SYNTHESIS OF BENZOXAZINE DERIVATIVES USING 2-AMINOPHENOL PRECURSORS

Ph.D. THESIS

by

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DEPARTMENT OF CHEMISTRY
INDIAN INSTITUTE OF TECHNOLOGY ROORKEE
ROORKEE – 247 667 (INDIA)

APRIL, 2014

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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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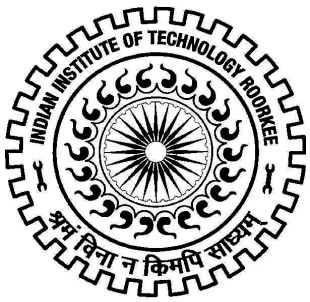

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CANDIDATE'S DECLARATION

I hereby certify that the work which is being presented in the thesis entitled **"Synthesis of benzoxazine derivatives using 2-aminophenol precursors"** 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 August 2009 to April 2014 under the supervision of Dr. Rama Krishna Peddinti, Associate Professor and Dr. Naseem Ahmed, 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 Institute.

(Ram Tilak Naganaboina)

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

(Naseem Ahmed) (R. K. Peddinti)

Date: _____ Supervisor Supervisor

The Ph.D. Viva-Voice Examination of **Mr. Ram Tilak Naganaboina**, Research Scholar, has been held on _____.

Signature of Supervisor Chairman, SRC Signature of External Examiner

Head of the Deptt./Chairman ODC

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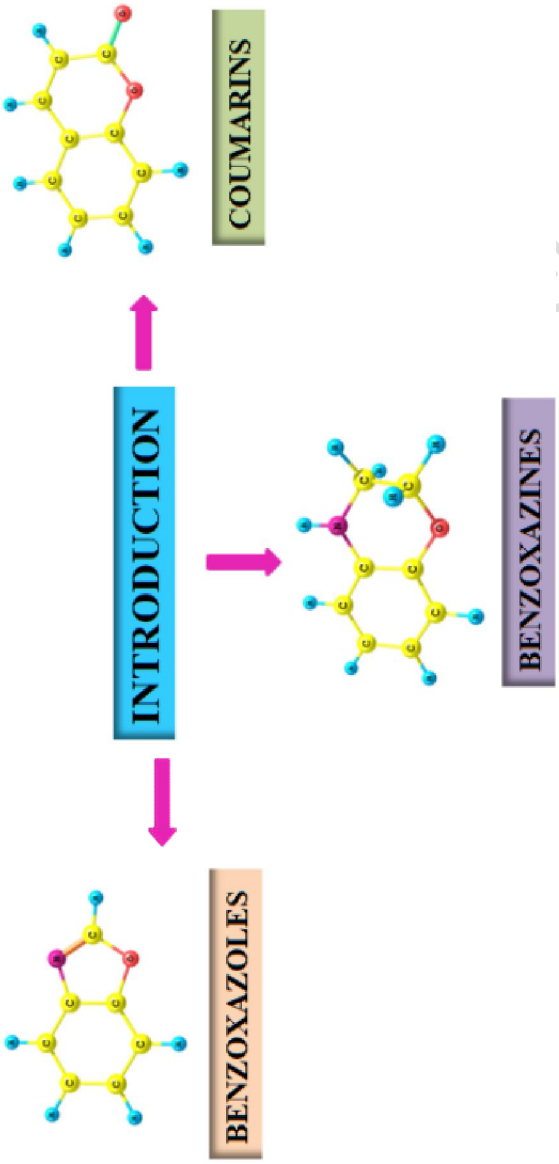
LIST OF ABBREVIATIONS

Ac-IBX	acetoxy *o*-iodoxybenzoic acid
BINAP	2,2′-bis(diphenylphosphino)-1,1′-binaphthyl
BQD	benzoylated quinidine
CDI	1,1′-carbonyldiimidazole
CNS	central nervous system
DA	Diels-Alder
DCE	1,2-dichloroethane
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DEPT	distortionless enhancement by polarization transfer
DIB	diacetoxyiodobenzene
DMF	dimethylformamide
DMP	Dess-Martin periodinane
DMSO	dimethylsulfoxide
DNA	deoxyribonucleic acid
DTBP	di-*tert*-butyl peroxide
EDG	electron-donating group
EVE	ethyl vinyl ether
EWG	electron-withdrawing group
HIV	human immunodeficiency virus
HOBt	1-hydroxybenzotriazole
HRMS	high resolution mass spectroscopy
IBX	2-iodoxybenzoic acid
IEDDA	inverse electron-demand Diels-Alder
IR	infrared
LTA	lead tetraacetate
MOB	masked *o*-benzoquinone
MW	microwave
NBS	*N*-bromosuccinimide
NMR	nuclear magnetic resonance

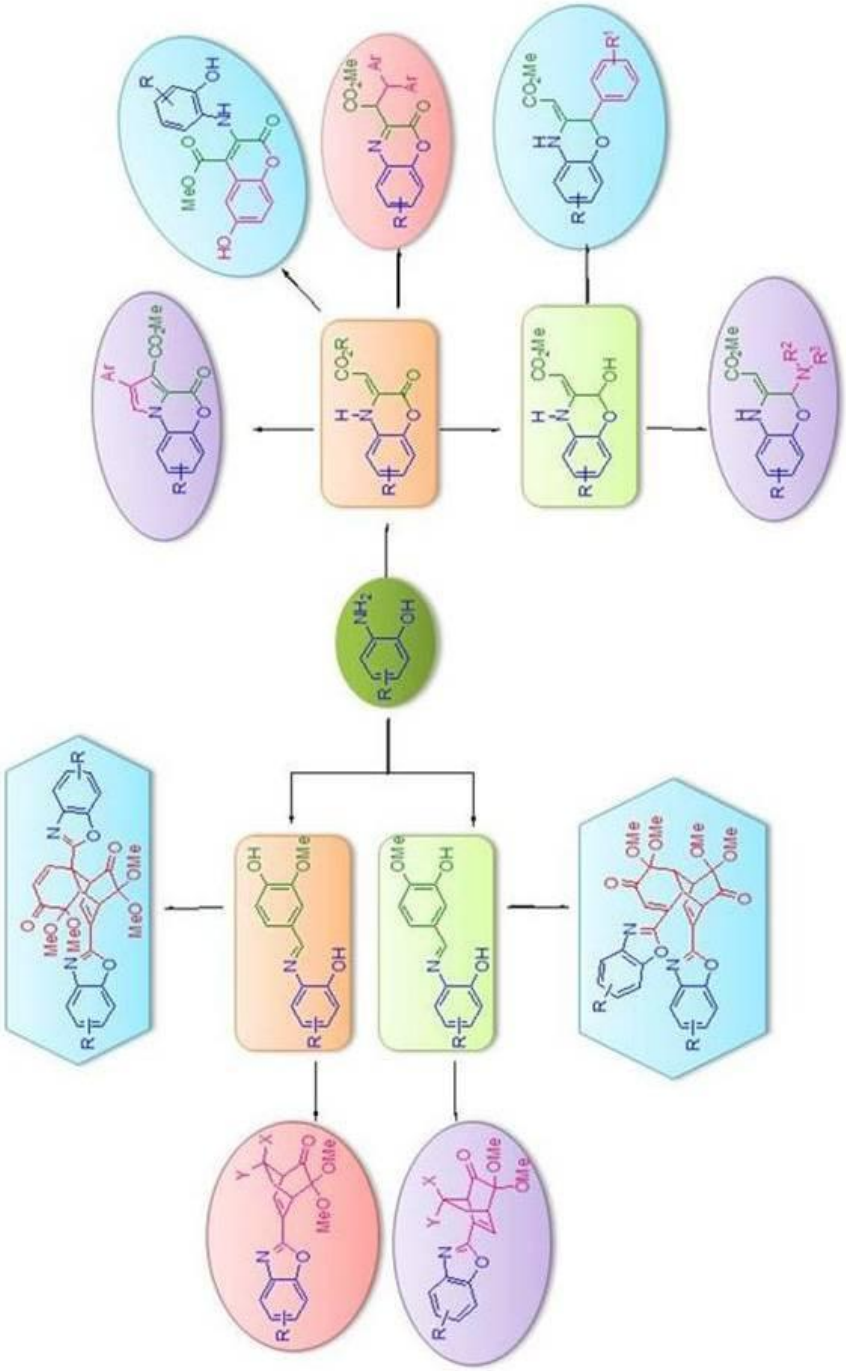
OLED	organic light-emitting diode
o-QMI	*o*-quinone monoamine
ORTEP	oak ridge thermal ellipsoid plot program
PCC	pyridinium chlorochromate
PPTS	pyridinium *p*-toluenesulfonate
TBAB	tetrabutylammonium bromide
TEBA	triethylammoniumbenzyl chloride
TFA	trifluoroacetic acid
THF	Tetrahydrofuran
TLC	thin layer chromatography
TMHD	2,2,6,6-tetramethyl-3,5-heptanedione
TMS	Tetramethylsilane
TMSCl	trimethylsilyl chloride
UV	Ultraviolet

SUMMARY IN SCHEMES

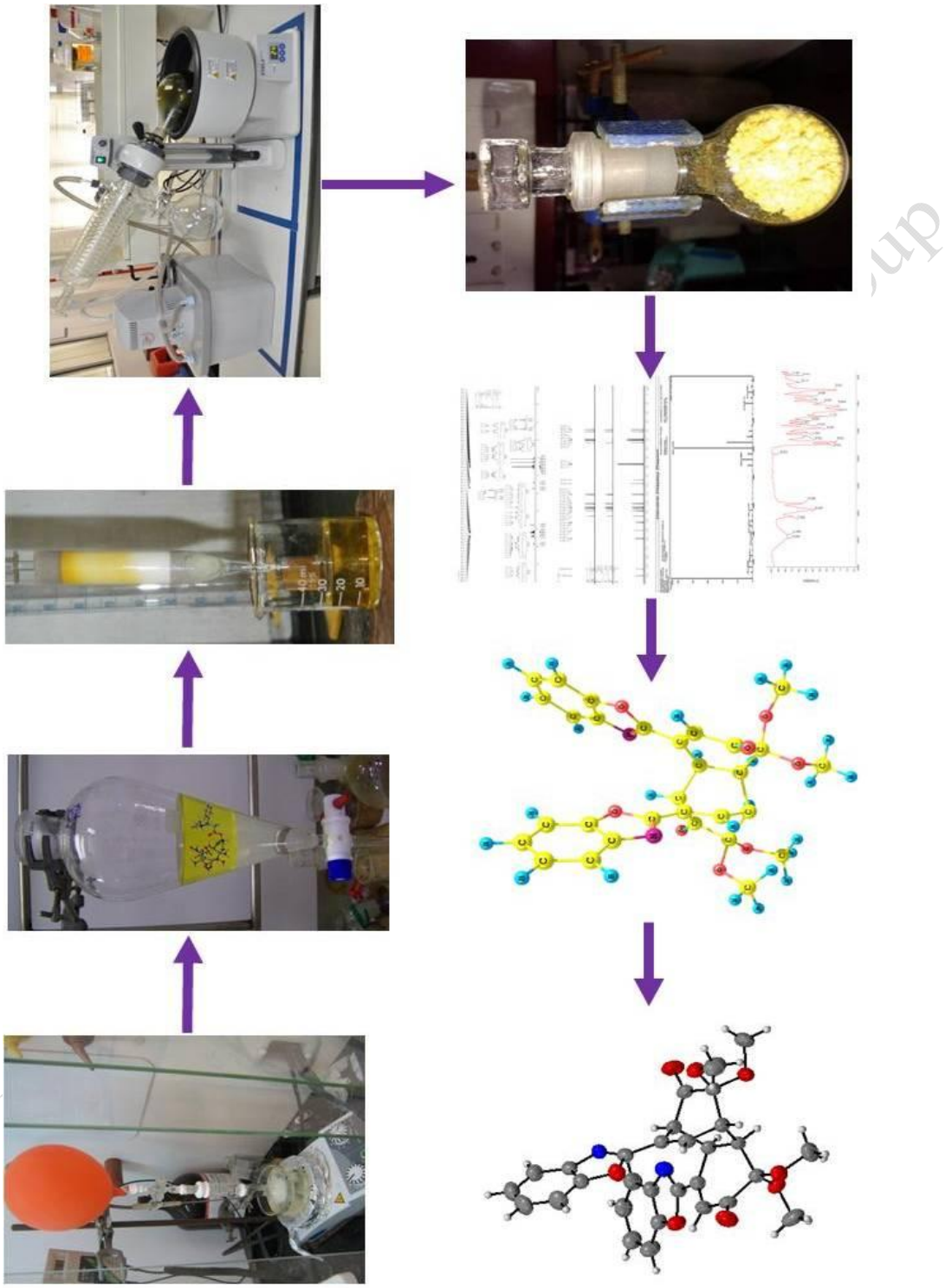
CHAPTER 1: INTRODUCTION



CHAPTER 2: OBJECTIVES, RESULTS AND DISCUSSION



CHAPTER 3: EXPERIMENTAL



ABSTRACT

The thesis entitled **"Synthesis of Benzoxazine Derivatives Using 2-Aminophenol Precursors"** is divided into three chapters, *viz*. (i) Introduction, (ii) Objectives, Results and Discussion, and (iii) Experimental. We have developed a one-pot domino oxidative cyclization–oxidative acetalization–Diels-Alder reaction for the synthesis of densely substituted (benzoxazol-2′-yl)bicyclo[2.2.2]octen-2-one derivatives using environmentally benign and inexpensive hypervalent iodine reagent diacetoxyiodobenzene (DIB). Further we have developed novel synthetic methodologies for the synthesis of numerous 1,4-benzoxazine and coumarin derivatives from a new class of vinylogous carbamates using Lewis and Brønsted acids.

Chapter 1: Introduction

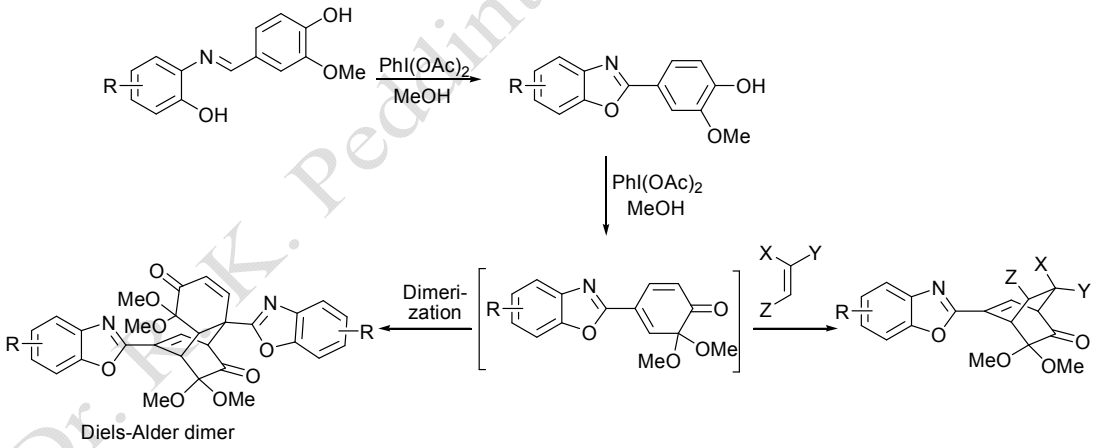
The organic compounds containing heteroatoms have engrossed a significant place in the modern organic synthesis as a result of their occurrence in various natural products and drug molecules. The synthesis of these heterocyclic compounds using readily available inexpensive reagents and environmentally benign methodologies has become a challenging task for the chemists. Among the various heterocyclic compounds, the benzoxazole and 1,4-benzoxazine derivatives found to exhibit a wide range of applications in pharma and agrochemical sectors. For example, benzoxazole core containing bicyclic systems calcimycin, cezomycin and routiennocin are isolated from the various strains of *Streptomyces*. and are found to act as good ionophore antibiotics. Benzoxazole derivatives act as estrogen receptor agonists, melotonin receptor agonists, anti tumor agents, and found to have applications in electronic devices, photoluminescent dyes and as sensors for metals, due to their fluorescent properties. The 1,4-benzoxazine derivatives also exhibit a wide range of biological activities such as antipsychotic agents, vasodilator agents, antibacterial agents, and antagonists, also been used in the treatment of heart disease, and diabetes. Apart from these, synthesis and screening of coumarin derivatives for drug discovery have become a subject of constant interest in pharmaceutical industry. Coumarins exhibit prominent biological activities such as antimicrobial, anticancer, antiallergic, and antiviral properties. The 3-*N*-substituted coumarins like novobiocin have been shown to bind to the C-terminal domain of heat shock protein 90 (hsp90), and thus become an exciting new target in cancer drug discovery.

Chapter 2: Objectives, Results and Discussion

This chapter deals with objectives, results and discussion which was further divided into six sections.

2.1. Facile one-pot synthesis of (benzoxazol-2′-yl)bicyclo[2.2.2]octen-2-one derivatives

In the first instance, we performed one-pot domino oxidative cyclization–oxidative acetalization–Diels-Alder reaction mediated by hypervalent iodine reagent diacetoxyiodobenzene (DIB) in methanol. The process involves the initial oxidation of the aldimine to give the benzoxazole derivative, which was further oxidised *in situ* to generate the masked *o*-benzoquinone as intermediate diene that was trapped with various dienophiles to afford the corresponding (benzoxazol-2′-yl)bicyclo[2.2.2]octen-2-one derivatives in good yields. The aldimines which were oxidised in absence of external dienophiles have undergone dimerization via Diels-Alder reaction to afford their respective dimers. The Diels-Alder reaction of benzoxazol-2′-yl MOBs with the various dienophiles was found to be regio- and stereo-selective, which was further confirmed by the 2D-NMR and ^{1}H-^{1}H decoupling experiments (Scheme 1).

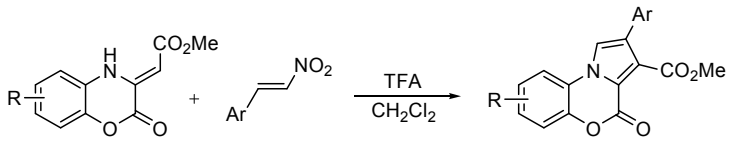


Scheme 1: Domino oxidative cyclization–oxidative acetalization–Diels-Alder reactions.

2.2. Synthesis of pyrrolobenzoxazine derivatives

We have developed a rapid and efficient methodology for the synthesis of pyrrolobenzoxazine mediated by trifluoroacetic acid. The initial step in this protocol involves the Michael addition of 1,4-benzoxazinone derivatives to the nitrostyrene

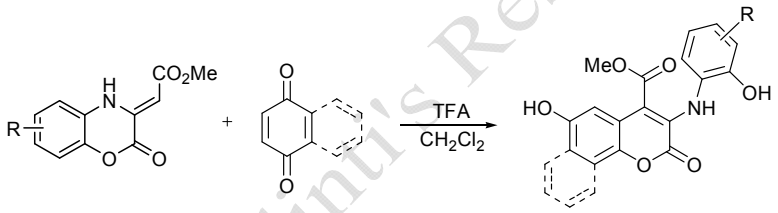
derivatives and further it undergoes the subsequent cyclization to give the corresponding pyrrolobenzoxazine derivatives in good to excellent yields (Scheme 2).



Scheme 2: Synthesis of pyrrolobenzoxazine derivatives.

2.3. Synthesis of 3-arylamino coumarin derivatives

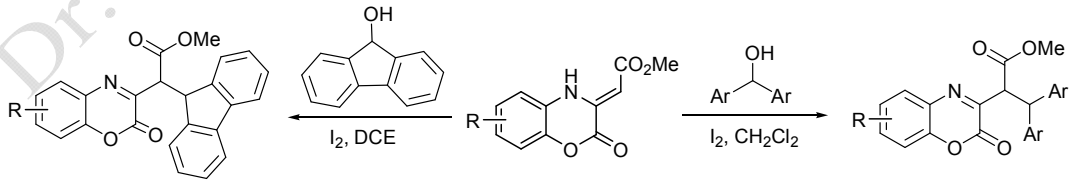
We have explored the reactivity of these novel class of vinylogous carbamates with *p*-benzoquinone derivatives. The reactions of 1,4-benzoxazinones with *p*-benzoquinone derivatives in presence of trifluoroacetic acid underwent smoothly and afforded the 3-arylamino coumarin derivatives in excellent yields. The reaction proceeds under mild conditions and obviates the use of column chromatography (Scheme 3).



Scheme 3: Synthesis of 3-arylamino coumarin derivatives.

2.4. Synthesis of 3-substituted 1,4-benzoxazinone derivatives

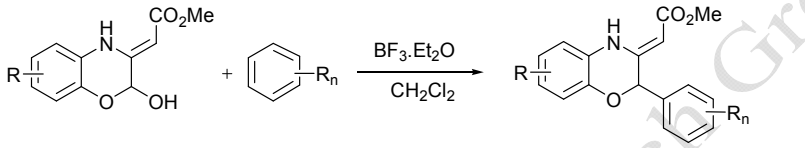
We have also developed a novel methodology for the alkylation of 1,4-benzoxazinone derivatives mediated by molecular iodine. These reactions proceeded efficiently with excellent yields and are compatible with various functional groups (Scheme 4).



Scheme 4: Molecular iodine-mediated alkylation reaction of 1,4-benzoxazinone derivatives.

2.5. Synthesis of 2-aryl 1,4-benzoxazine derivatives

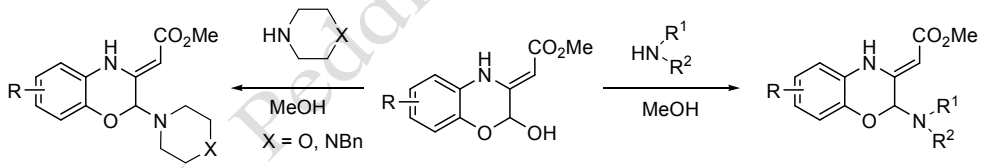
Further to uncover the reactivity of these 1,4-benzoxazinone derivatives, they were transformed to 2-hydroxy-1,4-benzoxazines by reducing with sodium borohydride. These 2-hydroxy-1,4-benzoxazines have undergone the Friedel-Crafts arylation reaction smoothly with various electron-rich arenes in presence BF_3.etherate. The current protocol provides an easy access for the synthesis of a series of densely substituted 2-aryl 1,4-benzoxazine derivatives under mild conditions (Scheme 5).



Scheme 5: Friedel–Crafts arylation reaction of 2-hydroxy-1,4-benzoxazines.

2.6. Synthesis of 2-amino 1,4-benzoxazine derivatives

In continuation of our interest to explore their reactivity, the 2-hydroxy-benzoxazine derivatives were reacted with cyclic and acyclic secondary amines to afford 2-amino-benzoxazine derivatives in good yields (Scheme 6).



Scheme 6: Synthesis of 2-amino 1,4-benzoxazine derivatives.

Chapter 3: Experimental

The third chapter provides experimental procedures in detail along with physical constants and spectral data.

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CHAPTER-1: INTRODUCTION

1.1. Substituted 1,3-benzoxazoles

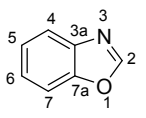
1.2. 1,4-Benzoxazines and 1,4-benzoxazinones

1.3. Synthesis of 1,4-benzoxazines from *o*-quinone monoimides and monoimines

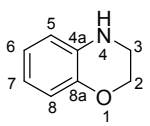
1.4. Coumarin derivatives

1. INTRODUCTION

The cyclic organic compounds which contain at least one heteroatom in their ring system are designated as heterocyclic compounds.[1,2] Nitrogen, oxygen and sulphur are the most commonly observed hetero atoms in many of the heterocyclic compounds. Apart from these, the compounds containing other hetero atoms are also well known in the literature. Heterocyclic compounds are ubiquitous in nature, found in many of the natural products and unnatural drug molecules. Remarkable and advanced synthetic technologies have been developed since last two decades in the field of heterocyclic chemistry. An enormous number of heterocyclic compounds have been synthesized till date and their number is increasing rapidly indicating the significance and necessity of such compounds in our day-to-day life. About more than half of the known compounds constituting these heterocycles are having a broad range of applications in diverse fields such as pharmaceutical industries, agricultural sectors and in material science as dyestuff, fluorescent sensors. Moreover, they also act as good organic conductors, semiconductors, photovoltaic cells, organic light-emitting diodes (OLEDs), light harvesting systems, chemically controllable switches, and liquid crystalline compounds.[3-6] Heterocyclic compounds like cinchona alkaloids which are readily available in nature are used as catalysts in various asymmetric transformations.[7,8] Metal complexes derived from heterocyclic compounds also have applications in asymmetric synthesis.[9] Many of these biologically active heterocyclic compounds which are obtained from the nature are biosynthesized by plants and animals. These wide range of applications have inspired chemists to continue their research in the development of novel heterocyclic compounds for their applications in various fields. Among various heterocyclic compounds, benzoxazoles and benzoxazine derivatives have engrossed a significant place due to their extensive applications in various fields.



1,3-benzoxazole



1,4-benzoxazine

Figure 1: Structures of 1,3-benzoxazole and 1,4-benzoxazine.

1.1. Substituted 1,3-benzoxazoles

Benzoxazole moiety is encountered in a number of natural products[10] and the compounds bearing benzoxazole are used widely in drug and agrochemical discovery sectors in addition to their various other applications. For instance, the benzoxazole core is found to occur in a variety of cytotoxic natural products such as the antimycobacterial pseudopteroxazole[11] and salvianen[12] (Figure 2). Benzoxazole containing molecule ERB-041 act as estrogen receptor agonist[13] and L-697,661 acts as HIV reverse transcriptase inhibitor.[14] Furthermore, benzoxazole derivatives have application as herbicides like fenoxaprop in agricultural sector.

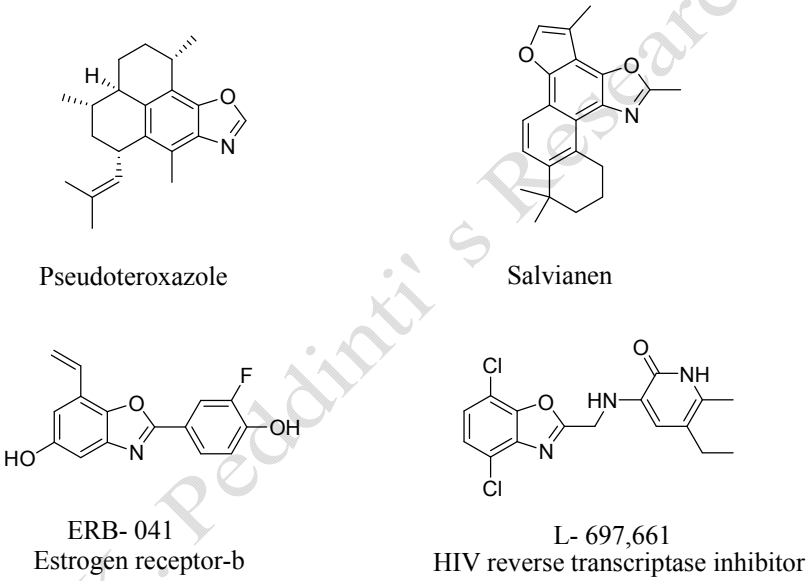


Figure 2: Representative drug candidates containing benzoxazole moiety.

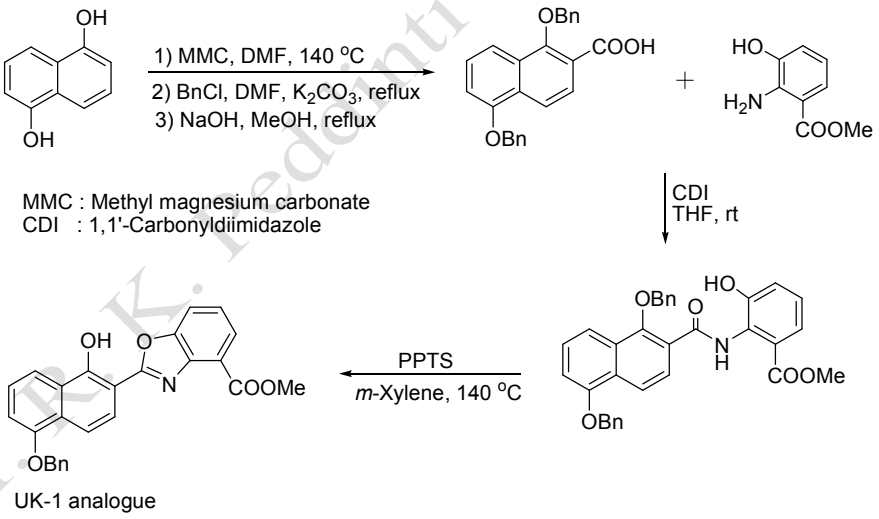
2-Aminophenols are the primary building blocks for the synthesis of diversely functionalized heterocyclic compounds. Exclusively benzoxazoles and 1,4-benzoxazines can be prepared easily from the commercially available 2-aminophenol derivatives. Several methods have been reported in literature for the synthesis of 2-aryl benzoxazole derivatives with 2-aminophenol precursors.[15]

The general methods available for synthesizing 2-substituted benzoxazoles are :

- The coupling of 2-aminophenols with carboxylic acid derivatives, which is either catalyzed by strong acids or requires microwave conditions.

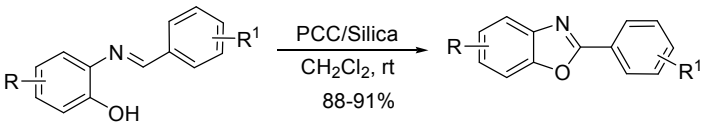
- Schiff bases derived from the condensation of 2-aminophenols with aldehydes are subjected to oxidative cyclizations in presence of various oxidants such as 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), $Mn(OAc)_3$, $PhI(OAc)_2$, and activated carbon.
- Metal or base catalyzed intramolecular cyclizations of suitably substituted 2-halo anilides.
- Coupling of benzoxazoles with aryl halides in presence of metal catalysts.

Ward *et al.* have synthesized the analogues of UK-1, by coupling of methyl 2-amino-3-hydroxybenzoate with acid derivatives.[16] UK-1 is a structurally unique bis(benzoxazole) natural product isolated from a strain of *Streptomyces*, which was found to exhibit anticancer activity.[17] The acid derivative was coupled with methyl 2-amino-3-hydroxybenzoate in presence of dehydrating agent and further it was subjected to intramolecular cyclization in presence of pyridinium *p*-toluenesulfonate to obtain the corresponding UK-1 analogue (Scheme 1).



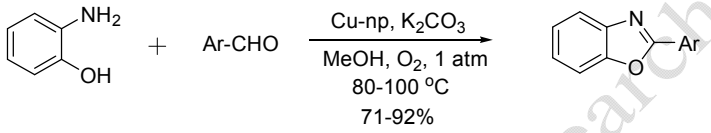
Scheme 1: Synthesis of benzoxazole derivative UK-1 analogue by coupling of 2-aminophenols with acid derivatives.

Praveen *et al.* have effectively used the pyridinium chlorochromate (PCC) supported silica gel in oxidative cyclization of structurally diverse phenolic Schiff bases to synthesize the corresponding 2-aryl benzoxazoles in high yields[18] (Scheme 2).



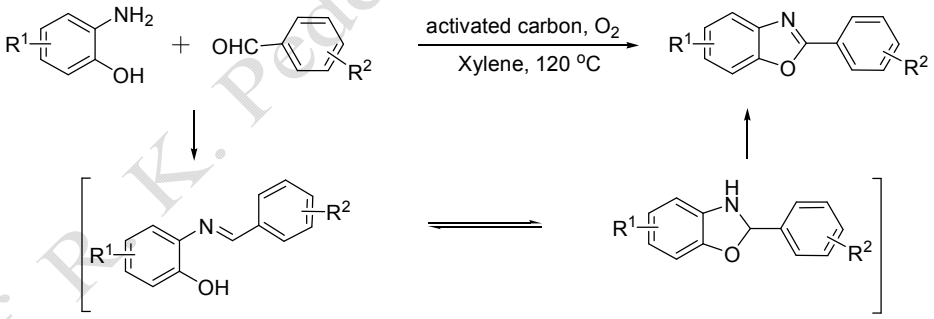
Scheme 2: Oxidative cyclization of Schiff bases using PCC-supported SiO_2.

Kidwai *et al.* have introduced the Cu-nanoparticles as an efficient catalyst for the synthesis of 2-aryl benzoxazoles.[19] The Schiff bases were prepared *in situ* by the reaction of 2-aminophenol with aryl aldehyde and further it was subjected to oxidation using catalytic amount of Cu-nanoparticles in the presence of K_2CO_3 in MeOH (Scheme 3).



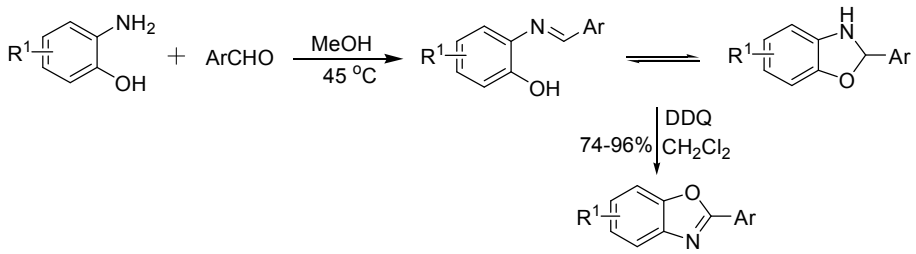
Scheme 3: Synthesis of 2-aryl benzoxazoles using Cu-nanoparticles.

Kawashita *et al.* have reported a practical synthesis of 2-aryl benzoxazoles under oxygen atmosphere in the presence of activated carbon from commercially available 2-aminophenols and aldehydes[20] (Scheme 4).



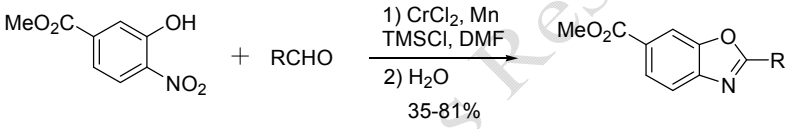
Scheme 4: Synthesis of 2-aryl benzoxazoles using activated carbon.

Chang *et al.* introduced a DDQ-mediated oxidative cyclization of phenolic Schiff bases for the synthesis of 2-aryl benzoxazole derivatives.[21] The Schiff bases obtained by the condensation of 2-aminophenol and aryl aldehydes underwent oxidative cyclization in presence of DDQ to afford the 2-aryl benzoxazole derivatives (Scheme 5).



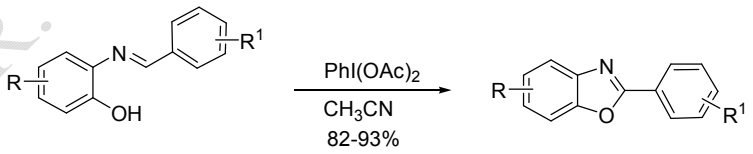
Scheme 5: DDQ-Mediated synthesis of 2-aryl benzoxazoles.

Hari *et al.* have developed one-pot domino process for the synthesis of 2-substituted benzoxazole derivatives in presence of chromium-manganese redox couple.[22] The chromium-manganese redox couple catalytically reduced the nitro group of the *o*-hydroxy nitroarene. The imine thus formed consequently underwent the oxidative cyclization to furnish the benzoxazole derivative (Scheme 6).



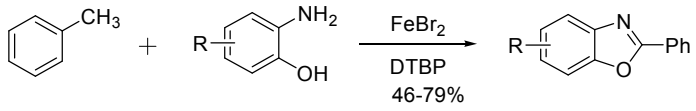
Scheme 6: Synthesis of 2-aryl benzoxazoles using chromium-manganese redox couple.

Varma *et al.* have developed a rapid protocol for the synthesis of 2-aryl benzoxazoles from the Schiff bases in the presence of diacetoxyiodobenzene (DIB).[23] The Schiff bases in presence of DIB underwent the oxidative cyclization and aromatization under mild reaction conditions to give desired products in high yields (Scheme 7).



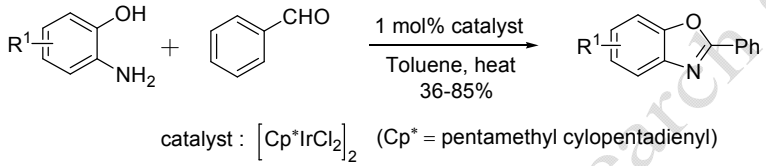
Scheme 7: DIB-Mediated synthesis of 2-aryl benzoxazoles.

Gu *et al.* developed a simple and efficient method to construct substituted benzoxazoles from commercially available 2-aminophenols and toluene derivatives.[24] The coupling of 2-aminophenols with toluene derivatives was catalyzed by iron(II) bromide in presence of di-*tert*-butyl peroxide (DTBP) (Scheme 8).



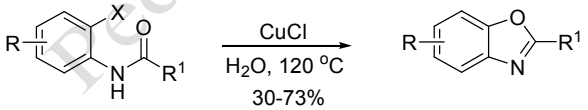
Scheme 8: Synthesis of 2-aryl benzoxazoles using iron(II) bromide.

Blacker *et al.* have synthesized the 2-aryl benzoxazole derivatives through a transition-metal-catalyzed hydrogen-transfer reaction.[25] The Schiff bases formed by the condensation of aldehyde and 2-aminophenol were oxidized in presence of catalytic amount of an iridium catalyst to obtain the 2-aryl benzoxazole derivatives in good yields (Scheme 9).



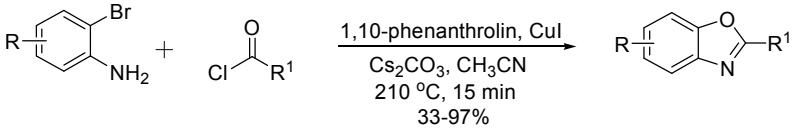
Scheme 9: Iridium-catalyzed synthesis of 2-aryl benzoxazoles.

Barbero *et al.* developed a copper(I) chloride catalyzed intramolecular *O*-arylation of substituted 2-haloanilides for the synthesis of 2-substituted benzoxazole derivatives.[26] The conveniently substituted 2-haloanilides cyclized in presence of catalytic amount of copper(I) chloride catalyst with water as a reaction medium (Scheme 10).



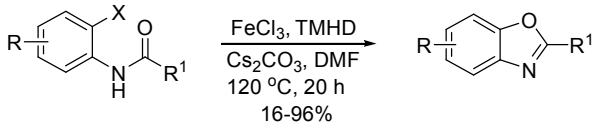
Scheme 10: Synthesis of 2-aryl benzoxazoles using copper(I) chloride.

Viirre *et al.* have developed a one-pot domino reaction for the synthesis of 2-substituted benzoxazole derivatives.[27] Initially the 2-bromoanilines were coupled with acyl chlorides and subsequent intramolecular C-O cross-coupling was mediated by a copper catalyst led to the formation of benzoxazole derivatives in high yields (Scheme 11).



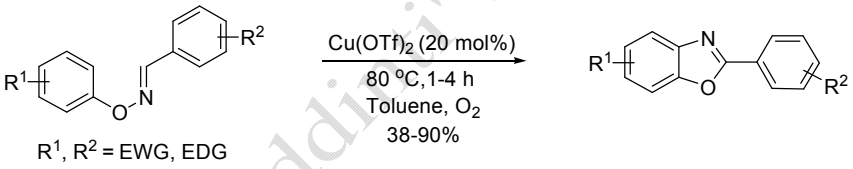
Scheme 11: Copper-catalyzed one-pot synthesis of 2-aryl benzoxazoles.

Bonnamour *et al.* have developed a practical iron-catalyzed *O*-arylation reaction for the synthesis of benzoxazole derivatives in high yields.[28] The key step in this method involves the use of $FeCl_3$ and 2,2,6,6-tetramethyl-3,5-heptanedione (TMHD) as a catalytic system for the intramolecular cyclization of 2-haloanilides (Scheme 12).



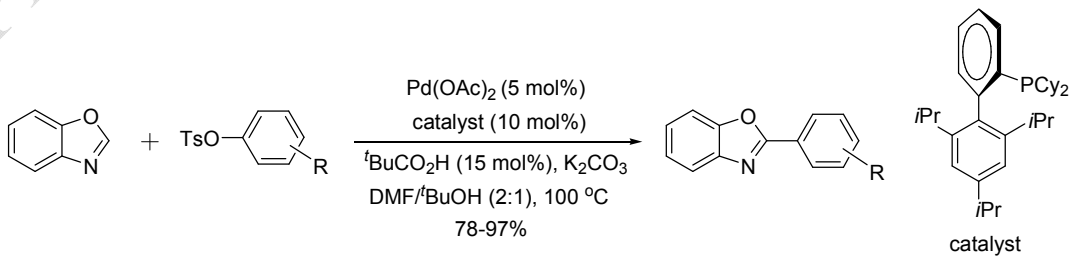
Scheme 12: Synthesis of 2-substituted benzoxazoles by intramolecular *O*-arylation.

Guru *et al.* have introduced an efficient method for the transformation of bisaryloxime ethers into 2-aryl benzoxazoles.[29] The bisaryloxime ethers when treated with the catalytic amount of copper(II) trifluoromethanesulfonate under oxygen atmosphere, it underwent rearrangement followed by cyclization reaction to furnish 2-aryl benzoxazole derivatives (Scheme 13).



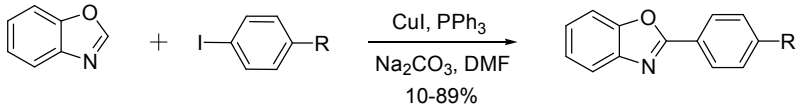
Scheme 13: Synthesis of 2-aryl benzoxazoles from bisaryloxime ethers.

Ackermann *et al.* have reported a palladium catalyzed cross-coupling of benzoxazoles with aryl tosylates/mesylates for the synthesis of 2-aryl benzoxazole derivatives.[30] In presence of a palladium-based catalytic system, the benzoxazoles were coupled with the aryl tosylates through the C-H functionalization (Scheme 14).



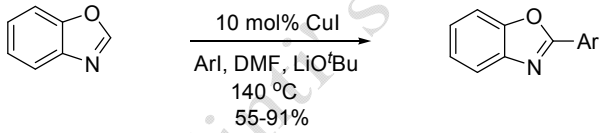
Scheme 14: Synthesis of 2-aryl benzoxazoles by cross coupling reaction.

Yoshizumi *et al.* developed an efficient method for the direct arylation of benzoxazole with aryl iodide for the synthesis of 2-aryl benzoxazole derivatives.[31] The coupling of 1,3-benzoxazole with the aryl iodides was promoted by the copper(I) iodide catalyst in presence of PPh_3 and Na_2CO_3 in DMF as a solvent (Scheme 15).



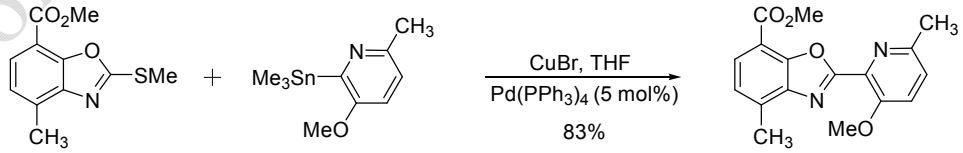
Scheme 15: Synthesis of 2-aryl benzoxazoles by copper(I) iodide-catalyzed coupling reactions.

Do *et al.* have reported a rapid and efficient method for the synthesis of 2-aryl benzoxazole derivatives through coupling reaction.[32] The arylation of the benzoxazole C-H bond was carried out by the catalytic amount of copper(I) iodide, in presence of lithium *tert*-butoxide and DMF (Scheme 16).



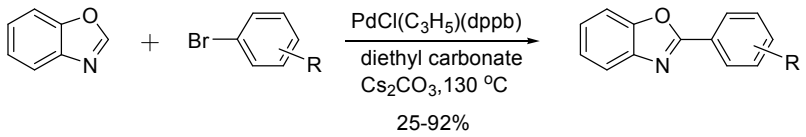
Scheme 16: Synthesis of 2-aryl benzoxazoles by copper-catalyzed arylation reaction.

Richardson *et al.* have synthesized the boxazomycin C analogues by palladium-catalyzed cross-coupling of 2-thiomethylbenzoxazoles with trialkylstannylpyridines.[33] The boxazomycins are the gram positive antibacterial agents which contain a biaryl bond between the benzoxazole and the pyridine moiety (Scheme 17).



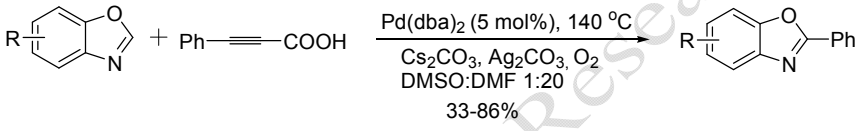
Scheme 17: Synthesis of 2-pyridinyl benzoxazoles by palladium-catalyzed coupling reaction.

Dong *et al.* reported[34] a palladium-catalyzed direct arylation of benzoxazole with aryl halides using the eco-friendly solvents such as diethyl carbonate (Scheme 18).



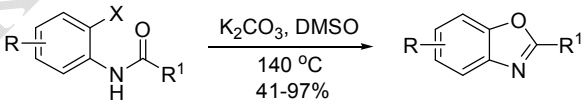
Scheme 18: Synthesis of 2-aryl benzoxazoles using palladium-based catalytic system.

Liu *et al.* developed a palladium-catalyzed one-pot decarboxylation, carbon-carbon triple bond oxidation and decarbonylative arylation of benzoxazole C-H bond for the synthesis of 2-aryl benzoxazole derivatives in good yields.[35] The initial step involves the decarboxylation in presence of Ag_2CO_3, then the triple bond gets oxidized with O_2 to a dicarbonyl intermediate. Consequently, it undergoes decarbonylative arylation with the benzoxazole derivative (Scheme 19).



Scheme 19: Synthesis of 2-aryl benzoxazoles using palladium-catalyzed coupling reaction.

Peng *et al.* introduced a transition-metal catalyst free intramolecular *O*-arylation of 2-haloanilides for the synthesis of 2-substituted benzoxazole derivatives in high yields.[36] The key step involves the cyclization of 2-haloanilides in the presence of K_2CO_3 in DMSO at 140 ^oC (Scheme 20).



Scheme 20: Synthesis of 2-aryl benzoxazoles by intramolecular *O*-arylation reaction.

1.2. 1,4-Benzoxazines and 1,4-benzoxazinones

1,4-Benzoxazine scaffolds have been studied extensively as important heterocyclic systems for building natural and synthetically designed biologically active drug molecules.[37] 1,4-Benzoxazine moiety is present in many of the drugs like ofloxacin, an antibiotic used in treating the infections caused by *E. coli*.[38] These derivatives act as antibacterial agents, used in treating infections caused by *Mycobacterium sp*.[39] and also help in inhibiting the

coagulation serine proteases factor Xa and factor VIIa.[40] Some of them are antipsychotic agents, CNS depressants, estrogen receptor β-agonists[41] and others are potential antithrombotic agents[42] (Figure 3). Benzoxazine derivatives are also used in the treatment of neurodegenerative illness in addition to cardiovascular, inflammatory and diabetic disorders.[43]

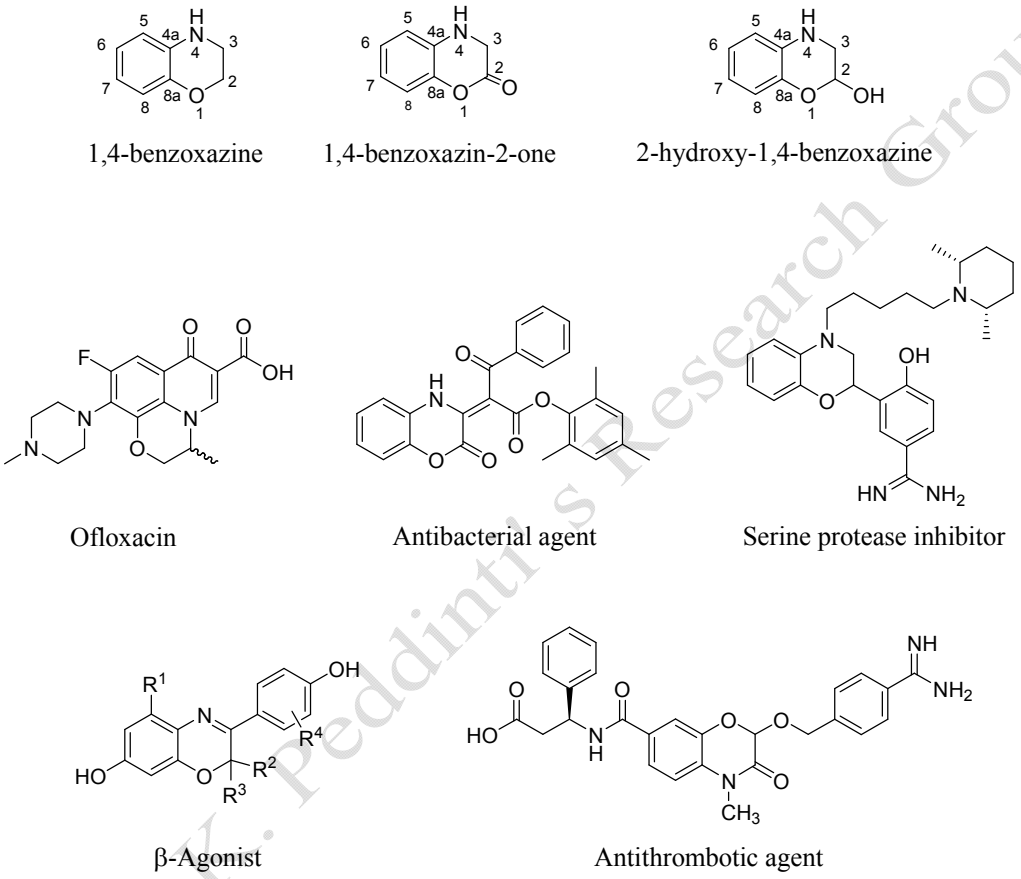
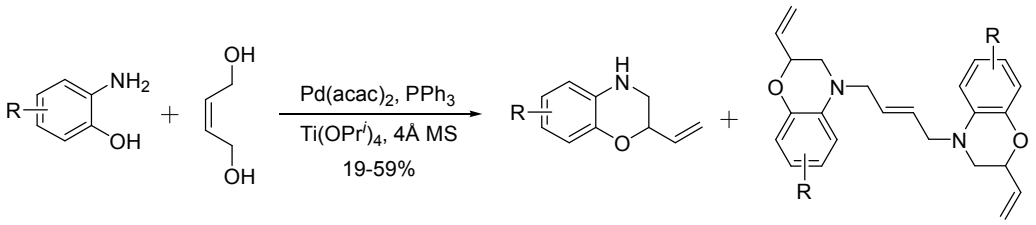


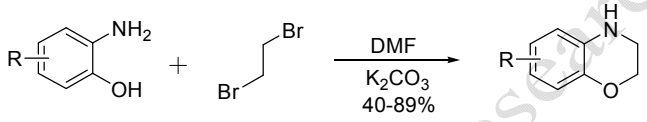
Figure 3: Biologically active molecules having 1,4-benzoxazine core.

Yang and co-workers carried out the direct activation of C–O bonds in 2-butene-1,4-diol by palladium complexes in presence of a titanium reagent for the synthesis of 3,4-dihydro-2-vinyl-2*H*-1,4-benzoxazines.[44] The reaction involves the palladium-catalyzed regiospecific tandem allylation of 2-aminophenols using 2-butene-1,4-diol in presence of $Ti(OPr^i)_4$. It was observed that the addition of $Ti(OPr^i)_4$ accelerated both the rate of the reaction and yield of the product (Scheme 21).



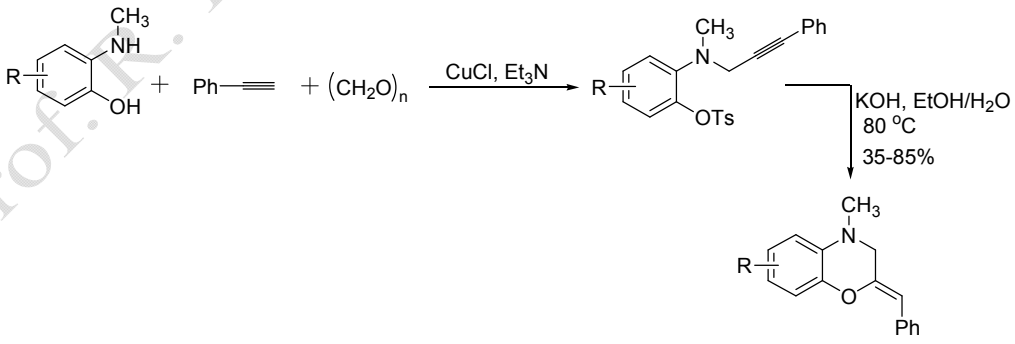
Scheme 21: Palladium catalyst-mediated synthesis of 1,4-benzoxazines.

Mizar *et al.* synthesized the 2*H*-1,4-benzoxazines from substituted 2-aminophenols and 1,2-dibromoethane in presence of base K_2CO_3 in good to excellent yields.[45] The cyclized products were further functionalized to *N*-substituted 3,4-dihydro-2*H*-1,4-benzoxazines by reaction with alkyl bromides.



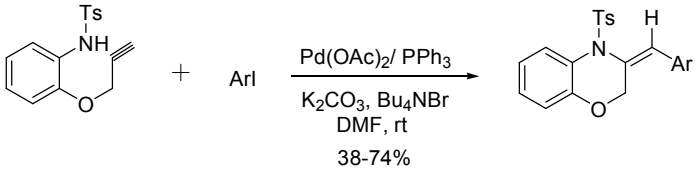
Scheme 22: K_2CO_3-Mediated synthesis of 1,4-benzoxazine derivatives.

Xu *et al.* have developed an efficient one-pot procedure for copper-catalyzed three-component coupling reaction leading to functionalized 1,4-benzoxazine derivatives in good to high yields.[46] The reaction involves the coupling of three components followed by the subsequent cyclization to a six-membered ring. Further, the *O*-annulation process was observed to be completely regio- and stereo-selective and only the *Z*-isomers with six-membered rings were obtained (Scheme 23).



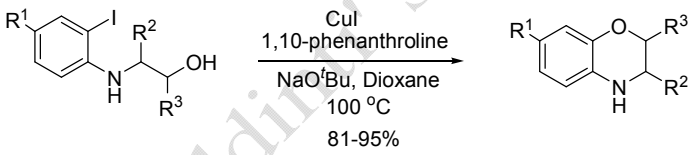
Scheme 23: Copper-catalyzed one-pot synthesis of functionalized 1,4-benzoxazine derivatives.

One-pot palladium catalyzed efficient synthesis of (*E*)-3-arylidene-3,4-dihydro-2*H*-1,4-benzoxazines at room temperature has been developed by Chowdhury and co-workers.[47] The reaction proceeds through a regio- and stereo-selective manner and it tolerates various functional groups (Scheme 24).



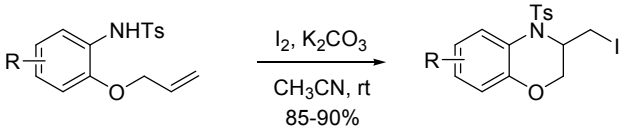
Scheme 24: Palladium-catalyzed synthesis of 1,4-benzoxazine derivatives.

Chen and co-workers synthesized 2,3-dihydro-1,4-benzoxazines through a mild intramolecular copper-catalyzed *O*-arylation reaction.[48] Substituted *β*-aminoalcohol derivatives were subjected to *O*-arylation reaction in presence of copper catalytic system to afford the benzoxazine derivatives in high yields (Scheme 25).



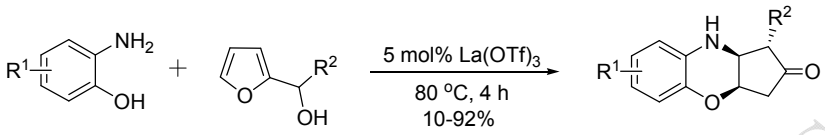
Scheme 25: Copper-catalyzed synthesis of 1,4-benzoxazine derivatives.

Majumdar *et al.* have introduced molecular iodine-mediated cyclization for the synthesis of 3,4-dihydro-2*H*-1,4-benzoxazine derivatives.[49] The iodocyclization reaction took place in presence of molecular iodine and potassium carbonate at room temperature. The reaction was operationally simple and afforded the products in good to excellent yields (Scheme 26).



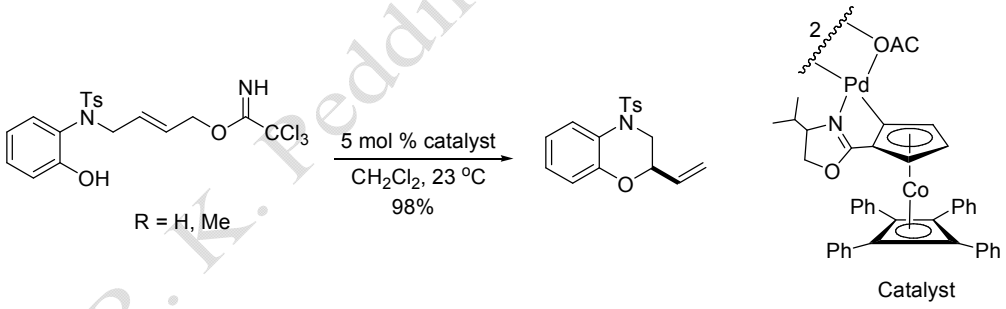
Scheme 26: Molecular iodine-promoted synthesis of 1,4-benzoxazine derivatives.

Liu *et al.* developed a domino reaction for the synthesis of *cis*-1,4-benzoxazine derivatives by a Piancatelli/C–N coupling/Michael addition reaction.[50] The reaction of 2-furylcarbinols with *o*-aminophenol derivatives takes place through a domino process catalyzed by $La(OTf)_3$ and the products were obtained as single diastereomers from readily available starting materials (Scheme 27).



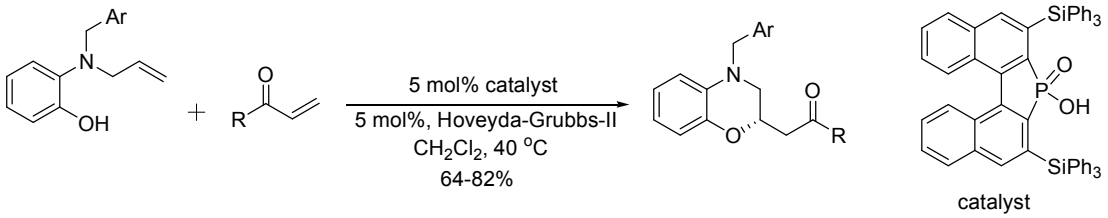
Scheme 27: Lanthanum(III) trifluoromethanesulfonate-mediated synthesis of *cis*-1,4-benzoxazine derivatives.

Cannon *et al.* synthesized 2,3-dihydro-2-vinyl-2*H*-1,4-benzoxazines in high yields and excellent enantiomeric purities up to 98% *ee* by $[COP\text{-}OAc]_2$-catalyzed cyclization reaction of phenolic (*E*)-allylic trichloroacetimidate precursors.[51] Further, computational and deuterium labelling experiments were in accordance with the cyclization reaction which occurs through an *anti*-oxypalladation/*syn*-deoxypalladation mechanism (Scheme 28).



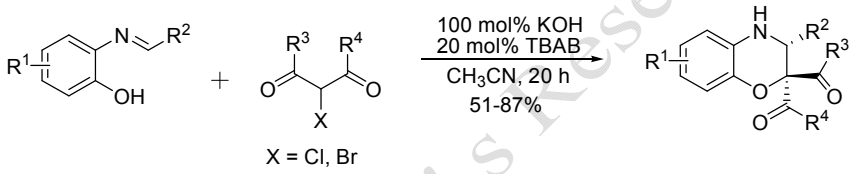
Scheme 28: Palladium(II)-catalyzed enantioselective synthesis of 2,3-dihydro-2-vinyl-2*H*-1,4-benzoxazines.

Zhang *et al.* developed a chiral phosphoric acid and Hoveyda–Grubbs II catalyzed olefin cross-metathesis–intramolecular oxo-Michael cascade reaction.[52] The reaction proceeds through a cross-metathesis–asymmetric oxo-Michael reaction affording a variety of functionalized benzoxazine derivatives (Scheme 29).



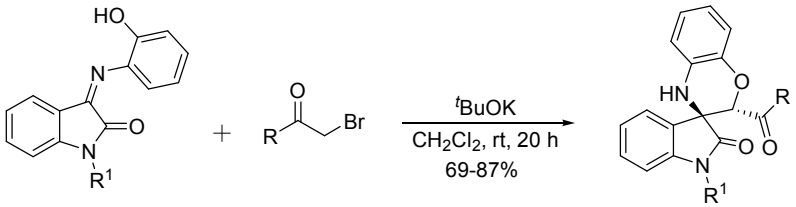
Scheme 29: Synthesis of 1,4-benzoxazine derivatives by cross-metathesis.

Zhang *et al.* synthesized the functionalized 2,3-dihydro-1,4-benzoxazines in moderate to excellent yields through a domino [5+1] annulation.[53] The reaction of 2-halo-1,3-dicarbonyl compounds with suitably substituted imines in presence of potassium hydroxide and tetrabutylammonium bromide resulted in functionalized tetracyclic-1,4-benzoxazines of biological significance under mild conditions (Scheme 30).



Scheme 30: Synthesis of 1,4-benzoxazine derivatives by [5+1] domino annulations.

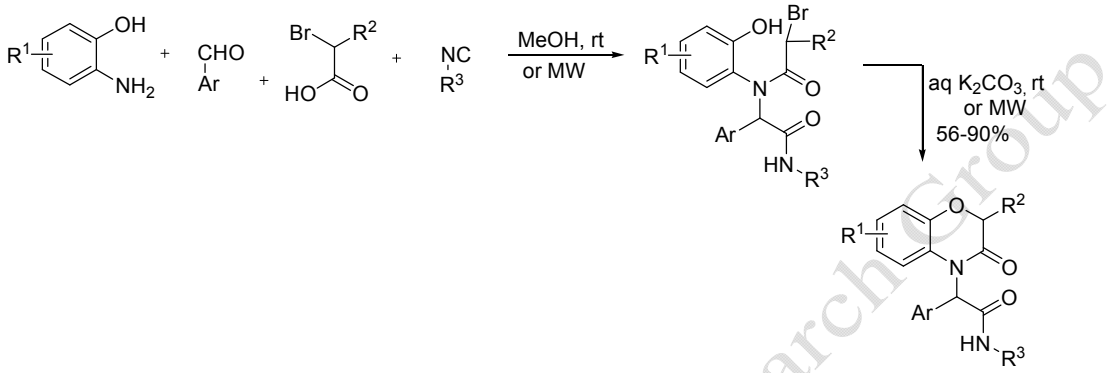
Huang *et al.* developed an efficient domino reaction for the synthesis of a series of spiro 1,4-benzoxazine oxindole derivatives.[54] The reaction proceeds *via* a domino Mannich-alkylation of α-halocarbonyl compounds with imines under mild conditions. The methodology provides an access for the diversely substituted 1,4-benzoxazine oxindole derivatives from the readily available starting materials (Scheme 31).



Scheme 31: Potassium *tert*-butoxide mediated synthesis of spiro 1,4-benzoxazine oxindole derivatives.

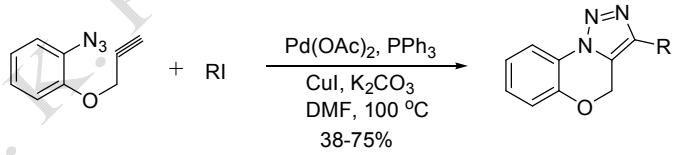
Xing *et al.* developed an efficient four-component Ugi reaction for rapid synthesis of highly functionalized 3,4-dihydro-3-oxo-2*H*-1,4-benzoxazines.[55] The mixture of four

components were taken in methanol and stirred at room temperature or subjected to microwave (MW) irradiation to obtain a bromo-intermediate. Further on addition of aqueous potassium carbonate, the bromo-intermediate underwent cyclization to furnish the desired benzoxazine derivatives in excellent yields (Scheme 32).



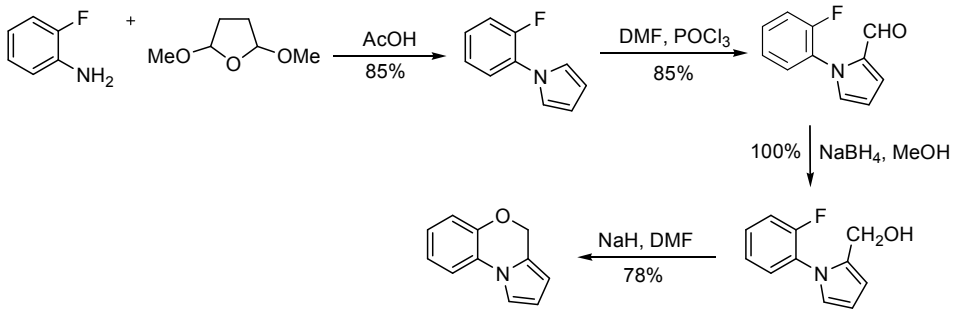
Scheme 32: Synthesis of benzoxazine derivatives by one-pot four component Ugi reaction.

Chowdhury and co-workers developed a general one-pot synthesis of [1,2,3]triazolo[5,1-*c*][1,4]benzoxazines from readily available starting materials.[56] The reactions of 1-azido-2-(prop-2-ynyloxy)benzene with aryl/vinyl iodides were carried out in presence of palladium-copper catalytic system to afford a wide variety of [1,2,3]triazolo[5,1-*c*][1,4]benzoxazine derivatives in excellent yields (Scheme 33).



Scheme 33: Palladium-copper catalyzed synthesis of [1,2,3]triazolo[5,1-*c*][1,4]benzoxazines.

Pujol and co-workers reported an efficient synthesis of pyrrolo[2,1-*c*][1,4]-benzoxazine derivatives.[57] The starting *N*-(2-fluorophenyl)pyrrole was prepared by condensation of 2-fluoroaniline with 2,5-dimethoxytetrahydrofuran in glacial acetic acid which underwent the formylation reaction in presence of DMF and $POCl_3$ to afford the aldehyde derivative. The reduction of aldehyde functionality was carried out with $NaBH_4$ and further cyclization in presence of sodium hydride in DMF to provide the desired [2,1-*c*][1,4]benzoxazine derivatives in good yields (Scheme 34).

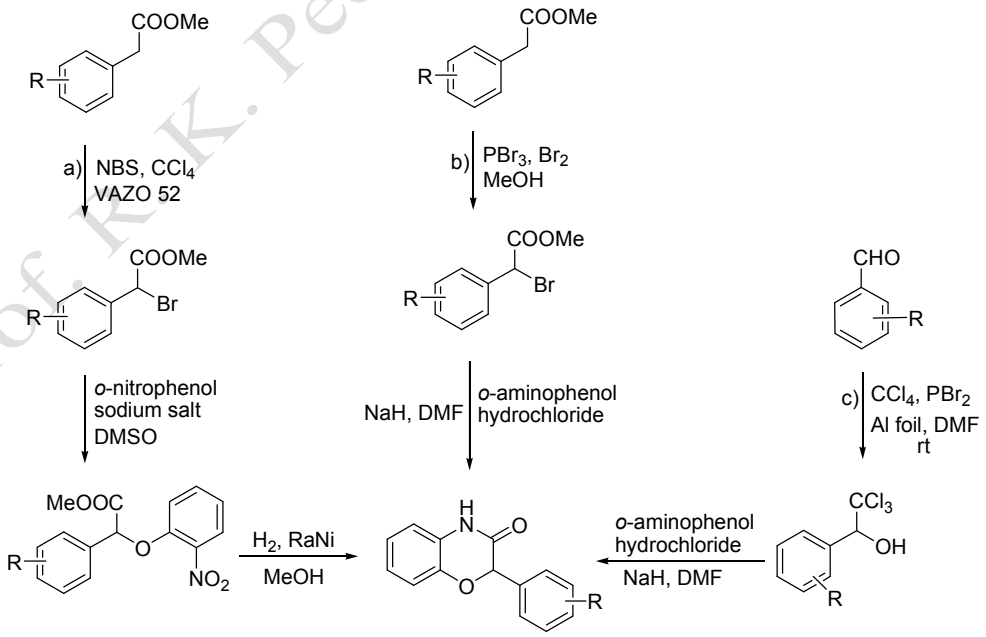


Scheme 34: Synthesis of pyrrolo[2,1-*c*][1,4]benzoxazine derivatives.

Dudley and co-workers designed a new class of 2-aryl benzoxazinone derivatives and carried out their biological activity as novel factor Xa inhibitors.[58] The precursors 2-aryl benzoxazine derivatives were synthesized in three different approaches (Scheme 35).

a) The α-aryl methyl acetate was brominated with NBS and in presence of a radical initiator, 2,2'-azobis(2,4-dimethylvaleronitrile) (VAZO 52) in carbon tetrachloride *via* radical reaction. Thus obtained bromo derivative was coupled with *o*-nitrophenol sodium salt and the subsequent reductive cyclization in presence of H_2-Raney Ni (RaNi) afforded the desired product.

b) Here the bromination of α-aryl methyl acetate was carried out in presence of PBr_3/Br_2 in methanol. The bromo derivative was reacted with *o*-aminophenol hydrochloride in presence

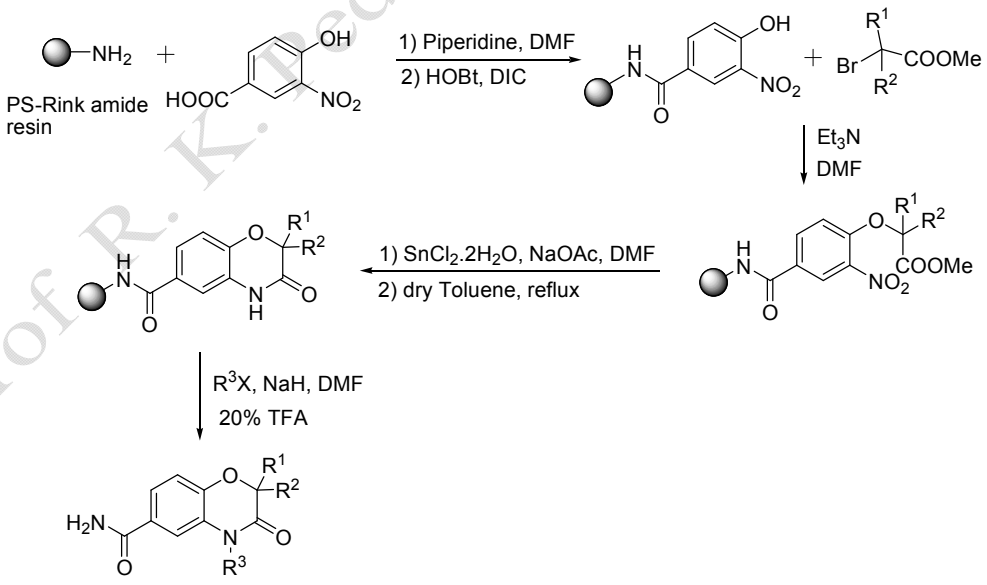


Scheme 35: Alternative approaches for synthesis of 2-aryl 1,4-benzoxazinone derivatives.

of sodium hydride, DMF to generate the corresponding 2-aryl benzoxazine derivative directly. This methodology is useful particularly to avoid the undesired over reduction side products.

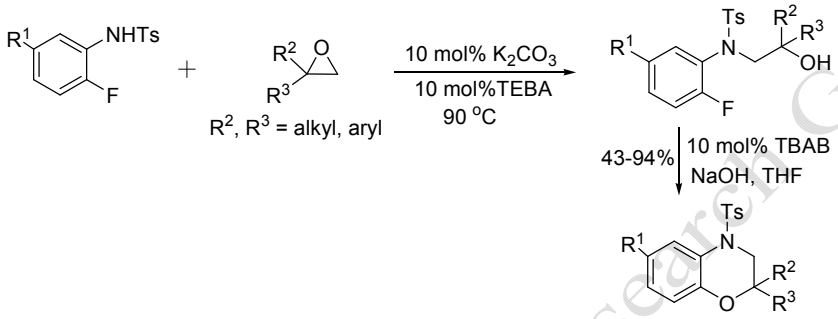
c) In this method, initially the trichloromethyl carbinol derivative was prepared from aryl aldehyde derivative, which was further reacted with *o*-aminophenol hydrochloride to obtain the 2-aryl benzoxazinone derivative.

Lee *et al.* reported the solid-phase synthesis of 1,4-benzoxazinone derivatives.[59] The deprotection of the Rink amide resin was done and the amide coupling reaction was carried out with 4-hydroxy-3-nitrobenzoic acid in presence of 1-hydroxybenzotriazole (HOBt) and *N*,*N*′-diisopropylcarbodiimide (DIC). Further the *O*-alkylation was performed with methyl bromo alkenoates in presence of triethylamine. Thus obtained aryl alkyl ether was subjected to reduction with tin(II) chloride dihydrate in presence of small amount of sodium acetate and cyclized to 1,4-benzoxazinone derivative in toluene at reflux temperature. The small amount of sodium acetate added act as the buffer and helps in preventing the early cleavage of *O*-alkylated product from the resin. Benzoxazinone derivatives thus obtained were functionalized further by reaction of the amide nitrogen with alkyl halides and acyl chlorides in presence of sodium hydride in anhydrous DMF (Scheme 36).



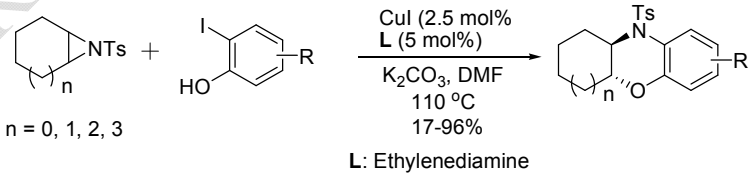
Scheme 36: Solid-phase combinatorial synthesis of 1,4-benzoxazinone derivatives.

Albanese *et al.* reported the synthesis of 1,4-benzoxazine derivatives by epoxide ring opening and subsequent intramolecular cyclization reaction.[60] The opening of epoxides was done with arylsulfonamides in presence of catalytic amount of K_2CO_3 and TEBA. The *N*-alkyl aniline derivative obtained further underwent intramolecular cyclization in presence of catalytic amount of tetrabutylammonium bromide and sodium hydroxide to give the desired 1,4-benzoxazine derivatives (Scheme 37).



Scheme 37: Synthesis of 1,4-benzoxazine derivatives by epoxide ring opening and cyclization reaction.

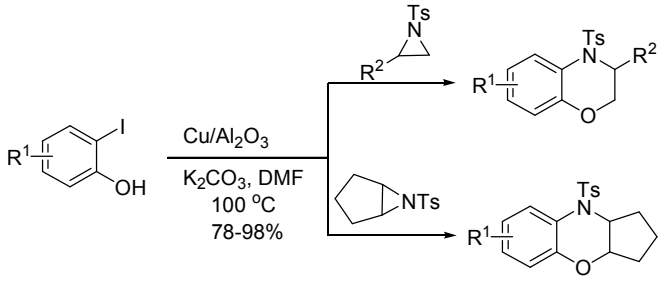
Sekar and co-workers developed a domino aziridine ring opening with 2-iodophenols followed by the copper-catalyzed coupling reaction.[61] The aziridine ring opening was done with 2-iodophenols and the subsequent cyclization was performed through a Goldberg coupling reaction in presence of ethylenediamine-CuI complex as catalyst and K_2CO_3 as base. The methodology provided an easy access for the synthesis of diversely substituted *trans*-1,4-benzoxazine derivatives from readily available starting materials (Scheme 38).



Scheme 38: Copper-catalyzed domino reaction for the synthesis of 1,4-benzoxazine derivatives.

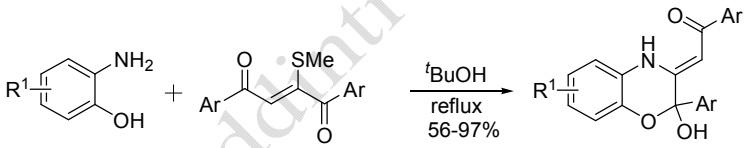
A sequential one-pot aziridine ring opening followed by the intramolecular cyclization was developed for the synthesis of functionalized 1,4-benzoxazine derivatives.[62] The ring opening and the cyclization was carried out by reacting the 2-iodophenol

derivatives with aziridine derivatives in presence of K_2CO_3 and alumina-supported copper(II) catalyst (Scheme 39).



Scheme 39: Synthesis of 1,4-benzoxazine derivatives by aziridine ring opening and cyclization reaction.

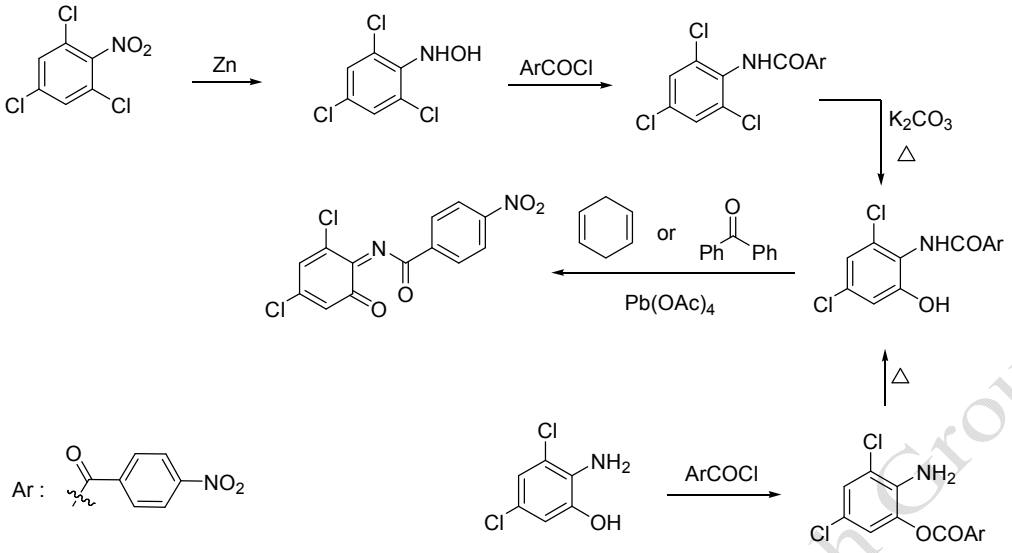
Zhang *et al.* reported the stereo-selective synthesis of densely substituted 1,4-benzoxazine derivatives from the readily available starting materials.[63] The 2-aryl substituted 1,4-benzoxazine derivatives were obtained by reacting *o*-aminophenol derivatives with 2-methylthio-1,4-enediones in *tert*-butanol at reflux temperature (Scheme 40).



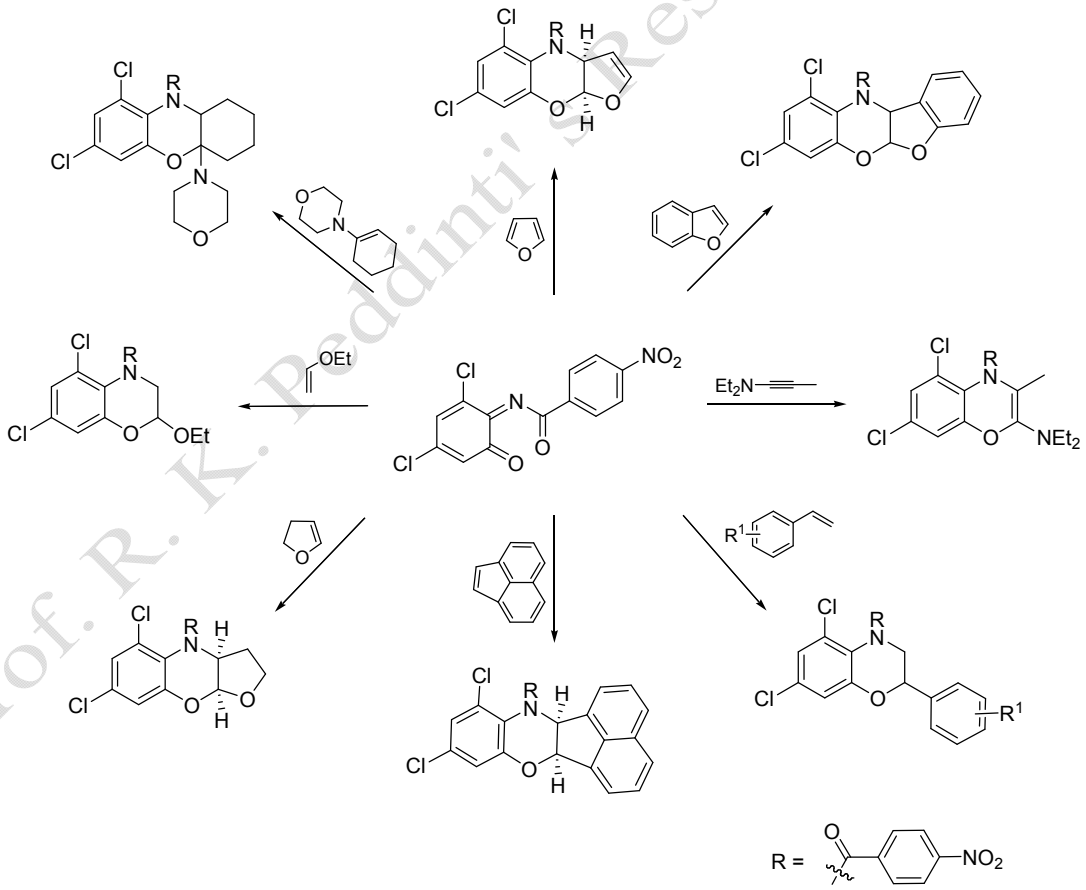
Scheme 40: Synthesis of 2-aryl 1,4-benzoxazine derivatives.

1.3. Synthesis of 1,4-benzoxazines from *o*-quinone monoimides and monoimines

In 1984 Heine and his co-workers synthesized *o*-quinone monoimides by introducing 4-nitrobenzoyl group on imine functionality and two chlorine atoms on the ring system.[64] They obtained this compound starting from either 3,5-dichloro-6-aminophenol or 2,4,6-trichloronitrobenzene in two different synthetic routes (Scheme 41). For the first time the authors used an *o*-benzoquinone monoimide as hetero diene in inverse electron-demand Diels-Alder (IEDDA) reaction with electron-rich dienophiles such as vinyl ethers, furans, enamines and styrenes. The reactions proceeded at room temperature to furnish a variety of 1,4-benzoxazine derivatives in 55-85% yields (Scheme 42).

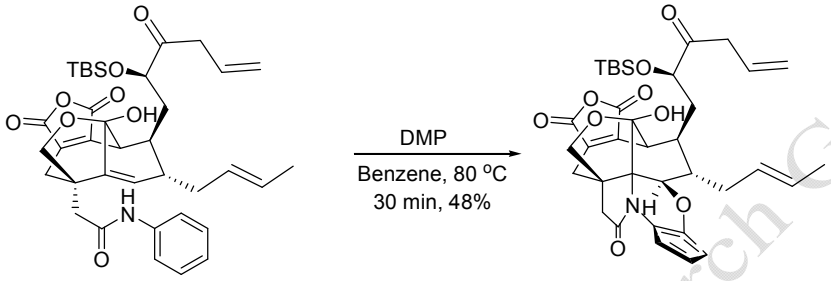


Scheme 41: Synthetic routes for *o*-quinone monoimide derivatives.



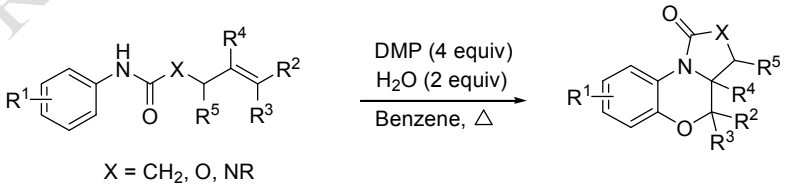
Scheme 42: Reaction of an *o*-quinone monoimide with different electron-rich olefins.

The construction of complex molecular structures from easily accessible starting materials is a challenging objective in contemporary organic synthesis. During the course of total synthesis of CP molecules, Nicolaou *et al.* observed an unexpected conversion of an anilide into a benzoxazine derivative by the oxidation with Dess-Martin periodinane (DMP) in benzene under reflux conditions[65] (Scheme 43).



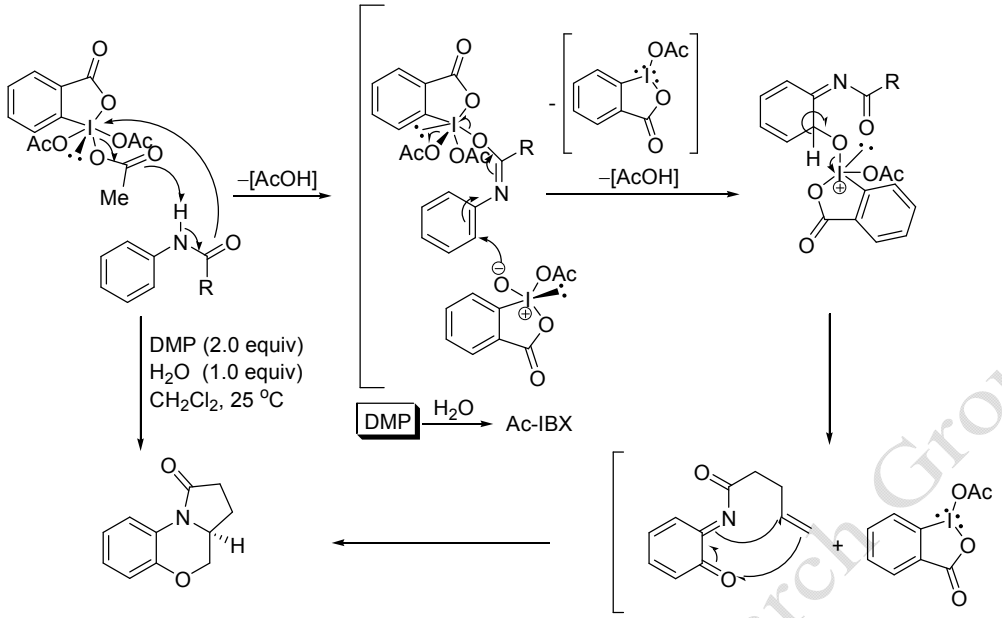
Scheme 43: Intramolecular Diels-Alder reaction of *in situ* generated *o*-quinone monoimide with olefin.

This serendipitous discovery led to a number of new processes and construction of a variety of a complex molecular structures. The treatment of simple anilides with DMP and water allowed the formation of *o*-quinone monoimide intermediate which underwent intramolecular Diels-Alder reaction with dienic part and furnished unusual complex molecular architectures (Scheme 44). From the optimization studies it was revealed that the amount and presence of the water in the reaction mixture is crucial for the success of the reaction. It was also observed that if the olefin moiety was part of the acyclic unit then the yield of the Diels-Alder adducts were poor owing to the more conformational freedom.



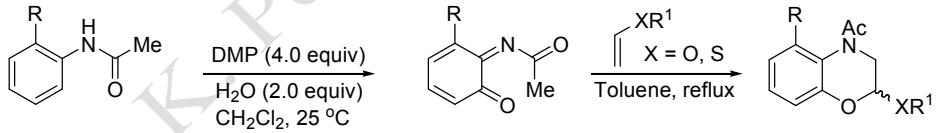
Scheme 44: Synthesis of polycyclic structures.

The labelling experiments confirmed that the oxygen atom of the *o*-QMI was coming from water, which explains the formation of acetoxy-*o*-iodoxybenzoic acid (Ac-IBX) upon attack of water on DMP[65] (Scheme 45).



Scheme 45: Proposed mechanism for the formation of benzoxazine derivative.

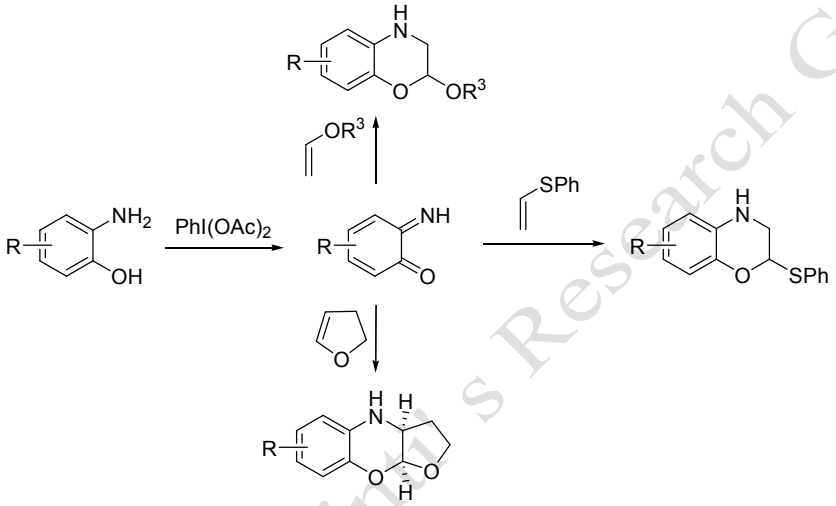
Subsequently, the authors isolated *o*-QMIs by introducing acetyl group on imine functionality and reacting the *o*-substituted anilides with DMP and water in dichloromethane at room temperature. These transient intermediates underwent IEDDA reaction with variety of vinyl ethers in toluene under reflux conditions to furnish both regio-isomers of benzoxazine derivatives in good to excellent yields[66,67] (Scheme 46).



Scheme 46: DMP-Mediated oxidation of anilides into *o*-quinone monoimides and subsequent Diels-Alder reaction with electron-rich olefins.

Our group has successfully developed a novel methodology for the generation of *o*-quinone monoimines from the corresponding *o*-aminophenols by using the less expensive hypervalent iodine reagents.[68] The *in situ* generated reactive *o*-quinone monoimines underwent the [4+2] cycloadddition reaction with various dienophiles such as vinyl ethers and vinyl sulfide with complete regio-selectivity to afford the 1,4-benzoxazine derivatives of diverse functionalities. The significant discovery of this study reveals that the incorporation of electron-withdrawing group on the aryl ring which avoids the polymerization of *o*-quinone

monoimines and favors the intermolecular Diels-Alder reactions. The more electron-rich carbon atom of the dienophilic enol ether added to the electrophilic nitrogen atom of the *o*-quinone monoimine. This can be attributed to the electron deficiency on the nitrogen atom due to the presence of more electronegative oxygen atom at the other end of the heterodiene (Scheme 47). The proposed mechanism for the DIB-mediated *in situ* generation of *o*-quinone monoamine and the consequent Diels-Alder reaction with various electron-rich dienophiles was depicted in Figure 4.



Scheme 47: DIB-Mediated synthesis of 1,4-benzoxazine derivatives.

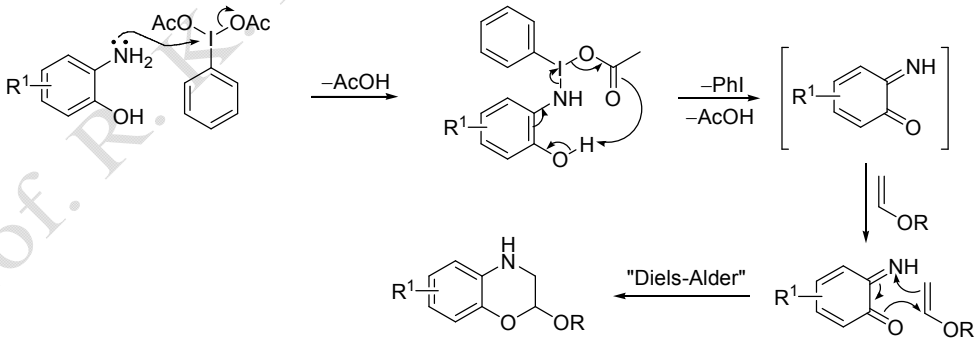
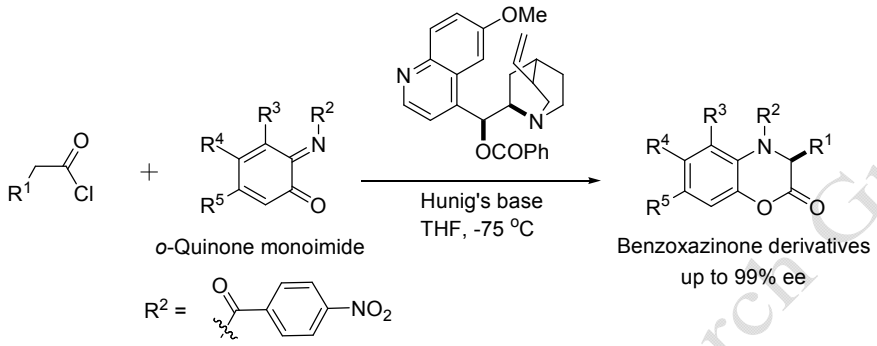


Figure 4: Proposed mechanism for DIB-mediated synthesis of 1,4-benzoxazine derivatives.

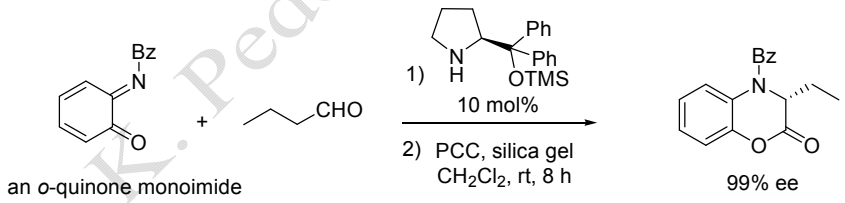
Lectka and co-workers designed an enantioselective route for the synthesis of α-amino acids from *o*-benzoquinone imides[69] The stable *o*-quinone imides underwent Diels-Alder reaction with chiral ketene enolate which formed by the action of benzoylated

quinidine (BQD) on acid chloride to provide enantiomerically enriched benzoxazinone derivatives in good yields. The nucleophilic attack on benzoxazinone derivatives led to α-amino acids. Finally oxidation by using ceric ammonium nitrate removed aryl moiety (Scheme 48).



Scheme 48: Enantioselective synthesis of benzoxazinones.

In a similar manner, the treatment of *o*-quinone monoimides and/or diimides with aliphatic aldehydes in the presence of catalytic amount of TMS ether of diphenylprolinol and subsequent oxidation with PCC furnished optically active benzoxazinone derivatives in excellent optical purities[70] (Scheme 49).

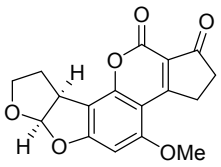


Scheme 49: A prolinol-based asymmetric synthesis of benzoxazinone derivatives.

1.4. Coumarin derivatives

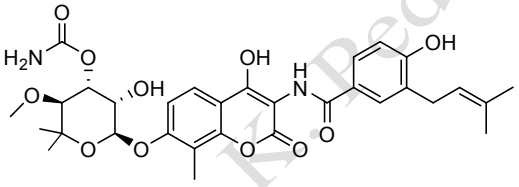
Coumarins belong to an interesting class of heterocyclic compounds which constitute a benzene ring fused to α-pyrone ring, the coumarin ring is present in a broad range of natural and unnatural products of biological interest.[71-76] Most of the coumarins occurring in the nature have been isolated from the higher plants whereas some of them have been identified in microorganisms. Aflatoxin B_1 is a coumarin derivative isolated from *Aspergillus*

species.[77] The high toxicity and carcinogenicity level of aflatoxins make them impractical to use as pharmacological agents since they act on cancer cells as well as on normal cells in the body. Therefore, only very few studies have been carried out to test their potential as drugs or pesticides.

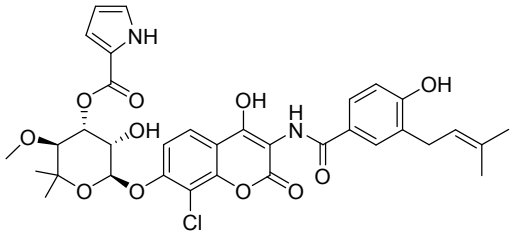


Aflotoxin B_1

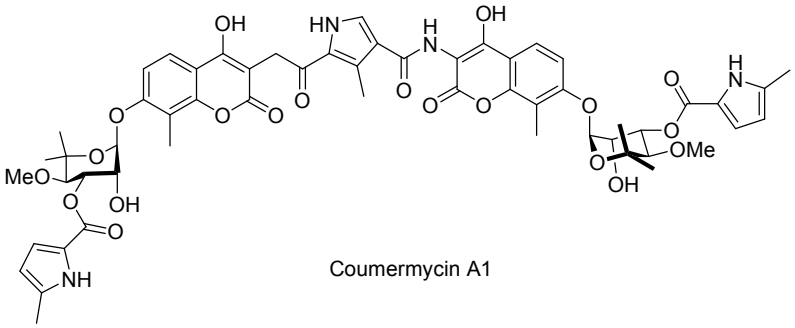
Novobiocin, chlorbiocin and coumermycin A1 are the antibiotics isolated from various *Streptomyces* species. All the three possess a 3-*N*-substituted coumarin moiety and a substituted deoxysugar in their structure. Chlorbiocin differs from novobiocin in that the methyl group at the C-8 of the coumarin ring is replaced by a chlorine atom. Recent work demonstrated that 3-aminocoumarin derivatives are potent inhibitors of DNA gyrase, binds to the C-terminal nucleotide-binding region of heat shock protein 90, an interesting new target in cancer drug discovery leading to decrease in hsp90 client proteins in various cancer cell lines.[78-81]



Novobiocin



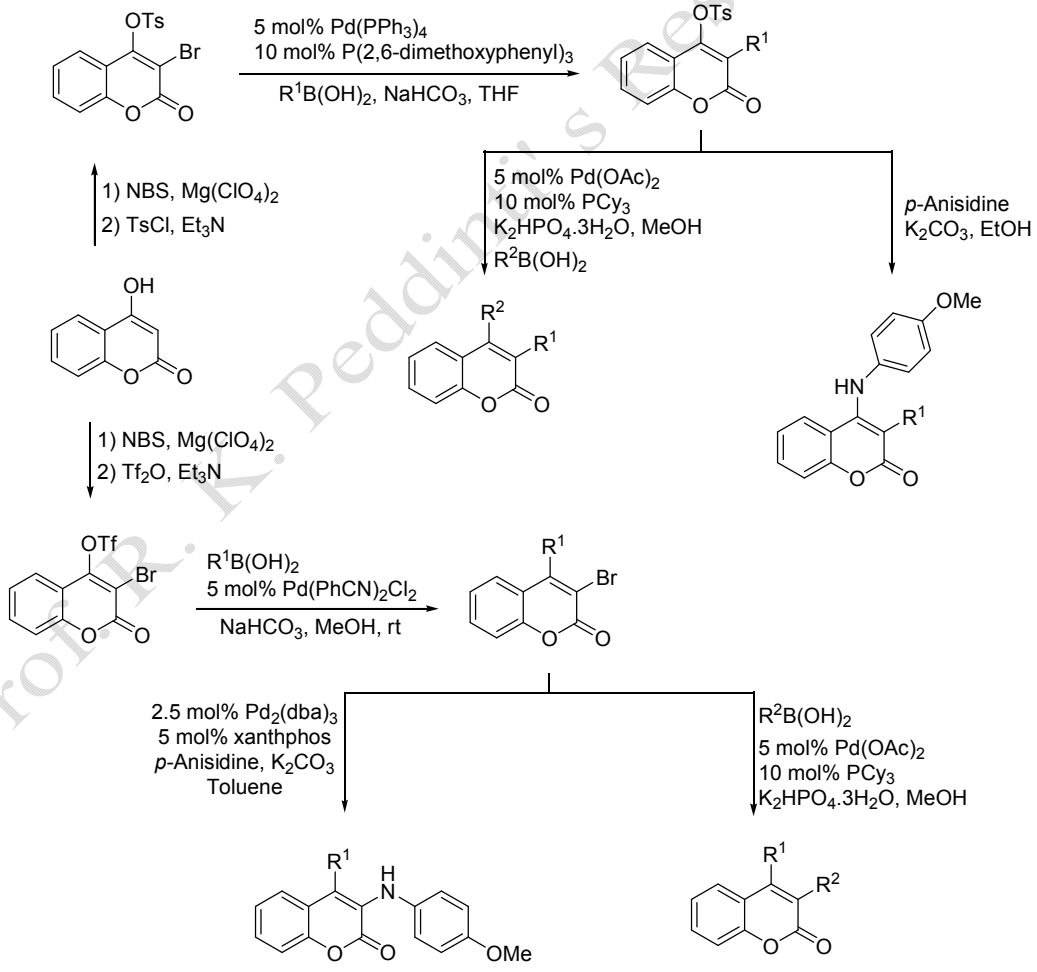
Chlorobiocin



Coumermycin A1

Over the past decades, synthesis and screening of various coumarin derivatives for drug discovery have been a subject of constant interest in medicinal chemistry because of their significant biological activities. The wide spectrum of these coumarin derivatives has inspired the chemists to design and develop simple and efficient synthetic routes for the construction of novel coumarin derivatives.

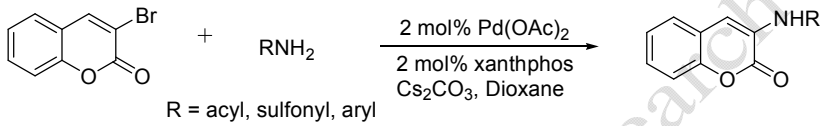
Zhang *et al.* developed a novel palladium-catalyzed site-selective coupling reactions of 3-bromo-4-trifloxycoumarins or 3-bromo-4-tosyloxycoumarins for the synthesis of diversely 3,4-disubstituted coumarin derivatives.[82] When the reaction of 3-bromo-4-trifloxycoumarin was carried out with arylboronic acid in presence of palladium catalyst, the reactivity of the vinyl trifloxy group was favored over vinyl bromide in coupling reactions. Similarly in the coupling reaction of 3-bromo-4-tosyloxycoumarins with arylboronic acid in



Scheme 50: Synthesis of functionalized coumarin derivatives by selective coupling reactions.

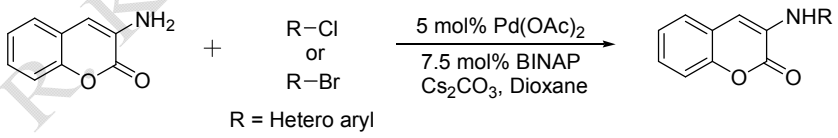
presence of palladium catalyst, the reactivity of bromide group was favored over the tosyloxy group. The trifloxy and tosyloxy groups present on the coumarin moiety provides a facile access for the selective synthesis of diversely substituted unsymmetrically 3,4-diarylated coumarin derivatives (Scheme 50).

Audisio *et al.* developed an efficient and selective Pd-mediated C–N coupling reactions of 3-bromocoumarins with various nucleophiles such as amides, sulfonamides and amines using palladium acetate and 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (xanthphos) as a catalytic system in presence of Cs_2CO_3 as a base[83] (Scheme 51).



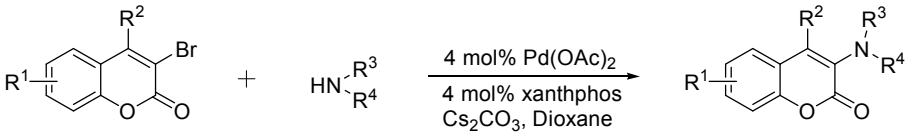
Scheme 51: Synthesis of 3-amino coumarin derivatives by coupling reactions.

Das *et al.* have synthesized 3-(heteroaryl) aminocoumarin derivatives from 3-aminocoumarin, by applying the optimized Buchwald–Hartwig amination reaction.[84] The 3-aminocoumarins were coupled with aryl halides using catalytic amount of palladium acetate, 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP) in presence of cesium carbonate. The target heteroaryl aminocoumarin derivatives were obtained in moderate to good yields (Scheme 52).



Scheme 52: Buchwald–Hartwig amination reaction of 3-amino coumarins with alkyl halides.

Soussi *et al.* developed a versatile and efficient palladium catalytic system for the coupling of a wide range of nitrogen-containing nucleophiles with 3-halo-substituted coumarins.[85] The reaction of 3-bromocoumarins with a variety of nitrogen containing nucleophiles such as azole, amide, lactam, sulfonamide, aniline, amine, and urea in presence of catalytic amounts of $Pd(OAc)_2$ and xanthphos provided an easy access for the synthesis of functionalized 3-aminocoumarin derivatives (Scheme 53).



Scheme 53: Palladium-catalyzed synthesis of 3-amino coumarin derivatives.

CHAPTER-2: OBJECTIVES, RESULTS AND DISCUSSION

2.1. Objectives

2.2. Results and Discussion

2.2.1. Synthesis of benzoxazol-2′-ylbicyclo[2.2.2]octenone derivatives

2.2.2. Synthesis of pyrrolobenzoxazine derivatives

2.2.3. Synthesis of 3-arylamino coumarin derivatives

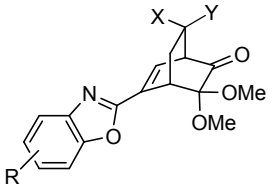
2.2.4. Synthesis of substituted 1,4-benzoxazinone derivatives

2.2.5. Synthesis of 2-aryl 1,4-benzoxazine derivatives

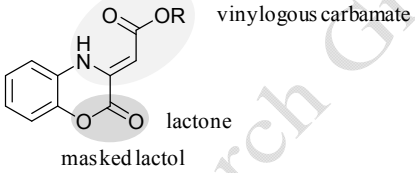
2.2.6. Synthesis of 2-amino-1,4-benzoxazine derivatives

2.1. OBJECTIVES

- Inspired by the simplicity in generation of *o*-benzoquinone monoketals and their utilization in the synthesis of complex natural products, we envisaged to incorporate a biologically significant benzoxazole core on to the bicyclo[2.2.2]octenones, which would lead to the synthesis of a novel class of benzoxazol-2′-yl bicyclo[2.2.2]octenone derivatives starting from 2-aminophenols.



benzoxazol-2'-yl bicyclo[2.2.2]octenones



1,4-benzoxazinone derivatives

- By applying the principles of green chemistry, we have developed a simple and efficient protocol for the synthesis of 1,4-benzoxazinone derivatives, a new class of vinylogous carbamates from 2-aminophenols. Further we became interested to extend our investigation to explore the various reactive sites of these vinylogous carbamates, which may provide an easy access for the synthesis of novel compounds of biological importance from the simple starting materials.

2.2. RESULTS AND DISCUSSION

In the previous chapter we have discussed the various synthetic methodologies developed for the synthesis of 2-aryl benzoxazole, 1,4-benzoxazine and coumarin derivatives. This chapter deals with the results and discussion, which was further divided into six sections as shown below.

1. Synthesis of benzoxazol-2′-yl bicyclo[2.2.2]octenone derivatives
2. Synthesis of pyrrolobenzoxazine derivatives
3. Synthesis of 3-arylamino coumarin derivatives
4. Synthesis of 3-substituted 1,4-benzoxazinone derivatives
5. Synthesis of 2-aryl 1,4-benzoxazine derivatives
6. Synthesis of 2-amino-1,4-benzoxazine derivatives

2.2.1. Synthesis of benzoxazol-2′-yl bicyclo[2.2.2]octenone derivatives

Organic compounds containing the benzoxazole scaffold belong to a significant class of heterocyclic compounds that are encountered in a number of natural products.[86-88] For example, benzoxazole core containing bicyclic systems calcimycin, cezomycin and routiennocin are isolated from the various strains of *Streptomyces*, and are found to act as good ionophore antibiotics (Figure 1).[89-91] Benzoxazole derivatives are found to have many applications in the field of medicinal chemistry. They act as estrogen receptor agonists,[92,93] melotonin receptor agonists,[94,95] anti tumor agents,[96] exhibit antimicrobial activities[97] and fatty acid amide hydrolase (FAAH) inhibitors.[98] These compounds are also found to have applications in electronic devices,[99] photoluminescent dyes[100] and as sensors for metals[101] due to their fluorescent properties.

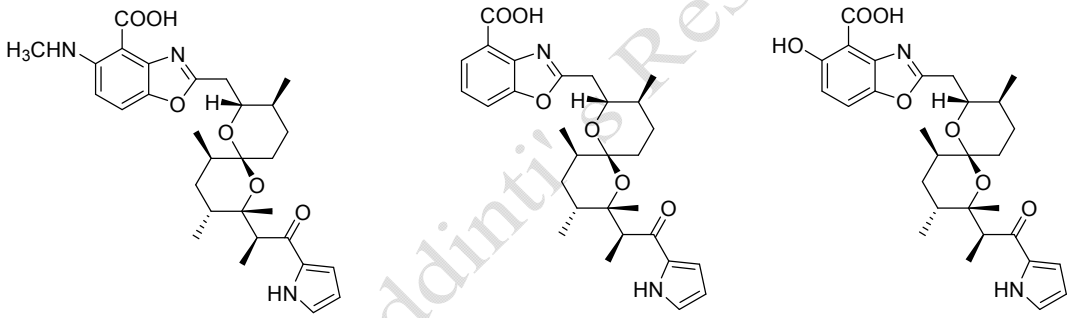
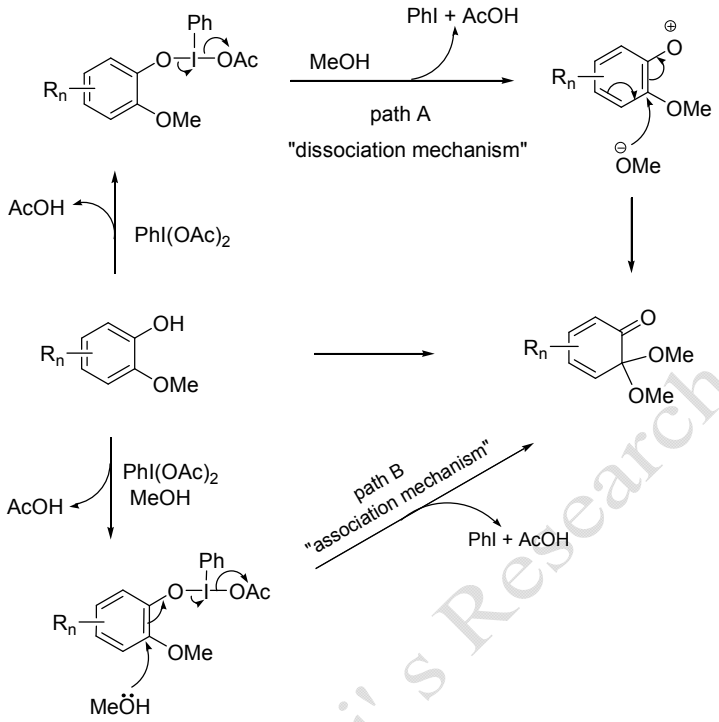


Figure 1: Biologically significant molecules containing benzoxazole moiety.

The oxidative dearomatization of phenol derivatives has become a very useful tactic in modern organic chemistry for the synthesis of complex natural products from simple and readily available starting materials.[102] The chemical[103-107] or electrochemical[108,109] oxidation of 2-methoxyphenol derivatives in presence of alcoholic reagents provides *o*-benzoquinone monoketals (*ortho*-benzoquinone monoketals) also called as masked *o*-benzoquinones (MOBs).[110-113] These MOBs belong to a class of linearly conjugated 2,4-cyclohexadienones, which can be transiently generated by the oxidative dearomatization of guaiacol derivatives in presence of alcoholic reagents with the help of hypervalent iodine reagents[114-117] such as phenyliodonium diacetate (PIDA) (also known as diacetoxyiodobenzene, DIB) and

phenyliodonium bis(trifluoroacetate) (PIFA). The formation of these ketals can be explained in two pathways, *viz* dissociation mechanism and association mechanism.[115,118,119]

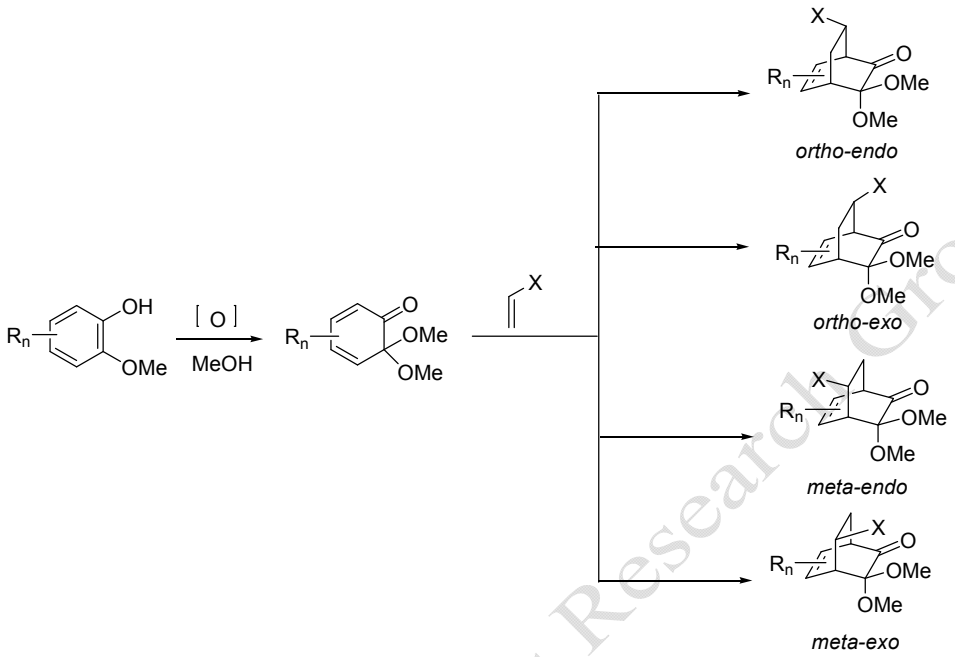


Scheme 1: Generation of *o*-benzoquinone monoketals using hypervalent iodine reagents.

Initially the nucleophilic oxygen of phenol attacks at the electrophilic iodine center, during which one of the carboxylate ligand is substituted by the reacting phenol (path A). The influence of the nucleofugality of the phenyliodanyl group helps the two-electron reduction of the iodine(III) center with concomitant elimination of a monovalent iodide and leaves solvated phenoxenium ions as intermediates. These species react further with methanol to give quinone monoketal. In the associate mechanism (path B), the direct attack of methanol on comparatively non-polar phenylaryloxyiodonium acetate (the common intermediate) affords the product (Scheme 1).

The masked orthobenzoquinones which are generated *in situ* from the oxidation of 2-methoxyphenol derivatives can be trapped often with dienophiles in Diels-Alder reaction to furnish the adducts with excellent stereo- and regio-selectivity[113,120-123] (Scheme 2). Liao exploited the Diels-Alder strategy of MOBs for the synthesis of bicyclo[2.2.2]octenones,

oxatricycles, triquinanes and bicyclo[4.2.2]decenones that are potential precursors in the construction of natural products of diverse structural nature.[113,123]



ortho: the electron-withdrawing/releasing group X is adjacent to the carbonyl function of bicyclo[2.2.2]octenone moiety

meta: the electron-withdrawing/releasing group X is adjacent to the acetal function of bicyclo[2.2.2]octenone moiety

endo: the electron-withdrawing/releasing group X is *anti* to the carbonyl/acetal functionality of bicyclo[2.2.2]octenone moiety

exo: the electron-withdrawing/releasing group X is *syn* to the carbonyl function of bicyclo[2.2.2]octenone moiety

Scheme 2: Intermolecular Diels-Alder reaction of *o*-benzoquinone monoketals.

The most recent examples of total synthesis based on MOB strategy are (+)-eudesmadiene-12,6-olide, (+)-frullanolide,[124] (+)-scabronine B, (−)-scabronine D, (−)-scabronine G,[125] (−)-anisatin,[126] (±)-penicillones A and B,[127] (−)-acutumine,[128] dalesconol B,[129] and (±)-chamaecypanone[130] (Figure 2).

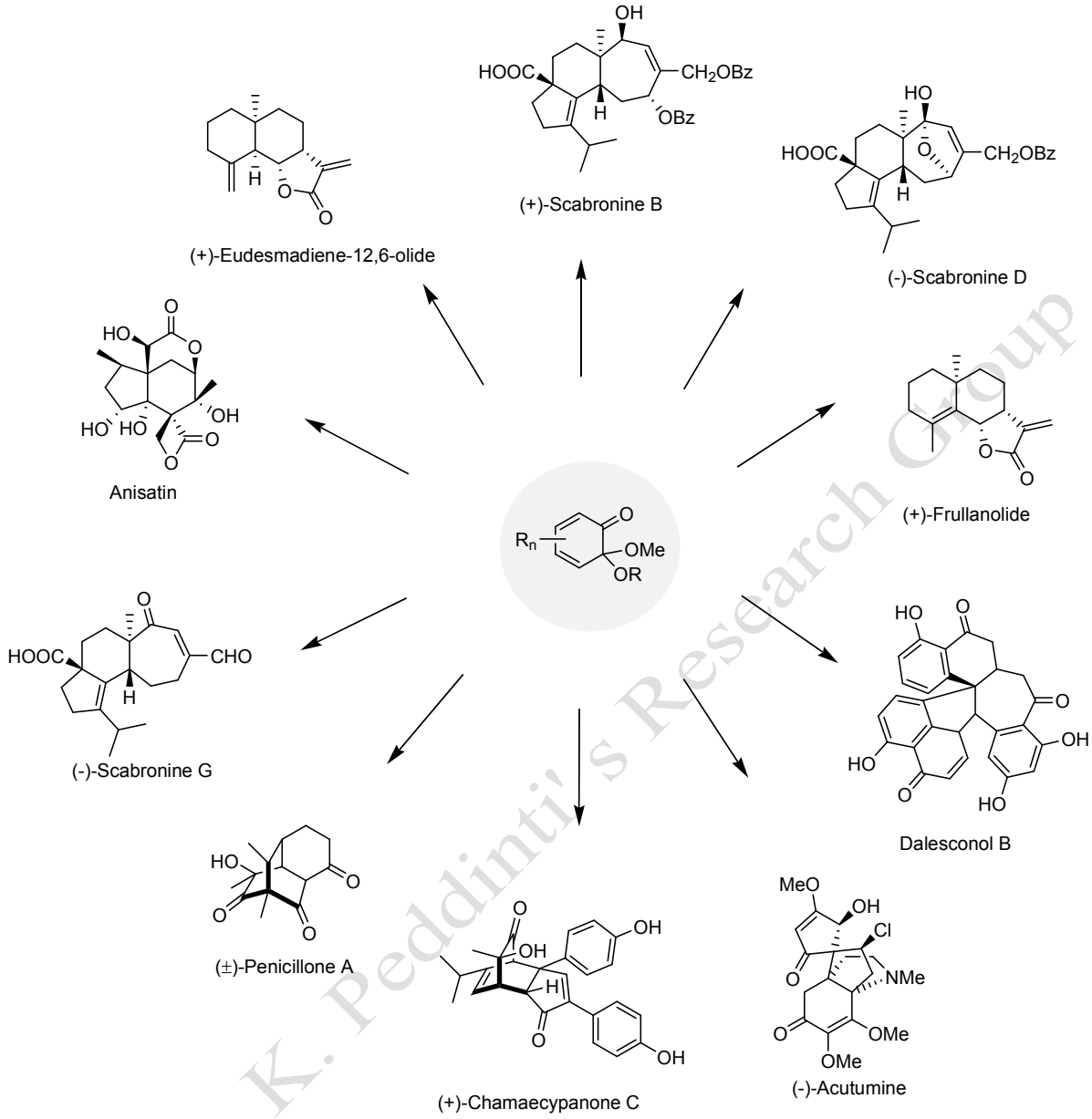
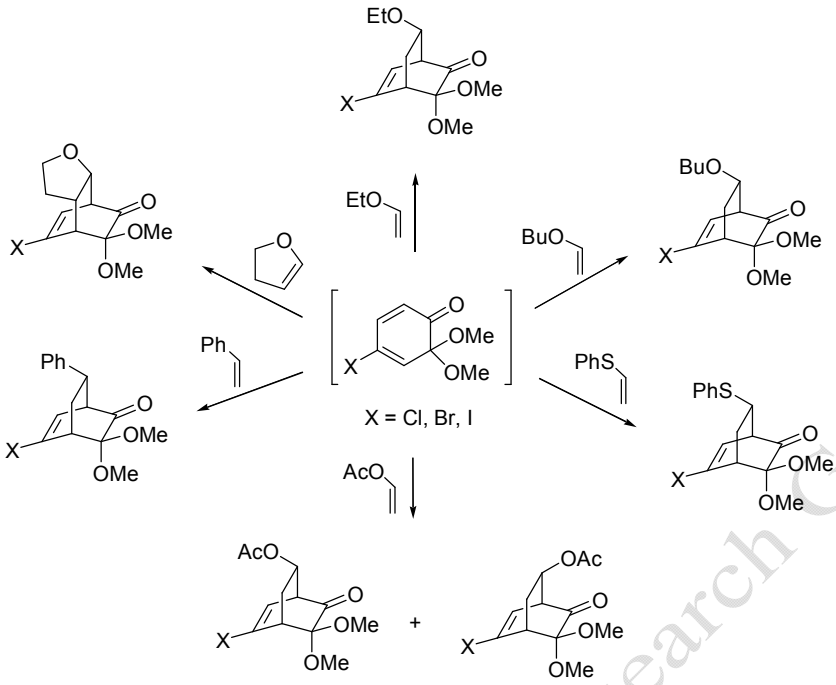
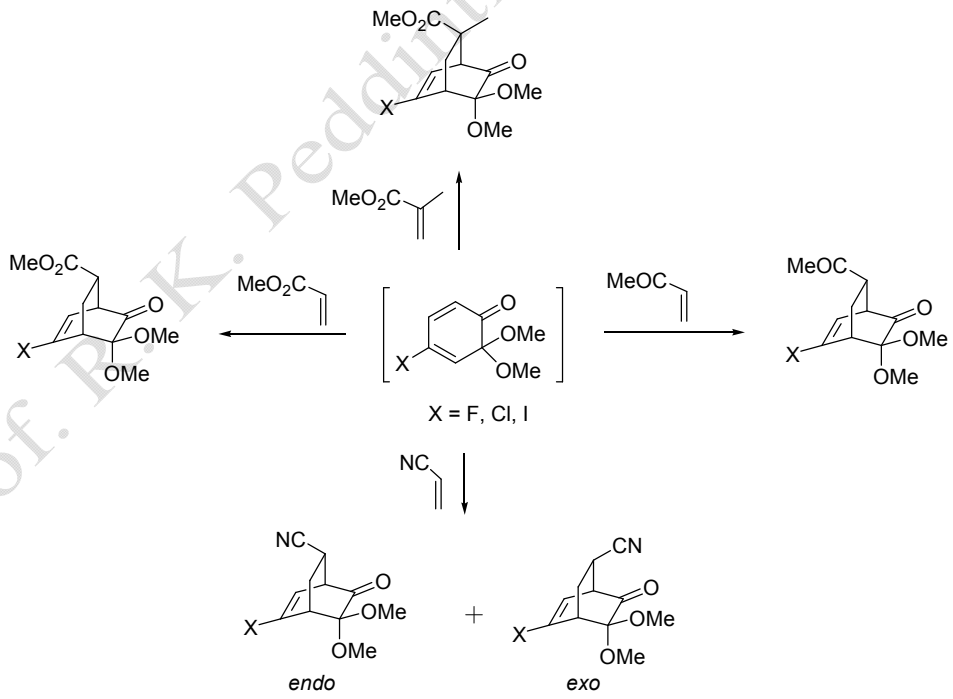


Figure 2: Synthesis of natural products using MOB strategy.

Our group has been interested in investigating oxidative dearomatization of phenolic substances. We have synthesized 4-halo bicyclo[2.2.2]octenone derivatives by highly regio- and stereo-selective Diels-Alder reaction between relatively stable dienic 4-halo MOBs and various 2π–components.[131,132] Further the studies also revealed that the 4-halo-*ortho*-benzoquinone monoketals are stable enough for the isolation and characterization (Schemes 3 and 4). We have also developed novel synthetic methodologies for synthesis of biaryls[133] and 1,4-benzoxazine derivatives.[68]



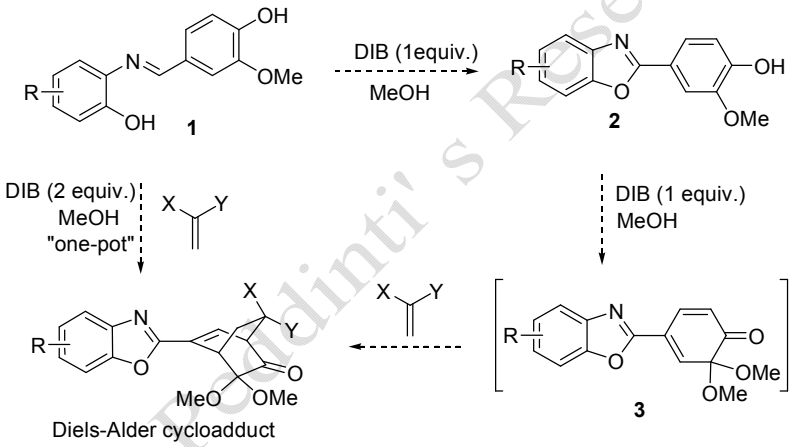
Scheme 3: Diels-Alder reaction of 4-halo MOBs with electron-rich dienophiles.



Scheme 4: Diels-Alder reaction of 4-halo MOBs with electron-deficient dienophiles.

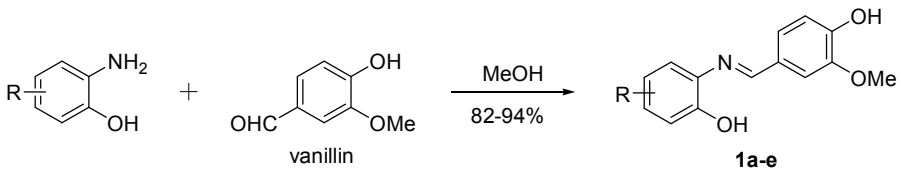
Several methodologies have been developed for the synthesis of various functionalized benzoxazoles and their derivatives.[15,134] The immense biological properties and wide spectrum of applications of benzoxazoles in various fields indicate the demand for development of novel synthetic methodologies for the synthesis of their derivatives.

Intrigued by the diverse applications of these 2-substituted benzoxazole derivatives, we envisaged that the introduction of biologically significant benzoxazole core on to the bicyclo[2.2.2]octenone system would provide a new class of densely substituted benzoxazol-2′-yl bicyclo[2.2.2]octenone derivatives. Accordingly we have designed a one-pot domino strategy for the synthesis of benzoxazolyl bicyclo[2.2.2]octenone derivatives from the readily available starting materials *o*-aminophenols and vanillin using the hypervalent iodine reagents (Scheme 5).



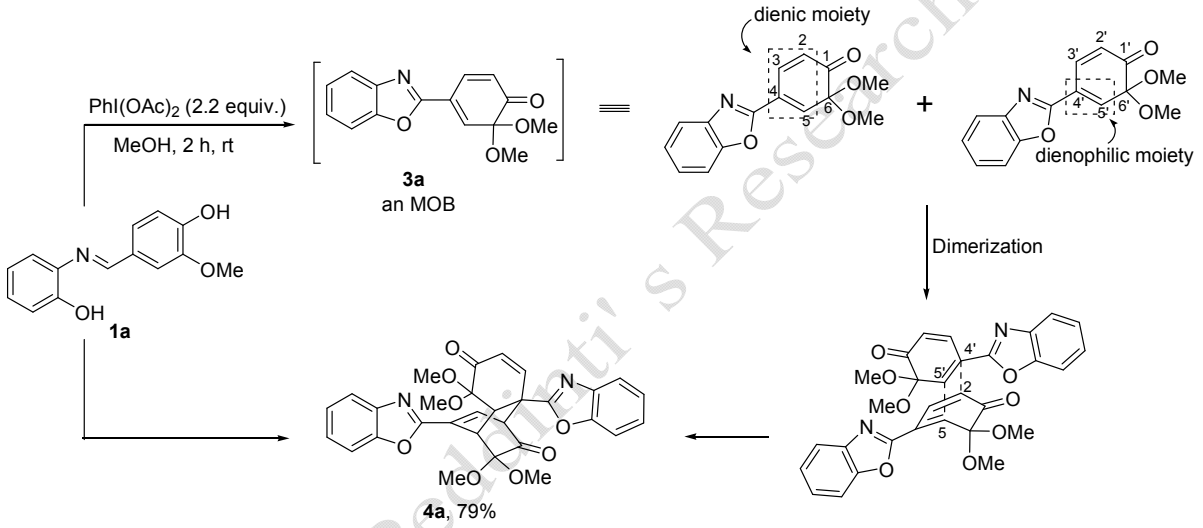
Scheme 5: Domino oxidative cyclization–oxidative acetalization–Diels-Alder strategy.

Our studies began with the synthesis of aldimines from the readily available *o*-aminophenol derivatives and vanillin. An aminophenol derivative and vanillin were dissolved in methanol and allowed to stir at room temperature. After completion of the reaction, the crude product was recrystallized to obtain the corresponding aldimines **1a-e** in high yields (Scheme 6).



Scheme 6: Synthesis of aldimines from 2-aminophenol derivatives and vanillin.

After synthesizing the Schiff bases **1a-e**, we have proceeded for the hypervalent iodine-mediated oxidation of aldimines. Aldimine **1a** was dissolved in methanol, and subjected to oxidation with 2.2 equiv. of diacetoxyiodobenzene (DIB) at room temperature. The *in situ* generated MOB underwent self-dimerization in 4 h in the absence of external reactant to afford the corresponding Diels-Alder dimer **4a** in 79% yield. Self-dimerization of reactive *ortho*-benzoquinone monoketals is known in literature.[135,136] Dimerization of MOBs which is also a Diels-Alder cycloaddition, proceeds in highly regio-, stereo- and chemo-selective manner. The $C_{4'}$-$C_{5'}$ bond acts as dienophile and the new bond formation takes place between C_2-$C_{4'}$ and C_5-$C_{5'}$ during the dimerization (Scheme 7).

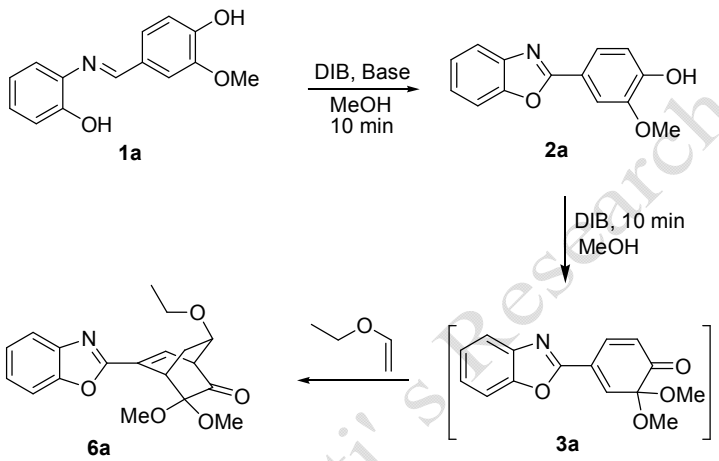


Scheme 7: Domino oxidative cyclization–oxidative acetalization–Diels-Alder dimerization.

We were delighted with this event and proceeded further to carry out the reaction of aldimine **1a** with external dienophiles. Thus, the reaction of **1a** with ethyl vinyl ether (5 equiv.) in 5 mL of methanol in the presence of 2.2 equiv. of DIB underwent smoothly to furnish the desired bicycloadduct **6a** in 82% yield *via* the Diels-Alder reaction of *in situ* generated MOB **3a**. Though the result obtained was encouraging, we were curious to know whether the first step was oxidative cyclization to benzoxazole or oxidative dearomatization to MOB. To understand the reaction sequence, we carried out the reaction with 1.1 equiv. of oxidizing agent. The product was formed in 10 min. with isolated yield of 80% and its ^{1}H and ^{13}C NMR analysis revealed that the product as benzoxazole derivative **2a**. The product **2a** obtained in the initial step was oxidized further with DIB (1.1 equiv.) in presence of ethyl

vinyl ether in methanol to afford the corresponding Diels-Alder adduct **6a** in 72% yield. As the overall chemical yield (58%) of **6a** obtained from the two individual steps is less than one-pot reaction (82%), we opted for one-pot synthesis of benzoxazolyl bicyclo[2.2.2]octenone derivatives. Further to optimize, the reaction was carried out in the presence of various bases like $NaHCO_3$, K_2CO_3, NEt_3 and $KHCO_3$ (Table 1).

Table 1: Optimization of reaction conditions.[a]



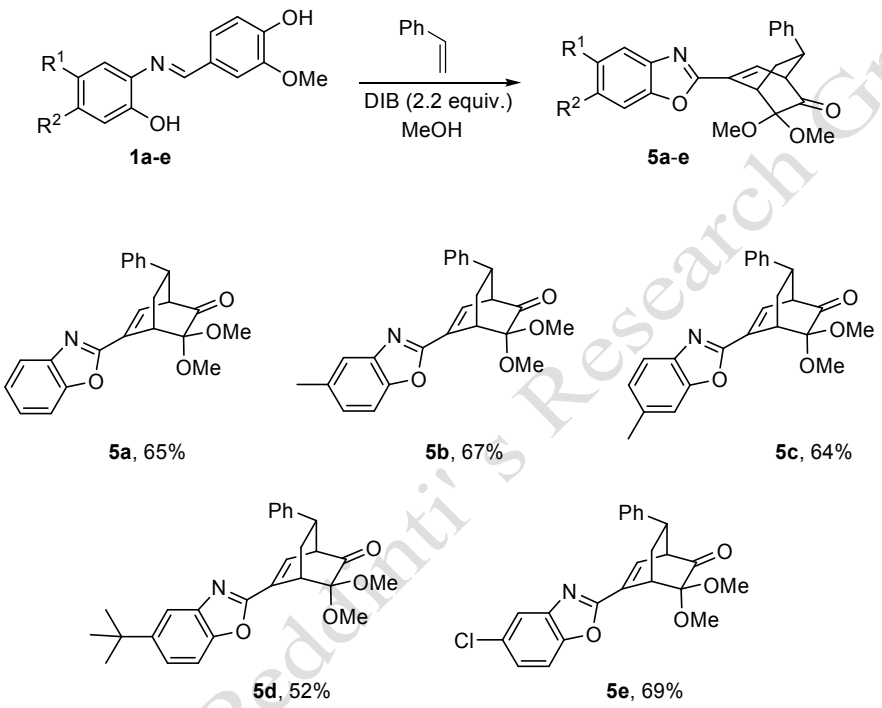
Entry	Substrate	Base	Product (yield)
1	**1a**	-	**6a** (82%)
2	**1a**	$NaHCO_3$	**2a** (trace)
3	**1a**	$KHCO_3$	**2a** (trace)
4	**1a**	K_2CO_3	**2a** (trace)
5	**1a**	Et_3N	**2a** (trace)

[a]reaction was carried out with aldimine **1a** (0.5 mmol), ethyl vinyl ether (2.5 mmol), base (1 mmol) and 1.1 mmol of DIB in 5 mL of methanol at rt for 20 min.

We expected that the base would facilitate the cyclization in the initial step, of transformation of the Schiff base into a benzoxazole moiety. However, in all the cases formation of benzoxazol-2'-yl guaiacol **2a** in trace amount was observed from the ^1H NMR.

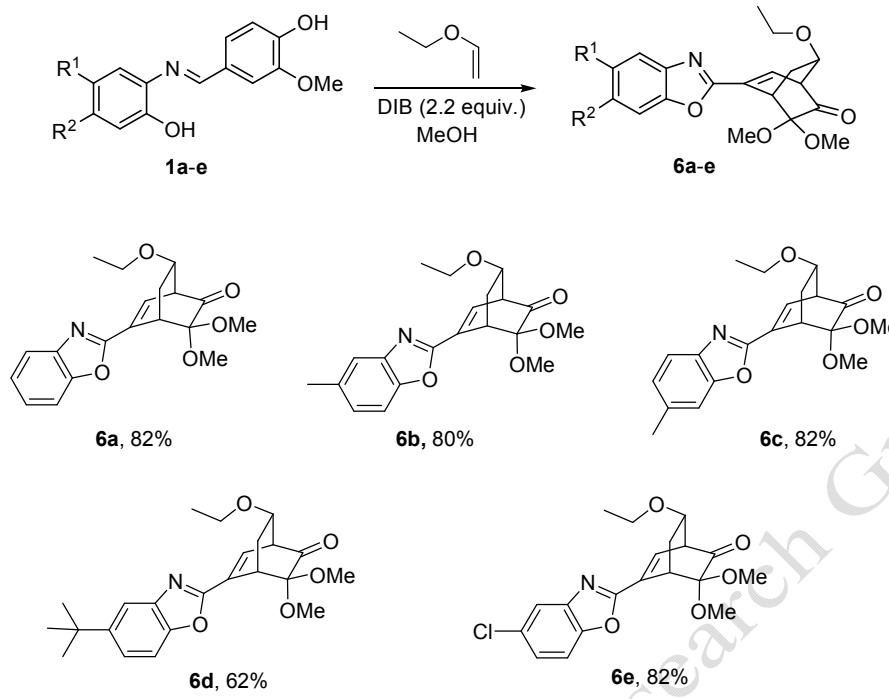
At this juncture, we turned our focus on improving the yield of the reaction by varying the amount of dienophile. When **1a** was oxidized with DIB in methanol in presence of 10 equiv. of styrene, the corresponding Diels-Alder adduct **5a** was obtained in 55% yield.

The similar reaction of **1a** in presence of 20 equiv. of the conjugative dienophile-styrene, the adduct **5a** was resulted in 10% higher yield. The other derivatives of aldimines **1b-e** were also oxidized in presence of the styrene and their respective Diels-Alder adducts **5b-e** were obtained in good yield. It was observed that the reaction of aldimine **1d** bearing the *tert*-butyl group with styrene provided the cycloadduct **5d** in slightly lower yield in comparison with those of other aldimines (Scheme 8).



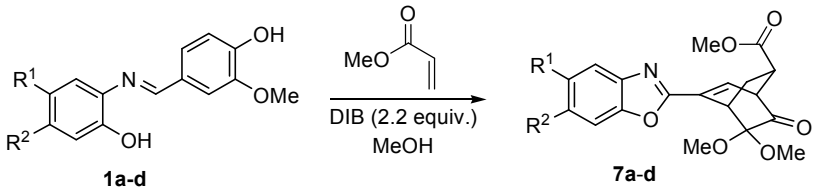
Scheme 8: DIB-Mediated reaction of aldimines **1a-e** with styrene.

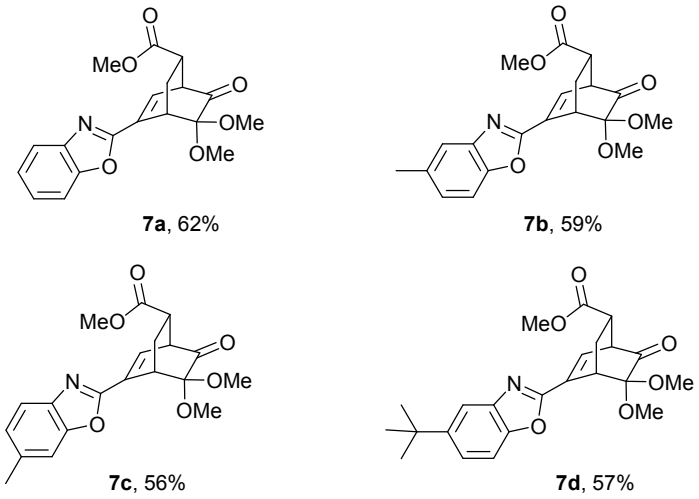
For uncovering the scope of this one-pot domino reaction, the reaction of **1a** was performed with 10 equiv. of ethyl vinyl ether, and no appreciable change was noticed on the chemical yield in comparison with that of the reaction carried out with 5 equiv. of ethyl vinyl ether. Thus the reaction of aldimines **1b-e** were also carried out with 5 equiv. of ethyl vinyl ether and the Diels-Alder adducts **6b-e** were obtained in excellent yields. The reaction of aldimine **1d** bearing the *tert*-butyl group with ethyl vinyl ether afforded the adduct **6d** in slightly lower yield in comparison to those of the adducts derived from the other aldimines (Scheme 9).



Scheme 9: DIB-Mediated reaction of aldimines **1a-e** with ethyl vinyl ether.

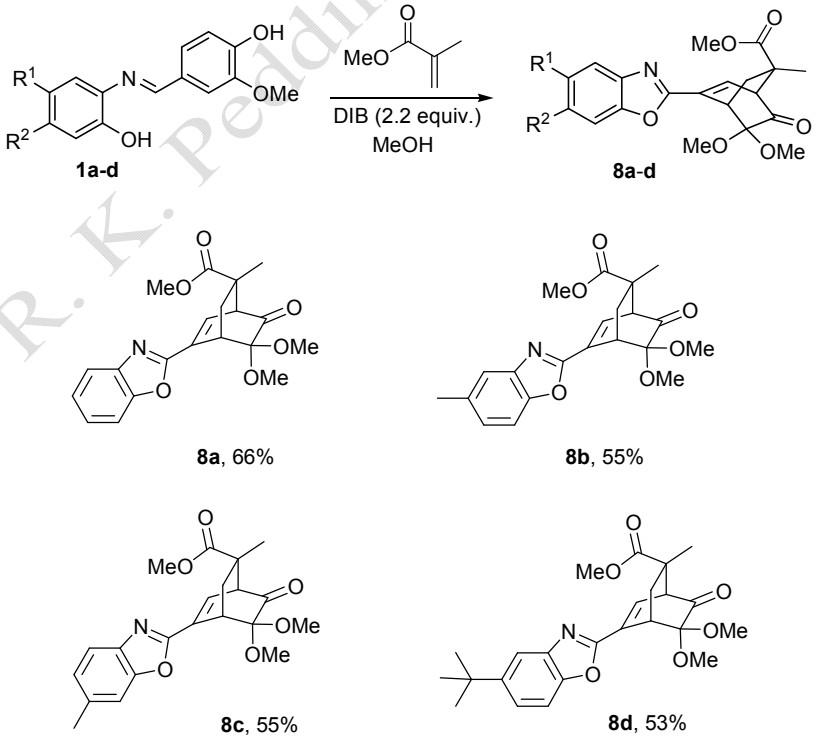
The hypervalent iodine-mediated domino oxidative cyclization-oxidative acetalization-Diels-Alder protocol was also extended to electron-deficient dienophiles. For this purpose, we performed the reaction of **1a** with 2.2 equiv. of DIB at rt in methanol in the presence of methyl acrylate (20 equiv.). The MOB which was generated *in situ* by the oxidative dearomatization of **1a**, successfully underwent inverse electron-demand Diels-Alder (IEDDA) reaction and was found to be completed in 40 min. Methanol was evaporated under reduced pressure and upon purification of crude reaction mixture by the silica gel column chromatography, the corresponding bicycloadduct **7a** was obtained in 62% yield. The generality of the cycloaddition of methyl acrylate in the current strategy was also tested with MOBs derived from other aldimines **1b-d**. The bicyclic adducts **7b-d** were synthesized in good yields. Unexpectedly, the Schiff base **1e** bearing chloro substituent did not afford the desired cycloadduct under similar reaction conditions (Scheme 10).





Scheme 10: DIB-Mediated reaction of aldimines **1a-d** with methyl acrylate.

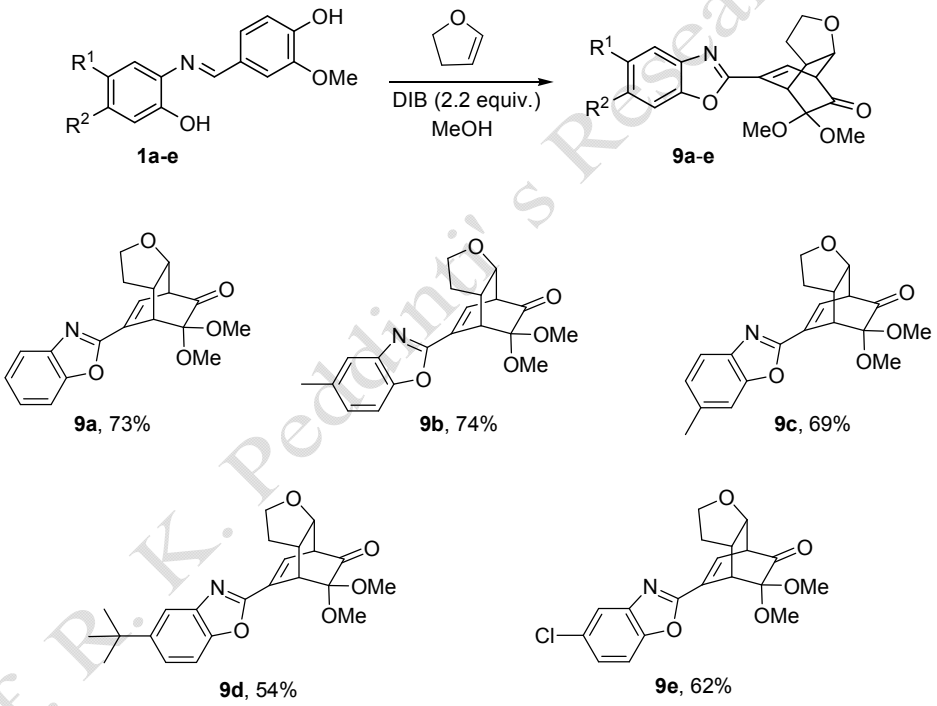
Further, to explore the substrate scope in the current protocol, we chose methyl methacrylate as a dienophile. When the oxidation of **1a** was carried out with DIB in methanol in presence of methyl methacrylate, the reaction underwent smoothly and the corresponding cycloadduct **8a** was obtained in 66% yield. The reactivity of aldimines **1b-d** were also tested with the methyl methacrylate and their respective cycloadducts **8b-d** were



Scheme 11: DIB-Mediated reaction of aldimines **1a-d** with methyl methacrylate.

isolated in good yields (Scheme 11). It is worth mentioning here that the Diels-Alder reaction of MOB derived from aldimines **1a-e** with electron-deficient dienophiles, unlike those with electron-rich dienophiles, furnished the cycloadducts **7** and **8** in slightly lower yields.

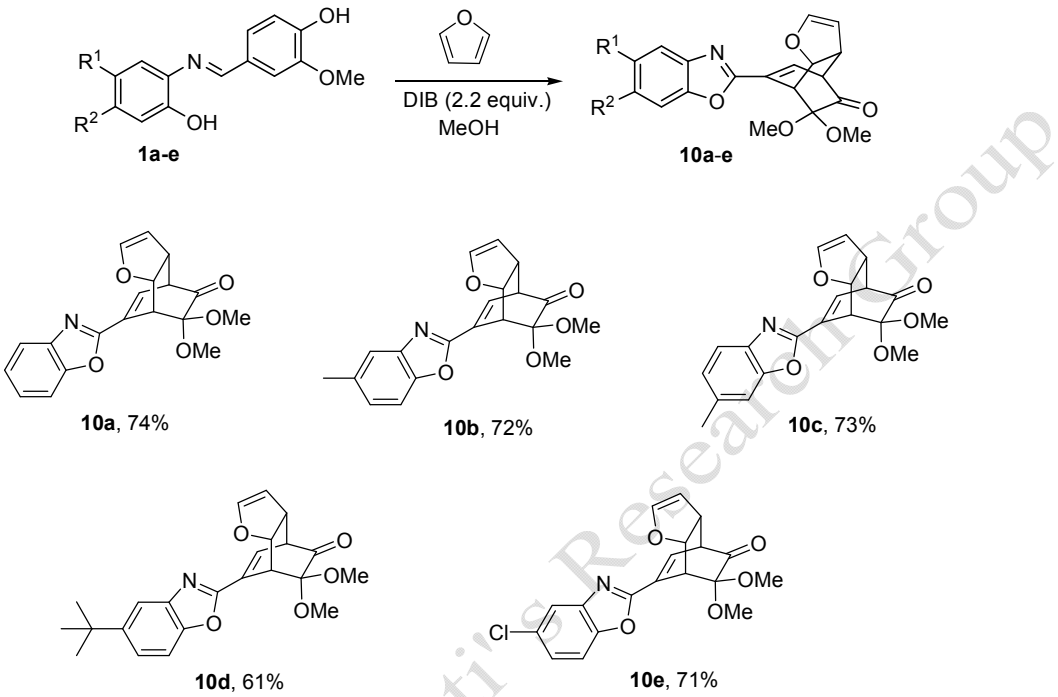
After successfully carrying out the one-pot domino Diels-Alder reactions of the aldimines **1a-e** with acyclic dienophiles such as styrene, ethyl vinyl ether, methyl acrylate and methyl methacrylate then we turned our focus on to the cyclic dienophiles. When **1a** was oxidized with DIB in methanol, the *in situ* generated MOB **3a** underwent [4+2] cycloaddition with the cyclic dienophile 2,3-dihydrofuran (5 equiv.) to provide the Diels-Alder adduct **9a** in 73% of isolated yield. The aldimines **1b-e** were reacted well with the 2,3-dihydrofuran and furnished the adducts **9b-e** in good yields (Scheme 12).



Scheme 12: DIB-Mediated reaction of aldimines **1a-e** with 2,3-dihydrofuran.

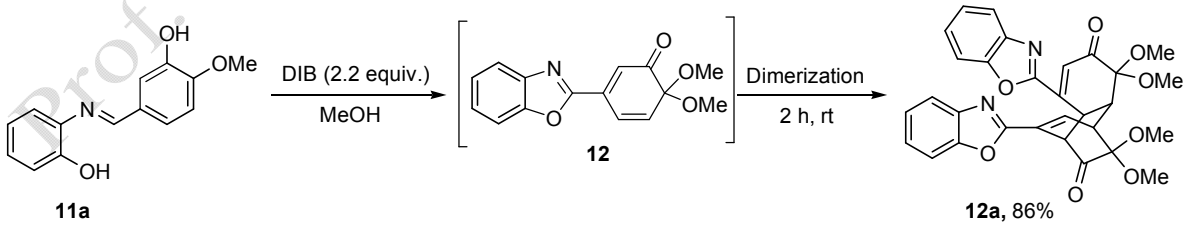
In the current study, the reactivity of furan was also tested. When the Schiff base **1a** was oxidized with DIB in methanol in presence of 20 equiv. of furan, the [4+2] cycloaddition reaction underwent smoothly and gave the corresponding product **10a** in 74% yield. In general the furan acts as a diene in [4+2] and [4+3] cycloaddition reactions[137-140] and as an olefin in [2+2] photocycloadditions.[141] However, in this Diels-Alder reaction, furan has efficiently participated as a dienophile and the MOB **3a** acted as diene. Such dienophilic

behavior of furan in Diels-Alder reaction with MOBs has literature precedence.[142,143] Under similar conditions, the aldimines **1b-e** resulted the Diels-Alder adducts **10b-e** in high yields (Scheme 13).



Scheme 13: DIB-Mediated reaction of aldimines **1a-e** with furan.

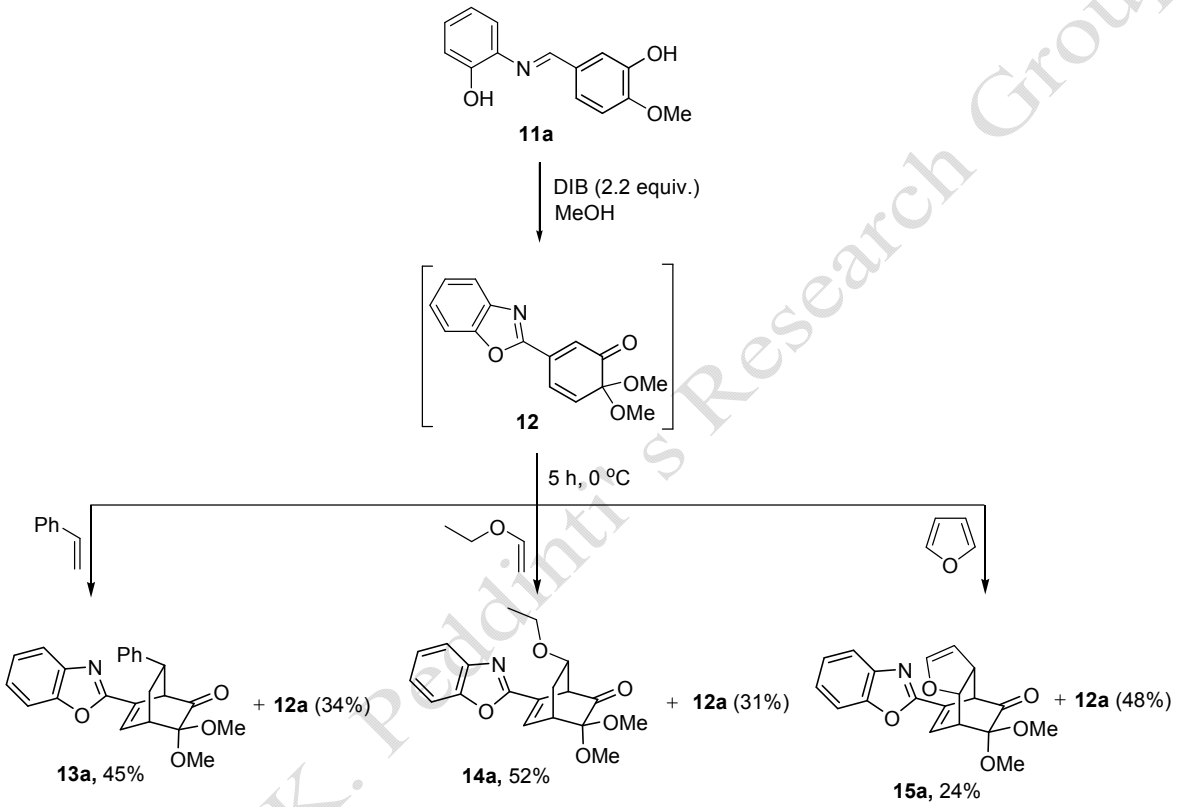
To expand the substarte scope in the present study, we have synthesized aldimine **11a** by the reaction of *o*-aminophenol with isovanillin. The oxidation of **11a** with DIB in methanol generated the MOB **12**, which underwent the self-dimerization reaction to provide the corresponding dimer **12a** in 86% yield in 2 h (Scheme 14).



Scheme 14: DIB-Mediated reaction of aldimine **11a** derived from isovanillin.

We have also applied the hypervalent iodine-mediated domino oxidative cyclization–oxidative acetalization–Diels-Alder strategy to the aldimine **11a** derived from *o*-

aminophenol and isovanillin. It is known from literature that the MOBs lacking substituents in 4th and 5th position, are found to be less stable and readily undergo Diels-Alder dimerization reaction at room temperature. So in order to decrease the extent of dimerization, we planned to carry out the oxidative acetalization of **11a** at 0 ^{o}C. Accordingly, when the aldimine **11a** was subjected to oxidation with DIB in methanol in presence of external dienophile styrene (20 equiv.), the reaction proceeded smoothly and found to be completed

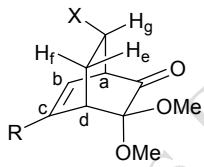


Scheme 15: DIB-Mediated reaction of aldimine **11a** derived from isovanillin with dienophiles.

in 5 h. The Diels-Alder adduct **13a** was obtained in 45% yield along with 34% of dimer **12a**. Under the similar conditions, the reaction of **11a** with ethyl vinyl ether provided the cycloadduct **14a** in 52% yield and the dimer **12a** in 31% yield. Further when **11a** was oxidized with DIB in presence of a cyclic dienophile furan, the cycloadduct **15a** was obtained in 24% yield in addition to 48% dimer **12a** (Scheme 15).

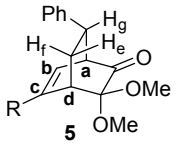
The structures of these Diels-Alder adducts were assigned based on IR, ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR, DEPT and HRMS spectral analysis. In order to identify the

chemical shifts of protons and carbon atoms, we have carried out ^1H-^1H decoupling experiments and 2D experiments such as ^1H-^1H COSY and Heteronuclear Multiple Quantum Correlation (HMQC). The protons H_a and H_d resonate in the range of δ 3.5-3.8 and 4.1-4.7 ppm, respectively. The coupling constants of H_d–H_e or H_d–H_f are observed predominantly in the range of J = 2.5-3.5 Hz, which are in agreement with the assigned *ortho*-regiochemistry (Table 2). The proton H_f resonates in the range of δ 1.5-2.1 ppm and H_e resonates at downfield in the range of δ 2.4-2.7 ppm. The higher chemical shift of H_e may be attributed predominantly to the magnetic anisotropic effect of *exo*-methoxy group of ketal function which lies in its proximity. The coupling constants (J = 6.0-7.0 Hz) between H_f–H_g, and those (J = 8.5-10.5 Hz) between H_e–H_g reveal the *cis* relationship of the protons H_e and H_g which confirms the assigned *endo*-stereochemistry.

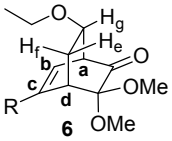


In the ^{13}C NMR of the Diels-Alder adducts, the ring carbonyl carbon appears at around 200 ppm and the ketal quaternary carbon appears at around 93 ppm (Table 5). Among the bridge-head carbons C_a (δ 55-57 ppm) and C_d (δ 39-40 ppm), the former which is positioned next to the ring carbonyl resonates downfield (Table 5). The cycloadducts exhibited IR absorptions at 1735-1745 cm^{-1}, a characteristic absorption of carbonyl function of bicyclo[2.2.2]octenones derived from MOBs. The selected ^1H and ^{13}C NMR chemical shifts of some of the cycloadducts are shown in Figure 3. The assigned regio- and stereo-selectivities are further established by the single crystal X-ray analysis of the product

Table 2: Selected coupling constants (*J* in Hz) of adducts **5**-**10**.



5



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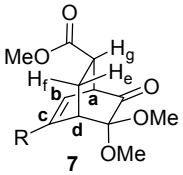

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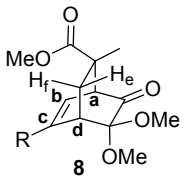

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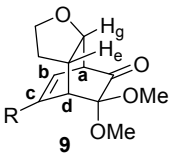

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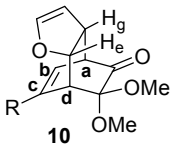


10

Entry	Adduct	*J* (Hz)			
		H_d-H_e	H_d-H_f	H_e-H_g	H_f-H_g
1	**5a**	3.0	2.5	8.5	6.5
2	**5b**	3.0	2.5	9.5	7.0
3	**5c**	3.0	3.0	9.5	7.0
4	**5d**	3.0	2.5	9.5	6.5
5	**5e**	3.0	3.0	10.0	7.0
6	**6a**	2.5	3.0	8.0	-
7	**6b**	3.0	3.5	8.5	-
8	**6c**	2.5	3.5	8.5	-
9	**6d**	2.5	3.5	8.0	-
10	**6e**	2.5	3.5	8.5	-
11	**7a**	3.0	3.0	10	6.0
12	**7b**	2.5	3.0	10	6.0
13	**7c**	-	2.5	-	6.0
14	**7d**	3.0	3.0	10.5	6.0
15	**8a**	3.5	2.0	-	-
16	**8b**	3.5	2.5	-	-
17	**8c**	3.5	2.5	-	-
18	**8d**	3.5	2.5	-	-
19	**9a**	3.0	-	8.0	-
20	**9b**	3.0	-	8.0	-
21	**9c**	3.0	-	8.0	-
22	**9d**	-	-	-	-
23	**9e**	-	-	-	-
24	**10a**	4.0	-	9.5	-
25	**10b**	4.0	-	9.5	-
26	**10c**	4.0	-	9.5	-
27	**10d**	4.0	-	9.5	-
28	**10e**	4.0	-	9.5	-

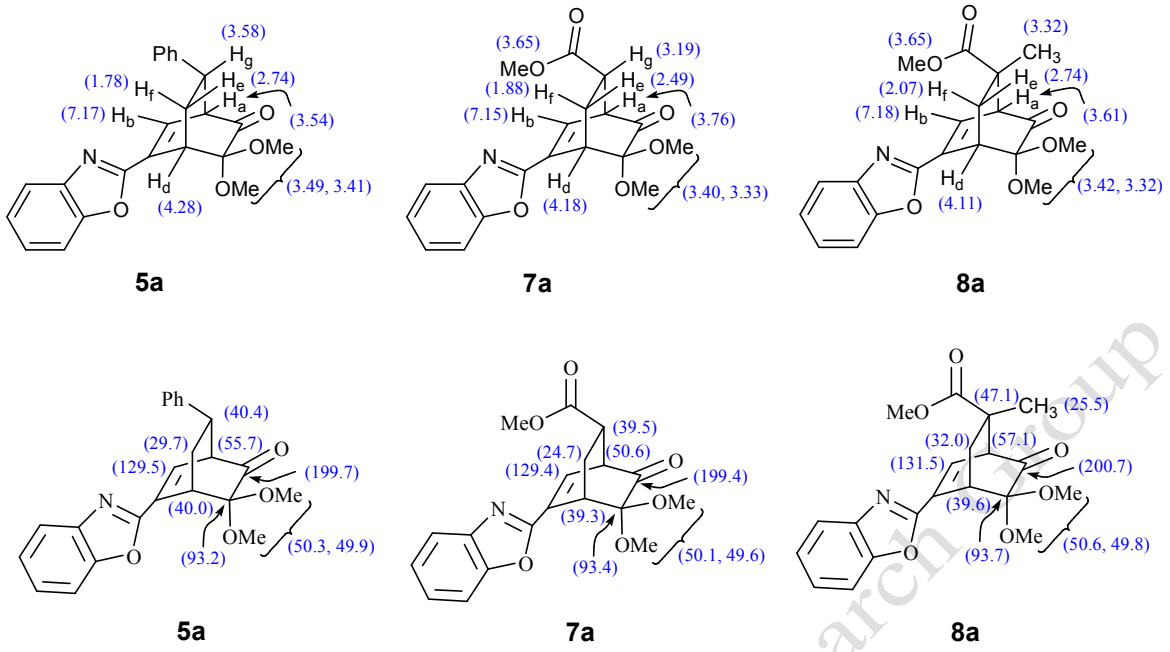
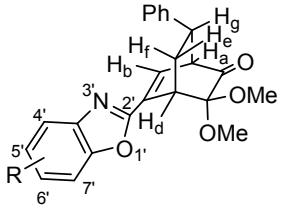
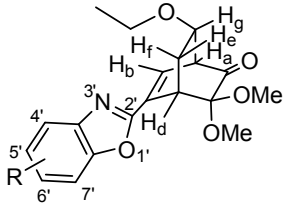
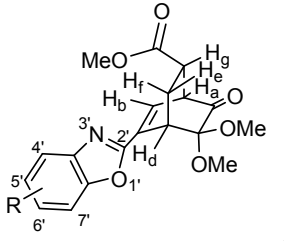


Figure 3: Selected ^{1}H and ^{13}C chemical shifts (in ppm) of the cycloadducts **5a**, **7a** and **8a**.

5e (Figure 4, Table 6). Of the eight possible isomers from the dimerization of substituted MOB **3a**, a single isomer **4a** was formed. The assigned structure of this dimer is unambiguously confirmed by its single crystal X-ray analysis (Figure 5, Table 7). The structure of the dimer **12a** was also confirmed by the single crystal X-ray analysis (Figure 6, Table 8). The regio-, stereo- and site-selectivity of the dimerization is in harmony with the literature precedents.[144] Selected ^{1}H and ^{13}C NMR chemical shifts are represented in Tables 3, 4 and 5 (Figure 3).

Table 3: Selected ^{1}H NMR chemical shifts (δ in ppm) of the Diels-Alder adducts **5-8**.

Adduct		R	H_a	H_b	H_d	H_e	H_f	H_g
	**5a**	H	3.54	7.17	4.28	2.74	1.78	3.58
	5b	5′-Me	3.51	7.16	4.23	2.70	1.76	3.56-3.53
	5c	6′-Me	3.52	7.20-7.11	4.25	2.72	1.77	3.58-3.54
	5d	5′-*tert*-butyl	3.52	7.22-7.19	4.26	2.73	1.78	3.58-3.55
	5e	5′-Cl	3.56	7.22-7.19	4.23	2.74	1.78	3.60-3.58
	**6a**	H	3.78	7.04	4.07-4.06	2.55	1.46	4.07-4.06
	6b	5′-Me	3.82	7.06	4.12-4.09	2.59	1.50	4.12-4.09
	6c	6′-Me	3.81	7.04	4.11-4.08	2.59	1.50	4.11-4.08
	6d	5′-*tert*-butyl	3.81	7.05	4.12-4.09	2.59	1.49	4.12-4.09
	6e	5′-Cl	3.84	7.11	4.14-4.11	2.60	1.50	4.14-4.11
	**7a**	H	3.76	7.15	4.18	2.49	1.88	3.19
	7b	5′-Me	3.75	7.12	4.17	2.49	1.88	3.19
	7c	6′-Me	3.75	7.13-.09	4.17-4.16	2.51-2.48	1.88	3.21-3.17
	7d	5′-*tert*-butyl	3.76	7.11	4.18	2.49	1.88	3.20

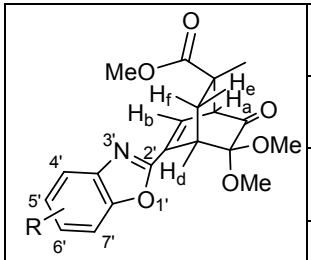
	**8a**	H	3.61	7.18	4.12-4.11	2.40	2.07	-
	8b	5′-Me	3.60	7.15-7.11	4.10-4.09	2.39	2.07	-
	8c	6′-Me	3.59	7.13-7.09	4.08-4.07	2.38	2.05	-
	8d	5′-*tert*-butyl	3.61	7.14	4.11-4.10	2.39	2.07	-

Table 4: Selected ^{1}H NMR chemical shifts (δ in ppm) of Diels-Alder adducts **9** and **10**.

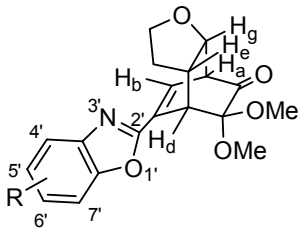
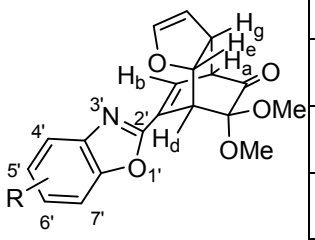
Adduct		R	H_a	H_b	H_d	H_e	H_g
	**9a**	H	3.84	7.14-7.11	4.21	3.12	4.47
	9b	5′-Me	3.82	7.08	4.19	3.11	4.45
	9c	6′-Me	3.84	7.10-7.08	4.21	3.12	4.48
	9d	5′-*tert*-butyl	3.82	7.10-7.08	4.21-4.20	3.14-3.08	4.46
	9e	5′-Cl	3.85	7.15-7.14	4.18-4.17	3.15-3.09	4.47
	**10a**	H	3.47	7.15-7.13	4.72-4.70	5.28	3.58
	10b	5′-Me	3.45	7.11	4.69	5.28	3.57
	10c	6′-Me	3.57-3.53	7.11	4.68	5.26	3.45
	10d	5′-*tert*-butyl	3.56	7.11	4.71	5.27	3.45
	10e	5′-Cl	3.59	7.17	4.68	5.29	3.49

Table 5: Selected ^{13}C NMR values of Diels-Alder adducts **5-9**.

Entry	Adduct	C_a	C_b	C_d	C_{ef}	C_g	C_{acetal}	ring carbonyl
1	**5a**	55.7	129.5	40.0	29.7	40.4	93.2	199.7
2	**5b**	55.8	129.2	40.2	30.0	40.6	93.4	200.1
3	**5c**	55.8	128.9	40.2	29.9	40.6	93.4	200.0
4	**5d**	56.0	129.2	40.3	30.0	40.8	93.5	200.3
5	**5e**	56.0	130.7	40.2	29.9	40.6	93.3	199.9
6	**6a**	54.7	128.8	38.8	30.0	64.4	93.3	199.9
7	**6b**	54.6	128.4	38.8	30.1	64.5	93.4	200.1
8	**6c**	54.7	128.1	38.9	30.1	64.4	93.4	200.0
9	**6d**	54.6	128.3	38.9	30.1	64.4	93.4	200.0
10	**6e**	54.7	129.8	38.8	30.0	64.5	93.2	199.8
11	**7a**	50.6	129.4	39.3	24.7	39.5	93.4	199.4
12	**7b**	50.6	129.0	39.4	24.8	39.6	93.4	199.4
13	**7c**	50.6	128.7	39.4	24.8	39.6	93.5	199.5
14	**7d**	50.6	128.9	39.4	24.7	39.6	93.5	199.5
15	**8a**	57.1	131.5	39.6	32.0	47.1	93.7	200.7
16	**8b**	57.1	131.1	39.6	32.0	47.1	93.6	200.7
17	**8c**	57.0	130.7	39.6	31.9	47.1	93.6	200.6
18	**8d**	57.1	131.0	39.7	31.7	47.2	93.7	200.7
19	**9a**	55.7	130.5	43.3	38.3	79.2	93.1	199.7
20	**9b**	55.6	130.0	43.2	38.2	79.1	93.0	199.7
21	**9c**	55.5	129.7	43.1	38.1	79.0	93.0	199.7
22	**9d**	55.7	130.0	43.3	38.2	79.2	93.1	199.8
23	**9e**	55.8	130.1	43.3	38.2	79.2	93.0	199.6

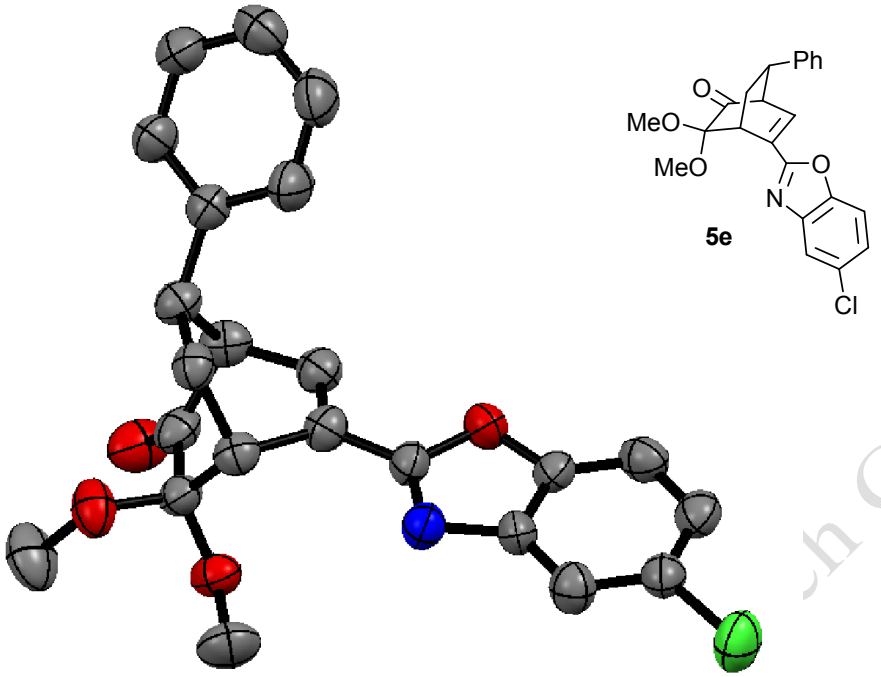


Figure 4: ORTEP Representation of crystal structure of Diels-Alder adduct **5e**.

Table 6: Crystallographic data for Diels-Alder adduct **5e**.

Formula	$C_{23}H_{20}ClNO_4$
Formula Wt.	409.85
Crystal habit	Blocks
Crystal color	Orange
Crystal system	Orthorhombic
Space group	-p 2ac 2ab
a (Å)	14.5001(17)
b (Å)	13.1869(11)
c (Å)	20.384(2)
α (deg)	90.00
β (deg)	90.00
γ (deg)	90.00
V (Å^3)	3897.6(7)
Z	8
D_{calc} (g cm^{-3})	1.397
T (K)	293(2)
λ (Mo-Kα)	0.71073
μ (mm^{-1})	0.227
2θ range (deg)	50.00

Limiting indices	$-12 \leq h \geq 17$ $-15 \leq k \geq 13$ $-21 \leq l \geq 24$
F(000)	1712
No. of Reflns. Measured	3427
No. of Parameters	265
GOF on F^2	0.846
R1 [$I>2\sigma(I)$]	0.1486
wR2	0.2233

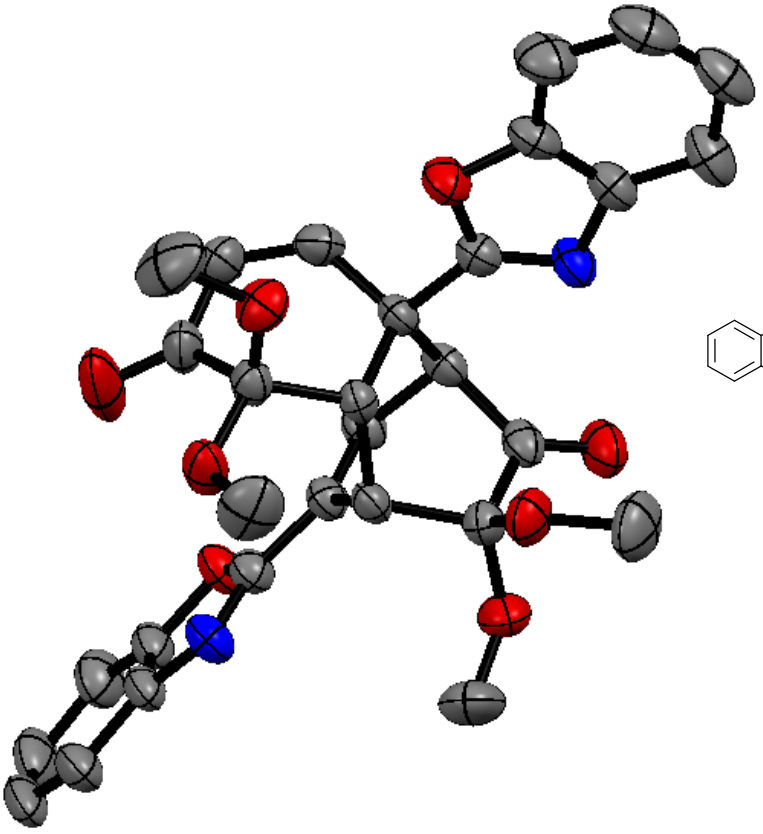


Figure 5: ORTEP Representation of crystal structure of Diels-Alder dimer **4a**.

Table 7: Crystallographic data for dimer **4a**.

Formula	$C_{30}H_{26}N_2O_8$
Formula Wt.	542.53
Crystal habit	Needle
Crystal color	Yellow
Crystal system	Monoclinic
Space group	-P 2ybc
a (Å)	11.237 (3)
b (Å)	12.150 (3)
c (Å)	19.687 (5)
α (deg)	90
β (deg)	97.946 (7)
γ (deg)	90
V (Å^3)	2661.9 (13)
Z	4
D_{calc} (g cm^{-3})	1.354
T (K)	296 (2)
λ (Mo-Kα)	0.71073
μ (mm^{-1})	0.099
2θ range (deg)	52.74
Limiting indices	$-14 \leq h \geq 14$
	$-15 \leq k \geq 15$
	$-24 \leq l \geq 24$
F(000)	1136
No. of Reflns. Measured	4231
No. of Parameters	365
GOF on F^2	0.980
R1 [I>2σ(I)]	0.1431
wR2	0.1885

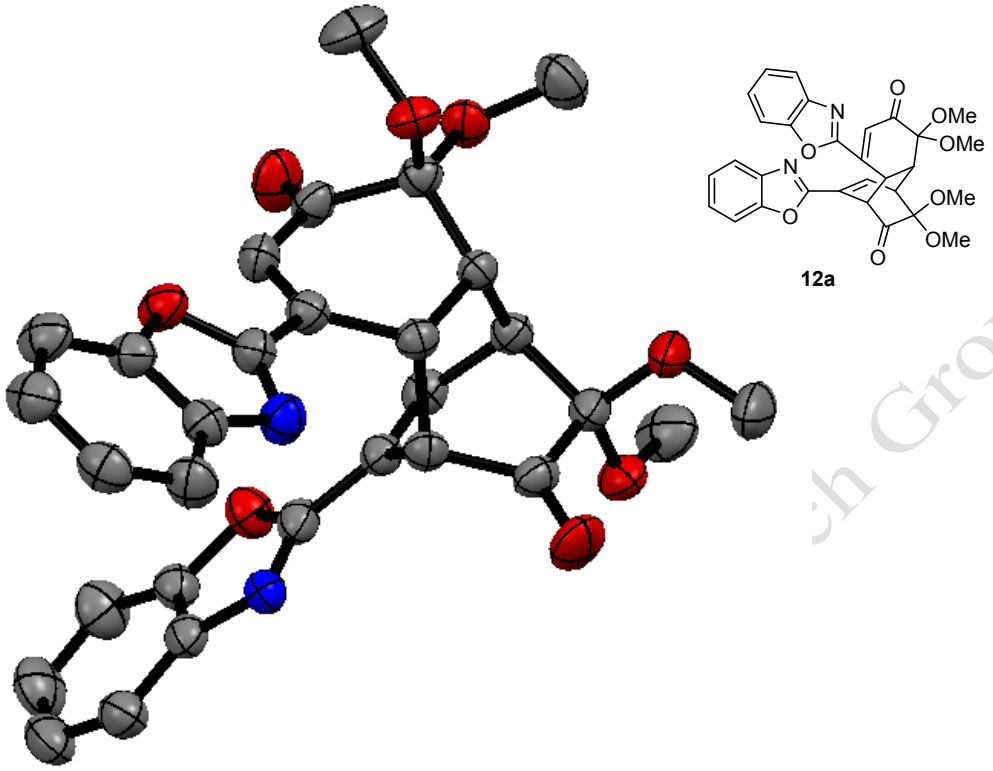


Figure 6: ORTEP Representation of crystal structure of Diels-Alder dimer **12a**.

Table 8: Crystallographic data for dimer **12a**.

Formula	$C_{30}H_{26}N_2O_8$
Formula Wt.	542.53
Crystal habit	Blocks
Crystal color	Yellow
Crystal system	Triclinic
Space group	-P 1
a (Å)	10.4060 (5)
b (Å)	10.5240 (6)
c (Å)	12.8850 (7)
α (deg)	86.860 (2)
β (deg)	71.130 (1)
γ (deg)	76.500 (2)

V (Å^3)	1298.01 (12)
Z	2
D_{calc} (g cm^{-3})	1.388
T (K)	296 (2)
λ (Mo-Kα)	0.71073
μ (mm^{-1})	0.102
2θ range (deg)	52.74
Limiting indices	-13 ≤ h ≥ 13
	-13 ≤ k ≥ 13
	-16 ≤ l ≥ 16
F(000)	568
No. of Reflns. Measured	5303
No. of Parameters	365
GOF on F^2	1.136
R1 [I>2σ(I)]	0.1368
wR2	0.1511

Two-dimensional nuclear magnetic resonance spectroscopy (2D NMR) is a set of nuclear magnetic resonance spectroscopic methods which gives data plotted in a space defined by two frequency axes instead of one. Two-dimensional NMR spectra provide more information about a molecule than one-dimensional NMR spectra and are especially useful in elucidating the structure of the molecules that are too complicated to work with using one-dimensional NMR. Two dimensional (2D NMR) spectroscopy includes Homonuclear and Heteronuclear correlation.

Homonuclear correlation

It is used to identify spins 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 double quantum transfer experiment

- Through space correlation:

  NOESY : Nuclear Overhauser effect spectroscopy

  ROESY : Rotating-frame nuclear Overhauser effect correlation spectroscopy

Heteronuclear correlation

The Heteronuclear correlation (also called ^{13}C-^{1}H COSY) shows connections between carbon atoms and the protons directly bonded to them.

- One-bond correlation

  HSQC : Heteronuclear single quantum correlation

  HMQC : Heteronuclear multiple-quantum correlation

- Long-range correlation

  HMBC : Heteronuclear multiple-bond correlation

The structural assignment of benzoxazol-2′-yl bicyclo[2.2.2]octenone derivatives was done by the analysis of data obtained from the proton-proton decoupling and 2D NMR experiments such as ^{1}H-^{1}H COSY, heteronuclear multiple quantum correlation spectroscopy (HMQC) measurements. The data obtained from the 2D NMR experiments for the Diels-Alder adducts **5a**, **7a** and **8a** are presented in Tables 9-11. The correlation between protons H_1-H_6, H_7-H_{8a}, H_7-H_{8b} is clearly visible from the ^{1}H-^{1}H COSY spectra. The C-H connectivities between C_1-H_1, C_4-H_4, C_6-H_6, C_7-H_7, and C_8-H_8, are confirmed by the HMQC spectra (Figures 7-12).

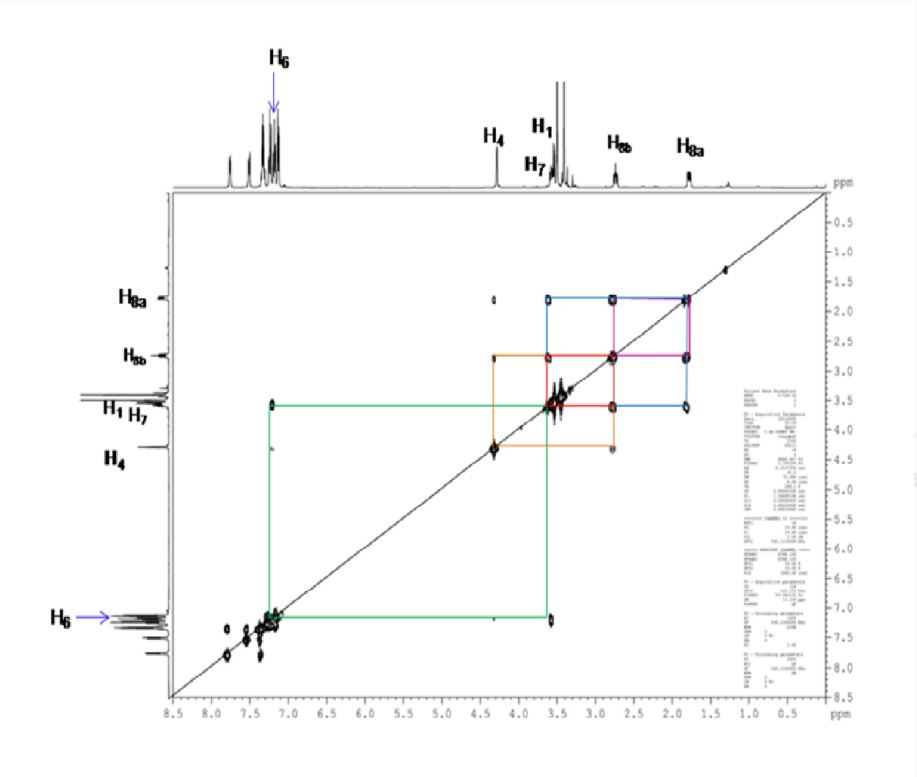
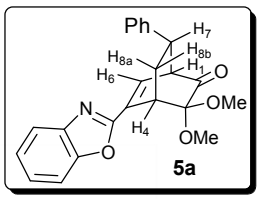


Figure 7: ^{1}H-^{1}H COSY Spectrum of cycloadduct **5a**.



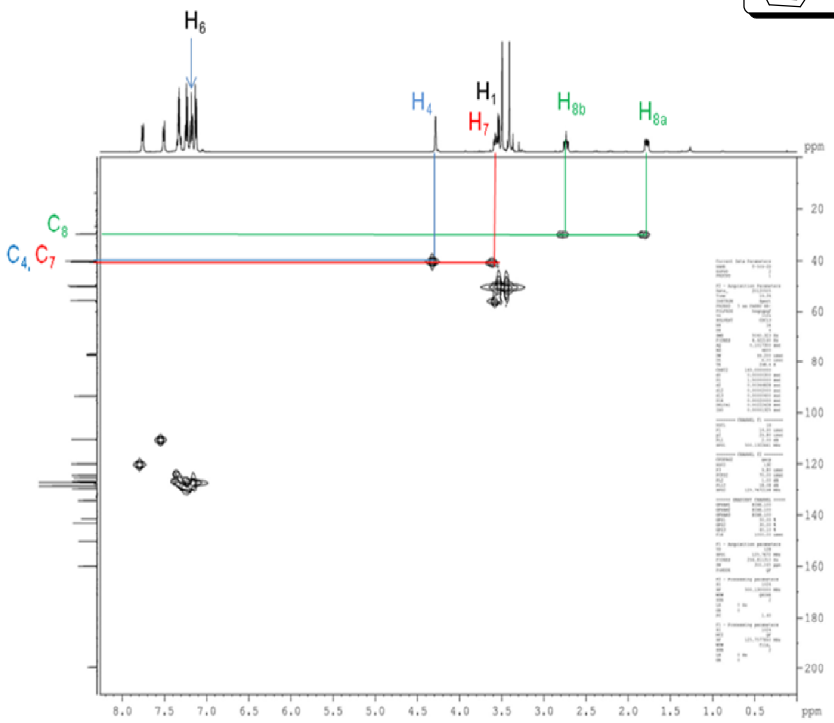
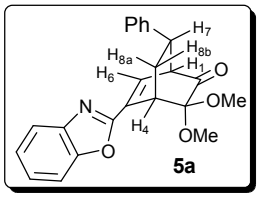
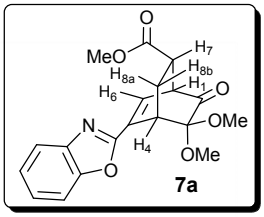


Figure 8: HMQC Spectrum of cycloadduct **5a**.

Table 9: Proton-proton and proton-carbon connectivity in **5a**.

^{13}C Signal		^{1}H-^{1}H COSY	Connectivity from HMQC
Carbon	δ (ppm)		
C_1	55.7	H_1-H_6	H_1-C_1
C_2	199.7	-	
C_3	93.2	-	
C_4	40.0	-	H_4-C_4
C_6	129.5	H_6-H_1	H_6-C_6
C_7	40.4	H_7-H_{8a} H_7-H_{8b}	H_7-C_7
C_8	29.7	H_{8a}-H_7 H_{8b}-H_7	H_{8a}-C_8 H_{8b}-C_8





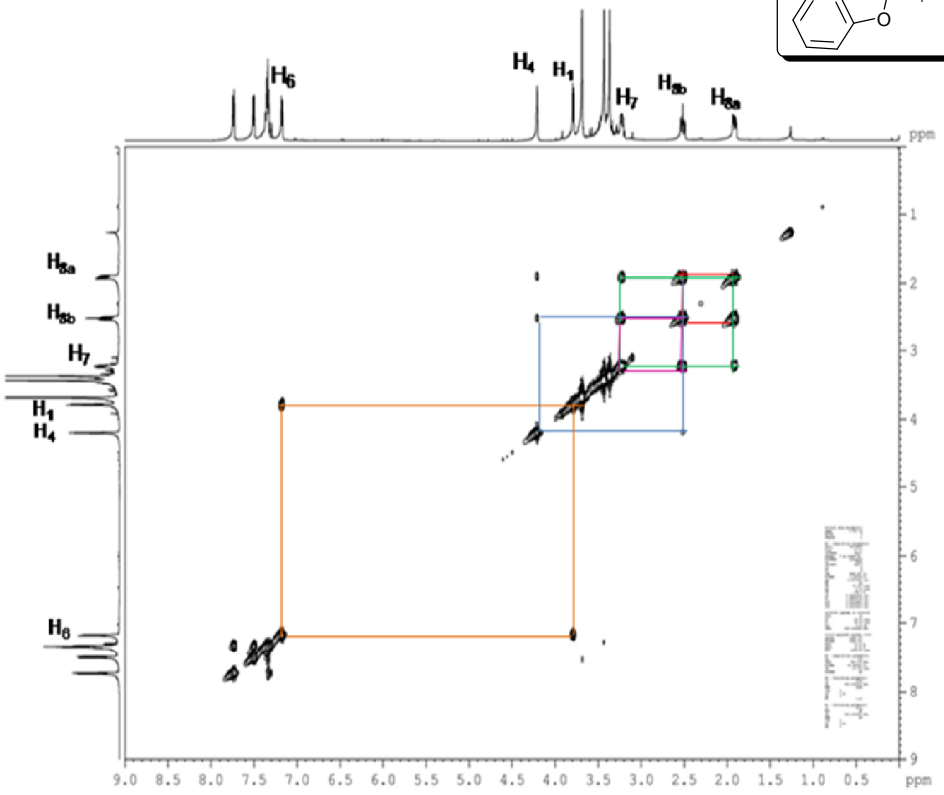


Figure 9: ^{1}H-^{1}H COSY Spectrum of cycloadduct **7a**.

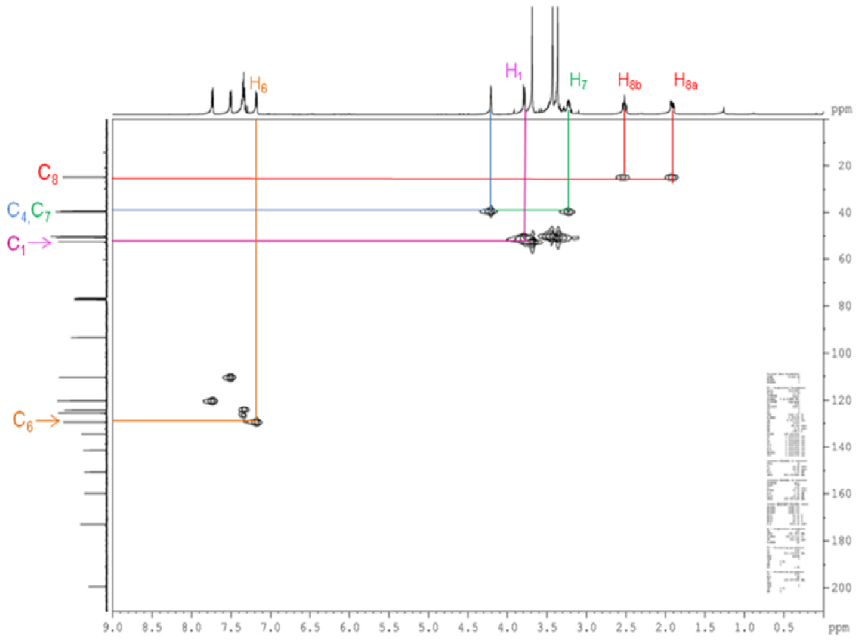


Figure 10: HMQC Spectrum of cycloadduct **7a**.

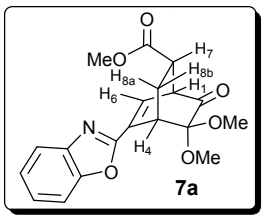


Table 10: Proton-proton and proton-carbon connectivity in **7a**.

^{13}C signal		^{1}H-^{1}H COSY	Connectivity from HMQC
Carbon	δ (ppm)		
C_1	50.6	H_1-H_6	H_1-C_1
C_2	199.4	-	
C_3	93.4	-	
C_4	39.3	-	H_4-C_4
C_6	129.4	H_6-H_1	H_6-C_6
C_7	39.5	H_7-H_{8a} H_7-H_{8b}	H_7-C_7
C_8	24.7	H_{8a}-H_7 H_{8b}-H_7	H_{8a}-C_8 H_{8b}-C_8

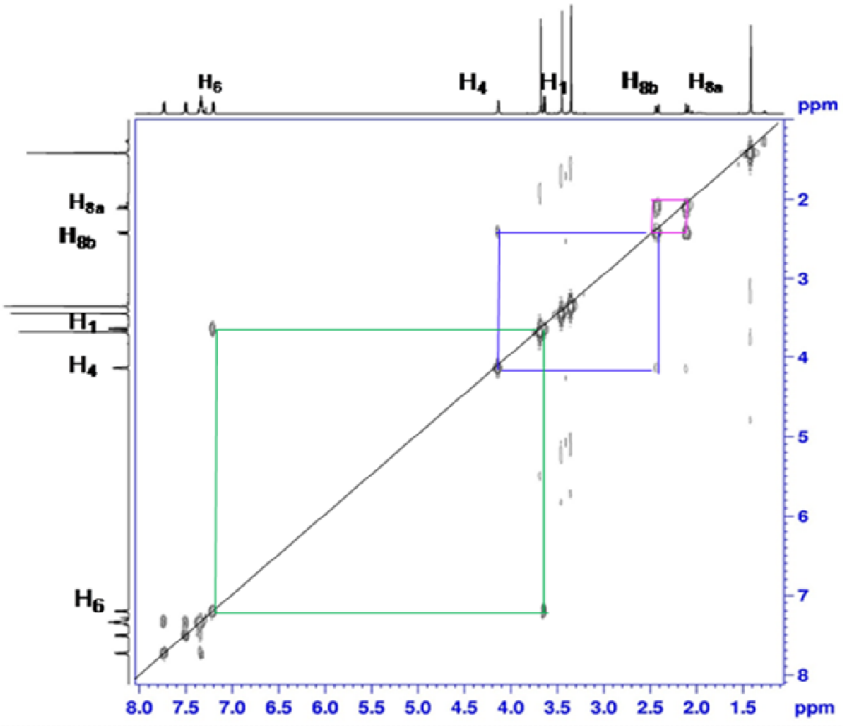
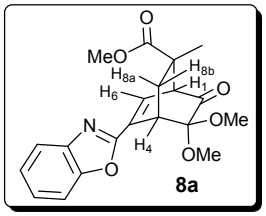


Figure 11: ^{1}H-^{1}H COSY Spectrum of cycloadduct **8a**.



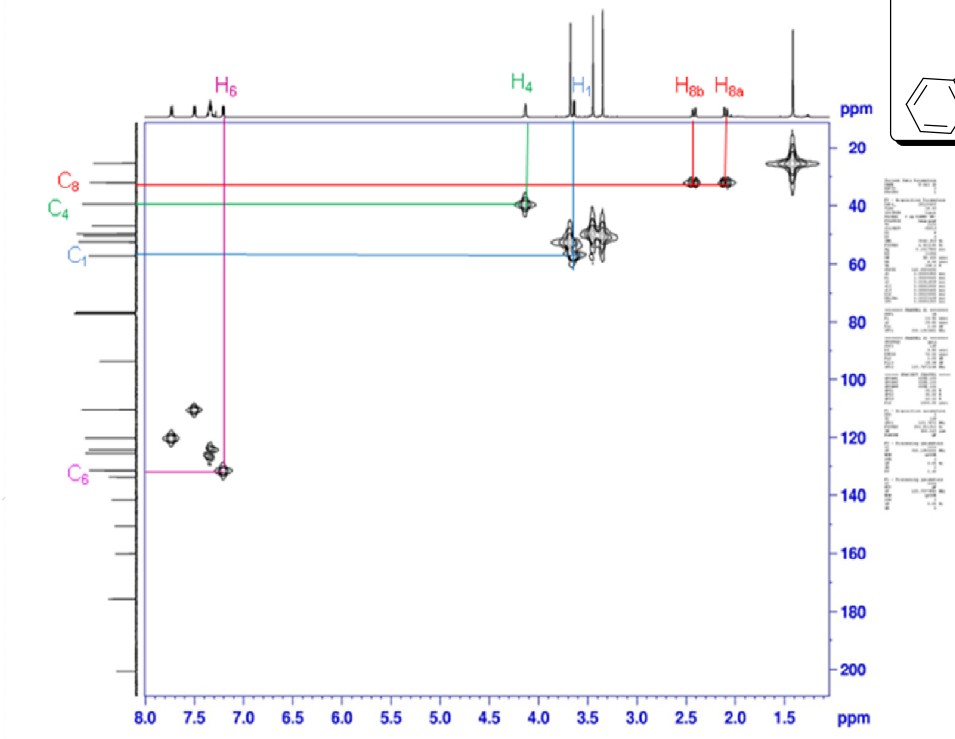
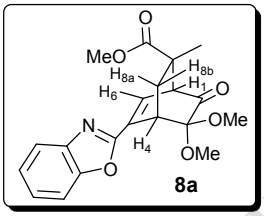


Figure 12: HMQC Spectrum of cycloadduct **8a**.

Table 11: Proton-proton and proton-carbon connectivity in **8a**.

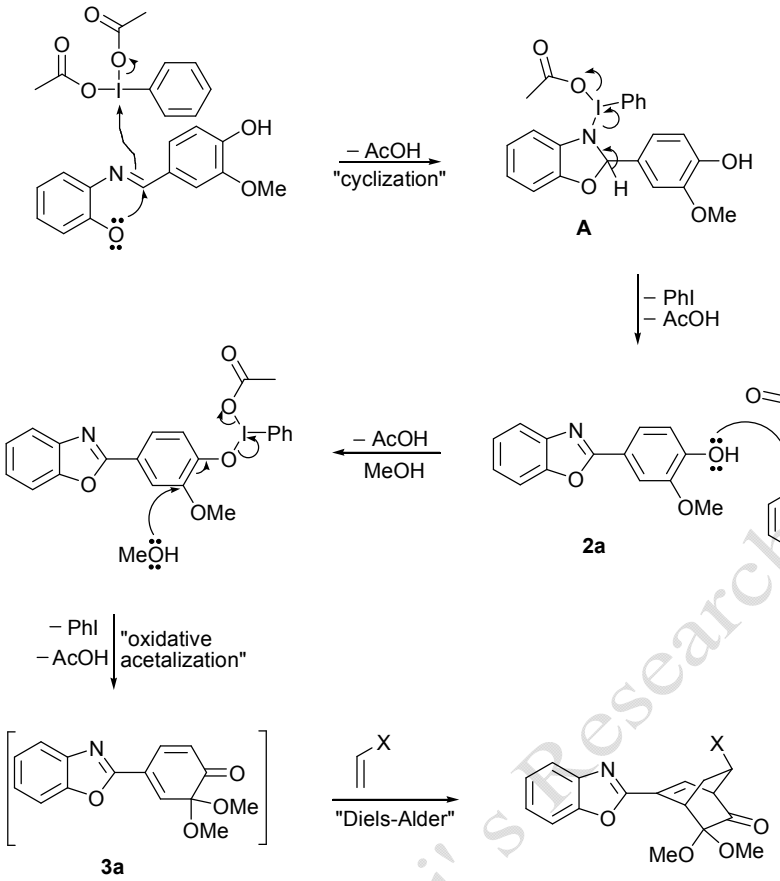
^{13}C signal		^{1}H-^{1}H COSY	Connectivity from HMQC
Carbon	δ (ppm)		
C_1	57.1	H_1-H_6	H_1-C_1
C_2	200.7	-	
C_3	93.4	-	
C_4	39.3	-	H_4-C_4
C_6	129.4	H_6-H_1	H_6-C_6
C_7	47.1	-	-
C_8	24.7	H_{8a}-H_{8b}	H_{8a}-C_8 H_{8b}-C_8



8a

In the initial step, the attack of imino nitrogen of aldimine on the Lewis acidic trivalent iodine centre makes the adjacent carbon more electrophilic, making more susceptible for the attack of nucleophilic oxygen atom leading to the benzoxazoline intermediate **A**. The subsequent aromatization of dihydro oxazole ring takes place along with the elimination of acetic acid and iodobenzene to give the benzoxazole derivative **2**. Now, the nucleophilic oxygen in the 4-(benzoxazol-2′-yl) guaiacol attacks on to the DIB with the elimination of acetic acid. Further the acetalization takes place with methanol to obtain the MOB **3**, which undergoes the [4+2] cycloaddition reaction with the dienophile to give the desired cycloadduct (Scheme 16).

In summary, an efficient hypervalent iodine mediated domino oxidative cyclization–oxidative acetalization–Diels-Alder protocol for highly selective synthesis of benzoxazole-2′-yl bicyclo[2.2.2]octenone derivatives was developed at ambient temperature. The yields of the title compounds bearing diverse functionalities obtained from this rapid synthesis shall be seen as overall yields of three steps.



Scheme 16: Plausible mechanism for the hypervalent iodine-mediated domino oxidative cyclization–oxidative acetalization–Diels-Alder strategy.

2.2.2. Synthesis of pyrrolobenzoxazine derivatives

Pyrrole fused heterocyclic compounds are wide spread in the nature and extensively found in many of the natural products and biologically active molecules.[145-150] These compounds possess a wide range of biological and pharmacological activities like antioxidant,[151] anticancer,[152-158] reversal of multidrug resistance (MDR),[159-162] antimicrobial activity,[163,164] human aldose reductase (h-ALR2) inhibition,[165] HIV-1 integrase inhibition and cell division inhibition.[166-168] The pyrrole fused compounds like pyrrolobenzoxazines and benzothiazines found to exhibit antihyperstensive and acts as central nervous system depressant agents[169] (Figure 13).

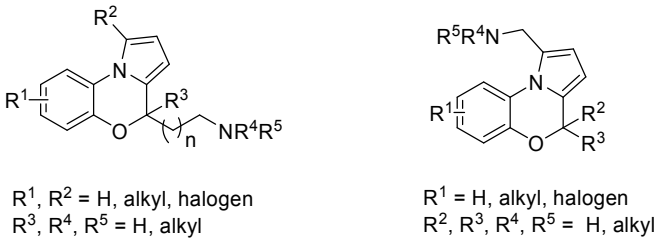
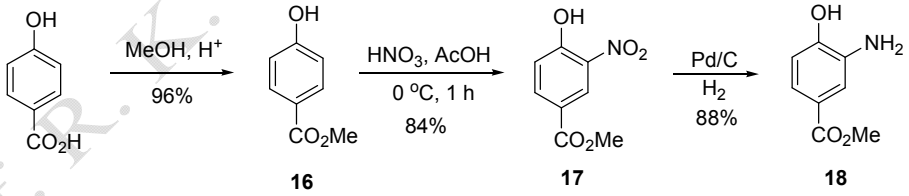


Figure 13: Biologically active pyrrolobenzoxazine derivatives.

In our laboratory, we have developed novel methodologies for the synthesis of heterocyclic compounds of biological significance.[68] A green approach for the synthesis of 1,4-benzoxazinone derivatives from the readily available starting materials is one among them.[170] Further we envisaged that these 1,4-benzoxazinone derivatives may serve as a new class of vinylogous carbamates. Herein, the reactions of these vinylogous carbamates with nitrostyrene leading to pyrrolobenzoxazines are described.

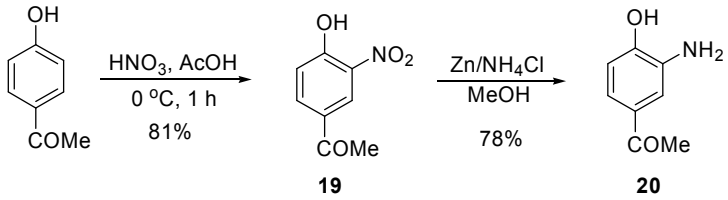
Synthesis of *o*-aminophenol derivatives

Esterification reaction of 4-hydroxybenzoic acid in methanol in the presence of a few drops of sulphuric acid provided methyl ester **16** of hydroxybenzoic acid in 96% yield which on nitration and followed by reduction with palladium charcoal furnished the aminophenol derivative **18** in good yield[171,172] (Scheme 17).



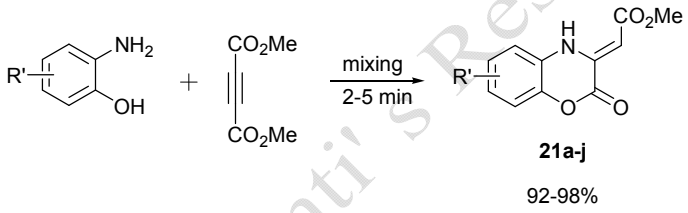
Scheme 17: Synthesis of methyl 3-amino-4-hydroxybenzoate (**18**).

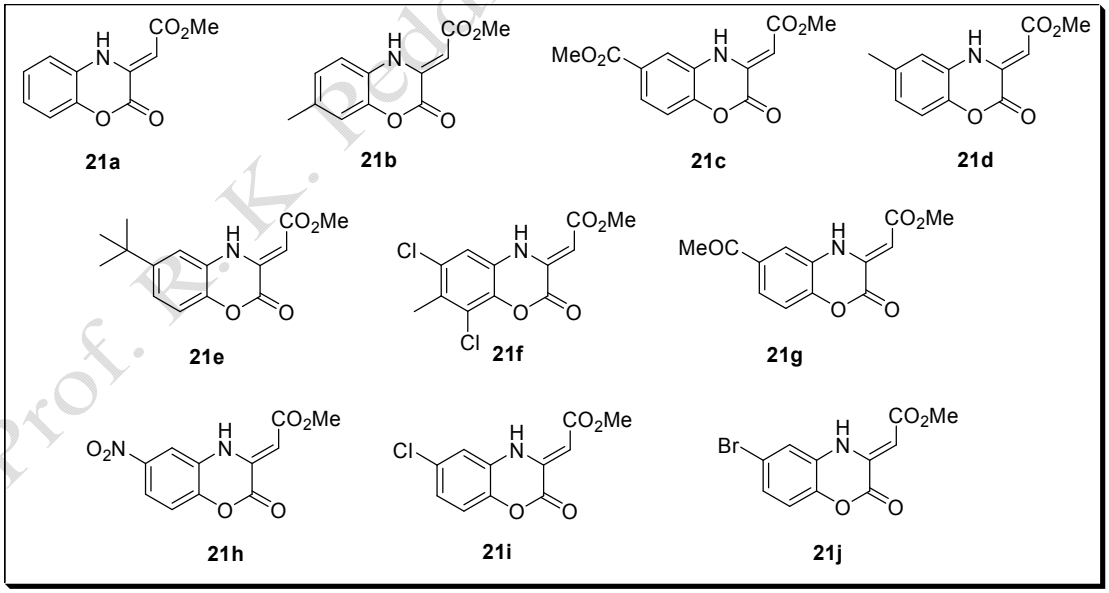
Nitration of 4-hydroxyacetophenone was employed with HNO_3/AcOH at 0 ^oC to obtain the 4-hydroxy-3-nitroacetophenone (**19)** in 81% yield. The reduction of nitro compound **19** was carried out in presence of zinc and ammonium chloride to afford the 3-amino-4-hydroxyacetophenone (**20**) in 78% yield (Scheme 18).



Scheme 18: Synthesis of 3-amino-4-hydroxyacetophenone (**20**).

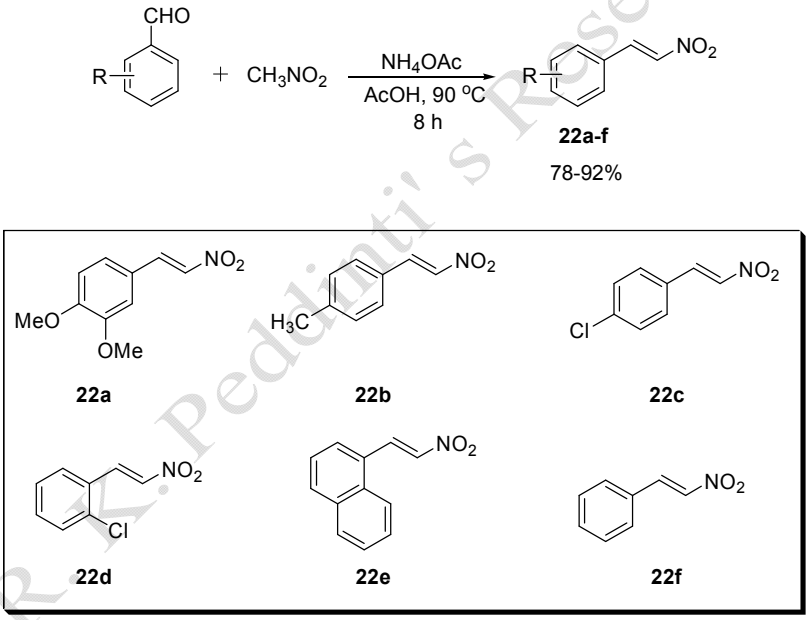
After having various derivatives of *o*-aminophenols in hand, we proceeded for the synthesis of vinylogous carbamates **21a-j** according to a green protocol developed in our laboratory.[170] In a Petri dish the *o*-aminophenol and dimethyl acetylenedicarboxylate were taken and mixed for 2-5 min. to obtain the corresponding vinylogous carbamate **21a** as a yellow coloured solid in quantitative yield. Similarly, the other 1,4-benzoxazinone derivatives **21b-i** were also prepared (Scheme 19).





Scheme 19: Synthesis of 1,4-benzoxazine-based vinylogous carbamates.

β-Nitrostyrene derivatives act as good Michael acceptors and the Michael adducts derived from these electron-poor species can be further functionalized by the cyclization β-Nitrostyrene derivatives act as good Michael acceptors and the Michael adducts derived from these electron-poor species can be further functionalized by the cyclization reaction, wherever possible, with concomitant elimination of the nitro functionality. Isoparvifuran and some other biologically important molecules can be synthesized easily with β-nitrostyrenes as the starting materials.[173-175] These β-nitrostyrenes were synthesized according to the reported procedure.[176] Thus a mixture of an aromatic aldehyde, nitromethane and ammonium acetate were dissolved in AcOH and allowed to heat overnight at 90 ^{o}C. The crude reaction mixture was recrystallized from methanol to obtain pure β-nitrostyrene derivatives **22a-f** in good to excellent yields (Scheme 20).

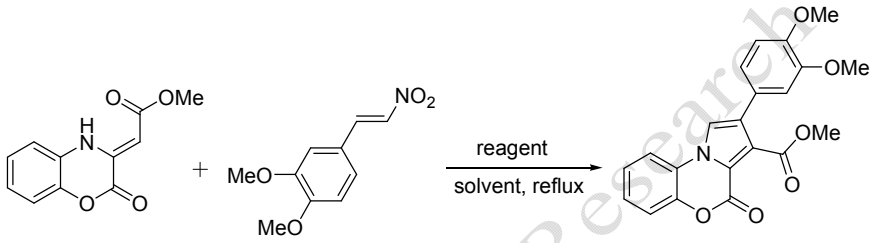


Scheme 20: Synthesis of β−nitrostyrenes.

In our initial attempts, a mixture of benzoxazinone derivative **21a** and 3,4-dimethoxy-nitrostyrene **22a** in 1,2-dichloroethane (DCE) in presence of triflic acid was allowed to reflux for 5 h. The reaction proceeded smoothly and after usual work up and purification by silica gel column chromatography a yellow coloured product was obtained. Upon careful analysis of the data obtained by ^{1}H, ^{13}C NMR and DEPT spectra, the product obtained was confirmed as a tetracyclic pyrrolobenzoxazine derivative **23a** (Table 12, entry 1). The formation of this

compound can be explained as follows. Initial step of the reaction takes place through the Michael addition and the Michael adduct undergoes the subsequent intramolecular cyclization with the concurrent elimination of nitro functionality to furnish pyrrolobenzoxazine **23a**. Inspired with the results obtained, we further proceeded for the screening of various Brønsted and Lewis acids to affect this transformation. Accordingly when the reaction of **21a** and **22a** was carried out in presence of *p*-TSA.H_2O the reaction was completed in 8 h to afford **23a** in 73% yield. Trifluoroacetic acid promoted reaction afforded the corresponding product **23a** with 82% yield in 5 h. Further screening various Lewis acids

Table 12: Optimization of reaction conditions.[a]



21a **22a** **23a**

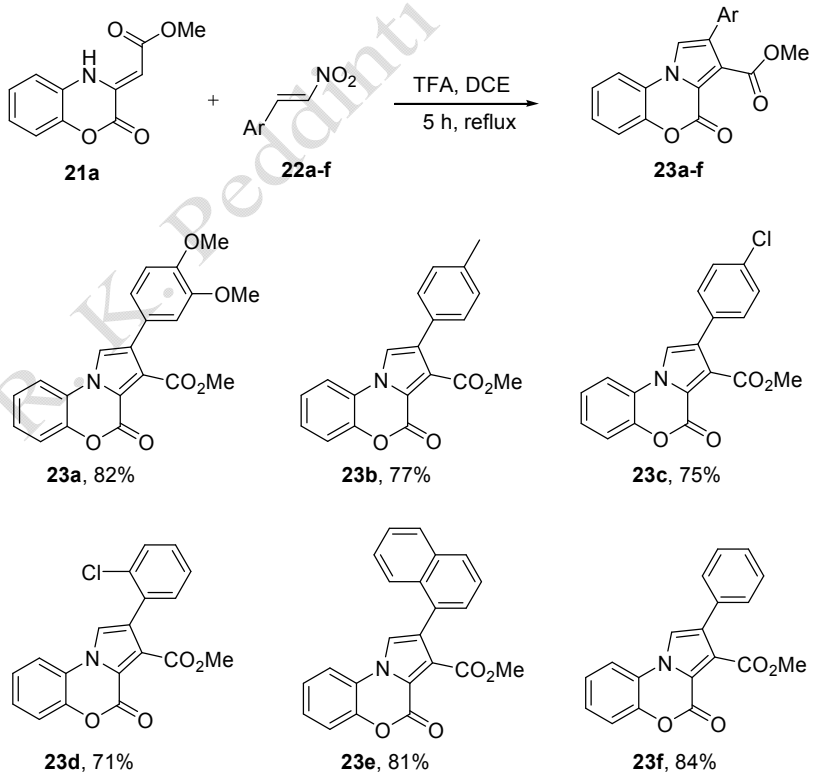
Entry	Reagent	Solvent	Time (h)	Yield[b] (%)
1	TfOH	DCE	5	57
2	*p*-TSA.H_2O	DCE	8	73
3	TFA	DCE	5	82
4	$ZrCl_4$	DCE	5	68
5	$ZnCl_2$	DCE	5	61
6	$FeCl_3$	DCE	5	72
7	$SnCl_4$	DCE	5	64
8	BF_3.etherate	DCE	5	76
9	-	DCE	12	-
10	TFA	CH_2Cl_2	8	69
11	TFA	THF	5	74
12	TFA	CH_3CN	5	71
13	TFA	Toluene	5	76

[a]reactions were performed with **21a** (0.5 mmol), 3,4-dimethoxy nitrostyrene **22a** (0.6 mmol) and reagent (0.75 mmol) in 4 mL of solvent.

[b]yield of pure and isolated product **23a**.

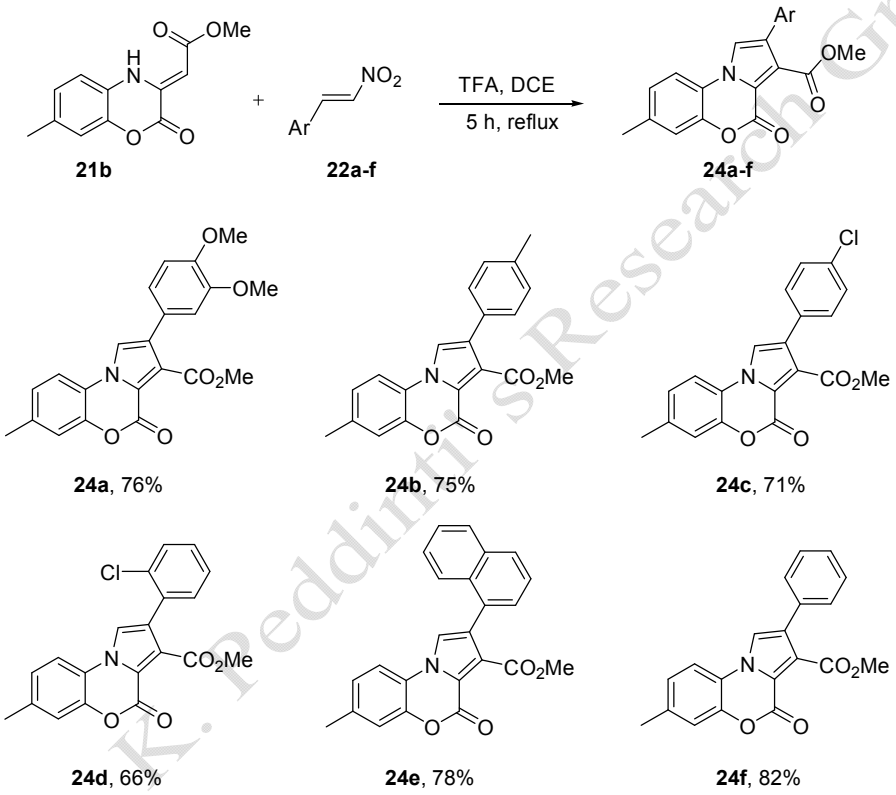
such as $ZrCl_4$, $ZnCl_2$, $FeCl_3$, $SnCl_4$ and BF_3.etherate also afforded the pyrrolobenzoxazine **23a** in varying quantities (Table 12, entries 4-8) nevertheless, the results revealed that they were less effective when compared to that of the trifluoroacetic acid. There was no formation of product in absence of any reagent (Table 12, entry 9). Subsequently, we have also tested various solvents such as toluene, CH_3CN, CH_2Cl_2, THF and it was found that DCE performed better for the current transformation (Table 12, entries 3 and 10-13).

With the optimized conditions in hand, we further explored the scope and generality of the present protocol with diversely substituted 1,4-benzoxazinones **21a-c** and nitrostyrene derivatives **22a-f**. The Michael addition-cyclization reaction of 1,4-benzoxazinone derivative **21a** with nitrostyrene derivatives **22b-d** in presence of TFA underwent smoothly and provided the corresponding pyrrolobenzoxazine derivatives **23b-d** in high yields. The reaction of naphthyl and phenyl nitrostyrenes **22e**, **22f** with 1,4-benzoxazinone **21a** also underwent effectively to afford the corresponding products **23e** and **23f** in 81 and 84% yields respectively (Scheme 21).



Scheme 21: Michael addition-cyclization reaction of 1,4-benzoxazinone **21a** with nitrostyrene derivatives **22a-f**.

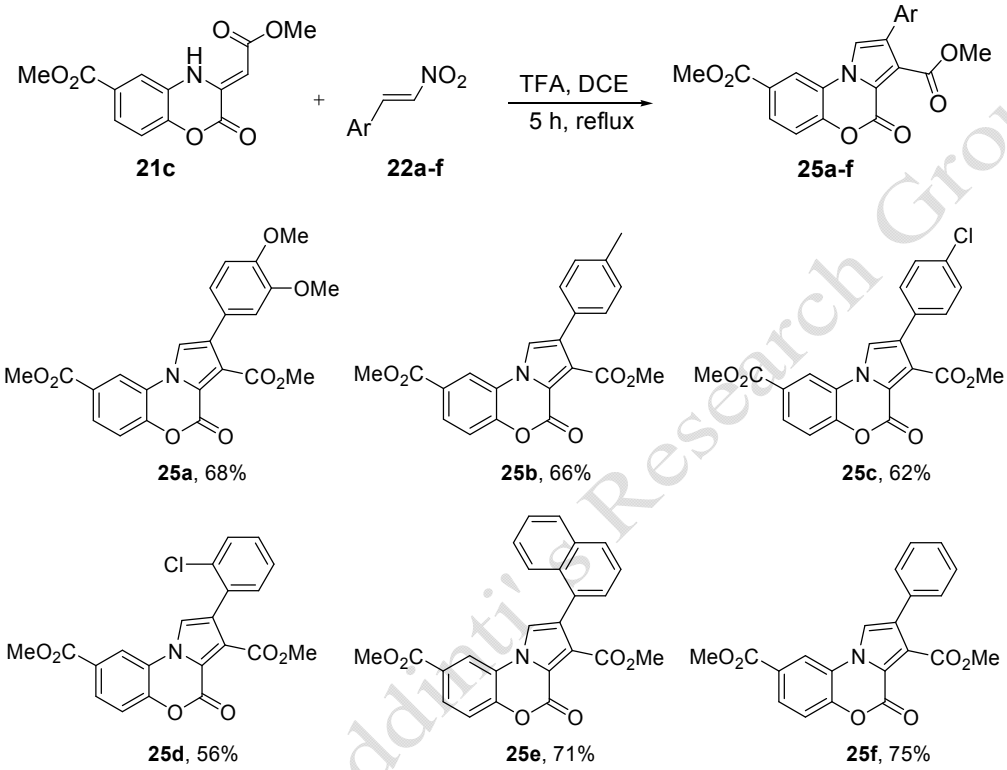
Further, the 1,4-benzoxazinone derivative bearing methyl substituent as a substrate was chosen in the current study. Under the standard conditions, the reaction of 1,4-benzoxazinone derivative **21b** with 3,4-dimethoxynitrostyrene **22a** afforded tetracyclic pyrrolobenzoxazinone derivative **24a** in 76% yield. Delighted with the results obtained, we performed the Michael addition-cyclization reaction of vinylogous carbamate **21b** with nitrostyrenes **22b-f**. All the reactions underwent effectively and afforded the desired products **24b-f** in high yields (Scheme 22).



Scheme 22: Michael addition-cyclization reaction of 1,4-benzoxazinone **21b** with nitro-styrene derivatives **22a-f**.

The present TFA-mediated Michael addition-cyclization methodology was extended to the 1,4-benzoxazinone derivative **21c** bearing the ester (CO_2Me) with nitrostyrene derivatives. The reaction of **21c** with nitrostyrenes **22a-f** proceeded effectively to provide the tetracyclic pyrrolobenzoxazinone derivatives **25a-f** in high yields. From the results obtained by the Michael addition-cyclization reaction of vinylogous carbamates **21a-c** with nitrostyrene derivatives, we observed that the benzoxazinone derivative bearing the electron-withdrawing ester group (CO_2Me) afforded the products **25a-f** (Scheme 23) in slightly

diminished yields when compared to those of products **23a-f**, **24a-f** (Schemes 21 and 22) obtained from the other two benzoxazinone derivatives **21a** and **21b**. The reason may be due to the moderate nucleophilicity of **21c**, bearing the electron-deficient ester (CO_2Me) substituent (Scheme 23).



Scheme 23: Michael addition-cyclization reaction of 1,4-benzoxazinone **21c** with nitro-styrene derivatives **22a-f**.

It is noteworthy to mention here that the reactions of 1,4-benzoxazinones **21a-c** with 2-chlorophenyl nitrostyrene **22d** furnished the products **23d**, **24d** and **25d** in slightly lower yields in comparison to those of products **23c**, **24c** and **25c** derived from 4-chlorophenyl nitrostyrene **22c**, which may be attributed to the steric encumbrance of the *ortho* substituent.

The structures of these pyrrolobenzoxazine derivatives were confirmed by the analysis of the data obtained from IR, ^{1}H, ^{13}C NMR, DEPT and HRMS spectral analysis. For instance, in compound **24f**, The stretching vibrational frequencies centered around 1734 and 1716 cm^{-1} are observed in the infrared spectrum reflecting the presence of C=O bonds of ester and lactone moieties, respectively. Similar trend is observed for other pyrrolo-

benzoxazine derivatives. The methoxy group (–OMe) of the ester moiety resonates at 3.92 ppm and methyl group present on the aromatic ring resonates at 2.41 ppm. The peak corresponding to CH of pyrrole ring resonates as a singlet at δ 7.64 ppm. HRMS analysis of the compound **24f** resulted in a peak at *m/z* 356.0893 which is in well agreement with the calculated value of *m/z* 356.0893. Further the structure of the compound **24f** was also confirmed by the single crystal X-ray analysis (Figure 14, Table 13).

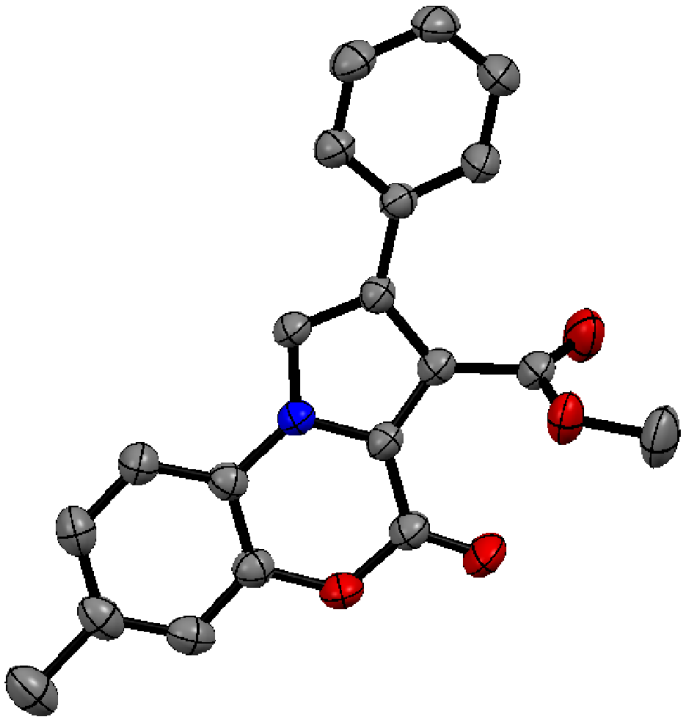


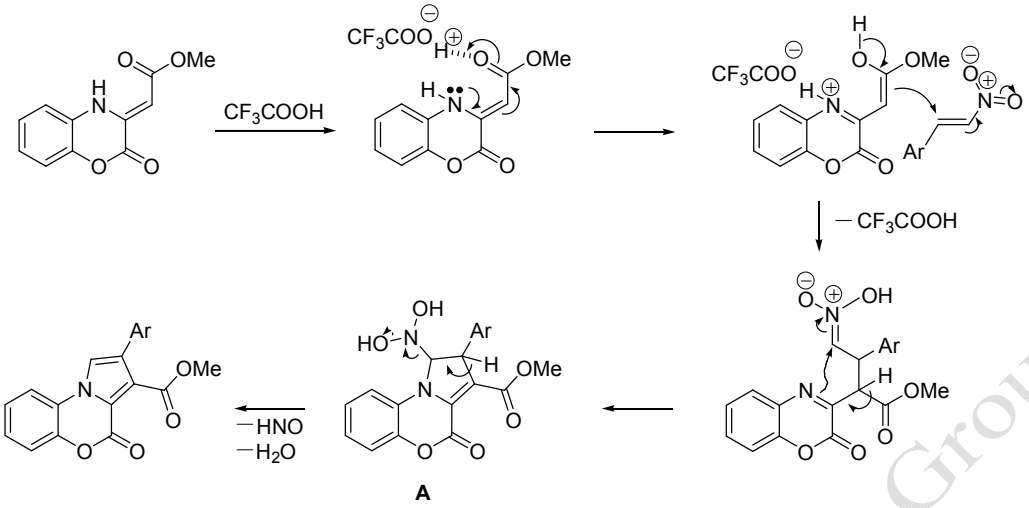
Figure 14: ORTEP Representation of crystal structure of **24f**.

Table 13: Crystallographic data for **24f**.

Formula	$C_{20}H_{15}NO_4$
Formula Wt.	333.32
Crystal habit	Blocks
Crystal color	White
Crystal system	Triclinic
Space group	-P 1
a (Å)	8.4042 (8)

b (Å)	9.8413 (9)
c (Å)	10.3659 (9)
α (deg)	76.972 (3)
β (deg)	72.998 (3)
γ (deg)	77.774 (3)
V (Å^3)	788.93 (13)
Z	2
D_{calc} (g cm^{-3})	1.403
T (K)	296 (2)
λ (Mo-Kα)	0.71073
μ (mm^{-1})	0.096
2θ range (deg)	50.52
Limiting indices	-13 ≤ h ≥ 13
	-23 ≤ k ≥ 23
	-12 ≤ l ≥ 11
F(000)	336
No. of Reflns. Measured	3226
No. of Parameters	228
GOF on F^2	1.252
R1 [I>2σ(I)]	0.0551
wR2	0.1573

A possible mechanism for the formation of pyrrolobenzoxazine derivatives is depicted in Scheme 24. In the presence of trifluoroacetic acid, initially the Michael addition of activated vinylogous carbamate takes place at the α-position of β-nitrostyrene, which further undergoes intramolecular cyclization. The aromatization to pyrrole ring and concomitant exclusion of HNO and H_2O from species **A** results in the formation of pyrrolobenzoxazine derivative.



Scheme 24: Plausible reaction mechanism for the synthesis of pyrrolobenzoxazine derivatives.

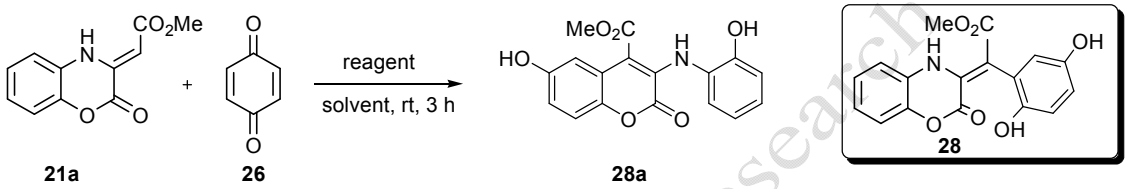
2.2.3. Synthesis of 3-arylamino coumarin derivatives

Coumarin derivatives are the prominent class of heterocyclic compounds exhibiting a wide range of biological activities.[72,73,177] Particularly, the 3-amino substituted coumarins are found in the naturally occurring antibiotics like novobiocin,[178,179] chlorbiocin,[180] and coumermycin A1.[181,182] The reported methods for the synthesis of 3-aminocoumarin derivatives involve multi-step procedures and expensive reagents.[85] Herein, we describe our results on a simple and efficient protocol for the synthesis of diversely substituted 3-arylamino coumarin derivatives from the readily available starting materials.

After exploring the unprecedented nucleophilicity of new class of vinylogous carbamates by reacting 1,4-benzoxazinone derivatives with β–nitrostyrenes in synthesizing the pyrrolobenzoxazine derivatives, we proceeded in investigating the reactivity of vinylogous carbamates **21a-h** with other Michael acceptors such as *p*-benzoquinone and naphthoquinone. Initially we started our investigation with the reaction between benzoxazinone **21a** and *p*-benzoquinone (**26**). In a typical reaction procedure, 1,4-benzoxazinone **1** and *p*-benzoquinone were dissolved in 4 mL of CH_2Cl_2, then trifluoroacetic acid was added and allowed the reaction mixture to stir at room temperature for 3 h. As the reaction proceeded, the product started precipitating out of the reaction mixture. After

completion of the reaction as shown by TLC, the reaction mixture was filtered to get as yellow precipitate, which was found to be a coumarin derivative **28a** (Table 14, entry 1). The coumarin derivative **28a** can be derived from the primary product **28**. With the preliminary results in hand, we chose the reaction of **21a** and **26** as our model reaction and proceeded for the optimization of reaction conditions. When the reaction was carried out with *p*-TSA.H_2O the desired product was obtained in 68% yield (Table 14, entry 2). However, no product was observed when the reaction was carried out with TfOH (Table 14, entry 3).

Table 14: Optimization of reaction conditions.[a]



21a **26** **28a**

Entry	Reagent	Solvent	Yield[b] (%)
1	TFA	CH_2Cl_2	88
2	*p*-TSA.H_2O	CH_2Cl_2	68
3	TfOH	CH_2Cl_2	-
4	$ZrCl_4$	CH_2Cl_2	71
5	$FeCl_3$	CH_2Cl_2	76
6	$SnCl_4$	CH_2Cl_2	62
7	BF_3.etherate	CH_2Cl_2	79
8	TFA	DCE	85
9	TFA	Toluene	84
10	TFA	THF	80
11	TFA	CH_3CN	78

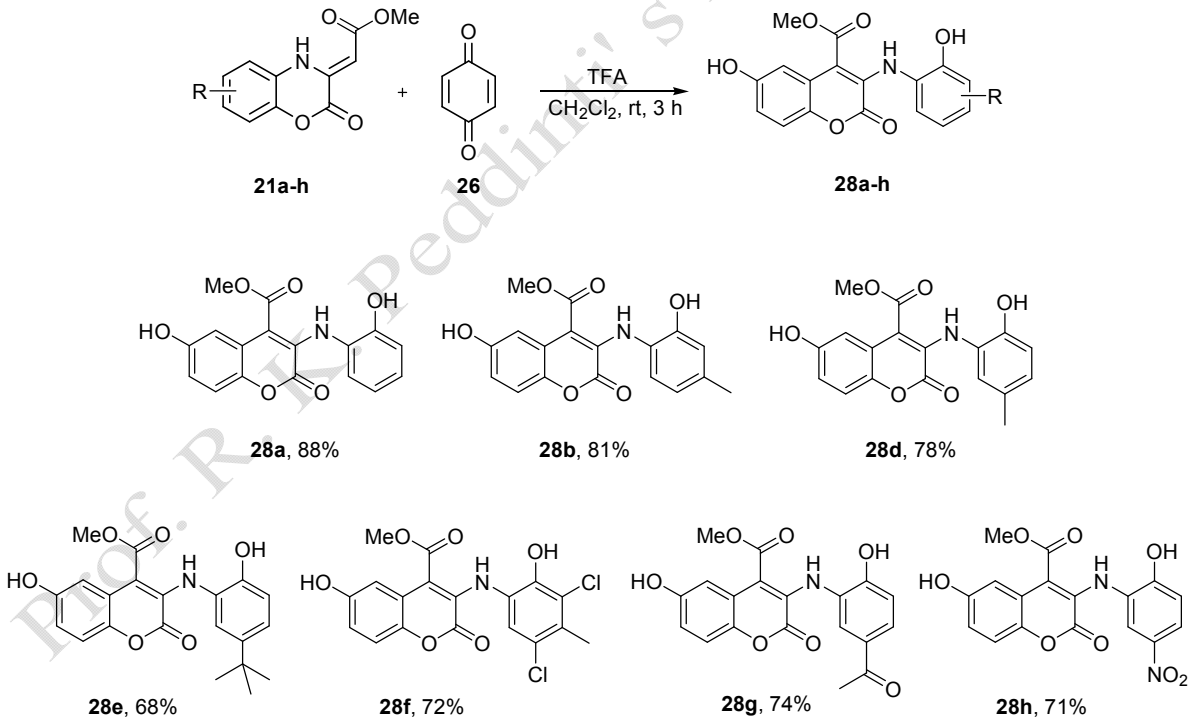
[a]reactions were performed with **21a** (0.5 mmol), *p*-benzoquinone (**26**) (0.6 mmol) and TFA (0.6 mmol) in 4 mL of solvent.

[b]yield of pure and isolated product **28a**.

Further the use of various Lewis acids such as $ZrCl_4$, $FeCl_3$, $SnCl_4$, and BF_3.etherate resulted in the formation of the desired product in moderate yields (Table 14, entries 4-7) Screening of various reagents disclosed that the trifluoroacetic acid affords the coumarin derivative **28a** in higher yield. Successive screening of various solvents like CH_2Cl_2, DCE,

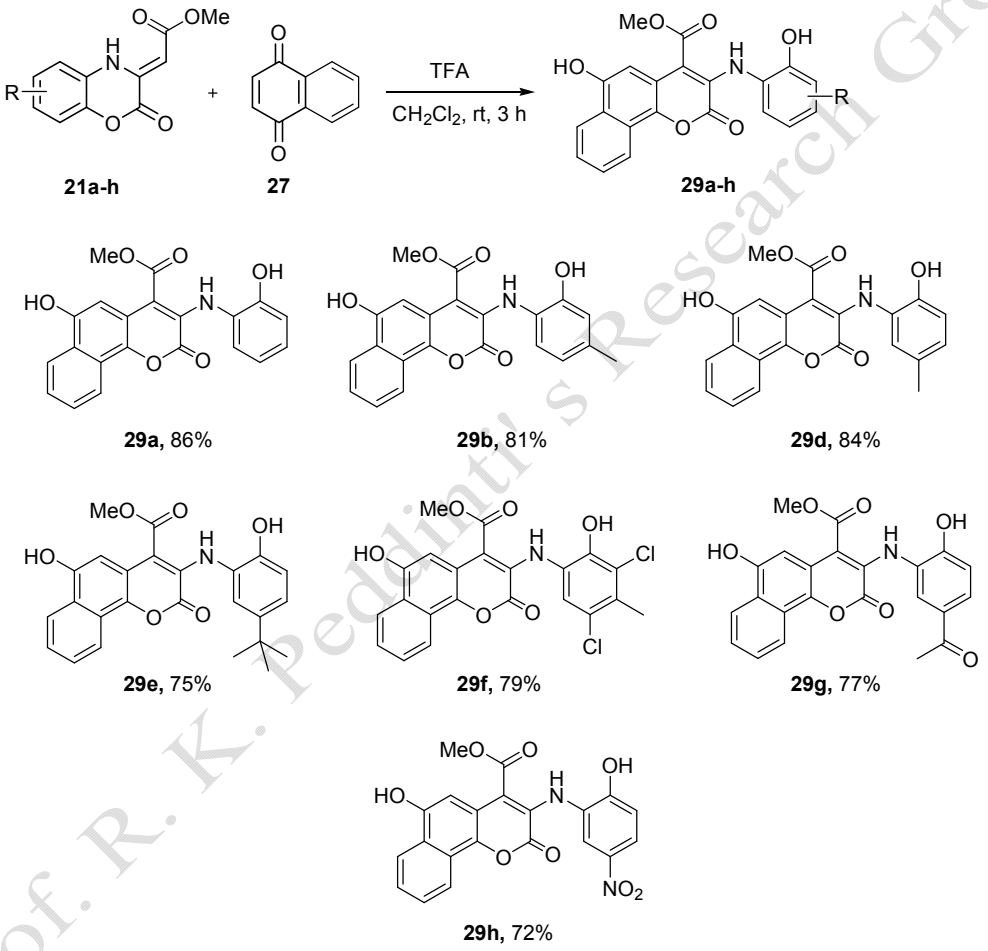
toluene, THF and CH_3CN, suggested that CH_2Cl_2 was the optimal solvent (Table 14, entries 8-11).

With the optimized protocol, we next set out to explore the substrate scope and limitation of the reaction. When the reaction of 1,4-benzoxazinone derivatives **21b** was carried out with *p*-benzoquinone, the reaction proceeded smoothly to give the coumarin derivative **28b** in 81% yield. Surprisingly, under similar conditions, the reaction of vinylogous carbamate **21c** with **26** did not afford the desired product **28c**. The 1,4-benzoxazinone derivatives **21d-h** reacted efficiently with the *p*-benzoquinone and afforded the corresponding 3-arylamino coumarin derivatives **28d-h** in high yields. This methodology also tolerated a variety of functional groups such as *tert*-butyl, chloro, nitro and acetyl groups. The benzoxazinone derivatives **21g** and **21h** bearing the electron-withdrawing groups provided the respective products in slightly lower yield in contrast to the other benzoxazinone derivatives (Scheme 25).



Scheme 25: Michael addition-cyclization reaction of vinylogous carbamates with *p*-benzoquinone.

Further we performed the reactions of 1,4-benzoxazinone derivatives **21a-h** with 1,4-naphthoquinone **27**. The reactions of **21a** and **21b** with naphthoquinone in presence of TFA were found to be completed in 3 h at the room temperature and delivered the corresponding coumarin derivatives **29a** and **29b** in 86 and 81% yields, respectively. Similar to *p*-benzoquinone, naphthoquinone also failed to give the product on reaction with **21c**. The benzoxazinone derivatives **21d-h** reacted efficiently with naphthoquinone to afford the desired products **29d-h** in high yields (Scheme 26).



Scheme 26: Michael addition-cyclization reaction of vinylogous carbamates with 1,4-naphthoquinone.

Structures of all the 3-arylamino coumarin derivatives were established on the basis of their IR, ^{1}H, ^{13}C NMR, DEPT and HRMS spectral data. The intense peaks observed in the range of 1706-1727 $cm^{-1}$and 1689-1653 cm^{-1} in IR spectrum show the presence of lactone and ester (CO_2Me) functionalities. The single crystal X-ray analysis of the

compound **28h** supported the assigned structures of the 3-arylamino coumarins (Figure 15, Table 15).

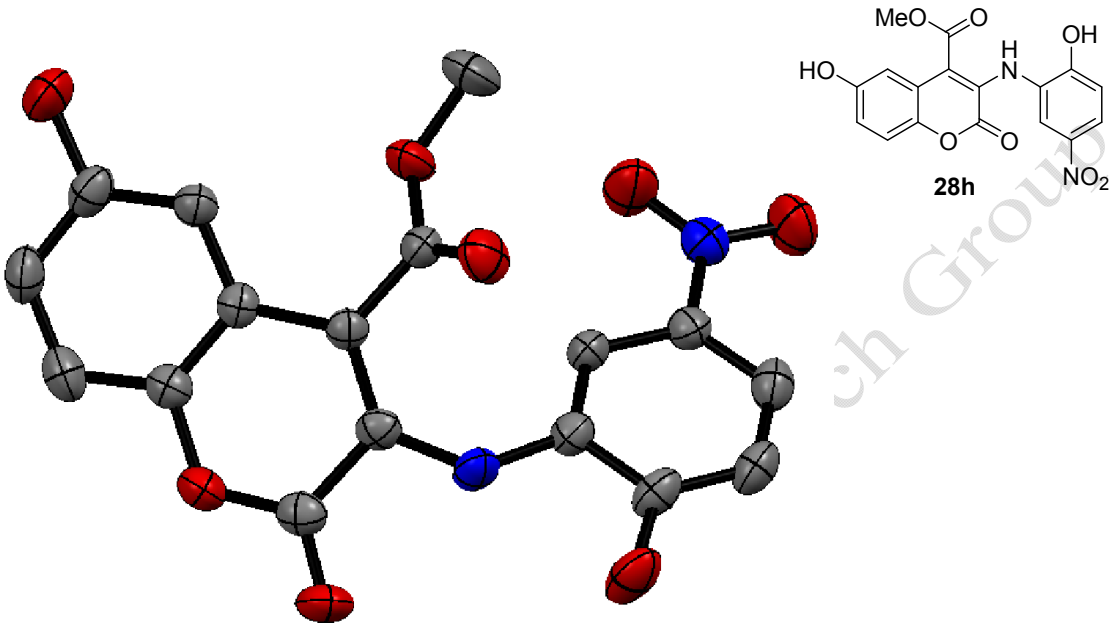


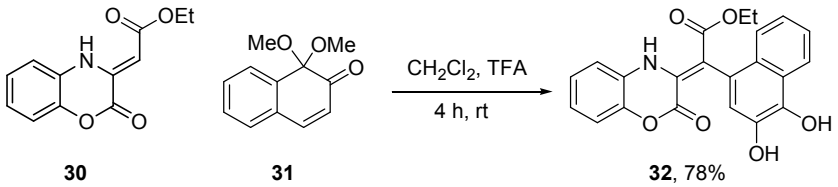
Figure 15: ORTEP Representation of crystal structure of **28h**.

Table 15: Crystallographic data for **28h**.

Formula	$C_{19}H_{18}N_2O_{10}S$
Formula Wt.	466.42
Crystal habit	Needle
Crystal color	Brown
Crystal system	Monoclinic
Space group	-P 2ybc
a (Å)	7.2807 (3)
b (Å)	23.1644 (11)
c (Å)	12.4215 (6)
α (deg)	90
β (deg)	98.89 (2)

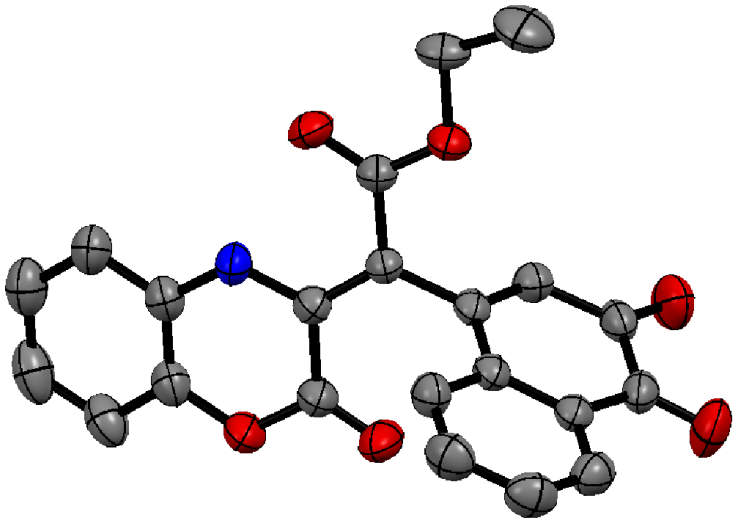
γ (deg)	90
V (Å^3)	2069.76 (16)
Z	4
D_{calc} (g cm^{-3})	1.497
T (K)	296 (2)
λ (Mo-Kα)	0.71073
μ (mm^{-1})	0.218
2θ range (deg)	52.74
Limiting indices	$-9 \leq h \geq 9$
	$-28 \leq k \geq 28$
	$-15 \leq l \geq 15$
F(000)	968
No. of Reflns. Measured	4231
No. of Parameters	289
GOF on F^2	1.099
R1 [I>2σ(I)]	0.0680
wR2	0.2480

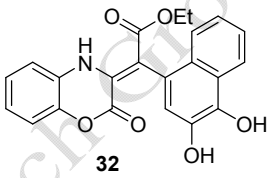
In further investigation to evaluate the substrate scope, we have also carried out the reaction of 1,4-benzoxazinone **30** with *ortho*-naphthoquinone monoketal **31** in presence of TFA at room temperature. The reaction underwent smoothly and reached to completion in 4 h. After usual workup and purification by column chromatography, the product **32** was obtained in 78% yield (Scheme 27). The structure of the product obtained was assigned by the analysis of the data obtained from ^{1}H, ^{13}C NMR, DEPT and HRMS analysis. In ^{1}H NMR the proton present on the nitrogen was observed as a broad singlet at 11.97 ppm. The proton present on the carbon adjacent to the hydroxyl group resonates at 6.27 ppm as a singlet. Further the structure of **32** was unambiguously confirmed by the single crystal X-ray analysis (Figure 16, Table 16).



30 **31** **32**, 78%

Scheme 27: Reaction of vinylogous carbamate **30** with *o*-naphthoquinone monoketal **31**.





32

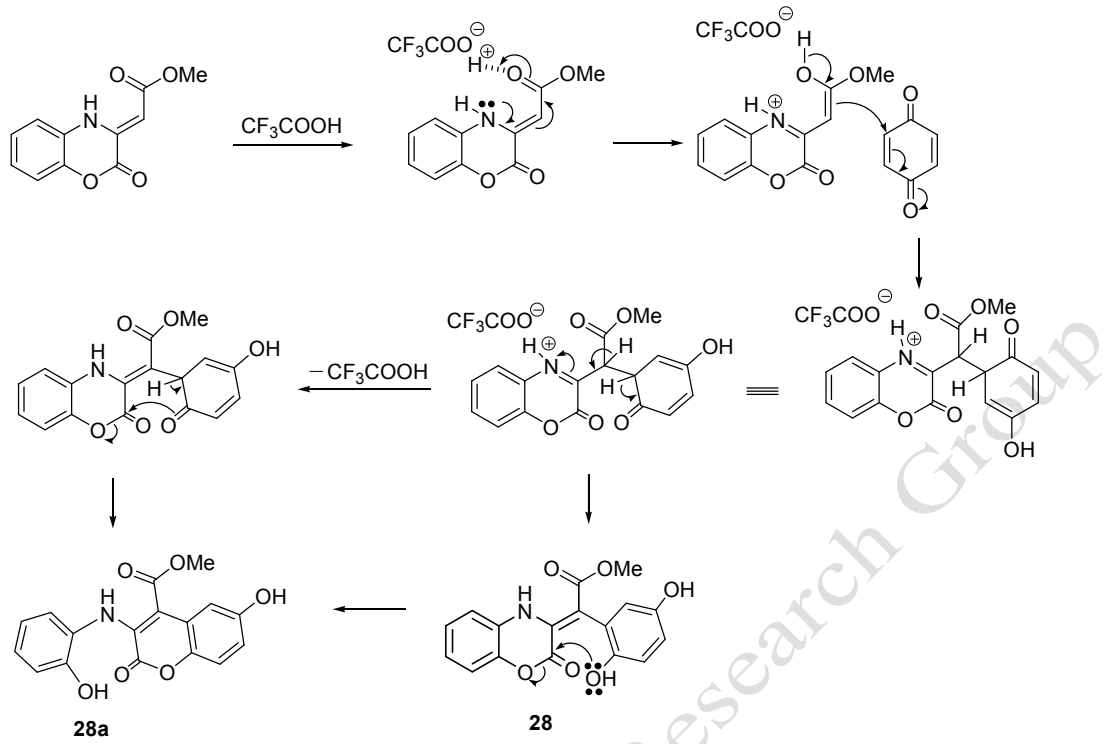
Figure 16: ORTEP Representation of crystal structure of **32**.

Table 16: Crystallographic data for **32**.

Formula	$C_{27}H_{15}NO_6$
Formula Wt.	391.11
Crystal habit	Needle
Crystal color	Brown
Crystal system	Monoclinic
Space group	-P 2ybc
a (Å)	8.447 (6)
b (Å)	9.631 (6)
c (Å)	22.349 (13)
α (deg)	90
β (deg)	91.54 (2)
γ (deg)	90

V (Å^3)	1818 (2)
Z	4
D_{calc} (g cm^{-3})	1.426
T (K)	296 (2)
λ (Mo-Kα)	0.71073
μ (mm^{-1})	0.105
2θ range (deg)	52.72
Limiting indices	$-10 \leq h \geq 10$
	$-12 \leq k \geq 12$
	$-27 \leq l \geq 27$
F(000)	812
No. of Reflns. Measured	3707
No. of Parameters	262
GOF on F^2	1.121
R1 [I>2σ(I)]	0.0763
wR2	0.1634

A plausible mechanism for TFA mediated Michael addition-cyclization reaction of 1,4-benzoxazinone derivatives with *p*-benzoquinone leading to coumarin derivatives is shown in Scheme 28. The 1,4-benzoxazinone derivative undergoes Michael addition with *p*-benzoquinone in the presence of trifluoroacetic acid. The intermediate thus obtained undergoes subsequent rearomatization and successive intramolecular ring opening of oxazinone ring and cyclization to pyranone ring to generate 3-arylamino coumarin derivative.



Scheme 28: Proposed mechanism for the synthesis of 3-arylamino coumarin.

2.2.4. Synthesis of 3-substituted 1,4-benzoxazinone derivatives

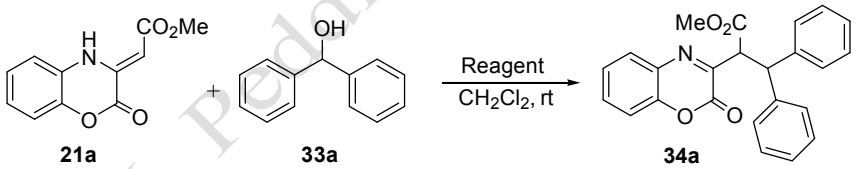
Owing to their occurrence in various natural products and drug molecules[183,184] the heterocyclic compounds have engrossed a significant place in the modern organic synthesis. Among the various heterocyclic compounds, benzoxazine derivatives found to exhibit a wide range of applications in pharma and agro chemical sectors.[37] These compounds act as potent 5-HT_1 receptor antagonists,[185,186] antibacterial agents[187] and also used in treatment of cancer[188] and cardiovascular diseases.[189,190]

Development of promising synthetic protocols using environmentally benign chemistry and by minimizing or eliminating the formation of hazardous byproducts have become a challenging task in the contemporary organic synthesis. In conventional method the halide derivatives are used as the alkylating agents, where the salts are obtained as the byproducts. Due to the environmental concerns, it has become a practice to employ alcohol derivatives as the alkylating agents instead of halides. Recently the alkylation reactions with alcohol derivatives have drawn considerable interest as alcohols can be easily activated under mild conditions using the Brønsted or Lewis acids and liberates water as a byproduct which

would be an environment friendly process.[191-197] We have explored various reactive sites of 1,4-benzoxazinone derivatives **21**, a new class of vinylogous carbamates. In further investigation, the nucleophilic nature of these vinylogous carbamates had insipired us to design a novel protocol for the alkylation of the 1,4-benzoxazinone derivatives with the alcohol derivatives leading to the generation of densely functionalized 1,4-benzoxazinone derivatives. Herein our results on the alkylation reaction of 1,4-benzoxazinone derivatives with alcohol derivatives are presented.

In our preliminary experiment, we carried out a reaction by treating the mixture of 1,4-benzoxazinone **21a** and diphenylmethanol **33a** in CH_2Cl_2 with triflic acid. The reaction proceeded smoothly and found to be completed in 30 min. as shown by the TLC. After purification by silica gel column chromatography afforded the desired product **34a** was obtained in 62% yield (Table 17, entry 1). Inspired with the results obtained, we further preceded for the optimization of the reaction conditions. When the reaction was carried out with other Brønsted acids such as *p*-TSA.H_2O and trifluoroacetic acid, the reaction was completed in 120 min. and the corresponding products were furnished in 67 and 74%

Table 17: Optimization of reaction conditions.[a]



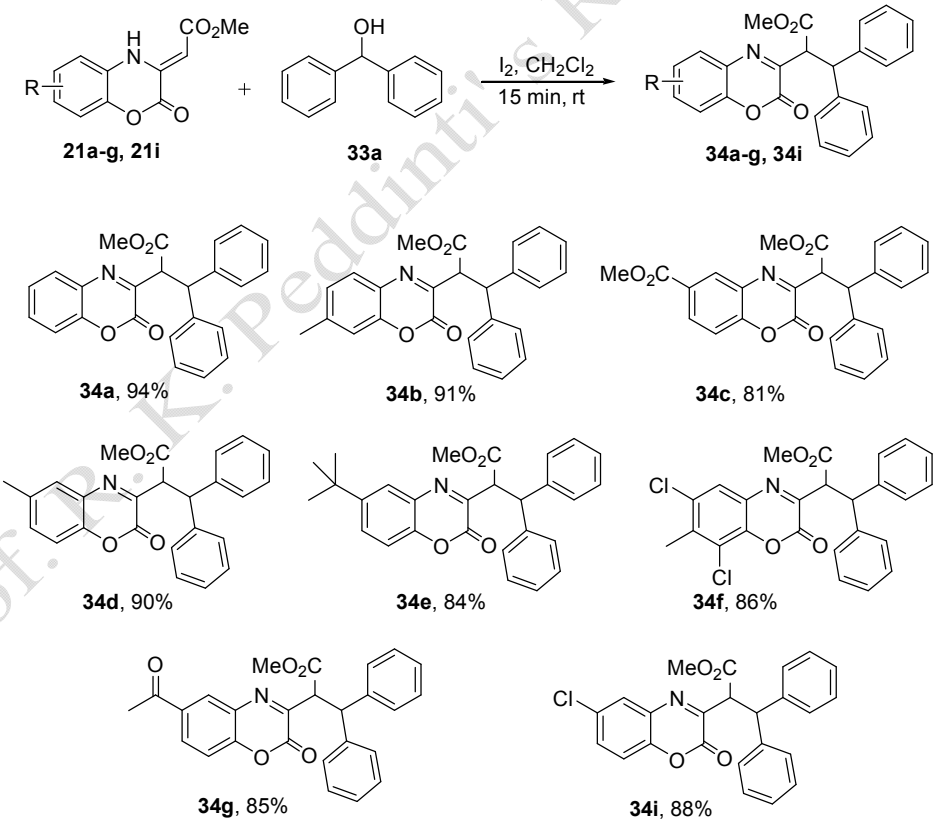
Entry	Reagent	Time (min)	Yield (%)[b]
1	TfOH	30	62
2	*p*-TSA.H_2O	120	67
3	TFA	120	74
4	$SnCl_4$	15	71
5	$FeCl_3$	15	78
6	$ZrCl_4$	15	80
7	BF_3.etherate	15	87
8	I_2	15	94

[a]reactions were carried out with **21a** (0.5 mmol), **33a** (0.6 mmol) and reagent (0.5 mmol) in CH_2Cl_2.

[b] yield of pure and isolated product **34a**.

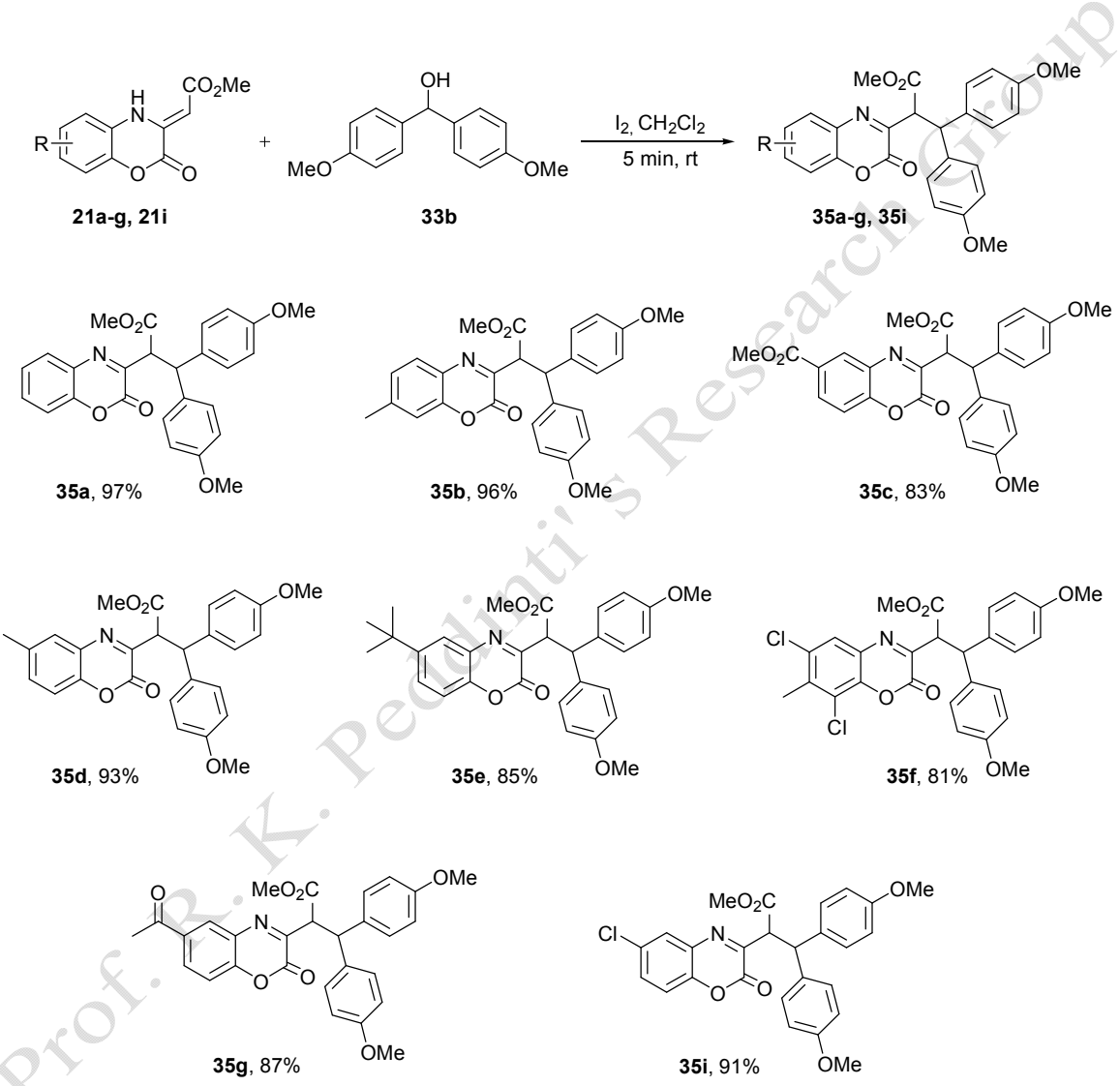
yields, respectively (Table 17, entries 2 and 3). On screening with Lewis acids such as $SnCl_4$, $FeCl_3$, $ZrCl_4$ and BF_3.etherate, the reaction was found to be completed in 15 min. (Table 17, entries 4-7). It was observed that in presence of these Lewis acids, the rate of the reaction as well as the yields of the product **34a** was also increased. The reaction promoted by molecular iodine was also completed in 15 min. and afforded the desired product **34a** in high yields compared to the other reagents.

With the optimized conditions in hand, we further proceeded to explore the substrate scope in the current protocol. Accordingly, we chose a set of vinylogous carbamates bearing both electron-donating and electron-withdrawing substituents. When the reaction of 1,4-benzoxazinone derivatives **21a-g, 21i** was carried out with diphenylmethanol (**33a**), all the reactions underwent smoothly and found to be completed in 15 min. to afford the corresponding products **34a-g, 34i** in excellent yields (Scheme 29).



Scheme 29: Molecular iodine-mediated dehydrative alkylation reaction of vinylogous carbamates with diphenylmethanol **33a**.

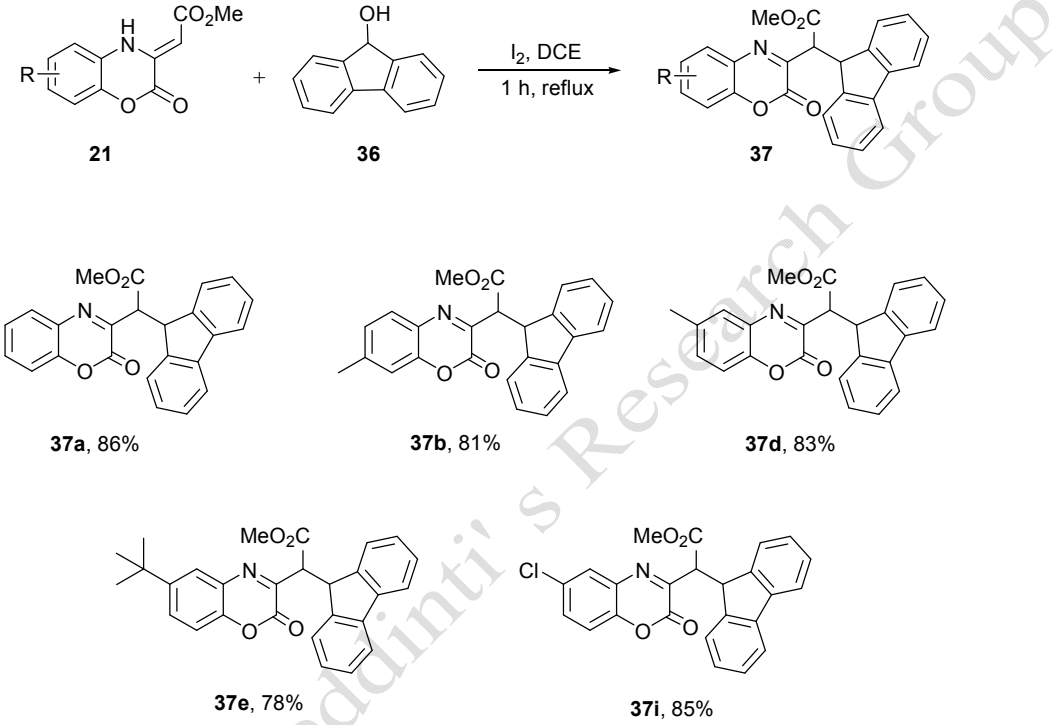
To expand the scope of the present methodology, we have employed the diphenylmethanol derivative **33b** as an alkylating agent. Under similar conditions, the reaction of diversely substituted vinylogous carbamates **21a-g, 21i** with **33b** were completed in 5 min. and delivered the anticipated products **35a-g, 35i** in excellent yields. The current protocol also tolerates a variety of benzoxazinone derivatives bearing both the electron-donating and electron-withdrawing substituents on benzoxazinone core (Scheme 30).



Scheme 30: Molecular iodine-promoted dehydrative alkylation reactions of 1,4-benzoxazinone derivatives with diarylcarbinol **33b**.

When the reaction of **21a** was carried out with **36** in CH_2Cl_2 in presence of molecular iodine, the reaction did not proceed under standard conditions or at prolonged reaction time. Only traces of product **37a** was observed after stirring at the room temperature for 24 h and

starting materials were recovered. At this juncture, the reaction was carried out in 1,2-dichloroethane (DCE) at reflux temperature and the reaction proceeded smoothly affording the product **37a** in 1 h in 86% yield. Under similar conditions the vinylogous carbamates **21a, 21b, 21d, 21e,** and **21i** reacted with **36**, to produce the corresponding products **37a-e**, **37i** in 1 h in good yields (Scheme 31).

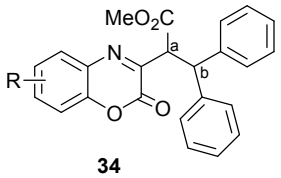


Scheme 31: Molecular iodine-mediated dehydrative alkylation reaction of 1,4-benzoxazinone derivatives **21**.

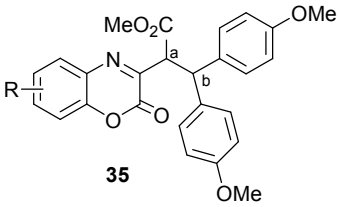
All the products obtained by the dehydrative alkylation of benzoxazinones with alcohol derivatives in presence of iodine are well characterized by the data obtained from IR, ^{1}H, ^{13}C NMR and DEPT analysis. In ^{1}H NMR of the products **34** and **35** the proton H_a on α-carbon, adjacent to the ester (CO_2Me) functionality resonate in the range of δ 5.50-5.28 ppm with a coupling constant of 12.0 Hz. In all the products the proton H_b on the carbon bearing two aryl rings resonates in the range of δ 5.16-5.01 ppm and the coupling constant value is observed around 12.0 Hz (Table 18). For the products **37**, the proton H_a on α-carbon, adjacent to the ester (CO_2Me) moiety, resonates in the range of 5.13-5.05 ppm and the coupling constant is observed around 4.5 Hz (Table 18). Similarly, the proton H_b on the carbon bearing the aryl moieties resonates in the range of 4.98-4.79 ppm with a coupling

constant around 5.0 Hz respectively. In IR spectra of all products the ester carbonyl absorb in the range of 1754-1738 cm^{-1}.

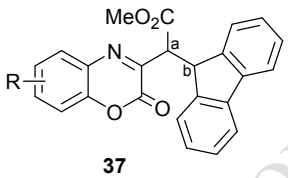
Table 18: Selective chemical shifts and coupling constants for products **34**, **35** and **37**.



34



35

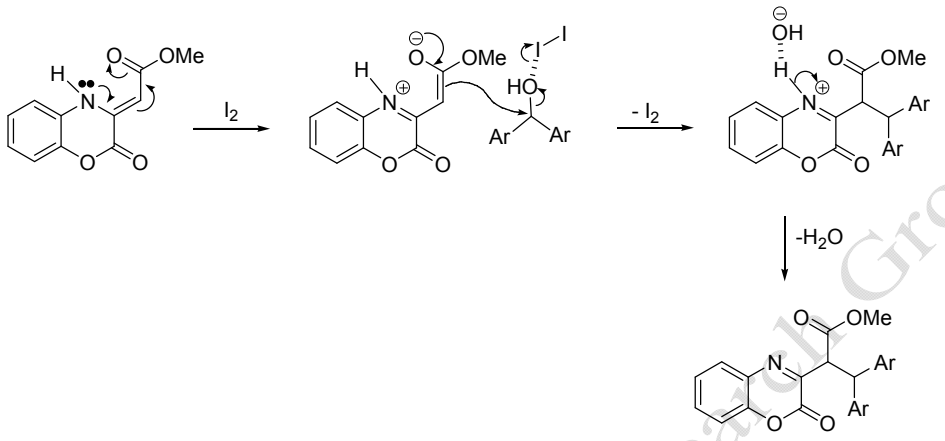


37

Entry	Product	H_a (δ in ppm)	H_b(δ in ppm)	J_{a-b} or J_{b-a} (Hz)
1	**34a**	5.40	5.14	12
2	**34b**	5.37	5.13	12
3	**34c**	5.39	5.14	12
4	**34d**	5.41	5.16	12
5	**34e**	5.50	5.13	12
6	**34f**	5.39	5.11	12
7	**34g**	5.39	5.13	12
8	**34i**	5.37	5.10	12
9	**35a**	5.30	5.03	12
10	**35b**	5.28	5.02	12
11	**35d**	5.29	5.02	12
12	**35e**	5.37	5.06	12
13	**35f**	5.30	5.01	12
14	**35i**	5.29	5.01	12
15	**37b**	5.10	4.92	4
16	**37d**	4.95	4.79	4
17	**37e**	5.13	4.80	4.5
18	**37i**	5.05	4.98	4

The possible mechanism for the molecular iodine-mediated alkylation reaction of benzoxazinone with alcohol derivatives is depicted in Scheme 32. The molecular iodine interacts with the hydroxy (–OH) group of the diarylmethanol, which in turn increases the

electrophilicity on the carbinol carbon. Since the benzoxazinone acts as a nucleophile, it attacks easily on to the electrophilic carbinol carbon and facilitates in the formation of alkylated product with simultaneous exclusion of water molecule.



Scheme 32: Proposed mechanism for the dehydrative alkylation reaction of 1,4-benzoxazinone derivatives.

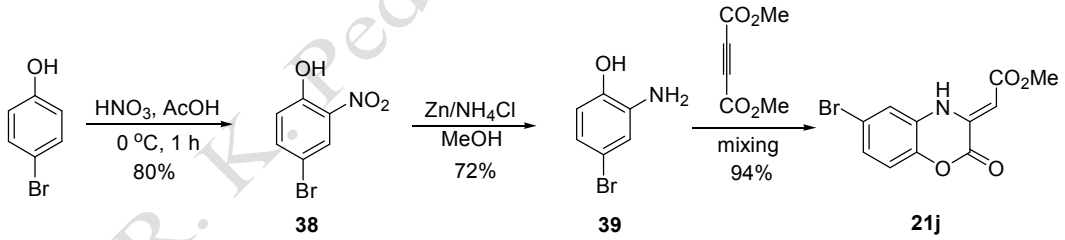
2.2.5. Synthesis of 2-aryl 1,4-benzoxazine derivatives

Carbon–carbon (C−C) bond-forming reactions have become very essential tools in modern organic synthesis because of their applications in the synthesis of various complex natural products.[198,199] Since heterocyclic compounds are ubiquitous in nature, the synthesis of novel derivatives of heterocyclic compounds by C−C bond-forming reactions has gained much importance recently.[200-207] A number of methodologies[208-215] for C−C bond construction have been developed. In particular, the formation of a C−C bond by direct reaction of a C−OH bond with a C−H bond would be an environmentally friendly process as it would generate water as the byproduct. Over the past decade, significant progress has been made in the development of direct dehydrative coupling methodologies.[216-220] In the field of heterocyclic chemistry, 1,4-benzoxazine derivatives have engrossed a significant place as a result of their occurrence in various natural products and biologically active molecules. 1,4-Benzoxazine derivatives were found to exhibit a wide range of biological activities such as antipsychotic agents,[221,222] vasodilator agents,[223] antibacterial agents,[224,225] and antagonists[226] and have also been used in the treatment of heart disease,[227] diabetes,[228] and neurode-

generative and cardiovascular disorders.[229,230] Recently, 2-aryl 1,4-benzoxazine derivatives were found to be active against *Toxoplasma gondiitachyzoite* proliferation.[231]

In continuation of our interest in exploring the various reactive sites of 1,4-benzoxazinone derivatives, we have developed a novel methodology for the conversion of 1,4-benzoxazinone derivatives into 2-hydroxy-1,4-benzoxazine derivatives using sodium borohydride under mild conditions.[232] We envisioned that these 2-hydroxy-1,4-benzoxazine derivatives would be excellent precursors for the synthesis of densely substituted 2-aryl-1,4-benzoxazine derivatives. Herein we illustrate our studies on the development of novel protocol for the synthesis of 2-aryl 1,4-benzoxazine derivatives by the arylation of 2-hydroxy-1,4-benzoxazine derivatives with various electron-rich arenes under mild conditions.

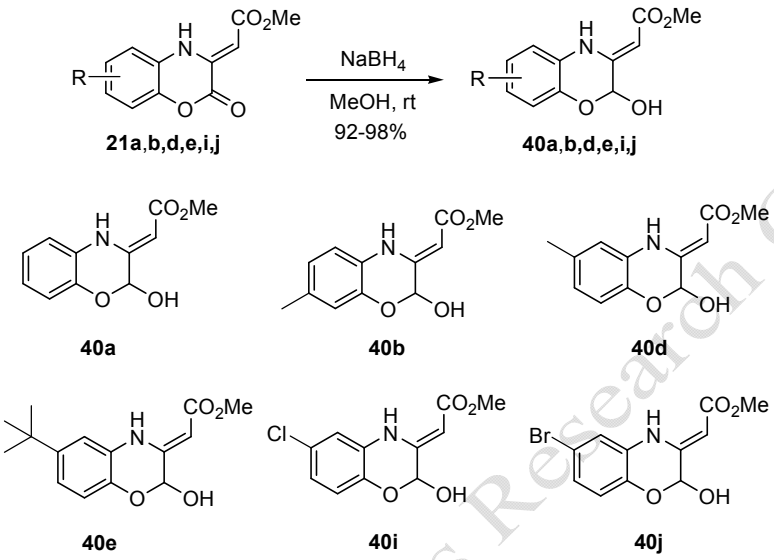
Initially the 4-bromo-2-nitrophenol **38** was synthesized in 80% yield by the nitration of *p*-bromophenol in presence of nitric acid and acetic acid. The nitro compound was subjected to reduction with Zn/NH_4Cl in methanol to afford the 2-amino 4-bromophenol **39** in 72% yield, which on reaction with dimethyl acetylenedicarboxylate gave the corresponding benzoxazinone derivative **21j** in 94% yield.



Scheme 33: Synthesis of bromobenzoxazinone derivative **21j**.

The benzoxazinone derivatives **21** were reduced to the 2-hydroxy-1,4-benzoxazinone derivatives **40** according to the procedure developed in our laboratory. In a typical reaction procedure, the benzoxazinone derivative (1 mmol) was suspended in 5 ml of methanol, cooled 0 ^oC. Then $NaBH_4$ (2.2 mmol) was added and allowed to stir for 15 min. Initially the benzoxazinone was having very less solubility in methanol but with the progress of the reaction, a clear solution was formed. After completion of the reaction, the methanol was removed completely with the help of rotary evaporator to give a semi-solid. Upon adding

water to the reaction mixture and by scratching with the help of spatula, a brown solid product separated out immediately from the reaction mixture. The solid was filtered and washed with water and dried to furnish pure 2-hydroxy-1,4-benzoxazine derivative in excellent yield (Scheme 34).

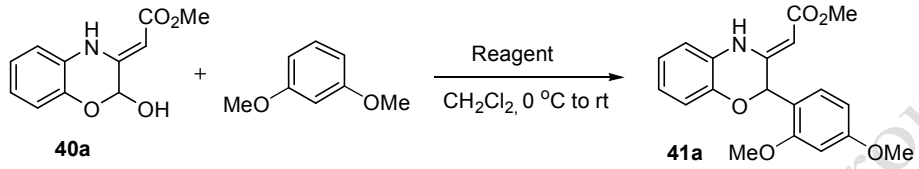


Scheme 34: Synthesis of 2-hydroxy-1,4-benzoxazine derivatives **40**.

After synthesizing a set of 2-hydroxy-1,4-benzoxazinone derivatives, we have focused on exploring the reactivity of these compounds with diversely substituted electron-rich arenes in presence of various reagents. In a preliminary experiment, a solution of 2-hydroxy-1,4-benzoxazine **40a** and 1,3-dimethoxybenzene in CH_2Cl_2 was cooled to 0° C, and trifluoroacetic acid (TFA) was added the reaction contents were then allowed to stir at room temperature. The reaction proceeded smoothly and was found to be completed in 4 h as shown by TLC. After purification by silica gel column chromatography, the corresponding 2-aryl benzoxazine derivative **41a** was isolated in 52% yield (Table 19, entry 1). Encouraged with the results obtained, we carried out the reaction of **40a** and 1,3-dimethoxybenzene under the influence of various Brønsted and Lewis acids for the optimization of reaction conditions. When the reaction was performed with Brønsted acids such as *p*-TSA.H_2O and TfOH, the product **41a** was obtained in 48 and 54% yields, respectively however, no product formation was observed from the reaction mediated by montmorillonite or amberlyst (Table 19, entries 2-5). Further we screened the reaction with Lewis acids such as $ZrCl_4$, $ZnCl_2$,

$FeCl_3$, $SnCl_4$, and BF_3.etherate. It was found that among the tested Lewis acids, BF_3.etherate afforded the desired product **41a** in better yield (Table 19, entries 6-11).

Table 19: Optimization of reaction conditions.[a]



Entry	Reagent	Time (h)	Yield (%)[b]
1	TFA	12	52
2	P-TSA.H_2O	4	48
3	TfOH	1	54
4	Montmorillonite	12	-
5	Amberlyst	12	-
6	$ZrCl_4$	3	61
7	$ZnCl_2$	3	58
8	$FeCl_3$	1	66
9	$SnCl_4$	1	71
10	**BF_3.etherate**	1	**79**
11	BF_3.etherate[d]	4	62
12	–	12	-

[a]reactions were performed with **40a** (0.5 mmol), 1,3-dimethoxybenzene (0.6 mmol) and reagent (0.5 mmol) in 5 mL of CH_2Cl_2.

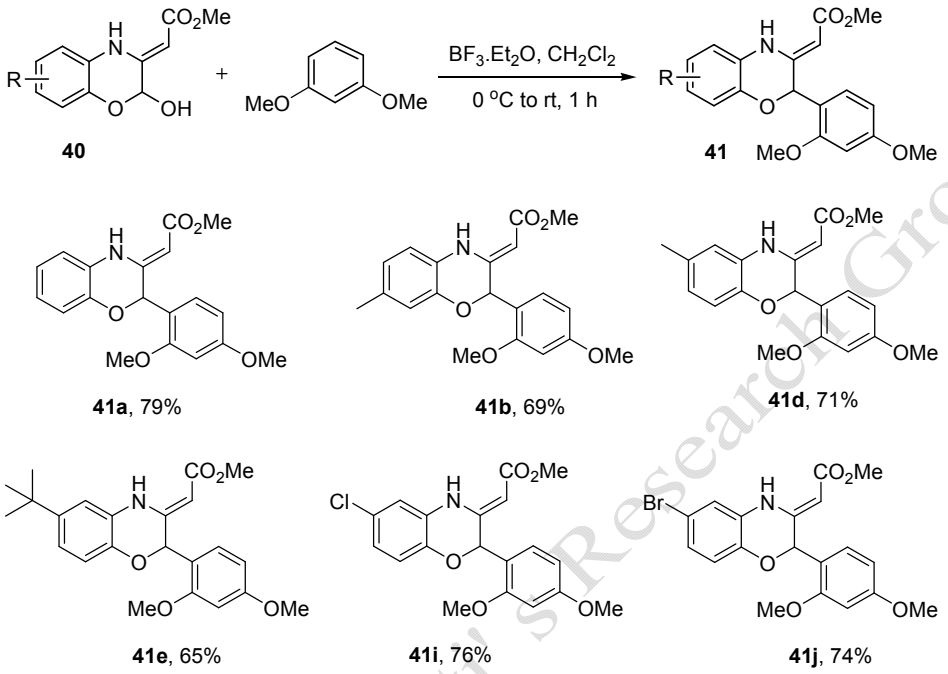
[b]yield of pure and isolated product **41a**.

[c]reaction was performed at rt.

[d]0.25 mmol of reagent was used.

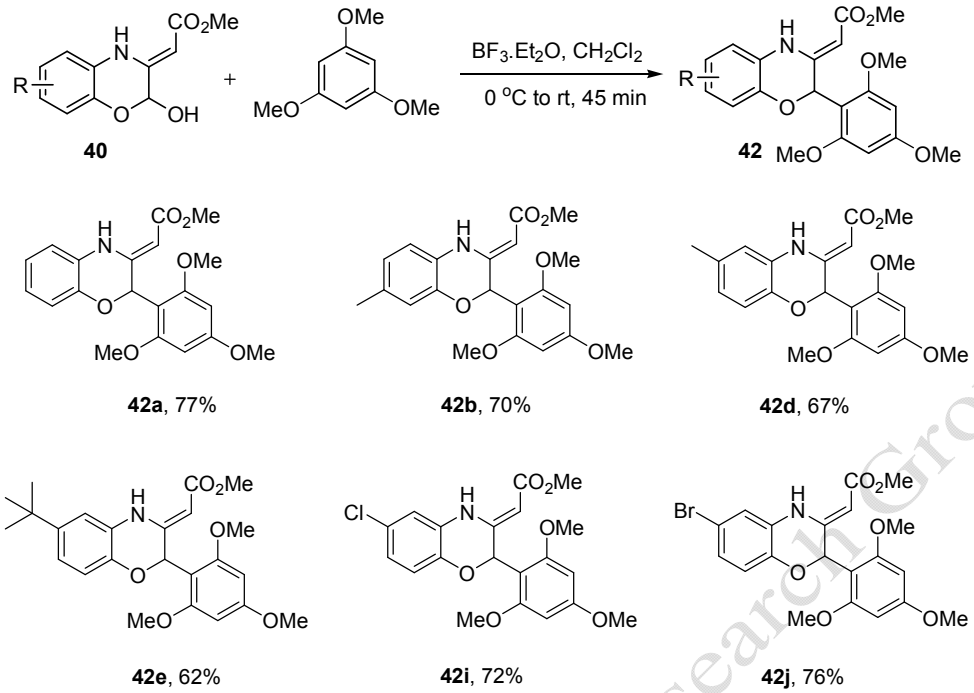
With the optimized conditions in hand, we then evaluated the scope of the reaction of diversely substituted 2-hydroxy-1,4-benzoxazine derivatives **40a**, **40b**, **40d**, **40e, 40i** and **40j** with various nucleophiles. When the reaction of 2-hydroxy-1,4-benzoxazine derivatives **40** were carried out with 1,3-dimethoxybenzene in presence of BF_3.etherate, the reactions proceeded smoothly to furnish the corresponding products **41b**, **41d**, **41e, 41i** and **41j** in good yields. It was observed that the benzoxazine derivatives possessing moderately

electron-withdrawing substituents such as –Cl, –Br on the aromatic ring gave the products **41i** and **41j** in marginally higher yields in comparison with those bearing electron-releasing substituents like –Me and *tert*-butyl **41b**, **41d** and **41e** (Scheme 35).



Scheme 35: Friedel-Crafts arylation reaction of 2-hydroxy-1,4-benzoxazine derivatives **40** with 1,3-dimethoxybenzene.

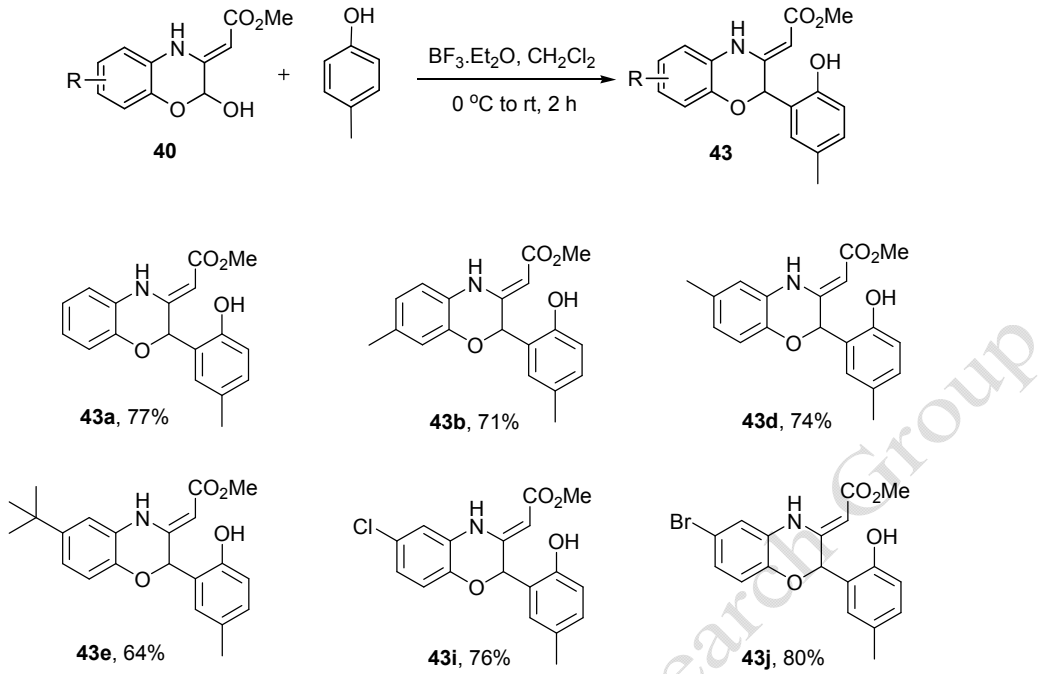
Under the standard conditions, 2-hydroxy-1,4-benzoxazine derivatives **40** reacted effectively with 1,3,5-trimethoxybenzene in presence of BF_3.etherate to furnish the expected products **42a**, **42b**, **42d**, **42e**, **42i**, and **42j** in good yields. It was noticed that, reactivity pattern of 1,3,5-trimethoxy benzene was similar to that of 1,3-dimethoxybenzene. For instance, the benzoxazine derivatives **40i** and **40j** having the –Cl and –Br substituents on the aromatic ring delivered the products **42i**, **42j** in 72 and 76% yields, respectively (Scheme 36). However, the benzoxazine derivatives **40b**, **40d**, **40e** carrying –Me, *tert*–butyl substituents provided the respective products **42b**, **42d**, **42e** in 70, 67 and 62% yields respectively (Scheme 36). The reactions of **40** with 1,3,5–trimethoxybenzene were completed in 45 min., whereas in case of 1,3-dimethoxybenzene, the reactions reached completion in 1 h, which may be due to the higher electron-rich character of the former arene.



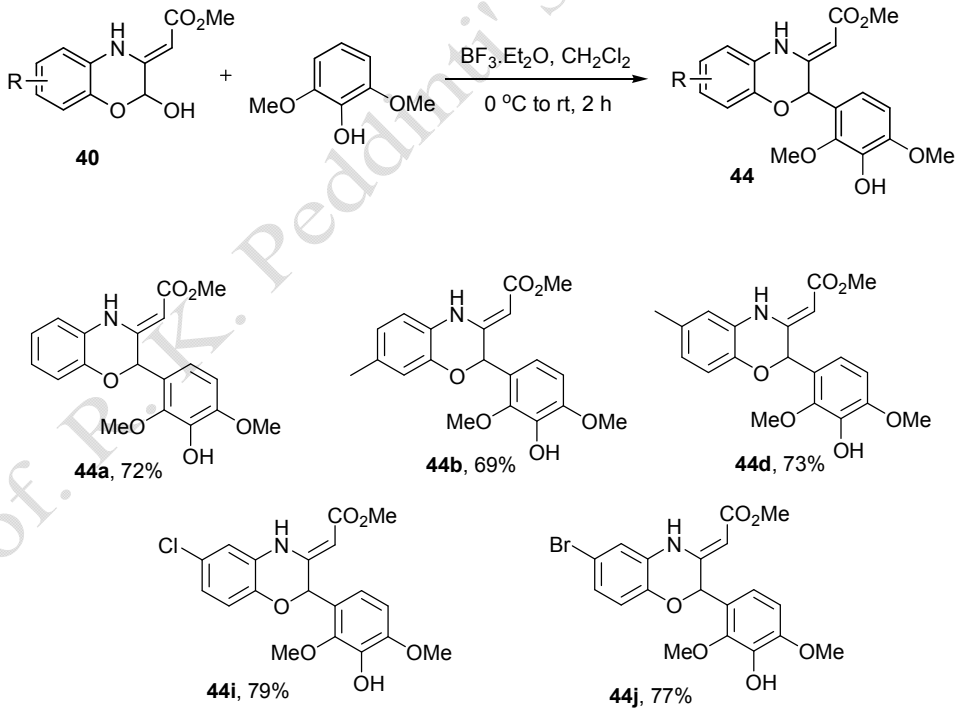
Scheme 36: Friedel-Crafts arylation reaction of 2-hydroxy-1,4-benzoxazine derivatives **40** with 1,3,5-trimethoxybenzene.

After successfully carrying out the reactions of **40** with electron-rich arenes such as 1,3-dimethoxybenzene and 1,3,5-trimethoxybenzene, we further advanced to explore the applicability of the current protocol to the phenolic nucleophiles. We then selected *p*-cresol for our study. The 2-hydroxy-1,4-benzoxazine derivatives **40** reacted with the *p*-cresol in presence of BF_3.etherate under the standard conditions to give the corresponding products **43a**, **43b**, **43d**, **43e**, **43i**, and **43j** with in 2 h in good yields (Scheme 37).

Similarly we also examined the reactivity of 2,6-dimethoxyphenol with the benzoxazine derivatives **40**. The treatment of 2,6-dimethoxyphenol with **40a** in presence of BF_3.etherate, provided the Friedel-Crafts adduct **44a** in 72% yield (Scheme 38). When the reactions of **40b**, **40d**, **40i** and **40j** was done with 2,6-dimethoxyphenol the desired products **44b**, **44d**, **44i** and **44j** were obtained in good yields. But unfortunately, under similar conditions the benzoxazine derivative **40e** bearing the *tert*-butyl group on treatment with 2,6-dimethoxyphenol failed to give any isolable product (Scheme 38).

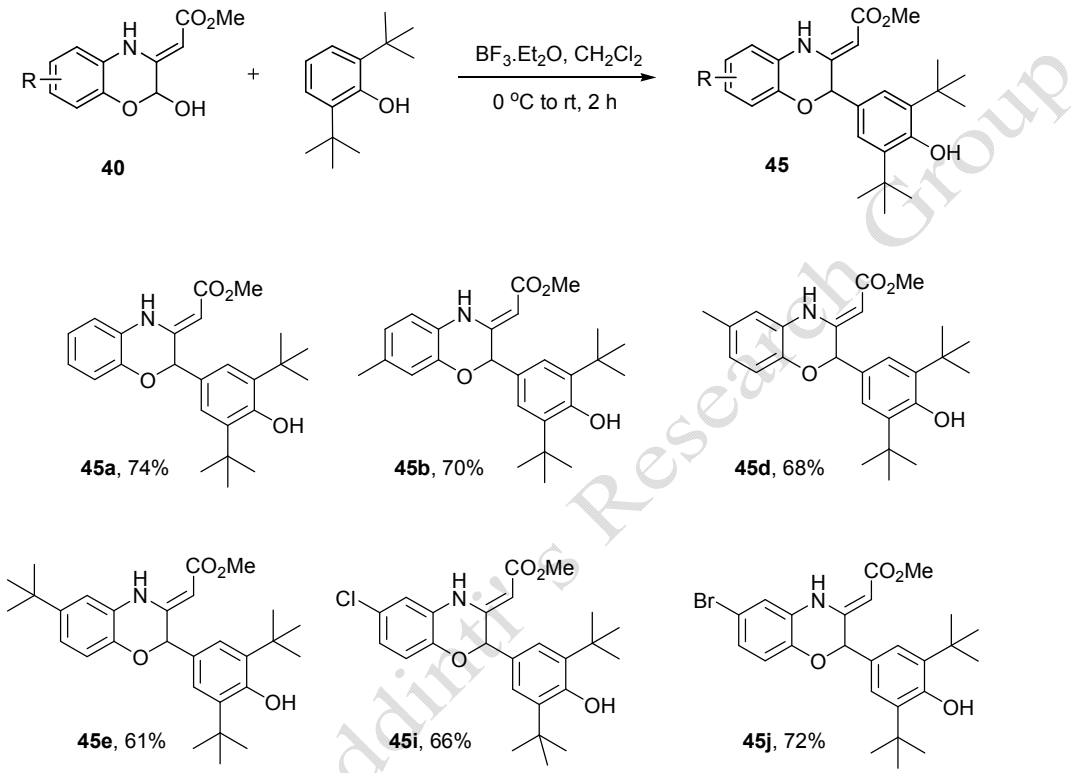


Scheme 37: Friedel-Crafts arylation reaction of 2-hydroxy-1,4-benzoxazine derivatives **40** with *p*-cresol.



Scheme 38: Friedel-Crafts arylation reaction of 2-hydroxy-1,4-benzoxazine derivatives **40** with 2,6-dimethoxyphenol.

The reactions of the benzoxazine derivatives **40** with 2,6-di-*tert*-butylphenol which was bearing the bulky *tert*-butyl groups also underwent smoothly and resulted in the formation of the Friedel-Crafts adducts **45a**, **45b**, **45d**, **45e**, **45i** and **45j** in good yields. The results are summarized in Scheme 39.



Scheme 39: Friedel-Crafts arylation reaction of 2-hydroxy-1,4-benzoxazine derivatives **40** with 2,6-di-*tert*-butylphenol.

The structure elucidation of all the pure and isolated products was done on the basis of the collective information obtained from the IR, ^{1}H, ^{13}C NMR, DEPT and HRMS spectral data. The presence of a broad singlet in the range of δ 10.37-10.60 ppm in the ^{1}H NMR spectra of these compounds indicates the NH proton. The vinylic proton on the α-carbon to ester functionality resonates in the range of δ 5.38-6.24 ppm. The proton on carbon-2 bearing aryl moiety resonates in the range of δ 4.35-4.51 ppm. The structure of the compound **42i** was further confirmed from its single crystal X-ray analysis (Figure 17, Table 20).

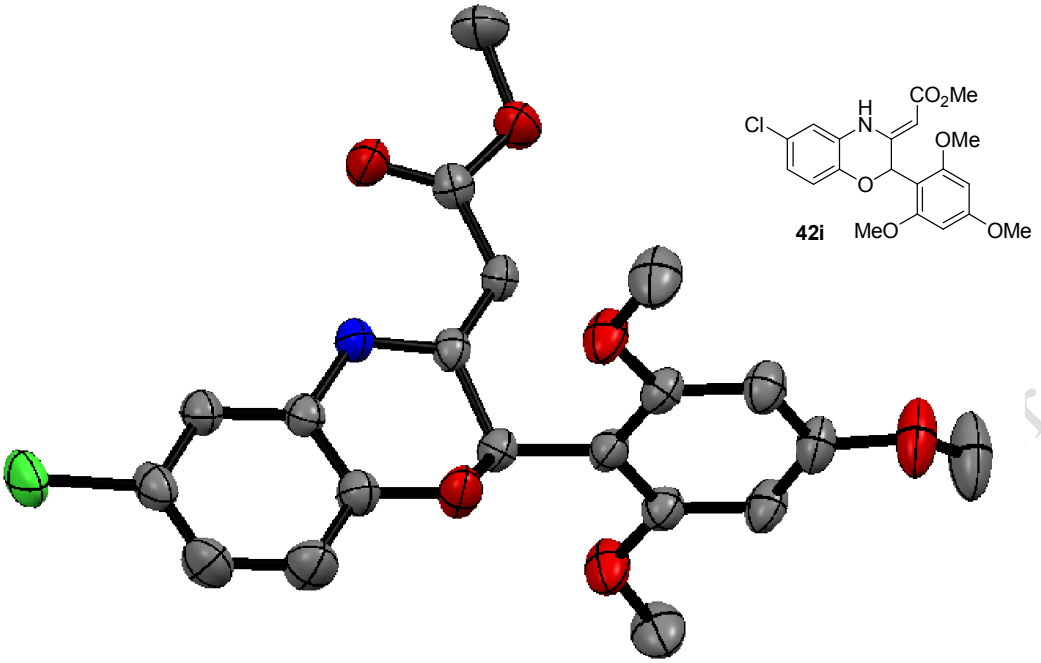


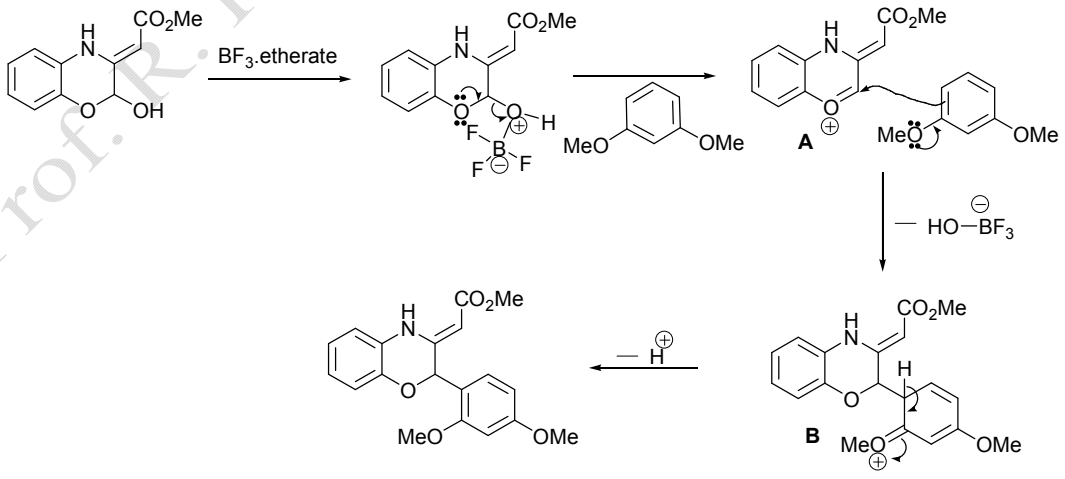
Figure 17: ORTEP Representation of crystal structure of **42i**.

Table 20: Crystallographic data for **42i.**

Formula	$C_{20}H_{19}ClNO_6$
Formula Wt.	404.81
Crystal habit	Blocks
Crystal color	White
Crystal system	Monoclinic
Space group	-P 2ybc
a (Å)	10.8408 (4)
b (Å)	18.4917 (7)
c (Å)	9.6835 (4)
α (deg)	90.00
β (deg)	90.00
γ (deg)	90.00
V (Å^3)	1911.11 (13)
Z	4

D_{calc} (g cm^{-3})	1.407
T (K)	296 (2)
λ (Mo-Kα)	0.71073
μ (mm^{-1})	0.237
2θ range (deg)	52.74
Limiting indices	-13 ≤ h ≥ 13
	-23 ≤ k ≥ 23
	-12 ≤ l ≥ 11
F(000)	844
No. of Reflns. Measured	3909
No. of Parameters	257
GOF on F^2	1.275
R1 [I>2σ(I)]	0.0542
wR2	0.1574

When the 2-hydroxy-1,4-benzoxazine derivatives reacted with electron-rich arene such as 1,3-dimethoxybenzene in presence of BF_3.etherate, the hydroxy group co-ordinates with BF_3.etherate and generates the oxonium ion intermediate **A**. Now the electron-rich arene attacks on to the oxonium ion and after subsequent rearomatization of species **B** affords the expected 2-aryl 1,4-benzoxazine derivative (Scheme 40).

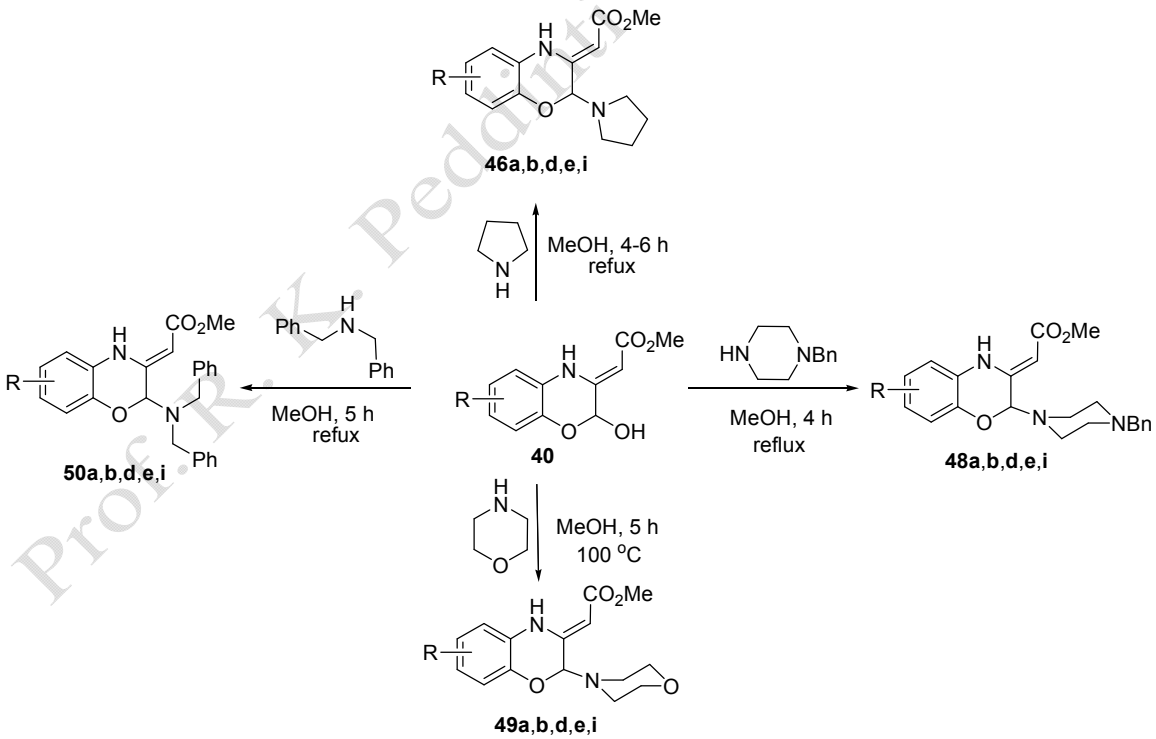


Scheme 40: Proposed mechanism for the synthesis of 2-aryl-1,4-benzoxazine derivative.

2.2.6. Synthesis of 2-amino-1,4-benzoxazine derivatives

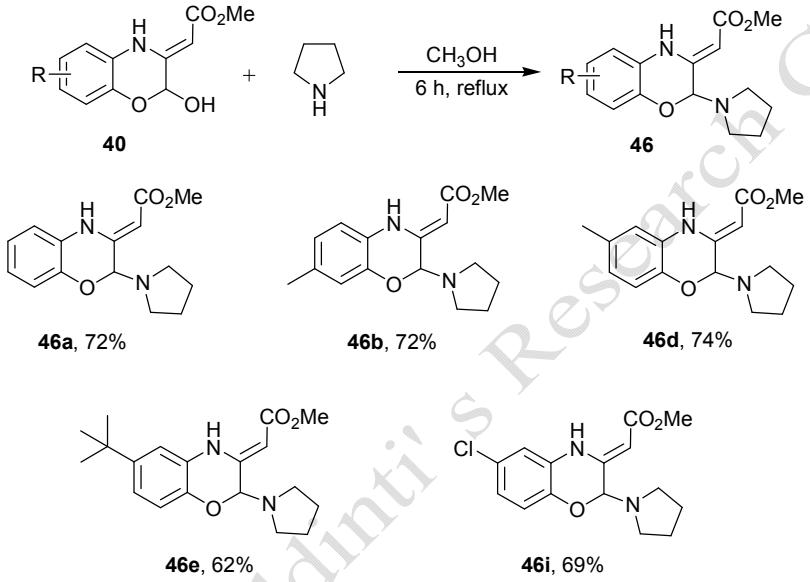
In organic synthesis, the transformations involving the selective carbon-heteroatom bond formation certainly play a prominent role in the construction of natural products. The carbon-nitrogen coupling reactions provide an easy access for the synthesis of wide variety of nitrogen containing derivatives. Such nitrogen-containing fragments are ubiquitous in nature, pharmaceuticals, herbicides and they are also used as precursors for the synthesis of complex natural products. Several methodologies have been developed for the construction of C-N bond, among them the metal mediated coupling reactions are widely used.[233-235]

After successfully exploring the reactivity of 2-hydroxy-1,4-benzoxazine derivatives **40** with nucleophiles such as electron-rich arenes, we envisaged that the reactions of these 2-hydroxy-1,4-benzoxazine derivatives with secondary amines would provide a simple and environment friendly procedure for the synthesis of novel target compounds like 2-amino benzoxazine derivatives.



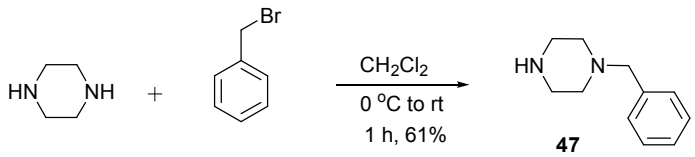
Scheme 41: Reaction of 2-hydroxy-1,4-benzoxazine derivatives **40** with secondary amines.

In our preliminary studies, we carried out the reaction of 2-hydroxy-1,4-benzoxazine derivative **40a** with pyrrolidine in methanol at reflux temperature. The reaction was found to be completed in 6 h and after purification by the silica gel column chromatography the desired product **46a** was obtained in 72% yield. Delighted with the results obtained, we then carried out the reaction of benzoxazinols **40b**, **40d**, **40e** and **40i** with pyrrolidine. All the reactions underwent smoothly and the 2-amino benzoxazine derivatives **46b**, **46d**, **46e**, and **46i** were isolated in good yields (Scheme 42).



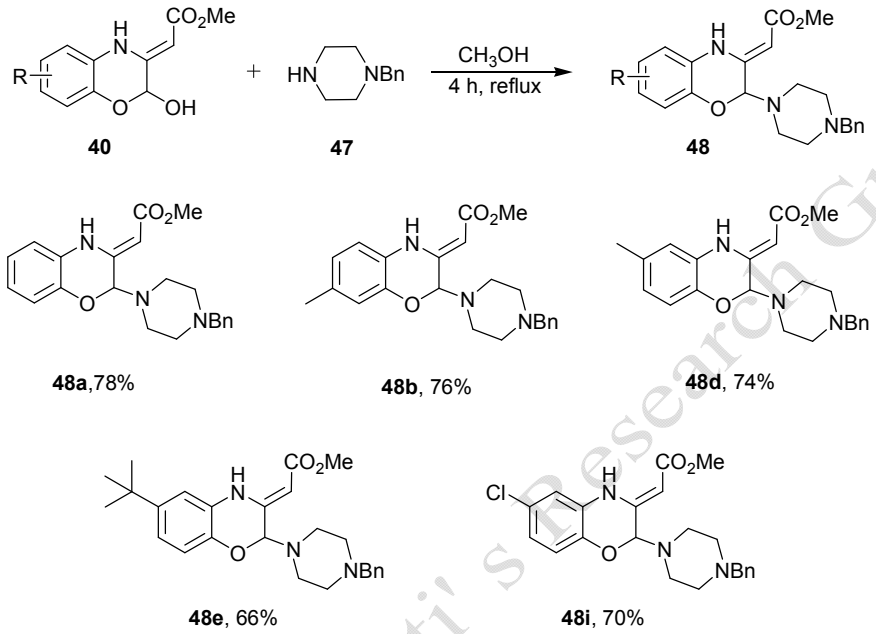
Scheme 42: Reaction of 2-hydroxy-1,4-benzoxazine derivatives **40** with pyrrolidine.

To investigate the reactivity of other secondary amines in the current protocol, we chose piperazine. When the reaction of **40a** was carried out with piperazine in methanol at reflux temperature, no isolable product was observed. At this stage we prepared the mono benzylated piperazine **47** by following the procedure reported in the literature.[236] To piperazine in CH_2Cl_2, was added the benzyl bromide dropwise at 0 °C. The reaction mixture was stirred at the same temperature for 1 h. After usual work up, the *N*-benzylpiperazine (**47**) was obtained in 61% yield as a colourless oil (Scheme 43).



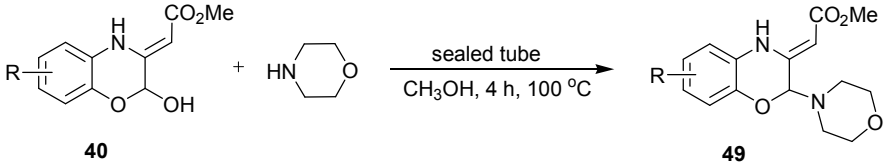
Scheme 43: Synthesis of *N*-benzylpiperazine (**47**).

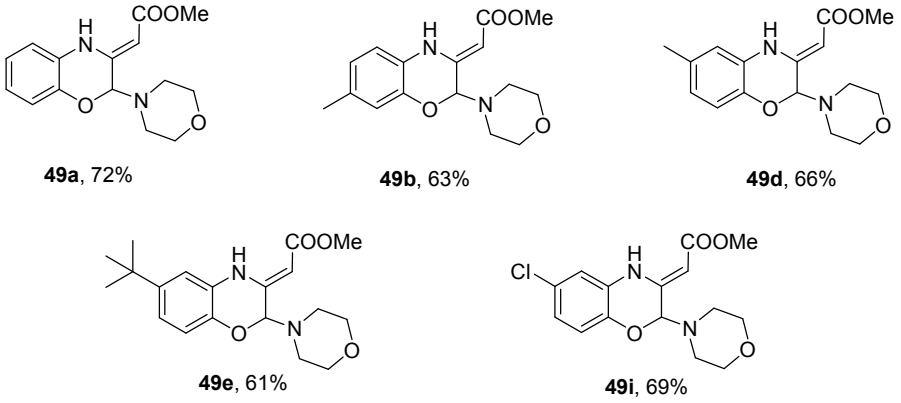
Thus obtained *N*-benzylpiperazine was reacted with 2-hydroxy-1,4-benzoxazine derivatives **40**. All the reactions underwent smoothly and found to be completed in 4 h. After purification by the silica gel column chromatography, the desired products **48a**, **48b**, **48d**, **48e**, and **48i** were obtained in high yields (Scheme 44).



Scheme 44: Reaction of 2-hydroxy-1,4-benzoxazine derivatives **40** with *N*-benzylpiperazine.

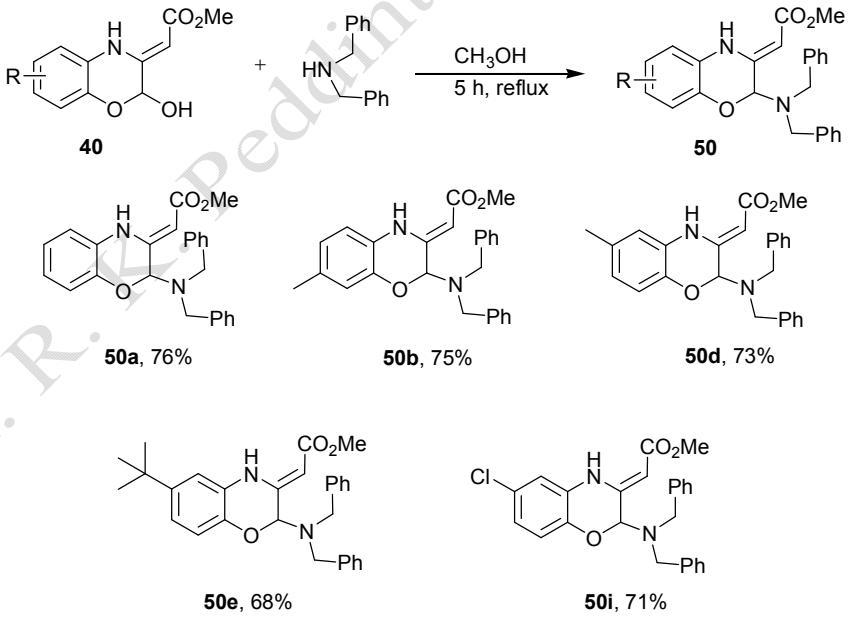
The reaction of **40a** with morpholine was also carried out in methanol at reflux temperature for 5 h. Surprisingly, there was no formation of expected product **49a** was observed, instead the starting material **40a** was recovered from the reaction. At this juncture, a mixture of **40a**, morpholine and methanol was heated in a sealed tube at 100 ^{o}C. The reaction reached completion in 4 h as shown by the TLC and after purification by silica gel column chromatography the desired product **49a** was isolated in 72% yield. In the same way the other benzoxazine derivatives **40b**, **40d**, **40e**, and **40i** reacted with morpholine to furnish the pure products **49b**, **49d**, **49e** and **49i** in good yields (Scheme 45).





Scheme 45: Reaction of 2-hydroxy-1,4-benzoxazine derivatives **40** with morpholine.

After successfully exploring the reactivity of 2-hydroxy-1,4-benzoxazine derivatives with cyclic secondary amines such as pyrrolidine, *N*-benzylpiperzine, and morpholine, we also studied the reactivity of acyclic secondary amine such as *N*,*N*-dibenzylamine. The reaction of benzoxazinols **40** with *N*,*N*-dibenzylamine in methanol at room temperature afforded the corresponding 2-amino benzoxazine derivatives **50a**, **50b**, **50d**, **50e** and **50i** in high yields.



Scheme 46: Reaction of 2-hydroxy-1,4-benzoxazine derivatives **40** with *N*,*N*-dibenzylamine.

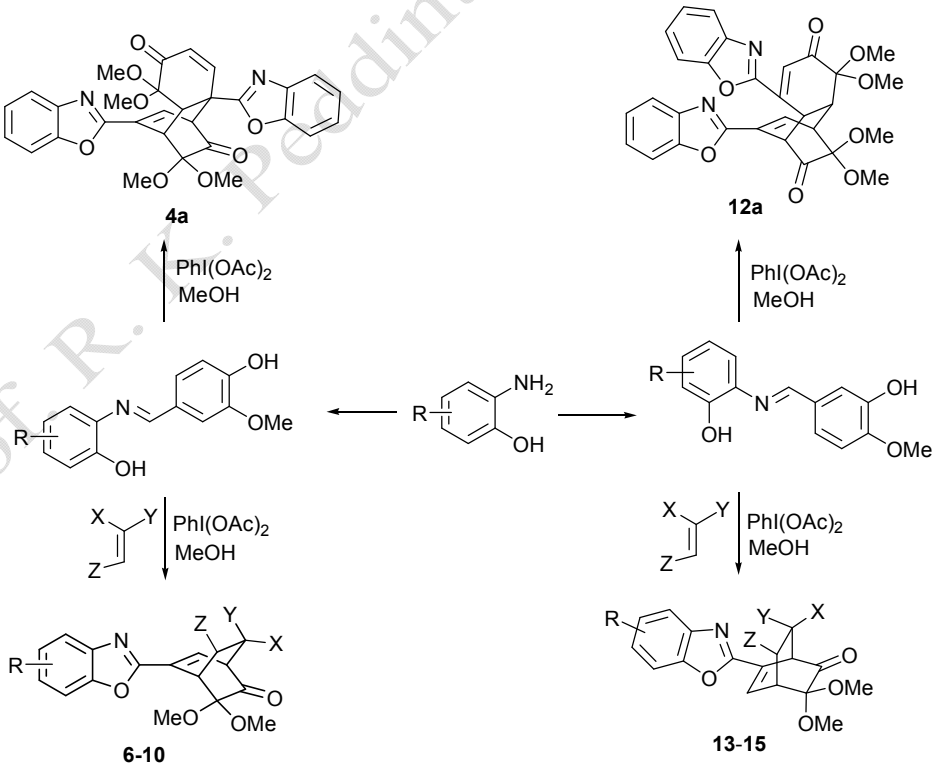
The structure of all the products was confirmed by the analysis of collective information obtained from ^{1}H, ^{13}C NMR, DEPT and IR spectra. In ^{1}H NMR the proton

attached to the nitrogen atom (NH) resonates in the range of 10.52-10.20 ppm. A peak in the range of 1674-1658 cm^{-1} was observed in IR spectra due to the ester functionality.

2.3. CONCLUSION

Synthesis of benzoxazole-2′-yl bicyclo[2.2.2]octenone derivatives

We have developed a simple and efficient one-pot domino reaction for the synthesis of benzoxazole-2′-yl bicyclo[2.2.2]octenone derivatives from the commercially available starting materials. In this methodology, the diacetoxyiodobenzene (DIB) mediated domino oxidative cyclization–oxidative acetalization–Diels-Alder reaction of aldimines facilitates the incorporation of benzoxazole moiety on to the bicyclo[2.2.2]octenone ring system. We have synthesized a new class of densely substituted benzoxazole-2′-yl bicyclo[2.2.2]octenone derivatives in good yields under mild conditions. The Diels-Alder reaction of benzoxazol-2′-yl MOBs with the various dienophiles was found to be regio- and stereo-selective, which was also further confirmed by the 2D-NMR and ^{1}H-^{1}H decoupling experiments (Scheme 47).



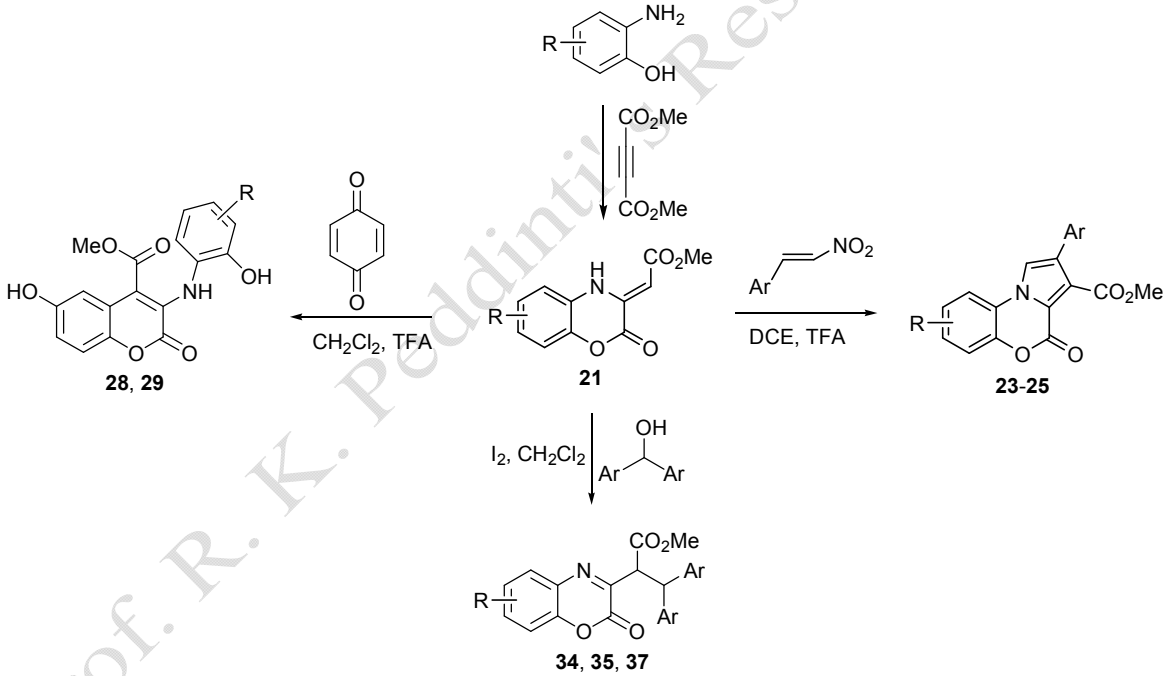
Scheme 47: DIB-Mediated reactions of aldimines.

Vinylogous Carbamates:

We have explored the reactivity of various unprecedented reactive sites of 3-(methoxycarbonyl)methylene-1,4-benzoxazinone derivatives, a new class of vinylogous carbamates in presence Brønsted and Lewis acids.

Synthesis of pyrrolobenzoxazine derivatives

The reactivity of 1,4-benzoxazinone derivatives as nucleophiles was investigated with β-nitrostyrene derivatives. The reaction of vinylogous carbamates with β-nitrostyrenes in presence of trifluoroacetic acid resulted in the formation of pyrrolobenzoxazine derivatives. We have introduced a novel protocol for the efficient synthesis of a series of pyrrolobenzoxazine derivatives from the readily available aminophenols and dialkyl acetylenedicarboxylates.



Scheme 48: Vinylogous carbamates: Reactions of 1,4-benzoxazinones.

Synthesis of 3-arylamino coumarin derivatives

Further we have also developed a simple and atom-economic protocol for the synthesis of 3-arylamino coumarin derivatives under mild conditions at ambient temperature. The reaction of these vinylogous carbamates with *p*-benzoquinone derivatives in presence of

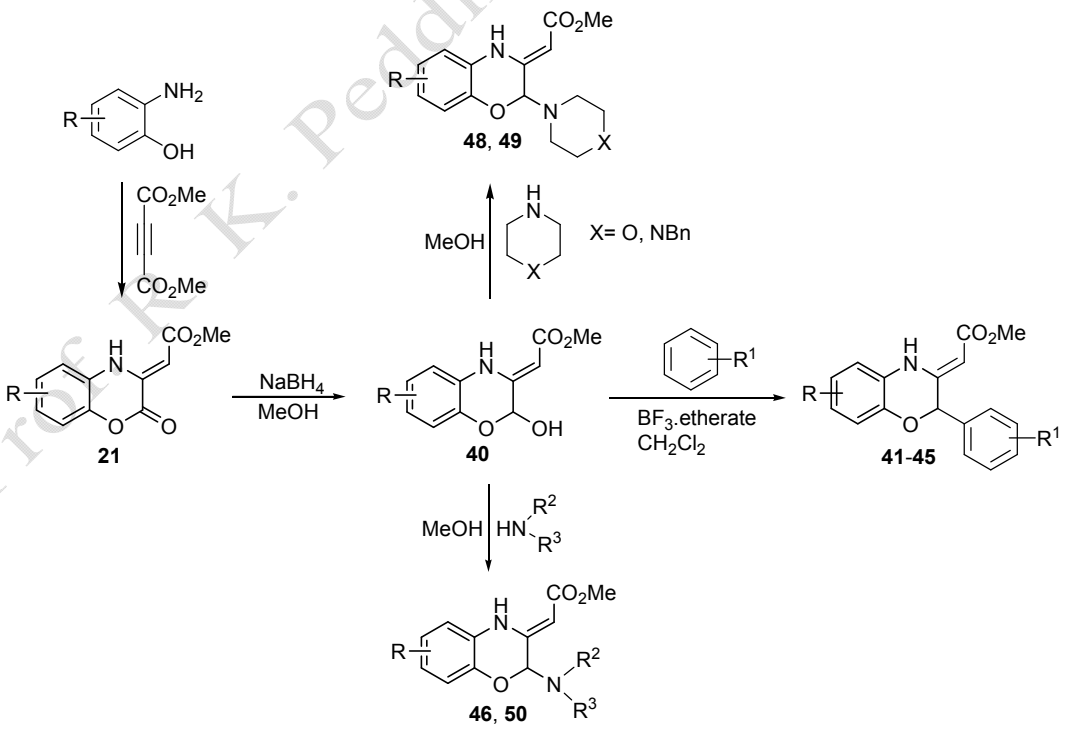
trifluoroacetic acid at room temperature provided the 3-arylamino coumarin derivatives in good to excellent yields. The reaction is easy to handle and incorporates all the reactants into the products without any byproducts. It is noteworthy to mention here that in synthesis of these coumarin derivatives obviates the use of column chromatography and the products can be isolated easily with simple filteration (Scheme 48).

Synthesis of 3-substituted 1,4-benzoxazinone derivatives

We explored the reactivity of vinylogous carbamates, as nucleophiles with the alcohol derivatives. The dehydrative alkylation reaction of 1,4-benzoxazinone derivatives with diaryl methanol derivatives in presence of molecular iodine provided the corresponding 3-substituted 1,4-benzoxazinone derivatives in excellent yields. We have developed a cost-effective, rapid and operationally simple synthetic methodology for the synthesis of 3-substituted 1,4-benzoxazinone derivatives (Scheme 48).

Synthesis of 2-aryl-1,4-benzoxazine derivatives

we have developed a new synthetic technology for the direct Friedel−Crafts arylation reaction of 2-hydroxy-1,4-benzoxazine derivatives. These 2-hydroxy-1,4-benzoxazine deriv-



Scheme 49: Vinylogous carbamates: Reactions of 2-hydroxy 1,4-benzoxazines.

atives in presence of BF_3.etherate, reacted efficiently with electron-rich arenes to afford the 2-aryl-1,4-benzoxazine derivatives in good yields. The methodology provides an easy access for the synthesis various substituted 2-arylbenzoxazine derivatives of potential biological significance under mild conditions (Scheme 49).

Synthesis of 2-amino-1,4-benzoxazine derivatives

An environmentally benign method has been developed by the dehydrative coupling of secondary amines with 2-hydroxy-1,4-benzoxazine derivatives for the synthesis of 2-amino-benzoxazine derivatives. The reaction proceeds smoothly in methanol without the aid of external reagents and provides an easy access for the synthesis of a series of 2-amino-benzoxazine derivatives (Scheme 49).

CHAPTER-3: EXPERIMENTAL

3.1. GENERAL REMARKS

3.2. SYNTHETIC PROCEDURES

3.1. GENERAL REMARKS

The reactions associated with the formation of gases and application of heat was 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. Chemicals

The solvents for anhydrous reactions were dried and purified according to standard techniques.

CH_3CN	**:**	Distilled over P_2O_5
CH_2Cl_2	**:**	Distilled over P_2O_5
DCE	**:**	Distilled over P_2O_5
EtOH	**:**	Distilled from magnesium cake
MeOH	**:**	Distilled from magnesium cake
THF	**:**	Distilled from Na/benzophenone ketyl radical

The chemicals were purchased from the companies Sigma-Aldrich, Across, Avra, Hi-Media, S. D. Fine chemicals and were used as received unless otherwise stated.

3.1.2. Chromatographic Methods

Thin Layer Chromatography

Support**:** TLC aluminium sheets of silica gel 60 F_{24} (*Merck*) with a fluorescent indicator.

Detection**:** 1) exposition to UV-light (λ = 254 nm).

2) exposed to iodine vapours.

Preparative Column Chromatography

Purification by gravity column chromatography were carried out on glass column (10-50 mm diameter) using silica gel with 100-200 mesh and silica gel (100-200 mesh) neutralized with triethylamine.

3.1.3. Determination of physical properties of the synthesized compounds

Melting points were measured in open glass capillaries with *Perfit* 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. Absorptions are given in wave numbers (cm^{-1}).

^{1}H NMR Spectroscopy

^{1}H NMR Spectra were recorded on Brüker AMX 500 instrument (500 MHz). Chemical shifts were given in ppm relative to tetramethylsilane (δ 0.00 ppm). Solvent residual peaks (from $CDCl_3$, δ 7.26 ppm; from DMSO, δ 2.50 ppm) were used as internal standards. Coupling patterns are described by the following abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), dt (doublet of triplet), td (triplet of doublet), br (broad). Coupling constants are given in Hertz.

^{13}C NMR Spectroscopy

^{13}C NMR Spectra were recorded on Brüker AMX 500 spectrometer (125 MHz). Chemical shifts were given in ppm and were determined by comparison with solvent residual peaks (from $CDCl_3$, δ 77.0 ppm; from DMSO, δ 39.5 ppm).

Mass Spectroscopy

High resolution mass spectra (HRMS) were recorded on microOTOF-Q II.

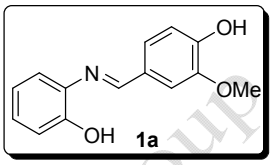
3.2. SYNTHETIC PROCEDURES

3.2.1. General procedure for the synthesis of aldimines 1a-e, 11a:

A 2-aminophenol derivative (10 mmol) and vanillin/isovanillin (10 mmol) were dissolved in methanol (4 mL) and allowed to stir at room temperature for 4 h. After completion of the reaction as shown by the TLC, methanol was evaporated under reduced pressure and the crude reaction mixture was dissolved in ethyl acetate (20 mL) and washed

twice with water (2 x 20 mL). The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Recrystallization of crude reaction mixture in ethanol gave the corresponding Schiff bases **1a-e** and **11a**.

(*E*)-4-((2′-Hydroxyphenylimino)methyl)-2-methoxyphenol (1a):



Yield: 2.13 g (87%) as brown solid.

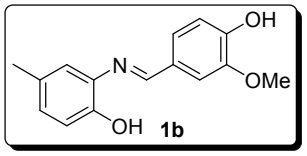
Mp: 101 ^{o}C.

IR (KBr): ν_{max} 3478, 1628, 1592, 1509, 1395, 1281 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.52 (s, 1H), 7.54 (s, 1H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 1H), 7.19-7.15 (m, 1H), 7.02 (dd, *J* = 1.5, 8.0 Hz, 1H), 6.99 (d, *J* = 8.0 Hz, 1H), 6.90 (d, *J* = 1.5, 7.5 Hz, 1H), 3.93 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 157.5, 151.7, 149.3, 147.0, 136.1, 128.2, 125.2, 120.1, 116.1, 114.9, 114.4, 108.6, 56.0 ppm.

(*E*)-4-((2′-Hydroxy-5′-methylphenylimino)methyl)-2-methoxyphenol (1b):



Yield: 2.20 g (85%) as brown solid.

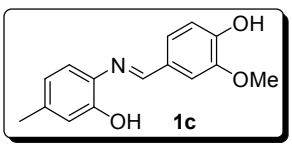
Mp: 118 ^{o}C.

IR (KBr): ν_{max} 3467, 1634, 1584, 1504, 1376, 1292 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.49 (s, 1H), 7.51 (s, 1H), 7.26 (d, *J* = 8.0 Hz, 1H), 7.13 (d, *J* = 8.0 Hz, 1H), 6.97 (d, *J* = 8.5 Hz, 1H), 6.82 (s, 1H), 6.69 (d, *J* = 1.5, 8.0 Hz, 1H), 3.92 (s, 3H), 2.31 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 156.0, 151.7, 149.1, 147.0, 138.6, 133.4, 128.8, 124.9, 120.8, 115.6, 115.4, 114.3, 108.5, 55.9, 21.3 ppm.

(*E*)-4-((2′-Hydroxy-4′-methylphenylimino)methyl)-2-methoxyphenol (1c):



Yield: 2.1 g (81%) as brown solid.

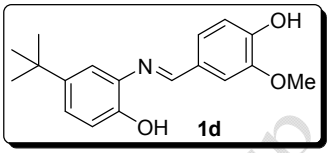
Mp: 100-101 ^{o}C.

IR (KBr): ν_{max} 3471, 1631, 1586, 1512, 1384, 1287 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.45 (s, 1H), 7.50 (s, 1H), 7.24 (d, *J* = 8.0 Hz, 1H), 7.01 (s, 1H), 6.97-6.94 (m, 2H), 6.89 (d, *J* = 8.5 Hz, 1H), 3.88 (s, 3H), 2.28 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 157.2, 149.5, 149.2, 147.0, 135.7, 129.3, 128.7, 128.7, 125.1, 116.7, 114.5, 114.3, 108.5, 55.9, 20.7 ppm.

(*E*)-4-((4′-*tert*-Butyl-2′-hydroxyphenylimino)methyl)-2-methoxyphenol (1d):



Yield: 2.28 g (76%) as brown solid.

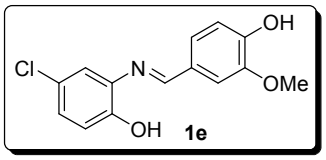
Mp: 102-103 °C.

IR (KBr): ν_{max} 3475, 1624, 1579, 1510, 1378, 1277 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.55 (s, 1H), 7.56 (d, *J* = 2.0 Hz, 1H), 7.33 (dd, *J* = 1.5, 8.0 Hz, 1H), 7.24 (d, *J* = 2.5 Hz, 1H), 7.22 (dd, *J* = 2.0, 8.5 Hz, 1H), 7.00 (d, *J* = 8.0 Hz, 1H), 6.95 (d, *J* = 8.5 Hz, 1H), 3.96 (s, 3H), 1.34 (s, 9H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 157.0, 149.4, 147.0, 135.7, 129.3, 128.7, 125.1, 116.7, 114.5, 114.3, 108.5, 55.9, 20.7 ppm.

(*E*)-4-((5′-Chloro-2′-hydroxyphenylimino)methyl)-2-methoxyphenol (1e):



Yield: 2.46 g (89%) as brown solid.

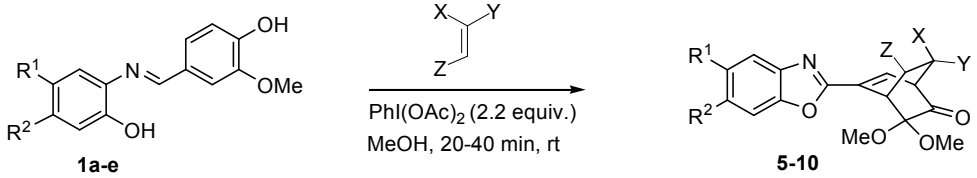
Mp: 121-122 °C.

IR (KBr): ν_{max} 3469, 1630, 1581, 1508, 1386, 1279 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.50 (s, 1H), 7.52 (d, *J* = 1.5 Hz, 1H), 7.32 (dd, *J* = 1.5, 8.0 Hz, 1H), 7.22 (d, *J* = 2.5 Hz, 1H), 7.12 (d, *J* = 2.5, 9.0 Hz, 1H), 7.01 (d, *J* = 8.0 Hz, 1H), 6.93 (d, *J* = 8.5 Hz, 1H), 3.98 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 158.7, 155.9, 149.7, 147.1, 135.9, 129.9, 128.3, 125.5, 122.1, 117.8, 114.6, 114.5, 108.8, 52.0 ppm.

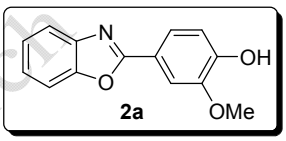
3.2.2. General procedure for the synthesis of 5-(benz[*d*]oxazol-2′-yl)bicyclo[2.2.2]-octen-2-one derivatives 5-10:



To a solution of aldimine **1** (0.5 mmol) and a dienophile [ethyl vinyl ether / dihydrofuran (5 eqiv.) styrene/ furan/ methyl acrylate/ methyl methacrylate (20 equiv)] in

methanol (5 mL), diacetoxyiodobenzene (DIB, 177 mg, 0.55 mmol) was added portion-wise at room temperature over a period of 5 min. and the resultant solution was allowed to stir for 5 min. After complete disappearance of starting material as shown by TLC, another portion of DIB (177 mg, 0.55 mmol) was added over a period of 5 min. and allowed to stir for additional 5 min. (25 min. in case of electron-deficient dienophile) at room temperature. After completion of the reaction as indicated by TLC, methanol was evaporated under reduced pressure and the crude reaction mixture was purified by silica gel column chromatography with (20-30%) ethyl acetate/hexanes as eluting system.

4-(Benz[*d*]oxazol-2′-yl)-2-methoxyphenol (2a):



2a

Yield: 97 mg (80%) as white solid.

Mp: 164-165 ^{o}C.

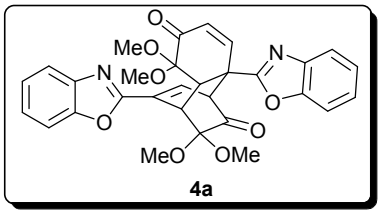
IR (KBr): ν_{max} 2924, 1601, 1500, 1457, 1302, 1255, 1180 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.81 (dd, *J* = 2.0, 8.5 Hz, 1H), 7.77 (d, *J* = 2.0 Hz, 1H), 7.74-7.72 (m, 1H), 7.56-7.54 (m, 1H), 7.34-7.31 (m, 2H), 7.05 (d, *J* = 8.0 Hz, 1H), 6.20 (br s, 1H), 4.01 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 163.2 (C), 150.7 (C), 149.1 (C), 146.9 (C), 142.2 (C), 124.7 (CH), 124.5 (CH), 121.9 (CH), 119.6 (CH), 119.3 (C), 114.8 (CH), 110.4 (CH), 109.8 (CH), 56.2 (OCH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{14}H_{12}NO_3+1]^+$: 242.0817, found: 242.0811.

(1*S,2*S**,7*R**,8*R**)-7,11-(bis-Benz[*d*]oxazol-2′-yl)-3,3,10,10-tetramethoxytricyclo-[6.2.2.0^{2,7}]dodeca-5,11-diene-4,9-dione (4a):**



4a

Yield: 106 mg (79%) as yellow solid.

Mp: 200-201 ^{o}C.

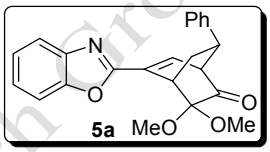
IR (KBr): ν_{max} 2947, 2830, 1745, 1708, 1590, 1533, 1449, 1237, 1115 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.78-7.75 (m, 2H), 7.56-7.54 (m, 1H), 7.50-7.48 (m, 1H), 7.40-7.36 (m, 2H), 7.35-7.30 (m, 2H), 7.02 (dd, *J* = 2.0, 7.0 Hz, 1H), 6.98 (d, *J* = 10.0 Hz, 1H), 6.17 (d, *J* = 10.0 Hz, 1H), 4.46 (s, 1H), 4.35 (t, *J* = 2.0 Hz, 1H), 3.76 (d, *J* = 7.0 Hz, 1H), 3.59 (s, 3H), 3.54 (s, 3H), 3.38 (s, 3H), 3.00 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 197.8 (cabonyl C=O), 192.0 (carbonyl C=O), 164.9 (C), 159.0 (C), 150.8 (C), 150.5 (C), 143.8 (CH), 141.5 (C), 140.6 (C), 132.7 (C), 130.7 (CH), 128.7 (CH), 125.7 (CH), 125.3 (CH), 124.6 (CH), 124.3 (CH), 120.8 (CH), 120.3 (CH), 110.5 (CH), 110.4 (CH), 97.5 (C_{acetal}), 94.1 (C_{acetal}), 58.9 (CH), 51.1 (OCH_3), 50.0 (OCH_3), 49.9 (OCH_3), 49.5 (OCH_3), 48.8 (C), 43.5 (CH), 41.2 (CH) ppm.

HRMS (ES$^+$): *m/z* calcd for $[C_{30}H_{26}N_2O_8+Na]^+$: 565.1581, found: 565.1587.

(1*S,4*R**,7*S**)-5-(Benz[*d*]oxazol-2′-yl)-3,3-dimethoxy-7-phenylbicyclo[2.2.2]oct-5-en-2-one (5a):**



Yield: 121 mg (65%) as yellow solid.

Mp: 99-100 ^oC.

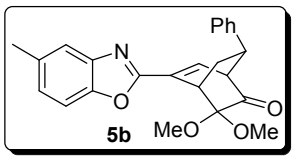
IR (KBr): ν_{max} 2949, 2830, 1737, 1633, 1529, 1447, 1132 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.76-7.49 (m, 1H), 7.52-7.49 (m, 1H), 7.34-7.30 (m, 2H), 7.25-7.22 (m, 2H), 7.20-7.16 (m, 2H), 7.14-7.12 (m, 2H), 4.28 (q, *J* = 2.5 Hz, 1H), 3.60-3.55 (m, 1H), 3.54 (dd, *J* = 1.5, 6.5 Hz, 1H), 3.49 (s, 3H), 3.41 (s, 3H), 2.74 (ddd, *J* = 3.0, 8.5, 13.0 Hz, 1H), 1.78 (ddd, *J* = 2.5, 6.5, 13.5 Hz, 1H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 199.7 (carbonyl C=O), 160.0 (C), 150.5 (C), 143.1 (C), 141.5 (C), 134.4 (C), 129.5 (CH), 128.4 (CH), 127.1 (CH), 126.7 (CH), 125.4 (CH), 124.3 (CH), 120.0 (CH), 110.3 (CH), 93.2 (C_{acetal}), 55.7 (CH), 50.3 (OCH_3), 49.9 (OCH_3), 40.4 (CH), 40.0 (CH), 29.7 (CH_2) ppm.

HRMS (ES$^+$): *m/z* calcd for $[C_{23}H_{21}NO_4+Na]^+$: 398.1363, found: 398.1363.

(1*S,4*R**,7*S**)-3,3-Dimethoxy-5-(5′-methylbenz[*d*]oxazol-2′-yl)-7-phenylbicyclo[2.2.2]-oct-5-en-2-one (5b):**



Yield: 131 mg (67%) as yellow solid.

Mp: 141-142 ^oC.

IR (KBr): ν_{max} 2942, 2839, 1744, 1647, 1534, 1452, 1139 cm^{-1}.

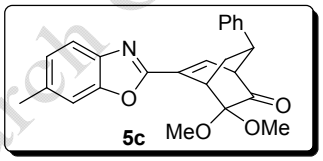
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52 (s, 1H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.24 (d, *J* = 3.0 Hz, 1H), 7.23 (s, 1H), 7.20 (d, *J* = 7.0 Hz, 1H), 7.16 (d, *J* = 9.5 Hz, 1H), 7.14-7.11 (m, 3H), 4.23 (q, *J* = 2.5 Hz, 1H), 3.56-3.53 (m, 1H), 3.51 (dd, *J* = 1.5, 6.5 Hz, 1H), 3.47 (s, 3H), 3.37 (s,

3H), 2.70 (ddd, *J* = 3.0, 9.5, 13.0 Hz, 1H), 2.46 (s, 3H), 1.76 (ddd, *J* = 2.5, 7.0, 13.5 Hz, 1H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 200.1 (carbonyl C=O), 160.3 (C), 148.9 (C), 143.3 (C), 141.8 (C), 134.7 (C), 134.4 (C), 129.2 (CH), 128.6 (CH), 127.3 (CH), 126.9 (CH), 126.8 (CH), 120.1 (CH), 109.8 (CH), 93.4 (C_{acetal}), 55.8 (CH), 50.5 (OCH_3), 50.2 (OCH_3), 40.6 (CH), 40.2 (CH), 30.0 (CH_2), 21.4 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{24}H_{23}NO_4+Na]^+$: 412.1525, found: 412.1522.

(1*S,4*R**,7*S**)-3,3-Dimethoxy-5-(6′-methylbenz[*d*]oxazol-2′-yl)-7-phenylbicyclo[2.2.2]-oct-5-en-2-one (5c):**



Yield: 123 mg (64%) as pale yellow solid.

Mp: 99-100 °C.

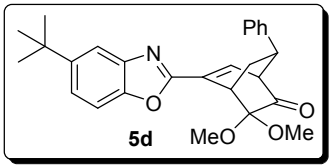
IR (KBr): ν_{max} 2937, 2834, 1742, 1631, 1530, 1449, 1245, 1128 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.62 (d, *J* = 8.0 Hz, 1H), 7.32 (s, 1H), 7.26-7.22 (m, 2H), 7.20-7.11 (m, 5H), 4.25 (q, *J* = 3.0 Hz, 1H), 3.58-3.54 (m, 1H), 3.52 (dd, *J* = 1.5, 6.5 Hz, 1H), 3.49 (s, 3H), 3.40 (s, 3H), 2.72 (ddd, *J* = 3.0, 9.5, 13.0 Hz, 1H), 2.48 (s, 3H), 1.77 (ddd, *J* = 3.0, 7.0, 13.5 Hz, 1H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 200.0 (carbonyl C=O), 159.7 (C), 151.0 (C), 143.3 (C), 139.5 (C), 136.2 (C), 134.7 (C), 128.9 (CH), 128.6 (CH), 127.3 (CH), 126.8 (CH), 125.8 (CH), 119.6 (CH), 110.6 (CH), 93.4 (C_{acetal}), 55.8 (CH), 50.5 (OCH_3), 50.1 (OCH_3), 40.6 (CH), 40.2 (CH), 29.9 (CH_2), 21.7 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{24}H_{23}NO_4+Na]^+$: 412.1519, found: 412.1513.

(1*S,4*R**,7*S**)-5-(5′-*tert*-Butylbenz[*d*]oxazol-2′-yl)-3,3-dimethoxy-7-phenylbicyclo[2.2.2]-oct-5-en-2-one (5d):**



Yield: 113 mg (52%) as pale yellow liquid.

IR (KBr): ν_{max} 2958, 2934, 1740, 1639, 1532, 1475, 1268, 1197 cm^{-1}.

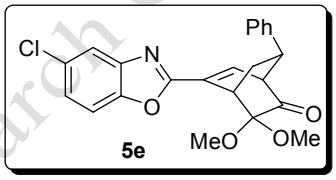
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.80-7.79 (m, 1H), 7.45-7.44 (m, 2H), 7.27-7.24 (m, 2H), 7.22-7.18 (m, 1H), 7.15-7.12 (m, 3H), 4.26 (q, *J* = 2.5 Hz, 1H), 3.58-3.55 (m, 1H), 3.52 (dd,

J = 1.5, 6.5 Hz, 1H), 3.49 (s, 3H), 3.40 (s, 3H), 2.73 (ddd, *J* = 3.0, 9.5, 13.0 Hz, 1H), 1.78 (ddd, *J* = 2.5, 6.5, 13.5 Hz, 1H), 1.39 (s, 9H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 200.3 (carbonyl C=O), 160.5 (C), 148.8 (C), 148.3 (C), 143.4 (C), 141.6 (C), 134.8 (C), 129.2 (CH), 128.7 (CH), 127.4 (CH), 127.0 (CH), 123.5 (CH), 116.8 (CH), 109.7 (CH), 93.5 (C_{acetal}), 56.0 (CH), 50.6 (OCH_3), 50.2 (OCH_3), 40.8 (CH), 40.3 (CH), 34.9 (C), 31.7 (CH_3), 30.0 (CH_2) ppm.

HRMS (ES$^+$): *m/z* calcd for $[C_{27}H_{29}NO_4+Na]^+$: 454.1989, found: 454.1976.

(1*S,4*R**,7*S**)-5-(5′-Chlorobenz[*d*]oxazol-2′-yl)-3,3-dimethoxy-7-phenylbicyclo[2.2.2]-oct-5-en-2-one (5e):**



5e

Yield: 142 mg (69%) as orange solid.

Mp: 173-174 ^oC.

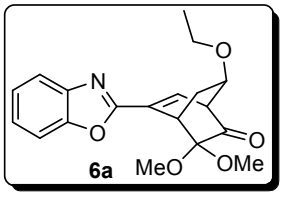
IR (KBr): ν_{max} 2943, 2836, 1736, 1626, 1527, 1453, 1127 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.73 (d, *J* = 2.0 Hz, 1H), 7.45 (d, *J* = 8.5 Hz, 1H), 7.32 (dd, *J* = 2.0, 8.5 Hz, 1H), 7.28-7.25 (m, 2H), 7.22-7.19 (m, 2H), 7.14-7.12 (m, 2H), 4.23 (q, *J* = 3.0 Hz, 1H), 3.60-3.58 (m, 1H), 3.56 (dd, *J* = 1.5, 6.5 Hz, 1H), 3.49 (s, 3H), 3.39 (s, 3H), 2.74 (ddd, *J* = 3.0, 10.0, 13.5 Hz, 1H), 1.78 (ddd, *J* = 3.0, 7.0, 13.5 Hz, 1H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 199.9 (carbonyl C=O), 161.4 (C), 149.3 (C), 143.2 (C), 142.8 (C), 134.3 (C), 130.7 (CH), 130.0 (C), 128.7 (CH), 127.3 (CH), 127.0 (CH), 125.9 (CH), 120.2 (CH), 111.2 (CH), 93.3 (C_{acetal}), 56.0 (CH), 50.6 (OCH_3), 50.2 (OCH_3), 40.6 (CH), 40.2 (CH), 29.9 (CH_2) ppm.

HRMS (ES$^+$): *m/z* calcd for $[C_{23}H_{20}ClNO_4+Na]^+$: 432.0973, found: 432.0991.

(1*S,4*R**,7*S**)-5-(Benz[*d*]oxazol-2′-yl)-3,3-dimethoxy-7-ethoxybicyclo[2.2.2]oct-5-en-2-one (6a):**



6a

Yield: 142 mg (82%) as yellow solid.

Mp: 101-102 ^oC.

IR (KBr): ν_{max} 2939, 2842, 1738, 1643, 1531, 1447, 1191 cm^{-1}.

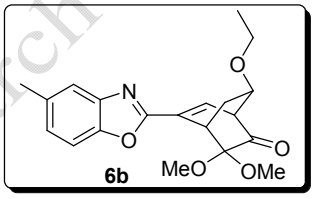
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.68-7.67 (m, 1H), 7.46-7.43 (m, 1H), 7.29-7.24 (m, 2H), 7.04 (d, *J* = 6.0 Hz, 1H), 4.07-4.06 (m, 2H), 3.78 (dd, *J* = 2.0, 6.0 Hz, 1H), 3.52-3.45 (m,

1H), 3.41-3.35 (m, 1H), 3.34 (s, 3H), 3.28 (s, 3H), 2.55 (ddd, *J* = 2.5, 8.0, 13.5 Hz, 1H), 1.46 (td, *J* = 3.0, 13.5 Hz, 1H), 1.10 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 199.9 (carbonyl C=O), 160.2 (C), 150.6 (C), 141.6 (C), 133.6 (C), 128.8 (CH), 125.5 (CH), 124.4 (CH), 120.1 (CH), 110.4 (CH), 93.3 (C_{acetal}), 74.9 (CH), 64.4 (CH_2), 54.7 (CH), 50.6 (OCH_3), 49.8 (OCH_3), 38.8 (CH), 30.0 (CH_2), 15.2 (CH_3) ppm.

HRMS (ES$^+$): *m/z* calcd for $[C_{19}H_{21}NO_5+Na]^+$: 366.1312, found: 366.1329.

(1*S,4*R**,7*S**)-3,3-Dimethoxy-7-ethoxy-5-(5′-methylbenz[*d*]oxazol-2′-yl)bicyclo[2.2.2]-oct-5-en-2-one (6b):**



6b

Yield: 142 mg (80%) as yellow solid.

Mp: 109-110 ^oC.

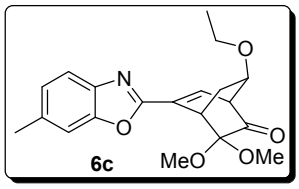
IR (KBr): ν_{max} 2972, 2843, 1738, 1643, 1534, 1447, 1128 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.50 (s, 1H), 7.37 (d, *J* = 8.5 Hz, 1H), 7.15 (dd, *J* = 1.5, 8.5 Hz, 1H), 7.06 (d, *J* = 6.5 Hz, 1H), 4.14-4.09 (m, 2H), 3.82 (dd, *J* = 2.5, 6.5 Hz, 1H), 3.57-3.51 (m, 1H), 3.46-3.41 (m, 1H), 3.38 (s, 3H), 3.32 (s, 3H), 2.59 (ddd, *J* = 3.0, 8.5, 14.0 Hz, 1H), 2.46 (s, 3H), 1.50 (td, *J* = 3.5, 14.0 Hz, 1H), 1.15 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 200.1 (carbonyl C=O), 160.3 (C), 148.9 (C), 141.8 (C), 134.3 (C), 133.8 (C), 128.4 (CH), 126.8 (CH), 120.1 (CH), 109.8 (CH), 93.4 (C_{acetal}), 75.0 (CH), 64.5 (CH_2), 54.6 (CH), 50.7 (OCH_3), 49.9 (OCH_3), 38.8 (CH), 30.1 (CH_2), 21.5 (CH_3), 15.2 (CH_3) ppm.

HRMS (ES$^+$): *m/z* calcd for $[C_{20}H_{23}NO_5+Na]^+$: 380.1474, found: 380.1462.

(1*S,4*R**,7*S**)-3,3-Dimethoxy-7-methoxy-5-(6′-methylbenz[*d*]oxazol-2′-yl)bicyclo[2.2.2] -oct-5-en-2-one (6c)**:



6c

Yield: 146 mg (82%) as thick brown liquid.

IR (KBr): ν_{max} 2934, 2865, 1741, 1638, 1533, 1449, 1244, 1102 cm^{-1}.

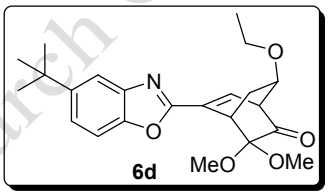
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.58 (d, *J* = 8.0 Hz, 1H), 7.29 (s, 1H), 7.12 (d, *J* = 8.0 Hz, 1H), 7.04 (d, *J* = 6.0 Hz, 1H), 4.12-4.08 (m, 2H), 3.81 (dd, *J* = 2.5, 6.0 Hz, 1H), 3.56-3.50

(m, 1H), 3.46-3.40 (m, 1H), 3.38 (s, 3H), 3.32 (s, 3H), 2.59 (ddd, *J* = 2.5, 8.5, 14.0 Hz, 1H), 2.47 (s, 3H), 1.50 (td, *J* = 3.5, 14.0 Hz, 1H), 1.48 (t, *J* = 6.5 Hz, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 200.2 (carbonyl C=O), 159.8 (C), 151.0 (C), 139.4 (C), 136.2 (C), 133.8 (C), 128.1 (CH), 125.8 (CH), 119.5 (CH), 110.6 (CH), 93.4 (C_{acetal}), 75.0 (CH), 64.4 (CH_2), 54.7 (CH), 50.7 (OCH_3), 49.9 (OCH_3), 38.9 (CH), 30.1 (CH_2), 21.8 (CH_3), 15.2 (CH_3) ppm.

HRMS (ES$^+$): *m/z* calcd for $[C_{20}H_{23}NO_5+Na]^+$: 380.1474, found: 380.1465.

(1*S,4*R**,7*S**)-5-(5′-*tert*-Butylbenz[*d*]oxazol-2′-yl)-3,3-dimethoxy-7-ethoxybicyclo[2.2.2]-oct-5-en-2-one (6d):**



6d

Yield: 124 mg (62%) as pale yellow liquid.

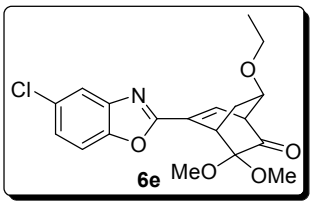
IR (KBr): ν_{max} 2965, 2865, 1741, 1639, 1534, 1475, 1360, 1271, 1103 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75 (s, 1H), 7.41-7.39 (m, 2H), 7.05 (dd, *J* = 1.5, 6.5 Hz, 1H), 4.12-4.09 (m, 2H), 3.81 (dd, *J* = 2.5, 6.5 Hz, 1H), 3.56-3.50 (m, 1H), 3.45-3.40 (m, 1H), 3.38 (s, 3H), 3.31 (s, 3H), 2.59 (ddd, *J* = 2.5, 8.0, 13.5 Hz, 1H), 1.49 (td, *J* = 3.5, 14.0 Hz, 1H), 1.36 (s, 9H), 1.14 (t, *J* = 5.5 Hz, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 200.0 (carbonyl C=O), 160.4 (C), 148.7 (C), 148.0 (C), 141.5 (C), 133.8 (C), 128.3 (CH), 123.4 (CH), 116.7 (CH), 109.6 (CH), 93.4 (C_{acetal}), 75.0 (CH), 64.4 (CH_2), 54.6 (CH), 50.7 (OCH_3), 49.9 (OCH_3), 38.9 (CH), 34.8 (C), 31.7 (CH_3), 30.1 (CH_2), 15.2 (CH_3) ppm.

HRMS (ES$^+$): *m/z* calcd for $[C_{23}H_{29}NO_5+Na]^+$: 422.1938, found: 422.1941.

(1*S,4*R**,7*S**)-5-(5′-Chlorobenz[*d*]oxazol-2′-yl)-3,3-dimethoxy-7-ethoxybicyclo[2.2.2]-oct-5-en-2-one (6e):**



6e

Yield: 154 mg (82%) as orange solid.

Mp: 80 ^{o}C.

IR (KBr): ν_{max} 2978, 2839, 1740, 1637, 1529, 1448, 1126 cm^{-1}.

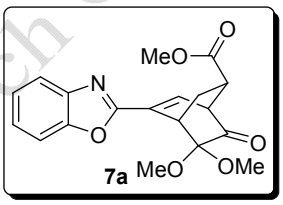
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.70-7.69 (m, 1H), 7.42 (d, *J* = 8.5 Hz, 1H), 7.33-7.30 (m, 1H), 7.11 (d, *J* = 7.5 Hz, 1H), 4.14-4.11 (m, 1H), 4.09-4.07 (m, 1H), 3.84 (dd, *J* = 2.5, 6.0

Hz, 1H), 3.57-3.51 (m, 1H), 3.46-3.40 (m, 1H), 3.38 (s, 3H), 3.31 (s, 3H), 2.60 (ddd, *J* = 2.5, 8.5, 14.0 Hz, 1H), 1.50 (td, *J* = 3.5, 14.0 Hz, 1H), 1.15 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 199.8 (carbonyl C=O), 161.4 (C), 149.2 (C), 142.7 (C), 133.3 (C), 129.9 (C), 129.8 (CH), 125.8 (CH), 120.1 (CH), 111.2 (CH), 93.2 (C_{acetal}), 74.9 (CH), 64.5 (CH_2), 54.7 (CH), 50.7 (OCH_3), 49.8 (OCH_3), 38.8 (CH), 30.0 (CH_2), 15.2 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{19}H_{20}ClNO_5+Na]^+$: 400.0928, found: 400.0917.

(1*S,4*R**,7*S**)-5-(Benz[*d*]oxazol-2′-yl)-3,3-dimethoxy-7-ethoxycarbonylbicyclo[2.2.2]-oct-5-en-2-one (7a):**



7a

Yield: 112 mg (62%) as thick yellow liquid.

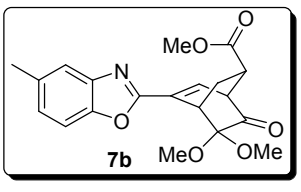
IR (KBr): ν_{max} 2952, 2839, 1737, 1636, 1525, 1443, 1332, 1165 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.73-7.69 (m, 1H), 7.49-7.46 (m, 1H), 7.34-7.29 (m, 2H), 7.15-7.13 (m, 1H), 4.18 (q, *J* = 2.5 Hz, 1H), 3.76 (dd, *J* = 2.0, 7.0 Hz, 1H), 3.66 (s, 3H), 3.40 (s, 3H), 3.33 (s, 3H), 3.19 (ddd, *J* = 1.5, 6.0, 10.0 Hz, 1H), 2.49 (ddd, *J* = 3.0, 10.0, 13.5 Hz, 1H), 1.88 (ddd, *J* = 3.0, 6.0, 13.5 Hz, 1H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 199.4 (carbonyl C=O), 172.8 (ester C=O), 160.0 (C), 150.6 (C), 141.5 (C), 134.4 (C), 129.4 (CH), 125.7 (CH), 124.5 (CH), 120.2 (CH), 110.4 (CH), 93.4 (C_{acetal}), 52.4 (OCH_3), 50.6 (CH), 50.6 (OCH_3), 50.1 (OCH_3), 39.5 (CH), 39.3 (CH), 24.7 (CH_2) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{19}H_{19}NO_6+Na]^+$: 380.1105, found: 380.1102.

(1*S,4*R**,7*S**)-3,3-Dimethoxy-7-methoxycarbonyl-5-(5′-methylbenz[*d*]oxazol-2′-yl)-bicyclo[2.2.2]oct-5-en-2-one (7b):**



7b

Yield: 109 mg (59%) as pale yellow solid.

Mp: 118-119 °C.

IR (KBr): ν_{max} 2946, 2838, 1738, 1633, 1527, 1440, 1323, 1143 cm^{-1}.

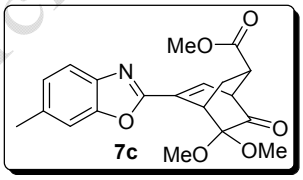
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.49 (s, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.12 (dt, *J* = 1.5, 9.0

Hz, 2H), 4.17 (q, *J* = 2.5 Hz, 1H), 3.75 (dd, *J* = 2.0, 6.5 Hz, 1H), 3.66 (s, 3H), 3.40 (s, 3H), 3.34 (s, 3H), 3.19 (ddd, *J* = 1.5, 6.0, 10.0 Hz, 1H), 2.49 (ddd, *J* = 2.5, 10.0, 13.0 Hz, 1H), 2.44 (s, 3H), 1.88 (ddd, *J* = 3.0, 6.0, 13.5 Hz, 1H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 199.4 (carbonyl C=O), 172.8 (ester C=O), 160.0 (C), 148.9 (C), 141.7 (C), 134.6 (C), 134.4 (C), 129.0 (CH), 126.9 (CH), 120.1 (CH), 109.8 (CH), 93.4 (C_{acetal}), 52.4 (OCH_3), 50.6 (CH), 50.5 (OCH_3), 50.1 (OCH_3), 39.6 (CH), 39.4 (CH), 24.8 (CH_2), 21.4 (CH_3) ppm.

HRMS (ES$^+$): *m/z* calcd for $[C_{20}H_{21}NO_6+Na]^+$: 394.1261, found: 394.1253.

(1*S,4*R**,7*S**)-3,3-Dimethoxy-7-methoxycarbonyl-5-(6′-methylbenz[*d*]oxazol-2′-yl)-bicyclo[2.2.2]oct-5-en-2-one (7c):**



Yield: 103 mg (56%) as pale yellow solid.

Mp: 95-96 ^oC.

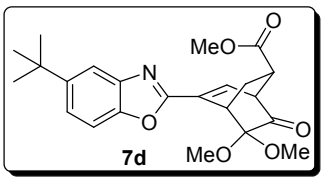
IR (KBr): ν_{max} 2952, 2839, 1740, 1626, 1528, 1444, 1327, 1184, 1136 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.57 (d, *J* = 8.0 Hz, 1H), 7.28 (s, 1H), 7.13-7.09 (m, 2H), 4.17-4.16 (m, 1H), 3.75 (d, *J* = 6.5 Hz, 1H), 3.67 (s, 3H), 3.40 (s, 3H), 3.34 (s, 3H), 3.21-3.17 (m, 1H), 2.51-2.48 (m, 1H), 2.46 (s, 3H), 1.88 (ddd, *J* = 2.5, 6.0, 13.0 Hz, 1H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 199.5 (carbonyl C=O), 172.8 (ester C=O), 159.5 (C), 151.0 (C), 139.4 (C), 136.3 (C), 134.6 (C), 128.7 (CH), 125.8 (CH), 119.6 (CH), 110.6 (CH), 93.5 (C_{acetal}), 52.4 (OCH_3), 50.6 (CH), 50.1 (OCH_3), 39.6 (CH), 39.4 (CH), 24.8 (CH_2), 21.8 (CH_3) ppm.

HRMS (ES$^+$): *m/z* calcd for $[C_{20}H_{21}NO_6+Na]^+$: 394.1261, found: 394.1251.

(1*S,4*R**,7*S**)-5-(5′-*tert*-Butylbenz[*d*]oxazol-2′-yl)-3,3-dimethoxy-7-methoxycarbonyl-bicyclo[2.2.2]oct-5-en-2-one (7d):**



Yield: 118 mg (57%) as yellow solid.

Mp: 94-95 ^oC.

IR (KBr): ν_{max} 2952, 2839, 1740, 1626, 1526, 1444, 1327, 1184 cm^{-1}.

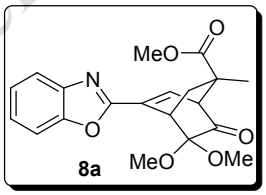
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.74 (s, 1H), 7.40 (s, 2H), 7.11 (dd, *J* = 2.0, 6.5 Hz, 1H),

4.18 (q, *J* = 2.5 Hz, 1H), 3.76 (dd, *J* = 2.0, 6.5 Hz, 1H), 3.66 (s, 3H), 3.40 (s, 3H), 3.34 (s, 3H), 3.20 (ddd, *J* = 1.5, 6.0, 10.0 Hz, 1H), 2.49 (ddd, *J* = 3.0, 10.5, 13.5 Hz, 1H), 1.88 (ddd, *J* = 3.0, 6.0, 13.5 Hz, 1H), 1.35 (s, 9H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 199.5 (carbonyl C=O), 172.8 (ester C=O), 160.1 (C), 148.7 (C), 148.1 (C), 141.4 (C), 134.6 (C), 128.9 (CH), 123.5 (CH), 116.7 (CH), 109.6 (CH), 93.5 (C_{acetal}), 52.4 (OCH_3), 50.6 (CH), 50.6 (OCH_3), 50.1 (OCH_3), 39.6 (CH), 39.4 (CH), 34.8 (C), 31.6 (CH_3), 24.7 (CH_2) ppm.

HRMS (ES$^+$): *m/z* calcd for $[C_{23}H_{27}NO_6+Na]^+$: 436.1736, found: 436.1736.

(1*S,4*R**,7*S**)-5-(Benz[*d*]oxazol-2′-yl)-3,3-dimethoxy-7-methoxycarbonyl-7-methyl-bicyclo[2.2.2]oct-5-en-2-one (8a):**



8a

Yield: 121 mg (66%) as yellow solid.

Mp: 101-102 ^oC.

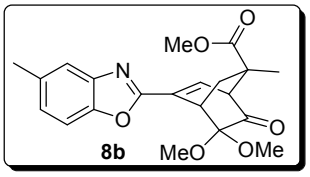
IR (KBr): ν_{max} 2949, 2843, 1739, 1634, 1531, 1447, 1204, 1149 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.71 (d, *J* = 7.5 Hz, 1H), 7.47 (d, *J* = 7.5 Hz, 1H), 7.34-7.28 (m, 2H), 7.18 (d, *J* = 6.5 Hz, 1H), 4.12-4.11 (m, 1H), 3.65 (s, 3H), 3.61 (d, *J* = 6.5 Hz, 1H), 3.42 (s, 3H), 3.32 (s, 3H), 2.40 (dd, *J* = 3.5, 14.0 Hz, 1H), 2.07 (dd, *J* = 2.0, 14.0 Hz, 1H), 1.39 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 200.7 (carbonyl C=O), 175.7 (ester C=O),160.1 (C), 150.6 (C), 141.6 (C), 133.8 (CH), 131.5 (CH), 125.7 (CH), 124.5 (CH), 120.2 (CH), 110.5 (C), 93.6 (C_{acetal}), 57.1 (CH), 52.6 (OCH_3), 50.6 (OCH_3), 49.8 (OCH_3), 47.1 (C), 39.6 (CH), 32.0 (CH_2), 25.5 (CH_3) ppm.

HRMS (ES$^+$): *m/z* calcd for $[C_{20}H_{21}NO_6+Na]^+$: 394.1261, found: 394.1247.

(1*S,4*R**,7*S**)-3,3-Dimethoxy-7-methoxycarbonyl-7-methyl-5-(5′-methylbenz[*d*]oxazol-2′-yl)bicyclo[2.2.2]oct-5-en-2-one (8b):**



8b

Yield: 106 mg (55%) as brown solid.

Mp: 98-99 ^oC.

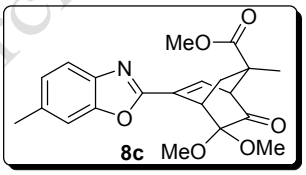
IR (KBr): ν_{max} 2949, 2839, 1738, 1634, 1530, 1452, 1382, 1256, 1113 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.48 (s, 1H), 7.34 (d, *J* = 8.5 Hz, 1H), 7.16-7.11 (m, 2H), 4.11-4.09 (m, 1H), 3.65 (s, 3H), 3.60 (d, *J* = 6.5 Hz, 1H), 3.42 (s, 3H), 3.32 (s, 3H), 2.43 (s, 3H), 2.39 (dd, *J* = 3.5, 14.0 Hz, 1H), 2.07 (dd, *J* = 2.5, 14.0 Hz, 1H), 1.38 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 200.7 (carbonyl C=O), 175.7 (ester C=O), 160.2 (C), 148.9 (C), 141.7 (C), 134.3 (C), 133.9 (C), 131.1 (CH), 126.8 (CH), 120.1 (CH), 109.8 (CH), 93.6 (C_{acetal}), 57.1 (CH), 52.6 (OCH_3), 50.5 (OCH_3), 49.8 (OCH_3), 47.1 (C), 39.6 (CH), 32.0 (CH_2), 25.5 (CH_3), 21.4 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{21}H_{23}NO_6+Na]^+$: 408.1418, found: 408.1401.

(1*S,4*R**,7*S**)-3,3-Dimethoxy-7-methoxycarbonyl-7-methyl-5-(6′-methylbenz[*d*]oxazol-2′-yl)bicyclo-[2.2.2]oct-5-en-2-one (8c):**



Yield: 106 mg (55%) as white solid.

Mp: 109-110 °C.

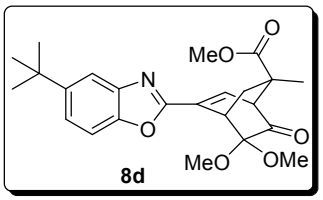
IR (KBr): ν_{max} 2951, 2837, 1733, 1625, 1530, 1446, 1326, 1211, 1144 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55 (d, *J* = 8.5 Hz, 1H), 7.25 (s, 1H), 7.13-7.09 (m, 2H), 4.08-4.07 (m, 1H), 3.64 (s, 3H), 3.59 (d, *J* = 6.0 Hz, 1H), 3.41 (s, 3H), 3.31 (s, 3H), 2.44 (s, 3H), 2.38 (dd, *J* = 3.5, 14.0 Hz, 1H), 2.05 (dd, *J* = 2.5, 14.0 Hz, 1H), 1.37 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 200.6 (carbonyl C=O), 175.7 (ester C=O), 159.7 (C), 150.9 (C), 139.3 (C), 136.2 (C), 133.9 (C), 130.7 (CH), 125.7 (CH), 119.5 (CH), 110.5 (CH), 93.6 (C_{acetal}), 57.0 (CH), 52.5 (OCH_3), 50.5 (OCH_3), 49.8 (OCH_3), 47.1 (C), 39.6 (CH), 31.9 (CH_2), 25.4 (CH_3), 21.7 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{21}H_{23}NO_6+Na]^+$: 408.1418, found: 408.1402.

(1*S,4*R**,7*S**)-5-(5′-*tert*-Butylbenz[*d*]oxazol-2′-yl)-3,3-dimethoxy-7-methoxycarbonyl-7-methylbicyclo[2.2.2]oct-5-en-2-one (8d):**



Yield: 114 mg (53%) as yellow solid.

Mp: 90 °C.

IR (KBr): ν_{max} 2961, 2878, 1734, 1634, 1534, 1468, 1382, 1264, 1208, 1114 cm^{-1}.

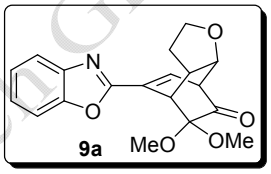
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.74 (s, 1H), 7.39 (s, 2H), 7.14 (dd, *J* = 2.0, 6.5 Hz, 1H), 4.11-4.10 (m, 1H), 3.65 (s, 3H), 3.61 (d, *J* = 6.5 Hz, 1H), 3.42 (s, 3H), 3.22 (s, 3H), 2.39 (dd,

J = 3.5, 14.0 Hz, 1H), 2.07 (dd, *J* = 2.5, 14.0 Hz, 1H), 1.38 (s, 3H), 1.35 (s, 9H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 200.7 (carbonyl C=O), 175.7 (ester C=O), 160.3 (C), 148.7 (C), 148.1 (C), 141.5 (C), 133.9 (C), 131.0 (CH), 123.5 (CH), 116.7 (CH), 109.6 (CH), 93.7 (C_{acetal}), 57.1 (CH), 52.6 (OCH_3), 50.5 (OCH_3), 49.8 (OCH_3), 47.2 (C), 39.7 (CH), 34.8 (C), 32.0 (CH_2), 31.7 (CH_3), 25.5 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{24}H_{29}NO_6 + Na]^+$: 450.1893, found: 450.1893.

(1*R,2*R**,6*R**,7*S**)-11-(Benz[*d*]oxazol-2′-yl)-8,8-dimethoxy-3-oxatricyclo[5.2.2.0^{2,6}]-undec-10-en-9-one (9a):**



9a

Yield: 124 mg (73%) as green colour solid.

Mp: 107-108 °C.

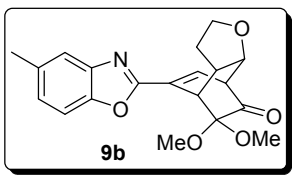
IR (KBr): ν_{max} 2939, 2843, 1737, 1643, 1539, 1448, 1230, 1146 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.76-7.73 (m, 1H), 7.52-7.50 (m, 1H), 7.38-7.31 (m, 2H), 7.14-7.11 (m, 1H), 4.47 (dd, *J* = 3.0, 8.0 Hz, 1H), 4.21 (t, *J* = 2.5 Hz, 1H), 3.84 (dd, *J* = 3.0, 6.0 Hz, 1H), 3.80-3.78 (m, 1H), 3.57-3.52 (m, 1H), 3.42 (s, 3H), 3.31 (s, 3H), 3.12 (ddd, *J* = 3.0, 8.0, 17.5 Hz, 1H), 2.18-2.11 (m, 1H), 1.57-1.50 (m, 1H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 199.7 (carbonyl C=O), 161.1 (C), 150.7 (C), 141.6 (C), 131.8 (CH), 130.5 (C), 125.8 (CH), 124.6 (CH), 120.3 (CH), 110.6 (CH), 93.1 (C_{acetal}), 79.2 (CH), 69.1 (CH_2), 55.7 (CH), 50.7 (OCH_3), 50.0 (OCH_3), 43.3 (CH), 38.3 (CH), 30.2 (CH_2) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{19}H_{19}NO_5 + Na]^+$: 364.1155, found: 364.1143.

(1*R,2*R**,6*R**,7*S**)-8,8-Dimethoxy-11-(5′-methylbenz[*d*]oxazol-2′-yl)-3-oxatricyclo-[5.2.2.0^{2,6}]undec-10-en-9-one (9b):**



9b

Yield: 126 mg (74%) as green solid.

Mp: 144-145 °C.

IR (KBr): ν_{max} 2939, 2878, 1737, 1636, 1526, 1451, 1262, 1146 cm^{-1}.

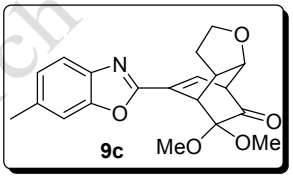
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.51 (s, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.15 (dd, *J* = 1.0, 8.5 Hz, 1H), 7.08 (d, *J* = 6.5 Hz, 1H), 4.45 (dd, *J* = 3.0, 8.5 Hz, 1H), 4.19 (t, *J* = 2.5 Hz, 1H), 3.82 (dd, *J* = 3.0, 6.5 Hz, 1H), 3.79 (dd, *J* = 3.0, 8.5 Hz, 1H), 3.56-3.50 (m, 1H), 3.40 (s,

3H), 3.30 (s, 3H), 3.11 (ddd, *J* = 3.0, 8.0, 18.0 Hz, 1H), 2.45 (s, 3H), 2.16-2.10 (m, 1H), 1.55-1.47 (m, 1H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 199.7 (carbonyl C=O), 161.7 (C), 148.9 (C), 141.8 (C), 134.4 (C), 131.9 (C), 130.0 (CH), 126.8 (CH), 120.1 (CH), 109.9 (CH), 93.0 (C_{acetal}), 79.1 (CH), 69.1 (CH_2), 55.6 (CH), 50.6 (OCH_3), 50.0 (OCH_3), 43.2 (CH), 38.2 (CH), 30.2 (CH_2), 21.4 (CH_3) ppm.

HRMS (ES$^+$): *m/z* calcd for $[C_{20}H_{21}NO_5+Na]^+$: 378.1312, found: 378.1312.

(1*R,2*R**,6*R**,7*S**)-8,8-Dimethoxy-11-(6′-methylbenz[*d*]oxazol-2′-yl)-3-oxatricyclo-[5.2.2.0^{2,6}]undec-10-en-9-one (9c):**



9c

Yield: 121 mg (69%) as brown solid.

Mp: 119-120 ^oC.

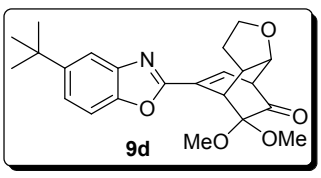
IR (KBr): ν_{max} 2939, 2863, 1735, 1630, 1530, 1449, 1232, 1141 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.61 (d, *J* = 8.0 Hz, 1H), 7.33 (s, 1H), 7.16 (d, *J* = 8.5 Hz, 1H), 7.10-7.08 (m, 1H), 4.48 (dd, *J* = 3.0, 8.5 Hz, 1H), 4.21 (t, *J* = 2.0 Hz, 1H), 3.84 (dd, *J* = 3.0, 6.5 Hz, 1H), 3.81 (dd, *J* = 3.0, 8.5 Hz, 1H), 3.58-3.53 (m, 1H), 3.42 (s, 3H), 3.32 (s, 3H), 3.12 (ddd, *J* = 3.0, 8.0, 17.5 Hz, 1H), 2.51 (s, 3H), 2.19-2.13 (m, 1H), 1.57-1.49 (m, 1H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 199.7 (carbonyl C=O), 160.6 (C), 150.8 (C), 139.2 (C), 136.3 (C), 131.7 (C), 129.7 (CH), 125.7 (CH), 119.5 (CH), 110.6 (CH), 93.0 (C_{acetal}), 79.0 (CH), 69.0 (CH_2), 55.5 (CH), 50.6 (OCH_3), 49.9 (OCH_3), 43.1 (CH), 38.1 (CH), 30.1 (CH_2), 21.7 (CH_3) ppm.

HRMS (ES$^+$): *m/z* calcd for $[C_{20}H_{21}NO_5+Na]^+$: 378.1312, found: 378.1320.

(1*R,2*R**,6*R**,7*S**)-11-(5′-*tert*-Butylbenz[*d*]oxazol-2′-yl)-8,8-dimethoxy-3-oxatricyclo-[5.2.2.0^{2,6}]undec-10-en-9-one (9d):**



9d

Yield: 106 mg (54%) as green colour solid.

Mp: 158-159 ^oC.

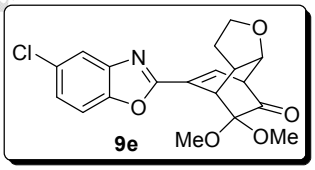
IR (KBr): ν_{max} 2952, 2894, 1743, 1639, 1532, 1269, 1141 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.80-7.77 (m, 1H), 7.43-7.42 (m, 2H), 7.10-7.08 (m, 1H), 4.46 (dd, *J* = 3.0, 8.0 Hz, 1H), 4.21-4.20 (m, 1H), 3.82 (dd, *J* = 3.0, 6.5 Hz, 1H), 3.79 (dt, *J* = 3.0, 8.5 Hz, 1H), 3.56-3.51 (m, 1H), 3.41 (s, 3H), 3.31 (s, 3H), 3.14-3.08 (m, 1H), 2.17-2.11 (m, 1H), 1.57-1.48 (m, 1H), 1.37 (s, 9H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 199.8 (carbonyl C=O), 161.3 (C), 148.7 (C), 148.2 (C), 141.5 (C), 131.9 (C), 130.0 (CH), 123.6 (CH), 116.8 (CH), 109.7 (CH), 93.1 (C_{acetal}), 79.2 (CH), 69.1 (CH_2), 55.7 (CH), 50.7 (OCH_3), 50.0 (OCH_3), 43.3 (CH), 38.2 (CH), 34.9 (C), 31.7 (CH_3), 30.2 (CH_2) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{23}H_{27}NO_5+Na]^+$: 420.1781, found: 420.1781.

(1*R,2*R**,6*R**,7*S**)-11-(5′-Chlorobenz[*d*]oxazol-2′-yl)-8,8-dimethoxy-3-oxatricyclo-[5.2.2.0^{2,6}]undec-10-en-9-one (9e):**



9e

Yield: 114 mg (62%) as yellow solid.

Mp: 127-128 ^oC.

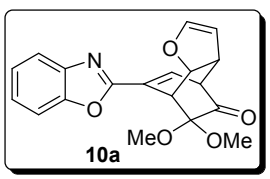
IR (KBr): ν_{max} 2940, 2882, 1740, 1589, 1499, 1450, 1275, 1218, 1130 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.71 (d, *J* = 2.0 Hz, 1H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.33 (d, *J* = 2.0, 9.0 Hz, 1H), 7.15-7.14 (m, 1H), 4.47 (dd, *J* = 3.0, 8.0 Hz, 1H), 4.18-4.17 (m, 1H), 3.85 (dd, *J* = 3.0, 6.5 Hz, 1H), 3.81 (dt, *J* = 3.0, 13.0 Hz, 1H), 3.57-3.52 (m, 1H), 3.42 (s, 3H), 3.31 (s, 3H), 3.15-3.09 (m, 1H), 2.19-2.14 (m, 1H), 1.54-1.46 (m, 1H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 199.6 (carbonyl C=O), 162.3 (C), 149.3 (C), 142.8 (C), 131.6 (C), 131.5 (CH), 130.1 (C),126.0 (CH), 120.3 (CH), 111.3 (CH), 93.0 (C_{acetal}), 79.2 (CH), 69.1 (CH_2), 55.8 (CH), 50.8 (OCH_3), 50.0 (OCH_3), 43.3 (CH), 38.2 (CH), 30.3 (CH_2) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{19}H_{18}ClNO_5+Na]^+$: 398.0766, found: 398.0766.

(1*R,2*R**,6*R**,7*S**)-9-(Benz[*d*]oxazol-2′-yl)-10,10-dimethoxy-3-oxatricyclo[5.2.2.0^{2,6}]-undeca-4,8-dien-11-one (10a):**



10a

Yield: 126 mg (74%) as pale yellow solid.

Mp: 129-130 ^oC.

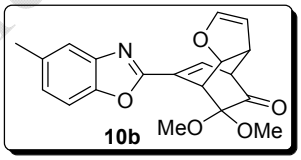
IR (KBr): ν_{max} 2953, 2839, 1743, 1621, 1534, 1456, 1135 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75-7.73 (m, 1H), 7.50-7.48 (m, 1H), 7.36-7.31 (m, 2H), 7.16-7.13 (m, 1H), 6.17-6.16 (m, 1H), 5.28 (dd, *J* = 4.0, 9.5 Hz, 1H), 4.78 (t, *J* = 2.5 Hz, 1H), 4.72-4.70 (m, 1H), 3.58 (dd, *J* = 1.5, 9.5 Hz, 1H), 3.47 (dd, *J* = 2.5, 7.0 Hz, 1H), 3.44 (s, 3H), 3.39 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 199.5 (carbonyl C=O), 160.7 (C), 150.6 (C), 148.4 (CH), 141.7 (C), 130.9 (CH), 129.8 (C), 125.6 (CH), 124.5 (CH), 120.5 (CH), 110.4 (CH), 100.0 (CH), 93.4 (C_{acetal}), 79.2 (CH), 52.9 (CH), 50.5 (OCH_3), 45.4 (CH), 44.4 (CH) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{19}H_{17}NO_5+Na]^+$: 362.0998, found: 362.0993.

(1*R,2*R**,6*R**,7*S**)-10,10-Dimethoxy-9-(5′-methylbenz[*d*]oxazol-2′-yl)-3-oxatricyclo-[5.2.2.0^{2,6}]undeca-4,8-dien-11-one (10b):**



10b

Yield: 127 mg (72 %) as pale orange solid.

Mp: 138-139 ^oC.

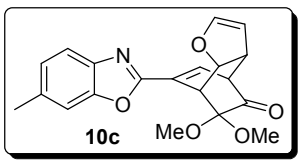
IR (KBr): ν_{max} 2952, 2847, 1741, 1613, 1526, 1454, 1135 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52 (s, 1H), 7.35 (d, *J* = 8.5 Hz, 1H), 7.14 (d, *J* = 8.0 Hz,1H), 7.11 (dd, *J* = 2.0, 7.0 Hz, 1H), 6.16 (t, *J* = 2.5 Hz, 1H), 5.28 (dd, *J* = 4.0, 9.5 Hz, 1H), 4.77 (t, *J* = 2.5 Hz, 1H), 4.69 (dd, *J* = 2.0, 4.0 Hz, 1H), 3.57 (dd, *J* = 2.0, 9.5 Hz, 1H), 3.45 (dd, *J* = 2.0, 7.0 Hz, 1H), 3.44 (s, 3H), 3.38 (s, 3H), 2.45 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 199.5 (carbonyl C=O), 160.7 (C), 148.8 (CH), 148.3 (C), 141.9 (C), 134.3 (C), 130.5 (CH), 129.8 (C), 126.7 (CH), 120.3 (CH), 109.7 (CH), 100.0 (CH), 93.4 (C_{acetal}), 79.2 (CH), 52.8 (CH), 50.5 (OCH_3), 50.4 (OCH_3), 45.4 (CH), 44.3 (CH), 21.4 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{20}H_{19}NO_5+Na]^+$: 376.1155, found: 376.1153.

(1*R,2*R**,6*R**,7*S**)-10,10-Dimethoxy-9-(6′-methylbenz[*d*]oxazol-2′-yl)-3-oxatricyclo-[5.2.2.0^{2,6}]undeca-4,8-dien-11-one (10c):**



10c

Yield: 126 mg (73%) as white solid.

Mp: 108-109 ^oC.

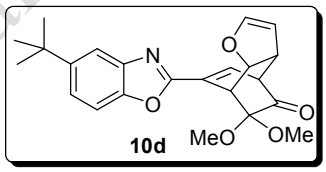
IR (KBr): ν_{max} 2940, 2834, 1738, 1621, 1534, 1456, 1234, 1139 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.58 (d, *J* = 11.5 Hz, 1H), 7.28 (s, 1H), 7.11 (dd, *J* = 1.0, 8.0 Hz, 1H), 7.08 (dd, *J* = 1.5, 5.5 Hz, 1H), 6.15 (dd, *J* = 2.0, 2.5 Hz, 1H), 5.26 (dd, *J* = 4.0, 9.5 Hz, 1H), 4.76 (t, *J* = 2.5 Hz, 1H), 4.68 (dd, *J* = 2.0, 3.5 Hz, 1H), 3.57-3.53 (m, 1H), 3.44 (dd, *J* = 2.5, 5.0 Hz, 1H), 3.43 (s, 3H), 3.37 (s, 3H), 2.45 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 199.4 (carbonyl C=O), 160.2 (C), 150.8 (C), 148.2 (CH), 139.4 (C), 136.1 (C), 130.2 (CH), 129.7 (C), 125.6 (CH), 119.7 (CH), 110.5 (CH), 100.0 (CH), 93.4 (C_{acetal}), 79.1 (CH), 52.8 (CH), 50.4 (OCH_3), 45.3 (CH), 44.3 (CH), 21.7 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{20}H_{19}NO_5+Na]^+$: 376.1155, found: 376.1142.

(1*R,2*R**,6*R**,7*S**)-9-(5′-*tert*-Butylbenz[*d*]oxazol-2′-yl)-10,10-dimethoxy-3-oxatricyclo-[5.2.2.0^{2,6}]undeca-4,8-dien-11-one (10d):**



10d

Yield: 121 mg (61%) as yellow solid.

Mp: 116-117 °C.

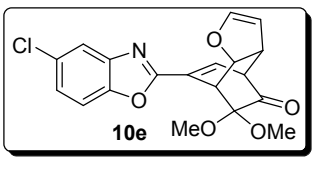
IR (KBr): ν_{max} 2960, 2846, 1739, 1626, 1537, 1472, 1267, 1139 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.79-7.77 (m, 1H), 7.41-7.40 (m, 2H), 7.11 (ddd, *J* = 1.0, 2.5, 7.0 Hz, 1H), 6.14 (dd, *J* = 1.5, 2.5 Hz, 1H), 5.27 (dd, *J* = 4.0, 9.5 Hz, 1H), 4.78-4.76 (m, 1H), 4.71 (dd, *J* = 2.0, 3.5 Hz, 1H), 3.56 (dd, *J* = 1.5, 9.5 Hz, 1H), 3.45 (dd, *J* = 2.0, 6.5 Hz, 1H), 3.44 (s, 3H), 3.38 (s, 3H), 1.36 (s, 9H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 199.5 (carbonyl C=O), 160.8 (C), 148.5 (C), 148.2 (CH), 148.0 (C), 141.5 (C), 130.4 (CH), 129.8 (C), 123.3 (CH), 116.9 (CH), 109.5 (CH), 100.0 (CH), 93.4 (C_{acetal}), 79.1 (CH), 52.8 (CH), 50.4 (OCH_3), 45.4 (CH), 44.3 (CH), 34.8 (C), 31.6 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{23}H_{25}NO_5+Na]^+$: 418.1625, found: 418.1649.

(1*R,2*R**,6*R**,7*S**)-9-(5′-Chlorobenz[*d*]oxazol-2′-yl)-10,10-dimethoxy-3-oxatricyclo-[5.2.2.0^{2,6}]undeca-4,8-dien-11-one (10e):**



10e

Yield: 132 mg (71%) as yellow solid.

Mp: 149-150 °C.

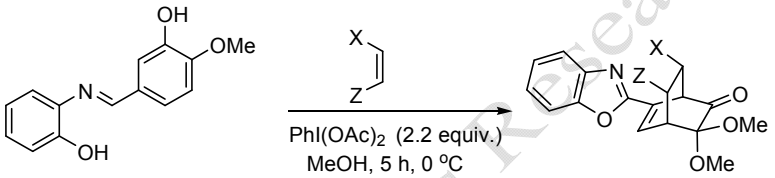
IR (KBr): ν_{max} 2943, 2839, 1739, 1634, 1530, 1454, 1138 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.71 (d, *J* = 2.0 Hz, 1H), 7.42 (d, *J* = 9.0 Hz, 1H), 7.31 (dd, *J* = 2.5, 9.0 Hz, 1H), 7.17 (dd, *J* = 2.5, 7.0 Hz, 1H), 6.18-6.17 (m, 1H), 5.29 (dd, *J* = 4.0, 9.5 Hz, 1H), 4.80 (t, *J* = 2.5 Hz, 1H), 4.68 (dd, *J* = 2.0, 3.5 Hz, 1H), 3.59 (dd, *J* = 1.5, 9.5 Hz, 1H), 3.49 (dd, *J* = 2.0, 6.5 Hz, 1H), 3.45 (s, 3H), 3.38 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 199.3 (carbonyl C=O), 161.9 (C), 149.2 (CH), 148.4 (C), 142.9 (C), 132.0 (CH), 130.0 (C), 129.5 (C), 125.9 (CH), 120.4 (CH), 111.2 (CH), 100.2 (CH), 93.4 (C_{acetal}), 79.2 (CH), 53.0 (OCH_3), 50.5 (OCH_3), 45.5 (CH), 44.4 (CH) ppm.

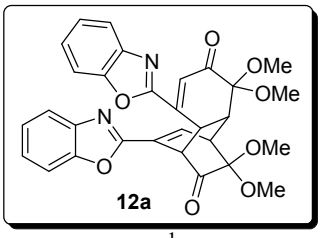
HRMS (ES^+): *m/z* calcd for $[C_{19}H_{16}ClNO_5+Na]^+$: 396.0615, found: 396.0610.

3.2.3. General procedure for the synthesis of 6-(benz[*d*]oxazol-2′-yl)bicyclo[2.2.2]oct-en-2-one derivatives 12-15:



To a solution of aldimine **11a** (0.5 mmol) and a dienophile such as ethyl vinyl ether /styrene /furan (20 equiv.) in methanol (5 mL), DIB (177 mg, 0.55 mmol) was added portion-wise at 0 °C over a period of 5 min., then the reaction mixture was allowed to stir for 5 min. at the same temperature. After complete disappearance of starting material as shown by TLC, another portion of DIB (177 mg, 0.55 mmol) was added over a period of 5 min. and the resultant solution was allowed to stir at 0 °C. After completion of the reaction as indicated by TLC, methanol was evaporated and the crude reaction mixture was purified by silica gel column chromatography with (20-30%) ethyl acetate/hexanes as eluting system.

(1*S,2*S**,7*R**,8*R**)-6,12-(bis-Benz[*d*]oxazol-2′-yl)-3,3,10,10-tetramethoxytricyclo-[6.2.2.0^{2,7}]dodeca-5,11-diene-4,9-dione (13a):**



Yield: 119 mg (86%) as yellow solid.

Mp: 194-195 °C.

IR (KBr): ν_{max} 2947, 2830, 1745, 1708, 1590, 1533, 1449, 1237, 1115, 1054 cm^{-1}.

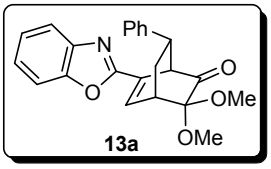
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.87-7.84 (m, 1H), 7.46-7.40 (m, 3H), 7.22-7.20 (m, 3H),

7.18-7.13 (m, 2H), 4.74 (dd, *J* = 2.0, 3.0 Hz, 1H), 4.43 (ddd, *J* = 0.5, 2.5, 8.0 Hz, 1H), 3.58 (dd, *J* = 1.0, 8.5 Hz, 1H), 3.54 (s, 3H), 3.47 (s, 3H), 3.46 (dd, *J* = 1.5, 7.0 Hz, 1H), 3.26 (s, 3H), 3.07 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 200.3 (carbonyl C=O), 193.1 (C), 159.5 (C), 159.1 (C), 150.5 (C), 150.4 (C), 141.9 (C), 141.2 (C), 141.2 (C), 134.4 (CH), 129.2 (CH), 128.7 (C), 126.8 (CH), 125.6 (CH), 125.0 (CH), 124.3 (CH), 121.1 (CH), 120.1 (CH), 110.7 (CH), 110.4 (CH), 98.4 (C), 94.5 (C_{acetal}), 53.3 (CH), 50.8 (OCH_3), 50.3 (OCH_3), 49.8 (OCH_3), 49.0 (OCH_3), 41.0 (CH), 38.8 (CH), 38.7 (CH) ppm.

HRMS (ES$^+$): *m/z* calcd for $[C_{30}H_{26}N_2O_8+Na]^+$: 565.1581, found: 565.1570.

(1*S,4*R**,7*S**)-6-(Benz[*d*]oxazol-2′-yl)-3,3-dimethoxy-7-phenylbicyclo[2.2.2]oct-5-en-2-one (12a):**



13a

Yield: 84 mg (45%) as white solid.

Mp: 98-99 ^oC.

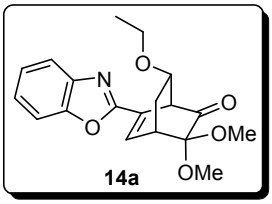
IR (KBr): ν_{max} 2943, 2834, 1732, 1635, 1529, 1447, 1335, 1240, 1124, 1036 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.65-7.63 (m, 1H), 7.62 (dd, *J* = 1.5, 7.0 Hz, 1H), 7.45-7.44 (m, 1H), 7.32-7.27 (m, 2H), 7.18-7.08 (m, 5H), 4.26 (t, *J* = 2.0 Hz, 1H), 3.62-3.58 (m, 1H), 3.51-3.50 (m, 1H), 3.46 (s, 3H), 3.37 (s, 3H), 2.68 (ddd, *J* = 2.5, 9.5, 26.0 Hz, 1H), 1.74 (ddd, *J* = 2.5, 6.5, 13.5 Hz, 1H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 200.3 (carbonyl C=O), 160.1 (C), 150.5 (C), 142.9 (C), 141.6 (C), 138.5 (CH), 128.6 (CH), 127.2 (C), 126.8 (CH), 126.1 (CH), 125.4 (CH), 124.4 (CH), 120.3 (CH), 110.3 (CH), 93.6 (C_{acetal}), 54.2 (CH), 50.5 (OCH_3), 49.9 (OCH_3), 39.9 (CH), 39.3 (CH), 29.6 (CH_2) ppm.

HRMS (ES$^+$): *m/z* calcd for $[C_{23}H_{21}NO_4+Na]^+$: 398.1363, found: 398.1345.

(1*S,4*R**,7*S**)-6-(Benz[*d*]oxazol-2′-yl)-3,3-dimethoxy-7-ethoxybicyclo[2.2.2]oct-5-en-2-one (14a):**



14a

Yield: 91 mg (52%) as brown solid.

Mp: 116-117 ^oC.

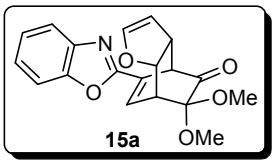
IR (KBr): ν_{max} 2939, 2878, 1738, 1639, 1521, 1446, 1248, 1106, 1038, 755 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.71-7.68 (m, 1H), 7.49-7.47 (m, 2H), 7.30-7.28 (m, 2H), 4.59-4.56 (m, 1H), 4.14 (td, *J* = 3.0, 8.5 Hz, 1H), 3.75-3.69 (m, 1H), 3.45-3.40 (m, 1H), 3.34 (s, 3H), 3.34-3.32 (m, 1H), 3.29 (s, 3H), 2.52 (ddd, *J* = 2.5, 8.0, 14.0 Hz, 1H), 1.43 (td, *J* = 3.5, 14.0 Hz, 1H), 1.04 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 200.5 (carbonyl C=O), 160.2 (C), 150.4 (C), 141.6 (C), 136.8 (CH), 125.3 (CH), 125.0 (C), 124.3 (CH), 120.1 (CH), 110.3 (CH), 93.5 (C_{acetal}), 73.9 (CH), 64.4 (C), 52.9 (CH), 50.5 (OCH_3), 49.4 (OCH_3), 38.7 (CH), 29.8 (CH_2), 15.0 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{19}H_{21}NO_5+Na]^+$: 366.1312, found: 366.1300.

(1*R,2*R**,6*R**,7*S**)-8-(Benz[*d*]oxazol-2′-yl)-10,10-dimethoxy-3-oxatricyclo[5.2.2.0^{2,6}]-undeca-4,8-dien-11-one (15a):**



15a

Yield: 42 mg (24%) as yellow solid.

Mp: 94-95 ^oC.

IR (KBr): ν_{max} 2945, 2845, 1740, 1612, 1532, 1451, 1241, 1138, 1056 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.72-7.70 (m, 1H), 7.50-7.48 (m, 1H), 7.33 (dd, *J* = 2.0, 4.0 Hz, 1H), 7.32 (dd, *J* = 3.0, 5.0 Hz, 1H), 7.26-7.24 (m, 1H), 6.16 (dd, *J* = 2.0, 3.0 Hz, 1H), 5.19 (dd, *J* = 3.5, 9.5 Hz, 1H), 4.80 (t, *J* = 2.5 Hz, 1H), 4.18 (t, *J* = 2.0 Hz, 1H), 3.95 (dd, *J* = 4.0, 7.0 Hz, 1H), 3.67 (qd, *J* = 2.0, 9.5 Hz, 1H), 3.43 (s, 3H), 3.35 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 199.7 (carbonyl C=O), 159.8 (C), 150.6 (C), 148.0 (CH), 141.6 (C), 133.6 (CH), 127.8 (C), 125.6 (CH), 124.6 (CH), 120.3 (CH), 110.5 (CH), 99.9 (CH), 93.5 (C_{acetal}), 79.5 (CH), 52.0 (CH), 50.3 (OCH_3), 50.2 (OCH_3), 45.4 (CH), 44.6 (CH) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{19}H_{17}NO5+Na]^+$: 362.1004, found: 362.0984.

Methyl 4-hydroxybenzoate (16):

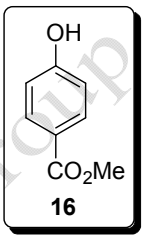
To a solution of 4-hydroxybenzoic acid (4.14 g, 30 mmol) in methanol (60 mL) two drops of conc. H_2SO_4 were added at room temperature. The reaction mixture was heated at 80 ^oC for 8 h after which the solvent was evaporated under reduced pressure then cold water

(50 mL) was added. The product was extracted twice with ethyl acetate (2 x 50 mL) and dried over anhydrous Na_2SO_4. The evaporation of solvent gave pure product **16**.

Yield: 4.38 g (96%) as white solid.

Mp: 122-123 ^oC (Lit.[237] Mp**:** 124-125 ^oC).

IR (KBr): ν_{max} 3421, 3042, 1741, 1623, 1598, 784 cm^{-1}.



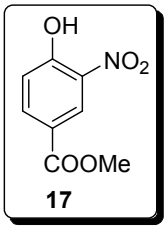
^{1}H NMR ($CDCl_3$, 500 MHz): δ 10.01 (br s, 1H), 8.12 (m, 2H), 7.34 (m, 2H), 3.90 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 125 MHz): δ 163.6, 155.2, 132.8, 130.2, 125.6, 52.6 ppm.

Methyl 4-hydroxy-2-nitrobenzoate (17):

A solution of methyl 4-hydroxybenzoate (3.04 g, 20 mmol) in acetic acid (15 mL) was added to a solution of conc. nitric acid (1.1 mL, 26 mmol,) in acetic acid (20 mL) at 0 ^oC. The reaction mixture was stirred at the same temperature for 2 h then cold water (100 mL) was added. The product was precipitated as yellow coloured solid which was filtered and dried. This compound was used as such in the next reaction.

Yield: 3.31 g (84%) as yellow solid.



Mp: 77-78 ^oC (Lit.[238] Mp**:** 76-77 ^oC).

IR (KBr): ν_{max} 3321, 3032, 1735, 1682, 923 cm^{-1}.

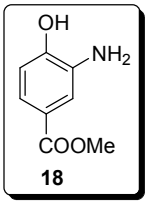
^{1}H NMR ($CDCl_3$, 500 MHz): δ 10.88 (br s, 1H), 8.79 (s, 1H), 8.23 (s, 1H), 7.22 (s, 1H), 3.95 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 125 MHz): δ 164.7, 158.1, 137.9, 133.2, 127.3, 122.7, 120.2, 52.6 ppm.

Methyl 3-amino-4-hydroxybenzoate (18):

To Pd/C (100 mg, 10%) in methanol (10 mL) was added a solution of methyl 4-hydroxy-3-nitrobenzoate (**17**, 2.95 g, 15 mmol) in methanol (10 mL) at room temperature. The reaction mixture was stirred under H_2 atmosphere for 6 h. After completion of the reaction as indicated by TLC, reaction mixture was filtered. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (100-200 mesh) by using 30% ethyl acetate and hexanes to furnish the aminophenol **18**.

Yield: 2.21 g (88%) as light brown solid.



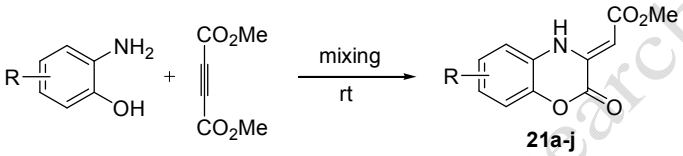
Mp: 130-131 ^{o}C (Lit.[239] Mp**:** 131-133 ^{o}C).

IR (KBr): ν_{max} 3318, 3062, 1752, 1593, 789 cm^{-1}.

^{1}H NMR (CDCl$_3$, 500 MHz): δ 10.00 (br s, 1H), 7.30 (d, *J* = 2.0 Hz, 1H), 7.16 (dd, *J* = 2.0, 8.0 Hz, 1H), 6.76 (d, *J* = 8.0 Hz, 1H), 4.83 (br s, 2H), 3.79 (s, 3H) ppm.

^{13}C NMR (CDCl$_3$, 125 MHz): δ 166.7, 148.7, 136.7, 120.8, 118.9, 114.8, 113.7, 51.5 ppm.

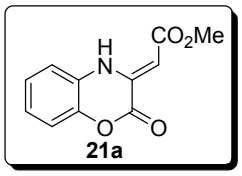
3.2.4. General procedure for the synthesis of vinylogous carbamates 21a-j:



The 1,4-benzoxazinone derivatives are synthesized according to the procedure developed in our laboratory[170]. An aminophenol derivative (2 mmol) was taken in a pre weighed Petri dish and then was added dialkyl acetylenedicarboxylate (2 mmol) slowly with thorough mixing over a period of 1-5 min. at room temperature with the help of a spatula to form a homogeneous paste. The progress of the reaction was monitored by TLC. After completion of reaction the products obtained were either opened to air or transferred to round bottom flask and vacuum was applied to remove the traces of methanol formed during the reaction. The products **21a-j** were obtained in analytically pure form after washing the reaction mixture with a few drops of methanol. All the products were solids and no standing was required.

(*Z*)-3-Methoxycarbonylmethylene-3,4-dihydro-2*H*-1,4-benzoxazin-2-one (21a):

Yield: 418 mg (98%) as yellow solid.



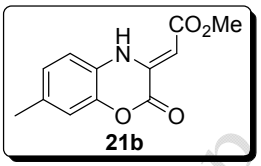
Mp: 166-167 ^{o}C.

IR (KBr): ν_{max} 3464, 1764, 1660, 1628, 1282 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$): δ 10.68 (br s, 1H), 7.16 (d, *J* = 8.0 Hz, 1H), 7.15 (t, *J* = 8.0 Hz, 1H), 7.03 (dt, *J* = 1.0, 8.0 Hz, 1H), 6.97 (d, *J* = 8.0 Hz, 1H) 5.94 (s, 1H), 3.78 (s, 3H, CH_3) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.3, 155.9, 140.0, 138.1, 125.7, 124.1, 122.8, 117.0, 114.8, 90.7, 51.5 ppm.

(*Z*)-3-Methoxycarbonylmethylene-7-methyl-3,4-dihydro-2*H*-1,4-benzoxazin-2-one (21b):



21b

Yield: 442 mg (95%) as yellow solid.

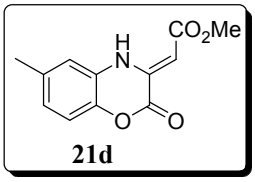
Mp: 170-171 ^{o}C.

IR (KBr): ν_{max} 3473, 1750, 1652, 1632, 1300 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.64 (br s, 1H), 6.97-6.93 (m, 2H), 6.85 (d, *J* = 8.0 Hz, 1H), 5.89 (s, 1H), 3.77 (s, 3H), 2.32 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.3, 156.1, 139.8, 138.2, 133.1, 126.3, 121.6, 117.3, 114.5, 89.9, 51.4, 20.8 ppm.

(*Z*)-3-Methoxycarbonylmethylene-6-methyl-3,4-dihydro-2*H*-1,4-benzoxazin-2-one (21d):



21d

Yield: 452 mg (97%) as yellow solid.

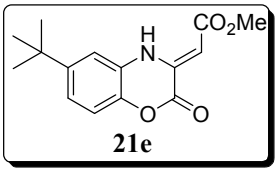
Mp: 144 ^{o}C.

IR (KBr): ν_{max} 3427, 1758, 1657, 1619, 1286 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.61 (br s, 1H), 7.03 (d, *J* = 8.0 Hz, 1H), 6.81 (d, *J* = 8.0 Hz, 1H), 6.77 (s, 1H), 5.91 (s, 1H), 3.78 (s, 3H), 2.32 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.3, 156.1, 138.2, 138.0, 135.7, 123.7, 123.5, 116.7, 115.1, 90.4, 51.4, 20.9 ppm.

(*Z*)- 3-Methoxycarbonylmethylene-6-*tert*-butyl-3,4-dihydro-2*H*-1,4-benzoxazin-2-one (21e):



21e

Yield: 508 mg (92%) as yellow solid.

Mp: 84-85 ^{o}C.

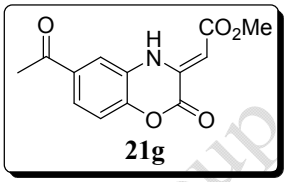
IR (KBr): ν_{max} 3461, 1773, 1668, 1621, 1276 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.70 (br s, 1H), 7.08 (d, *J* = 8.5 Hz, 1H), 7.05 (dd, *J* = 2.0, 9.0 Hz, 1H), 6.97 (d, *J* = 2.0 Hz, 1H), 5.92 (s, 1H), 3.80 (s, 3H), 1.29 (s, 9H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.4, 156.1, 147.6, 138.4, 137.8, 123.4, 120.0, 116.4, 111.9, 90.2, 61.3, 36.8, 31.3 ppm.

Methyl (*Z*)-2-(6-acetyl-2-oxo-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (21g):

Yield: 512 mg (98%) as yellow solid.



21g

Mp: 147-148 °C.

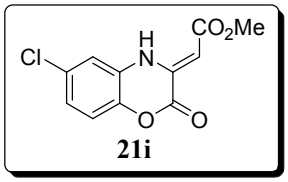
IR (KBr): ν_{max} 3456, 1764, 1662, 1643, 1278 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.75 (br s, 1H), 7.62 (d, *J* = 8.5 Hz, 1H), 7.60 (s, 1H), 7.21(d, *J* = 8.0 Hz, 1H), 5.98 (s, 1H), 3.80 (s, 3H), 2.59 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 196.0, 170.0, 155.3, 143.1, 137.4, 134.6, 124.4, 123.2, 117.2, 114.8, 92.2, 51.7, 26.5 ppm.

(*Z*)-3-Methoxycarbonylmethylene-6-chloro-3,4-dihydro-2*H*-1,4-benzoxazin-2-one (21i):

Yield: 482 mg (95%) as yellow solid.



21i

Mp: 165-166 °C.

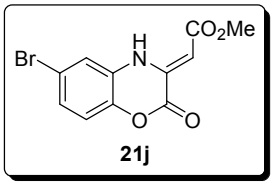
IR (KBr): ν_{max} 3386, 1778, 1654, 1631, 1288 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.65 (br s, 1H), 7.09-7.06 (m, 1H), 6.99-6.96 (m, 2H), 5.97 (s, 1H), 3.79 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.1, 155.4, 138.6, 137.4, 130.9, 125.1, 122.6, 118.1, 114.7, 92.2, 51.7 ppm.

Methyl (*Z*)-2-(6-bromo-2-oxo-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (21j):

Yield: 568 mg (96%) as yellow solid.



21j

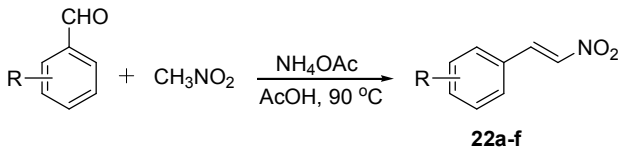
Mp: 156-157 °C.

IR (KBr): ν_{max} 3456, 1768, 1657, 1624, 1265 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.64 (br s, 1H), 7.13-7.10 (m, 2H), 7.02 (d, *J* = 8.0Hz, 1H), 5.97 (s, 1H), 3.79 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.0, 155.4, 139.0, 137.3, 125.5, 125.4, 188.4, 118.1, 117.5, 92.2, 51.7 ppm.

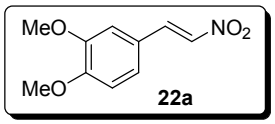
3.2.5. General procedure for the synthesis of β-nitrostyrenes 22a-f:



22a-f

A mixture of a benzaldehyde derivative (15 mmol), nitromethane (6 mL, 110 mmol) and ammonium acetate (5.2 mmol) in glacial acetic acid (40 mL) was heated at 90 °C for 8 h. Then the hot solution was poured into 400 mL of ice-cold water in a beaker. Immediately the product began to precipitate out. To get the complete precipitation, the beaker was kept in refrigerator at 0 °C for 4 h. The precipitate was filtered under reduced pressure, washed with water and dried under vacuum to afford pure β-nitrostyrene.

(*E*)-1,2-Dimethoxy-4-(2-nitrovinyl)benzene (22a):



22a

Yield: 2.89 g (92%) as yellow solid.

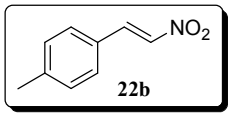
Mp: 141-142 °C (Lit.[240] Mp**:**144 °C).

IR (KBr): ν_{max} 3105, 1601, 1502, 1423, 1315, 1165, 1023 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.96 (d, *J* = 13.5 Hz, 1H), 7.53 (d, *J* = 13.5 Hz, 1H), 7.17 (d, *J* = 2.0, 8.5 Hz, 1H), 7.00 (d, *J* = 2.0 Hz, 1H), 6.91 (d, *J* = 8.0 Hz, 1H), 3.94 (s, 3H), 3.92 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 152.8, 149.5, 139.3, 135.1, 124.6, 122.7, 111.3, 110.1, 56.1, 56.0 ppm.

(*E*)-1-Methyl-4-(2-nitrovinyl)benzene (22b):



22b

Yield: 2.06 g (84%) as pale yellow crystalline solid.

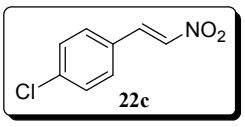
Mp: 99-100 °C (Lit.[3] Mp**:** 102 °C).

IR (KBr): ν_{max} 3102, 1635, 1601, 1499, 1415, 1337, 1177 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.99 (d, *J* = 13.5 Hz, 1H), 7.57 (d, *J* = 14.0 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 2H), 7.27-7.24 (m, 2H), 2.41 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 143.1, 139.1, 136.2, 130.1, 129.1, 127.2, 21.6 ppm.

(*E*)-1-Chloro-4-(2-nitrovinyl)benzene (22c):



Yield: 2.24 g (81%) pale yellow crystalline solid.

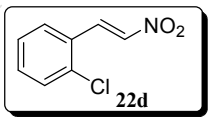
Mp: 112-113 °C (Lit.[3] Mp**:** 113 °C).

IR (KBr): ν_{max} 3100, 1631, 1586, 1495, 1335, 1079 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.96 (d, *J* = 14.0 Hz, 1H), 7.56 (d, *J* = 13.5 Hz, 1H), 7.50-7.48 (m, 2H), 7.45-7.43 (m, 2H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 138.2, 137.6, 137.4, 130.2, 129.7, 128.5 ppm.

(*E*)-1-Chloro-2-(2-nitrovinyl)benzene (22d):



Yield: 2.15 g (78%) as pale yellow solid.

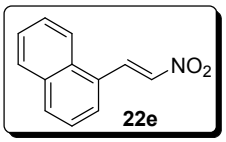
Mp: 45-46 °C (Lit.[241] Mp**:** 48 °C).

IR (KBr): ν_{max} 3106, 1643, 1576, 1482, 1335, 1069, 972, 821 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.38 (d, *J* = 13.0 Hz, 1H), 7.61-7.56 (m, 2H), 7.48 (dd, *J* = 1.5, 8.0 Hz, 1H), 7.42 (td, *J* = 1.5, 8.0 Hz, 1H), 7.34 (td, *J* = 1.5, 7.5 Hz, 1H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 138.9, 136.1, 135.2, 133.0, 130.8, 128.7, 128.6, 127.6 ppm.

(*E*)-1-(2-Nitrovinyl)naphthalene (22e):



Yield: 2.14 g (86%) as yellow crystalline solid.

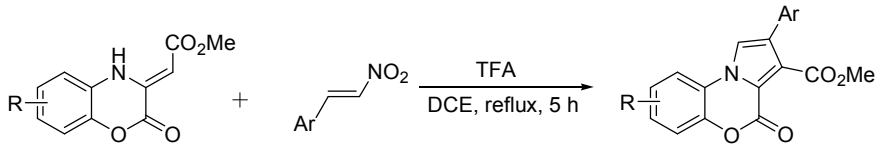
Mp: 75-76 °C (Lit.[242] Mp**:** 76 °C).

IR (KBr): ν_{max} 3104, 1623, 1507, 1334, 956, 776 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.85 (d, *J* = 13.0 Hz, 1H), 8.15 (d, *J* = 8.5 Hz, 1H), 8.01 (d, *J* = 8.0 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.77 (d, *J* = 7.5 Hz, 1H), 7.68-7.64 (m, 2H), 7.60 (t, *J* = 8.5 Hz, 1H), 7.53 (t, *J* = 8.0 Hz, 1H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 138.5, 136.0, 133.7, 132.5, 131.5, 129.0, 127.7, 127.0, 126.8, 126.3, 125.4, 122.9 ppm.

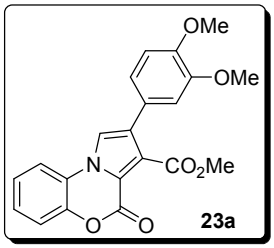
3.2.6. General procedure for the synthesis of pyrrolobenzoxazine derivatives 23-25:



21a-c **22 a-f** **23-25**

To a mixture of 1,4-benzoxazinone derivative (**21**, 0.5 mmol) and β-nitrostyrene (**22**, 0.6 mmol) in 4 mL of 1,2-dichloroethane, trifluoroacetic acid (0.75 mmol) was added dropwise, and the mixture was allowed to reflux for 5 h. After completion of the reaction as shown by TLC, the reaction was quenched with 4 mL of saturated $NaHCO_3$ solution. The organic layer was separated, washed twice with water, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude reaction mixture was purified by column chromatography on silica gel (100-200 Mesh) using 20-40% ethyl acetate/hexanes as the eluting system to obtain pure pyrrolobenzoxazine derivative.

Methyl 2-(3′,4′-dimethoxyphenyl)-4-oxo-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazine-3-carboxylate (23a):



Yield: 156 mg (82%) as yellow solid.

Mp: 150-151 ^{o}C.

IR (KBr): ν_{max} 1732, 1721, 1598, 1410, 1256, 1116, 1031 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.65 (s, 1H), 7.60 (d, *J* = 7.0 Hz, 1H), 7.32-7.26 (m, 3H), 6.99-6.95 (m, 2H), 6.82 (d, *J* = 8.5 Hz, 1H), 3.93 (s, 3H), 3.87 (s, 3H), 3.86 (s, 3H) ppm.

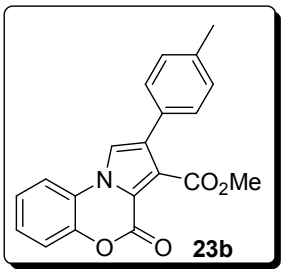
^{13}C NMR (125 MHz, $CDCl_3$): δ 165.4 (C), 151.9 (C), 148.8 (C), 148.7 (C), 142.8 (C), 128.8 (C), 126.9 (CH), 124.9 (CH), 124.4 (C), 121.5 (C), 121.3 (C), 119.9 (CH), 118.1 (CH), 115.4 (CH), 115.4 (C), 114.4 (CH), 111.1 (CH), 110.7 (CH), 55.7 (OCH_3), 52.8 (OCH_3) ppm.

HRMS (ES^{+}): *m/z* calcd for $[C_{21}H_{17}NO_6+Na]^{+}$: 402.0948, found: 402.0945.

Methyl 2-(4′-methylphenyl)-4-oxo-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazine-3-carboxylate (23b):

Yield: 128 mg (77%) as yellow solid.

Mp: 162-163 °C.



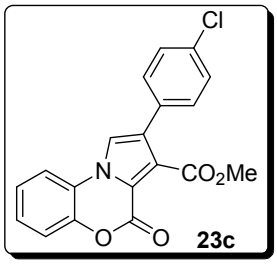
IR (KBr): ν_{max} 1743, 1724, 1595, 1400, 1238, 1112, 1023 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.65 (s, 1H), 7.61-7.59 (m, 1H), 7.36-7.27 (m, 5H), 7.17 (d, *J* = 8.0 Hz, 2H), 3.92 (s, 3H), 2.34 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 165.3 (C), 152.1 (C), 142.9 (C), 137.8 (C), 129.4 (CH), 129.2 (C), 128.9 (C), 127.4 (CH), 127.1 (CH), 125.0 (CH), 121.8 (C), 121.5 (C), 118.3 (CH), 115.6 (C), 115.5 (CH), 114.4 (CH), 52.8 (OCH_3), 21.1 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{20}H_{15}NO_4+Na]^+$: 356.0893, found: 356.0888.

Methyl 2-(4′-chlorophenyl)-4-oxo-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazine-3-carboxylate (23c):



Yield: 132 mg (75%) as orange solid.

Mp: 178-179 °C.

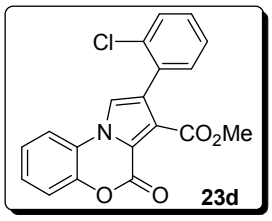
IR (KBr): ν_{max} 1748, 1726, 1598, 1409, 1240, 1125, 1010 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.67 (s, 1H), 7.64-7.62 (m, 1H), 7.38-7.36 (m, 2H), 7.36-7.35 (m, 1H), 7.34-7.33 (m, 2H), 7.33-7.29 (m, 2H), 3.91 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 165.0 (C), 151.9 (C), 143.0 (C), 134.0 (C), 130.4 (C), 129.0 (CH), 128.9 (CH), 128.1 (C), 127.3 (CH), 125.1 (CH), 121.8 (C), 121.4 (C), 118.4 (CH), 115.9 (C), 115.7 (CH), 114.4 (CH), 52.9 (OCH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{19}H_{12}ClNO_4+Na]^+$: 376.0347, found: 376.0346.

Methyl 2-(2′-chlorophenyl)-4-oxo-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazine-3-carboxylate (23d):



Yield: 126 mg (71%) as yellow solid.

Mp: 160-161 °C.

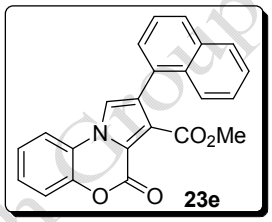
IR (KBr): ν_{max} 1730, 1721, 1606, 1524, 1412, 1372, 1247, 1068 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.71 (s, 1H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.44 (dd, *J* = 3.0, 5.5 Hz, 1H), 7.38-7.28 (m, 6H), 3.80 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 163.8 (C), 151.6 (C), 143.1 (C), 133.3 (C), 131.4 (CH), 131.2 (C), 129.7 (CH), 129.3 (CH), 127.3 (CH), 127.1 (C), 126.7 (CH), 125.0 (CH), 123.1 (C), 121.4 (C), 118.2 (CH), 117.6 (CH), 115.7 (C), 114.5 (CH), 52.5 (OCH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{19}H_{12}ClNO_4+Na]^+$: 376.0347, found: 376.0343.

Methyl 2-(1′-naphthyl)-4-oxo-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazine-3-carboxylate (23e):



Yield: 149 mg (81%) as yellow solid.

Mp: 136-137 °C.

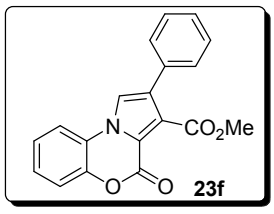
IR (KBr): ν_{max} 1745, 1725, 1598, 1381, 1259, 1089 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): 7.88-7.85 (m, 3H), 7.71 (s, 1H), 7.60 (dd, *J* = 1.5, 8.0 Hz, 1H), 7.51-7.40 (m, 5H), 7.36 (dt, *J* = 1.5, 7.0 Hz, 1H), 7.30 (dt, *J* = 1.5, 8.0 Hz, 1H), 3.59 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 164.1 (C), 151.8 (C), 143.1 (C), 133.4 (C), 132.0 (C), 129.9 (C), 128.5 (CH), 128.3 (CH), 128.2 (C), 127.8 (CH), 127.2 (CH), 126.3 (CH), 125.9 (CH), 125.1 (CH), 125.0 (CH), 123.8 (C), 121.5 (C), 118.3 (CH), 117.7 (CH), 115.6 (C), 114.5 (CH), 52.3 (OCH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{23}H_{15}NO_4+Na]^+$: 392.0893, found: 392.0883.

Methyl 4-oxo-2-phenyl 4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazine-3-carboxylate (23f):



Yield: 134 mg (84%) as brown solid.

Mp: 168-169 °C.

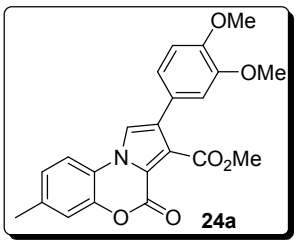
IR (KBr): ν_{max} 1741, 1722, 1530, 1468, 1384, 1250, 1138 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.68 (s, 1H), 7.62-7.60 (m, 1H), 7.45-7.43 (m, 2H), 7.38-7.35 (m, 2H), 7.34-7.29 (m, 4H), 3.91 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 165.2 (C), 152.0 (C), 142.9 (C), 131.9 (C), 129.2 (C), 128.7 (CH), 127.8 (CH), 127.6 (CH), 127.1 (CH), 125.0 (CH), 121.9 (C), 121.4 (C), 118.3 (CH), 115.7 (CH), 115.7 (C), 114.4 (CH), 52.8 (OCH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{19}H_{13}NO_4+Na]^+$: 342.0737, found: 342.0735.

Methyl 2-(3′,4′-dimethoxyphenyl)-7-methyl-4-oxo-2-phenyl-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazine-3-carboxylate (24a):



Yield: 151 mg (76%) as brown solid.

Mp: 143-144 ^{o}C.

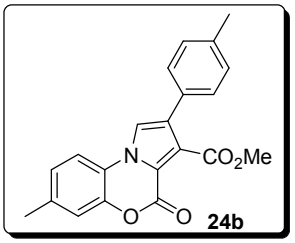
IR (KBr): ν_{max} 1738, 1716, 1595, 1397, 1261, 1115, 1032 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.58 (s, 1H), 7.36 (d, *J* = 1.0 Hz, 1H), 7.15 (d, *J* = 8.5 Hz, 1H), 7.06 (dd, *J* = 1.5, 8.5 Hz, 1H), 6.97 (d, *J* = 2.0 Hz, 1H), 6.95 (dd, *J* = 2.0, 8.0 Hz, 1H), 6.81 (d, *J* = 8.0 Hz, 1H), 3.91 (s, 3H), 3.86 (s, 3H), 3.85 (s, 3H), 2.40 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 165.5 (C), 152.1 (C), 148.8 (C), 148.7 (C), 140.7 (C), 135.2 (C), 128.6 (C), 127.7 (CH), 124.5 (C), 121.4 (C), 120.8 (C), 119.9 (CH), 117.7 (CH), 115.4 (C), 115.2 (CH), 114.5 (CH), 111.1 (CH), 110.6 (CH), 55.7 (OCH_3), 52.8 (OCH_3), 20.9 (OCH_3) ppm.

HRMS (ES^{+}): *m/z* calcd for $[C_{22}H_{19}NO_6+Na]^{+}$: 416.1105, found: 416.1105.

Methyl 2-(4′-methylphenyl)-7-methyl-4-oxo-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazine-3-carboxylate (24b):



Yield: 131 mg (75%) as brown solid.

Mp: 182-183 ^{o}C.

IR (KBr): ν_{max} 1739, 1719, 1594, 1410, 1272, 1119, 1029 cm^{-1}.

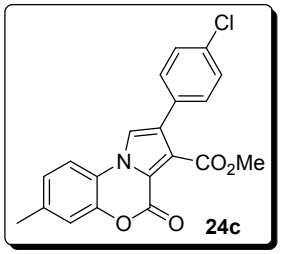
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.59 (s, 1H), 7.46 (d, *J* = 8.5 Hz, 1H), 7.33 (d, *J* = 8.5 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 7.13 (s, 1H), 7.08 (dd, *J* = 1.0, 8.0 Hz, 1H), 3.92 (s, 3H), 2.40 (s, 3H), 2.35 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 165.4 (C), 152.2 (C), 142.8 (C), 137.7 (C), 129.4 (CH), 129.1 (C), 129.0 (C), 127.5 (CH), 125.7 (CH), 121.5 (C), 119.2 (C), 118.4 (CH), 115.5 (C), 115.3 (CH), 114.0 (CH), 52.8 (OCH_3), 21.1 (CH_3), 21.0 (CH_3) ppm.

HRMS (ES^{+}): *m/z* calcd for $[C_{21}H_{17}NO_4+Na]^{+}$: 370.1050, found: 370.1048.

Methyl 2-(4′-chlorophenyl)-7-methyl-4-oxo-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazine-3-carboxylate (24c):

Yield: 131 mg (71%) as yellow solid.



Mp: 180-181 ^{o}C.

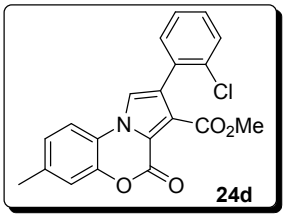
IR (KBr): ν_{max} 1739, 1721, 1539, 1368, 1235, 1124, 1024 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.63 (s, 1H), 7.50 (d, *J* = 8.5 Hz, 1H), 7.37 (q, *J* = 7.5 Hz, 4H), 7.18-7.17 (m, 1H), 7.12 (d, *J* = 8.0Hz, 1H), 3.91 (s, 3H), 2.42 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 165.1 (C), 152.2 (C), 142.9 (C), 138.1 (C), 134.0 (C), 130.7 (C), 129.1 (CH), 129.0 (CH), 128.0 (C), 125.9 (CH), 121.6 (C), 119.1 (C), 118.6 (CH), 115.9 (C), 115.5 (CH), 114.1 (CH), 52.9 (OCH_3), 21.2 (CH_3) ppm.

HRMS (ES^{+}): *m/z* calcd for $[C_{20}H_{14}ClNO_4+Na]^{+}$: 390.0504, found: 390.0505.

Methyl 2-(2′-chlorophenyl)-7-methyl-4-oxo-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazine-3-carboxylate (24d):



Yield: 122 mg (66%) as yellow solid.

Mp: 168-169 ^{o}C.

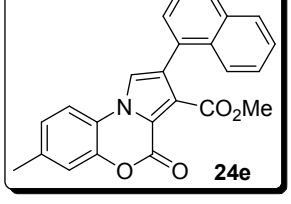
IR (KBr): ν_{max} 1744, 1728, 1576, 1382, 1264, 1058 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.66 (s, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.45 (dd, *J* = 3.5, 5.5 Hz, 1H), 7.37 (dd, *J* = 3.5, 5.5 Hz, 1H), 7.31-7.27 (m, 2H), 7.17 (s, 1H), 7.10 (d, *J* = 8.5 Hz, 1H), 3.80 (s, 3H), 2.42 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 163.9 (C), 151.8 (C), 142.9 (C), 138.0 (C), 133.3 (C), 131.5 (CH), 131.4 (C), 129.7 (CH), 129.3 (CH), 126.9 (CH), 126.7 (C), 125.7 (CH), 122.8 (C), 119.1 (C), 118.3 (CH), 117.4 (CH), 115.3 (C), 114.2 (CH), 52.4 (OCH_3), 21.1 (CH_3) ppm.

HRMS (ES^{+}): *m/z* calcd for $[C_{20}H_{14}ClNO_4+Na]^{+}$: 390.0505, found: 390.0509.

Methyl 7-methyl-2-(1-naphthyl)-4-oxo-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazine-3-carboxylate (24e):



Yield: 149 mg (78%) as yellow solid.

Mp: 167-168 ^{o}C.

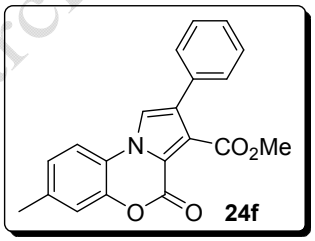
IR (KBr): ν_{max} 1744, 1724, 1593, 1394, 1259, 1075 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.89-7.86 (m, 3H), 7.67 (s, 1H), 7.51-7.43 (m, 5H), 7.22 (s, 1H), 7.10 (d, *J* = 8.5 Hz, 1H), 3.59 (s, 3H), 2.44 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 164.2 (C), 152.0 (C), 143.0 (C), 137.9 (C), 133.5 (C), 132.1 (C), 130.0 (C), 128.5 (CH), 128.3 (CH), 128.1 (C), 127.8 (CH), 126.3 (CH), 125.9 (CH), 125.8 (CH), 125.2 (CH), 125.1 (CH), 123.5 (C), 119.2 (C), 118.4 (CH), 117.4 (CH), 115.5 (C), 114.2 (CH), 52.3 (OCH_3), 21.1 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{24}H_{17}NO_4+Na]^+$: 406.1050, found: 406.1049.

Methyl 7-methyl-4-oxo-2-phenyl-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazine-3-carboxylate (24f):



Yield: 137 mg (82%) as yellow solid.

Mp: 166-167 °C.

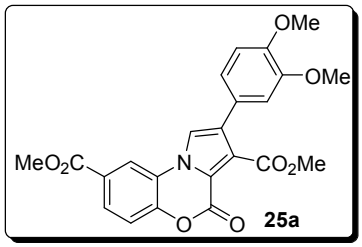
IR (KBr): ν_{max} 1734, 1716, 1594, 1409, 1265, 1117, 1028 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.64 (s, 1H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.47-7.46 (m, 2H), 7.39 (t, *J* = 7.0 Hz, 2H), 7.35-7.32 (m, 1H), 7.16 (s, 1H), 7.11 (d, *J* = 8.0 Hz, 1H), 3.92 (s, 3H), 2.41 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 165.3 (C), 152.3 (C), 142.9 (C), 137.8 (C), 132.1 (C), 129.1 (C), 128.8 (CH), 127.9 (CH), 127.7 (CH), 125.8 (CH), 121.6 (C), 119.2 (C), 118.5 (CH), 115.6 (C), 115.5 (CH), 114.1 (CH), 52.8 (OCH_3), 21.1 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{20}H_{15}NO_4+Na]^+$: 356.0893, found: 356.0893.

Dimethyl 2-(3′,4′-dimethoxyphenyl)-4-oxo-2-phenyl-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazine-3,8-dicarboxylate (25a):



Yield: 148 mg (68%) as yellow solid.

Mp: 180-181 °C.

IR (KBr): ν_{max} 1742, 1722, 1595, 1397, 1262, 1119, 1015 cm^{-1}.

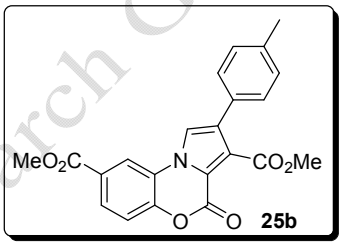
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.30 (s, 1H), 7.98 (d, *J* = 8.5 Hz, 1H), 7.74 (s, 1H), 7.40 (d, *J* = 8.5 Hz, 1H), 6.98 (d, *J* = 7.5 Hz, 2H), 6.84 (d, *J* = 8.5 Hz, 1H), 3.96 (s, 3H), 3.93 (s, 3H),

3.88 (s, 3H), 3.87 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 165.3 (C), 165.2 (C), 151.2 (C), 149.0 (C), 148.9 (C), 146.0 (C), 129.4 (C), 128.2 (CH), 127.0 (C), 124.2 (C), 122.3 (C), 121.5 (C), 120.0 (CH), 118.3 (CH), 116.1 (CH), 115.9 (CH), 115.1 (C), 111.2 (CH), 110.7 (CH), 55.8 (OCH_3), 55.8 (OCH_3), 52.9 (OCH_3), 52.6 (OCH_3) ppm.

HRMS (ES$^+$): *m/z* calcd for $[C_{23}H_{19}NO_8+Na]^+$: 460.1003, found: 460.1014.

Dimethyl 2-(4′-methylphenyl)-4-oxo-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazine-3,8-dicarb-oxylate (25b):



Yield: 129 mg (66%) as brown solid.

Mp: 150-151 ^oC.

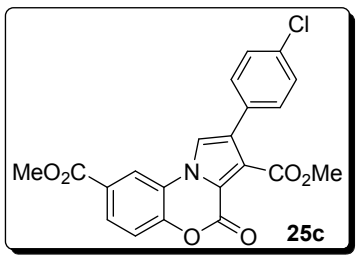
IR (KBr): ν_{max} 1749, 1726, 1604, 1391, 1254, 1117, 1058 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.28 (s, 1H), 7.98 (d, *J* = 8.5 Hz, 1H), 7.75 (s, 1H), 7.38 (d, *J* = 8.5 Hz, 1H), 7.30 (d, *J* = 7.5 Hz, 2H), 7.14 (d, *J* = 8.0 Hz, 2H), 3.96 (s, 3H), 3.95 (s, 3H), 2.33 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 165.2 (C), 165.1 (C), 151.2 (C), 145.9 (C), 137.8 (C), 129.4 (C), 129.4 (CH), 128.5 (C), 128.1 (CH), 127.2 (CH), 126.9 (C), 122.3 (C), 121.4 (C), 118.2 (CH), 116.1 (CH), 116.1 (CH), 115.1 (C), 52.8 (OCH_3), 52.5 (OCH_3), 21.0 (CH_3) ppm.

HRMS (ES$^+$): *m/z* calcd for $[C_{22}H_{17}NO_6+Na]^+$: 414.0948, found: 414.0948.

Dimethyl 2-(4′-chlorophenyl)-4-oxo-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazine-3-dicarb-oxylate (25c):



Yield: 128 mg (62%) as orange solid.

Mp: 154-155 ^oC.

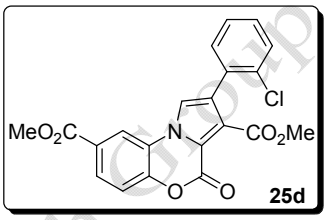
IR (KBr): ν_{max} 1746, 1724, 1604, 1398, 1260, 1119, 1069 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.33 (d, *J* = 1.5 Hz, 1H), 8.03 (dd, *J* = 1.5, 8.5 Hz, 1H), 7.78 (s, 1H), 7.44 (d, *J* = 8.5 Hz, 1H), 7.39 (q, *J* = 8.0 Hz, 4 H), 3.97 (s, 3H), 3.93 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 165.2 (C), 164.7 (C), 151.1 (C), 146.1 (C), 134.2 (C), 130.2 (C), 129.1 (CH), 129.0 (CH), 128.6 (C), 128.5 (CH), 127.1 (C), 122.5 (C), 121.4 (C), 118.5 (CH), 116.2 (CH), 115.6 (C), 53.0 (OCH_3), 52.7 (OCH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{21}H_{14}ClNO_6+Na]^+$: 434.0402 , found: 434.0403.

Dimethyl 2-(2′-chlorophenyl)-4-oxo-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazine-3-dicarboxylate (25d):



Yield: 116 mg (56%) as white solid.

Mp: 184-185 °C.

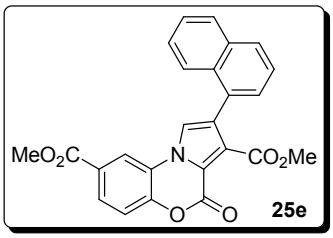
IR (KBr): ν_{max} 1736, 1712, 1595, 1398, 1259, 1115, 1062 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.33 (d, *J* = 1.5 Hz, 1H), 8.02 (dd, *J* = 1.5, 8.5 Hz, 1H), 7.82 (s, 1H), 7.46-7.43 (m, 2H), 7.38-7.36 (m, 1H), 7.32-7.29 (m, 2H), 3.95 (s, 3H), 3.81 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 165.2 (C), 163.6 (C), 150.8 (C), 146.2 (C), 133.3 (C), 131.4 (CH), 131.0 (C), 129.7 (CH), 129.5 (CH), 128.5 (CH), 127.6 (C), 127.0 (C), 126.7 (CH), 123.8 (C), 121.5 (C), 118.3 (CH), 118.1 (CH), 116.3 (CH), 115.3 (C), 52.6 (OCH_3), 52.6 (OCH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{21}H_{14}ClNO_6+Na]^+$: 434.0402, found: 434.0402.

Dimethyl 2-(1-naphthyl)-4-oxo-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazine-3-dicarboxylate (25e):



Yield: 152 mg (71%) as brown solid.

Mp: 208-209 °C.

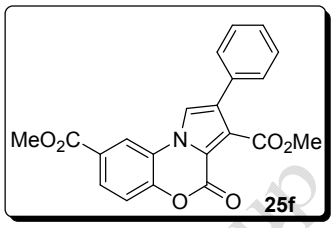
IR (KBr): ν_{max} 1738, 1723, 1593, 1393, 1263, 1118, 1076 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.32 (d, *J* = 2.0 Hz, 1H), 8.04 (dd, *J* = 1.5, 8.5 Hz, 1H), 7.89-7.84 (m, 3H), 7.83 (s, 1H), 7.52-7.44 (m, 5H), 3.95 (s, 3H), 3.61 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 165.2 (C), 163.8 (C), 151.0 (C), 146.2 (C), 133.5 (C), 131.9 (C), 129.5 (C), 128.7 (CH), 128.5 (CH), 128.4 (CH), 127.9 (CH), 127.1 (C), 126.4 (CH), 126.0 (CH), 125.1 (CH), 125.1 (CH), 124.6 (C), 121.6 (C), 118.4 (CH), 118.2 (CH), 116.3 (CH), 115.3 (C), 52.6 (OCH_3), 52.3 (OCH_3) ppm.

HRMS (ES$^+$): *m/z* calcd for $[C_{25}H_{17}NO_6+Na]^+$: 450.0948, found: 450.0955.

Dimethyl 4-oxo-2-phenyl-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazine-3-dicarboxylate (25f):



Yield: 142 mg (75%) as yellow solid.

Mp: 158-159 ^oC.

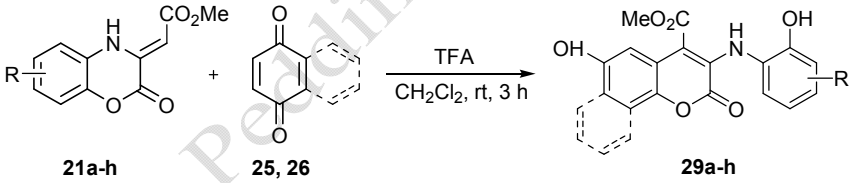
IR (KBr): ν_{max} 1730, 1714, 1603 1465, 1364, 1261, 1006 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.28 (d, *J* = 1.5 Hz, 1H), 7.96 (dd, *J* = 2.0, 9.0 Hz, 1H), 7.77 (s, 1H), 7.41 (d, *J* = 7.0 Hz, 2H), 7.37 (d, *J* = 9.0 Hz, 1H), 7.33 (t, *J* = 7.0 Hz, 2H), 7.28 (d, *J* = 7.5 Hz, 1H), 3.93 (s, 3H), 3.92 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 165.1 (C), 164.9 (C), 151.1 (C), 145.9 (C), 131.4 (C), 129.4 (C), 128.6 (CH), 128.2 (C), 127.9 (C), 127.4 (CH), 126.9 (C), 122.4 (C), 121.4 (C), 118.2 (CH), 116.2 (CH), 116.1 (CH), 115.2 (C), 52.8 (OCH_3), 52.5 (OCH_3) ppm.

HRMS (ES$^+$): *m/z* calcd for $[C_{21}H_{15}NO_6+Na]^+$: 400.0792, found: 400.0791.

3.2.7. General procedure for the synthesis of 3-arylamino coumarin derivatives 29a-h:



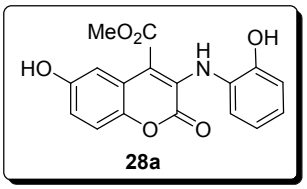
21a-h **25, 26** **29a-h**

To a mixture of 1,4-benzoxazinone derivative **21**, (0.5 mmol) and *p*-benzoquinone (**25**)/naphthoquinone (**26**) (0.6 mmol) in 4 mL of CH_2Cl_2, trifluoroacetic acid (TFA) (0.6 mmol) was added dropwise and the mixture was allowed to stir at room temperature for 3 h. As the reaction proceeded, the product started precipitating out. After completion of the reaction, as shown by TLC, the reaction mixture was filtered and the resultant precipitate was washed with 5 mL of CH_2Cl_2 and dried under vacuum to furnish a yellow coloured solid.

Methyl 6-hydroxy-3-(2′-hydroxyphenylamino)-2-oxo-2*H*-chromene-4-carboxylate (28a):

Yield: 144 mg (88%) as yellow solid.

Mp: 154-155 °C.



28a

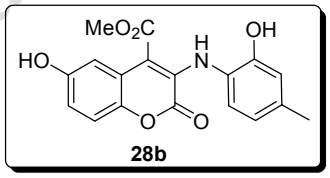
IR (KBr): ν_{max} 3334, 1712, 1663, 1506, 1497, 1350, 1247, 1024 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ 9.54 (s, 2H), 7.82 (s, 1H), 7.22 (d, *J* = 9.0 Hz, 1H), 6.97 (d, *J* = 6.5 Hz, 2H), 6.87-6.83 (m, 2H), 6.78-6.73 (m, 2H), 3.17 (s, 3H) ppm.

^{13}C NMR (125 MHz, DMSO-d_6): δ 165.4 (C), 159.5 (C), 154.5 (C), 151.0 (C), 141.1 (C), 130.0 (C), 127.3 (CH), 126.1 (CH), 124.9 (C), 119.4 (CH), 119.2 (C), 117.5 (CH), 116.4 (CH), 115.2 (CH), 111.6 (C), 105.2 (CH), 51.9 (OCH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{17}H_{13}NO_6+Na]^+$: 350.0635, found: 350.0637.

Methyl 6-hydroxy-3-(2′-hydroxy-4′-methylphenylamino)-2-oxo-2*H*-chromene-4-carboxylate (28b):



28b

Yield: 138 mg (81%) as yellow solid.

Mp: 178-179 °C.

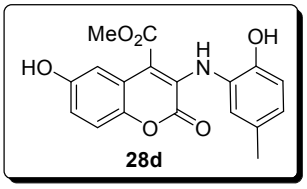
IR (KBr): ν_{max} 3375, 1727, 1689, 1524, 1500, 1344, 1274, 1028 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ 9.74 (br s, 1H), 9.57 (br s, 1H), 7.61 (s, 1H), 7.19 (d, *J* = 8.5 Hz, 1H), 6.81 (d, *J* = 8.0 Hz, 1H), 6.75-6.72 (m, 2H), 6.64-6.63 (m, 1H), 6.55 (dd, *J* = 1.5, 8.0 Hz, 1H), 3.18 (s, 3H), 2.17 (s, 3H) ppm.

^{13}C NMR (125 MHz, DMSO-d_6): δ 165.7 (C), 159.6 (C), 154.6 (C), 151.3 (C), 141.0 (C), 136.2 (C), 130.4 (C), 125.6 (CH), 124.5 (C), 120.1 (CH), 119.4 (C), 117.6 (CH), 117.0 (CH), 115.2 (CH), 110.9 (C), 108.2 (CH), 52.1 (OCH_3), 21.2 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{18}H_{15}NO_6+Na]^+$: 364.0792, found: 364.0791.

Methyl 6-hydroxy-3-(2′-hydroxy-5′-methylphenylamino)-2-oxo-2*H*-chromene-4-carboxylate (28d):



28d

Yield: 133 mg (78%) as yellow solid.

Mp: 164-165 °C.

IR (KBr): ν_{max} 3358, 1724, 1683, 1577, 1524, 1450, 1344, 1257, 1021 cm^{-1}.

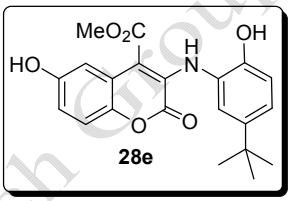
^{1}H NMR (500 MHz, DMSO-d_6): δ 9.69 (br s, 1H), 9.41 (br s, 1H), 7.59 (s, 1H), 7.10 (d, *J* =

9.0 Hz, 1H), 6.83 (d, *J* = 2.5 Hz, 1H), 6.77-6.70 (m, 4H), 3.20 (s, 3H), 2.13 (s, 3H) ppm.

^{13}C NMR (125 MHz, DMSO-*d*$_6$): δ 165.4 (C), 159.4 (C), 154.5 (C), 148.3 (C), 141.0 (C), 129.8 (C), 128.0 (C), 126.9 (C), 126.2 (CH), 124.5 (CH), 119.1 (C), 117.4 (CH), 116.1 (CH), 115.2 (C), 111.5 (C), 108.2 (CH), 51.7 (OCH_3), 20.4 (CH_3) ppm.

HRMS (ES$^+$): *m/z* calcd for $[C_{18}H_{15}NO_6+Na]^+$: 364.0792, found: 364.0789.

Methyl 3-(5′-*tert*-butyl-2′-hydroxyphenylamino)-6-hydroxy-2-oxo-2*H*-chromene-4-carboxylate (28e):



28e

Yield: 132 mg (68%) as yellow solid.

Mp: 184-185 ^{o}C.

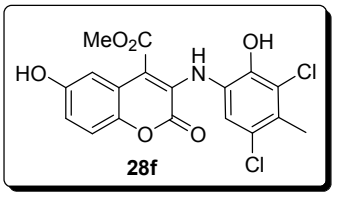
IR (KBr): ν_{max} 3359, 1714, 1649, 1563, 1526, 1344, 1241, 1042 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-*d*$_6$): δ 9.51 (br s, 1H), 9.32 (br s, 1H), 7.69 (s, 1H), 7.21 (d, *J* = 9.0 Hz, 1H), 6.99 (dd, *J* = 2.0, 8.0 Hz, 1H), 6.96 (d, *J* = 2.5 Hz, 1H), 6.92 (d, *J* = 3.0 Hz, 1H), 6.78 (d, *J* = 8.5 Hz, 1H), 6.76 (dd, *J* = 2.5, 8.5 Hz, 1H), 3.08 (s, 3H), 1.22 (s, 9H) ppm.

^{13}C NMR (125 MHz, DMSO-*d*$_6$): δ 165.0 (C), 159.2 (C), 154.2 (C), 148.0 (C), 141.2 (C), 140.6 (C), 129.9 (C), 126.2 (C), 122.3 (CH), 120.4 (CH), 119.0 (C), 117.0 (CH), 115.7 (CH), 114.5 (CH), 109.8 (C), 107.8 (CH), 51.2 (OCH_3), 33.7 (C), 31.2 (CH_3) ppm.

HRMS (ES$^+$): *m/z* calcd for $[C_{21}H_{21}NO_6+Na]^+$: 406.1261, found: 406.1273.

Methyl 3-(3′,5′-dichloro-2′-hydroxy-4′-methylphenylamino)-6-hydroxy-2-oxo-2*H*-chromene-4-carboxylate (28f):



28f

Yield: 152 mg (72%) as yellow solid.

Mp: 198-199 ^{o}C.

IR (KBr): ν_{max} 3387, 1718, 1674, 1603, 1530, 1444, 206, 1017 cm^{-1}.

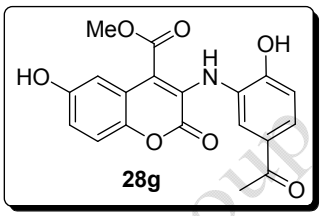
^{1}H NMR (500 MHz, DMSO-*d*$_6$): δ 9.74 (br s, 1H), 7.91 (s, 1H), 7.21 (d, *J* = 9.0 Hz, 1H), 7.02 (s, 1H), 6.79 (dd, *J* = 3.0, 9.0 Hz, 1H), 6.76 (d, *J* = 2.5 Hz, 1H), 3.29 (s, 3H), 2.33 (s, 3H) ppm.

^{13}C NMR (125 MHz, DMSO-*d*$_6$): δ 164.8 (C), 158.6 (C), 154.2 (C), 146.7 (C), 141.1 (C), 130.3 (C), 129.6 (C), 127.5 (C), 123.5 (CH), 122.8 (C), 122.4 (C), 118.5 (C), 117.1 (CH),

115.3 (CH), 113.0 (C), 107.9 (CH), 51.5 (OCH_3), 17.3 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{18}H_{13}Cl_2NO_6+Na]^+$: 432.0012, found: 432.0017.

Methyl 3-(5′-acetyl-2′-hydroxyphenylamino)-6-hydroxy-2-oxo-2*H*-chromene-4-carboxylate (28g):



Yield: 137 mg (74%) as yellow solid.

Mp: 184-185 °C.

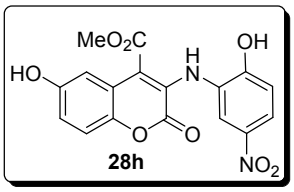
IR (KBr): ν_{max} 3361, 1709, 1653, 1586, 1506, 1450, 1338, 1074 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-*d*$_6$): δ 10.67 (br s, 1H), 9.65 (br s, 1H), 7.84 (s, 1H), 7.63 (dd, *J* = 2.0, 8.5 Hz, 1H), 7.58 (d, *J* = 2.0 Hz, 1H), 7.23 (d, *J* = 8.5 Hz, 1H), 6.93 (d, *J* = 8.5 Hz, 1H), 6.84 (d, *J* = 2.5 Hz, 1H), 6.80 (dd, *J* = 2.5, 8.5 Hz, 1H), 3.20 (s, 3H), 2.45 (s, 3H) ppm.

^{13}C NMR (125 MHz, DMSO-*d*$_6$): δ 196.2 (C), 165.2 (C), 159.0 (C), 155.4 (C), 154.4 (C), 141.1 (C), 129.5 (C), 128.6 (C), 127.4 (C), 126.6 (CH), 124.6 (CH), 118.7 (C), 117.3 (CH), 115.8 (CH), 115.3 (CH), 112.7 (C), 108.1 (CH), 51.7 (OCH_3), 26.4 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{19}H_{15}NO_7+Na]^+$: 392.0741, found: 392.0746.

Methyl 6-hydroxy-3-(2′-hydroxy-5′-nitrophenylamino)-2-oxo-2*H*-chromene-4-carboxylate (28h):



Yield: 132 mg (71%) as yellow solid.

Mp: 171-172 °C.

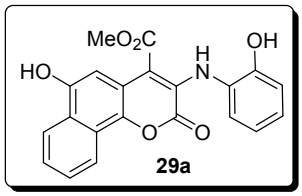
IR (KBr): ν_{max} 3326, 1712, 1674, 1592, 1527, 1361, 1241, 1079 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-*d*$_6$): δ 11.38 (br s, 1H), 8.05 (br s, 1H), 7.89 (d, *J* = 9.0 Hz, 1H), 7.87-7.85 (m, 1H), 7.24 (d, *J* = 8.5 Hz, 1H), 7.00 (d, *J* = 9.0 Hz, 1H), 6.91 (s, 1H), 6.84 (dd, *J* = 2.5, 8.5 Hz, 1H), 3.36 (s, 3H) ppm.

^{13}C NMR (125 MHz, DMSO-*d*$_6$): δ 165.0 (C), 158.7 (C), 156.7 (C), 156.7 (C), 154.3 (C), 141.7 (C), 139.3 (C), 128.9 (C), 128.8 (C), 121.1 (CH), 118.5 (CH), 118.2 (C), 117.4 (CH), 116.1 (CH), 115.6 (CH), 108.5 (CH), 52.0 (OCH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{17}H_{12}N_2O_8+Na]^+$: 395.0486, found: 395.0497.

Methyl 6-hydroxy-3-(2′-hydroxyphenylamino)-2-oxo-2*H*-benzo[*h*]chromene-4-carboxylate (29a):



Yield: 162 mg (86%) as yellow solid.

Mp: 176-177 ^{o}C.

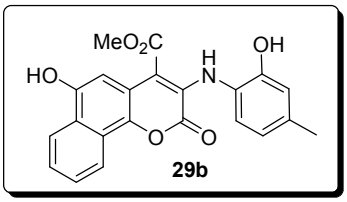
IR (KBr): ν_{max} 3382, 1711, 1677, 1592, 1577, 1409, 1245, 1078 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ 10.29 (br s, 1H), 9.56 (br s, 1H), 8.23 (d, *J* = 8.5 Hz, 1H), 8.14 (d, *J* = 8.0 Hz, 1H), 7.89 (s, 1H), 7.66 (t, *J* = 7.5 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.02-6.97 (m, 2H), 6.95 (s, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 6.76 (t, *J* = 7.5 Hz, 1H), 3.23 (s, 3H) ppm.

^{13}C NMR (125 MHz, DMSO-d_6): δ 165.2 (C), 158.9 (C), 150.7 (C), 150.0 (C), 135.8 (C), 130.1 (C), 127.6 (CH), 127.1 (C), 125.7 (CH), 125.5 (CH), 124.6 (CH), 123.6 (C), 123.3 (C), 122.4 (CH), 120.1 (CH), 118.8 (CH), 116.0 (CH), 114.4 (C), 112.3 (C), 100.8 (CH), 51.4 (OCH_3) ppm.

HRMS (ES^{+}): *m/z* calcd for $[C_{21}H_{15}NO_6+Na]^{+}$: 400.0792, found: 400.0800.

Methyl 6-hydroxy-3-(2′-hydroxy-4′-methylphenylamino)-2-oxo-2*H*-benzo[*h*]chromene-4-carboxylate (29b):



Yield: 159 mg (81%) as yellow solid.

Mp: 216-217 ^{o}C.

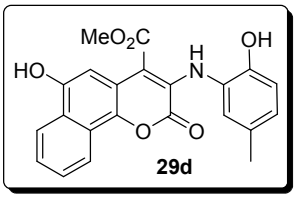
IR (KBr): ν_{max} 3358, 1709, 1674, 1592, 1559, 1421, 1232, 1085 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ 10.29 (br s, 1H), 9.43 (br s, 1H), 8.22 (d, *J* = 8.5 Hz, 1H), 8.15 (d, *J* = 8.5 Hz, 1H), 7.81 (s, 1H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.53 (t, *J* = 8.0 Hz, 1H), 6.94 (s, 1H), 6.91 (d, *J* = 8.0 Hz, 1H), 6.70 (s, 1H), 6.58 (d, *J* = 8.0 Hz, 1H), 3.25 (s, 3H), 2.22 (s, 3H) ppm.

^{13}C NMR (125 MHz, DMSO-d_6): δ 165.3 (C), 159.0 (C), 151.0 (C), 150.1 (C), 135.6 (C), 135.3 (C), 130.4 (C), 127.6 (CH), 125.6 (CH), 125.1 (CH), 124.3 (C), 123.5 (C), 123.4 (C), 122.4 (CH), 120.0 (CH), 119.4 (CH), 116.6 (CH), 114.6 (C), 111.5 (C), 100.8 (CH), 51.5 (OCH_3), 20.7 (CH_3) ppm.

HRMS (ES^{+}): *m/z* calcd for $[C_{22}H_{17}NO_6+Na]^{+}$: 414.0948, found: 414.0960.

Methyl 6-hydroxy-3-(2′-hydroxy-5′-methylphenylamino)-2-oxo-2*H*-benzo[*h*]chromene-4-carboxylate (29d):



29d

Yield: 164 mg (84%) as yellow solid.

Mp: 208-209 ^{o}C.

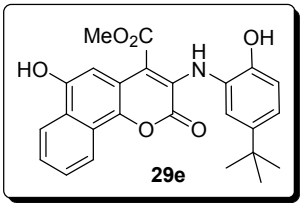
IR (KBr): ν_{max} 3352, 1712, 1689, 1589, 1562, 1430, 1206, 1085 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ 10.31 (br s, 1H), 9.33 (br s, 1H), 8.23 (d, *J* = 8.5 Hz, 1H), 8.14 (d, *J* = 8.5 Hz, 1H), 7.79 (s, 1H), 7.67 (t, *J* = 7.0 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 1H), 6.97 (s, 1H), 6.81-6.74 (m, 3H), 3.25 (s, 3H), 2.17 (s, 3H) ppm.

^{13}C NMR (125 MHz, DMSO-d_6): δ 165.3 (C), 159.1 (C), 150.1 (C), 148.2 (C), 136.0 (C), 130.0 (C), 127.7 (CH), 127.6 (C), 126.8 (C), 125.8 (CH), 124.3 (CH), 123.7 (C), 123.4 (C), 122.5 (CH), 120.2 (CH), 115.9 (CH), 114.4 (C), 112.5 (C), 101.0 (CH), 51.5 (OCH_3), 20.2 (CH_3) ppm.

HRMS (ES^{+}): *m/z* calcd for $[C_{22}H_{17}NO_6+Na]^{+}$: 414.0948, found: 414.0963.

Methyl 3-(5′-*tert*-butyl-2′-hydroxyphenylamino)-6-hydroxy-2-oxo-2*H*-benzo[*h*]-chromene-4-carboxylate (29e):



29e

Yield: 162 mg (75%) as yellow solid.

Mp: 202-203 ^{o}C.

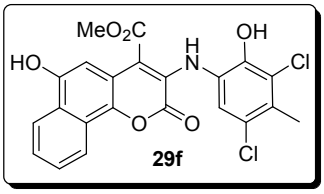
IR (KBr): ν_{max} 3364, 1721, 1657, 1572, 1509, 1352, 1238, 1063 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ 10.27 (br s, 1H), 9.38 (br s, 1H), 8.23 (d, *J* = 8.5 Hz, 1H), 8.16 (d, *J* = 8.5 Hz, 1H), 7.78 (s, 1H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.07 (s, 1H), 7.03 (s, 1H), 6.99 (d, *J* = 8.5 Hz, 1H), 6.84 (d, *J* = 8.5 Hz, 1H), 3.15 (s, 3H), 1.20 (s, 9H) ppm.

^{13}C NMR (125 MHz, DMSO-d_6): δ 165.2 (C), 159.2 (C), 150.1 (C), 148.1 (C), 141.3 (C), 135.8 (C), 130.3 (C), 127.5 (CH), 126.3 (C), 125.6 (C), 123.7 (C), 123.4 (C), 122.4 (CH), 122.3 (CH), 120.4 (CH), 120.1 (CH), 115.8 (CH), 114.6 (C), 111.3 (C), 101.0 (CH), 51.3 (OCH_3) ppm.

HRMS (ES^{+}): *m/z* calcd for $[C_{25}H_{23}NO_6+Na]^{+}$: 456.1418, found: 456.1428.

Methyl 3-(3′,5′-dichloro-2′-hydroxy-4-methylphenylamino)-6-hydroxy-2-oxo-2*H*-benzo[*h*]chromene-4-carboxylate (29f):



29f

Yield: 182 mg (79%) as yellow solid.

Mp: 220-221 ^{o}C.

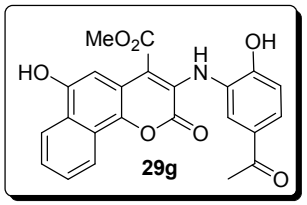
IR (KBr): ν_{max} 3368, 1714, 1689, 1546, 1468, 1268, 1082 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ 10.32 (br s, 1H), 9.75 (br s, 1H), 8.24 (d, *J* = 8.5 Hz, 1H), 8.16 (d, *J* = 8.5 Hz, 1H), 8.05 (s, 1H), 7.67 (t, *J* = 7.5 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.11 (s, 1H), 6.89 (s, 1H), 3.39 (s, 3H), 2.37 (s, 3H) ppm.

^{13}C NMR (125 MHz, DMSO-d_6): δ 165.1 (C), 158.6 (C), 150.1 (C), 146.7 (C), 136.6 (C), 130.2 (C), 129.8 (C), 127.7 (C), 127.6 (CH), 126.0 (CH), 124.0 (C), 123.3 (CH), 123.3 (C), 122.9 (C), 122.5 (CH), 122.5 (C), 120.2 (CH), 114.8 (C), 113.9 (C), 100.8 (CH), 51.7 (OCH_3), 17.3 (CH_3) ppm.

HRMS (ES^{+}): *m/z* calcd for $[C_{22}H_{15}C_{l2}NO_6+Na]^{+}$: 482.0169, found: 482.0178.

Methyl 3-(5′-acetyl-2′-hydroxyphenylamino)-6-hydroxy-2-oxo-2*H*-benzo[*h*]chromene-4-carboxylate (29g):



29g

Yield: 162 mg (77%) as yellow solid.

Mp: 202-203 ^{o}C.

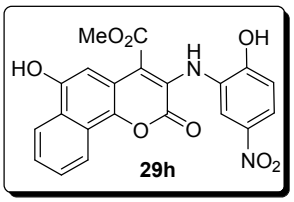
IR (KBr): ν_{max} 3387, 1706, 1656, 1586, 1562, 1415, 1321 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ 10.34 (br s, 1H), 8.24 (d, *J* = 8.5Hz, 1H), 8.15 (d, *J* = 8.5 Hz, 1H), 7.93 (s, 1H), 7.68-7.64 (m, 3H), 7.56 (t, *J* = 8.0 Hz, 1H), 6.96-6.94 (m, 2H), 3.26 (s, 3H), 2.47 (s, 3H) ppm.

^{13}C NMR (125 MHz, DMSO-d_6): δ 195.9 (C), 165.2 (C), 158.8 (C), 155.3 (C), 150.1 (C), 136.3 (C), 129.7 (C), 128.5 (C), 127.6 (CH), 127.4 (C), 126.3 (CH), 125.9 (CH), 124.5 (CH), 123.9 (C), 123.3 (C), 122.4 (CH), 120.2 (CH), 115.7 (CH), 114.1 (C), 114.0 (C), 100.9 (CH), 51.6 (OCH_3), 26.2 (CH_3) ppm.

HRMS (ES^{+}): *m/z* calcd for $[C_{23}H_{17}NO_7+Na]^{+}$: 442.0897, found: 442.0905.

Methyl 6-hydroxy-3-(2′-hydroxy-5′-nitrophenylamino)-2-oxo-2*H*-benzo[*h*]chromene-4-carboxylate (29h):



29h

Yield: 152 mg (72%) as yellow solid.

Mp: 194-195 ^{o}C.

IR (KBr): ν_{max} 3364, 1724, 1677, 1589, 1559, 1421, 1318, 1079 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ 11.40 (br s, 1H), 10.35 (br s, 1H), 8.19-8.05 (m, 2H), 8.05 (s, 1H), 7.86 (s, 2H), 7.61-7.53 (m, 2H), 7.01-6.94 (m, 2H), 3.42 (s, 3H) ppm.

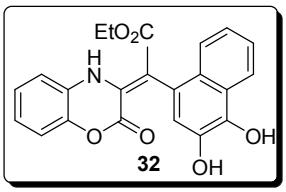
^{13}C NMR (125 MHz, DMSO-d_6): δ 164.3 (C), 157.7 (C), 155.6 (C), 149.3 (C), 138.5 (C), 136.6 (C), 128.1 (C), 128.0 (C), 126.8 (CH), 125.4 (CH), 123.5 (C), 122.5 (C), 121.6 (CH), 119.9 (CH), 119.6 (CH), 117.2 (CH), 117.0 (C), 114.7 (CH), 112.8 (C), 100.2 (CH), 51.1 (OCH_3) ppm.

HRMS (ES^{+}): *m/z* calcd for $[C_{21}H_{14}N_2O_8+Na]^{+}$: 445.0642, found: 445.0647.

Synthesis of ethyl (*Z*)-2-(3′,4′-dihydroxynaphthalen-1-yl)-2-(2-oxo-2*H*-benzo[*b*][1,4]-oxazin-3(4*H*)-ylidene)acetate (32):

To a mixture of 1,4-benzoxazinone derivative **30** (0.5 mmol) and naphthoquinone monoketal **31**, (0.6 mmol) in 4 mL of CH_2Cl_2, trifluoroacetic acid (0.6 mmol) was added dropwise, and the mixture was allowed to stir at room temperature for 4 h. After completion of the reaction, as shown by TLC, the reaction was quenched with 4 mL of saturated $NaHCO_3$ solution. The organic layer was separated, washed twice with water (2 x 15 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude reaction mixture was purified by column chromatography on silica gel (100-200 mesh) using 30-50% ethyl acetate/hexanes as the eluting system.

Yield: 153 mg (78%) as brown solid.



32

Mp: 168-169 ^{o}C.

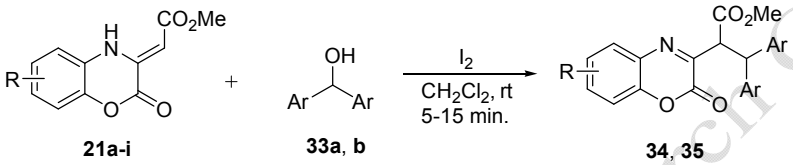
IR (KBr): ν_{max} 3352, 1726, 1678, 1593, 1394, 1279, 1085 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 11.97 (br s, 1H), 8.12-8.10 (m, 1H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.44 (t, *J* = 7.5 Hz, 1H), 7.26 (d, *J* = 7.5 Hz, 1H), 7.19-7.14 (m, 1H), 7.12-7.03 (m, 3H), 6.27 (s, 1H), 4.20-4.15 (m, 2H), 1.12-1.09 (m, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 180.7 (C), 179.6 (C), 168.5 (C), 154.0 (C), 153.1 (C), 140.4 (C), 136.7 (C), 136.3 (C), 135.3 (CH), 131.1 (C), 130.1 (CH), 129.9 (CH), 128.1 (CH), 127.0 (CH), 125.8 (CH), 123.6 (CH), 123.5 (C), 116.7 (CH), 115.4(CH), 100.0 (C), 61.5(CH_2), 13.9 (CH_3) ppm.

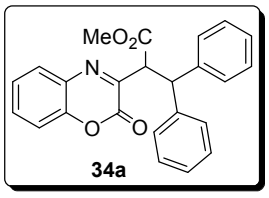
HRMS (ES^+): *m/z* calcd for $[C_{22}H_{17}NO_6+Na]^+$: 414.0948, found: 414.0938.

3.2.8. General procedure for the synthesis of 3-(2′,2′-diaryl-1′-methoxycarbonyl) ethyl-1,4-benzoxazinone derivatives 34 and 35:



To a mixture of 1,4-benzoxazinone derivative **21**, (0.5 mmol) and diarylmethanol derivative **33**, (0.6 mmol) in 4 mL of CH_2Cl_2, molecular iodine (127 mg, 0.5 mmol) was added and the reaction mixture was allowed to stir at room temperature for 5-15 min. After completion of the reaction as shown by TLC, the reaction was quenched with 4 mL of saturated $Na_2S_2O_3$ solution. The organic layer was separated, washed twice with water (2 x 15 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude reaction mixture was purified by column chromatography on silica gel (100-200 mesh) using 20-30% ethyl acetate/hexanes as the eluting system.

Methyl 2-(2-oxo-2*H*-benzo[*b*][1,4]oxazin-3-yl)-3,3-diphenylpropanoate (34a):



Yield: 179 mg (94%) as white solid.

Mp: 159-160 ^oC.

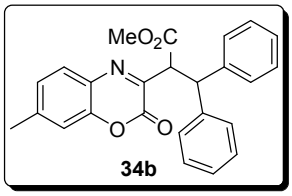
IR (KBr): ν_{max} 1745, 1603, 1568, 1450, 1327, 1262 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.77 (d, *J* = 8.0 Hz, 1H), 7.48-7.42 (m, 3H), 7.34-7.28 (m, 5H), 7.20 (dd, *J* = 7.5, 12.5 Hz, 2H), 7.14 (t, *J* = 8.0 Hz, 2H), 7.04 (t, *J* = 7.0 Hz, 1H), 5.40 (d, *J* = 12.0 Hz, 1H), 5.14 (d, *J* = 12.0 Hz, 1H), 3.51 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 169.7 (C), 152.8 (C), 152.4 (C), 146.0 (C), 141.9 (C), 141.2 (C), 131.4 (CH), 130.9 (C), 129.3 (CH), 128.5 (CH), 128.5 (CH), 128.1 (CH), 127.9 (CH), 126.8 (CH), 126.6 (CH), 125.4 (CH), 116.2 (CH), 52.4 (CH_3), 52.2 (CH), 51.9 (CH)

ppm.

Methyl 2-(7-methyl-2-oxo-2*H*-benzo[*b*][1,4]oxazin-3-yl)-3,3-diphenylpropanoate (34b):



34b

Yield: 182 mg (91%) as white solid.

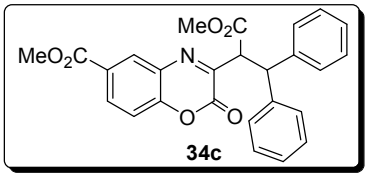
Mp: 184-185 ^{o}C.

IR (KBr): ν_{max} 1739, 1624, 1508, 1444, 1265, 1159 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.65 (d, *J* = 8.5 Hz, 1H), 7.46 (d, *J* = 7.5 Hz, 2H), 7.32-7.27 (m, 4H), 7.20 (t, *J* = 7.0 Hz, 1H), 7.15-7.12 (m, 3H), 7.03 (t, *J* = 7.0 Hz, 1H), 6.98 (s, 1H), 5.37 (d, *J* = 12.0 Hz, 1H), 5.13 (d, *J* = 12.0 Hz, 1H), 3.50 (s, 3H), 2.41 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 169.9 (C), 152.7 (C), 151.4 (C), 145.9 (C), 142.9 (C), 142.0 (C), 141.3 (C), 129.1 (C), 128.9 (CH), 128.5 (CH), 128.5 (CH), 128.1 (CH), 127.9 (CH), 126.8 (CH), 126.6 (CH), 126.6 (CH), 126.6 (C), 116.3 (CH), 52.4 (OCH_3), 52.0 (CH), 52.0 (CH), 21.6 (CH_3) ppm.

Methyl 3-(1-methoxy-1-oxo-3,3-diphenylpropan-2-yl)-2-oxo-2*H*-benzo[*b*][1,4]oxazine-6-carboxylate (34c):



34c

Yield: 180 mg (81%) as pale yellow solid.

Mp: 150-151 ^{o}C.

IR (KBr): ν_{max} 1754, 1727, 1615, 1565, 1433, 1224 cm^{-1}.

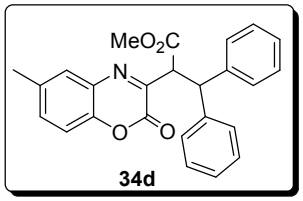
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.44 (d, *J* = 1.5 Hz, 1H), 8.08 (d, *J* = 8.5 Hz, 1H), 7.45 (d, *J* = 7.5 Hz, 2H), 7.32-7.28 (m, 4H), 7.22-7.16 (m, 2H), 7.13 (t, *J* = 7.5 Hz, 2H), 7.02 (t, *J* = 7.0 Hz, 1H), 5.39 (d, *J* = 12.0 Hz, 1H), 5.14 (d, *J* = 12.0 Hz, 1H), 3.92 (s, 3H), 3.48 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 169.3 (C), 165.1 (C), 153.7 (C), 151.5 (C), 148.8 (C), 141.6 (C), 140.9 (C), 132.2 (CH), 130.9 (CH), 130.2 (C), 128.5 (CH), 128.4 (CH), 127.9 (CH), 127.7 (CH), 127.6 (C), 127.0 (C), 126.7 (CH), 126.6 (CH), 116.4 (CH), 52.4 (OCH_3), 52.3 (OCH_3), 52.2 (CH), 51.8 (CH) ppm.

Methyl 2-(6-methyl-2-oxo-2*H*-benzo[*b*][1,4]oxazin-3-yl)-3,3-diphenylpropanoate (34d):

Yield: 179 mg (90%) as white solid.

Mp: 134-135 ^{o}C.



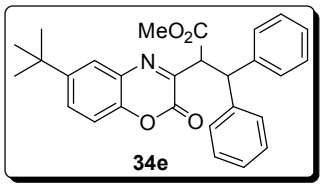
34d

IR (KBr): ν_{max} 1742, 1624, 1529, 1457, 1259 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.58 (s, 1H), 7.47 (d, *J* = 7.5 Hz, 2H), 7.35-7.30 (m, 4H), 7.25-7.19 (m, 2H), 7.15 (t, *J* = 7.5 Hz, 2H), 7.08-7.02 (m, 2H), 5.41 (d, *J* = 12.0 Hz, 1H), 5.16 (d, *J* = 12.0 Hz, 1H), 3.50 (s, 3H), 2.39 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 169.7 (C), 152.6 (C), 152.5 (C), 143.8 (C), 141.9 (C), 141.2 (C), 135.3 (C), 132.3 (CH), 130.6 (C), 129.1 (CH), 128.5 (CH), 128.0 (CH), 127.8 (CH), 126.7 (CH), 126.5 (CH), 115.7 (CH), 52.3 (OCH_3), 52.0 (CH), 52.0 (CH), 20.6 (CH_3) ppm.

Methyl 2-(6-*tert*-butyl-2-oxo-2*H*-benzo[*b*][1,4]oxazin-3-yl)-3,3-diphenylpropanoate (34e):



34e

Yield: 185 mg (84%) as yellow solid.

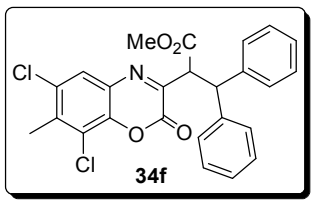
Mp: 157-158 ^{o}C.

IR (KBr): ν_{max} 1739, 1609, 1592, 1450, 1261, 1134 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.84 (d, *J* = 1.5 Hz, 1H), 7.54-7.50 (m, 3H), 7.37-7.33 (m, 4H), 7.23 (t, *J* = 7.0 Hz, 1H), 7.18 (q, *J* = 7.5 Hz, 3H), 7.06 (t, *J* = 7.5 Hz, 1H), 5.50 (d, *J* = 12.0 Hz, 1H), 5.13 (d, *J* = 12.0 Hz, 1H), 3.53 (s, 3H), 1.40 (s, 9H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 169.7 (C), 152.6 (C), 152.4 (C), 148.8 (C), 143.7 (C), 142.0 (C), 141.1 (C), 130.4 (C), 129.0 (CH), 128.4 (CH), 128.0 (CH), 127.8 (CH), 126.7 (CH), 126.5 (CH), 125.8 (CH), 115.5 (CH), 52.3 (OCH_3), 52.0 (CH), 51.8 (CH) ppm.

Methyl 2-(6,8-dichloro-7-methyl-2-oxo-2*H*-benzo[*b*][1,4]oxazin-3-yl)-3,3-diphenyl propanoate (34f):



34f

Yield: 202 mg (86%) as pale yellow solid.

Mp: 120-121 ^{o}C.

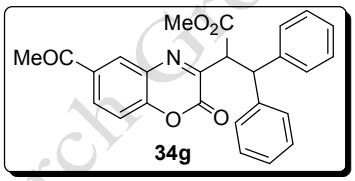
IR (KBr): ν_{max} 1748, 1603, 1550, 1450, 1262, 1197 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75 (s, 1H), 7.45 (d, *J* = 7.5 Hz, 2H), 7.33 (t, *J* = 7.5 Hz, 2H), 7.29 (d, *J* = 7.0 Hz, 2H), 7.23 (t, *J* = 7.0 Hz, 1H), 7.19 (t, *J* = 7.0 Hz, 2H), 7.08 (t, *J* =

7.5 Hz, 1H), 5.39 (d, *J* = 12.0 Hz, 1H), 5.11 (d, *J* = 12.0 Hz, 1H), 3.52 (s, 3H), 2.57 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 169.4 (C), 153.6 (C), 151.3 (C), 141.7 (C), 141.2 (C), 141.0 (C), 138.6 (C), 131.2 (C), 129.7 (C), 128.7 (CH), 128.6 (CH), 128.0 (CH), 127.9 (CH), 127.1 (CH), 126.9 (CH), 126.8 (CH), 121.9 (C), 52.5 (OCH_3), 52.3 (CH), 52.0 (CH), 18.0 (CH_3) ppm.

Methyl 2-(6-acetyl-2-oxo-2*H*-benzo[*b*][1,4]oxazin-3-yl)-3,3-diphenylpropanoate (34g):



34g

Yield: 182 mg (85%) as white solid.

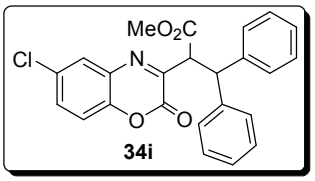
Mp: 150-151 ^{o}C.

IR (KBr): ν_{max} 1742, 1677, 1606, 1495, 1253, 1127 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.35 (s, 1H), 8.08 (d, *J* = 8.5 Hz, 1H), 7.45 (d, *J* = 7.5 Hz, 2H), 7.35-7.27 (m, 5H), 7.21 (t, *J* = 6.5 Hz, 1H), 7.15 (t, *J* = 7.0 Hz, 2H), 7.05 (t, *J* = 7.0 Hz, 1H), 5.39 (d, *J* = 12.0 Hz, 1H), 5.13 (d, *J* = 12.0 Hz, 1H), 3.52 (s, 3H), 2.65 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 195.7 (C), 169.5 (C), 154.0 (C), 151.6 (C), 149.0 (C), 141.7 (C), 141.0 (C), 134.5 (C), 131.0 (CH), 130.4 (C),130.0 (CH), 128.6 (CH), 128.6 (CH), 128.0 (CH), 127.8 (CH), 126.9 (CH), 126.7 (CH), 116.8 (CH), 52.5 (OCH_3), 52.3 (CH), 52.1 (CH), 26.5 (CH_3) ppm.

Methyl 2-(6-chloro-2-oxo-2*H*-benzo[*b*][1,4]oxazin-3-yl)-3,3-diphenylpropanoate (34i):



34i

Yield: 186 mg (88%) as white solid.

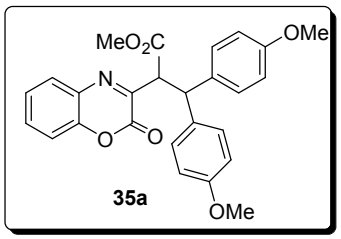
Mp: 126-127 ^{o}C.

IR (KBr): ν_{max} 1748, 1603, 1559, 1447, 1259, 1168 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.78 (d, *J* = 2.5 Hz, 1H), 7.45-7.41 (m, 3H), 7.32 (t, *J* = 8.0 Hz, 2H), 7.28-7.27 (m, 2H), 7.22 (t, *J* = 7.5 Hz, 1H), 7.19-7.15 (m, 3H), 7.07 (t, *J* = 7.0 Hz, 1H), 5.37 (d, *J* = 12.0 Hz, 1H), 5.10 (d, *J* = 12.0 Hz, 1H), 3.52 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 169.4 (C), 154.1 (C), 151.8 (C), 144.4 (C), 141.7 (C), 141.0 (C), 131.2 (CH), 130.5 (C), 128.7 (CH), 128.5 (CH), 128.0 (CH), 127.8 (CH), 126.8 (CH), 126.7 (CH), 126.4 (C), 117.3 (CH), 52.4 (OCH_3), 52.3 (CH), 51.9 (CH) ppm.

Methyl 3,3-bis(4′-methoxyphenyl)-2-(2-oxo-2*H*-benzo[*b*][1,4]oxazin-3-yl)propanoate (35a):



Yield: 216 mg (97%) as yellow solid.

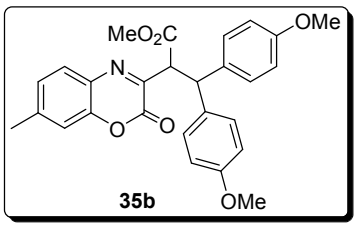
Mp: 118-119 ^{o}C.

IR (KBr): ν_{max} 1742, 1612, 1509, 1462, 1312, 1253, 1177 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.0 Hz, 1H), 7.44 (t, *J* = 7.5 Hz, 1H), 7.36-7.30 (m, 3H), 7.20-7.17 (m, 3H), 6.84 (d, *J* = 8.5 Hz, 2H), 6.67 (d, *J* = 8.5 Hz, 2H), 5.30 (d, *J* = 12.0 Hz, 1H), 5.03 (d, *J* = 12.0 Hz, 1H), 3.75 (s, 3H), 3.61 (s, 3H), 3.52 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 169.8 (C), 158.2 (C), 158.0 (C), 152.9 (C), 152.4 (C), 146.0 (C), 134.5 (C), 133.7 (C), 131.4 (CH), 131.0 (C), 129.3 (CH), 128.9 (CH), 128.7 (CH), 125.4 (CH), 116.2 (CH), 113.9 (CH), 113.9 (CH), 55.1 (OCH_3), 55.0 (OCH_3), 52.5 (OCH_3), 52.4 (CH), 50.4 (CH) ppm.

Methyl 3,3-bis(4′-methoxyphenyl)-2-(7-methyl-2-oxo-2*H*-benzo[*b*][1,4]oxazin-3-yl)propanoate (35b):



Yield: 221 mg (96%) as yellow solid.

Mp: 130-131 ^{o}C.

IR (KBr): ν_{max} 1745, 1618, 1603, 1506, 1456, 1238 cm^{-1}.

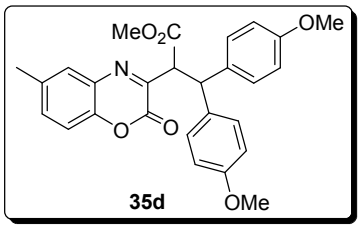
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.65 (d, *J* = 8.0 Hz, 1H), 7.35 (d, *J* = 9.0 Hz, 2H), 7.17 (d, *J* = 8.5 Hz, 2H), 7.12 (dd, *J* = 1.0, 8.0 Hz, 1H), 6.98 (s, 1H), 6.83 (d, *J* = 8.5 Hz, 2H), 6.66 (d, *J* = 9.0 Hz, 2H), 5.28 (d, *J* = 12.0 Hz, 1H), 5.02 (d, *J* = 12.0 Hz, 1H), 3.75 (s, 3H), 3.63 (s, 3H), 3.51 (s, 3H), 2.40 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 169.9 (C), 158.1 (C), 157.9 (C), 152.7 (C), 151.5 (C), 145.8 (C), 142.8 (C), 134.5 (C), 133.7 (C), 129.0 (C), 128.9 (CH), 128.9 (CH), 128.7 (CH), 126.5 (CH), 116.2 (CH), 113.8 (CH), 113.8 (CH), 55.0 (OCH_3), 54.9 (OCH_3), 52.3 (OCH_3), 52.3 (CH), 50.4 (CH), 21.5 (CH_3) ppm.

Methyl 3,3-bis(4′-methoxyphenyl)-2-(6-methyl-2-oxo-2*H*-benzo[*b*][1,4]oxazin-3-yl)propanoate (35d):

Yield: 214 mg (93%) as yellow solid.

Mp: 156-157 ^{o}C.

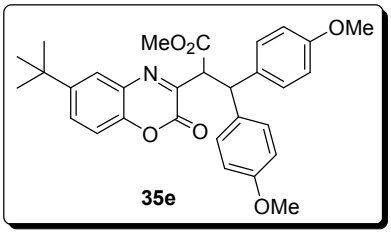


IR (KBr): ν_{max} 1748, 1621, 1506, 1459, 1312, 1235, 1180 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.65 (d, *J* = 8.0 Hz, 1H), 7.35 (d, *J* = 8.5 Hz, 2H), 7.18 (d, *J* = 8.5 Hz, 2H), 7.11 (d, *J* = 8.0 Hz, 1H), 6.97 (s, 1H), 6.84 (d, *J* = 8.5 Hz, 2H), 6.66 (d, *J* = 8.5 Hz, 2H), 5.29 (d, *J* = 12.0 Hz, 1H), 5.02 (d, *J* = 12.0 Hz, 1H), 3.74 (s, 3H), 3.62 (s, 3H), 3.51 (s, 3H), 2.39 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 169.9 (C), 158.1 (C), 157.9 (C), 152.6 (C), 151.4 (C), 145.8 (C), 142.7 (C), 134.5 (C), 133.7 (C), 129.0 (C), 128.9 (CH), 128.8 (CH), 128.6 (CH), 126.5 (CH),116.2 (CH), 113.8 (CH), 113.7 (CH), 55.0 (OCH_3), 54.9 (OCH_3), 52.3 (OCH_3), 52.2 (CH), 50.4 (CH), 21.5 (CH_3) ppm.

Methyl 2-(6-*tert*-butyl-2-oxo-2*H*-benzo[*b*][1,4]oxazin-3-yl)-3,3-bis(4′-methoxyphenyl)propanoate (35e):



Yield: 212 mg (85%) as yellow solid.

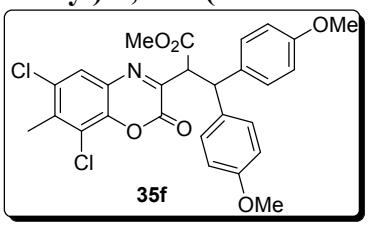
Mp: 120-121 ^{o}C.

IR (KBr): ν_{max} 1748, 1603, 1509, 1368, 1259, 1157 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.80 (d, *J* = 2.0 Hz, 1H), 7.49 (dd, *J* = 2.5, 8.5 Hz, 1H), 7.37 (d, *J* = 8.5 Hz, 2H), 7.21 (d, *J* = 9.0 Hz, 2H), 7.11 (d, *J* = 8.5 Hz, 1H), 6.84 (d, *J* = 8.5 Hz, 2H), 6.67 (d, *J* = 9.0 Hz, 2H), 5.37 (d, *J* = 12.5 Hz, 1H), 5.06 (d, *J* = 12.0 Hz, 1H), 3.72 (s, 3H), 3.59 (s, 3H), 3.50 (s, 3H), 1.34 (s, 9H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 169.7 (C), 158.0 (C), 157.8 (C), 152.6 (C), 152.5 (C), 148.7 (C), 143.6 (C), 134.4 (C), 133.5 (C), 130.4 (C), 128.9 (CH), 128.8 (CH), 128.6 (CH), 125.7 (CH), 115.5 (CH), 113.7 (CH), 54.8 (OCH_3), 54.7 (OCH_3), 52.2 (OCH_3), 52.1 (CH), 50.5 (CH), 34.4 (C), 31.1 (CH_3) ppm.

Methyl 2-(6,8-dichloro-7-methyl-2-oxo-2*H*-benzo[*b*][1,4]oxazin-3-yl)-3,3-bis(4′-methoxyphenyl)propanoate (35f):



Yield: 213 mg (81%) as yellow solid.

Mp: 169-170 ^{o}C.

IR (KBr): ν_{max} 1745, 1603, 1512, 1459, 1262, 1177 cm^{-1}.

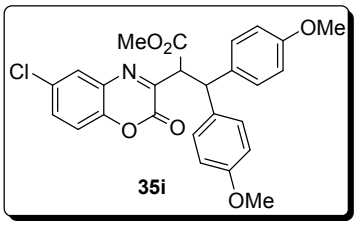
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.69 (s, 1H), 7.34 (d, *J* = 8.5 Hz, 2H), 7.18 (d, *J* = 8.5 Hz, 2H), 6.84 (d, *J* = 8.5 Hz, 2H), 6.69 (d, *J* = 8.5 Hz, 2H), 5.30 (d, *J* = 12.0 Hz, 1H), 5.01 (d, *J* = 12.0 Hz, 1H), 3.75 (s, 3H), 3.64 (s, 3H), 3.51 (s, 3H), 2.49 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 169.3 (C), 158.2 (C), 158.0 (C), 153.6 (C), 151.2 (C), 141.0 (C), 138.4 (C), 134.1 (C), 133.4 (C), 131.0 (C), 129.6 (C), 128.8 (CH), 128.6 (CH), 126.9 (CH), 121.7 (C), 113.9 (CH), 113.8 (CH), 55.0 (OCH_3), 54.9 (OCH_3), 52.5 (OCH_3), 52.5 (CH), 50.4 (CH), 17.8 (CH_3) ppm.

Methyl 2-(6-chloro-2-oxo-2*H*-benzo[*b*][1,4]oxazin-3-yl)-3,3-bis(4′-methoxyphenyl)propanoate (35i):

Yield: 219 mg (91%) as yellow solid.

Mp: 95-96 °C.

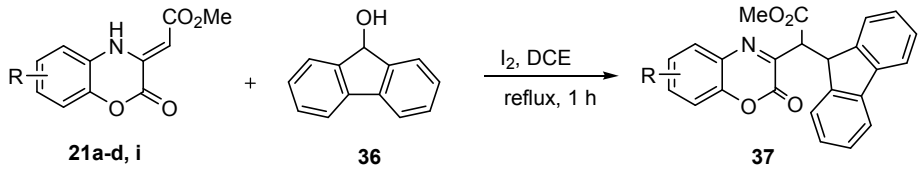


IR (KBr): ν_{max} 1743, 1607, 1511, 1435, 1262, 1178 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.76 (d, *J* = 2.5 Hz, 1H), 7.37 (dd, *J* = 2.5, 6.5 Hz,1H), 7.34 (d, *J* = 8.5 Hz, 2H), 7.17 (d, *J* = 8.5 Hz, 2H), 7.11 (d, *J* = 9.0 Hz, 1H), 6.84 (d, *J* = 8.5 Hz, 2H), 6.68 (d, *J* = 8.5 Hz, 2H), 5.29 (d, *J* = 12.0 Hz, 1H), 5.01 (d, *J* = 12.0 Hz, 1H), 3.75 (s, 3H), 3.64 (s, 3H), 3.51 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 169.5 (C), 158.2 (C), 158.0 (C), 154.2 (C), 151.8 (C), 144.4 (C), 134.2 (C), 133.4 (C), 131.3 (C), 131.2 (CH), 130.5 (C), 128.8 (CH), 128.7 (CH), 128.7 (CH), 117.4 (CH), 113.9 (CH), 113.9 (CH), 55.0 (OCH_3), 54.9 (OCH_3), 52.6 (CH), 52.5 (OCH_3), 50.4 (CH) ppm.

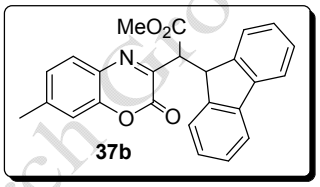
3.2.9. General procedure for the synthesis of 2-(fluren-9′-yl)methoxycarbonylmethyl-1,4-benzoxazinones 37:



To a mixture of 1,4-benzoxazinone derivative **21**, (0.5 mmol) and **36** (0.6 mmol) in 4 mL of 1,2-dichloroethane molecular iodine (127 mg, 0.5 mmol) was added and the reaction

mixture was allowed to heat at reflux temperature for 1 h. After completion of the reaction as shown by TLC, the reaction was quenched with 4 mL of saturated $Na_2S_2O_3$ solution. The organic layer was separated, washed twice with water (2 x 15 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude reaction mixture was purified by column chromatography on silica gel (100-200 mesh) using 20-30% ethyl acetate/hexanes as the eluting system.

Methyl 2-(9*H*-fluoren-9′-yl)-2-(7-methyl-2-oxo-2*H*-benzo[*b*][1,4]oxazin-3-yl)acetate (37b):



37b

Yield: 162 mg (81%) as yellow solid.

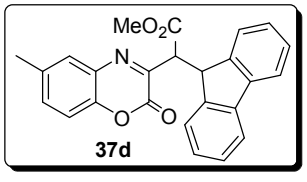
Mp: 108-109 ^{o}C.

IR (KBr): ν_{max} 1744, 1638, 1509, 1448, 1267 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.76 (t, *J* = 7.5 Hz, 2H), 7.65 (d, *J* = 7.5 Hz, 1H), 7.58 (d, *J* = 8.0 Hz, 1H), 7.45 (d, *J* =7.5 Hz, 1H), 7.40 (q, *J* = 7.5 Hz, 2H), 7.30-7.26 (m, 2H), 7.18 (d, *J* = 8.0, 1H), 7.10 (s, 1H), 5.10 (d, *J* = 4.5 Hz, 1H), 4.92 (d, *J* = 4.5 Hz, 1H), 3.51 (s, 3H), 2.45 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 169.7 (C), 152.9 (C), 151.5 (C), 146.4 (C), 144.8 (C), 143.7 (C), 142.9 (C), 141.4 (C), 141.3 (C), 129.0 (CH), 128.6 (C), 127.6 (CH), 127.4 (CH), 127.0 (CH), 126.8 (CH), 126.6 (CH), 125.6 (CH), 124.6 (CH), 119.7 (CH), 119.7 (CH), 116.4 (CH), 52.1 (CH), 51.8 (CH_3), 46.2 (CH), 21.7 (CH_3) ppm.

Methyl 2-(9*H*-fluoren-9′-yl)-2-(6-methyl-2-oxo-2*H*-benzo[*b*][1,4]oxazin-3-yl) acetate (37d):



37d

Yield: 165 mg (83%) as yellow solid.

Mp: 118-119 ^{o}C.

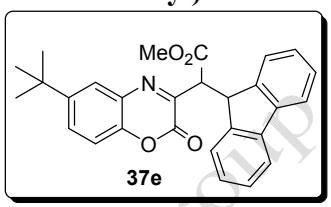
IR (KBr): ν_{max} 1747, 1657, 1521, 1463, 1237 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.61 (t, *J* = 7.5 Hz, 2H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.35 (s, 1H), 7.30 (d, *J* = 7.5 Hz, 1H), 7.25 (q, *J* = 8.0 Hz, 2H), 7.18-7.12 (m, 3H), 7.04 (d, *J* = 8.5 Hz, 1H), 4.95 (d, *J* = 4.0 Hz, 1H), 4.79 (d, *J* = 4.0 Hz, 1H), 3.36 (s, 3H), 2.29 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 196.6 (C), 152.8 (C), 152.7 (C), 144.8 (C), 144.4 (C),

143.7 (C), 141.4 (C), 141.3 (C), 135.5 (C), 132.3 (CH), 130.3 (C), 129.2 (CH), 127.6 (CH), 127.4 (CH), 127.0 (CH), 126.8 (CH), 125.6 (CH), 124.5 (CH), 119.7 (CH), 119.6 (CH), 115.9 (CH), 52.1 (CH_3), 51.9 (CH), 46.1 (CH), 20.6 (CH_3) ppm.

Methyl 2-(6-*tert*-butyl-2-oxo-2*H*-benzo[*b*][1,4]oxazin-3-yl)-2-(9*H*-fluoren-9′-yl)acetate (37e):



37e

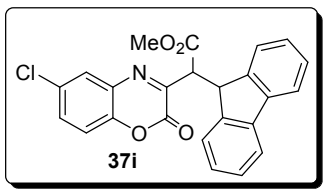
Yield: 172 mg (78%) as thick brown liquid.

IR (KBr): ν_{max} 1743, 1676, 1514, 1437, 1254 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.70 (dd, *J* = 5.0, 7.5 Hz, 2H), 7.74 (d, *J* = 2.5 Hz, 1H), 7.64 (d, *J* = 7.5 Hz, 1H), 7.60 (dd, *J* = 2.5, 9.0 Hz, 1H), 7.42-7.38 (m, 3H), 7.30-7.27 (m, 3H), 5.13 (d, *J* = 4.5 Hz,1H), 4.80 (d, *J* = 5.0 Hz, 1H), 3.51 (s, 3H), 1.40 (s, 9H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 169.7 (C), 153.0 (C), 152.8 (C), 149.2 (C), 144.9 (C), 144.3 (C), 143.8 (C), 141.5 (C), 141.4 (C), 130.2 (C), 129.1 (CH), 127.7 (CH), 127.6 (CH), 127.1 (CH), 126.9 (CH), 126.0 (CH), 125.7 (CH), 124.6 (CH), 119.9 (CH), 119.8 (CH), 115.8 (CH), 52.2 (CH_3), 52.1 (CH), 46.3 (CH), 34.7 (C), 31.3 (CH_3) ppm.

Methyl 2-(6-chloro-2-oxo-2*H*-benzo[*b*][1,4]oxazin-3-yl)-2-(9*H*-fluoren-9′-yl)acetate (37i):



37i

Yield: 177 mg (85%) as a white solid.

Mp: 98-99 ^oC.

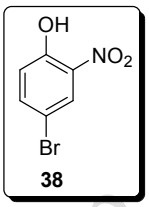
IR (KBr): ν_{max} 1742, 1609, 1574, 1447, 1347, 1238, 1153 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.76 (d, *J* = 7.5 Hz, 1H), 7.75 (d, *J* = 9.0 Hz, 1H), 7.62-7.60 (m, 2H), 7.47-7.43 (m, 2H), 7.41 (d, *J* = 7.5 Hz, 1H), 7.38 (d, *J* = 7.5 Hz, 1H), 7.32-7.27 (m, 2H), 7.23 (d, *J* = 8.5 Hz, 1H), 5.05 (d, *J* = 4.0 Hz, 1H), 4.98 (d, *J* = 4.5 Hz, 1H), 3.54 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 169.4 (C), 154.0 (C), 152.0 (C), 145.0 (C), 144.5 (C), 143.4 (C), 141.4 (C), 141.4 (C), 131.3 (CH), 130.9 (C), 130.6 (C), 128.7 (CH), 127.7 (CH), 127.6 (CH), 127.0 (CH), 126.9 (CH), 125.4 (CH), 124.5 (CH), 119.8 (CH), 119.7 (CH), 117.5 (CH), 52.3 (CH_3), 51.7 (CH), 46.1 (CH) ppm.

4-Bromo-2-nitrophenol (38):

The nitration of *p*-bromophenol was carried out by following the procedure described for the synthesis of **17**.



Yield: 3.46g (80%) as yellow solid.

Mp: 90-91 ^{o}C (Lit.[243] Mp**:** 88-89 ^{o}C).

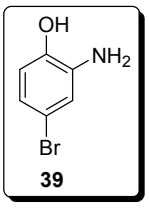
IR (KBr): ν_{max} 3273, 1527, 1313, 970, 883 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.49 (s, 1H), 8.24 (d, *J* = 2.0 Hz, 1H), 7.66 (dd, *J* = 2.0, 8.0 Hz, 1H), 7.07 (d, *J* = 8.0 Hz, 1H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 154.1, 142.9, 140.3, 127.3, 121.7, 111.7 ppm.

2-Amino-4-bromophenol (39):

To a mixture of 2-nitro-4-bromophenol (**38**, 3.24 g, 15 mmol) and zinc powder (6.8 g, 105 mmol) in methanol (20 mL) was added followed by ammonium chloride (5.6 g, 105 mmol) dissolved in 15 mL of water was added slowly at 0 ^{o}C and allowed to stir at room temperature for 1 h. After completion of reaction as shown by TLC, the reaction mixture was filtered off and extracted twice with ethyl acetate (2 x 30 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude reaction mixture was further purified by silica gel (100-200 mesh) column chromatography using 40% ethyl acetate/hexanes as eluting system.



Yield: 2.03 g (72%) as brown solid.

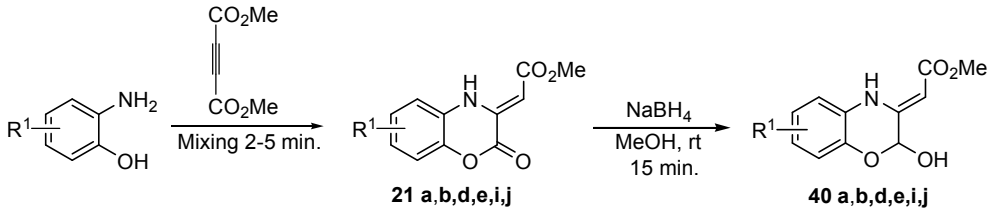
Mp: 131-132 ^{o}C (Lit.[244] Mp**:** 133-135).

IR (KBr): ν_{max} 3062, 1497, 1444, 1437, 1279 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 6.89 (d, *J* = 2.5 Hz, 1H), 6.78 (dd, *J* = 2.5, 8.5 Hz, 1H), 6.61 (d, *J* = 8.0 Hz, 1H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): 142.8, 136.2, 121.7, 119.2, 116.5, 113.4 ppm.

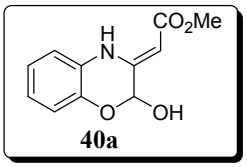
3.2.10. General procedure for the synthesis of 2-hydroxy-1,4-benzoxazine derivatives 40:



21 a,b,d,e,i,j **40 a,b,d,e,i,j**

In a typical reaction procedure, aminophenol derivative (2 mmol) was mixed with dimethyl acetylenedicarboxylate (2 mmol) for 2-5 min. at room temperature. The product obtained was transferred into a round bottomed flask, followed by addition of $NaBH_4$ (4.4 mmol) and the reaction mixture was stirred for 15 min. in methanol. After completion of the reaction, methanol was removed completely with the help of rotary evaporator and the reaction mixture was found stuck on the inner walls of the reaction vessel in semi solid form. After adding tap water to the reaction vessel and scratching the inner walls with the help of spatula, a brown solid product separated out immediately from the mixture. It was filtered and washed with water and dried to afford the corresponding 2-hydroxy-1,4-benzoxazine derivatives.

Methyl (*Z*)-2-(2-hydroxy-2*H*-benzo-1,4-oxazin-3(4*H*)-ylidene)acetate (40a):



40a

Yield: 416 mg (94%) as brown solid.

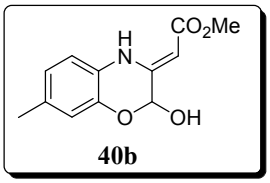
Mp: 172-173 °C.

IR (KBr): ν_{max} 3286, 1738, 1667, 1597, 1275 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.03 (br s, 1H), 6.98-6.91 (m, 3H), 6.86 (d, *J* = 7.5 Hz, 1H), 5.70 (s, 1H), 4.90 (s, 1H), 3.67 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.4, 149.2, 141.2, 126.4, 122.3, 122.2, 117.3, 115.0, 90.3, 83.4, 50.4 ppm.

Methyl (*Z*)-2-(2-hydroxy-7-methyl-2*H*-benzo-1,4-oxazin-3(4*H*)-ylidene)acetate (40b) :



40b

Yield: 448 mg (95%) as brown solid.

Mp: 113-114 °C.

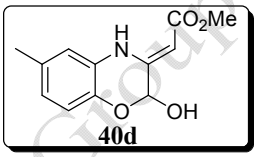
IR (KBr): ν_{max} 3324, 2980, 1652, 1621, 1513, 1367, 1287 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ10.09 (br s, 1H), 6.95-6.93 (m, 2H), 6.85 (d, *J* = 8.0 Hz, 1H), 5.71 (s, 1H), 3.70 (s, 3H), 2.33 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.3, 156.1, 139.8, 138.2, 133.1, 126.3, 121.6, 117.3, 114.5, 89.9, 83.5, 51.4, 20.8 ppm.

Methyl (*Z*)-2-(2-hydroxy-6-methyl-2*H*-benzo-1,4-oxazin-3(4*H*)-ylidene)acetate (40d):

Yield: 462 mg (98%) as brown solid.



40d

Mp: 158-159 ℃.

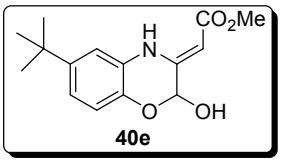
IR (KBr): ν_{max} 3336, 2925, 1659, 1623, 1351, 1290 cm^{-1}.

^{1}HNMR (500 MHz, $CDCl_3$): δ 9.97 (br s, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 6.72 (d, *J* = 8.5 Hz, 1H), 6.68 (s, 1H), 5.67 (s, 1H), 4.88 (s, 1H), 3.67 (s, 3H), 3.49 (br s, 1H), 2.28 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.7, 149.4, 139.5, 132.2, 126.2, 123.0, 117.3, 115.7, 90.6, 83.5, 50.6, 20.7 ppm.

Methyl (*Z*)-2-(6-*tert*-butyl-2-hydroxy-2*H*-benzo-1,4-oxazin-3(4*H*)-ylidene)acetate (40e):

Yield: 512 mg (92%) as brown solid.



40e

Mp: 135-136 ℃.

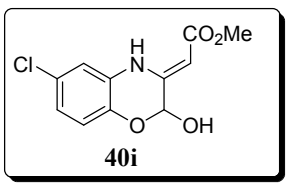
IR (KBr): ν_{max} 3377, 2957, 1656, 1613, 1506, 1437, 1294 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.06 (br s, 1H), 6.95 (dd, *J* = 2.0, 8.5 Hz, 1H), 6.91 (s, 1H), 6.88 (d, *J* = 2.0 Hz, 1H), 5.69 (s, 1H), 4.89 (s, 1H), 3.67 (s, 3H), 1.29 (s, 9H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.5, 149.4, 145.5, 138.9, 125.6, 119.1, 116.6, 112.2, 90.3, 83.0, 50.3, 33.9, 31.1 ppm.

Methyl (*Z*)-2-(6-chloro-2-hydroxy-2*H*-benzo-1,4-oxazin-3(4*H*)-ylidene)acetate (40i):

Yield: 476 mg (93%) as brown solid.



40i

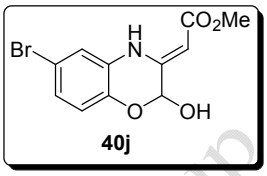
Mp: 175-176 ℃.

IR (KBr): ν_{max} 3321, 2982, 1653, 1624, 1515, 1464, 1289 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ10.04 (br s, 1H), 6.90-6.86 (m, 3H), 5.71 (s, 1H), 4.94 (s, 1H), 3.71 (s, 3H), 3.40 (br s, 1H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 169.2, 148.0, 140.1, 128.9, 125.9, 121.4, 119.0, 115.8, 90.0, 84.7, 50.5 ppm.

Methyl (*Z*)-2-(6-bromo-2-hydroxy-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (40j):



40j

Yield: 556 mg (92%) as brown solid.

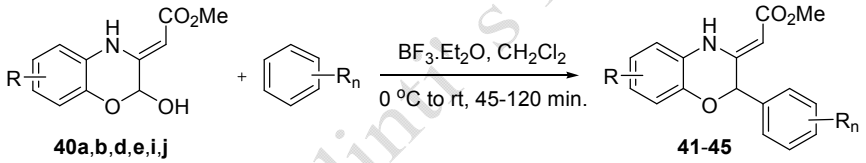
Mp: 147-148 ^{o}C.

IR (KBr): ν_{max} 3368, 2966, 1661, 1627, 1519, 1424, 1278 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.06 (br s, 1H), 7.57 (d, *J* = 2.5 Hz, 1H), 7.01 (dd, *J* = 2.0, 8.0Hz, 1H), 6.86 (d, *J* = 8.5 Hz, 1H), 5.73 (s, 1H), 4.88 (s, 1H), 3.63 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 169.0, 148.2, 140.8, 128.9, 124.6, 119.3, 118.5, 113.7, 90.0, 84.9, 50.6 ppm.

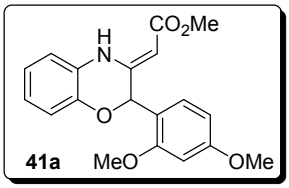
3.2.11. General procedure for the synthesis of 2-aryl 1,4-benzoxazine derivatives 41-45:



40a,b,d,e,i,j **41-45**

To a mixture of benzoxazine derivative **40**, (0.5 mmol) and electron-rich arene (0.6 mmol), 5 mL of CH_2Cl_2 was added, cooled to 0 ^{o}C and BF_3.etherate (0.6 mmol) was added slowly dropwise and allowed to stir at room temperature for 45-120 min. After completion of the reaction as shown by TLC, the reaction was quenched with 5 mL of saturated $NaHCO_3$ solution. The organic layer was separated washed twice with water, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude reaction mixture was purified by silica gel (100-200 mesh) column chromatography using 10-20% ethyl acetate/hexanes as the eluting system.

Methyl (*Z*)-2-(2-(2′,4′-dimethoxyphenyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (41a):



41a

Yield: 134 mg (79%) as white solid.

Mp: 108-109 ^{o}C.

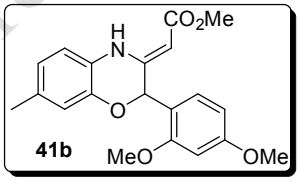
IR (KBr): ν_{max} 3312, 1660, 1613, 1507, 1218, 1115, 1039 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.48 (br s, 1H), 7.26 (d, *J* = 9.5 Hz, 1H), 6.96-6.84 (m, 4H), 6.51-6.49 (m, 2H), 5.94 (s, 1H), 4.39 (s, 1H), 3.83 (s, 3H), 3.81 (s, 3H), 3.67 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.7 (C), 161.5 (C), 158.3 (C), 152.7 (C), 144.8 (C), 129.5 (CH), 127.3 (C), 122.5 (CH), 122.5 (CH), 117.1 (CH), 116.9 (C), 115.3 (CH), 104.8 (CH), 98.4 (CH), 84.2 (CH), 71.1 (CH), 55.6 (OCH_3), 55.3 (OCH_3), 50.6 (OCH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{19}H_{19}NO_5+Na]^+$: 364.1155, found: 364.1149.

Methyl (*Z*)-2-(2-(2′,4′-dimethoxyphenyl)-7-methyl-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (41b):



Yield: 122 mg (69%) as white solid.

Mp: 128-129 °C.

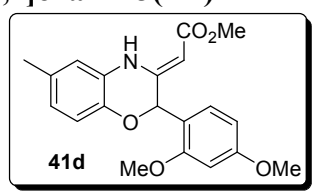
IR (KBr): ν_{max} 3374, 1665, 1607, 1515, 1398, 1273, 1153, 1035 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.45 (br s, 1H), 7.26 (d, *J* = 9.0 Hz, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 6.74-6.71 (m, 2H), 6.49-6.47 (m, 2H), 5.93 (s, 1H), 4.37 (s, 1H), 3.82 (s, 3H), 3.80 (s, 3H), 3.66 (s, 3H), 2.24 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.7 (C), 161.4 (C), 158.2 (C), 152.6 (C), 144.5 (C), 132.4 (C), 129.5(CH), 124.7 (C), 122.9 (CH), 117.6 (CH), 116.9 (C), 115.0 (CH), 104.7 (CH), 98.4 (CH), 83.5 (CH), 71.0 (CH), 55.5 (OCH_3), 55.2 (OCH_3), 50.4 (OCH_3), 20.8 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{20}H_{21}NO_5+Na]^+$: 378.1312, found: 378.1322.

Methyl (*Z*)-2-(2-(2′,4′-dimethoxyphenyl)-6-methyl-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene) acetate (41d):



Yield: 128 mg (71%) as white solid.

Mp: 138-139 °C.

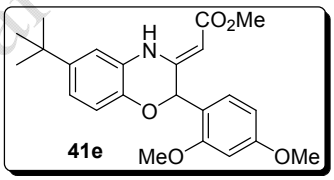
IR (KBr): ν_{max} 3270, 1665, 1617, 1507, 1282, 1155, 1039 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.43 (br s, 1H), 7.26 (d, *J* = 9.5 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 6.72 (s, 1H), 6.67 (dd, *J* = 1.5, 8.0 Hz, 1H), 6.50-6.48 (m, 2H), 5.91 (s, 1H), 4.38 (s, 1H), 3.82 (s, 3H), 3.80 (s, 3H), 3.66 (s, 3H), 2.28 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.6 (C), 161.4 (C), 158.2 (C), 152.8 (C), 142.6 (C), 132.0 (CH), 129.5 (C), 126.9 (C), 122.9 (CH), 116.9 (C), 116.7 (CH), 115.8 (CH), 104.8 (CH), 98.4 (CH), 84.0 (CH), 71.1 (CH), 55.6 (OCH_3), 55.2 (OCH_3), 50.5 (OCH_3), 20.7 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{20}H_{21}NO_5+Na]^+$: 378.1312, found: 378.1325.

Methyl (*Z*)-2-(6-*tert*-butyl-2-(2′,4′-dimethoxyphenyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (41e):



Yield: 128 mg (65%) as brown solid.

Mp: 146-147 °C.

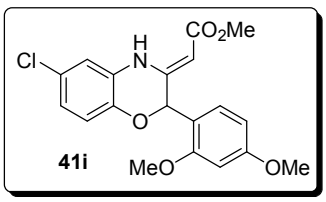
IR (KBr): ν_{max} 3297, 1671, 1612, 1507, 1261, 1117, 1004 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.51 (br s, 1H), 7.28 (d, *J* = 8.5 Hz, 1H), 6.93 (d, *J* = 2.5 Hz, 1H), 6.90 (dd, *J* = 2.0, 8.5 Hz, 1H), 6.84 (d, *J* = 8.5 Hz, 1H), 6.52 (dd, *J* = 2.5, 8.5 Hz, 1H), 6.49 (d, *J* = 2.0 Hz, 1H), 5.93 (s, 1H), 4.35 (s, 1H), 3.81 (s, 3H), 3.81 (s, 3H), 3.67 (s, 3H), 1.30 (s, 9H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.8 (C), 161.4 (C), 158.3 (C), 153.1 (C), 145.7 (C), 142.6 (C), 129.6 (CH), 126.6 (C), 119.3 (CH), 116.9 (C), 116.3 (CH), 112.6 (CH), 104.9 (CH), 98.4 (CH), 83.8 (CH), 71.1 (CH), 55.6 (OCH_3), 55.3 (OCH_3), 50.5 (OCH_3), 34.3 (C), 31.4 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{23}H_{27}NO_5+Na]^+$: 420.1781, found: 420.1780.

Methyl (*Z*)-2-(6-chloro-2-(2′,4′-dimethoxyphenyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (41i):



Yield: 143 mg (76%) as white solid.

Mp: 158-159 °C.

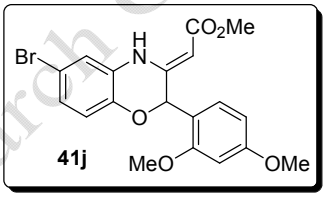
IR (KBr): ν_{max} 3360, 1656, 1605, 1504, 1398, 1264, 1114, 1073 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.46 (br s, 1H), 7.21 (d, *J* = 9.0 Hz, 1H), 6.88 (t, *J* = 1.0 Hz, 1H), 6.79 (d, *J* = 1.0 Hz, 2H), 6.49-6.48 (m, 2H), 5.90 (s, 1H), 4.42 (s, 1H), 3.82 (s, 3H), 3.81 (s, 3H), 3.66 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.5 (C), 161.6 (C), 158.3 (C), 151.8 (C), 143.3 (C), 129.5 (CH), 128.3 (C), 127.1 (C), 122.0 (CH), 118.1 (CH), 116.5 (C), 115.1 (CH), 104.8 (CH), 98.5 (CH), 85.5 (CH), 71.2 (CH), 55.6 (OCH_3), 55.3 (OCH_3), 50.7 (OCH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{19}H_{18}ClNO_5+Na]^+$: 398.0766, found: 398.0765.

Methyl (*Z*)-2-(6-bromo-2-(2′,4′-dimethoxyphenyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)ylidene)acetate (41j).



Yield: 154 mg (74%) as white solid.

Mp: 168-169 °C.

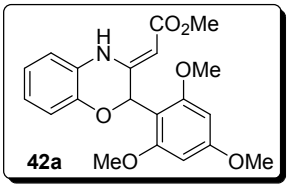
IR (KBr): ν_{max} 3358, 1657, 1608, 1510, 1385, 1259, 1120, 1062 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.46 (br s, 1H), 7.22 (d, *J* = 9.5 Hz, 1H), 7.02 (d, *J* = 2.0 Hz, 1H), 6.94 (dd, *J* = 2.5, 9.0 Hz, 1H), 6.74 (d, *J* = 8.5 Hz, 1H), 6.49-6.48 (m, 2H), 5.90 (s, 1H), 4.42 (d, *J* = 1.0 Hz, 1H), 3.82 (s, 3H), 3.81 (s, 3H), 3.66 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.6 (C), 161.6 (C), 158.3 (C), 151.7 (C), 143.9 (C), 129.5 (CH), 128.7 (C), 125.0 (CH), 118.5 (CH), 117.9 (CH), 116.5 (C), 114.3 (C), 104.9 (CH), 98.5 (CH), 85.5 (CH), 71.2 (CH), 55.7 (OCH_3), 55.4 (OCH_3), 50.7 (OCH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{19}H_{18}BrNO_5+Na]^+$: 442.0261, found: 442.0260.

Methyl (*Z*)-2-(2-(2′,4′,6′-trimethoxyphenyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene) acetate (42a):



Yield: 142 mg (77%) as brown solid.

Mp: 110-111 °C.

IR (KBr): ν_{max} 3346, 1661, 1605, 1503, 1218, 1155, 1066 cm^{-1}.

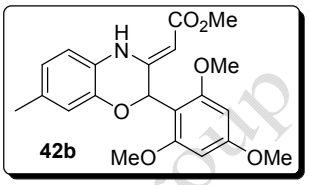
^{1}H NMR (500 MHz, $CDCl_3$): δ 10.57 (br s, 1H), 6.90-6.82 (m, 4H), 6.24 (s, 1H), 6.15 (s, 2H), 4.40 (s, 1H), 3.80 (s, 3H), 3.71 (s, 6H), 3.65 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.7 (C), 162.2 (C), 159.8 (C), 154.7 (C), 145.1 (C),

126.6 (C), 122.0 (CH), 121.7 (CH), 116.3 (CH), 114.8 (CH), 105.3 (C), 90.9 (CH), 80.8 (CH), 68.8 (CH), 55.6 (OCH_3), 55.0 (OCH_3), 50.2 (OCH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{20}H_{21}NO_6+Na]^+$: 394.1261, found: 394.1255.

Methyl (*Z*)-2-(7-methyl-2-(2′,4′,6′-trimethoxyphenyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (42b):



Yield: 135 mg (70%) as white solid.

Mp: 118-119 °C.

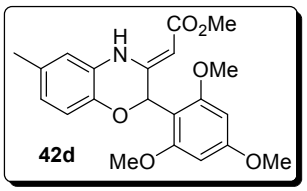
IR (KBr): ν_{max} 3240, 1662, 1614, 1517, 1462, 1270, 979 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.51 (br s, 1H), 6.75 (d, *J* = 7.5 Hz, 1H), 6.71 (s, 1H), 6.69 (s, 1H), 6.20 (s, 1H), 6.15 (s, 2H), 4.35 (s, 1H), 3.81 (s, 3H), 3.72 (s, 6H), 3.64 (s, 3H), 2.24 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.8 (C), 162.2 (C), 159.8 (C), 154.9 (C), 145.0 (C), 131.9 (C), 124.2 (CH), 122.2 (C), 117.0 (CH), 114.6 (CH), 105.4 (C), 91.0 (CH), 80.2 (CH), 68.9 (CH), 55.7 (OCH_3), 55.1 (OCH_3), 50.2 (OCH_3), 20.7 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{21}H_{23}NO_6+Na]^+$: 408.1418, found: 408.1417.

Methyl (*Z*)-2-(6-methyl-2-(2′,4′,6′-trimethoxyphenyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (42d):



Yield: 129 mg (67%) as brown solid.

Mp: 128-129 °C.

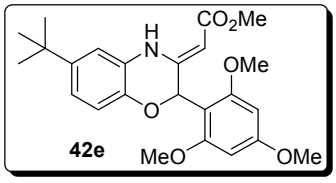
IR (KBr): ν_{max} 3284, 1665, 1600, 1504, 1280, 1116, 1003 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.49 (br s, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 6.68 (s, 1H), 6.65 (d, *J* = 8.0 Hz, 1H), 6.18 (s, 1H), 6.15 (s, 2H), 4.36 (s, 1H), 3.82 (s, 3H), 3.73 (s, 6H), 3.65 (s, 3H), 2.78 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.8 (C), 162.2 (C), 159.9 (C), 155.1 (C), 143.1 (C), 131.3 (C), 126.5 (C), 122.5 (CH), 116.2 (CH), 115.5 (CH), 105.4 (C), 91.1 (CH), 80.8 (CH), 69.0 (CH), 55.8 (OCH_3), 55.2 (OCH_3), 50.3 (OCH_3), 20.7 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{21}H_{23}NO_6+Na]^+$: 408.1418, found: 408.1418.

Methyl (*Z*)-2-(6-*tert*-butyl-2-(2′,4′,6′-trimethoxyphenyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (42e):



Yield: 131 mg (62%) as brown solid.

Mp: 138-139 ^{o}C.

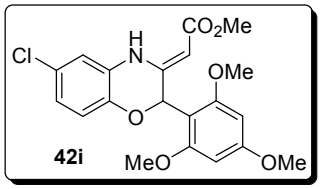
IR (KBr): ν_{max} 3384, 1662, 1608, 1507, 1258, 1114, 1043 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.60 (br s, 1H), 6.92 (s, 1H), 6.90 (d, *J* = 8.0 Hz, 1H), 6.83 (d, *J* = 8.5 Hz, 1H), 6.22 (s, 1H), 6.16 (s, 2H), 4.38 (s, 1H), 3.80 (s, 3H), 3.71 (s, 6H), 3.65 (s, 3H), 1.31 (s, 9H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.8 (C), 162.2 (C), 159.8 (C), 155.1 (C), 144.9 (C), 142.9 (C), 126.1 (C), 118.8 (CH), 115.7 (CH), 112.1 (CH), 105.3 (C), 91.0 (CH), 80.5 (CH), 68.9 (CH), 55.6 (OCH_3), 55.0 (OCH_3), 50.1 (OCH_3), 34.0 (C), 31.2 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{24}H_{29}NO_6+Na]^+$: 450.1887, found: 450.1880.

Methyl (*Z*)-2-(6-chloro-2-(2′,4′,6′-trimethoxyphenyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (42i):



Yield: 147 mg (72%) as pale yellow crystals.

Mp: 136-137 ^{o}C.

IR (KBr): ν_{max} 3381, 1657, 1619, 1499, 1272, 1117, 1041 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.53 (br s, 1H), 6.84 (t. *J* = 1.5 Hz, 1H), 6.77 (d, *J* = 1.0 Hz, 2H), 6.19 (s, 1H), 6.14 (s, 2H), 4.41 (d, *J* = 1.0 Hz, 1H), 3.81 (s, 3H), 3.71 (s, 6H), 3.64 (s, 3H) ppm.

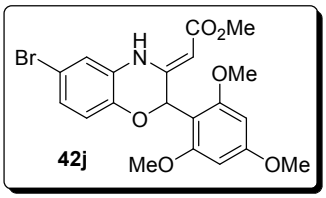
^{13}C NMR (125 MHz, $CDCl_3$): δ 170.7 (C), 162.4 (C), 159.8 (C), 154.0 (C), 143.8 (C), 127.7 (C), 126.3 (C), 121.5 (CH), 117.3 (CH), 114.7 (CH), 105.3 (C), 91.1 (CH), 82.2 (CH), 68.9 (CH), 55.8 (OCH_3), 55.2 (OCH_3), 50.4 (OCH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{20}H_{20}ClNO_6+Na]^+$: 428.0871, found: 428.0876.

Methyl (*Z*)-2-(6-bromo-2-(2′,4′,6′-trimethoxyphenyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (42j):

Yield: 171 mg (76%) as brown solid.

Mp: 158-159 ^{o}C.



42j

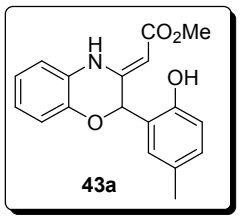
IR (KBr): ν_{max} 3244, 1656, 1615, 1521, 1466, 1269, 1034 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.52 (br s, 1H), 6.98 (d, *J* = 2.0 Hz, 1H), 6.92 (dd, *J* = 2.0, 8.5 Hz, 1H), 6.72 (d, *J* = 8.5 Hz, 1H), 6.19 (s, 1H), 6.14 (s, 2H), 4.40 (d, *J* = 1.0 Hz, 1H), 3.82 (s, 3H), 3.72 (s, 6H), 3.64 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.7 (C), 162.4 (C), 159.9 (C), 154.0 (C), 144.3 (C), 128.1 (C), 124.5 (CH), 117.8 (CH), 117.5 (CH), 113.4 (C), 105.4 (C), 91.1 (CH), 82.2 (CH), 68.9 (CH), 55.8 (OCH_3), 55.3 (OCH_3), 50.5 (OCH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{20}H_{20}BrNO_6+Na]^+$: 472.0366 , found: 472.0364.

Methyl (*Z*)-2-(2-(2′-hydroxy-5′-methylphenyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene) acetate (43a):



43a

Yield: 119 mg (77%) as brown solid.

Mp: 140-141 ^{o}C.

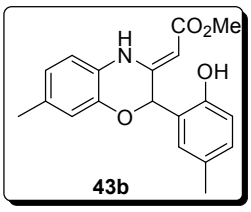
IR (KBr): ν_{max} 3442, 1658, 1619, 1502, 1285, 1230, 1169 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.41 (br s, 1H), 7.07 (d, *J* = 8.0 Hz, 1H), 6.98-6.94 (m, 3H), 6.89 (d, *J* = 8.0 Hz, 2H), 6.83 (d, *J* = 8.0 Hz, 1H), 6.35 (br s, 1H), 5.73 (s, 1H), 4.47 (s, 1H), 3.68 (s, 3H), 2.26 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.6 (C), 152.6 (C), 150.7 (C), 143.8 (C), 131.3 (CH), 129.8 (C), 129.4 (CH), 127.4 (C), 123.5 (CH), 122.5 (CH), 120.3 (C), 117.1 (CH), 116.8 (CH), 115.6 (CH), 85.1 (CH), 75.7 (CH), 50.8 (OCH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{18}H_{17}NO_4+Na]^+$: 334.1050, found: 334.1045.

Methyl (*Z*)-2-(2-(2′-hydroxy-5′-methylphenyl)-7-methyl-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (43b):



43b

Yield: 115 mg (71%) as brown solid.

Mp: 114-115 ^{o}C.

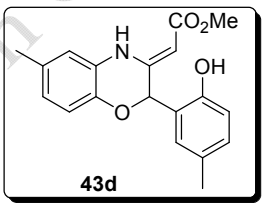
IR (KBr): ν_{max} 3441, 2962, 1659, 1609, 1508, 1441, 1256, 1231, 1169 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.37 (br s, 1H), 7.06 (d, *J* = 8.5 Hz,1H), 6.94 (s, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 6.77-6.76 (m, 3H), 6.46 (br s, 1H), 5.70 (s, 1H), 4.44 (s, 1H), 3.68 (s, 3H), 2.25 (s, 3H), 2.24 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.6 (C), 152.8 (C), 150.6 (C), 143.6 (C), 132.6 (C), 131.3 (CH), 129.7 (C), 129.3 (CH), 125.0 (C), 124.0 (CH), 120.4 (C), 117.6 (CH), 116.9 (CH), 115.4 (CH), 84.6 (CH), 75.9 (CH), 50.7 (OCH_3), 20.8 (CH_3), 20.5 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{19}H_{19}NO4+Na]^+$: 348.1206, found: 348.1215.

Methyl (*Z*)-2-(2-(2′-hydroxy-5′-methylphenyl)-6-methyl-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (43d):



43d

Yield: 120 mg (74%) as brown solid.

Mp: 120-121 °C.

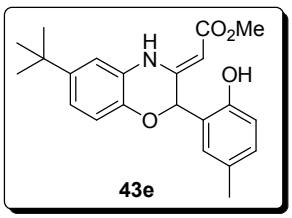
IR (KBr): ν_{max} 3432, 2958, 1668, 1618, 1511, 1448, 1261, 1228, 1166 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.35 (br s, 1H), 7.06 (dd, *J* = 1.5, 8.0 Hz, 1H), 6.93 (s, 1H), 6.83 (d, *J* = 8.0 Hz, 2H), 6.69 (s, 1H), 6.67 (d, *J* = 8.0 Hz, 1H), 6.34 (br s, 1H), 5.67 (s, 1H), 4.46 (s, 1H), 3.68 (s, 3H), 2.27 (s, 3H), 2.25 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.6 (C), 152.8 (C), 150.6 (C), 141.5 (C), 133.3 (C), 131.3 (CH), 129.7 (C), 129.4 (CH), 127.1 (C), 123.1 (CH), 120.2 (C), 117.0 (CH), 116.8 (CH), 116.2 (CH), 85.1 (CH), 50.7 (OCH_3), 20.8 (CH_3), 20.5 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{19}H_{19}NO_4+Na]^+$: 348.1206 , found: 348.1210.

Methyl (*Z*)-2-(6-*tert*-butyl-2-(2′-hydroxy-5′-methylphenyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (43e):



43e

Yield: 118 mg (64%) as brown solid.

Mp: 178-179 °C.

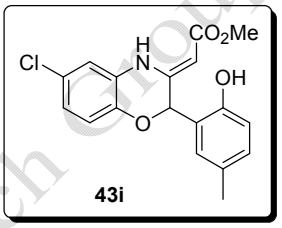
IR (KBr): ν_{max} 3430, 2954, 1663, 1621, 1504, 1436, 1264, 1226, 1166 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.44 (br s, 1H), 7.07 (dd, *J* = 2.0, 8.0 Hz, 1H), 6.95 (d, *J* = 2.0 Hz, 1H), 6.93-6.88 (m, 3H), 6.83 (d, *J* = 8.0 Hz, 1H), 5.69 (s, 1H), 4.43 (s, 1H), 3.68 (s, 3H), 2.26 (s, 3H), 1.29 (s, 9H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.7 (C), 152.9 (C), 151.0 (C), 146.9 (C), 141.6 (C), 131.3 (CH), 129.7 (C), 129.6 (CH), 126.9 (CH), 126.8 (C), 120.3 (C), 119.5 (CH), 117.0 (CH), 116.4 (CH), 112.9 (CH), 76.3 (CH), 50.7 (OCH_3), 34.4 (C), 31.4 (CH_3), 20.5 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{22}H_{25}NO_4+Na]^+$: 390.1676, found: 390.1679.

Methyl (*Z*)-2-(6-chloro-2-(2′-hydroxy-5′-methylphenyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (43i):



43i

Yield: 132 mg (76%) as pale yellow solid.

Mp: 150-151 °C.

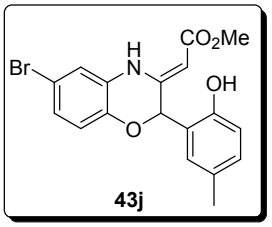
IR (KBr): ν_{max} 3368, 2916, 1645, 1602, 1495, 1437, 1272, 1226, 1169 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.41 (br s, 1H), 7.07 (dd, *J* = 2.0, 8.5 Hz, 1H), 6.94 (d, *J* = 1.5 Hz, 1H), 6.88 (d, *J* = 2.0 Hz, 1H), 6.86-6.84 (m, 1H), 6.82-6.80 (m, 2H), 6.03 (br s, 1H), 5.71 (s, 1H), 4.51 (s, 1H), 3.69 (s, 3H), 2.25 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.4 (C), 152.4 (C), 149.9 (C), 142.4 (C), 131.5 (CH), 130.0 (C), 129.3 (CH), 128.4 (C), 128.2 (C), 122.2 (CH), 120.1 (C), 118.1 (CH), 116.8 (CH), 115.5 (CH), 86.4 (CH), 75.5 (CH), 50.9 (OCH_3), 20.5 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{18}H_{16}ClNO_4+Na]^+$: 368.0660, found: 368.0644.

Methyl (*Z*)-2-(6-bromo-2-(2′-hydroxy-5′-methylphenyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (43j):



43j

Yield: 156 mg (80%) as brown solid.

Mp: 134-135 °C.

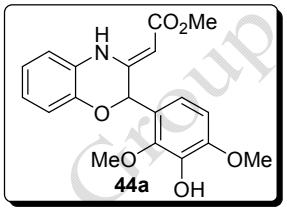
IR (KBr): ν_{max} 3385, 2922, 1663, 1607, 1598, 1497, 1297, 1268, 1223, 1164 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.41 (br s, 1H), 7.07 (dd, *J* = 1.5, 8.5 Hz, 1H), 7.03 (d, *J* = 2.0 Hz, 1H), 6.96 (dd, *J* = 2.5, 8.5 Hz, 1H), 6.94 (d, *J* = 1.5 Hz, 1H), 6.81 (d, *J* = 6.0 Hz, 1H), 6.80 (d, *J* = 5.5 Hz, 1H), 5.98 (br s, 1H), 5.72 (s, 1H), 4.51 (d, *J* = 0.5 Hz, 1H), 3.69 (s, 3H), 2.25 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.4 (C), 152.5 (C), 149.8 (C), 142.9 (C), 131.5 (CH), 130.1 (C), 129.3 (CH), 128.9 (C), 125.1 (CH), 120.2 (C), 118.6 (CH), 118.4 (CH), 116.9 (CH), 115.5 (C), 86.5 (CH), 75.6 (CH), 50.9 (OCH_3), 20.5 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{18}H_{16}BrNO_4+Na]^+$: 412.0155, found: 412.0158.

Methyl (*Z*)-2-(2-(3′-hydroxy-2′,4′-dimethoxyphenyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (44a):



44a

Yield: 128 mg (72%) as brown solid.

Mp: 108-109 ^oC.

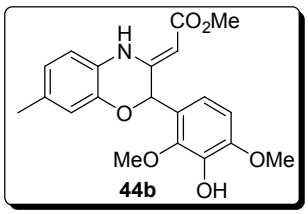
IR (KBr): ν_{max} 3480, 2940, 1666, 1620, 1500, 1448, 1266, 1225, 1163 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.49 (br s, 1H), 6.95-6.92 (m, 1H), 6.91-6.88 (m, 1H), 6.87-6.85 (m, 2H), 6.84 (d, *J* = 8.5 Hz, 1H), 6.64 (d, *J* = 8.5 Hz, 1H), 5.88 (s, 1H), 5.63 (br s, 1H), 4.40 (d, *J* = 0.5 Hz, 1H), 3.95 (s, 3H), 3.88 (s, 3H), 3.66 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.7 (C), 152.5 (C), 148.4 (C), 145.5 (C), 144.5 (C), 138.4 (C), 127.3 (C), 122.6 (CH), 122.5 (CH), 122.3 (C), 118.9 (CH), 117.1 (CH), 115.3 (CH), 106.4 (CH), 84.5 (CH), 71.8 (CH), 61.3 (OCH_3), 56.2 (OCH_3), 50.7 (OCH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{19}H_{19}NO_6+Na]^+$: 380.1105, found: 380.1100.

Methyl (*Z*)-2-(2-(3′-hydroxy-2′,4′-dimethoxy phenyl)-7-methyl-2*H*-benzo [*b*][1,4]-oxazin-3(4*H*)-ylidene)acetate (44b):



44b

Yield: 128 mg (69%) as brown solid.

Mp: 138-139 ^oC.

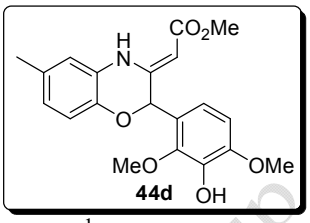
IR (KBr): ν_{max} 3404, 2946, 1669, 1612, 1517, 1470, 1277, 1222, 1163 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.45 (br s, 1H), 6.82 (d, *J* = 8.5 Hz, 1H), 6.79 (d, *J* = 8.0 Hz, 1H), 6.74-6.72 (m, 1H), 6.69 (s, 1H), 6.63 (d, *J* = 8.5 Hz, 1H), 5.86 (s, 1H), 5.60 (br s, 1H), 4.38 (s, 1H), 3.95 (s, 3H), 3.88 (s, 3H), 3.66 (s, 3H), 2.24 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.8 (C), 152.5 (C), 148.3 (C), 145.6 (C), 144.3 (C), 138.4 (C), 132.6 (C), 124.8 (C), 123.1 (CH), 122.5 (C), 118.9 (CH), 117.7 (CH), 115.1 (CH), 106.4 (CH), 83.9 (CH), 71.8 (CH), 61.3 (OCH_3), 56.2 (OCH_3), 50.6 (OCH_3), 20.9 (CH_3) ppm.

HRMS (ES$^+$): *m/z* calcd for $[C_{20}H_{21}NO_6+Na]^+$: 394.1261, found: 394.1264.

Methyl (*Z*)-2-(2-(3′-hydroxy-2′,4′-dimethoxyphenyl)-6-methyl-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate(44d):



44d

Yield: 135 mg (73%) as white solid.

Mp: 123-124 ^oC.

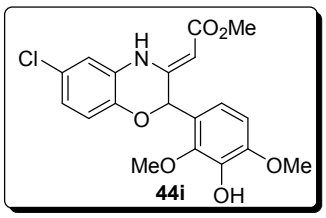
IR (KBr): ν_{max} 3468, 2938, 1652, 1626, 1504, 1452, 1274, 1237, 1156 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.45 (br s, 1H), 6.82 (d, *J* = 8.5 Hz, 1H), 6.79 (d, *J* = 8.0 Hz, 1H), 6.73 (dd, *J* = 1.0, 8.0 Hz, 1H), 6.69 (s, 1H), 6.63 (d, *J* = 9.0 Hz, 1H), 5.86 (s, 1H), 5.60 (br s, 1H), 4.38 (s, 1H), 3.95 (s, 3H), 3.88 (s, 3H), 3.66 (s, 3H), 2.24 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.8 (C), 152.5 (C), 148.3 (C), 145.6 (C), 144.3 (C), 138.4 (C), 132.6 (C), 124.8 (C), 123.1 (CH), 122.5 (C), 118.9 (CH), 117.7 (CH), 115.1 (CH), 106.4 (CH), 83.9 (CH), 71.8 (CH), 61.3 (OCH_3), 56.2 (OCH_3), 50.6 (OCH_3), 20.9 (CH_3) ppm.

HRMS (ES$^+$): *m/z* calcd for $[C_{20}H_{21}NO_6+Na]^+$: 394.1261, found: 394.1254.

Methyl (*Z*)-2-(6-chloro-2-(3′-hydroxy-2′,4′-dimethoxyphenyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (44i):



44i

Yield: 156 mg (79%) as brown solid.

Mp: 160-161 ^oC.

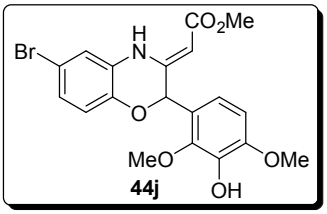
IR (KBr): ν_{max} 3465, 2931, 1665, 1622, 1503, 1456, 1265, 1228, 1172 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.49 (br s, 1H), 6.89 (d, *J* = 2.0 Hz, 1H), 6.81-6.76 (m, 3H), 6.63 (d, *J* = 8.5 Hz, 1H), 5.86 (s, 1H), 5.65 (br s, 1H), 4.45 (d, *J* = 0.5 Hz, 1H), 3.94 (s, 3H), 3.88 (s, 3H), 3.66 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.5 (C), 151.6 (C), 148.5 (C), 145.5 (C), 143.0 (C), 138.4 (C), 128.2 (C), 127.3 (C), 122.1 (CH), 122.0 (C), 118.8 (CH), 118.1 (CH), 115.2 (CH), 106.3 (CH), 85.7 (CH), 71.9 (CH), 61.2 (OCH_3), 56.2 (OCH_3), 50.8 (OCH_3) ppm.

HRMS (ES$^+$): *m/z* calcd for $[C_{19}H_{18}ClNO_6+Na]^+$: 414.0715 , found: 414.0712.

Methyl (*Z*)-2-(6-bromo-2-(3′-hydroxy-2′,4′-dimethoxyphenyl)-2*H*-benzo[*b*] [1,4]oxazin-3(4*H*)-ylidene)acetate (44j):



44j

Yield: 168 mg (77%) as brown solid.

Mp: 168-169 ^{o}C.

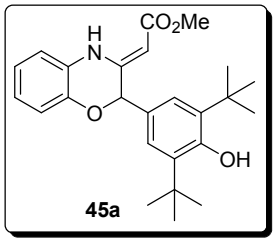
IR (KBr): ν_{max} 3472, 2936, 1658, 1626, 1498, 1447, 1256, 1220, 1162 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.48 (br s, 1H), 7.03 (d, *J* = 2.0 Hz, 1H), 6.94 (dd, *J* = 2.0, 8.5 Hz, 1H), 6.79 (d, *J* = 8.5 Hz, 1H), 6.73 (d, *J* = 9.0 Hz, 1H), 6.63 (d, *J* = 8.5 Hz, 1H), 5.85 (s, 1H), 5.61 (br s, 1H), 4.45 (s, 1H), 3.94 (s, 3H), 3.89 (s, 3H), 3.66 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.5 (C), 151.5 (C), 148.5 (C), 145.4 (C), 143.5 (C), 138.4 (C), 128.6 (C), 125.1 (CH), 122.1 (C), 118.8 (CH), 118.6 (CH), 118.0 (CH), 114.5 (C), 106.3 (CH), 85.8 (CH), 71.9 (CH), 61.2 (OCH_3), 56.2 (OCH_3), 50.8 (OCH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{19}H_{18}BrNO_6+Na]^+$: 458.0210, found: 458.0209.

Methyl (*Z*)-2-(2-(3′,5′-di-*tert*-butyl-4′-hydroxyphenyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (45a):



45a

Yield: 151 mg (74%) as yellow solid.

Mp: 180-181 ^{o}C.

IR (KBr): ν_{max} 3626, 2953, 1662, 1600, 1501, 1435, 1268, 1222, 1160 cm^{-1}.

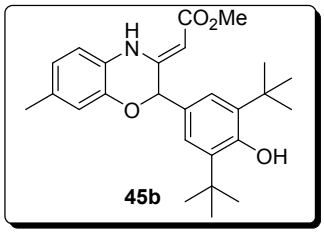
^{1}H NMR (500 MHz, $CDCl_3$): δ 10.45 (br s, 1H), 7.18 (s, 2H), 6.93 (dt, *J* = 1.5, 7.5 Hz, 2H), 6.89-6.87 (m, 2H), 5.42 (s, 1H), 5.31 (s, 1H), 4.42 (s, 1H), 3.69 (s, 3H), 1.42 (s, 18H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.7 (C), 154.5 (C), 152.8 (C), 144.7 (C), 136.0 (C), 127.4 (C), 126.5 (C), 125.0 (CH), 122.6 (CH), 122.5 (CH), 117.2 (CH), 115.3 (CH), 85.1 (CH), 78.2 (CH), 50.7 (OCH_3), 34.3 (C), 30.2 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{25}H_{31}NO_4+Na]^+$: 432.2145, found: 432.2144.

Methyl (*Z*)-2-(2-(3′,5′-di-*tert*-butyl-4′-hydroxyphenyl)-7-methyl-2*H*-benzo[*b*][1,4]-oxazin-3(4*H*)-ylidene)acetate (45b):

Yield: 148 mg (70%) as yellow solid.



45b

Mp: 171-172 ^{o}C.

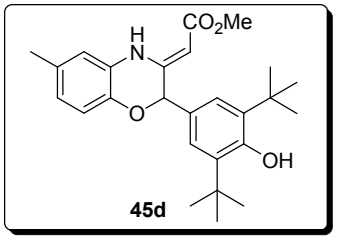
IR (KBr): ν_{max} 3630, 2958, 1665, 1617, 1516, 1436, 1273, 1226, 1158 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.44 (br s, 1H), 7.21 (s, 2H), 6.79-6.74 (m, 3H), 5.42 (s, 1H), 5.33 (s, 1H), 4.42 (s, 1H), 3.70 (s, 3H), 2.27 (s, 3H), 1.44 (s, 18H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.7 (C), 154.4 (C), 152.8 (C), 144.5 (C), 135.9 (C), 132.4 (C), 126.6 (C), 125.0 (CH), 124.9 (C), 123.0 (CH), 117.7 (CH), 115.0 (CH), 84.4 (CH), 76.7 (CH), 50.6 (OCH_3), 34.3 (C), 30.2 (CH_3), 20.9 (CH_3) ppm.

HRMS (ES^{+}): *m/z* calcd for $[C_{26}H_{33}NO_4+Na]^{+}$: 446.2302, found: 446.2317.

Methyl (*Z*)-2-(2-(3′,5′-di-*tert*-butyl-4′-hydroxyphenyl)-6-methyl-2*H*-benzo[*b*][1,4]-oxazin-3(4*H*)-ylidene)acetate (45d):



45d

Yield: 144 mg (68%) as yellow solid.

Mp: 182-183 ^{o}C.

IR (KBr): ν_{max} 3643, 2944, 1654, 1621, 1528, 1425, 1264, 1224, 1159 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.39 (br s, 1H), 7.18 (s, 2H), 6.83 (d, *J* = 8.5 Hz, 1H), 6.70 (s, 1H), 6.68 (d, *J* = 8.0 Hz, 1H), 5.38 (s, 1H), 5.30 (s, 1H), 4.40 (s, 1H), 3.69 (s, 3H), 2.28 (s, 3H), 1.42 (s, 18H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.6 (C), 154.4 (C), 153.0 (C), 142.6 (C), 136.0 (C), 132.2 (C), 127.1 (C), 126.6 (C), 125.0 (CH), 123.0 (CH), 116.8 (CH), 115.9 (CH), 85.0 (CH), 78.3 (CH), 50.6 (OCH_3), 34.4 (C), 30.2 (CH_3), 20.8 (CH_3) ppm.

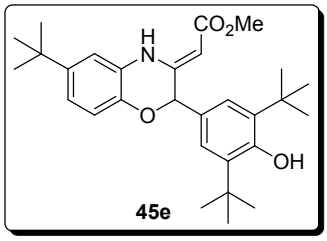
HRMS (ES^{+}): *m/z* calcd for $[C_{26}H_{33}NO_4+Na]^{+}$: 446.2302, found: 446.2297.

Methyl (*Z*)-2-(6-*tert*-butyl-2-(3′,5′-di-*tert*-butyl-4′-hydroxyphenyl)-2*H*-benzo[*b*][1,4]-oxazin -3(4*H*)-ylidene)acetate (45e):

Yield: 141 mg (61%) as brown solid.

Mp: 140-141 ^{o}C.

IR (KBr): ν_{max} 3610, 2952, 1659, 1624, 1434, 1261, 1227, 1158 cm^{-1}.



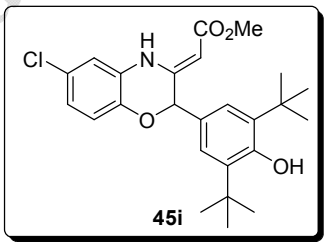
45e

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.51 (br s, 1H), 7.19 (s, 2H), 6.94 (s, 1H), 6.92 (dd, *J* = 2.0, 8.5 Hz, 1H), 6.88 (d, *J* = 8.5 Hz, 1H), 5.42 (s, 1H), 5.33 (s, 1H), 4.42 (s, 1H), 3.71 (s, 3H), 1.43 (s, 18H), 1.31 (s, 9H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.7 (C), 154.5 (C), 153.2 (C), 145.8 (C), 142.4 (C), 135.9 (C), 126.7 (C), 126.7 (C), 125.0 (CH), 119.4 (CH), 116.5 (CH), 112.6 (CH), 84.6 (CH), 78.3 (CH), 50.6 (CH_3), 34.3 (C), 34.3 (C), 31.4 (CH_3), 30.1 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{29}H_{39}NO_4+Na]^+$: 488.2771, found: 488.2768.

Methyl (*Z*)-2-(6-chloro-2-(3′,5′-di-*tert*-butyl-4′-hydroxyphenyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (45i):



45i

Yield: 146 mg (66%) as yellow solid.

Mp: 188-189 °C.

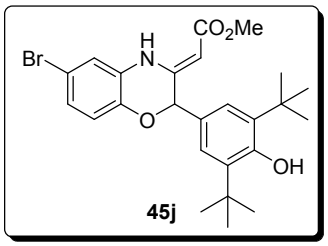
IR (KBr): ν_{max} 3631, 2953, 1672, 1623, 1499, 1435, 1262, 1220, 1160 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.44 (br s, 1H), 7.17 (s, 2H), 6.88-6.86 (m, 1H), 6.85 (s, 1H), 6.82 (dd, *J* = 1.5, 8.5 Hz, 1H), 5.40 (s, 1H), 5.33 (s, 1H), 4.47 (s, 1H), 3.70 (s, 3H), 1.42 (s, 18H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.5 (C), 154.6 (C), 151.9 (C), 143.3 (C), 136.1 (C), 128.4 (C), 127.3 (C), 126.1 (C), 125.0 (CH), 122.1 (CH), 118.2 (CH), 115.2 (CH), 86.4 (CH), 76.7 (CH), 50.8 (CH_3), 34.4 (C), 30.2 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{25}H_{30}ClNO_4+Na]^+$: 466.1756, found: 466.1742.

Methyl (*Z*)-2-(6-bromo-2-(3′,5′-di-*tert*-butyl-4′-hydroxyphenyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (45j):



45j

Yield: 176 mg (72%) as yellow solid.

Mp: 180-181 °C.

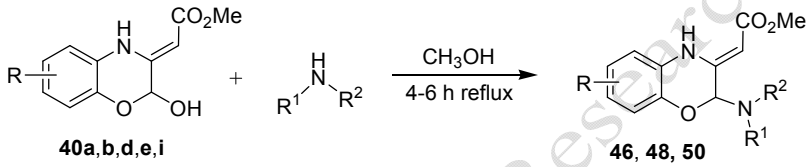
IR (KBr): ν_{max} 3629, 2953, 1672, 1622, 1598, 1497, 1433, 1265, 1219, 1156 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.42 (br s, 1H), 7.15 (s, 2H), 7.01 (d, *J* = 2.0 Hz, 1H), 6.96 (dd, *J* = 2.0, 8.5 Hz, 1H), 6.80 (d, *J* = 8.5 Hz, 1H), 5.39 (s, 1H), 5.31 (s, 1H), 4.46 (s, 1H), 3.69 (s, 3H), 1.41 (s, 18H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.5 (C), 154.6 (C), 151.9 (C), 143.3 (C), 136.1 (C), 128.4 (C), 127.3 (C), 126.1 (C), 125.0 (CH), 122.1 (CH), 118.2 (CH), 115.2 (CH), 86.4 (CH), 76.7 (CH), 50.8 (CH_3), 34.4 (C), 30.2 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{25}H_{30}BrNO_4+Na]^+$: 510.1250, found: 510.1252.

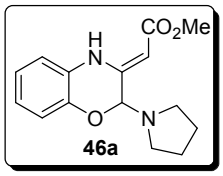
3.2.12. General procedure for synthesis of 2-amino-benzoxazine derivatives 46, 48 and 50:



In a typical reaction procedure, a secondary amine (pyrrolidine/ *N*-benzyl piperazine /dibenzylamine, 0.75 mmol) was added to a solution of 2-hydroxy-1,4-benzoxazine derivative **40**, **(**0.5 mmol) in methanol (4 mL) and the resulting mixture was stirred at the reflux temperature until the starting material was completely consumed. The progress of the reaction was monitored by TLC, after completion of the reaction the solvent was evaporated under reduced pressure. The crude reaction mixture was subjected to column chromatography on silica gel (100-200 mesh, pre-treated with triethylamine) and purified by using 10% ethyl acetate in hexanes as eluent to obtain the pure products.

Methyl (*Z*)-2-(2-(pyrrolidin-1′-yl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (46a):

Yield: 99 mg (72%) thick brown liquid.



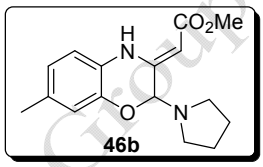
IR (KBr): ν_{max} 3300, 2950, 2840, 1667, 1622, 1501, 1429, 1269, 1226, 1145 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.26 (br s, 1H), 6.90-6.85 (m, 3H), 6.81-6.78 (m, 1H), 5.29 (s, 1H), 5.04 (s, 1H), 3.05-3.00 (m, 2H), 2.90-2.85 (m, 2H), 3.72 (s, 3H), 1.81-1.75 (m, 4H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 171.1 (C), 150.4 (C), 144.1 (C), 126.8 (C), 122.5 (CH), 122.1 (CH), 116.7 (CH), 115.1 (CH), 87.5 (CH), 83.9 (CH), 50.7 (OCH_3), 40.8 (CH_2), 24.5 (CH_2) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{15}H_{18}N_2O_3+Na]^+$: 297.1209, found: 297.1214.

Methyl (*Z*)-2-(7-methyl-2-(pyrrolidin-1′-yl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)-acetate (46b):



46b

Yield: 104 mg (72%) thick brown liquid.

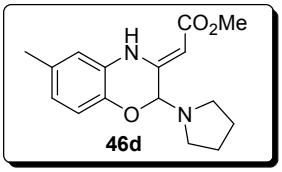
IR (KBr): ν_{max} 3287, 2967, 2861, 1663, 1614, 1516, 1430, 1387, 1271, 1217, 1145 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.23 (br s, 1H), 6.72 (s, 1H), 6.69-6.68 (m, 2H), 5.26 (s, 1H), 4.99 (s, 1H), 3.71 (s, 3H), 3.03-2.98 (m, 2H), 2.88-2.83 (m, 2H), 2.26 (s, 3H) 1.80-1.74 (m, 4H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 171.0 (C), 150.3 (C), 143.8 (C), 132.3 (C), 124.2 (CH), 122.4 (C), 117.1 (CH), 114.6 (CH), 87.4 (CH), 83.1 (CH), 50.5 (OCH_3), 47.7 (CH_2), 24.4 (CH_2), 20.7 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{16}H_{20}N_2O_3+Na]^+$: 311.1366, found: 311.1369.

Methyl (*Z*)-2-(6-methyl-2-(pyrrolidin-1′-yl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene) - acetate (46d):



46d

Yield: 107 mg (74%) thick brown liquid.

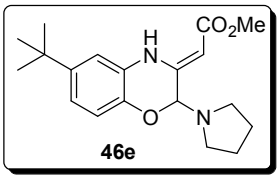
IR (KBr): ν_{max} 3278, 2948, 2871, 1667, 1623, 1502, 1434, 1275, 1234, 1164 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.20 (br s, 1H), 6.77 (d, *J* = 8.0 Hz, 1H), 6.69-6.61 (m, 2H), 5.23 (s, 1H), 5.01 (s, 1H), 3.72 (s, 3H), 3.04-2.98 (m, 2H), 2.87-2.84 (m, 2H), 2.26 (s, 3H) 1.81-1.74 (m, 4H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.0 (C), 149.5 (C), 140.9 (C), 130.6 (C), 125.5 (C), 122.0 (CH), 115.3 (CH), 114.6 (CH), 86.5 (CH), 82.7 (CH), 49.6 (OCH_3), 46.9 (CH_2), 23.4 (CH_2), 19.8 (CH_3) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{16}H_{20}N_2O_3+Na]^+$: 311.1366, found: 311.1356.

Methyl (*Z*)-2-(6-*tert*-butyl-2-(pyrrolidin-1′-yl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)-acetate (46e):



46e

Yield: 103 mg (62%) as thick brown liquid.

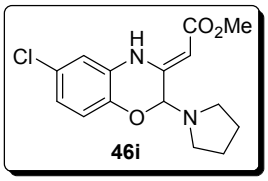
IR (KBr): ν_{max} 3451, 2960, 2866, 1664, 1620, 1513, 1458, 1383, 1255, 1223, 1174 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.29 (br s, 1H), 6.88 (dd, *J* = 2.5, 8.5 Hz, 1H), 6.82 (d, *J* = 2.0 Hz, 1H), 6.81 (d, *J* = 8.5 Hz, 1H), 6.80 (s, 1H), 5.28 (s, 1H), 5.03 (d, *J* = 1.0 Hz, 1H), 3.72 (s, 3H), 3.05-3.00 (m, 2H), 2.90-2.85 (m, 2H), 1.81-1.76 (m, 4H), 1.27 (s, 9H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 171.2 (C), 150.7 (C), 145.3 (C), 141.8 (C), 126.0 (C), 119.4 (CH), 116.0 (CH), 112.4 (CH), 87.5 (CH), 83.4 (CH), 50.6 (OCH_3), 47.8 (CH_2), 34.2 (C), 31.4 (CH_3), 24.5 (CH_2) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{19}H_{26}N_2O_3+Na]^+$: 353.1835, found: 353.1839.

Methyl (*Z*)-2-(6-chloro-2-(pyrrolidin-1′-yl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)ylidene)-acetate (46i):



46i

Yield: 106 mg (69%) as thick brown liquid.

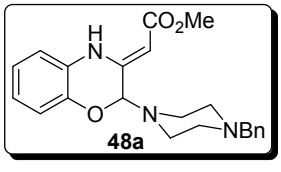
IR (KBr): ν_{max} 3280, 2953, 1669, 1629, 1498, 1379, 1265, 1158 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.24 (br s, 1H), 6.80-6.79 (m, 2H), 6.78-6.77 (m, 1H), 5.25 (s, 1H), 5.06 (s, 1H), 3.71 (s, 3H), 3.01-2.97 (m, 2H), 2.87-2.83 (m, 2H), 1.80-1.74 (m, 4H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.8 (C), 149.5 (C), 142.7 (C), 127.8 (C), 126.6 (C), 122.0 (CH), 117.6 (CH), 114.8 (CH), 87.7 (CH), 85.1 (CH), 50.7 (OCH_3), 47.8 (CH_2), 24.4 (CH_2) ppm.

HRMS (ES^+): *m/z* calcd for $[C_{15}H_{17}ClN_2O_3+Na]^+$: 331.0820, found:331.0816.

Methyl (*Z*)- 2-(2-(4′-benzylpiperazin-1′-yl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)-acetate (48a):



48a

Yield: 148 mg (78%) as pale yellow solid.

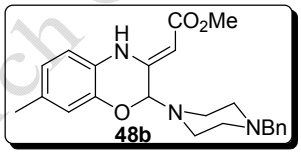
Mp: 80-81 ^oC.

IR (KBr): ν_{max} 3264, 1674, 1624, 1506, 1450, 1376, 1268 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.43 (br s, 1H), 7.37-7.35 (m, 4H), 7.31-7.27 (m, 1H), 6.94-6.90 (m, 3H), 6.84-6.81 (m, 1H), 5.19 (s, 1H), 5.13 (s, 1H), 3.77 (s, 3H), 3.55 (s, 2H), 3.15-3.10 (m, 2H), 2.80 (td, *J* = 4.5, 10.0 Hz, 2H), 2.60-2.41 (m, 4H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.9 (C), 149.6 (C), 143.9 (C), 137.8 (C), 129.0 (CH), 128.0 (CH), 126.9 (CH), 126.2 (C), 122.5 (CH), 121.9 (CH), 116.5 (CH), 114.8 (CH), 89.4 (CH), 83.3 (CH), 62.8 (CH_2), 53.0 (CH_2), 50.5 (OCH_3) ppm.

Methyl (*Z*)-2-(2-(4′-benzylpiperazin-1′-yl)-7-methyl-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (48b):



48b

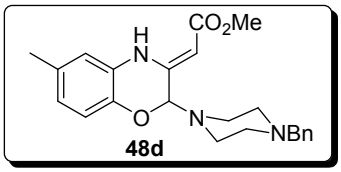
Yield: 149 mg (76%) as thick brown liquid.

IR (KBr): ν_{max} 3264, 1656, 1614, 1513, 1462, 1371, 1264 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.32 (br s, 1H), 7.33-7.31 (m, 4H), 7.27-7.26 (m, 1H), 6.71 (s, 1H), 6.80 (s, 2H), 5.15 (s, 1H), 5.02 (s, 1H), 3.72 (s, 3H), 3.53 (s, 2H), 3.11-3.06 (m, 2H), 2.80-2.75 (m, 2H), 2.55-2.44 (m, 4H), 2.26 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 171.1 (C), 149.8 (C), 143.8 (C), 132.6 (C), 129.2 (CH), 128.2 (CH), 127.0 (CH), 123.8 (C), 122.5 (CH), 117.1 (CH), 114.7 (CH), 89.5 (CH), 82.8 (CH), 62.9 (CH_2), 53.0 (CH_2), 50.6 (OCH_3), 20.8 (CH_3) ppm.

Methyl (*Z*)-2-(2-(4′-benzylpiperazin-1′-yl)-6-methyl-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (48d):



48d

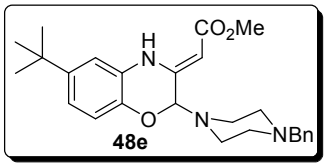
Yield: 145 mg (74%) as orange thick liquid.

IR (KBr): ν_{max} 3274, 1657, 1621, 1513, 1434, 1382, 1254 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.33 (br s, 1H), 7.34 (d, *J* = 4.0 HZ, 4H), 7.31-7.27 (m, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 6.70 (d, *J* = 8.5 Hz, 1H), 6.63 (s, 1H), 5.14 (s, 1H), 5.08 (s, 1H), 3.75 (s, 3H), 3.53 (s, 2H), 3.13-3.07 (m, 2H), 2.78 (td, *J* = 4.5, 10.0 Hz, 2H), 2.60-2.49 (s, 4H), 2.83 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 171.0 (C), 149.9 (C), 141.8 (C), 138.0 (C), 131.6 (C), 129.1 (CH), 128.1 (CH), 127.0 (CH), 126.0 (C), 123.0 (CH), 116.3 (CH), 115.5 (CH), 89.5 (CH), 83.3 (CH), 62.9 (CH_2), 53.1 (CH_2), 50.6 (OCH_3), 20.7 (CH_3) ppm.

Methyl (*Z*)-2-(2-(4′-benzylpiperazin-1′-yl)-6-*tert*-butyl-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (48e):



48e

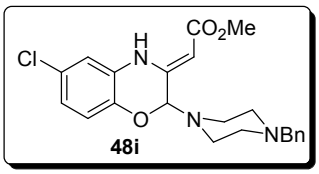
Yield: 144 mg (66%) as thick brown liquid.

IR (KBr): ν_{max} 3226, 1665, 1615, 1509, 1450, 1365, 1256 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.38 (br s, 1H), 7.32-7.31 (m, 5H), 6.89 (dd, *J* = 2.0, 8.0 Hz, 1H), 6.82-6.79 (m, 2H), 5.16 (s, 1H), 5.07 (s, 1H), 3.73 (s, 3H), 3.51 (s, 2H), 3.11-3.04 (m, 2H), 2.81-2.74 (m, 2H), 2.53-2.44 (m, 4H), 1.26 (s, 9H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 171.2 (C), 150.2 (C), 145.4 (C), 141.7 (C), 129.2 (CH), 128.2 (CH), 127.0 (CH), 125.6 (C), 119.5 (CH), 116.0 (CH), 112.3 (CH), 89.6 (CH), 83.0 (CH), 63.0 (CH_2), 53.2 (CH_2), 50.7 (OCH_3), 34.3 (C), 31.4 (CH_3) ppm.

Methyl (*Z*)-2-(2-(4′-benzylpiperazin-1′-yl)-6-chloro-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (48i):



48i

Yield: 146 mg (70%) as orange solid.

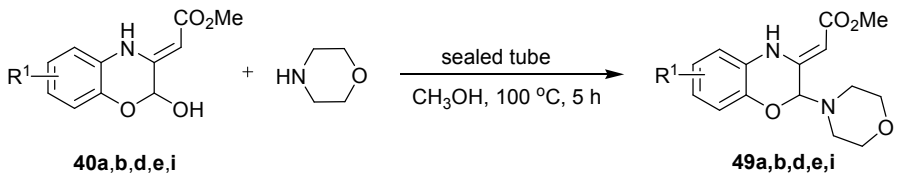
Mp: 84-85 °C.

IR (KBr): ν_{max} 3248, 1668, 1615, 1518, 1438, 1374, 1249 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.37 (br s, 1H), 7.34 (d, *J* = 4.5 Hz, 4H), 7.31-7.26 (m, 1H), 6.84-6.82 (m, 2H), 6.80 (s, 1H), 5.16 (s, 1H), 5.12 (s, 1H), 3.75 (s, 3H), 3.54 (s, 2H), 3.10-3.07 (m, 2H), 2.78 (td, *J* = 4.5, 10.5 Hz, 2H), 2.56-2.45 (m, 4H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.8 (C), 148.9 (C), 142.6 (C), 129.2 (CH), 128.2 (CH), 127.3 (C), 127.1 (CH), 126.7 (C), 122.1 (CH), 117.6 (CH), 114.8 (CH), 89.6 (CH), 84.8 (CH), 62.9 (CH_2), 53.0 (CH_2), 50.8 (OCH_3) ppm.

3.2.13. General procedure for the reaction of 2-hydroxy-1,4-benzoxazine derivatives with morpholine:



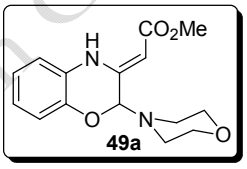
40a,b,d,e,i **49a,b,d,e,i**

In a dry sealed tube 2-hydroxy-1,4-benzoxazine derivative **40**, (0.5 mmol) was dissolved in methanol (4 mL) and morpholine (2 mmol) was added. The reaction mixture was allowed to heat at 100 ^{o}C for 5 h. After completion of the reaction as shown by the TLC, methanol was evaporated under reduced pressure and the crude reaction mixture was subjected to column chromatography on silica gel (100-200 mesh, pre-treated with triethylamine) and eluted with 10% ethyl acetate in hexanes to obtain the pure products **49**.

Methyl (*Z*)-2-(2-morpholino-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (49a):

Yield: 105 mg (72%) as yellow solid.

Mp: 78-79 ^{o}C.



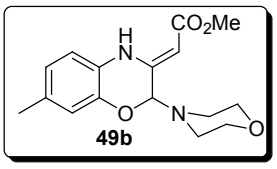
49a

IR (KBr): ν_{max} 3261, 1671, 1630, 1518, 1462, 1362, 1271cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.35 (br s, 1H), 6.92-6.87 (m, 3H), 6.81-6.79 (m, 1H), 5.12 (s, 1H), 5.08 (s, 1H), 3.73 (s, 3H), 3.70 (t, *J* = 5.0 Hz, 4H), 3.04 (td, *J* = 4.5, 11.5 Hz, 2H), 2.74 (td, *J* = 4.5, 11.0 Hz, 2H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 171.0 (C), 149.3 (C), 143.8 (C), 126.4 (C), 122.7 (CH), 122.3 (CH), 116.7 (CH), 115.1 (CH), 89.6 (CH), 83.7 (CH), 67.0 (CH_2), 50.8 (OCH_3), 48.1 (CH_2) ppm.

Methyl (*Z*)-2-(7-methyl-2-morpholino-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (49b):



49b

Yield: 96 mg (63%) as yellow solid.

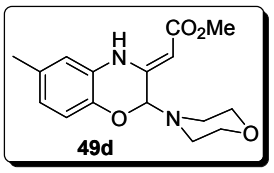
Mp: 95-96 ^{o}C.

IR (KBr): ν_{max} 3261, 1671, 1630, 1507, 1443, 1367, 1271 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.30 (br s, 1H), 6.70 (s, 1H), 6.65 (s, 2H), 5.04 (s, 1H), 5.00 (s, 1H), 3.68 (s, 3H), 3.65 (t, *J* = 4.5 Hz, 4H), 2.99 (td, *J* = 4.5, 11.5 Hz, 2H), 2.68 (td, *J* = 4.5, 9.5 Hz, 2H), 2.23 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.7 (C), 149.1 (C), 143.4 (C), 132.4 (C), 123.7 (C), 122.5 (CH), 116.9 (CH), 114.6 (CH), 89.4 (CH), 82.9 (CH), 66.7 (CH_2), 50.4 (OCH_3), 47.8 (CH_2), 20.6 (CH_3) ppm.

Methyl (*Z*)-2-(6-methyl-2-morpholino-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (49d):



Yield: 101 mg (66%) as yellow solid.

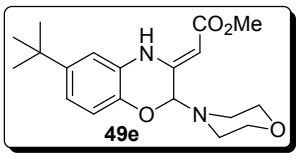
Mp: 72-73 ^{o}C.

IR (KBr): ν_{max} 3265, 1674, 1632, 1512, 1434, 1378, 1246 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.28 (br s, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 6.67 (d, *J* = 8.0 Hz, 1H), 6.61 (s, 1H), 5.05 (s, 1H), 5.04 (s, 1H), 3.71 (s, 3H), 3.69 (t, *J* = 4.5 Hz, 4H), 3.02 (td, *J* = 4.0, 10.5 Hz, 2H), 2.72 (td, *J* = 4.5, 10.0 Hz, 2H), 2.25 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.9 (C), 149.4 (C), 141.5 (C), 131.9 (C), 126.0 (C), 123.1 (CH), 116.3 (CH), 115.6 (CH), 89.6 (CH), 83.6 (CH), 67.0 (CH_2), 50.7 (OCH_3), 48.0 (CH_2), 20.7 (CH_3) ppm.

Methyl (*Z*)-2-(6-*tert*-butyl-2-morpholino-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (49e):



Yield: 106 mg (61%) as pale yellow solid.

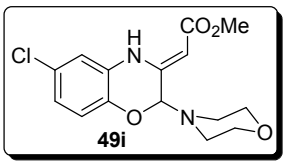
Mp: 114-115 ^{o}C.

IR (KBr): ν_{max} 3249, 1668, 1615, 1518, 1436, 1371, 1250 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.41 (br s, 1H), 6.93 (dd, *J* = 2.0, 8.5 Hz, 1H), 6.86 (s, 1H), 6.84 (s, 1H), 5.13 (s, 1H), 5.10 (s, 1H), 3.75 (s, 3H), 3.73 (t, *J* = 4.5 HZ, 4H), 3.07 (td, *J* = 4.5, 10.0 Hz, 2H), 2.77 (td, *J* = 5.0, 10.0 Hz, 2H), 1.29 (s, 9H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 171.1 (C), 149.7 (C), 145.6 (C),141.4 (C), 125.6 (C), 119.6 (CH), 116.0 (CH), 112.3 (CH), 89.6 (CH), 83.2 (CH), 66.9 (CH_2), 50.7 (OCH_3), 48.1 (CH_2), 34.3 (C), 31.4 (CH_3) ppm.

Methyl (*Z*)-2-(6-chloro-2-morpholino-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (49i):



Yield: 112 mg (69%) as yellow solid.

Mp: 100-101 ^{o}C.

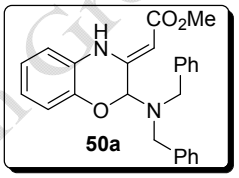
IR (KBr): ν_{max} 3243, 1668, 1630, 1520, 1465, 1389, 1265 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.32 (br s, 1H), 6.80 (s, 2H), 6.78 (d, *J* = 0.5 Hz, 1H), 5.09 (s, 1H), 5.06 (s, 1H), 3.71 (s, 3H), 3.68 (t, *J* = 5.0 Hz, 4H), 2.99 (td, *J* = 4.5, 11.5 Hz, 2H), 2.71 (td, *J* = 5.0, 10.0 Hz, 2H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.6 (C), 148.3 (C), 142.3 (C), 127.3 (C), 126.9 (C), 122.1 (CH), 117.6 (CH), 114.8 (CH), 89.6 (CH), 85.0 (CH), 66.8 (CH_2), 50.8 (OCH_3), 48.0 (CH_2) ppm.

Methyl (*Z*)-2-(2-(dibenzylamino)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (50a):

Yield: 152 mg (76%) as pale yellow solid.



Mp: 72-73 ^oC.

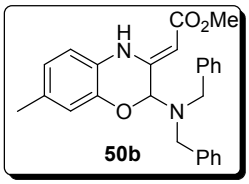
IR (KBr): ν_{max} 3271, 1659, 1612, 1514, 1456, 1374, 1247 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.51 (br s, 1H), 7.46 (d, *J* = 7.5 Hz, 4H), 7.38 (t, *J* = 7.5 Hz, 4H), 7.31 (t, *J* = 7.0 Hz, 2H), 7.05-7.02 (m, 1H), 6.97-6.91 (m, 2H), 6.85-6.81 (m, 1H), 5.39 (s, 1H), 5.32 (s, 1H), 4.14 (d, *J* = 14.0 Hz, 2H), 3.92 (d, *J* = 14.0 Hz, 2H), 3.77 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 171.0 (C), 151.4 (C), 144.0 (C), 138.3 (C), 128.6 (CH), 128.5 (CH), 127.3 (CH), 126.4 (C), 122.6 (CH), 122.2 (CH), 116.6 (CH), 115.0 (CH), 85.7 (CH), 83.0 (CH), 52.9 (CH_2), 50.7 (OCH_3) ppm.

Methyl (*Z*)-2-(2-(dibenzylamino)-7-methyl-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)-acetate(50b):

Yield: 156mg (75%) as yellow solid.



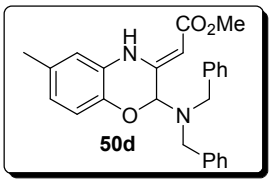
Mp: 78-79 ^oC.

IR (KBr): ν_{max} 3261, 1665, 1619, 1517, 1452, 1383, 1277cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.52 (br s, 1H), 7.50 (d, *J* = 7.5 Hz, 4H), 7.41 (t, *J* = 7.5 Hz, 4H), 7.33 (t, *J* = 7.5 Hz, 2H), 6.89 (s, 1H), 6.77-6.73 (m, 2H), 5.40 (s, 1H), 5.33 (s, 1H), 4.17 (d, *J* = 14.0 Hz, 2H), 3.95 (d, *J* = 14.0 Hz, 2H), 3.79 (s, 3H), 2.36 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 171.0 (C), 151.3 (C), 143.7 (C), 138.2 (C), 132.5 (C), 128.5 (CH), 128.4 (CH), 127.2 (CH), 123.8 (C), 122.6 (CH), 117.1 (CH), 114.7 (CH), 85.6 (CH), 82.3 (CH), 52.7 (CH_2), 50.5 (OCH_3), 20.8 (CH_3) ppm.

Methyl (*Z*)-2-(2-(dibenzylamino)-6-methyl-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)-acetate (50d):



Yield: 152 mg (73%) as orange solid.

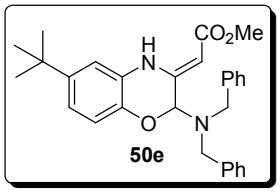
Mp: 80-81 ^{o}C.

IR (KBr): ν_{max} 3269, 1663, 1624, 1525, 1491, 1377, 1279 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.41 (br s, 1H), 7.44 (d, *J* = 7.0 Hz, 4H), 7.37 (t, *J* = 7.5 Hz, 4H), 7.30-7.27 (m, 2H), 6.90 (t, *J* = 8.0 Hz, 1H), 6.74 (dd, *J* = 1.0, 8.0 Hz, 1H), 6.63 (d, *J* = 1.5 Hz, 1H), 5.40 (s, 1H), 5.25 (s, 1H), 4.11 (d, *J* = 14.0 Hz, 2H), 3.89 (d, *J* = 14.0Hz, 2H), 3.75 (s, 3H), 2.29 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 171.0 (C), 151.5 (C), 141.8 (C), 138.3 (C), 131.8 (C), 128.6 (CH), 128.5 (CH), 127.2 (CH), 126.1 (C), 123.1 (CH), 116.3 (CH), 115.5 (CH), 85.7 (CH), 82.8 (CH), 52.8 (CH_2), 50.7 (OCH_3), 20.8 (CH_3) ppm.

Methyl (*Z*)-2-(6-*tert*-butyl-2-(dibenzylamino)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)-acetate (50e):



Yield: 156 mg (68%) as yellow solid.

Mp: 98-99 ^{o}C.

IR (KBr): ν_{max} 3272, 1665, 1618, 1521, 1492, 1383, 1259 cm^{-1}.

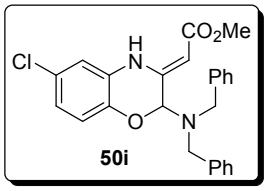
^{1}H NMR (500 MHz, $CDCl_3$): δ 10.49 (br s, 1H), 7.44 (d, *J* = 7.5 Hz, 4H), 7.36 (t, *J* = 7.5 Hz, 4H), 7.28 (t, *J* = 7.0 Hz, 2H), 6.97-6.92 (m, 2H), 6.84 (d, *J* = 1.5 Hz, 1H), 5.37 (s, 1H), 5.26 (s, 1H), 4.11 (d, *J* = 14.0 Hz, 2H), 3.90 (d, *J* = 14.0 Hz, 2H), 3.75 (s, 3H), 1.30 (s, 9H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ171.2 (C), 151.7 (C), 145.5 (C), 141.6 (C), 138.3 (C), 128.6 (CH), 128.5 (CH), 127.3 (CH), 125.7 (C), 119.5 (CH), 116.0 (CH), 112.3 (CH), 85.7 (CH), 82.5 (CH), 52.8 (CH_2), 50.7 (OCH_3), 34.3 (C), 31.4 (CH_3) ppm.

Methyl (*Z*)-2-(6-chloro-2-(dibenzylamino)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-ylidene)acetate (50i):

Yield: 154 mg (71%) as pale yellow solid.

Mp: 108-109 ^{o}C.



50i

IR (KBr): ν_{max} 3257, 1662, 1617, 1518, 1454, 1363, 1232 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.46 (br s, 1H), 7.42-7.41 (m, 4H), 7.37 (t, *J* = 7.5 Hz, 4H), 7.29 (t, *J* = 7.5 Hz, 2H), 6.92-6.90 (m, 1H), 6.87 (dd, *J* = 2.0, 8.5 Hz, 1H), 6.79 (d, *J* = 2.0 Hz, 1H), 5.39 (s, 1H), 5.27 (s, 1H), 4.10 (d, *J* = 13.5 Hz, 2H), 3.87 (d, *J* = 14.0 Hz, 2H), 3.75 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.8 (C), 150.4 (C), 142.5 (C), 138.0 (C), 128.5 (CH), 128.5 (CH), 127.3 (CH), 126.9 (C), 122.1 (CH), 117.5 (CH), 114.8 (CH), 85.9 (CH), 84.2 (CH), 52.8 (CH_2), 50.8 (OCH_3) ppm.

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NMR SPECTRA FOR SELECTED COMPOUNDS

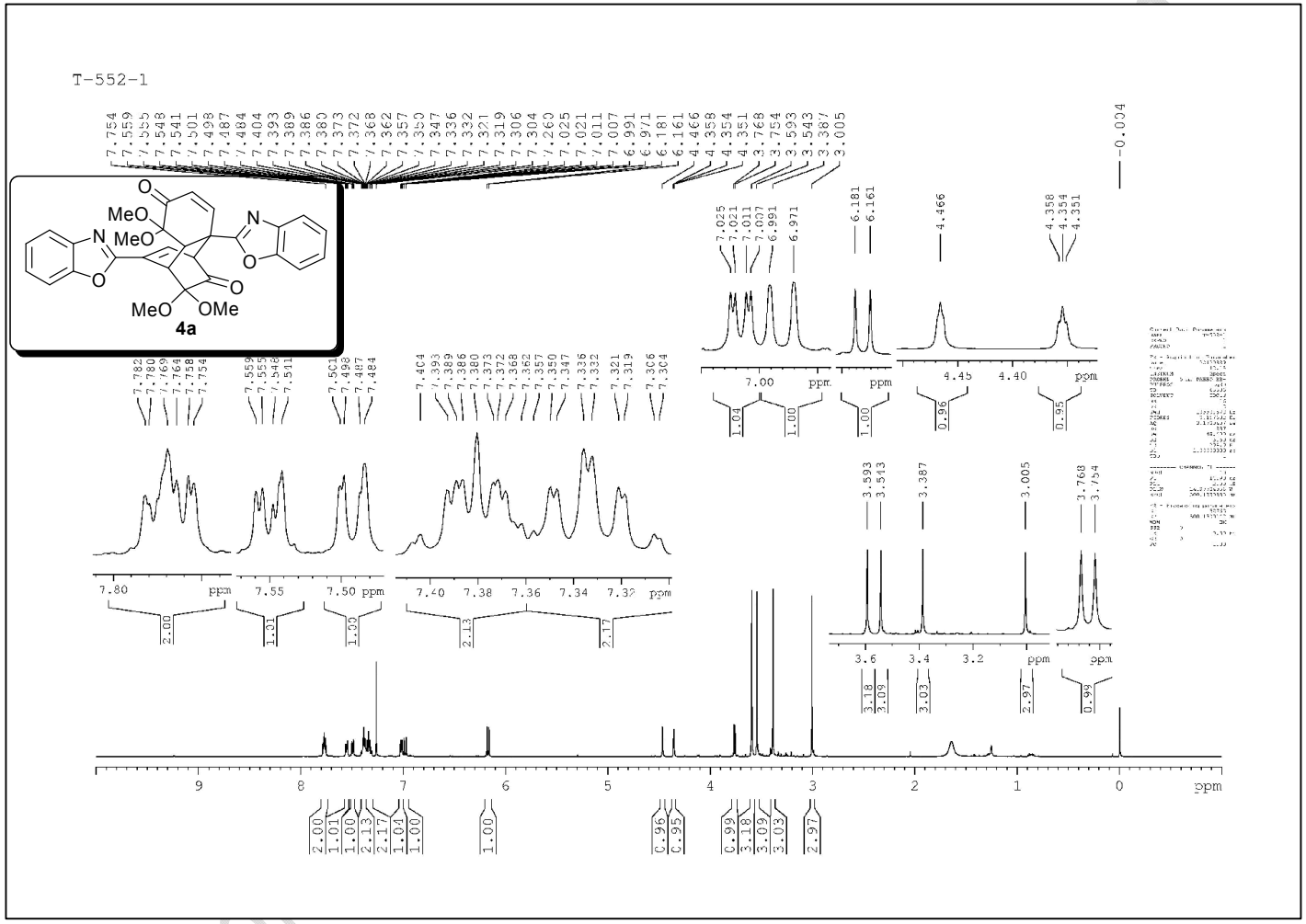


Figure S-1: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **4a.**

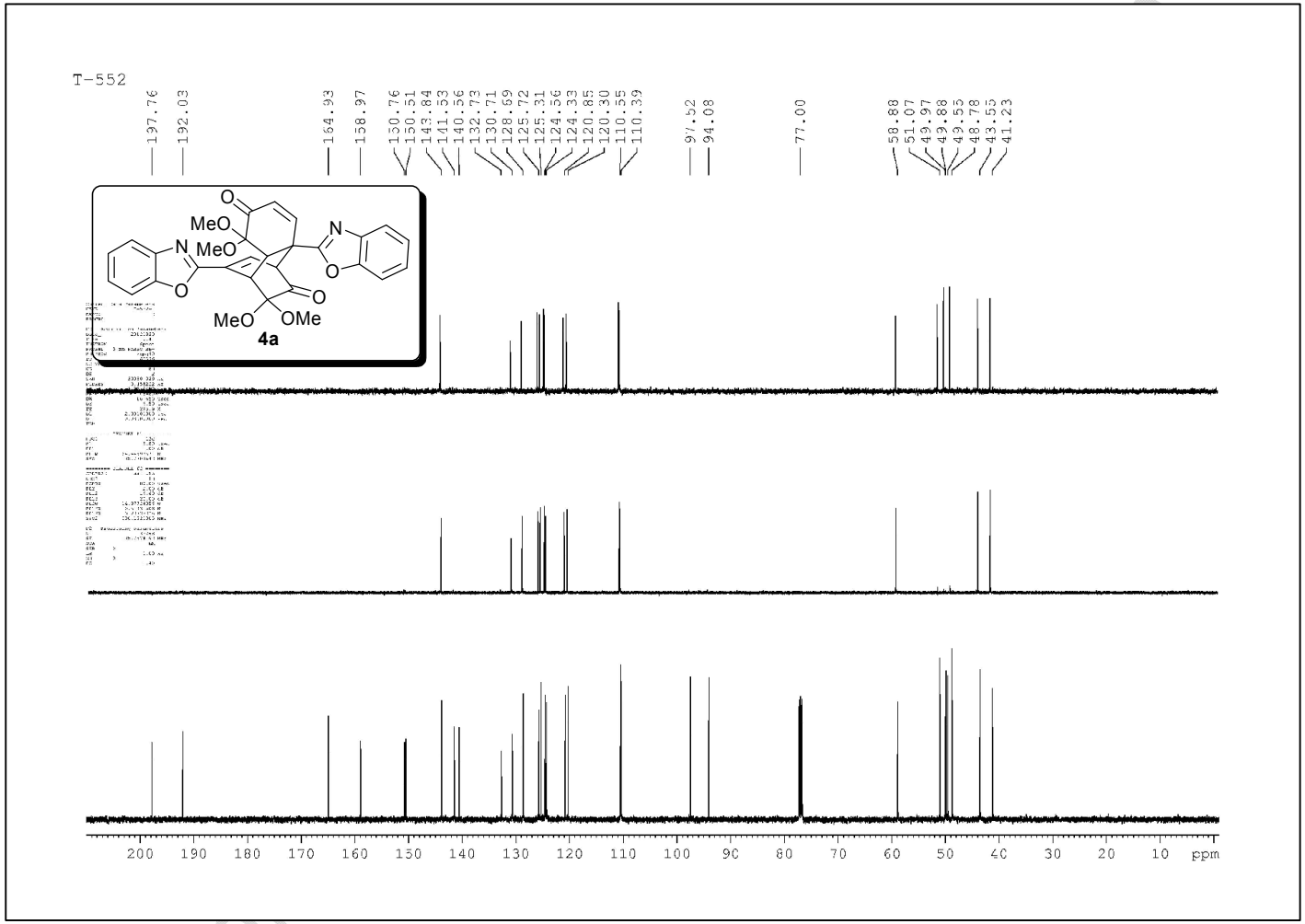


Figure S-2: ^{13}C and DEPT (125 MHz, $CDCl_3$) Spectra of **4a**.

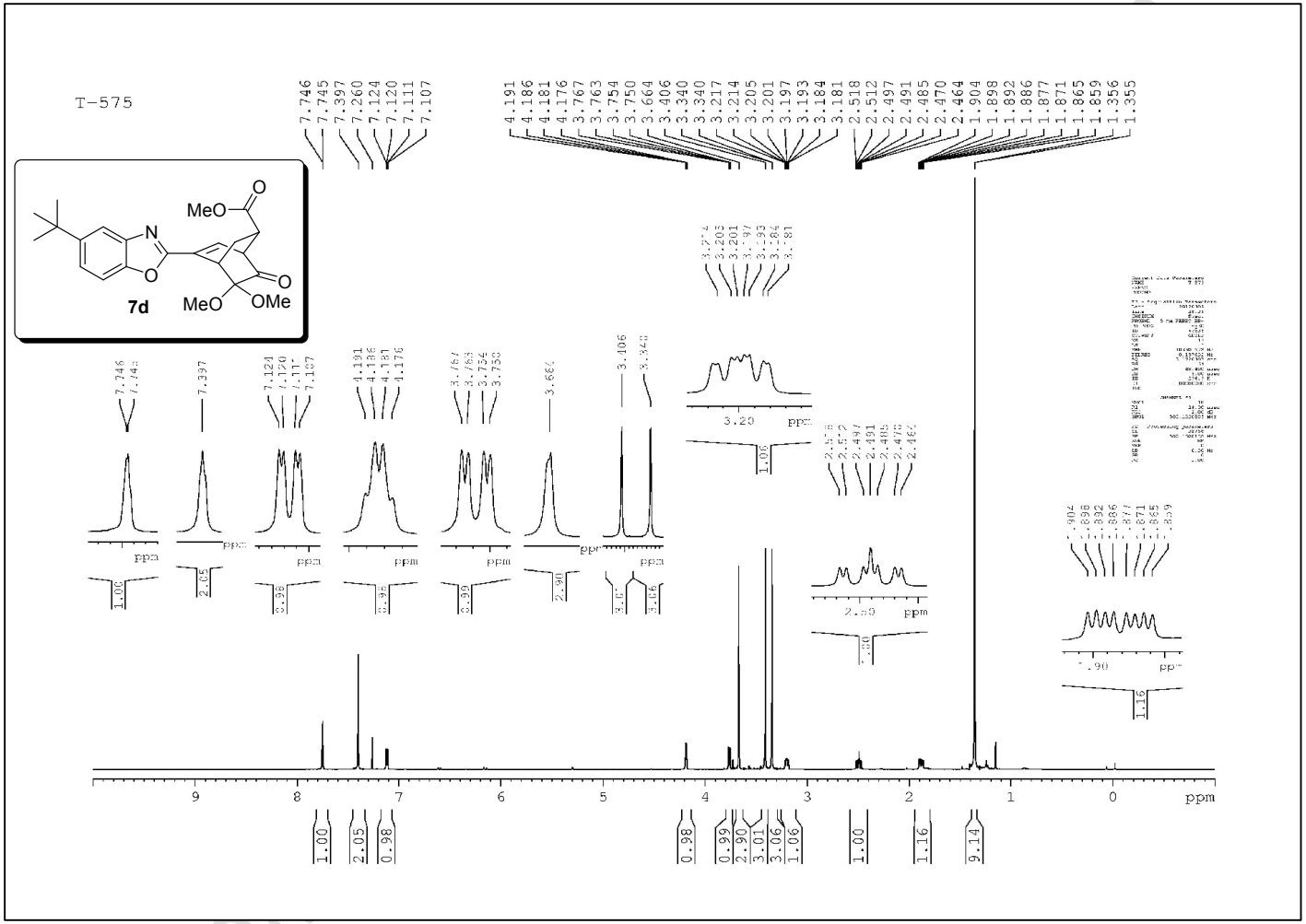


Figure S-3: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **7d.**

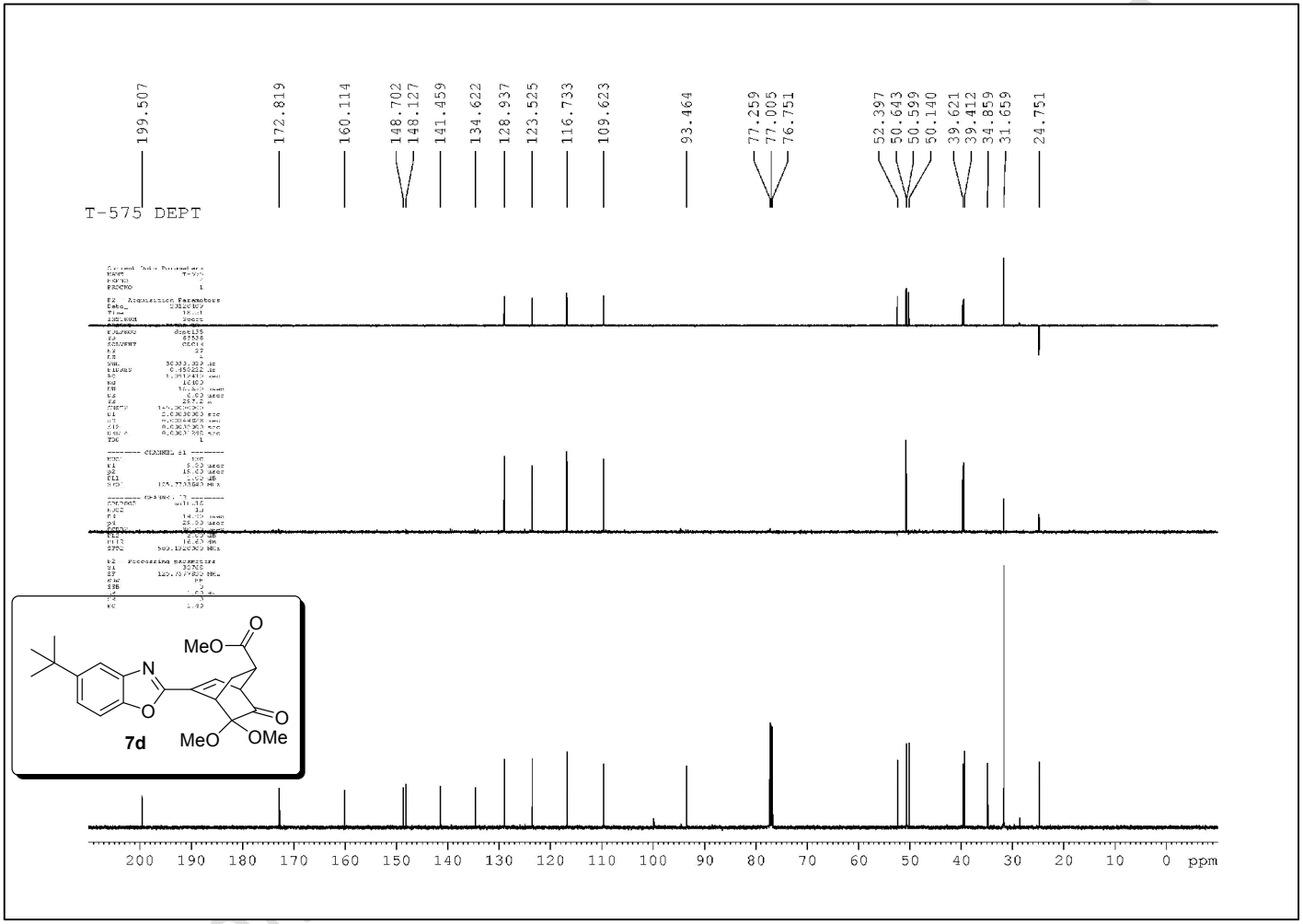


Figure S-4: ^{13}C and DEPT (125 MHz, $CDCl_3$) Spectra of **7d**.

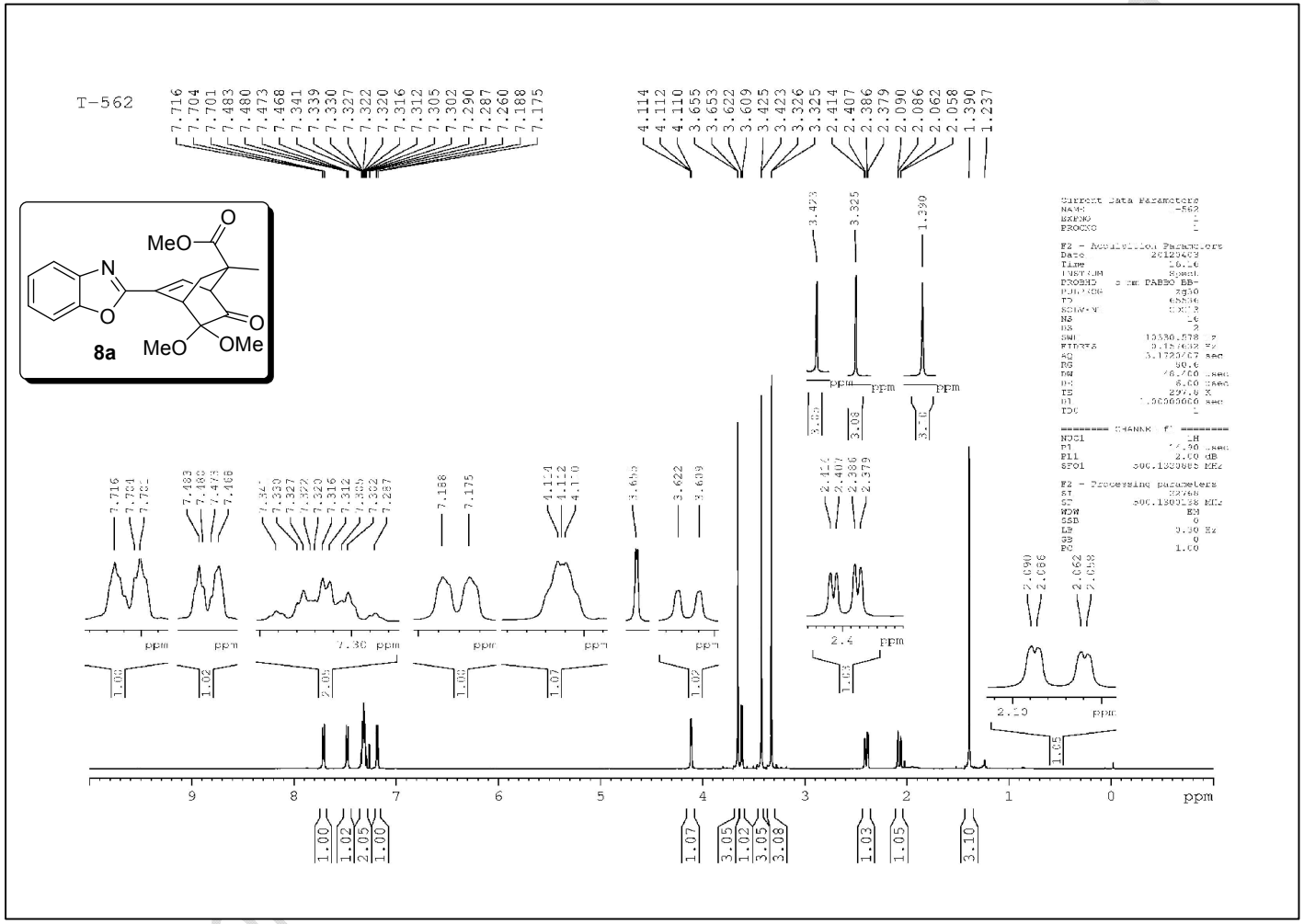


Figure S-5: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **8a.**

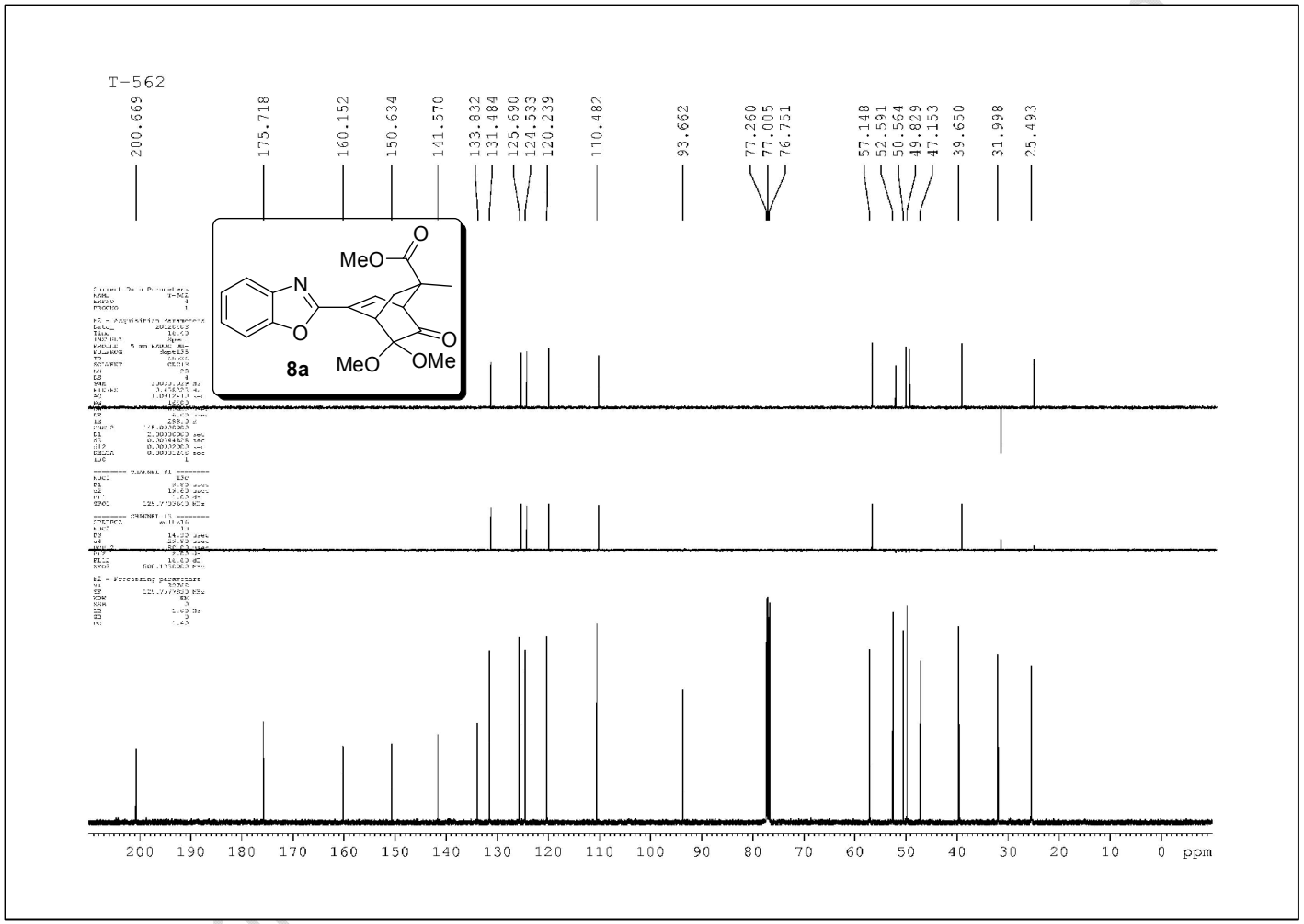


Figure S-6: ^{13}C and DEPT (125 MHz, $CDCl_3$) Spectra of **8a**.

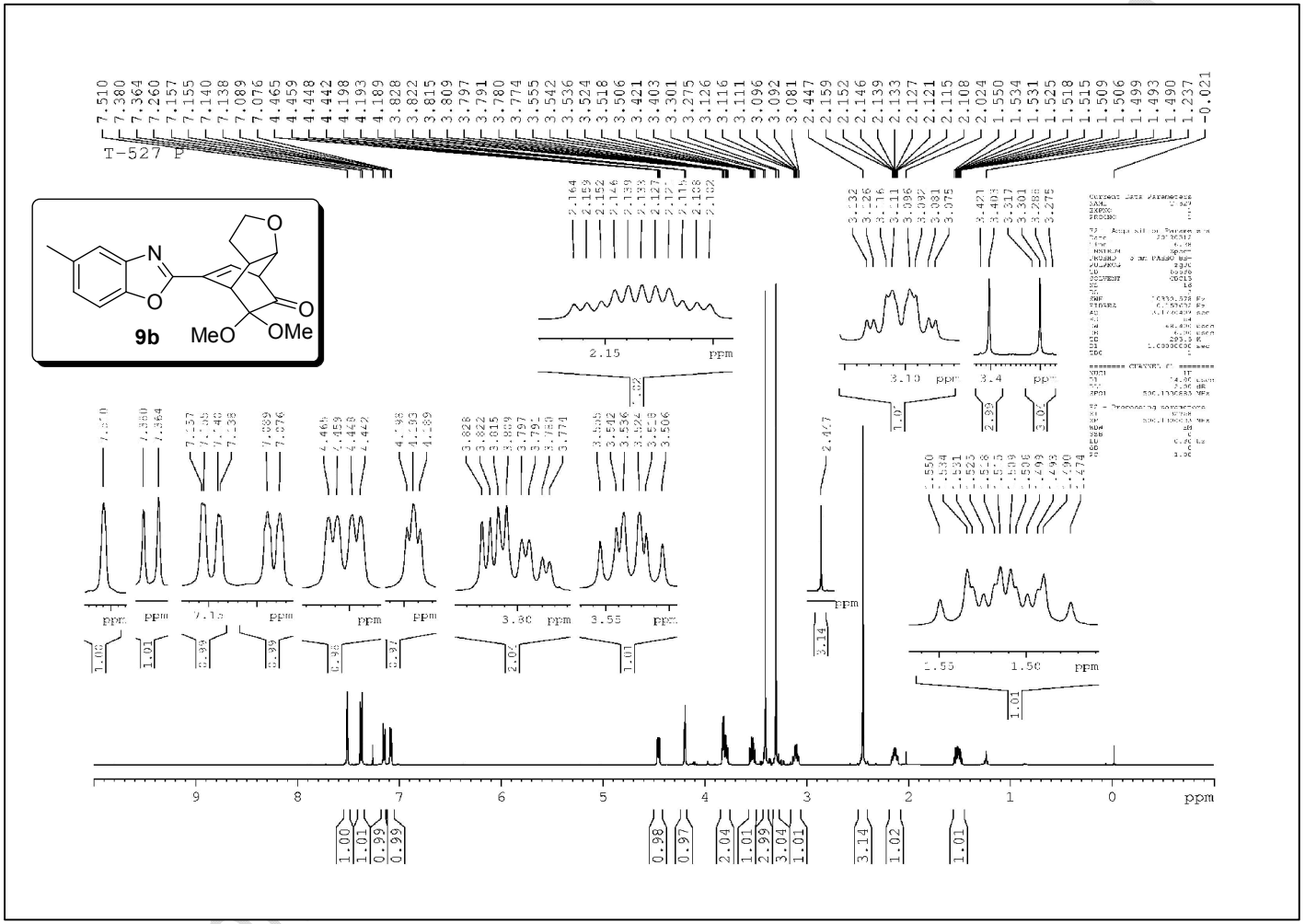


Figure S-7: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **9b**.

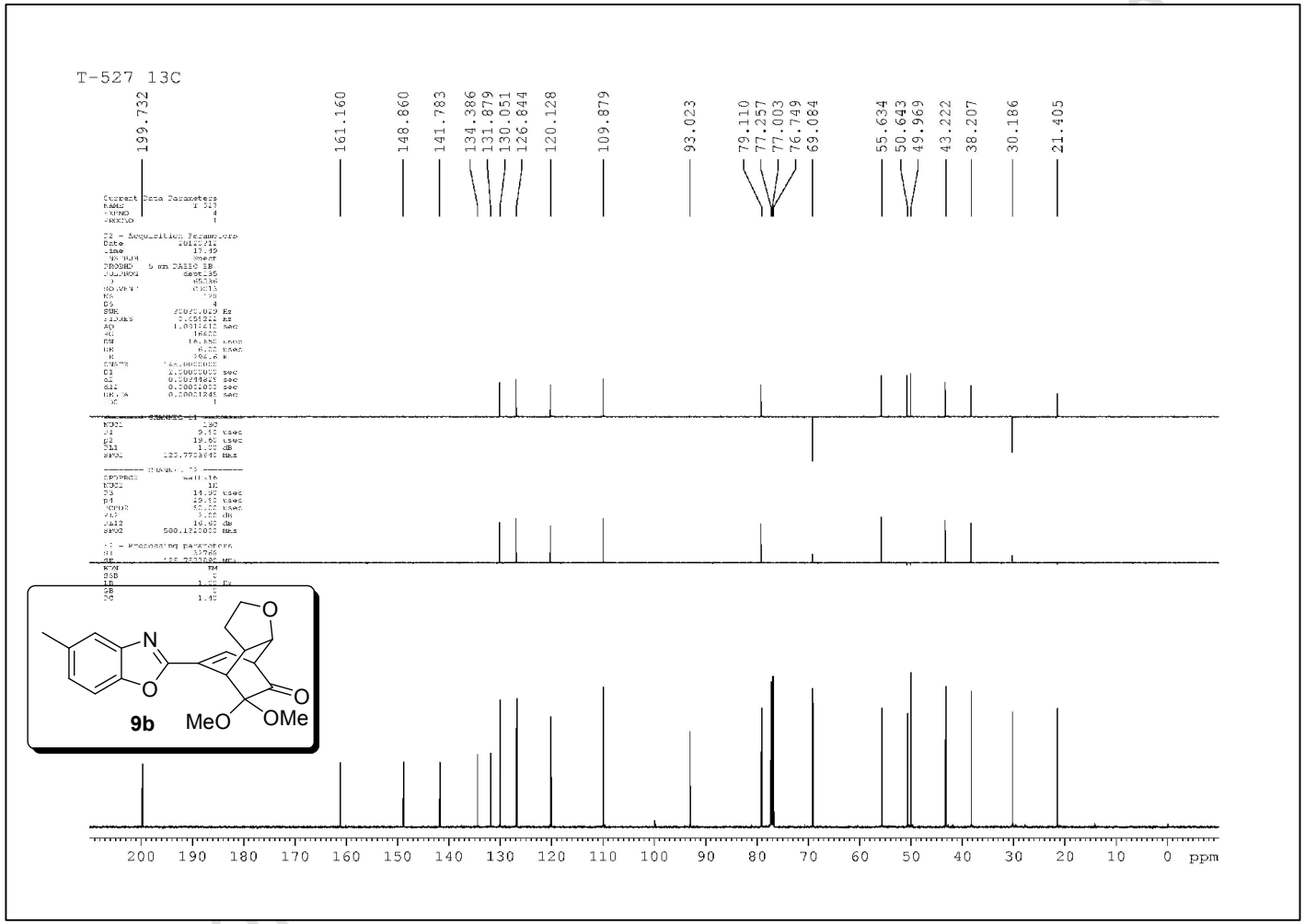


Figure S-8: ^{13}C and DEPT (125 MHz, $CDCl_3$) Spectra of **9b**.

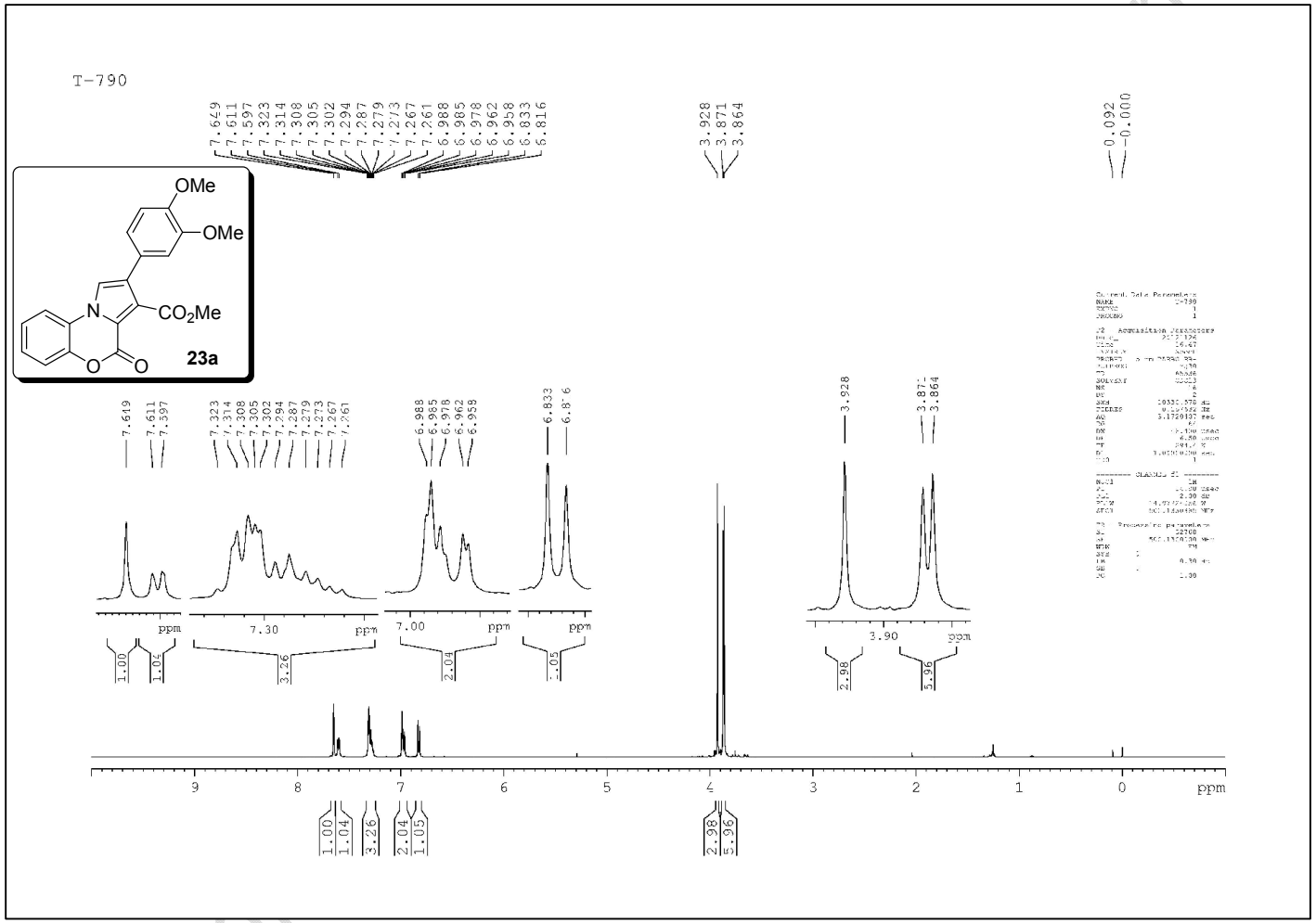


Figure S-9: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **23a**.

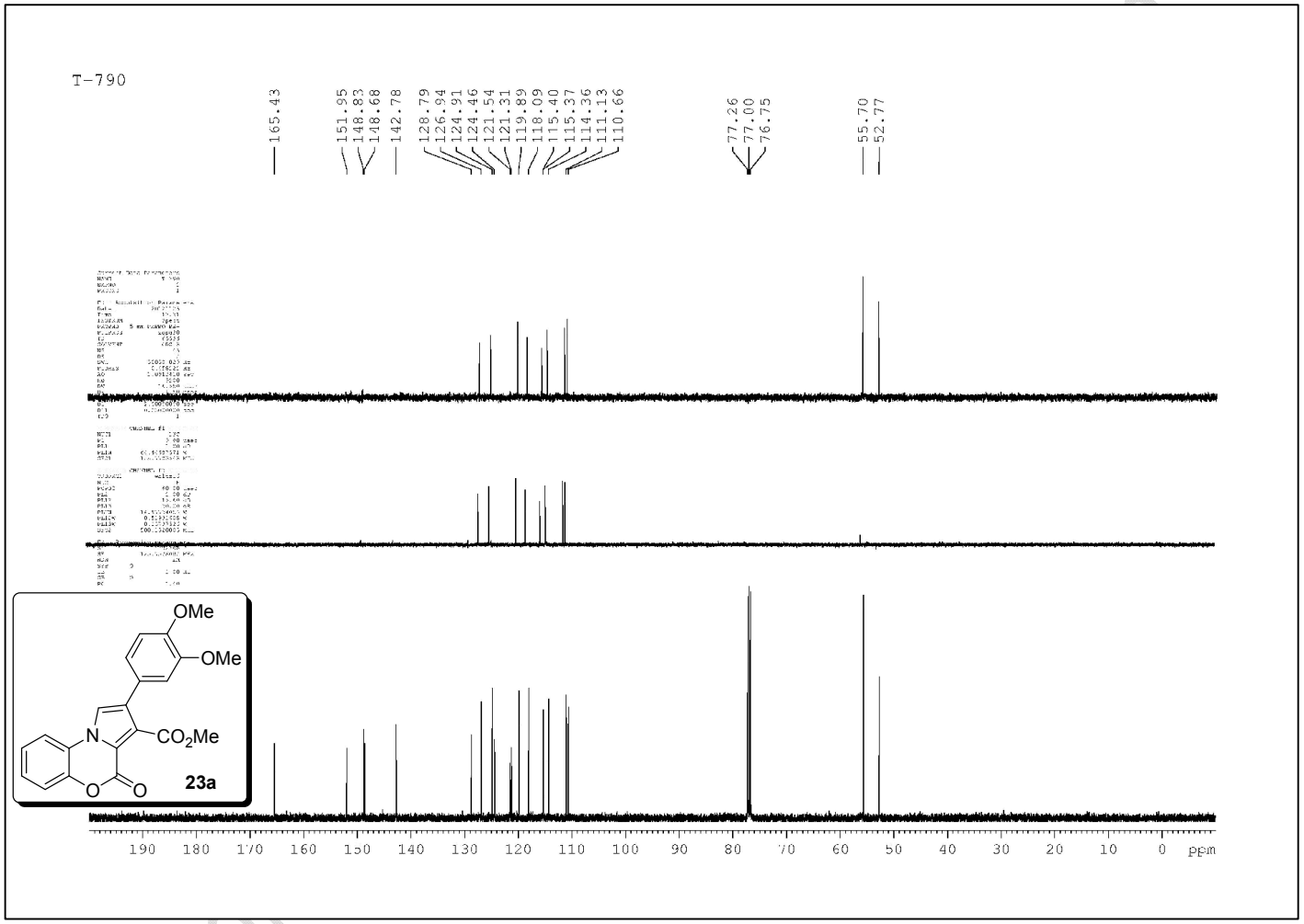


Figure S-10: ^{13}C and DEPT (125 MHz, $CDCl_3$) Spectra of **23a**.

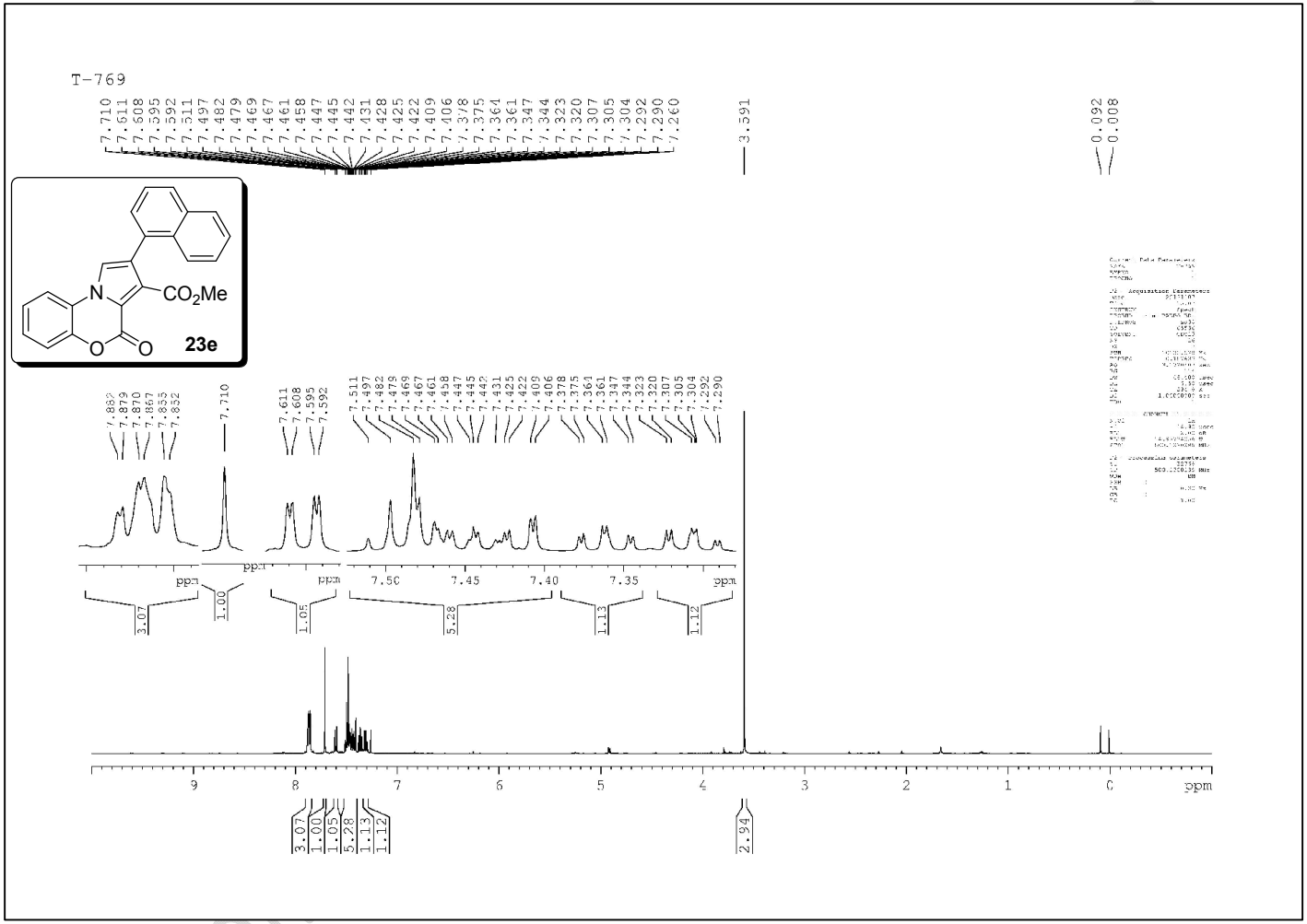


Figure S-11: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **23e**.

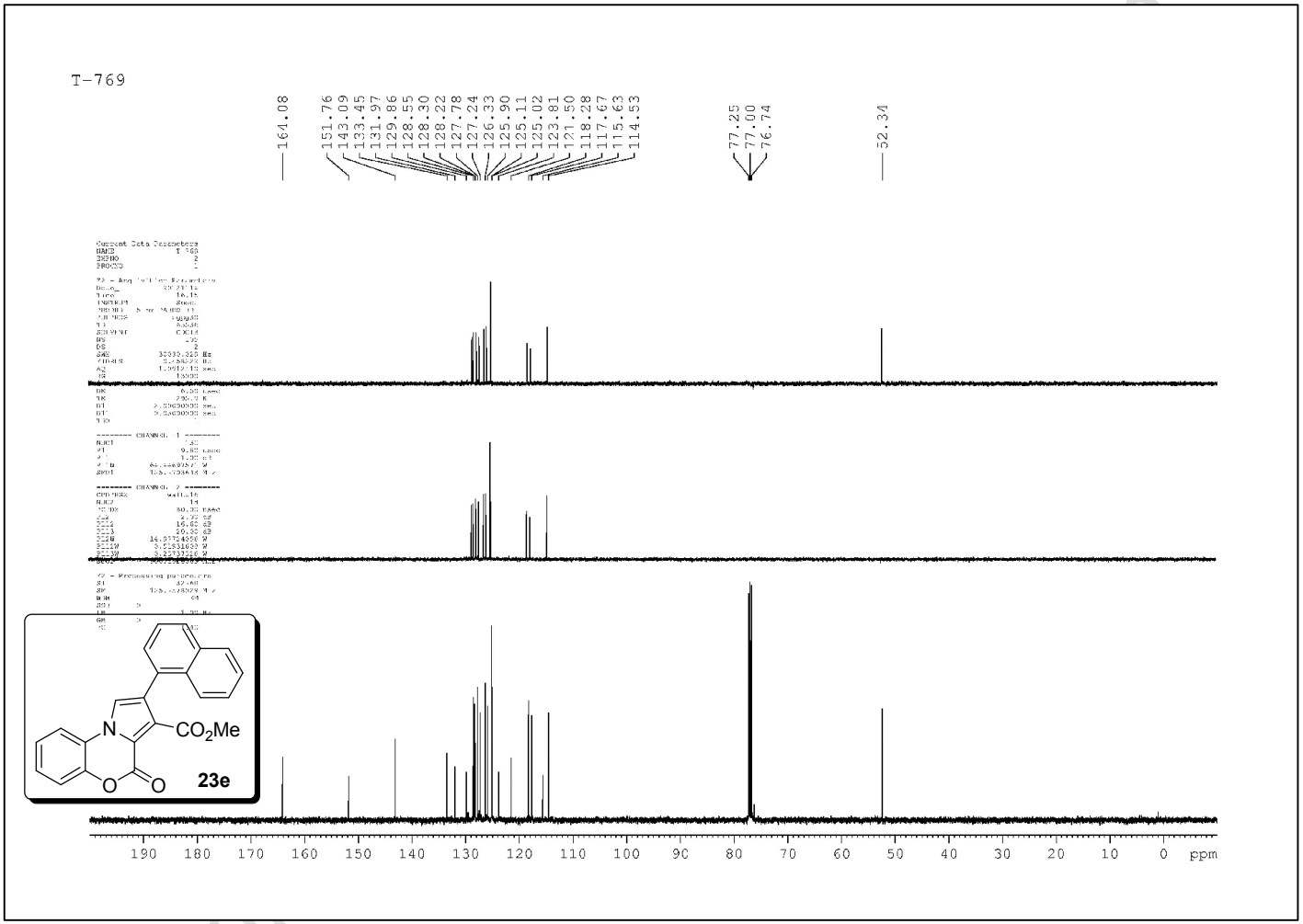


Figure S-12: ^{13}C and DEPT (125 MHz, $CDCl_3$) Spectra of **23e**.

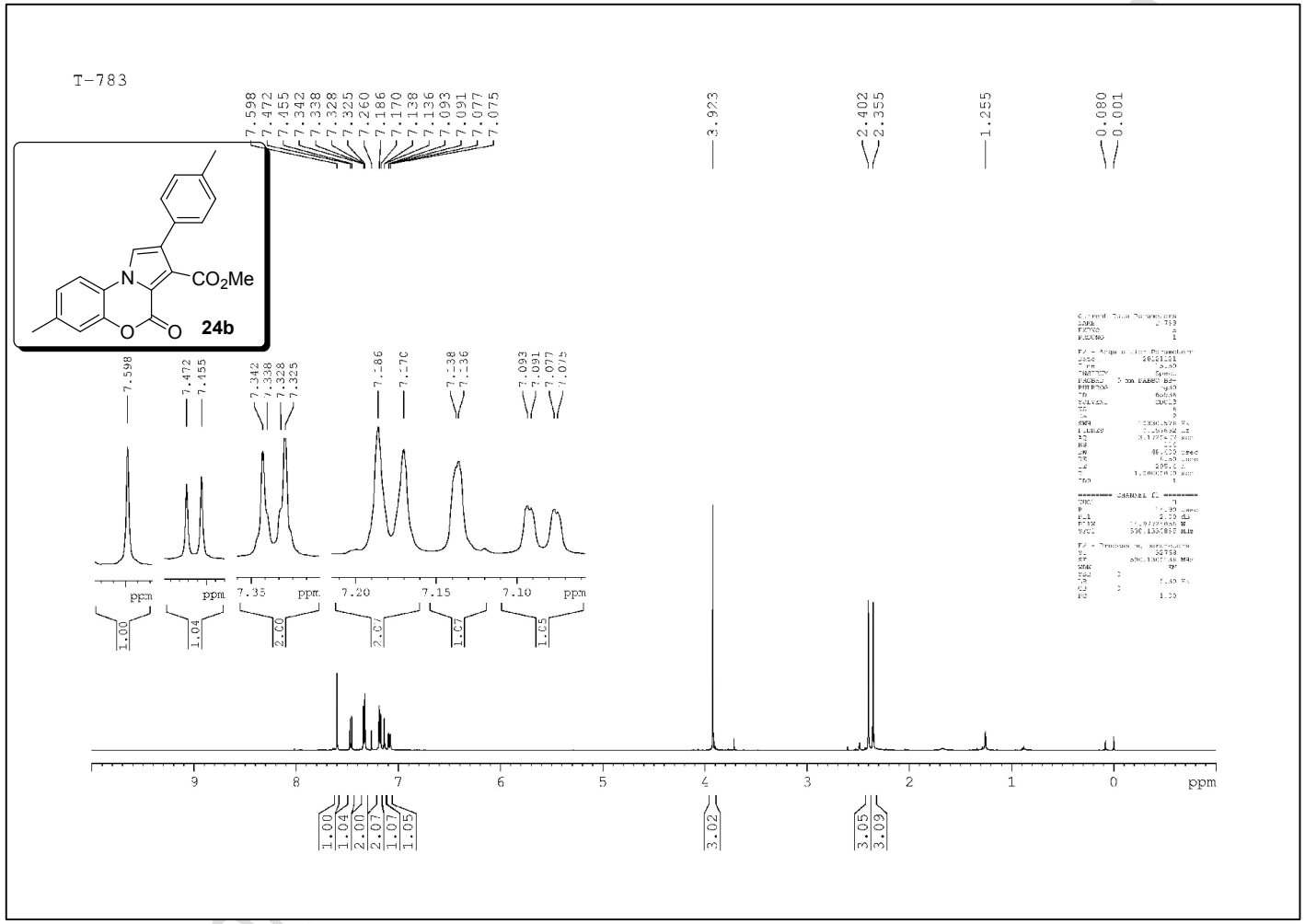


Figure S-13: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **24b**.

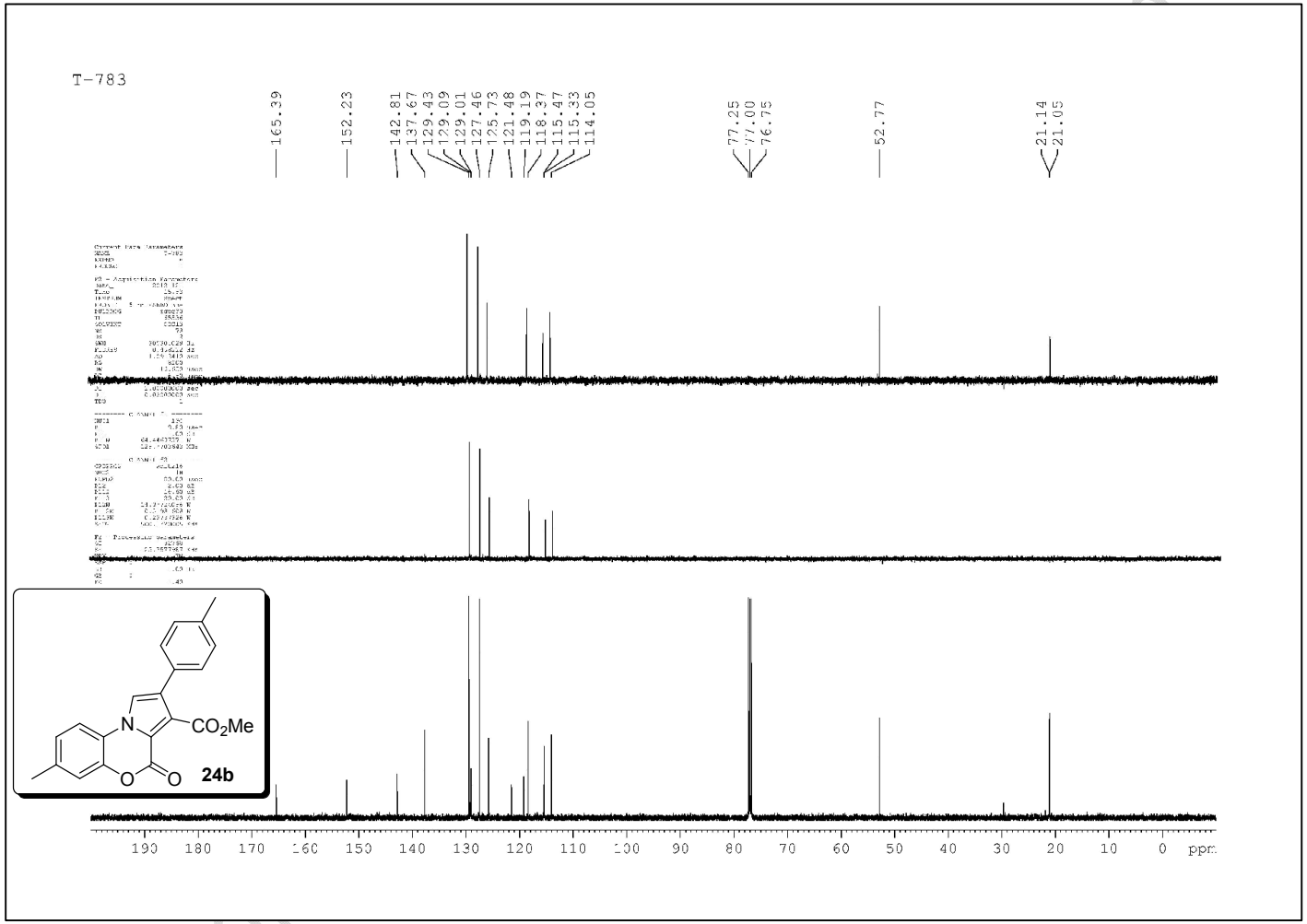


Figure S-14: ^{13}C and DEPT (125 MHz, $CDCl_3$) Spectra of **24b**.

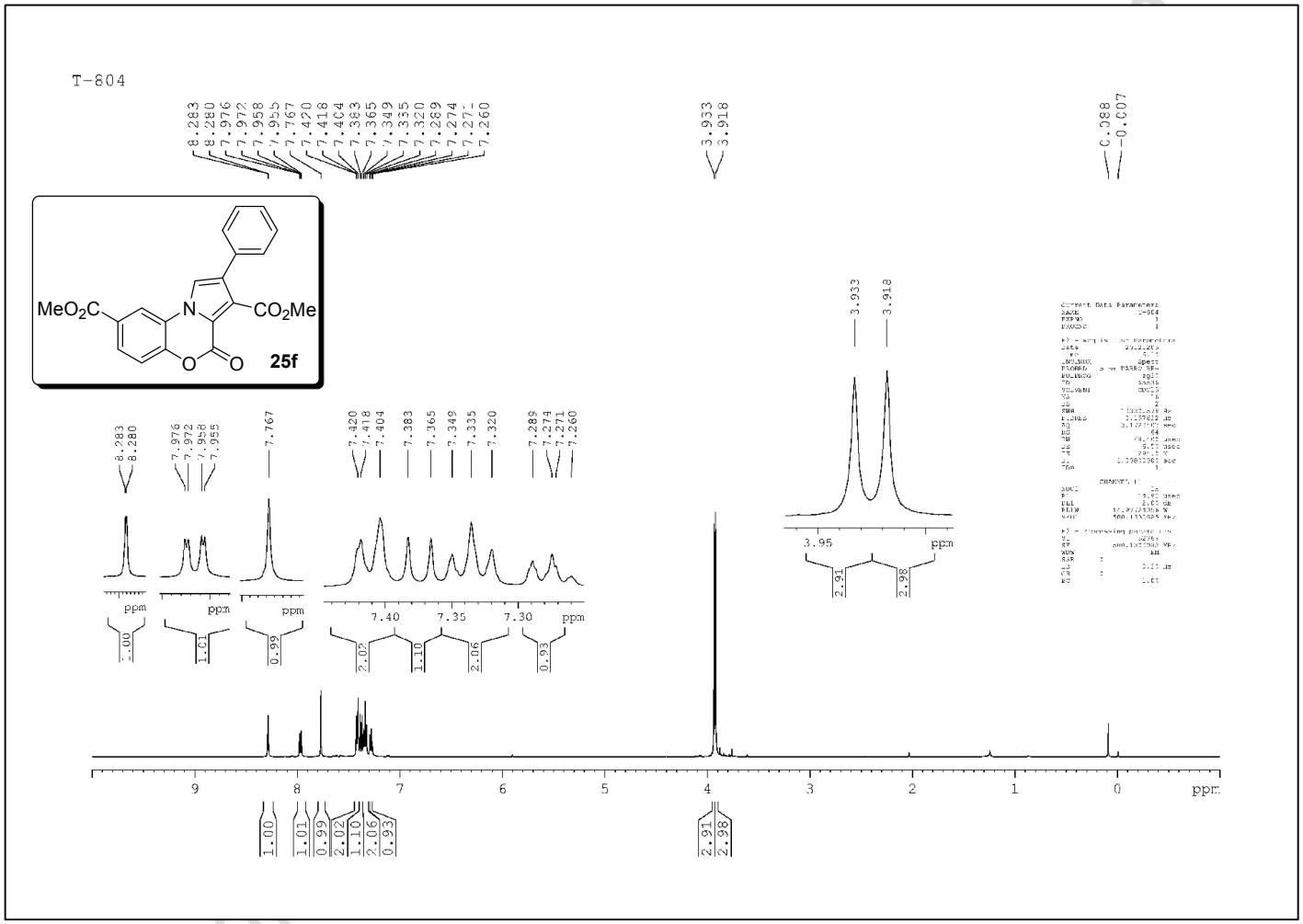


Figure S-15: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **25f**.

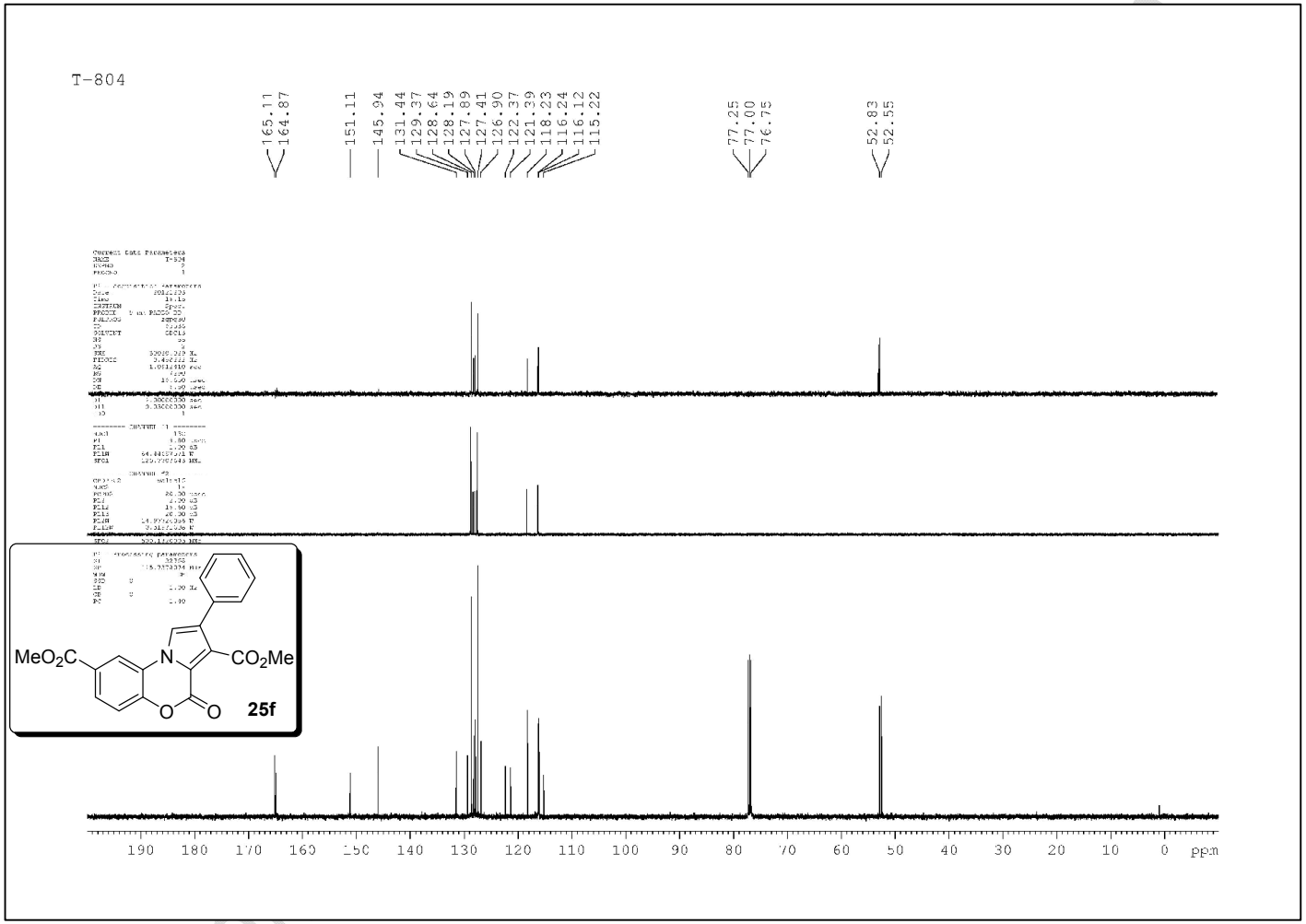


Figure S-16: ^{13}C and DEPT (125 MHz, $CDCl_3$) Spectra of **25f**.

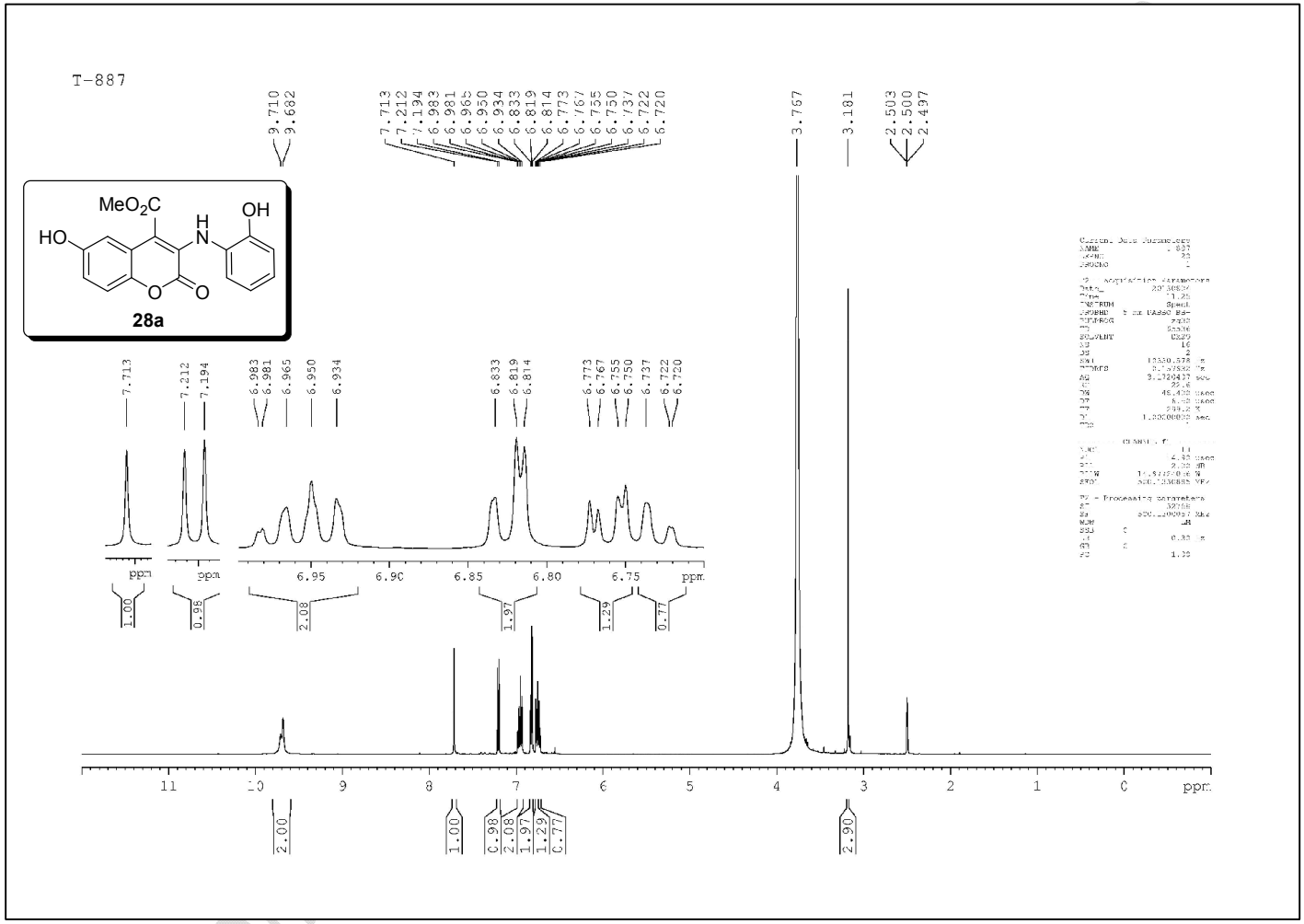


Figure S-17: ^{1}H NMR (500 MHz, DMSO-d_6) Spectrum of **28a**.

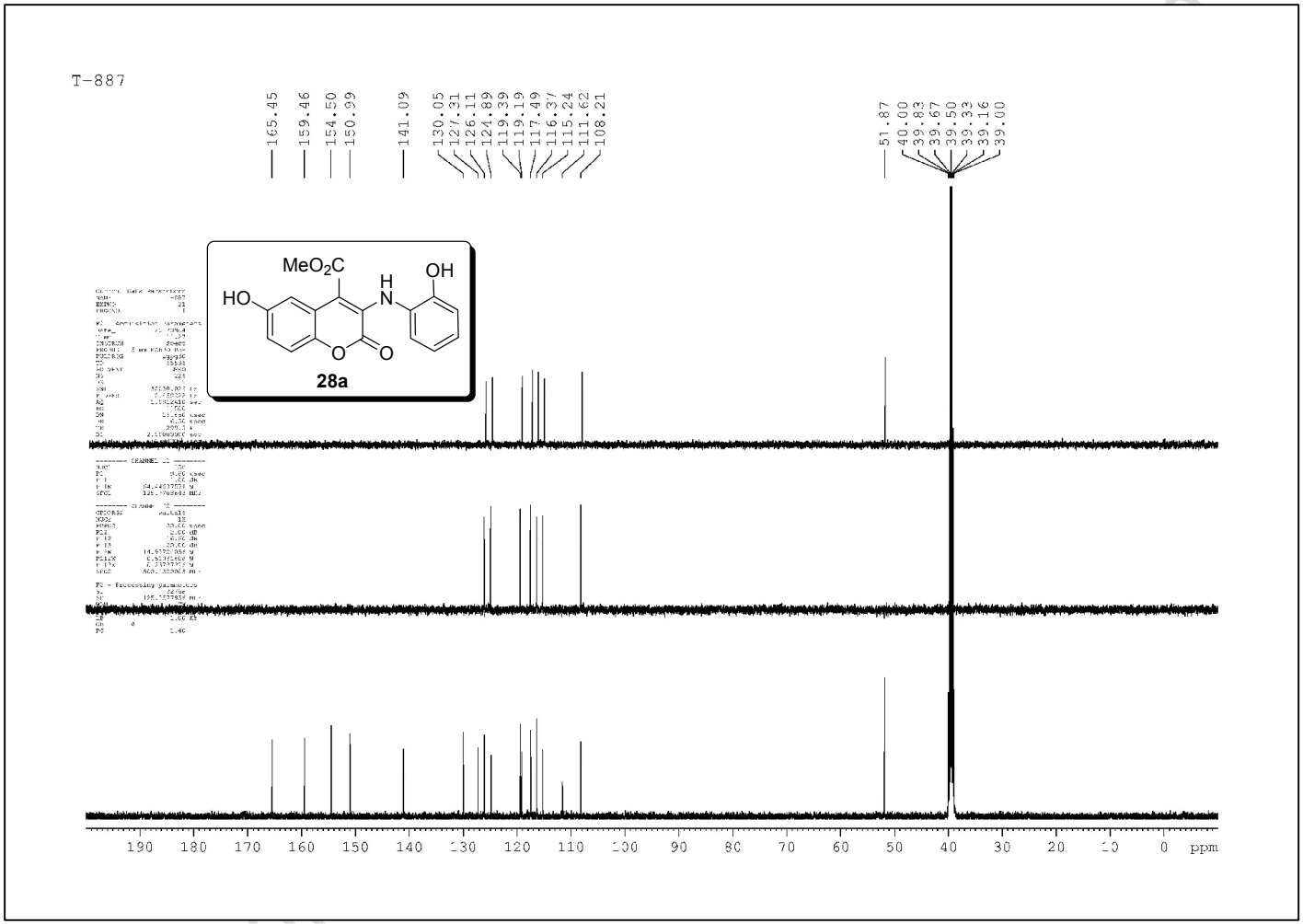


Figure S-18: ^{13}C and DEPT (125 MHz, DMSO-d_6) Spectra of **28a**.

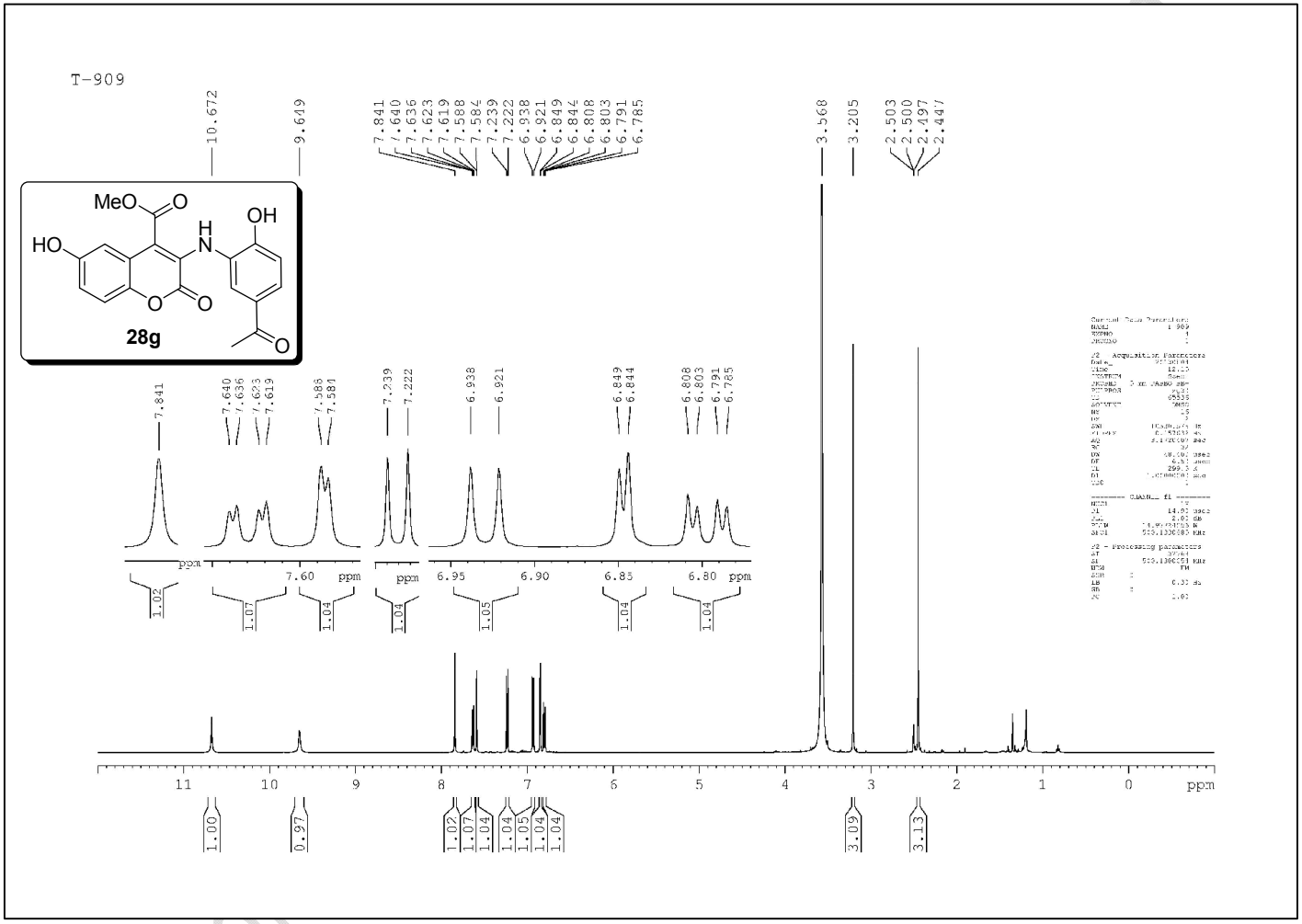


Figure S-19: ^{1}H NMR (500 MHz, DMSO-d_6) Spectrum of **28g**.

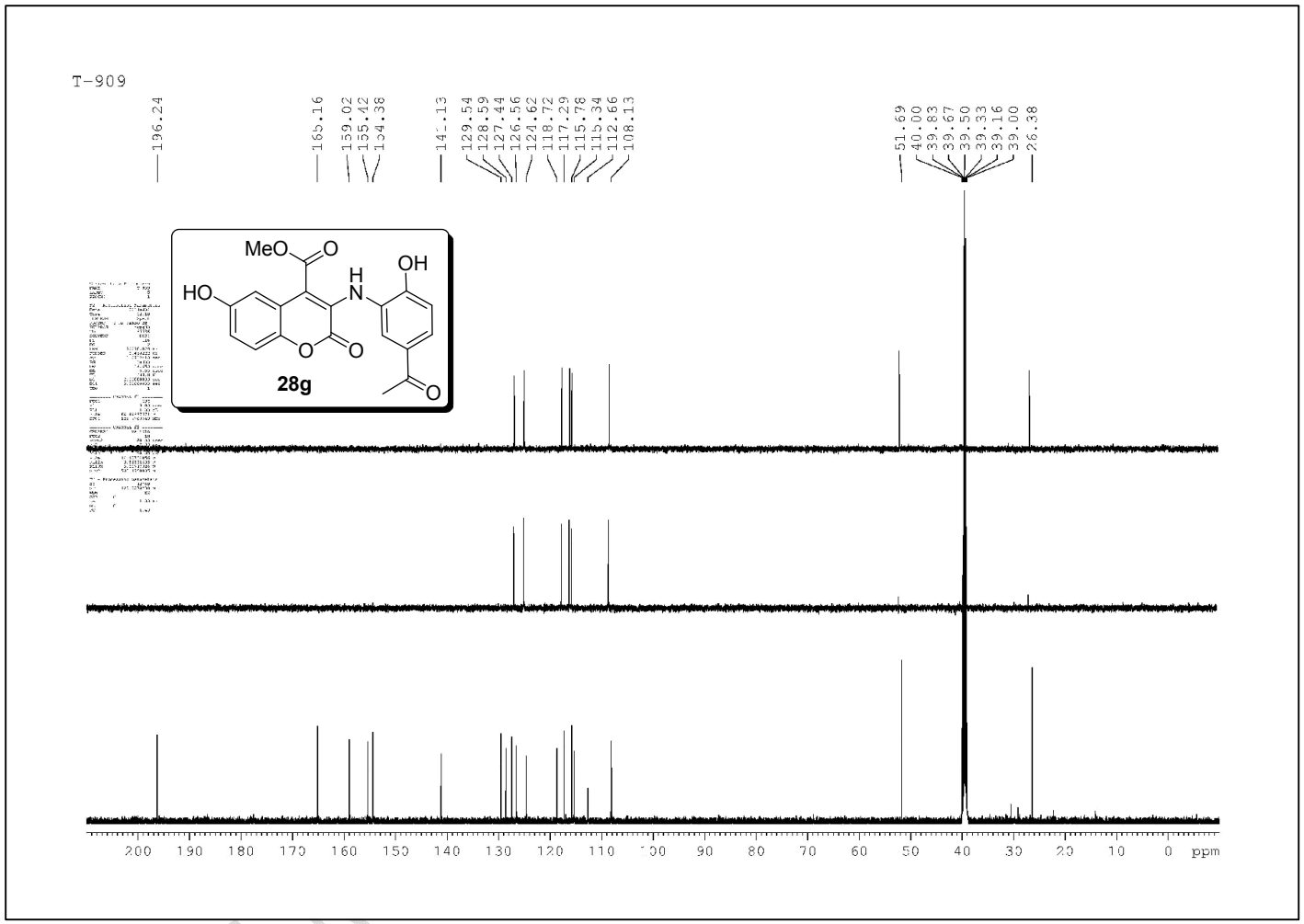


Figure S-20: ^{13}C and DEPT (125 MHz, DMSO-d_6) Spectra of **28g**.

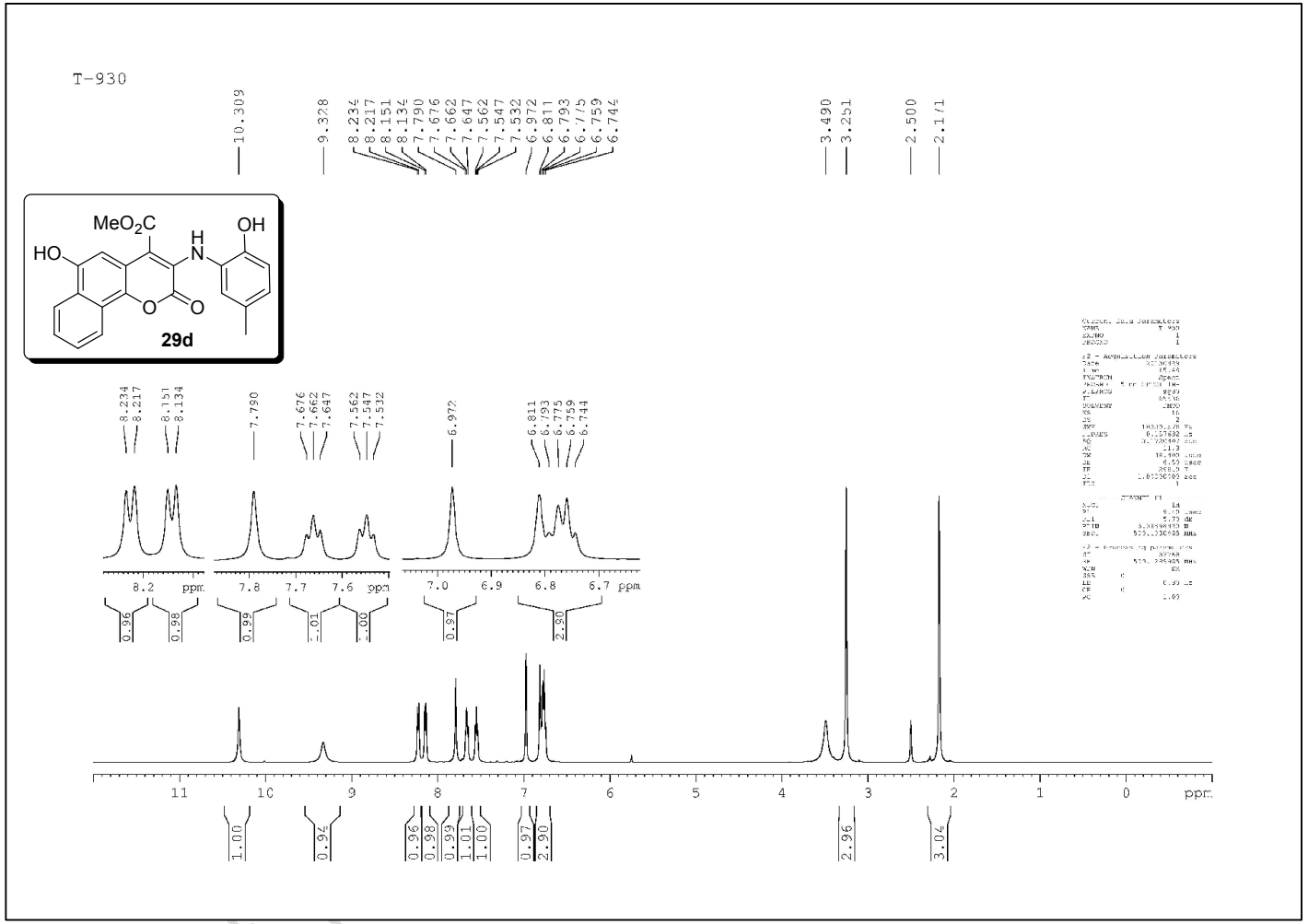


Figure S-21: ^{1}H NMR (500 MHz, DMSO-d_6) Spectrum of **29d**.

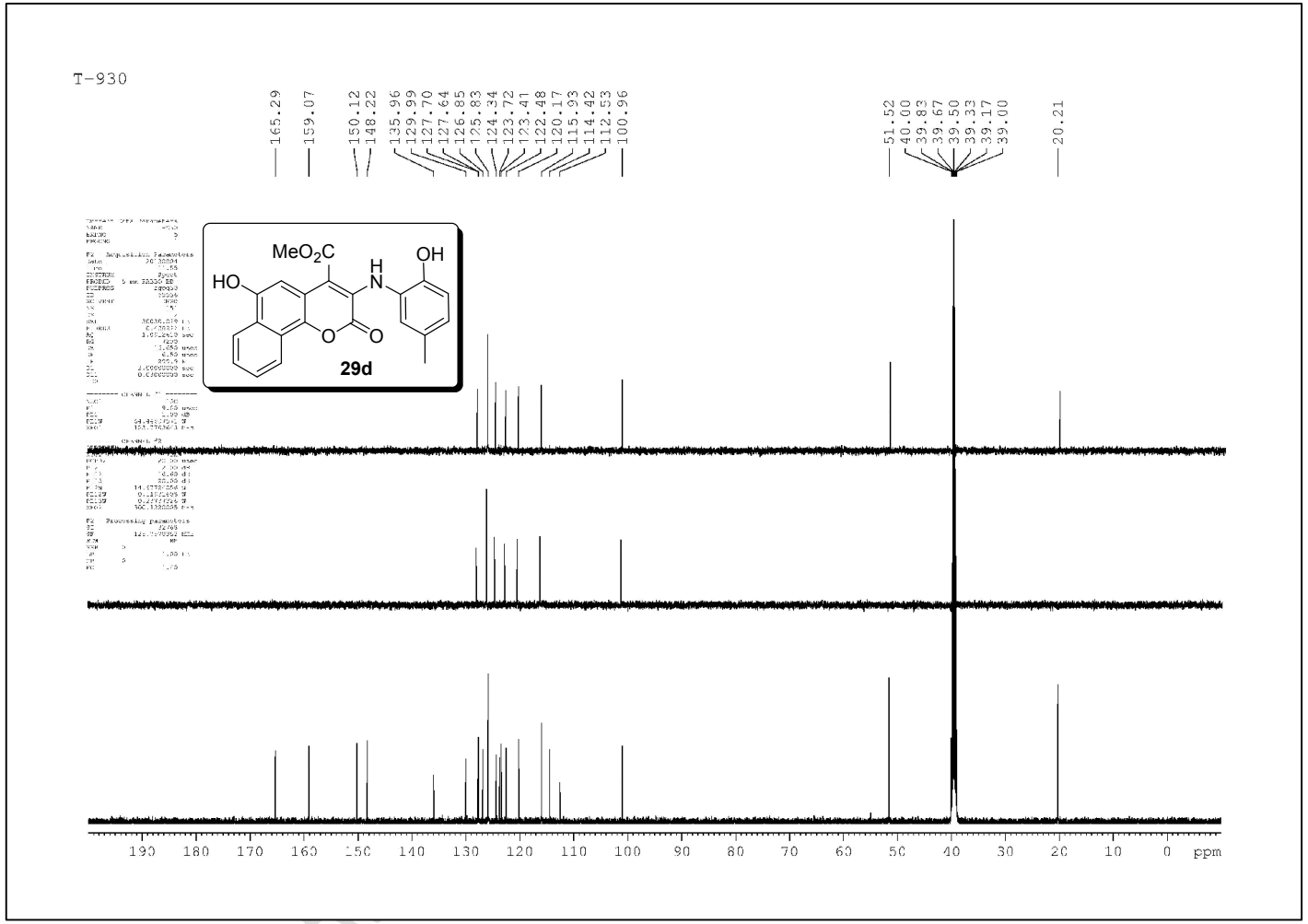


Figure S-22: ^{13}C and DEPT (125 MHz, DMSO-d_6) Spectra of **29d**.

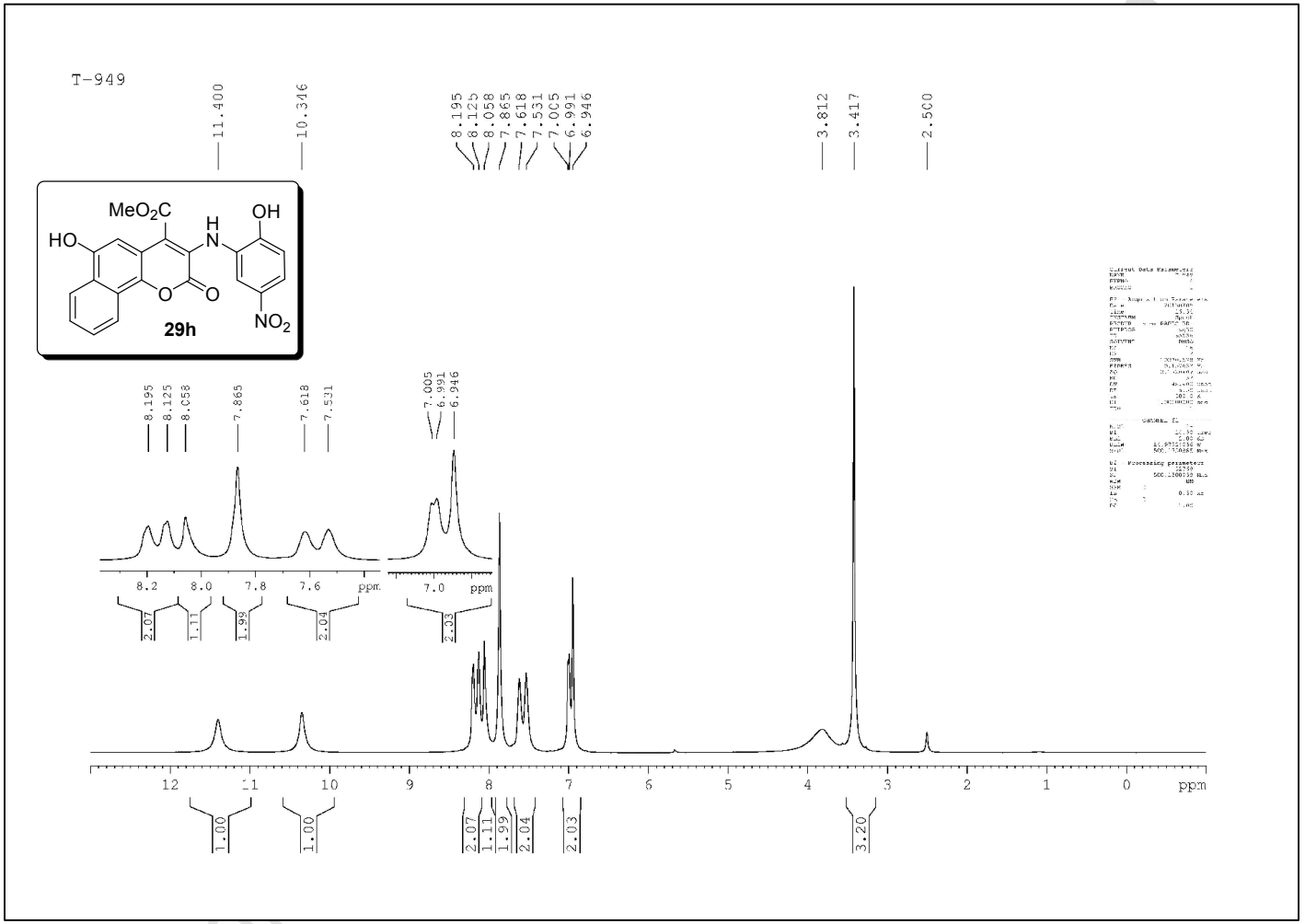


Figure S-23: ^{1}H NMR (500 MHz, DMSO-d_6) Spectrum of **29h**.

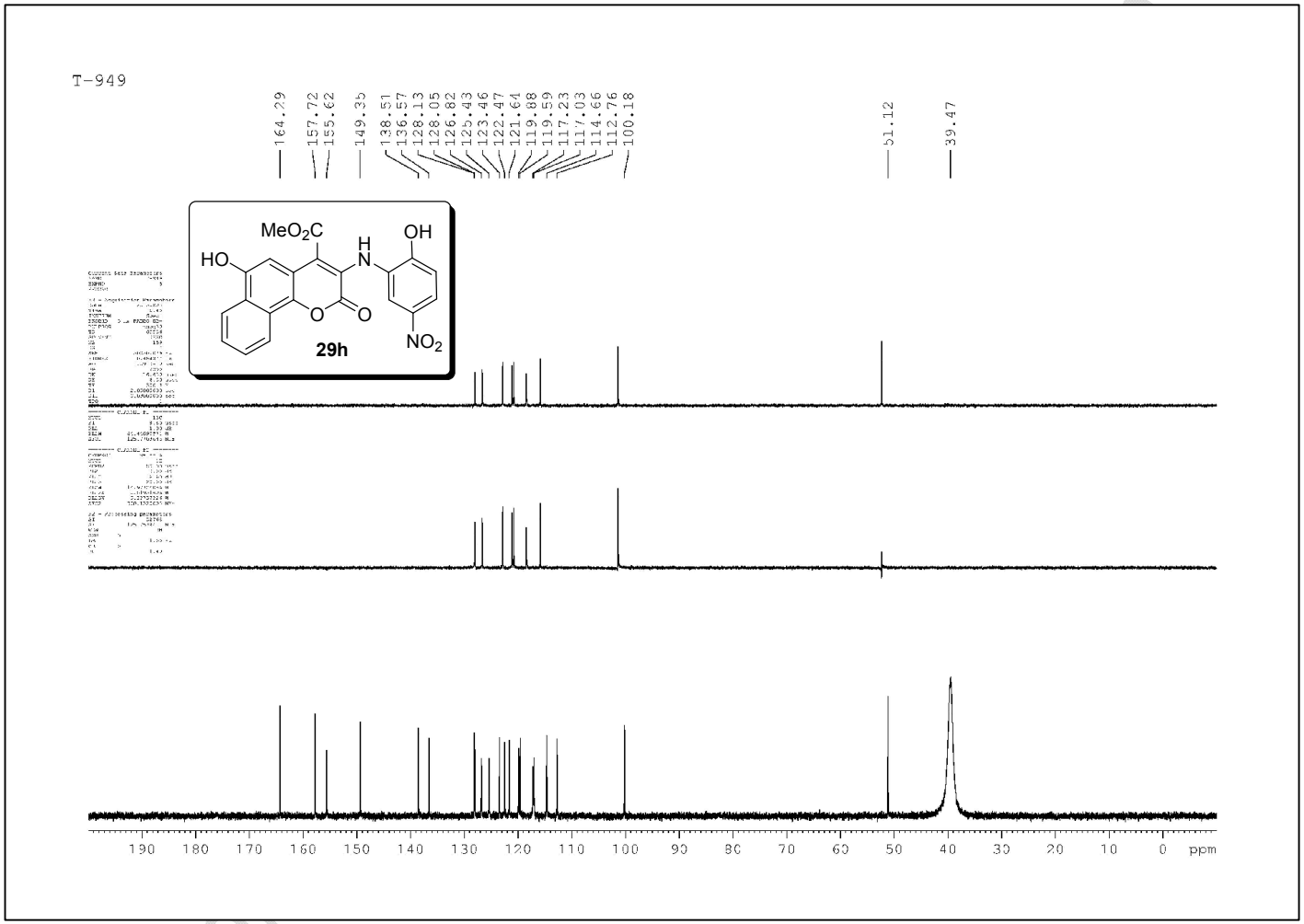


Figure S-24: ^{13}C and DEPT (125 MHz, DMSO-d_6) Spectra of **29h**.

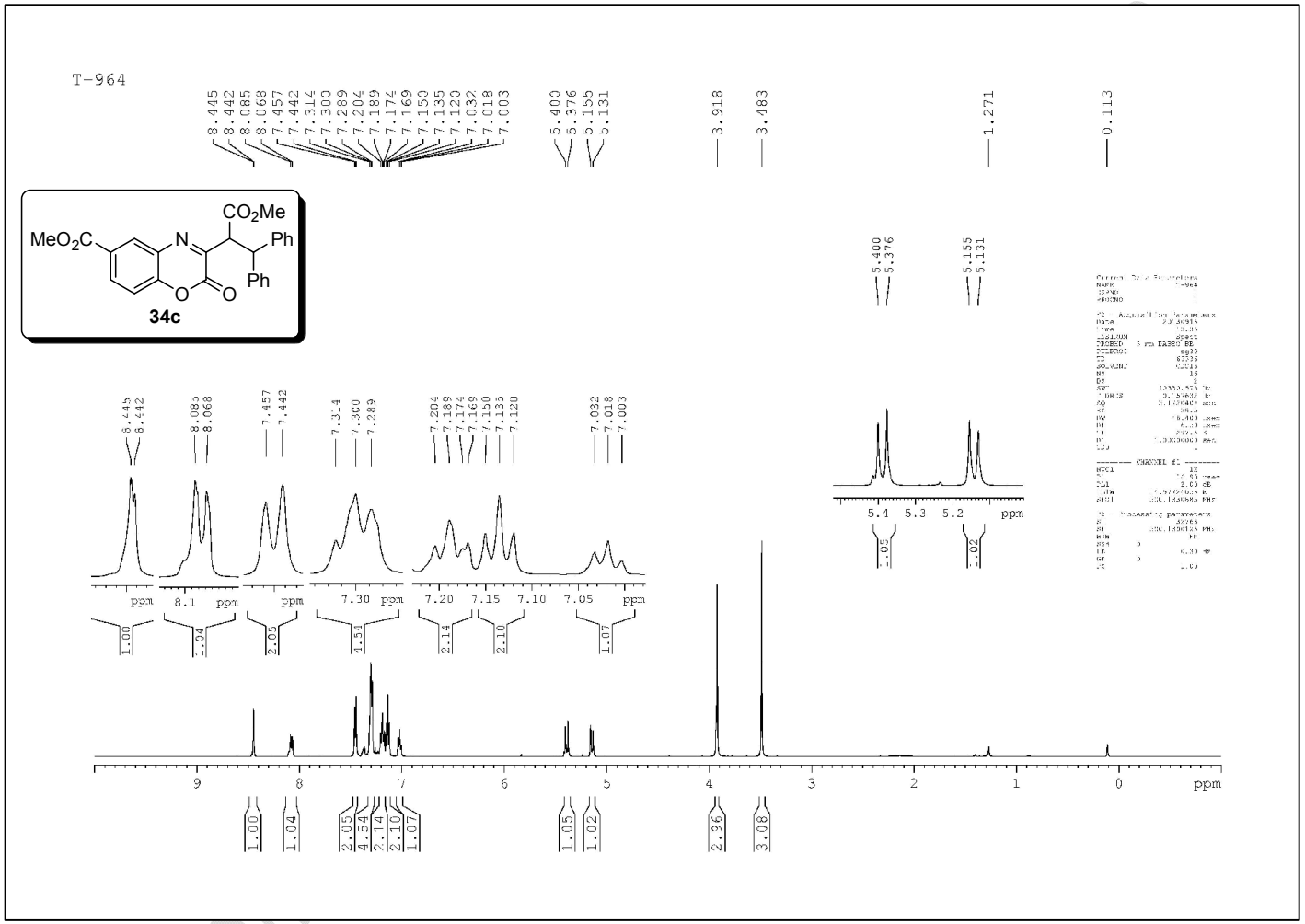


Figure S-25: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **34c**.

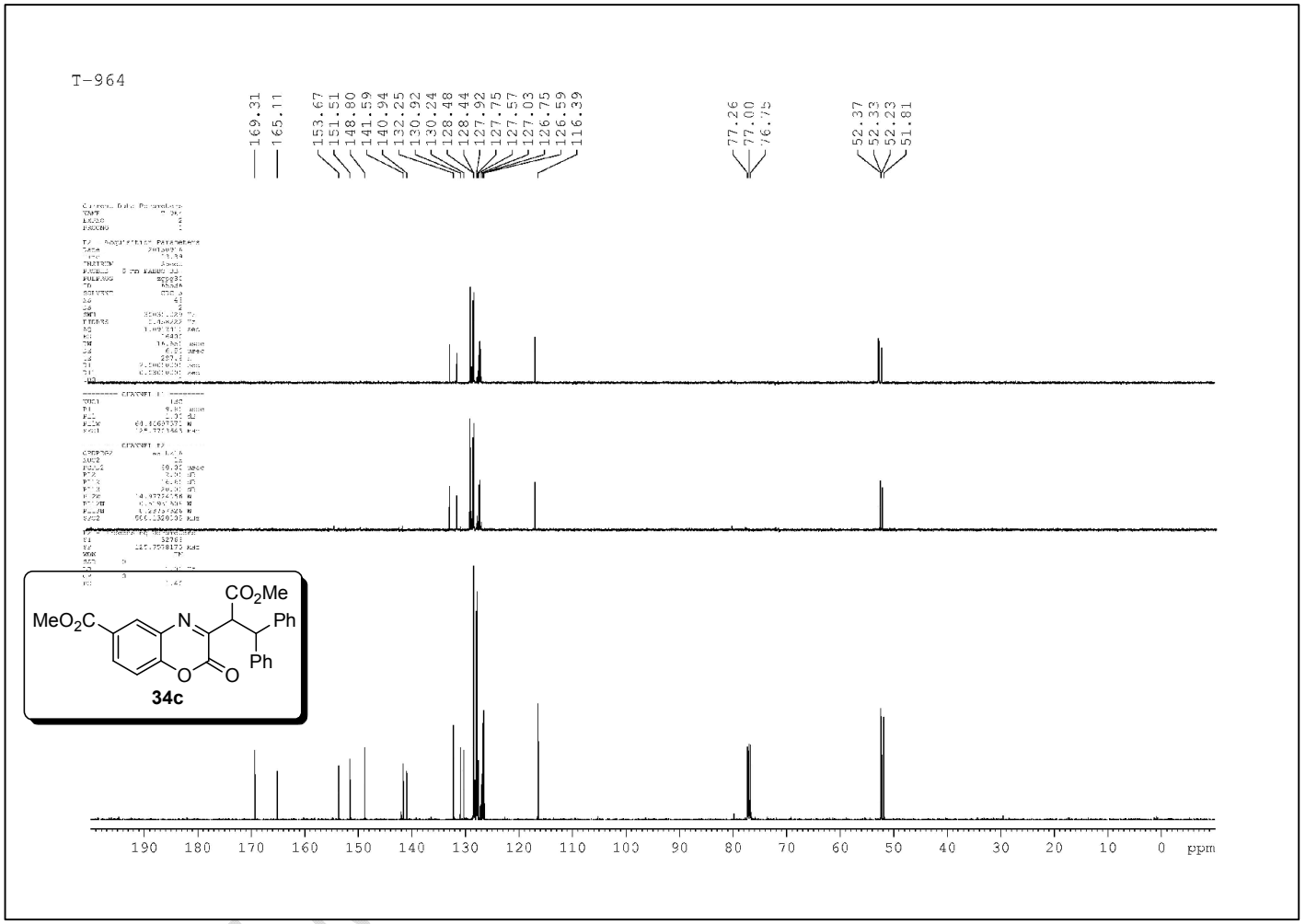


Figure S-26: ^{13}C and DEPT (125 MHz, $CDCl_3$) Spectra of **34c**.

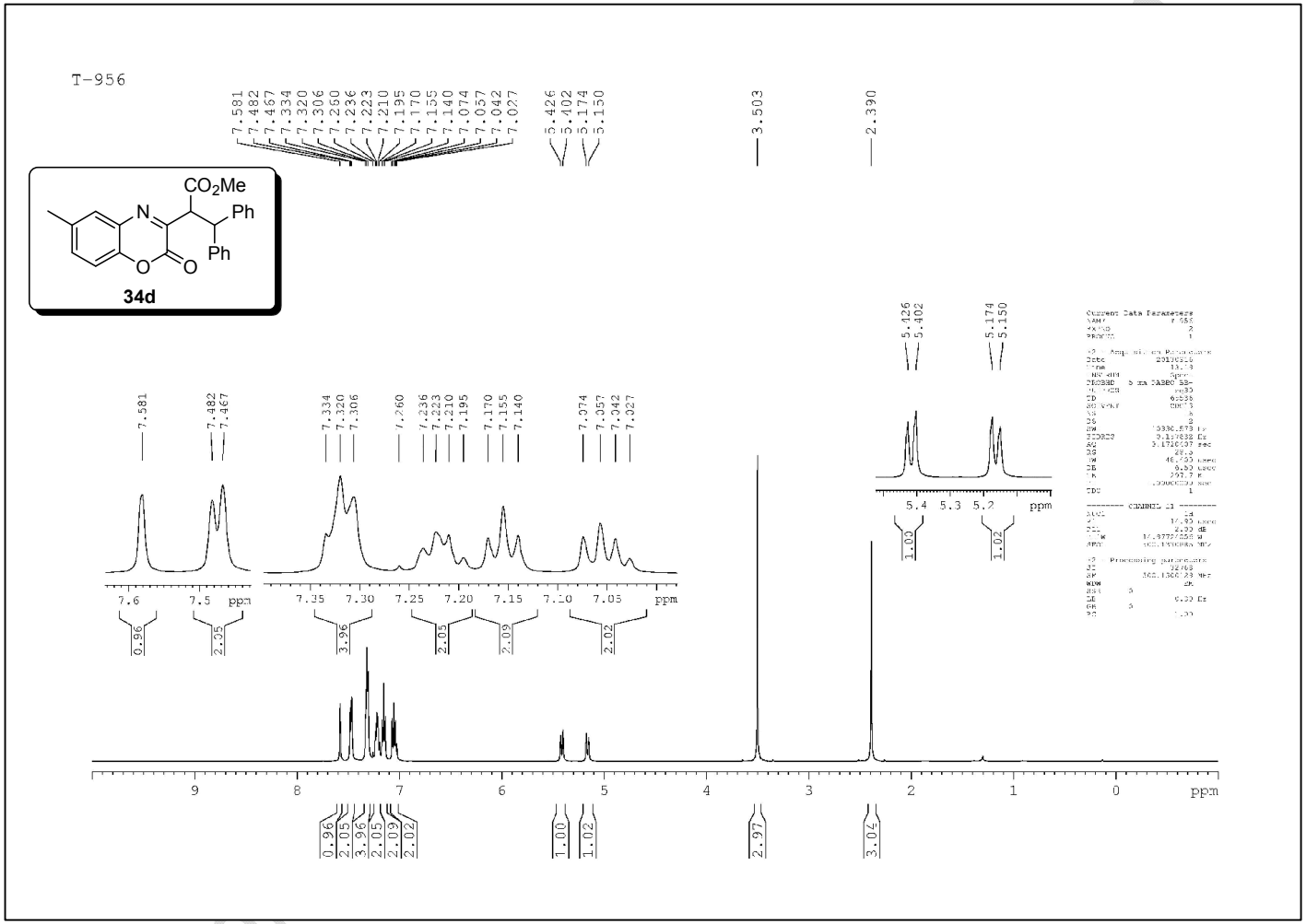


Figure S-27: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **34d**.

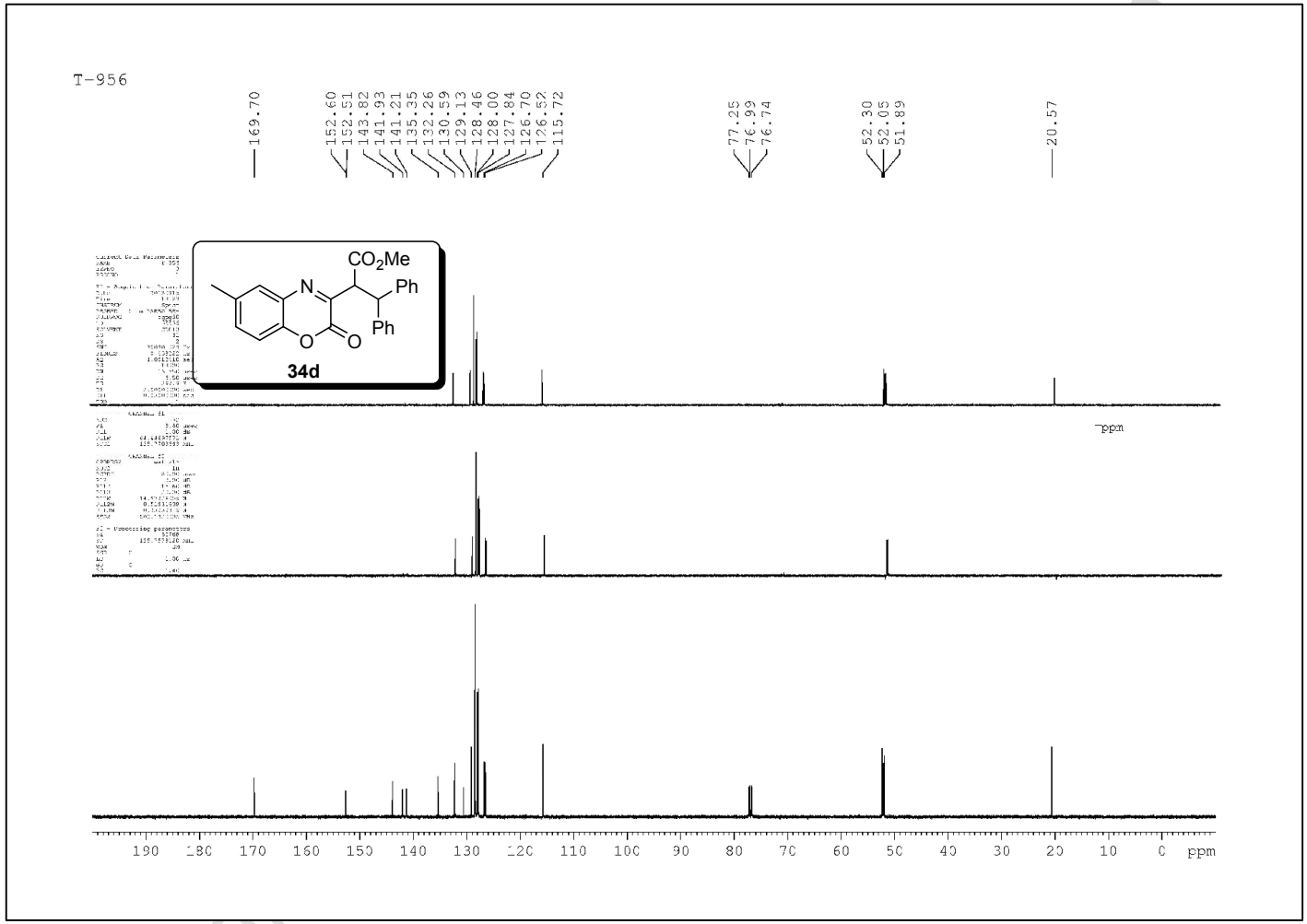


Figure S-28: ^{13}C and DEPT (125 MHz, $CDCl_3$) Spectra of **34d**.

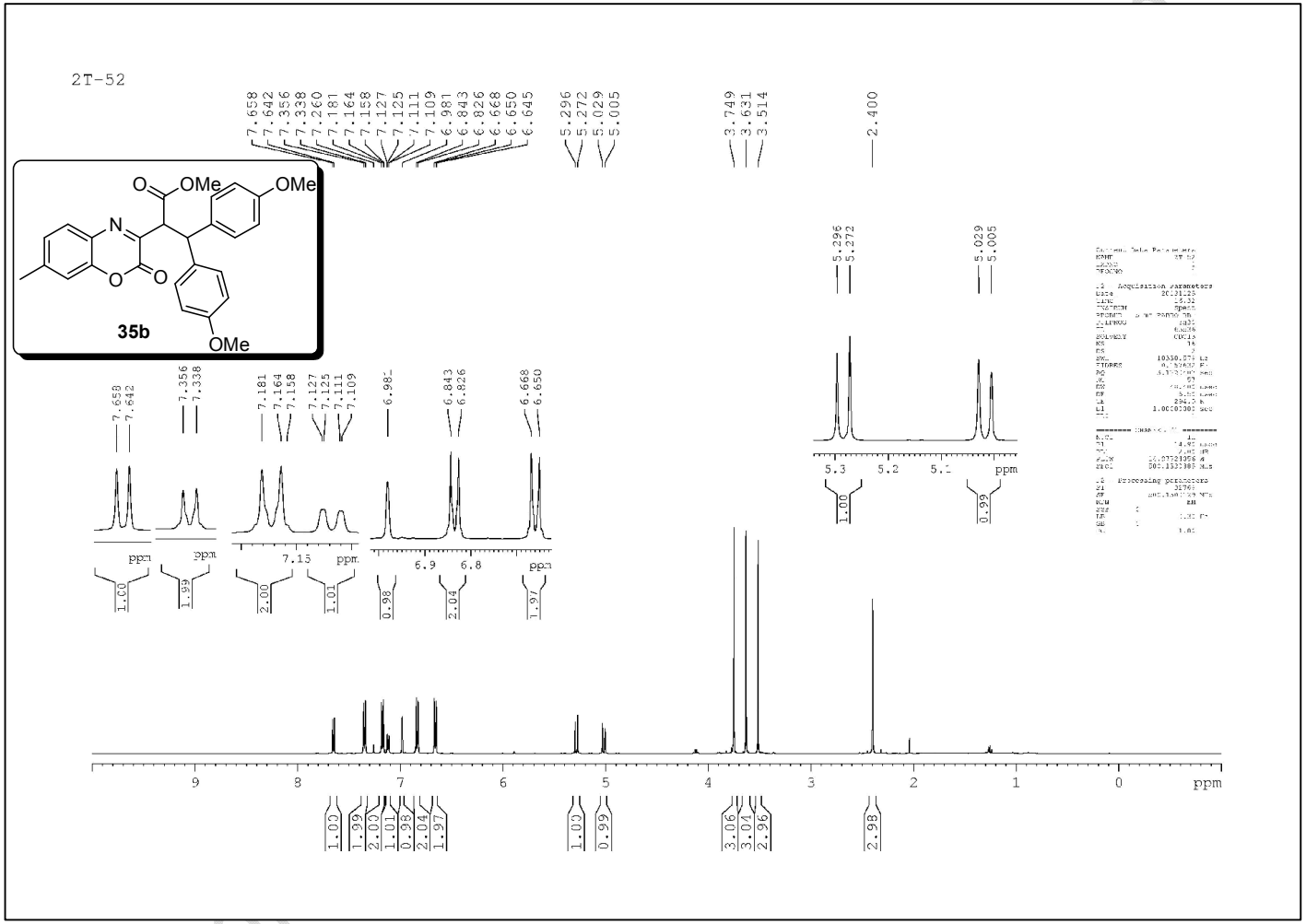


Figure S-29: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **35b**.

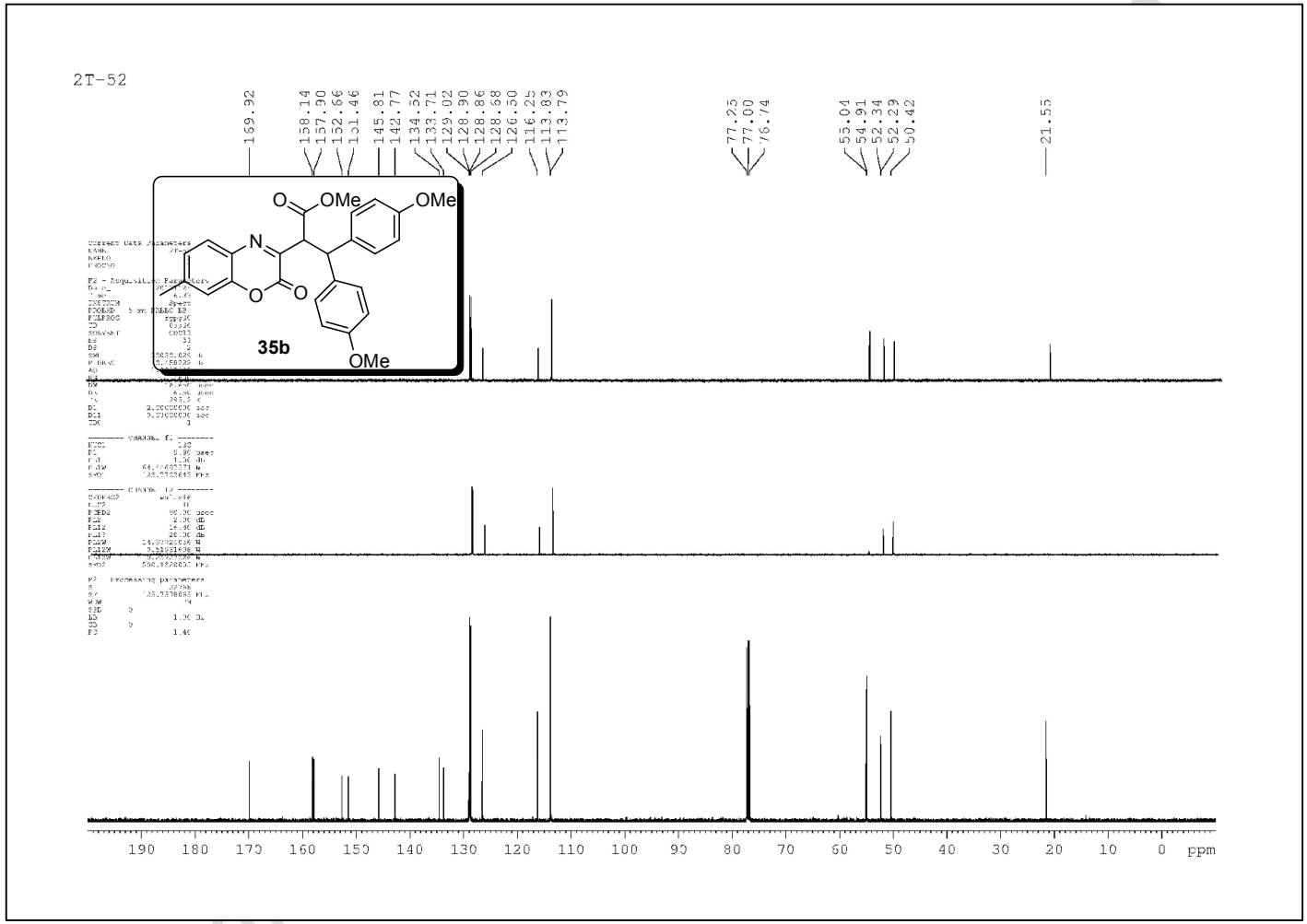


Figure S-30: ^{13}C and DEPT (125 MHz, $CDCl_3$) Spectra of **35b**.

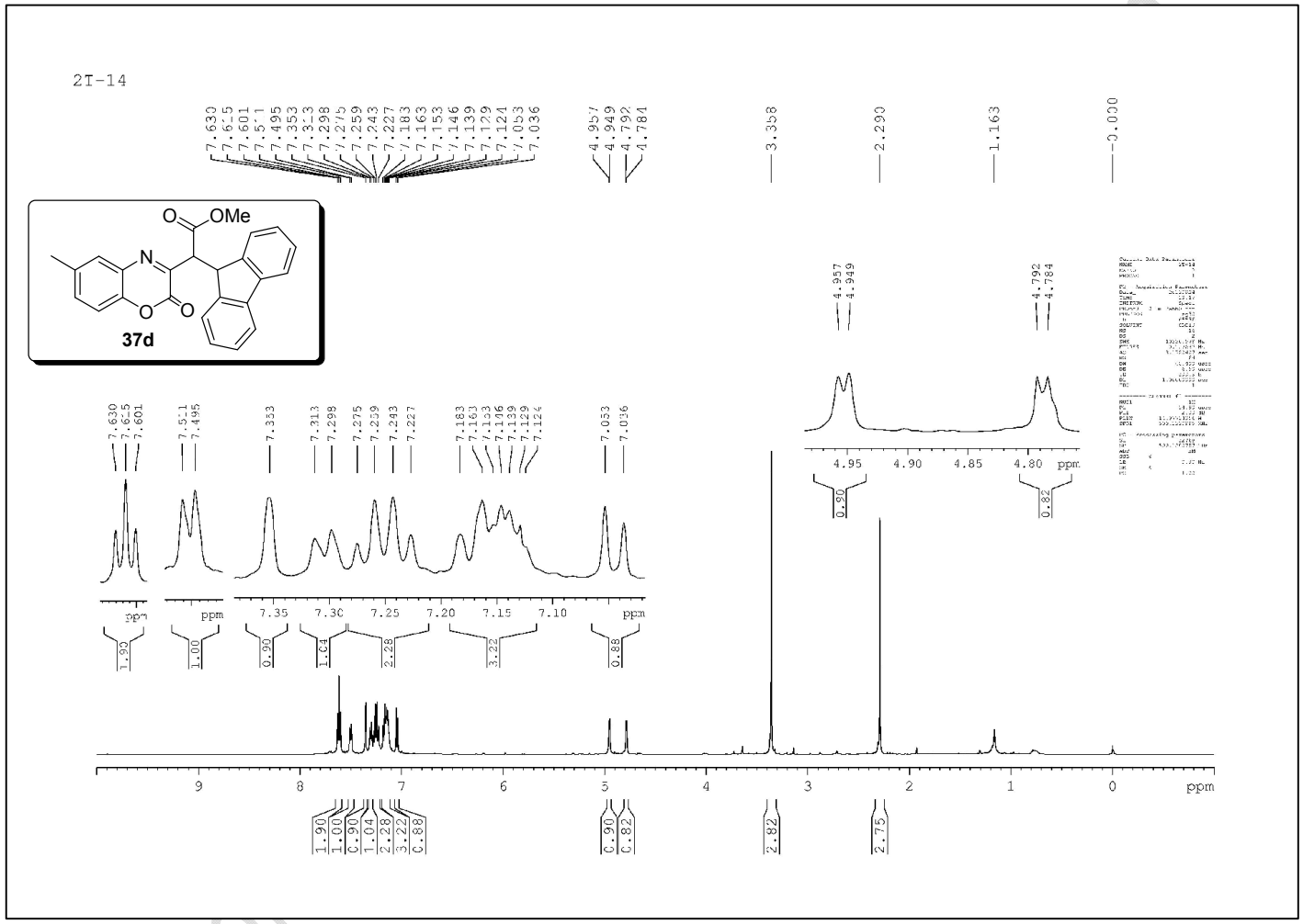


Figure S-31: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **37d**.

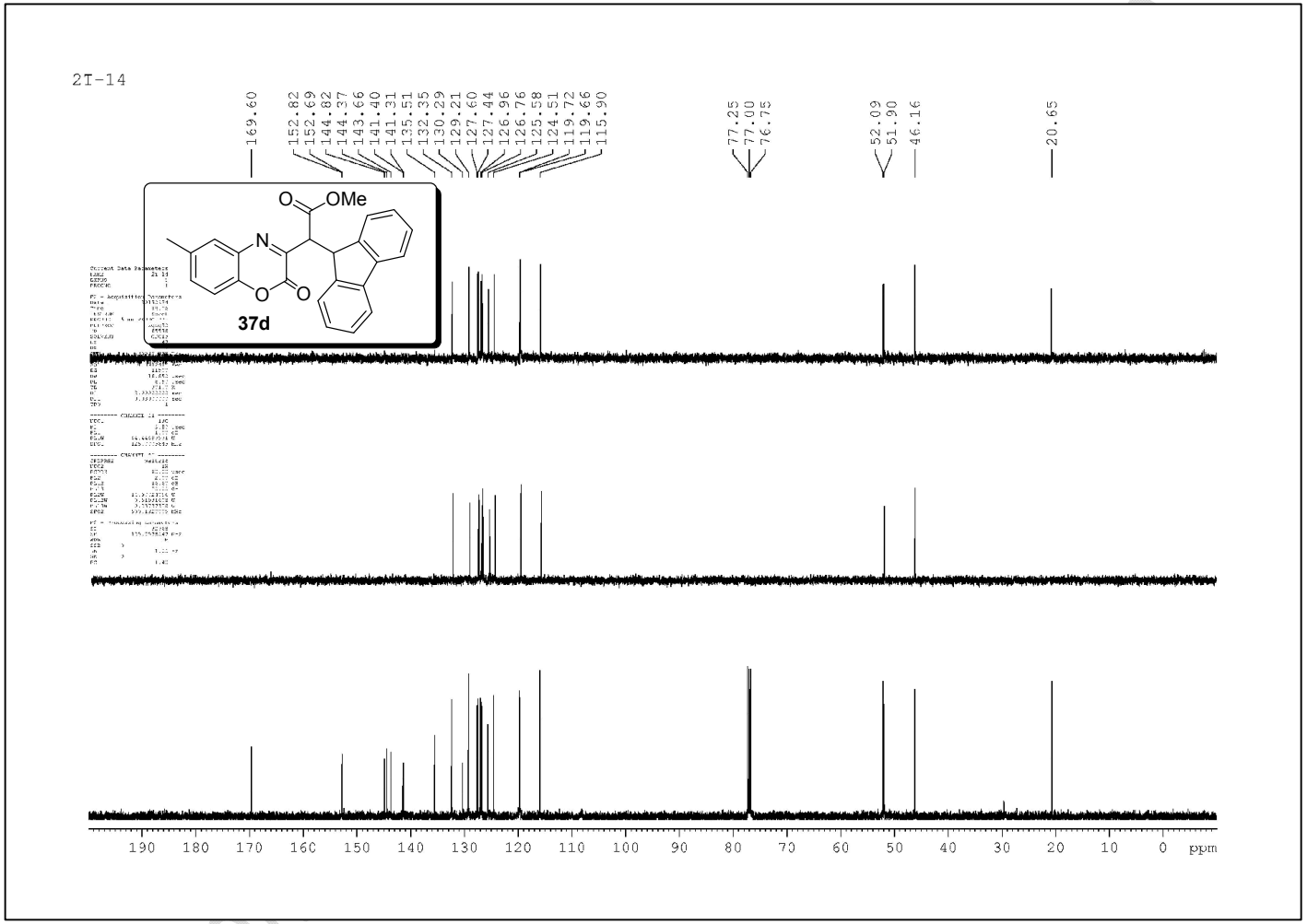


Figure S-32: ^{13}C and DEPT (125 MHz, $CDCl_3$) Spectra of **37d**.

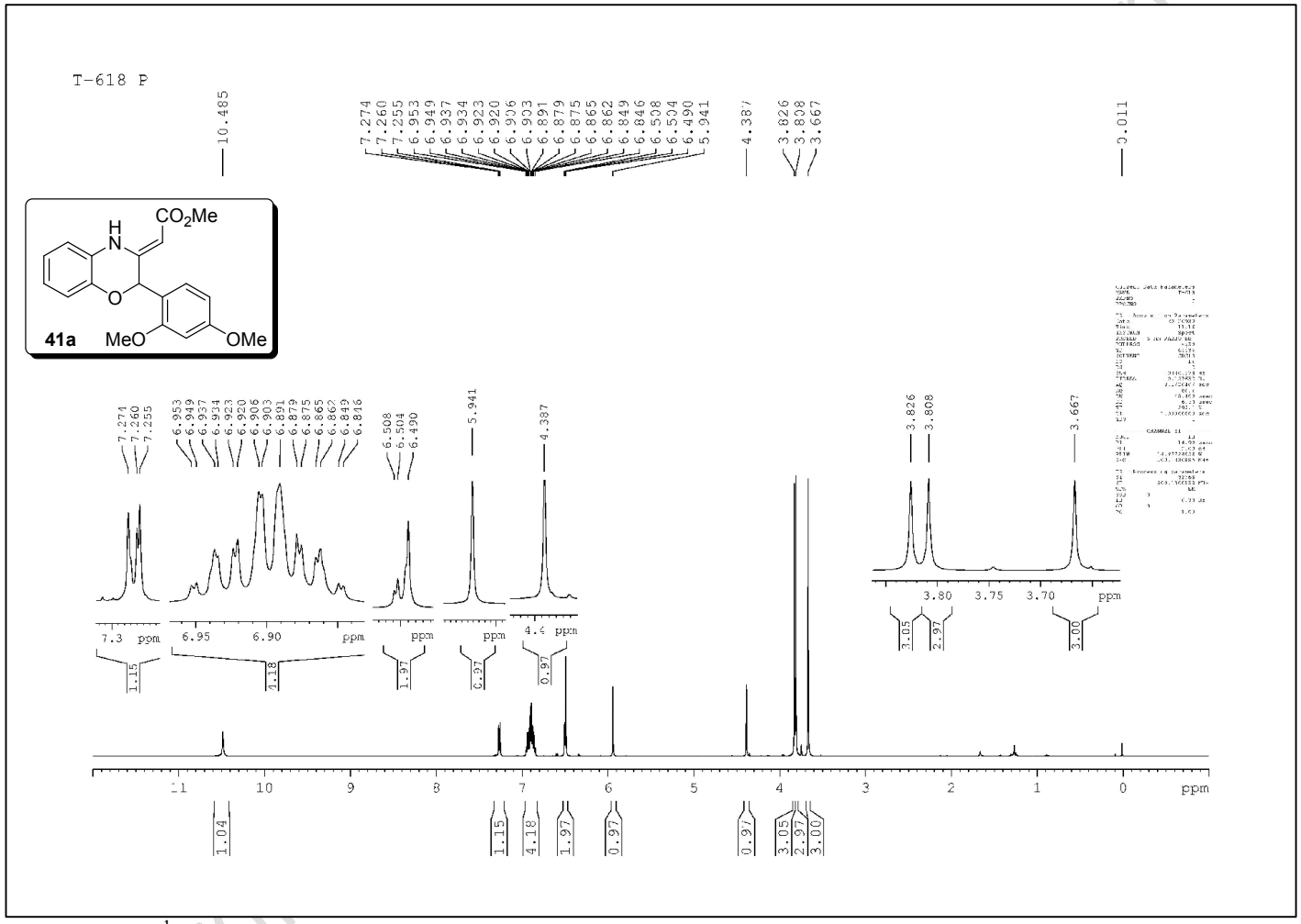


Figure S-33: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **41a**.

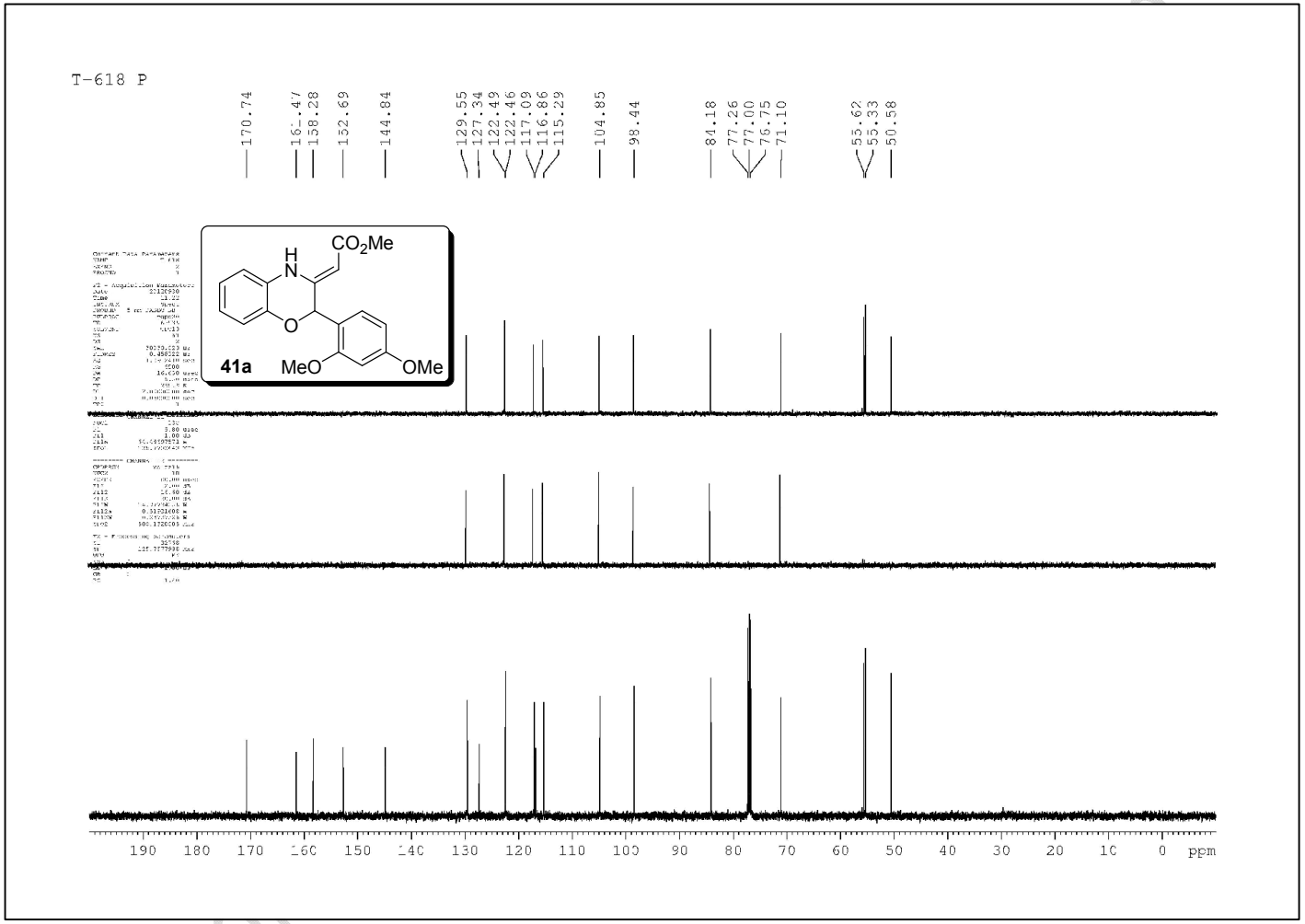


Figure S-34: ^{13}C NMR (125 MHz, $CDCl_3$) Spectra of **41a**.

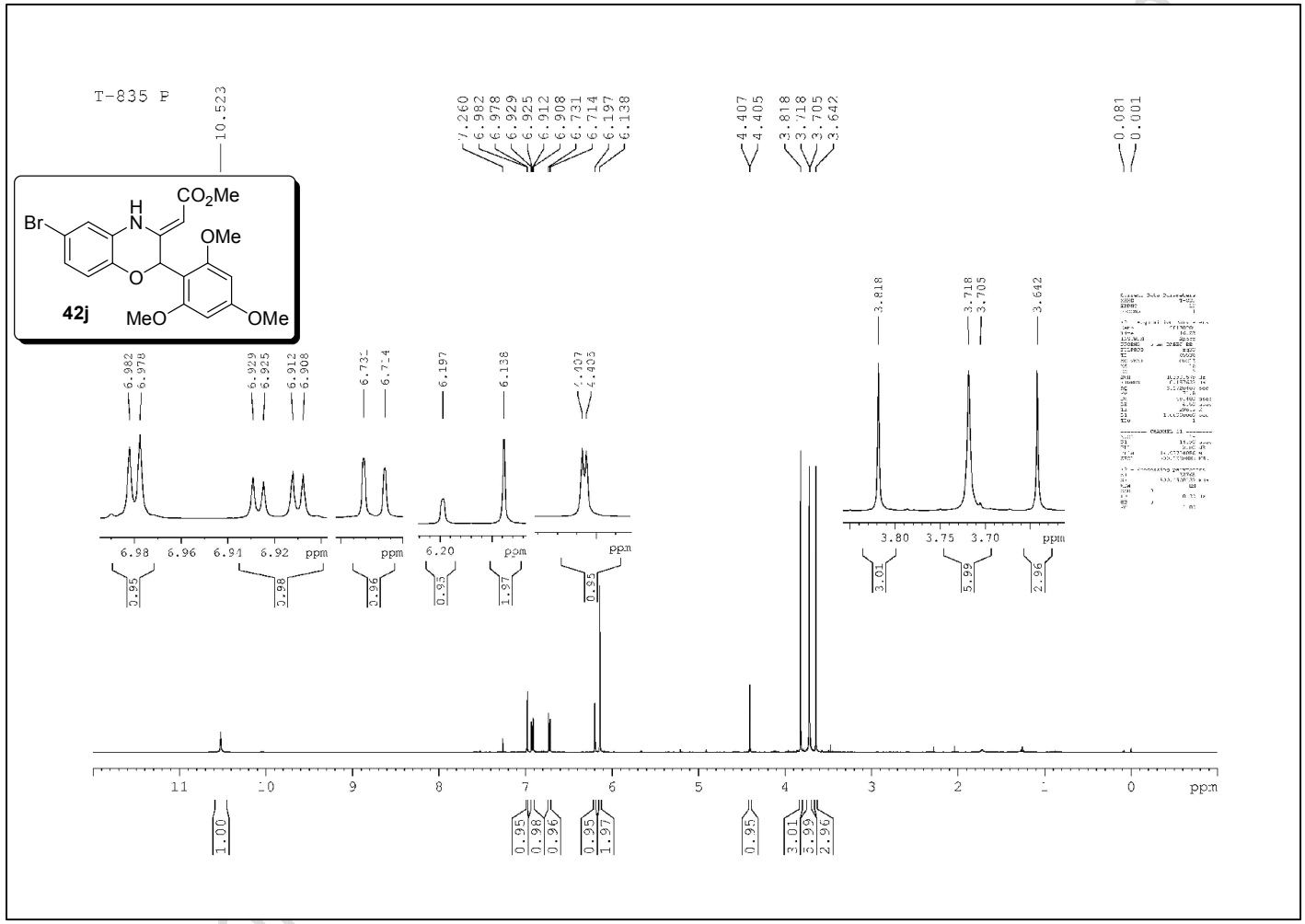


Figure S-35: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **42j**.

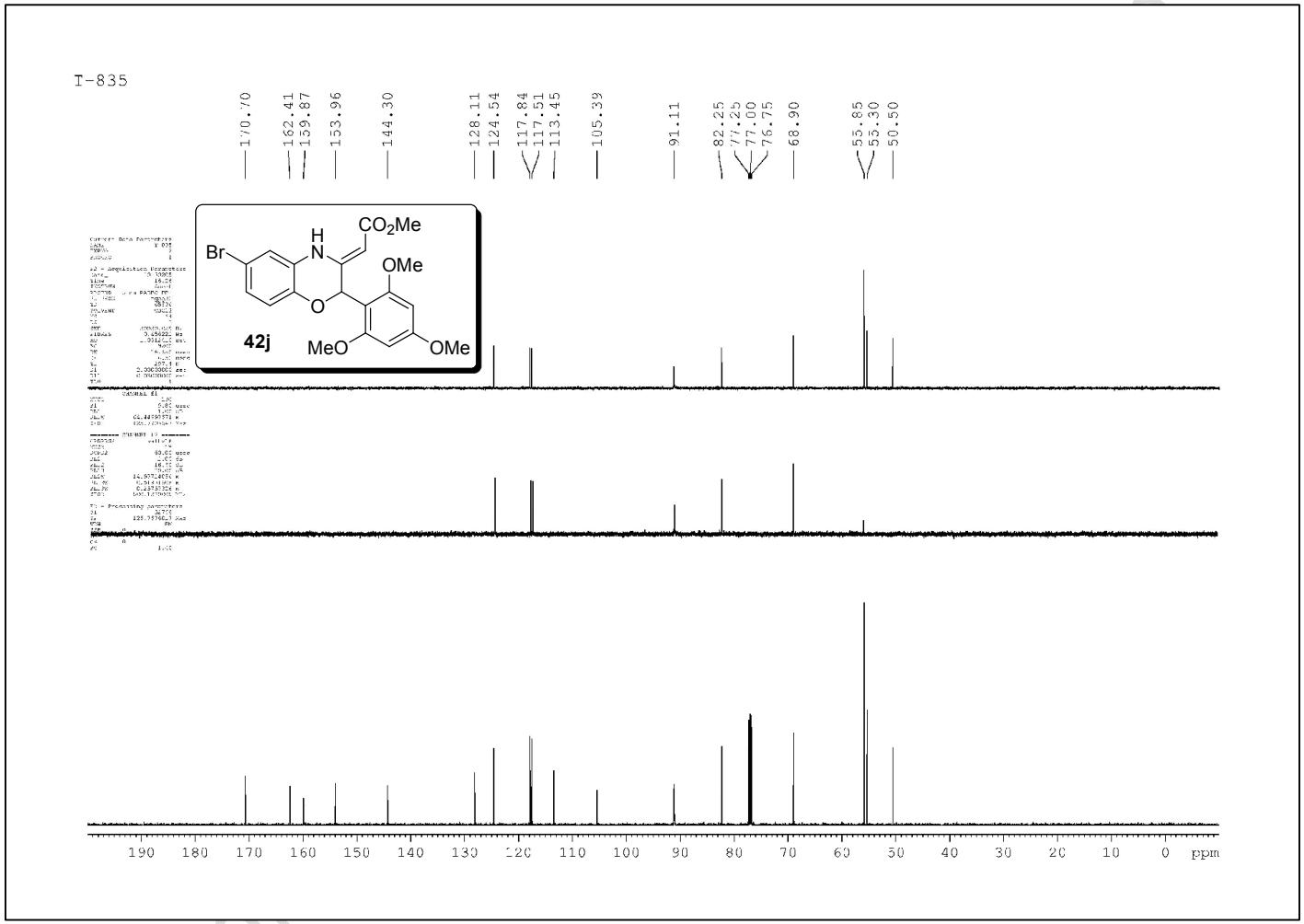


Figure S-36: ^{13}C and DEPT (125 MHz, $CDCl_3$) Spectra of **42j**.

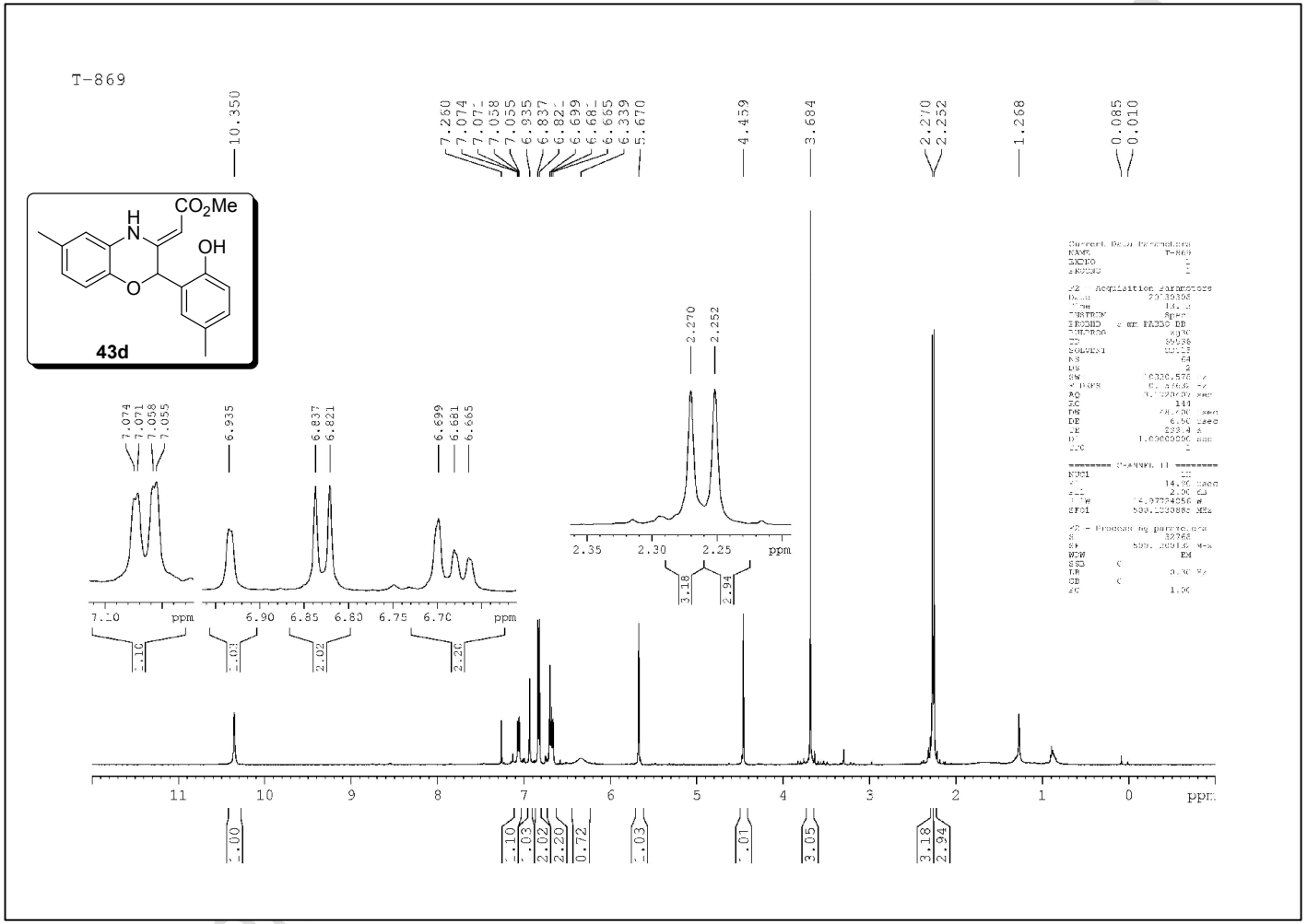


Figure S-37: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **43d**.

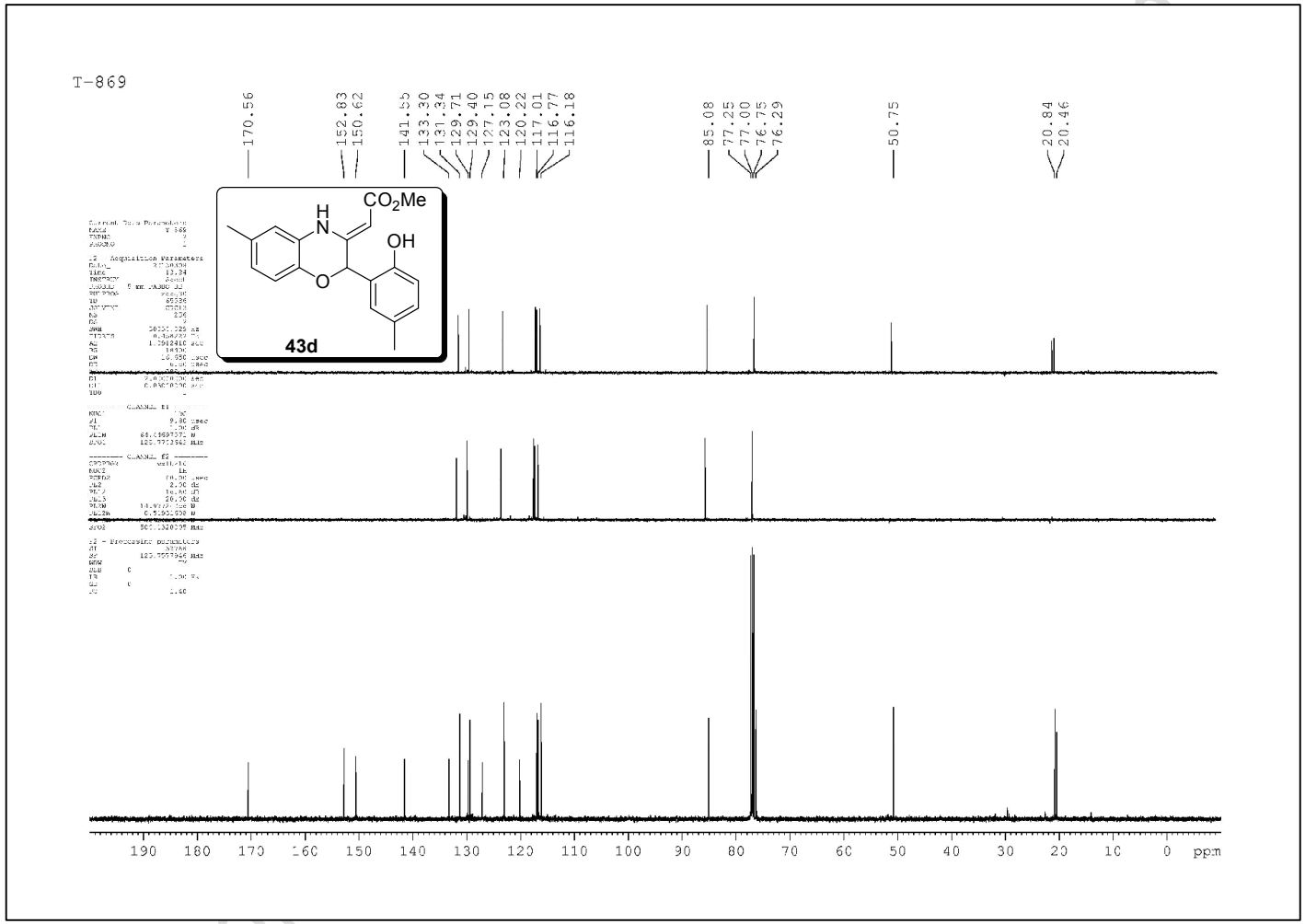


Figure S-38: ^{13}C and DEPT (125 MHz, $CDCl_3$) Spectra of **43d**.

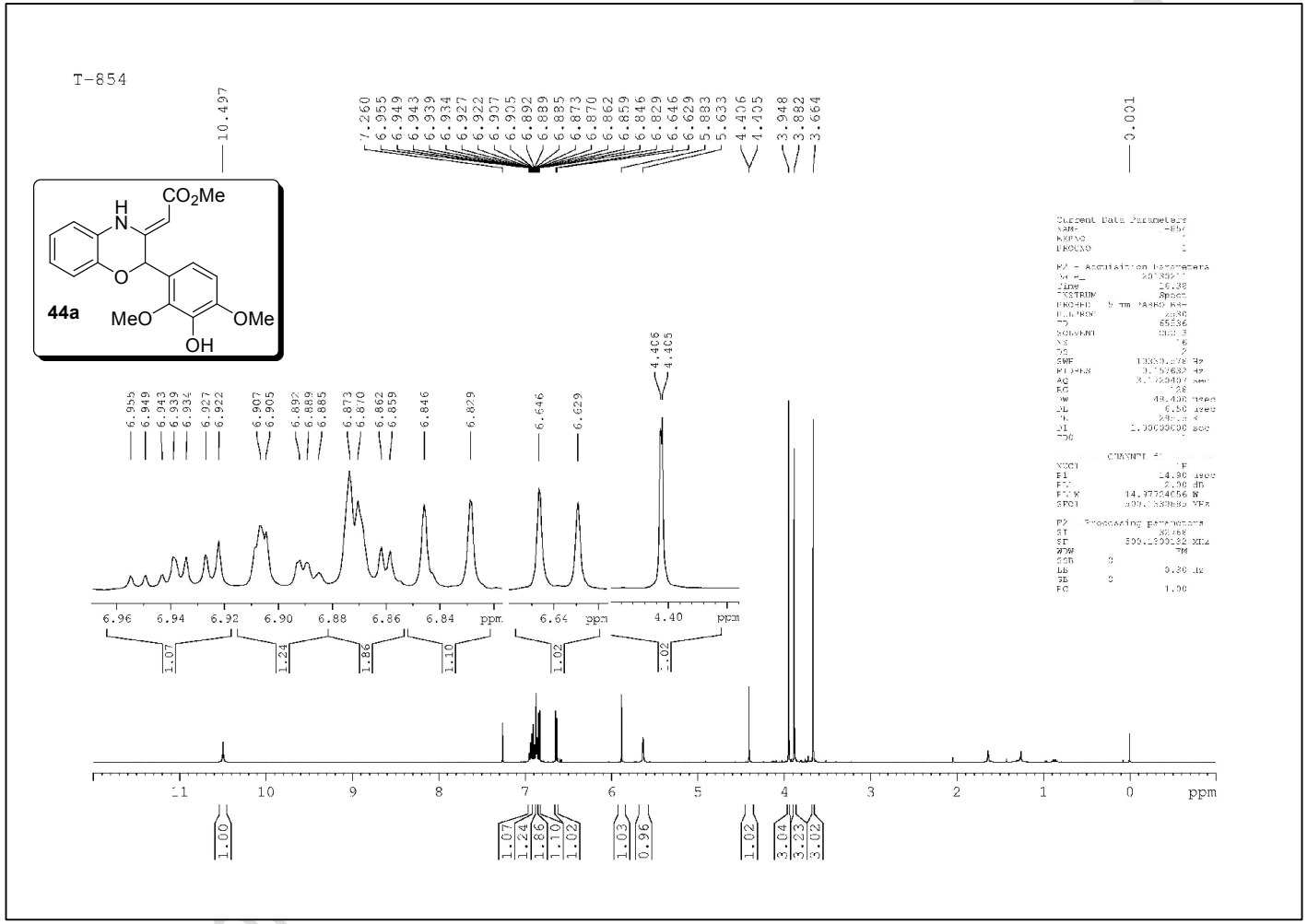


Figure S-39: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **44a**.

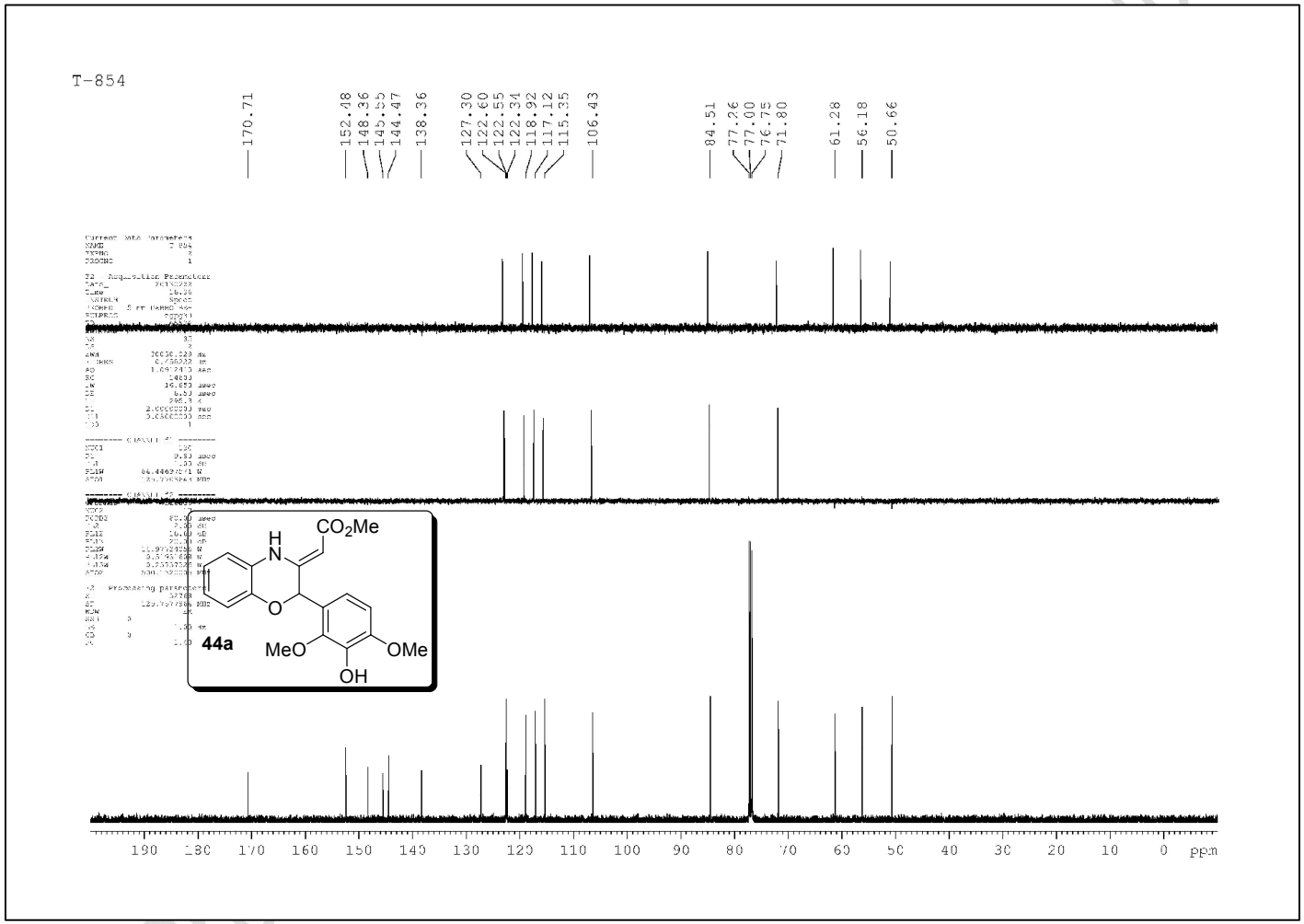


Figure S-40: ^{13}C and DEPT (125 MHz, $CDCl_3$) Spectra of **44a**.

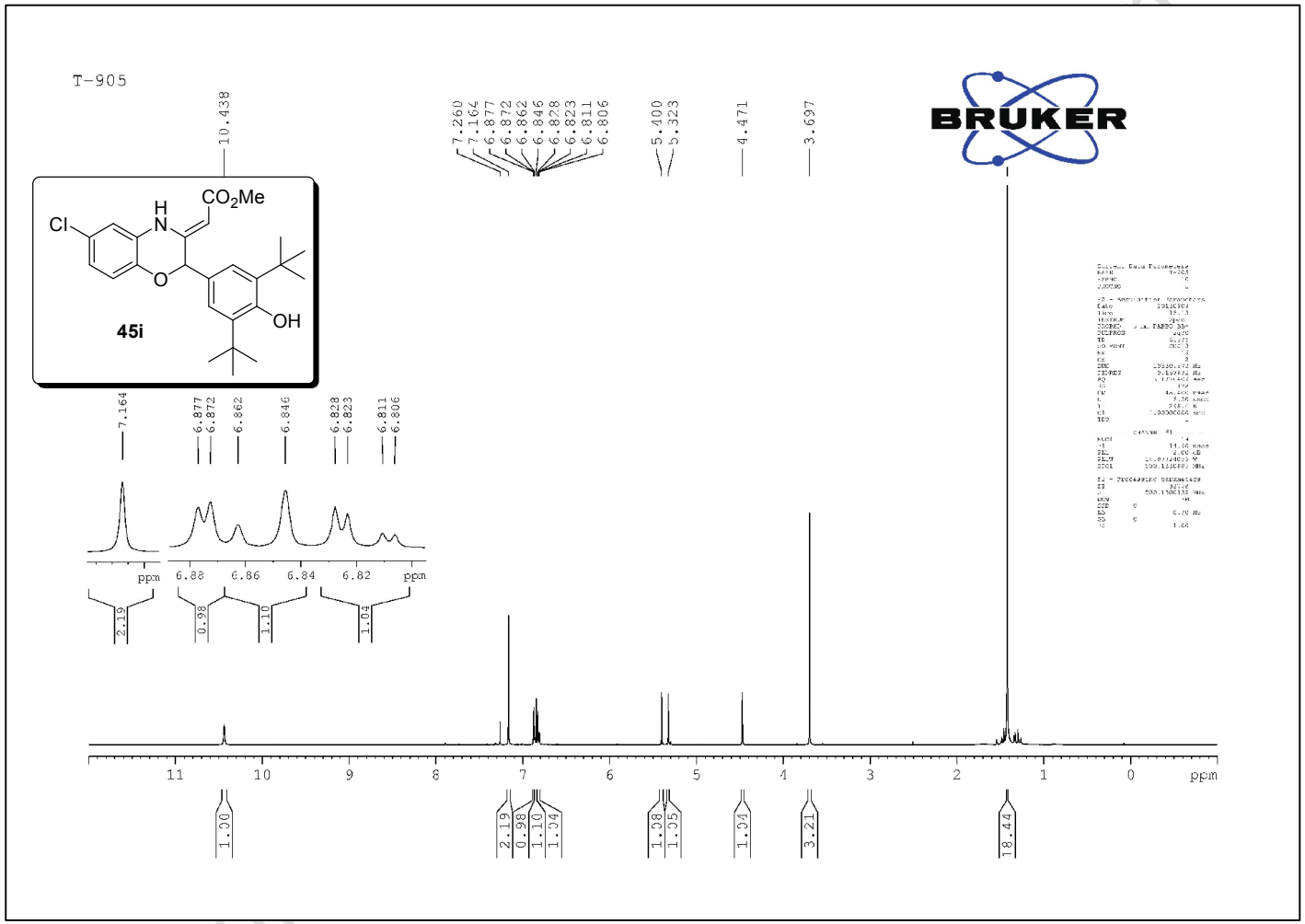


Figure S-41: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **45i**.

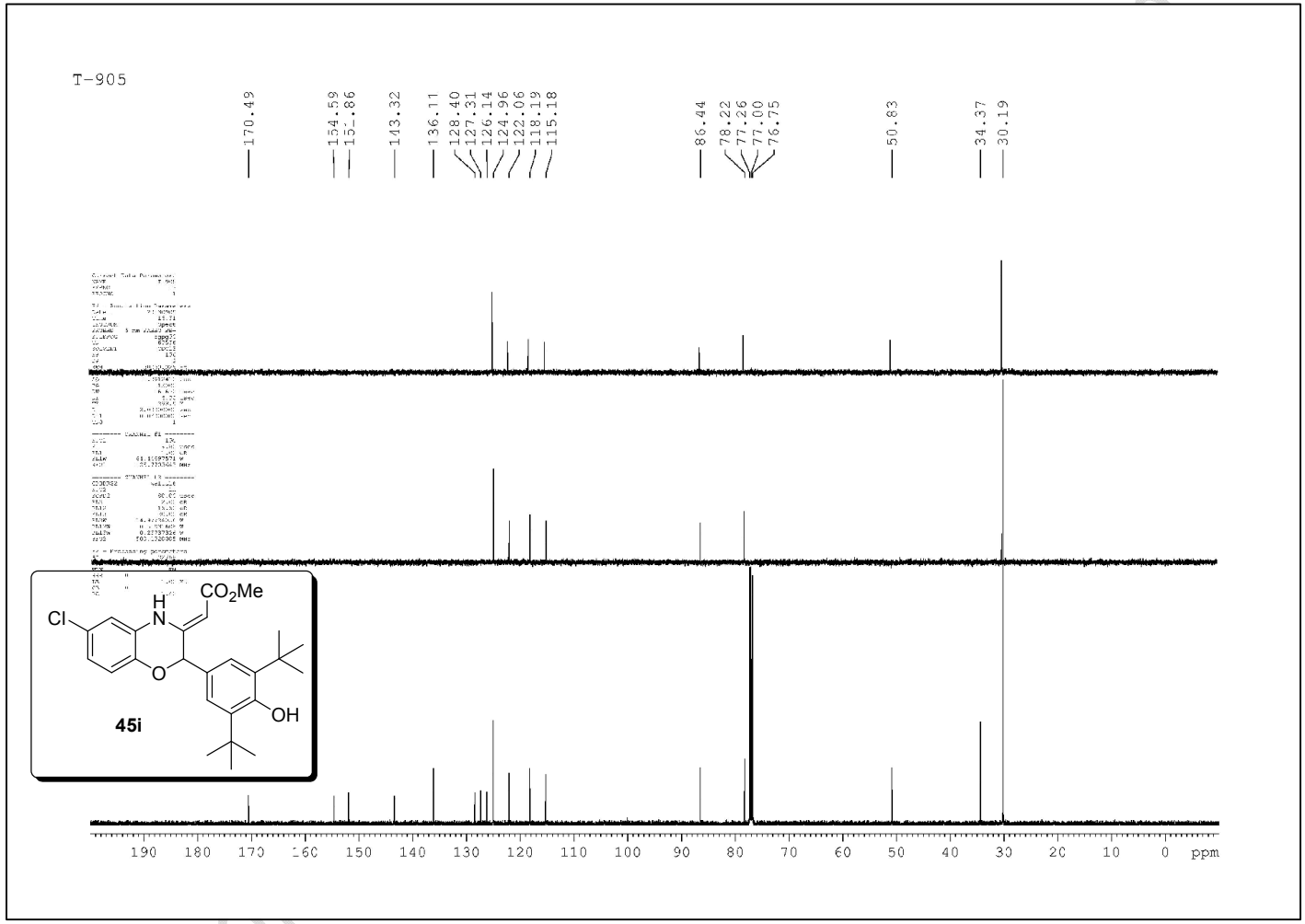


Figure S-42: ^{13}C and DEPT (125 MHz, $CDCl_3$) Spectra of **45i**.

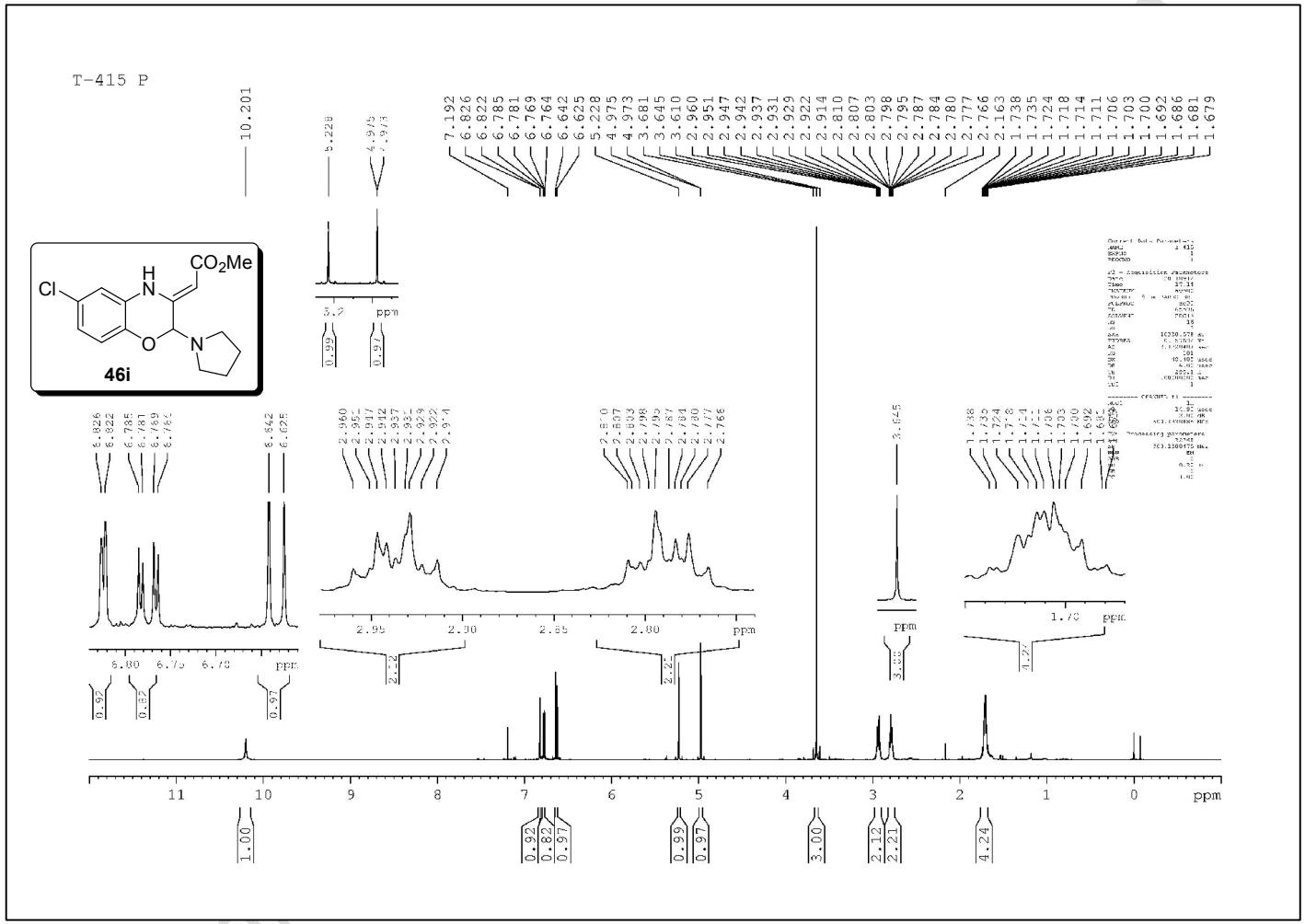


Figure S-43: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **46i**.

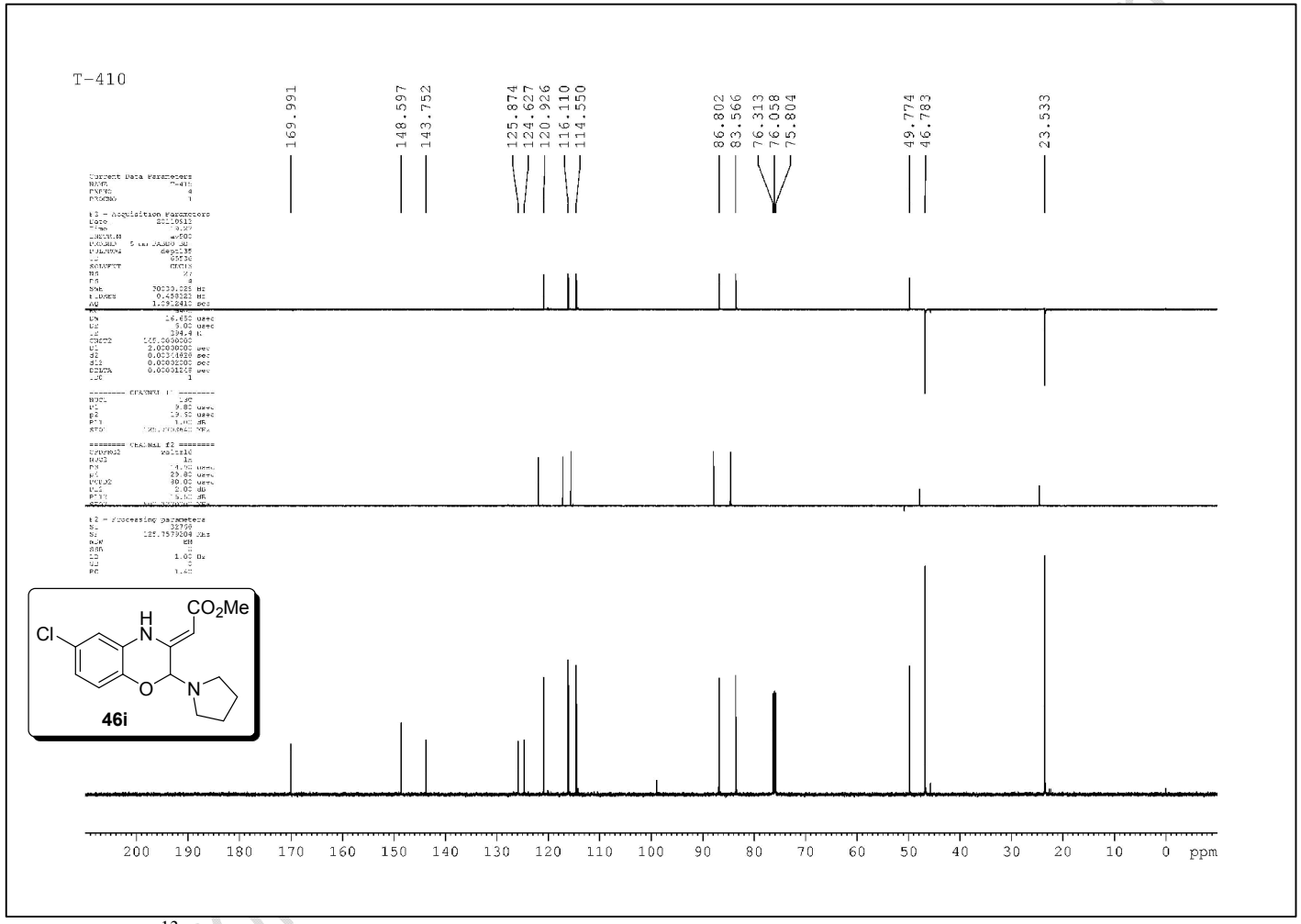


Figure S-44: ^{13}C and DEPT (125 MHz, $CDCl_3$) Spectra **46i**.

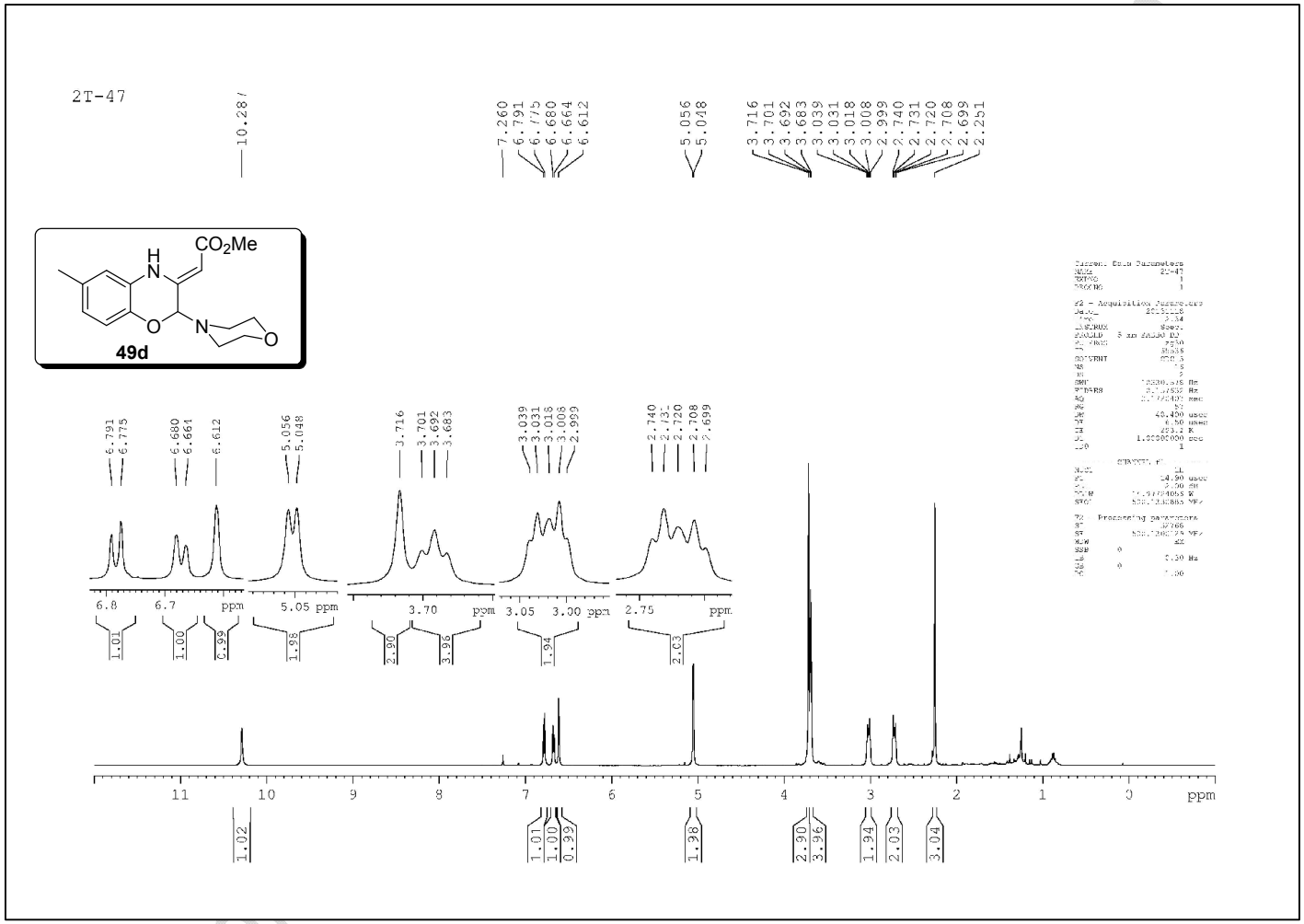


Figure S-45: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **49d**.

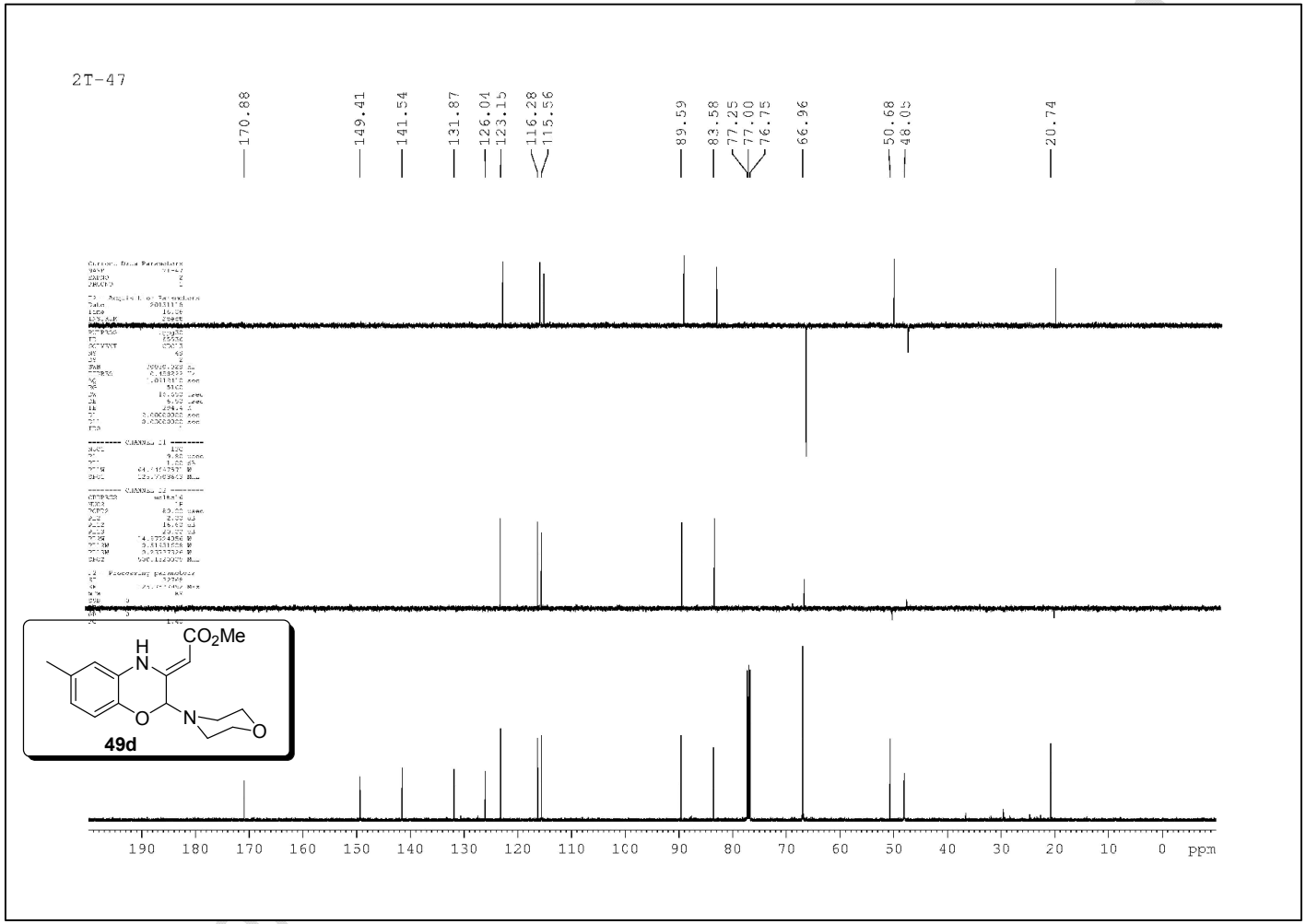


Figure S-46: ^{13}C and DEPT (125 MHz, $CDCl_3$) Spectra of **49d**.

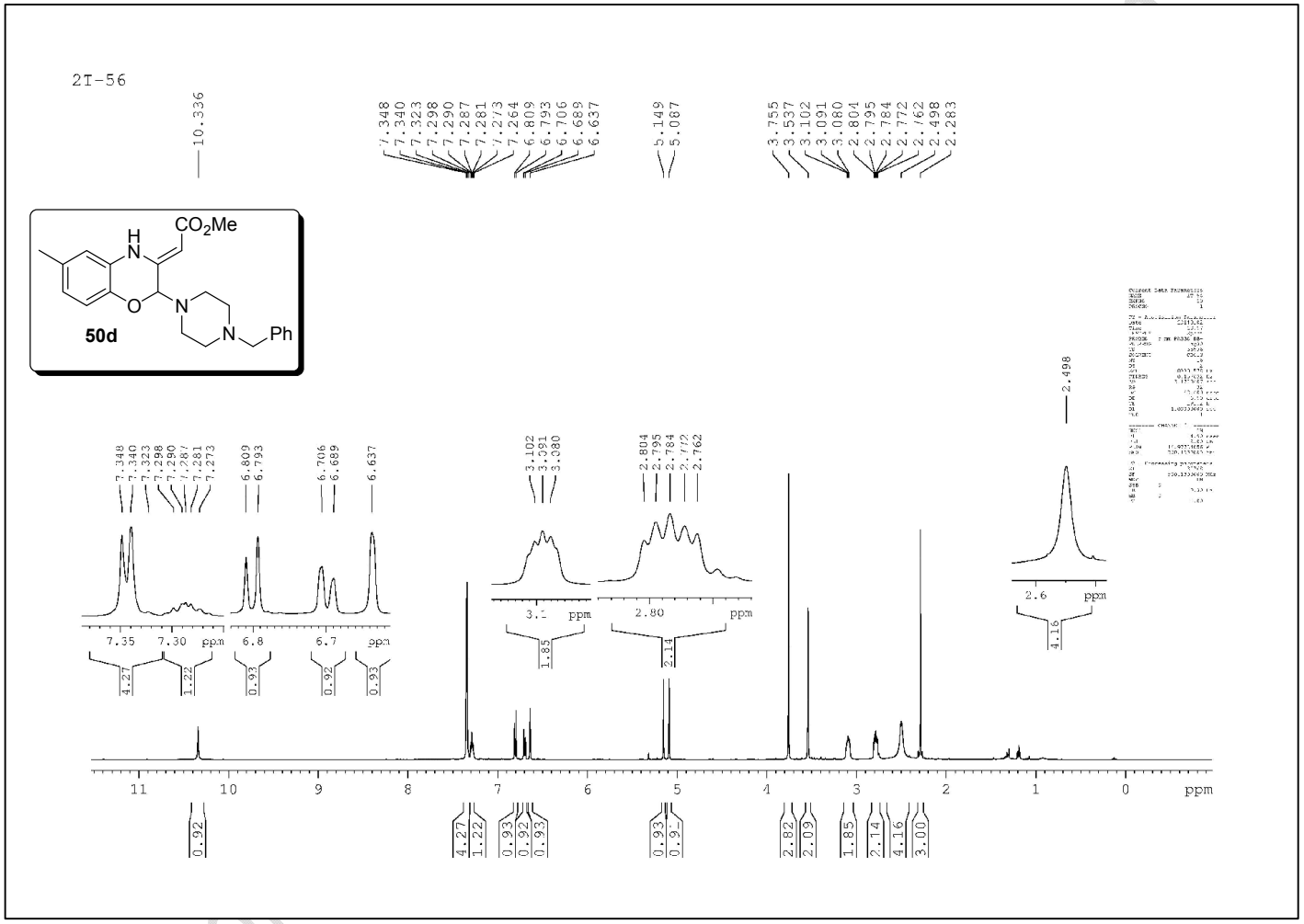


Figure S-47: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **50d**.

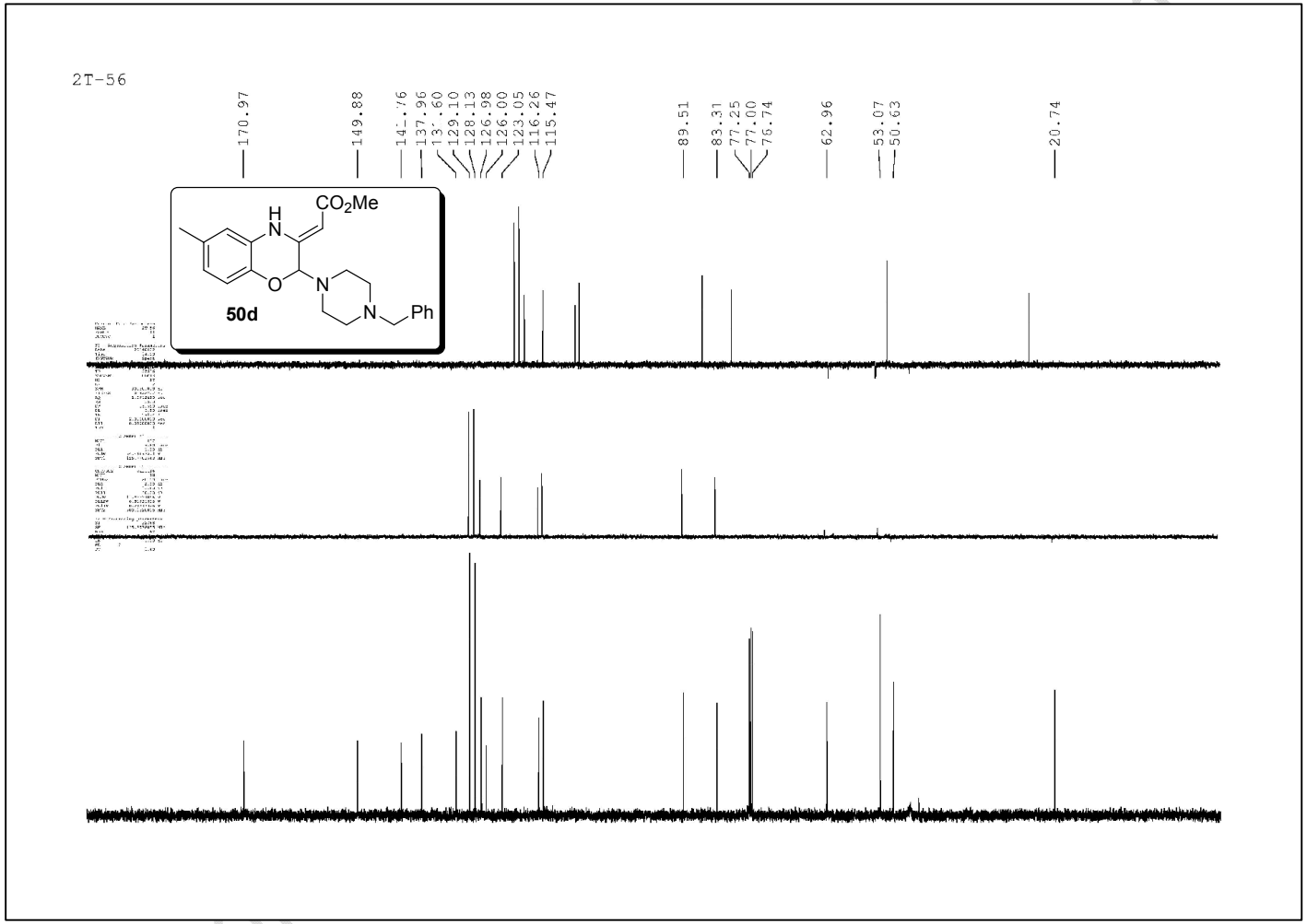


Figure S-48: ^{13}C and DEPT (125 MHz, $CDCl_3$) Spectra of **50d**.

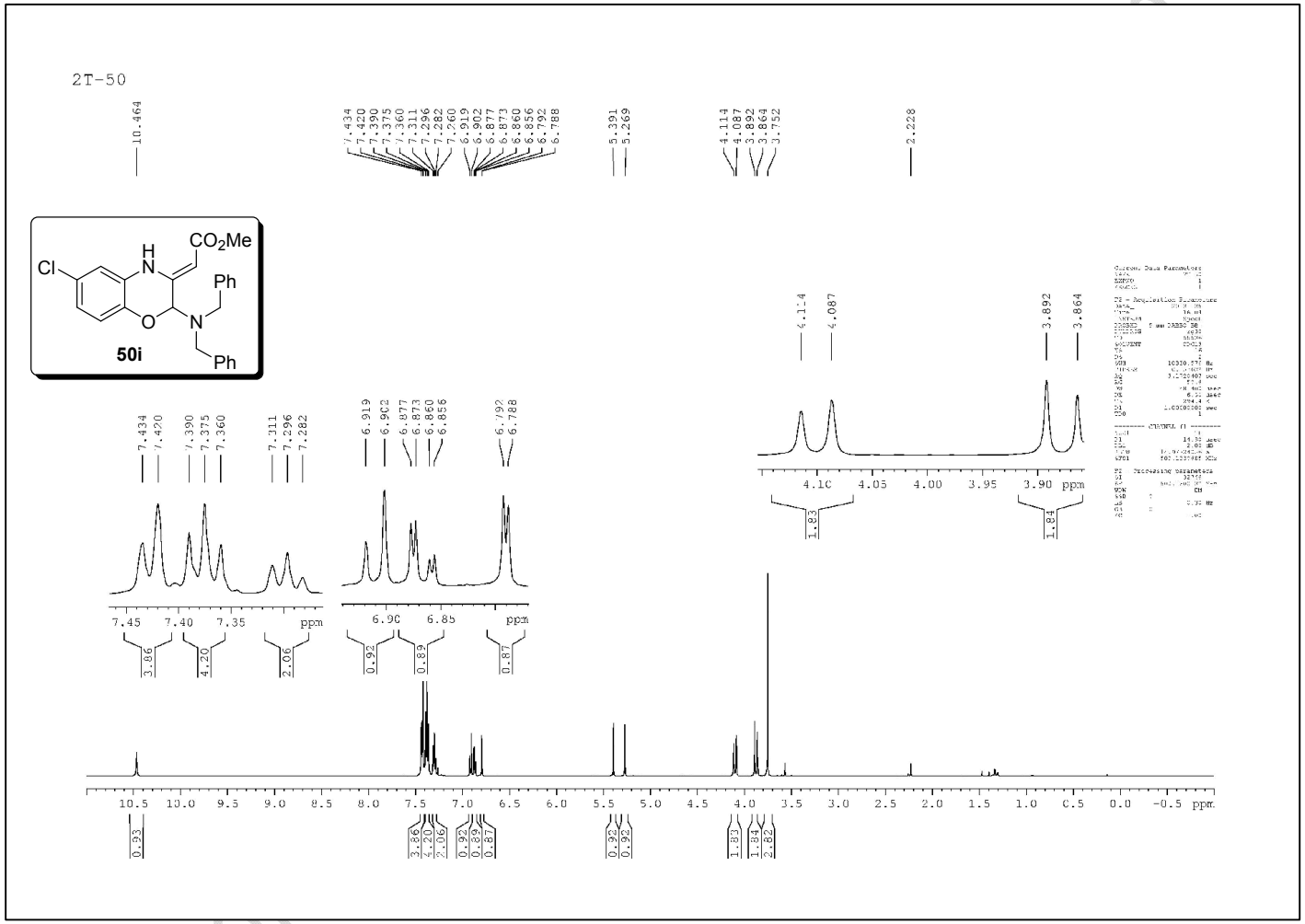


Figure S-49: ^{1}H NMR (500 MHz, $CDCl_3$) Spectra of **50i**.

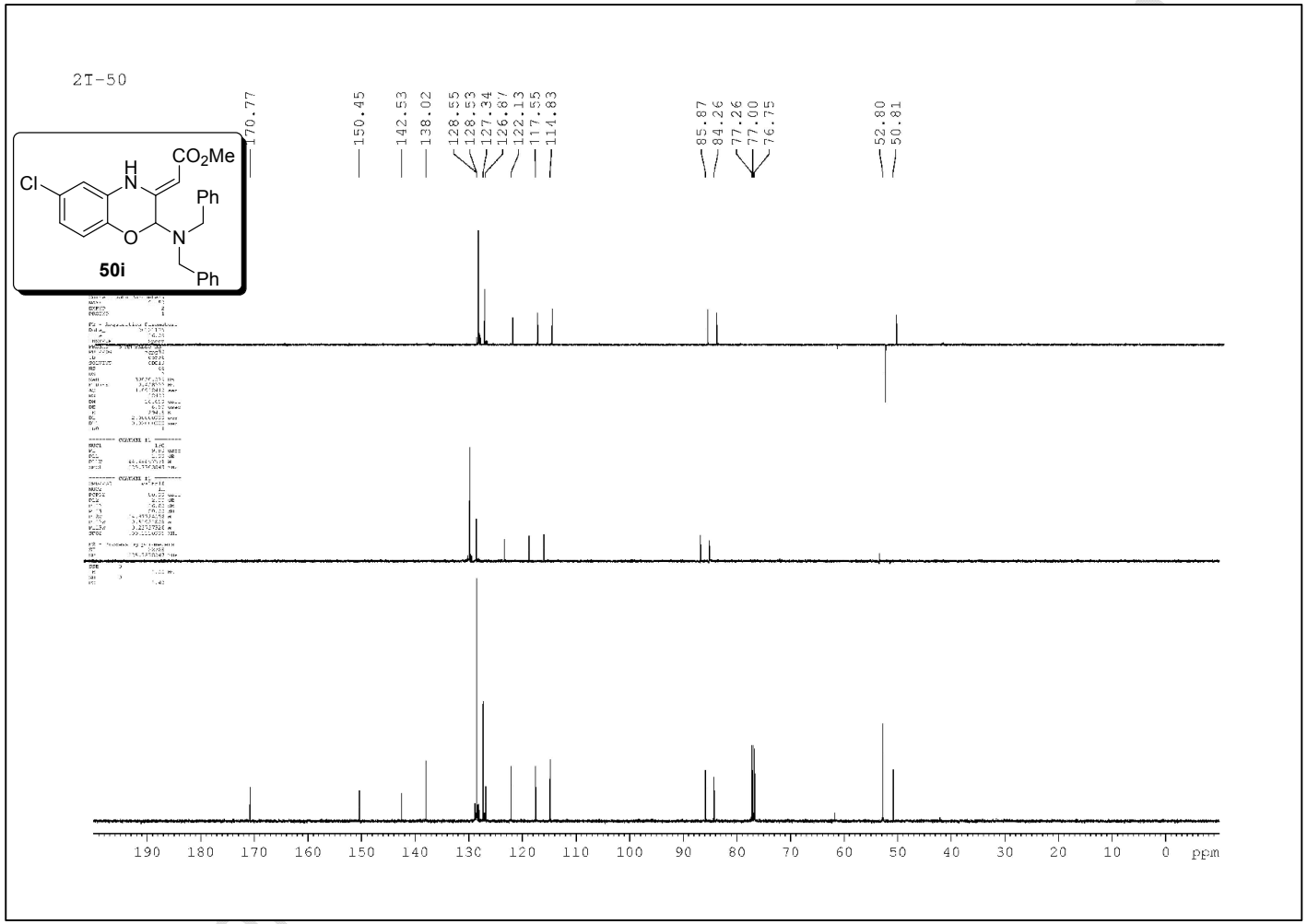
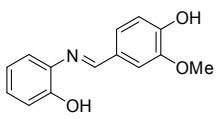


Figure S-50: ^{13}C and DEPT (125 MHz, $CDCl_3$) Spectra of **50i**.

STRUCTURES OF COMPOUNDS FROM THESIS



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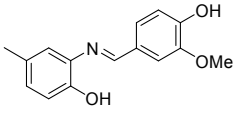

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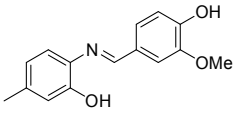

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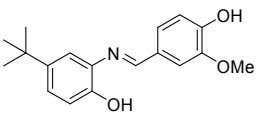

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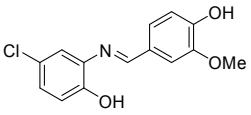

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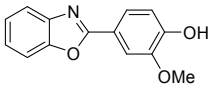

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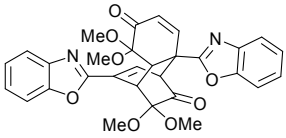

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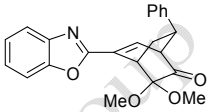

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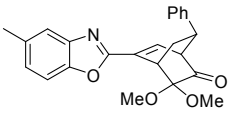

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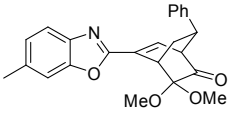

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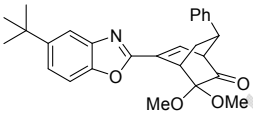

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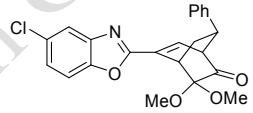

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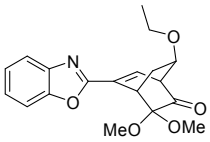

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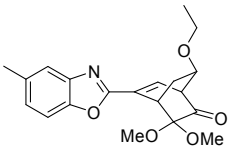

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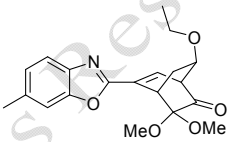

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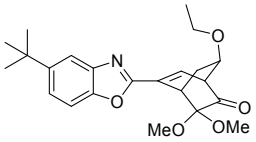

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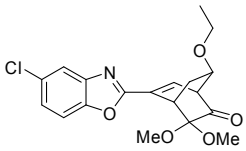

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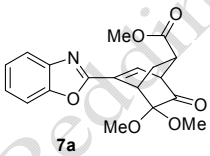

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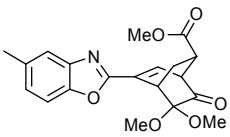

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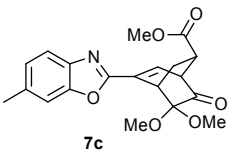

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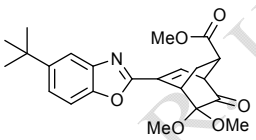

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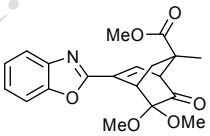

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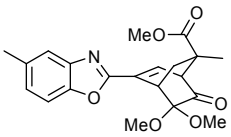

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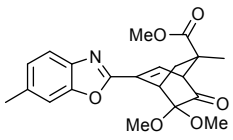

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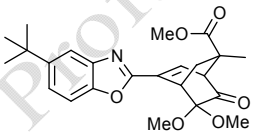

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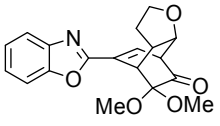

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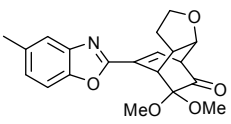

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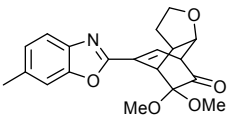

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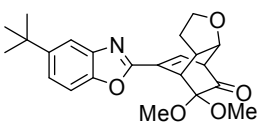

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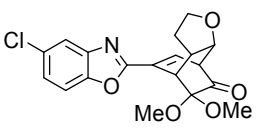

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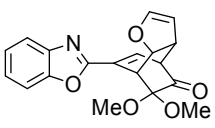

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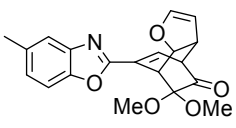

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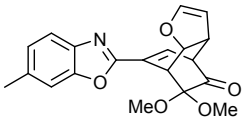

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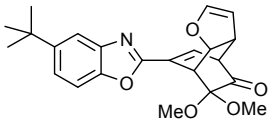

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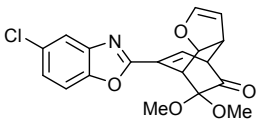

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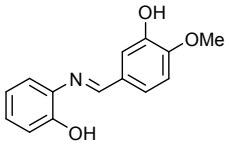

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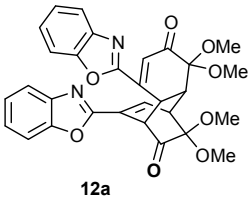

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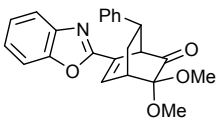

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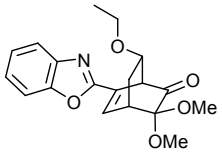

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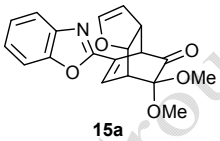

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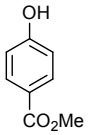

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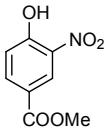

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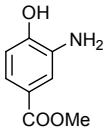

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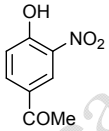

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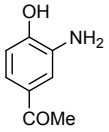

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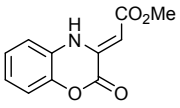

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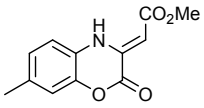

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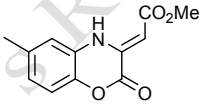

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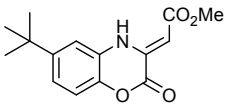

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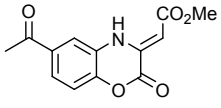

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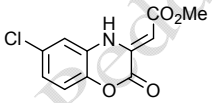

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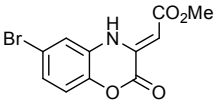

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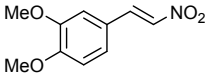

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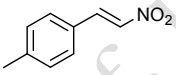

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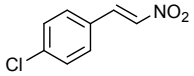

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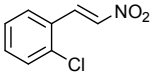

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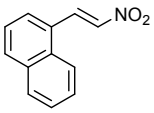

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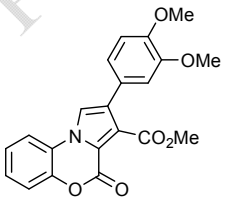

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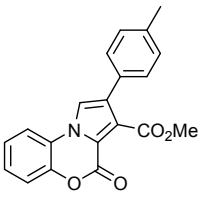

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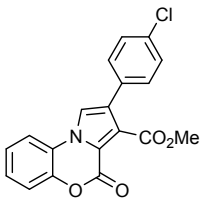

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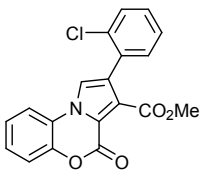

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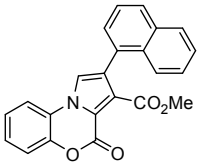

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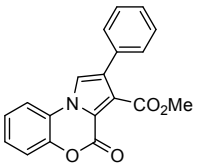

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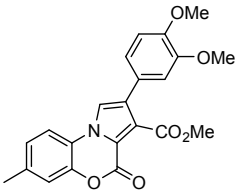

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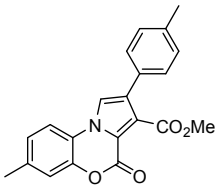

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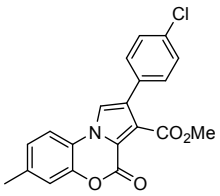

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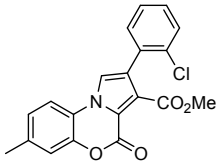

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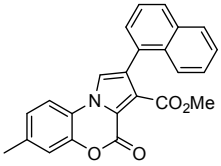

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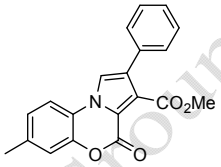

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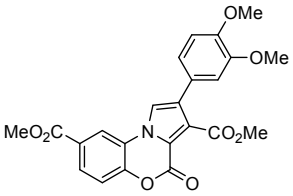

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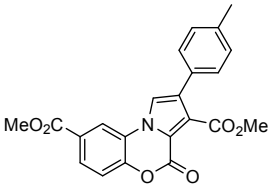

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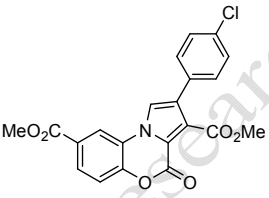

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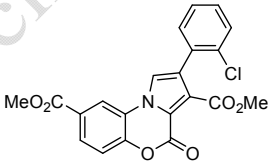

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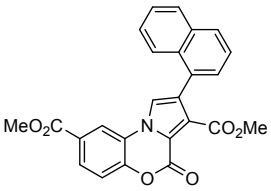

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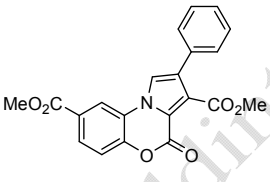

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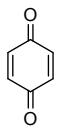

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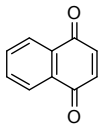

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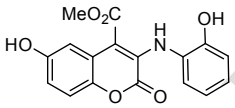

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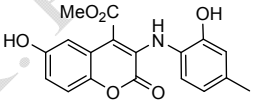

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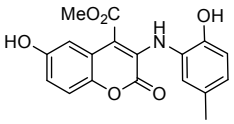

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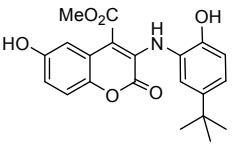

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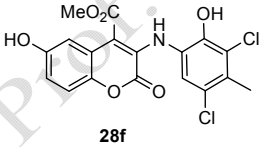

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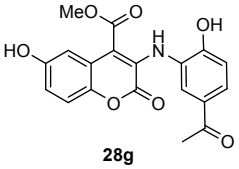

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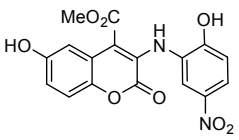

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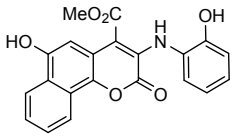

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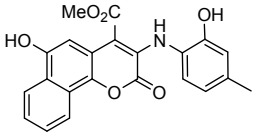

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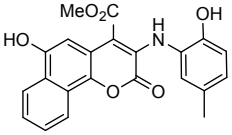

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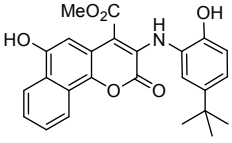

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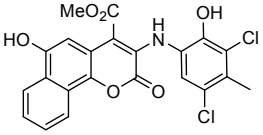

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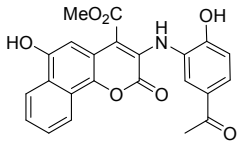

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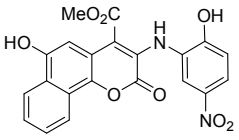

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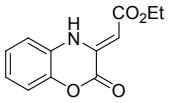

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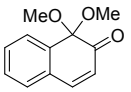

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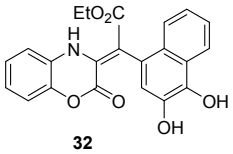

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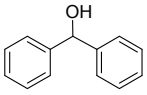

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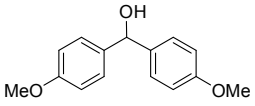

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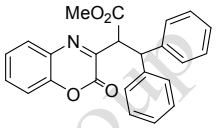

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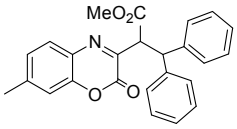

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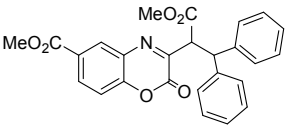

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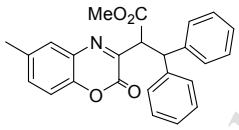

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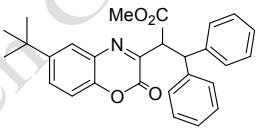

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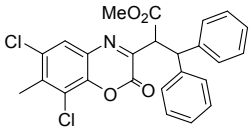

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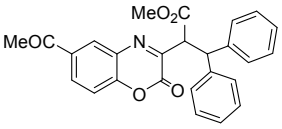

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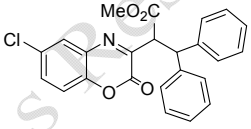

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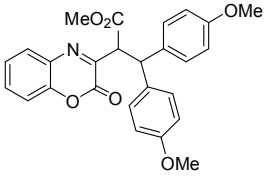

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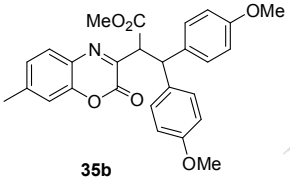

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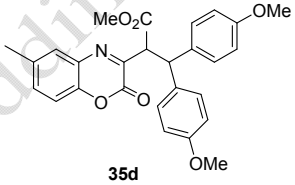

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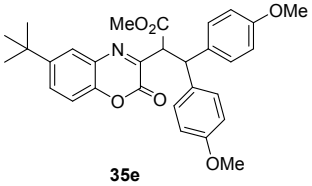

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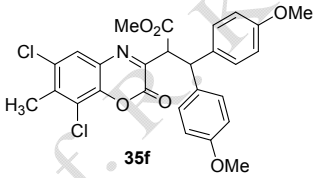

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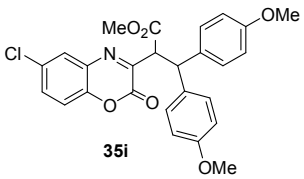

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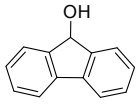

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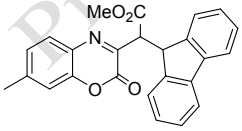

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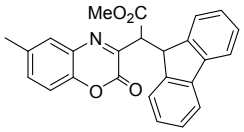

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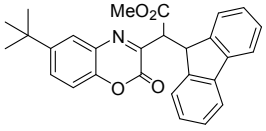

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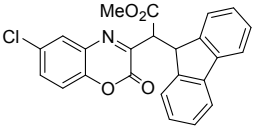

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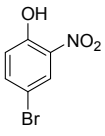

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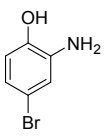

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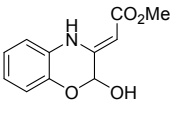

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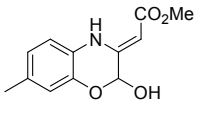

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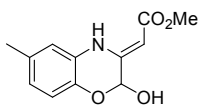

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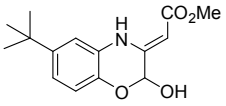

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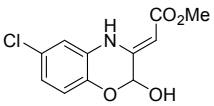

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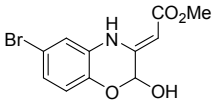

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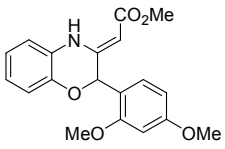

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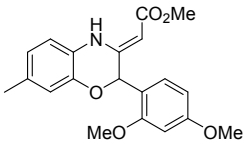

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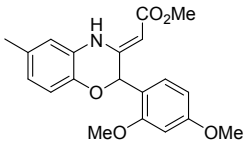

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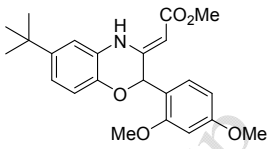

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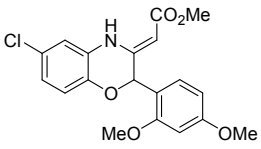

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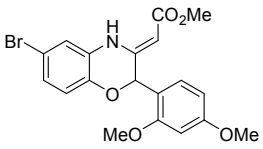

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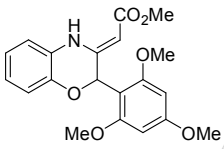

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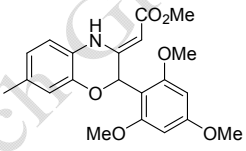

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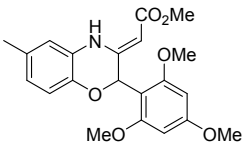

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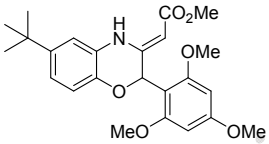

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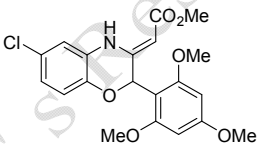

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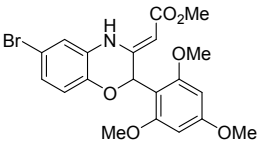

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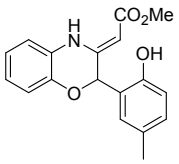

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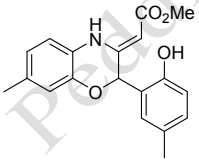

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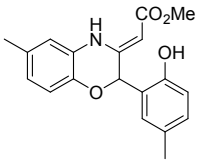

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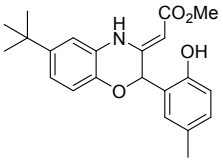

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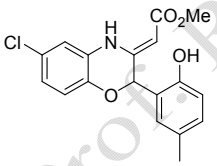

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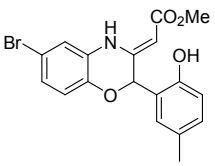

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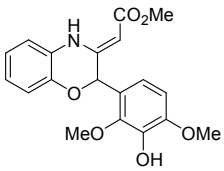

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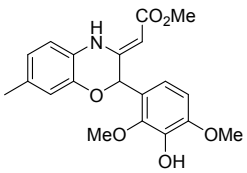

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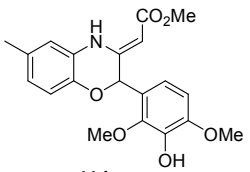

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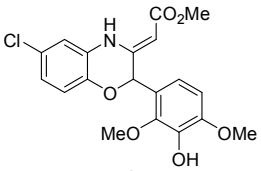

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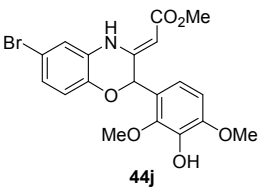

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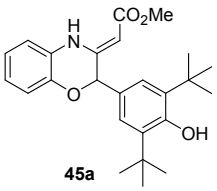

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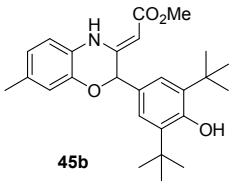

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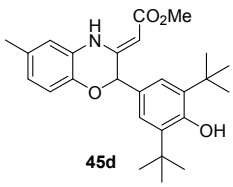

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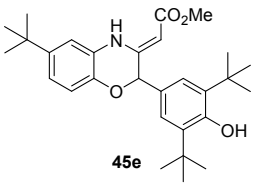

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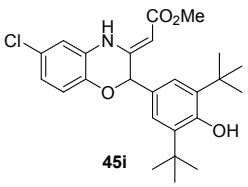

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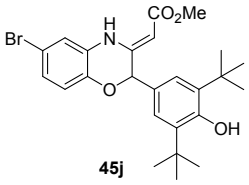

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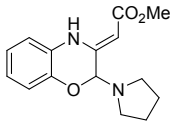

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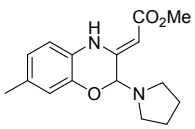

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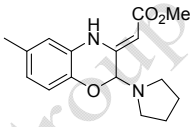

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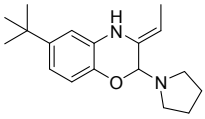

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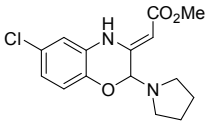

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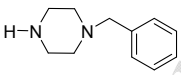

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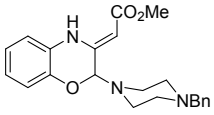

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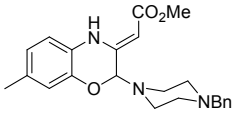

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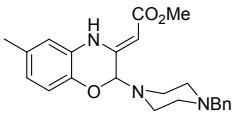

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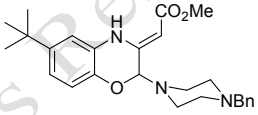

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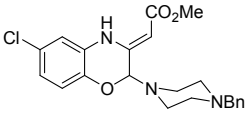

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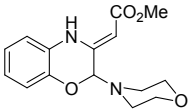

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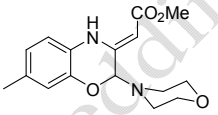

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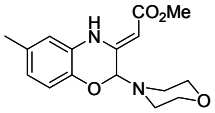

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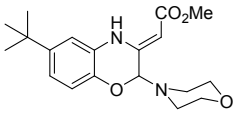

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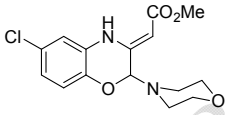

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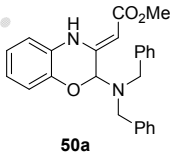

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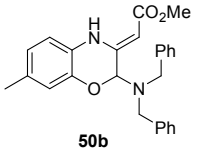

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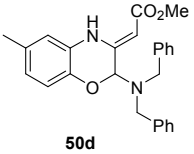

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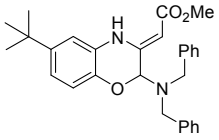

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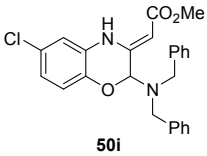

50i

VITAE

The author was born on 4th September 1985, at Deshaipet, Warangal, Andhra Pradesh. Following his early education he joined Chaitanya Degree College, Hanamkonda, Warangal and received his B. Sc degree from Kakatiya University in 2006. He joined A. V. College, Osmania University for M.Sc and obtained the degree in 2008. He registered for Ph. D in July 2009 at Indian Institute of Technology Roorkee. He was awarded JRF and SRF by CSIR, New Delhi.

LIST OF PUBLICATIONS

1. An Expedient and Green Protocol for the Michael Addition of Malonates, Diketones and β-keto Esters to the Nitrostyrenes.
   J. Agarwal, **R.T. Naganaboina**, R. K. Peddinti *Ind. J. Chem*. **2013**, *52B*, 511-518.

2. BF_3·Etherate-Mediated Friedel-Crafts Arylation of 2-Hydroxy-1,4-benzoxazines: Synthesis of 2-Aryl-1,4-benzoxazine Derivatives.
   R. T. Naganaboina, R. K. Peddinti, *J. Org. Chem*. **2013**, *78*, 12819-12824.

3. Synthesis of Novel 1,4-Benzoxazine and Butenolide Derivatives.
   G. Choudhary, **R.T. Naganaboina**, R. K. Peddinti, *RSC Adv*. **2014**, *4*, 17969-17979.

4. Trifluoroacetic Acid-Mediated Michael Addition–Cyclization Reactions of Vinylogous Carbamates.
   R. T. Naganaboina, R. K. Peddinti, *Org. Biomol. Chem.* **2014**, DOI: 10.1039/ c4ob00437j.

5. Facile One-Pot Synthesis of (Benzoxazol-2′-yl)bicyclo[2.2.2]octen-2-one Derivatives.
   R. T. Naganaboina, R. K. Peddinti, *(Communicated)*.

6. Molecular Iodine-Mediated Friedel-Crafts Alkylation of 1,4-Benzoxazinone Derivatives.
   R. T. Naganaboina, R. K. Peddinti, *(Manuscript in preparation)*.

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