REGIOSELECTIVE SYNTHESIS OF β-HYDROXY SULFIDES, SPIROOXINDOLES AND BENZYLIDENE SUCCINIMIDE-TETHERED PROPANONES SCAFFOLDS

Ph.D. THESIS

by

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JULY, 2019

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CANDIDATE'S DECLARATION

I hereby certify that the work which is being presented in the thesis entitled "**REGIOSELECTIVE SYNTHESIS OF β-HYDROXY SULFIDES, SPIROOXINDOLES AND BENZYLIDENE SUCCINIMIDE-TETHERED PROPANONES SCAFFOLDS**" in partial fulfilment 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 of July, 2014 to July, 2019 under the supervision of Dr. Rama Krishna Peddinti, Professor, Department of Chemistry, Indian Institute of Technology Roorkee, Roorkee.

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

(**PIYUSH TEHRI**)

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

Date: July 9, 2019. (R. K. Peddinti)
Supervisor

The Ph.D. Viva-Voce Examination of **Mr. Piyush Tehri**, research scholar has been held on 23-09-2019.

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This is certify that the student has made all the corrections in the thesis.

Signature of Supervisor **Head of the Department**

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List of abbreviations

ACN	Acetonitrile
b_{mim}	1-Butyl-3-methylimidazolium
Bn	Benzyl
BHT	Dibutylhydroxytoluene
Boc	*tert*-Butyloxycarbonyl
Calc.	Calcined
CCDC	Cambridge crystallographic data centre
CD	Circular dichroism
COSY	Correlation spectroscopy
Cp	Cyclopentadienyl
DABCO	1,4-Diazabicyclo[2.2.2]octane
dba	*E,E*-Dibenzylidene acetone
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
DCE	1,2-Dichloroethane
DCM	Dichloromethane
DDQ	2,3-Dichloro-5,6-dicyano-1,4-benzoquinone
DFT	Density functional theory
DIB	Diacetoxyiodobenzene
DIPEA	*N,N*-Diisopropylethylamine
DMF	Dimethylformamide
DMSO	Dimethyl sulfoxide
dr	Diastereomeric ratio
ee	Enantiomeric excess
DROC	Domino ring-opening cyclization
EDG	Electron donating group
equiv.	Equivalent
ESI	Electron spray ionization
EWG	Electron withdrawing group
HFIP	Hexafluoro-2-propanol
HIV	Human immunodeficiency virus

HSQC	Heteronuclear Single-Quantum Correlation
HMBC	Heteronuclear Multiple Bond Correlation
HRMS	High-resolution mass spectrometry
Hz	Hertz
IMDA	Intramolecular Diels−Alder
IPA	Isopropyl alcohol
IR	Infrared
LR	Lawesson's reagent
mL	Milliliter
MVK	Methyl vinyl ketone
NCS	*N*-Chlorosuccinimide
NMR	Nuclear magnetic resonance
NOE	nuclear Overhauser effect
NOESY	Nuclear Overhauser Effect Spectroscopy
ORTEP	Oak Ridge Thermal Ellipsoid Plot
rt	Room temperature
SN^1	unimolecular nucleophilic substitutions
TBHP	*tert*-Butyl hydroperoxide
TEMPO	2,2,6,6-Tetramethylpiperidine-1-oxyl
TFA	Trifluoroacetic acid
THF	Tetrahydrofuran
TLC	Thin-layer Chromatography
TMM	Trimethylenemethane
TMS	Trimethylsilyl
TOCO	Thiol-olefin co-oxidation
PA	Phosphoric acid
PG	Protecting group
pH	Power of hydrogen
ppm	parts per million
PTSA	*p*-Toluenesulfonic acid
UV	Ultraviolet

Abstract

The thesis entitled "**Regioselective synthesis of *β*-hydroxy sulfides, spirooxindoles and benzylidene succinimide-tethered propanones scaffolds**" is divided into three chapters, *viz*. (i) Introduction, (ii) Objectives, Results and Discussion, and (iii) Experimental.

Chapter 1: Introduction

Regioselective synthesis has always been the point initial concern as this affects the outcome of nearly all kind of reactions involving carbon–carbon and carbon–heteroatom bond formation formation. Consequently, it is attracting much attention since last few decades. Various methods have been developed for the synthesis of C–C and C–X bonds. However, some protocols involve transition metals, expensive reagents or additives and therefore this area is still under exploration to develop environment friendly strategies for the construction of important scaffolds having biologically significant moieties like oxindoles, spirooxindoles and biaryls. There have been many synthetic protocols such as radical addition, cycloaddition, Michael addition and domino reactions to construct C–C and C–X bonds. A few of such strategies have been employed successfully to access useful scaffolds such as *β*-hydroxy sulfides, benzylidene succinimide-tethered propanones, spirooxindoles which are having significance similarities to bio-active scaffolds.

Chapter 2: Objectives, Results and Discussion

This chapter deals with the objectives, results and discussion which are divided into four sections.

2.1. Synthesis of substituted *β*-hydroxy sulfides

we have developed a metal-free, green and environmentally friendly, highly regioselective method for the synthesis of *β*-hydroxy sulfides in good to excellent yields from styrenes and thiophenols using an inexpensive, nontoxic and eco-friendly iodine/DMSO system. The reaction involves single step C–S and C–O bonds construction. The results obtained from iodine-mediated synthesis of various sulfur containing compounds are presented here.

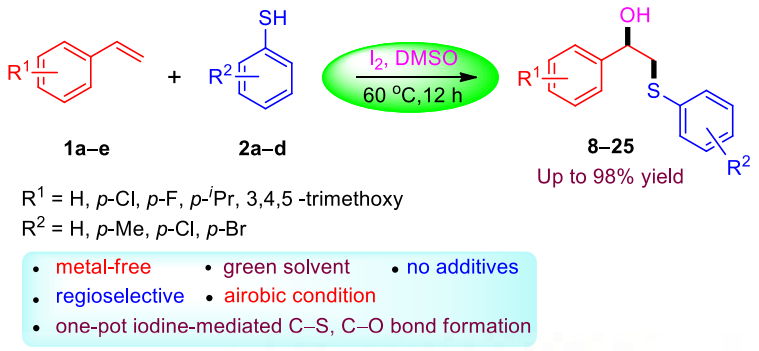


Figure 18: Iodine-catalyzed synthesis of *β*-hydroxy sulfides.

2.2. Synthesis of highly substituted spirooxindolic-cyclopentanes *via* [3 + 2] cycloaddition reactions

We have successfully demonstrated a DBU-catalyzed regioselective synthesis of a series of spirooxindoles *via* a [3 + 2] cycloaddition strategy using mild reaction conditions. The current rapid protocol offers valuable fully substituted cyclopentanes with five contiguous stereocenters in good yields with excellent diastereoselectivity in regioselective manner from easily accessible starting materials. Moreover, this methodology is simple and does not require purification steps such as recrystallization and column chromatography.

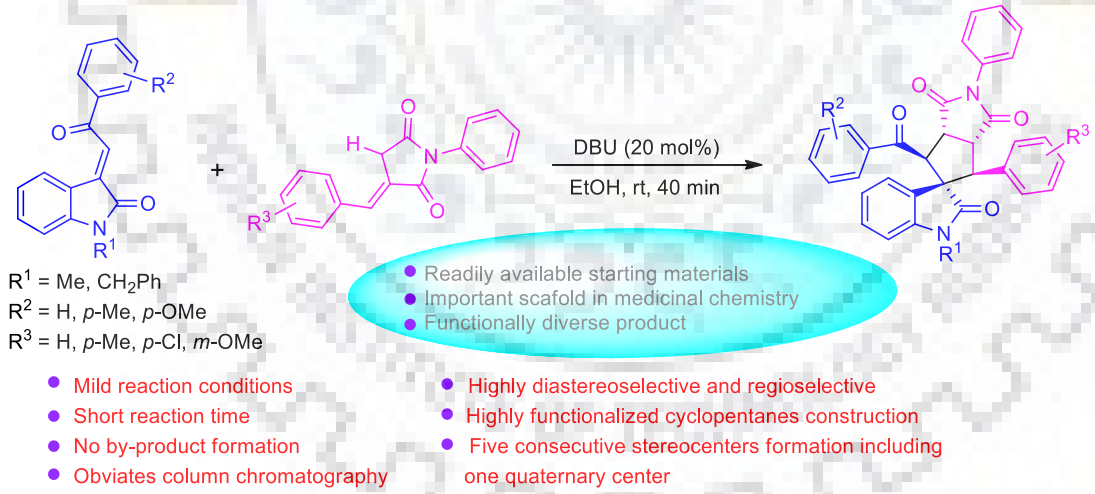


Figure 19: DBU-catalyzed highly diastereoselective synthesis of substituted spirooxindoles.

2.3. Synthesis of benzylidene succinimide-tethered propanones *via* Michael addition reactions

We have illustrated a novel approach to access benzylidene succinimide-tethered propanones *via* an efficient, metal-free, base mediated protocol. The present work involves a simple Michael addition strategy of 3-benzylidene succinimides as a readily available

nucleophile source for chalcones through C–C bond formation. All the products were obtained in good yields with excellent regeo- and diastereoselectivity and the products can be obtained just by simple filtration followed by simple washing with ethanol.

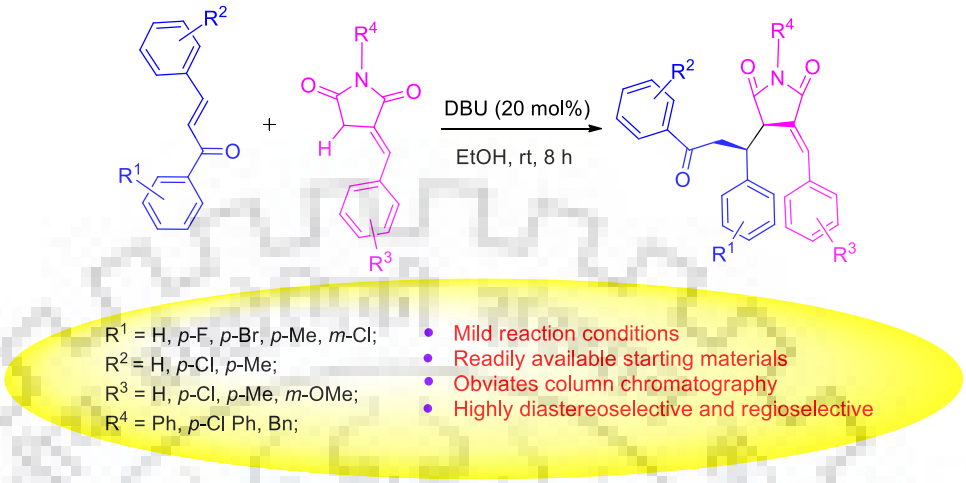


Figure 20: DBU-calalyzed highly diastereoselective synthesis of benzylidene succinimide-tethered propanones.

2.4. Synthesis of highly conjugated xanthene-tethered unsymmetrical biarylic spirooxindoles *via* domino reactions

We investigated Brønsted acid assisted domino ring opening cyclization between donor–acceptor cyclopropanes and *β*-naphthols. The protocol involves the construction of three C–C and one C–O bonds during the course of reaction in one-pot manner to furnish the highly conjugated biaryl-xanthene-spirooxindoles hybrid with one quaternary carbon atom regioselectively.

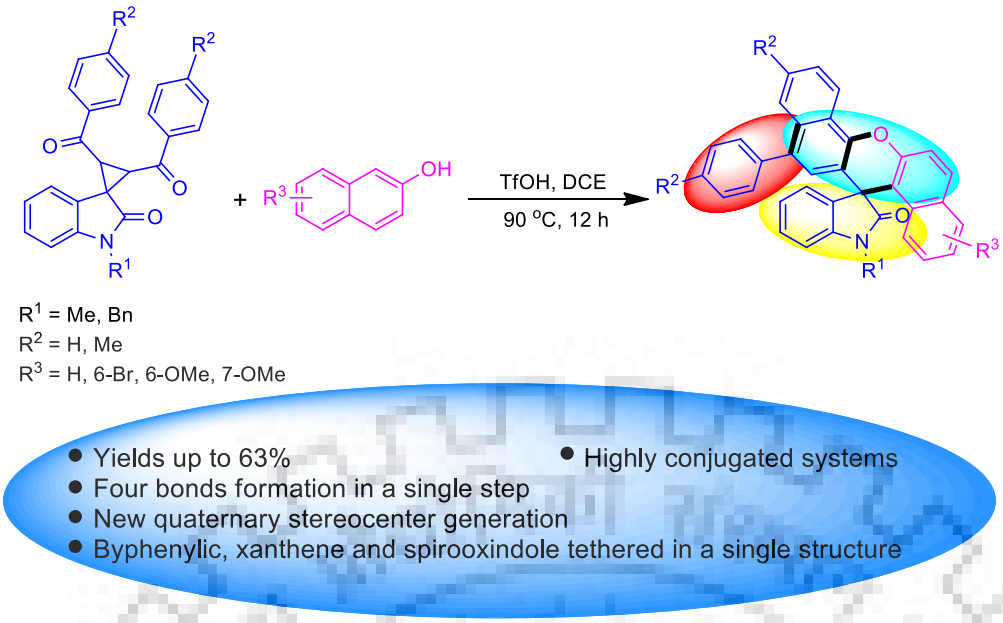


Figure 21: Triflic acid mediated synthesis of xanthene-tethered biarylic spirooxindoles.

Chapter 3: Experimental

The third chapter provides experimental procedures in detail along with physical and spectroscopic data such as MP, yield, ^{1}H and ^{13}C NMR and mass spectral data.

1. Introduction

Organic synthesis is a branch of synthetic chemistry that belongs to building of organic frameworks [1]. The first ever report in the history available is the synthesis of natural product urea from ammonium isocyanate by Wöhler in 1828, and the journey of never ending development of organic chemistry started. In 1856, Perkin synthesized the first industrial organic product *i.e.* mauveine (aniline purple) which replaced the natural dye, Tyrian purple (at the time cost more than gold) [2]. Organic chemistry connects to medicinal world *via* medicinal chemistry, also involves many important areas of research such as total synthesis, semisynthesis and methodology development.

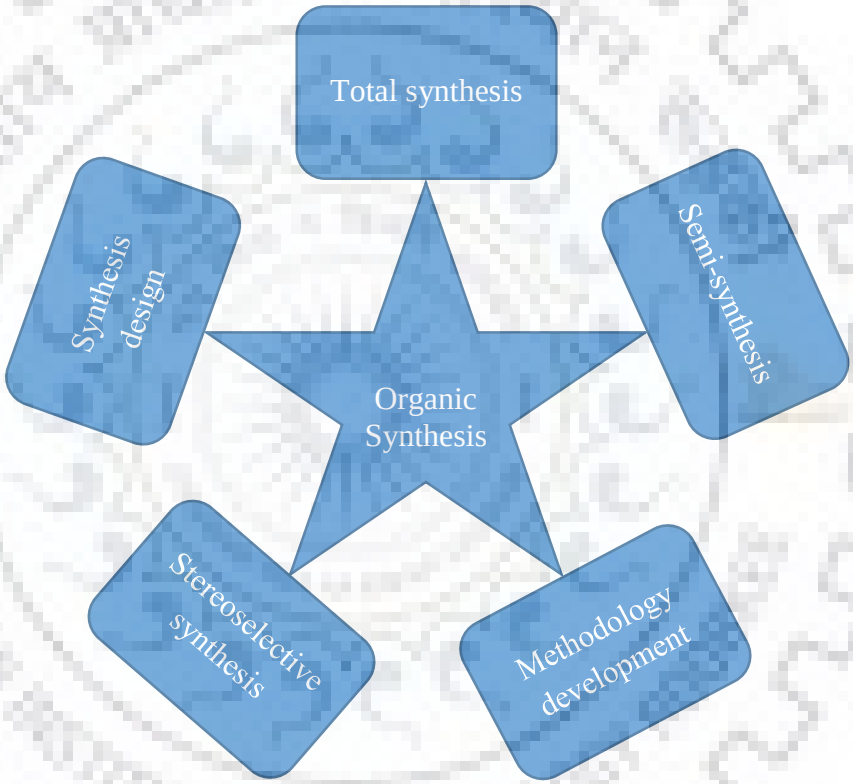


Figure 1: Areas of research in organic chemistry.

Total synthesis this is one of the outstanding fields of organic synthesis which deals with the synthesis of targeted chemical architectures. Total synthesis may be achieved through linear synthesis or convergent approach in several steps to furnish the desired product [3].

Semisynthesis involves the synthesis of novel organic scaffolds with distinct chemical and medicinal properties from the precursors isolated from natural resources. This may involve the synthesis of complex structures. It is very useful in drug discovery and cheaper than total synthesis with less number of steps.

Methodology development is all about accomplishment of the reactions to deliver easy to handle protocols for the synthesis of early synthetic intermediates or some useful compounds with high yields and broad substrate scope after the testing of various conditions of temperature, solvent, reaction time [4].

Stereoselective synthesis involves the construction of pure isomers by using specially designed catalysts. Historically, asymmetric synthesis was accomplished in two ways: synthesis followed by resolution. This technique provides synthetic approach to access pure enantiomers without the need of any resolution which was a big challenge in early 2000s.

Synthetic design was first reported by Elias James Corey. It is a formal approach about planning a synthesis before carrying it out. In this method a backward synthesis is planned from the product to simple precursors, using a set of rules in such a way that makes the synthesis achievable [5].

1.1. Isatin & Oxindole

Isatin, also known as tribulin, indoline-2,3-dione or indole-1*H*-2,3-dione (Figure 2), is a time-honored natural product found in the plants of genus *Isatis*, *Calanthe discolor* and in *Couroupita guianensis Aubl*. It was first synthesized by the oxidation of indigo dye by Erdman and Laurent in 1840, and its present structure was proposed by Kekule (Scheme 1). Isatin can be found in mammalian tissues, metabolic derivative of adrenaline [6]. It forms a blue dye known as blue indophenin when mixed with sulfuric acid and crude benzene [7].

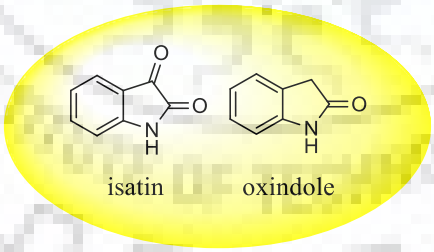
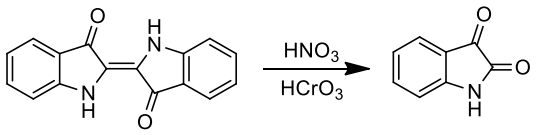


Figure 2: Structures of isatin and oxindole.

One of its derivatives known as oxindole having carbonyl functionality at second position in the five membered cyclic system (Figure 1), found in *Uncaria tomentosa* and in body fluids [8]. Oxindoles are found as integral part in many important natural products and biologically privileged scaffolds [9–13].



Scheme 1: First synthesis of isatin.

Isatin and its analogoues have become an important field of research especially in organic and medicinal chemistry because of interesting findings, which uncovered their potential as antioxidant, antitubercular, antitumor, antimicrobial, antidepressant, cytotoxic, antiviral, spermicidal, anticonvulsant, anti-corrosive, antiepileptic, and analgesic properties in recent years [14–27] (Figure 3).

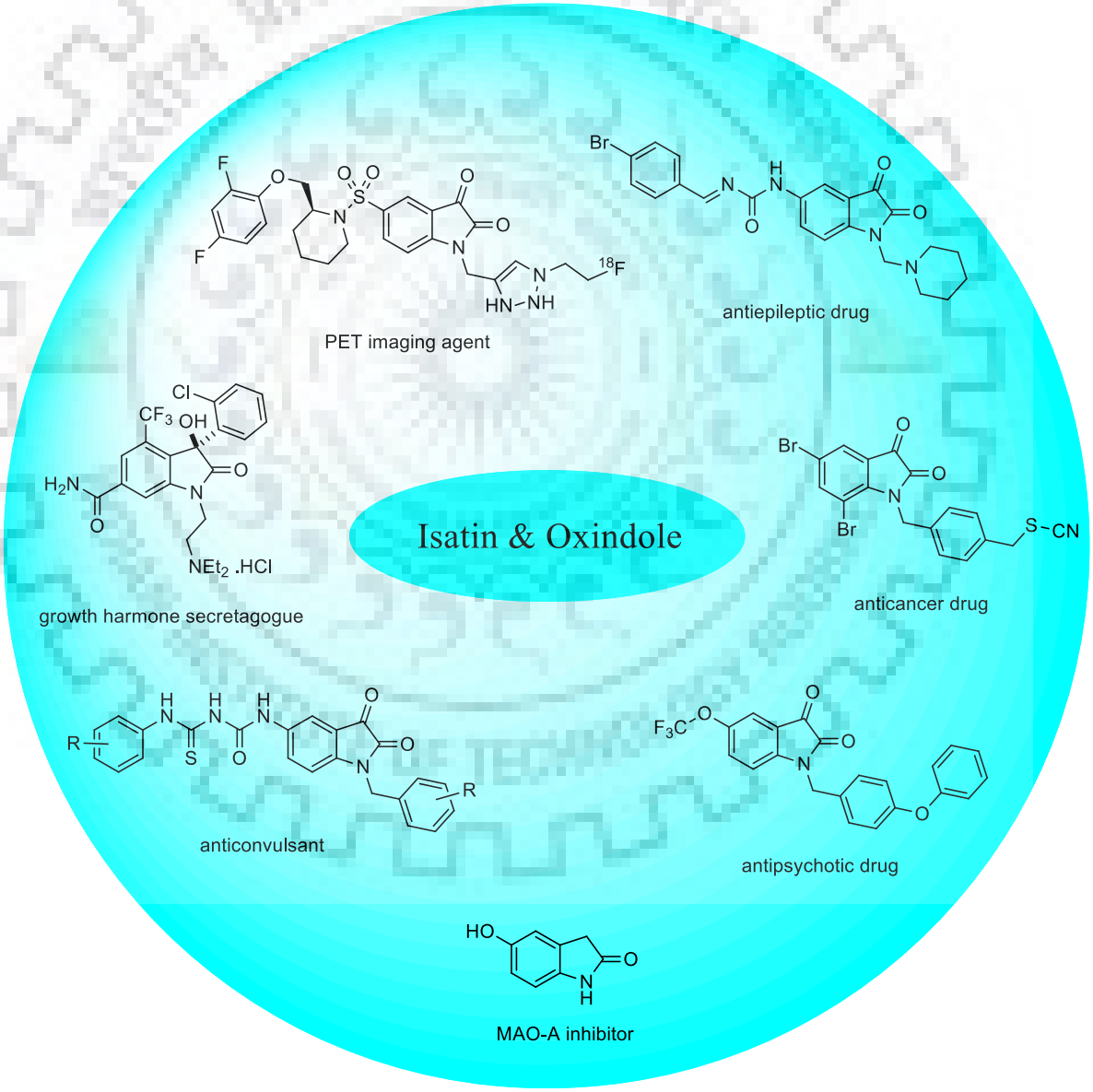
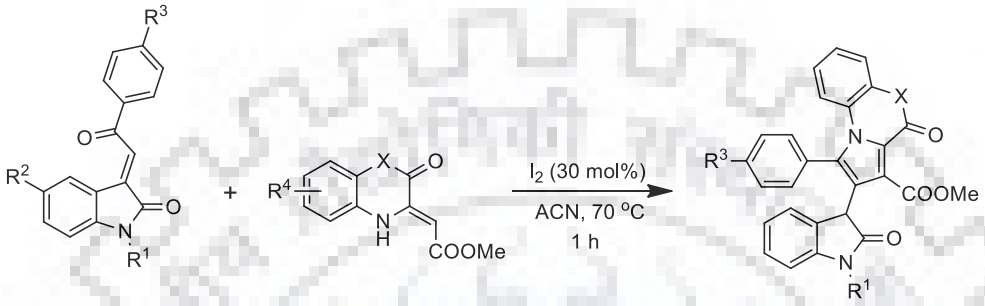


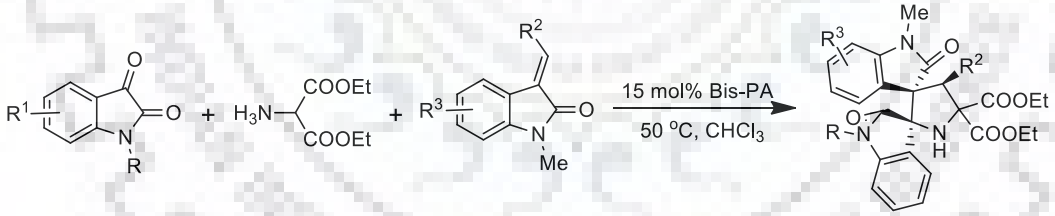
Figure 3: Medicinally important isatin and oxindole scaffolds.

In 2017, our group established the synthesis of highly substituted polyheterocyclic pyrroles from 3-ylidene oxindoles and benzoxazines in the presence of iodine in a highly regioselective manner. The protocol works under mild conditions and products can be isolated by simple filtration in good to excellent yields, making this an environmentally benign methodology. This one-pot protocol is highly atom economic and involves the formation of contiguous C–C and C–N bonds through a cascade approach [28] (Scheme 2).



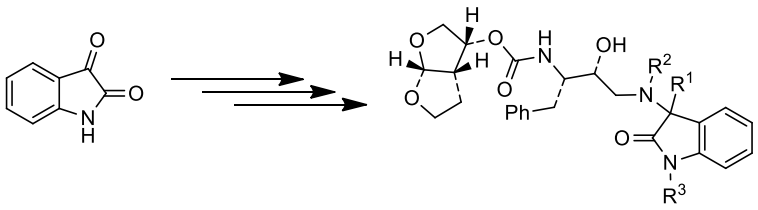
Scheme 2: Synthesis of multisubstiuted pyrroles.

Dai *et al*. introduced a novel bis-phosphoric acid catalyst for the synthesis of 3′-pyrrolidinyldispirooxindole *via* 1,3-dipolar cycloadditions through dual activation strategy. The spirooxindole products were synthesized in a highly stereoselective fashion from isatin-derived azomethine and methyleneindolinones in excellent enantioselectivity [29] (Scheme 3).



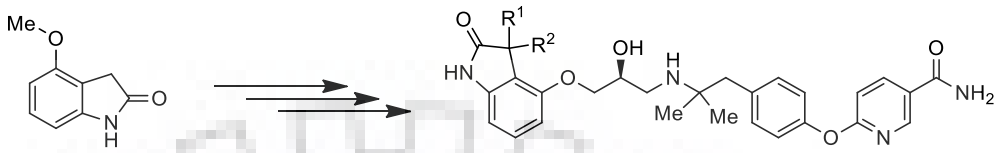
Scheme 3: Construction of 3,3-pyrrolidinyldispirooxindoles.

Mitsuya and co-workers discovered oxindole derived novel HIV-1 protease inhibtors. After design and synthesis of spirocyclic systems with different substituents and ring sizes, they evaluated anti HIV-protease activity of the products. They also investigated the potency of spiro oxyindoles systems as P20-ligands and found that acyclic inhibitors are considerably more potent than their cyclic counterparts [30] (Scheme 4).



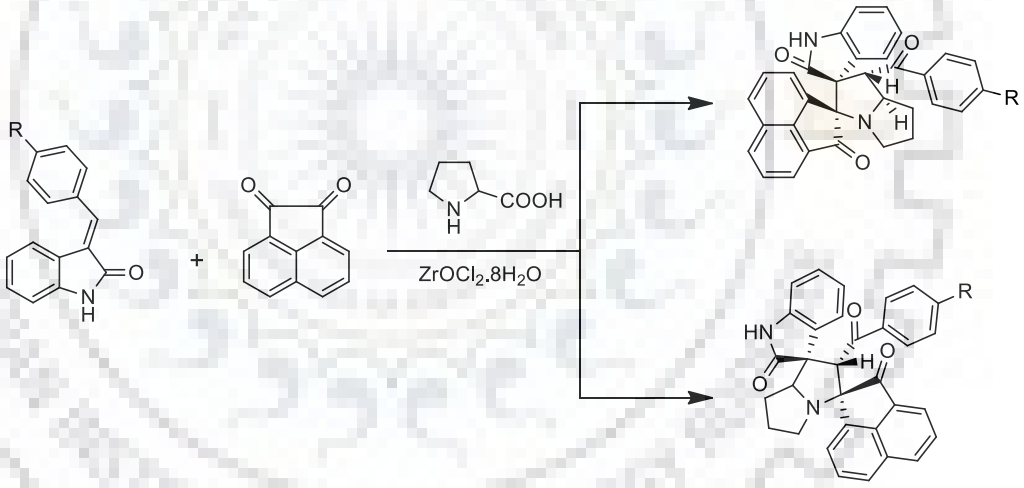
Scheme 4: Synthesis of oxindole-derived protease inhibitors.

Jesudason and co-workers revealed a series of oxindole b3 adrenergic receptor agonists. They carried out multistep synthesis from 4-methoxyindolin-2-one leading to the formation of 3-isopropyloxindole derivatives followed by structure activity relationship studies and evaluated the effect of steric bulk in the 3-position of oxindole in modulating rat atrial tachycardia in vitro [31] (Scheme 5).



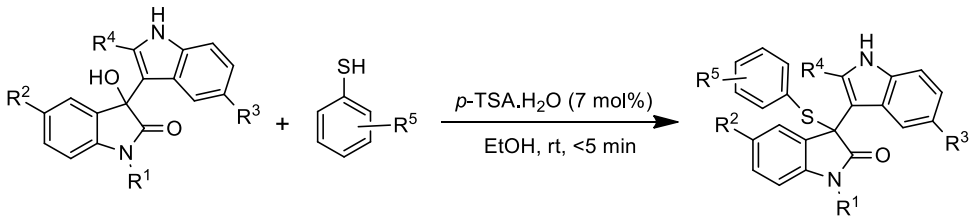
Scheme 5: Synthesis of b3 adrenergic receptors agonists.

Babu *et al.* explored [3 + 2] cycloaddition reactions for the synthesis of dispiro-oxindolopyrrolidines and dispiro-pyrrolizidines in the presence of solid supported zirconium oxychlorideoctahydrate catalyst. The protocol delivered the products in high regio- and stereo-selectivity under mild set of reaction conditions from acenaphthenequinone, sarcosine and L-prolineand 3-ylidene oxindoles in good yields [32] (Scheme 6).



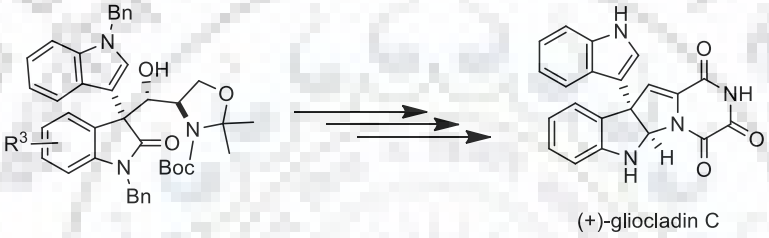
Scheme 6: $ZrOCl_2.8H_2O$ mediated synthesis of novel dispiroheterocycles.

Our group demonstrated the sulfenylation of 3-hydroxy bisindoles in the presence of *p*-TSA.H_2O. The methodology provides an environmentally benign catalytic approach through S_N1 catalytic pathway regioselectively to furnish C-3 substituted oxindoles. The mechanism is further supported by theoretical studies. All the products were obtained in excellent yield [33] (Scheme 7).



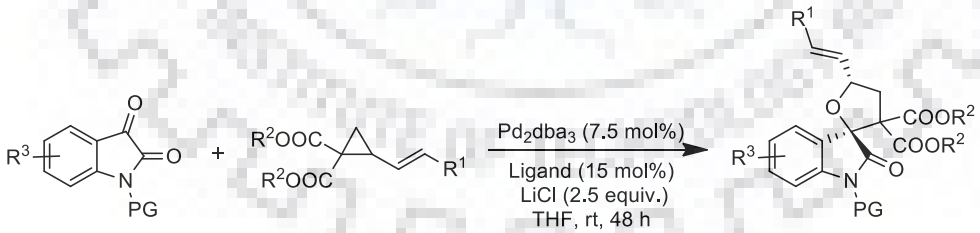
Scheme 7: *p*-TSA·H_2O-catalyzed C-3 functionalization of 3-hydroxy bisindoles.

Shin and co-workers reported the total synthesis of gliocladin C starting from simple substrate like isatin. The protocol was designed and executed in 21 steps including enantioselective Mukaiyama aldol reaction with overall yield of 4% and well-established absolute configuration at stereogenic centers. This was the first report for the synthesis of this marine alkaloid derived from fungas [34] (Scheme 8).



Scheme 8: Total Synthesis of (+)-gliocladin C.

Mei *et al*. disclosed the synthesis of spirooxindoles from *N*-protected isatins and vinylcyclopropanes in the presence of $Pd_2(dba)_3$ and imidazoline-phosphine as a novel ligand to furnish the products in excellent diastereo- and enantioselectivities with good yields. The reaction followed [3 + 2] cycloaddition and the product was utilized further to carry out important conversions [35] (Scheme 9).



Scheme 9: Palladium-catalyzed [3 + 2]-cycloaddition of vinyl cyclopropanes.

1.2. Domino reactions

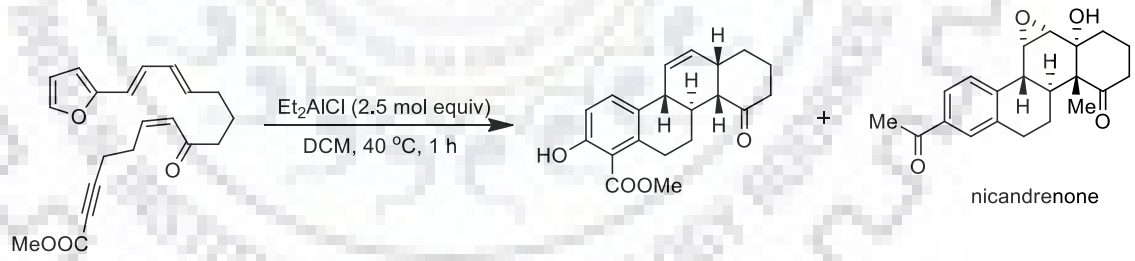
The domino reaction follows a sequence of transformations resulting in the formation of two or more bonds (usually C–C) through the involvement of the functionalities generated under the reaction conditions without adding any other promoter in one-pot manner. It is obvious that environment friendly protocols are in great demand and hence an exponential increase in utilization of this concept have been observed in the last few decades [36, 37].

Domino reactions are broadly divided into 5 types:

1. Electrophilic domino reactions
2. Nucleophilic domino reactions
3. Radical domino reactions
4. Pericyclic domino reactions
5. Transition metal catalyzed domino reactions

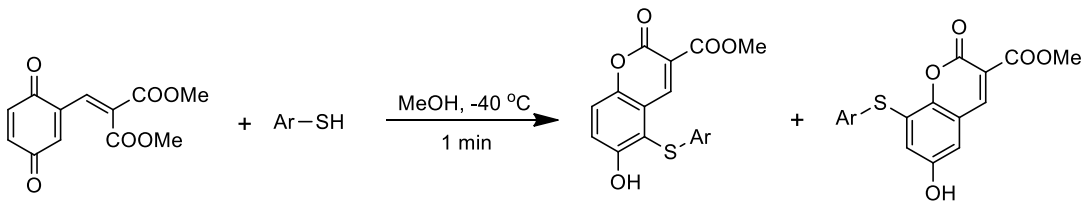
In 1992 Heathcock performed the total synthesis of dihydro-proto-daphniphylline using enamine-iminium ion chemistry [38]. In 1999 Corey revealed the total synthesis of (–)-aspidophytine utilizing the same concept [39]. Later the same group reported the total synthesis of glabrescol by sequential epoxide openings [40]. In 2003, Holton displayed the total synthesis of hemibrevetoxin B by epoxy-olefin cyclization in a domino fashion [41]. Qin and co-workers reported total synthesis of (+)-perophoramidine in 2010 [42]. As domino reactions are helpful to carry out multistep syntheses in a single pot and therefore directly affect the usage of solvents, reagents, energy as well as the human labour [43–50].

Sherburn and co-workers reported the synthesis of nicandrenone, an insect repellent and antifeedant agent. The domino strategy involved intramolecular Diels-Alder reactions in the formation of four rings in a sequential manner. This Lewis acid mediated approach allowed creation of high molecular complexity in one single step [51] (Scheme 10).



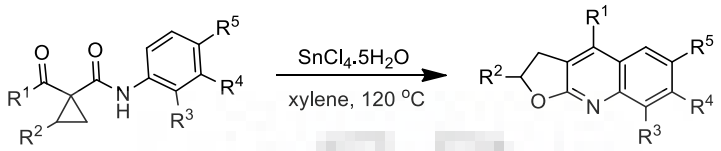
Scheme 10: Construction of tetracyclic nicandrenone scaffolds.

Our group demonstrated Michael addition initiated domino strategy to accomplish the synthesis of biologically important coumarin aryl sulphides from *p*-benzoquinones and thiophenols. All the products were obtained in good to excellent yields and the observed regioselectivity was further supported by theoretical studies [52] (Scheme 11).



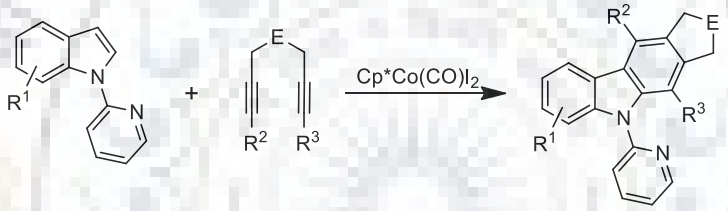
Scheme 11: Synthesis of coumarin aryl sulfides through domino strategy.

Zhang *et al*. reported $SnCl_4$ promoted domino approach for the synthesis of furoquinoline derivatives, a class of useful bioactive scaffolds known for their wide pharmacological profiles. The strategy utilized the doubly activated cyclopropanes to undergo ring-opening/recyclization in highly chemo- and regioselective manner [53] (Scheme 12).



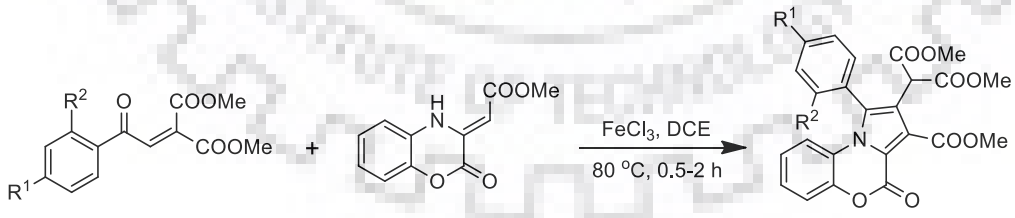
Scheme 12: Synthesis of furo[2,3-*b*]quinolones.

Wang and co-workers disclosed cobalt catalysed protocol for the highly regioselective synthesis of carbazole scaffolds *via* C–H activation strategy of indoles followed by domino annulation reaction with diynes. This reaction displayed broad substrate scope and high functional group compatibility [54] (Scheme 13).



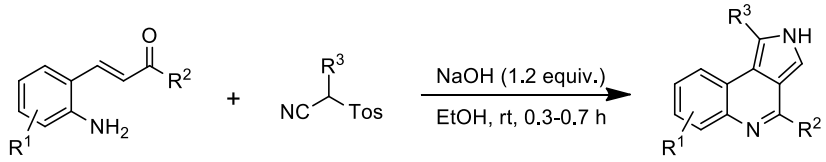
Scheme 13: Co-catalyzed regioselective synthesis of cyclopenta[*b*]carbazoles.

Our group reported the synthesis of highly substituted complex pyrrolobenzoxazines from aroylmethylidene malonates and benzoxazinones in the presence of $FeCl_3$. The presented protocol showing high functional group tolerance with wide substrate scope and furnished the desired products in high yields with excellent regioselectivity [55] (Scheme 14).



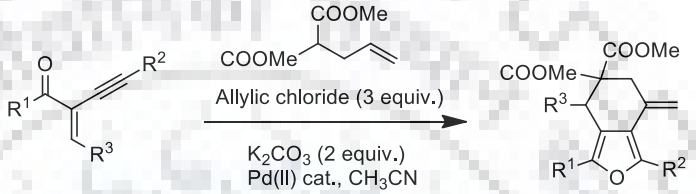
Scheme 14: $FeCl_3$ mediated synthesis of pyrrolobenzoxazine derivatives.

Hu *et al*. explored a domino strategy to accomplish the synthesis of pyrrolo[3,4-*c*]quinolines in the presence of sodium hydroxide from aminochalcones and tosylmethyl isocyanides. The reaction involves the formation of three bonds and two rings during the course of reaction with high selectivity *via* formal [3 + 2] cycloadditon/cyclization [56] (Scheme 15).



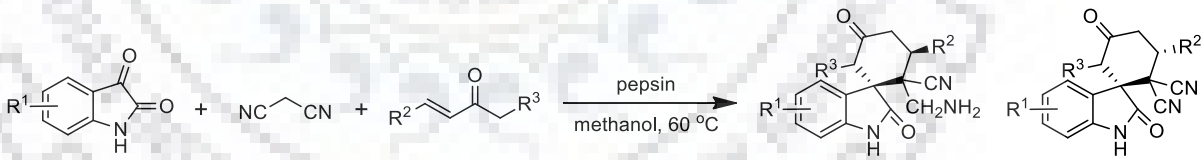
Scheme 15: NaOH promoted synthesis of pyrrolo[3,4-*c*]quinolones.

Li *et al*. reported the syntheses of multifunctionalized cyclopentanes, cyclohexanes and hexahydro-1*H*-inden-4(2*H*)-ones from electron-deficient enynes and malonate-derived α,β-unsaturated esters/ketones. The reaction involved base-catalysed stereoselective domino transformations [57] (Scheme 16).



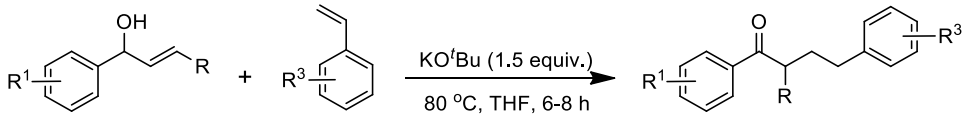
Scheme 16: Base-catalyzed synthesis of multi-functionalized cyclopentanes.

Guan and co-workers established a novel biocatalytic strategy for the synthesis of spirocyclicoxindole systems from isatin, malononitrile and benzalacetone. The use of pepsin from porcine, makes the protocol environment friendly and makes the reaction to move on a domino path *via* a series of Knoevenagel/Michael/Michael reactions furnishing the products with yields up to 99% with excellent diastereoselectivity with a wide substrate scope [58] (Scheme 17).



Scheme 17: Porcine pepsin catalyzed synthesis of spirooxindoles.

Satyanarayana and co-workers introduced a metal-free strategy for internal hydrogen transfer for the synthesis of alkylated ketones from allylic alcohols and styrenes in the presence of KO^{t}Bu. The protocol utilizes domino isomerization and alkylation through *in situ* generated ketones in a domino fashion and furnished the desired products in good yields [59] (Scheme 18).

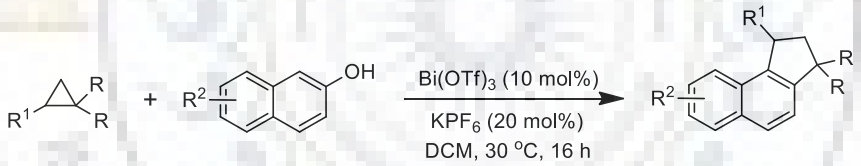


Scheme 18: KO^{t}Bu-promoted synthesis of alkylated ketones.

1.3. Donor-acceptor (D-A) cyclopropanes

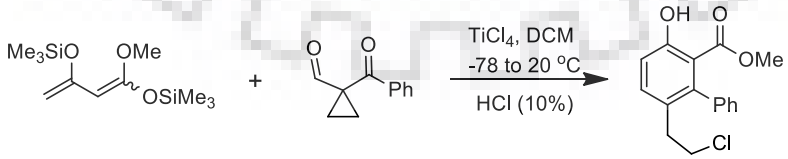
Cyclopropanes are very high in energy, having ring strain of nearly 115 kJmol^{-1} and are kinetically inert. These molecules are less likely to give up their ring structures [60]. To utilize the ring strain of cyclopropanes in a flourishing way, electron-donating and electron-accepting groups were attached to it, thus a new term evolved, so called donor-acceptor (D-A) cyclopropanes. It was first introduced by Reissig in 1980s, however activated cyclopropanes carried only electron accepting groups were known in 1960s and 1970s [61]. Their high reactivity profile might be well understood in terms of 1,3-zwitterionic relationship. These molecules are under intense consideration to carry out various enantioselective transformations, domino reactions because of their key role in total syntheses of various natural products [62–64].

Biju and co-workers reported the Lewis acid catalysed tunable reactivity of cyclopropanes while treating with 2-naphthols. The protocol leads to the formation of naphthalene-fused cyclopentanes when treated in the presence of $Bi(OTf)_3$ and functionalized 2-naphthols when $Sc(OTf)_3$ was used as a promoter. All the product were furnished in good to high yields with high regioselectivity [65] (Scheme 19).



Scheme 19: Bismuth-catalyzed dehydrative [3 + 2] cyclopentannulation.

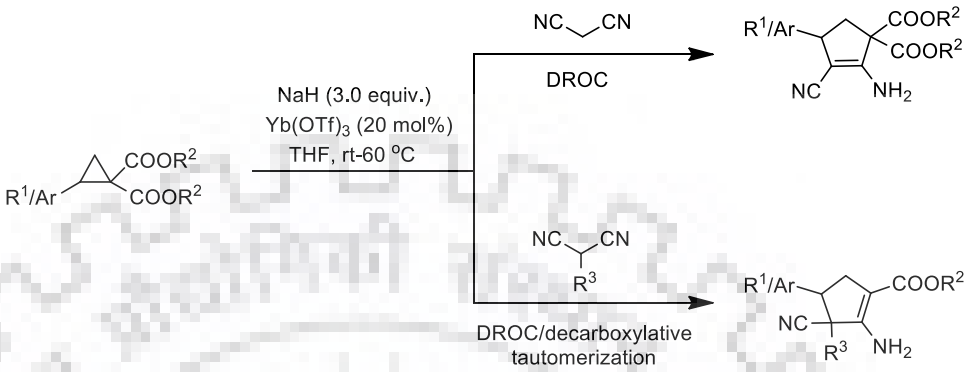
Riahi *et al*. revealed the regioselective synthesis of 3-aryl-4-(chloroethyl)phenols by treating 1,3-bis(silyloxy)-1,3-butadienes and 1-benzoyl-1-formylcyclopropane in the presence of $TiCl_4$. The reaction underwent in domino fashion through regioselective [3 + 3] cyclization and homo-Michael reactions [66] (Scheme 20).



Scheme 20: $TiCl_4$-mediated synthesis of 6-aryl-5-(chloroethyl)salicylates.

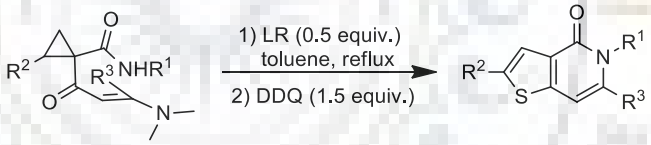
Ghorai and co-workers explored domino ring-opening cyclization (DROC) strategy of donor-acceptor cyclopropanes for the construction of carbocyclic from activated cyclopropanes in the presence of sodium hydride and $Yb(OTf)_3$. The reaction produced 4,5-dihydropyrroles as final products when the D-A cyclopropanes were treated with

malononitrile *via* DROC however, reaction followed DROC/decarboxylative tautomerization with 2-benzylmalononitrile leading to the formation of enaminonitriles and *β*-enaminoesters and the authors also presented the enantioselective variants of the above strategies [67] (Scheme 21).



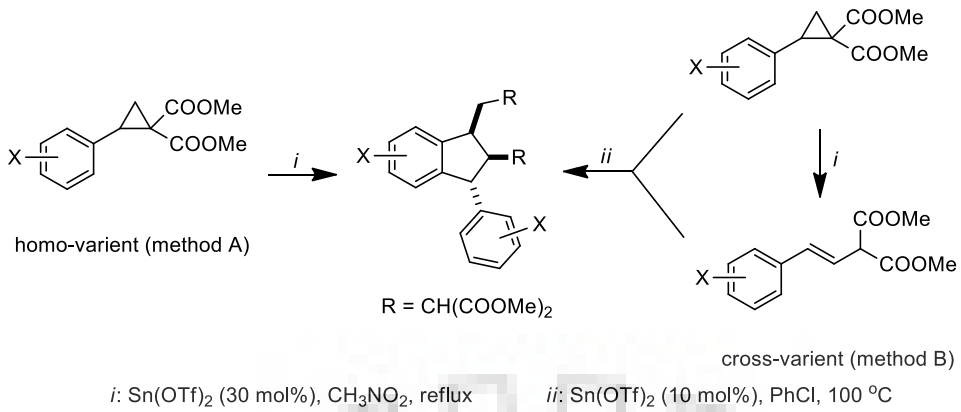
Scheme 21: Syntheses of enaminonitriles and *β*-enaminoesters.

Huang *et al*. utilized the activating capability of Lawesson's reagent to carry out the synthesis of thieno[3,2-*c*]pyridines derivatives. The protocol involves one-pot three-step synthesis *via* sequential reactions in presence of DDQ as oxidant from simple substrate [68] (Scheme 22).



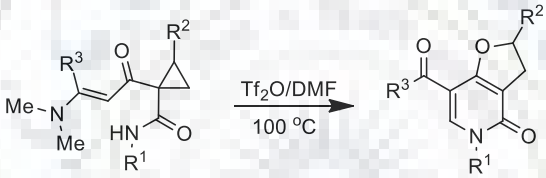
Scheme 22: Synthesis of thieno[3,2-*c*]pyridinones.

Ivanova *et al*. established a novel route for the synthesis of polyoxygenated indanes and cyclopentannulated heteroarene derivatives and these products were revealed as good cytotoxic agents while being non-toxic to normal cells. Acid catalyzed protocols with easy handling and excellent control over chemo-, regio- and diastereoselectivity [69] (Scheme 23).



Scheme 23: Synthesis of indanes and cyclopentannulated hetarenes.

Huang *et al*. triflic anhydride mediated domino reaction to excess 2,3-dihydrofuro[3,2-*c*]pyridin-4(5*H*)-ones from 1-carbamoyl-1-dimethylaminoalkenoylcyclopropanes in DMF. The protocol involves a sequence of formylation, intramolecular cyclization followed by ring-enlargement [70] (Scheme 24).



Scheme 24: One-pot synthesis of 2,3-dihydrofuro[3,2-*c*]pyridin-4(5H)-ones.

1.4. Synthesis of *β*-hydroxy sulfides

Carbon–heteroatom bond formation has been a highly flourishing field in the recent time because of its tremendous applications in organic synthesis. A large number of reactions known for their construction and most of them utilize transition metal catalysis. Therefore, this field is under further exploration to develop green synthetic protocols [71–74]. Synthesis of *β*-hydroxyl sulfides most likely involves the construction of C–S or C–O bonds or both. Such scaffolds have been integral part of leukotrienes such as LTC_4, LTD_4 and LTE_4, eicosanoid inflammatory mediators produced in leukocytes, which makes it more interesting for synthetic chemists [75, 76] (Figure 4). There have been many reports known in the literature for the synthesis of *β*-hydroxy sulfides and some of them are described here.

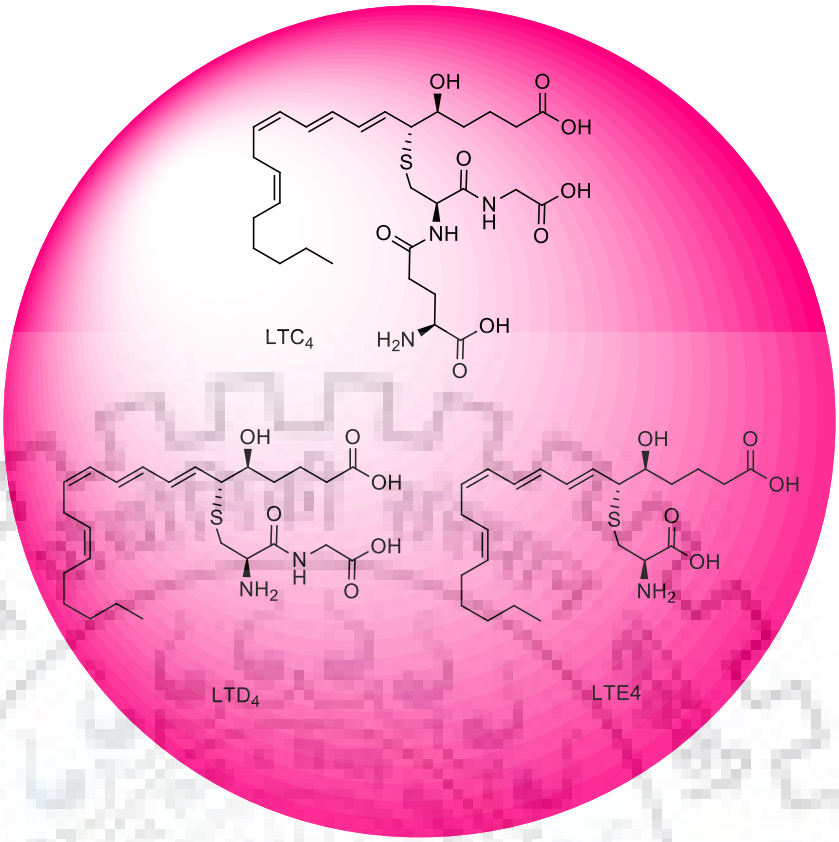
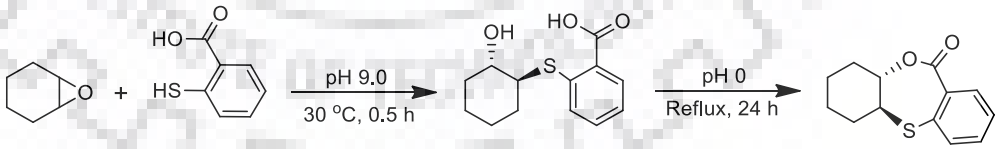


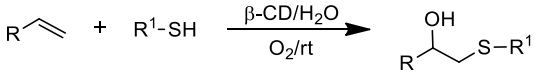
Figure 4: Structures of leukotrienes LTC_4, LTD_4 and LTE_4 having *β*-hydroxy sulfide core.

Vaccaro and co-workers reported the diasteroselective and regioselective synthesis of benzo[*e*]1,4-oxathiepin-5-ones under solvent-free conditions by nucleophilic ring opening of 1,2-epoxides with thiosalycilic acid in a one-pot manner with very good yields. Thiosalicylic acid itself activated the reaction with anti-stereoselectivity. Catalyst-free neat reaction conditions make this protocol atom-economical and environmentally benign [77] (Scheme 25).



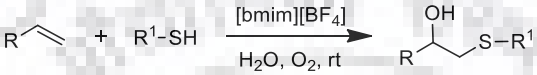
Scheme 25: One-pot synthesis of benzo[*e*]1,4-oxathiepin-5-ones.

Surendra *et al*. for the first time utilized cyclodextrin (CD) to excess *β*-hydroxysulfides directly from alkenes. CD being nontoxic and safe from metabolic point of view, this protocol is environmental friendly. Further the reaction was carried out under mild conditions in water as solvent with short reaction time and high selectivity. The method has become more economical by recycling the catalyst to generate the products in high efficiency [78] (Scheme 26).



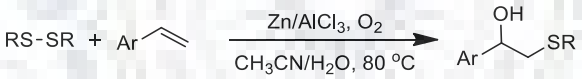
Scheme 26: Cyclodextrin catalyzed synthesis of *β*-hydroxy sulfides.

Rajendar and co-workers developed the first of its kind activation of inert alkenes using an ionic liquid for the construction of *β*-hydroxy sulfides from the reaction of terminal olefins and alkenes. These ionic liquid-catalyzed reaction makes available a green strategy by avoiding the use of heavy metals, Lewis acids also obviates aqueous workup for the isolation of the desired products with high selectivity with a recyclable catalyst [79] (Scheme 27).



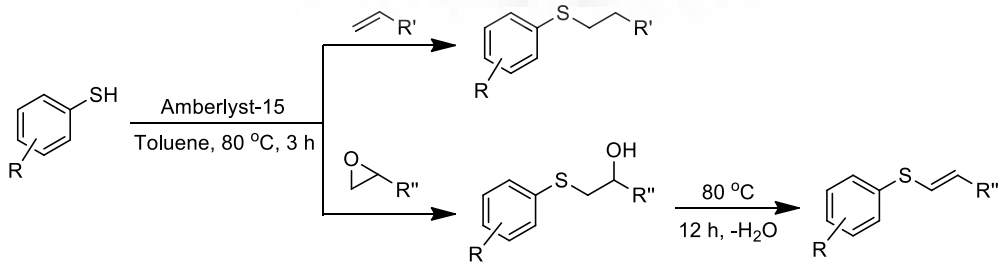
Scheme 27: liquid [bmim][BF_4] mediated synthesis of *β*-hydroxy sulfides.

Navidi and co-workers used thiolate anions in the reaction with styrenes for the synthesis of *β*-hydroxy sulfides. The reactions proceeded regioselectively in an anti-Markovnikov fashion under mild conditions leading to terminal olefin functionalization in short reaction time with simple precursors [80] (Scheme 28).



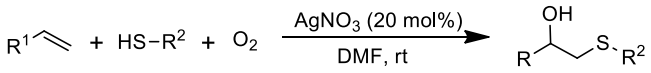
Scheme 28: Zn/$AlCl_3$ promoted synthesis of *β*-hydroxy sulfides.

Lanke *et al*. performed C–S bond construction under metal-free conditions using Amberlyst-15© reusable catalyst. The catalyst was reported to work up to five consecutive cycles effectively, without any loss in its activity, with high atom economy leading to the formation of diorganyl sulfides, *β*-hydroxy sulfides and phenyl(styryl)sulfanes in good to excellent yields regioselectively by anti-Markovnikov addition of thiols to alkenes and thiolysis of 1,2-epoxides [81] (Scheme 29).



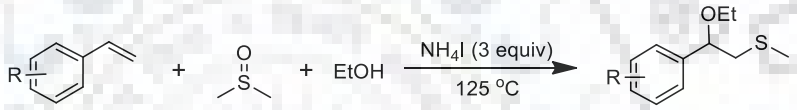
Scheme 29: Amberlyst-15 mediated anti-Markovnikov addition of thiols to alkenes/alkynes.

Singh *et al*. demonstrated an efficient synthesis of *β*-keto sulfones and *β*-hydroxy sulfides from olefins and thiophenols using silver nitrate as catalyst in one-pot operation. The protocol involves formation of C–O, C–S and S–O bonds through radical pathway followed by oxidation [82] (Scheme 30).



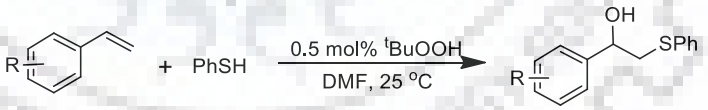
Scheme 30: $AgNO_3$ catalysed synthesis of *β*-hydroxy sulfides.

Li and co-workers displayed a novel synthesis of *β*-alkoxy methyl sulfides *via* NH_4I-mediated three-component oxysulfenylation reaction. The reaction shows broad substrate scope with easily affordable starting materials such as styrenes, DMSO and alcohols. Preliminary mechanistic studies were performed using TEMPO and BHT to ensure the radical pathways being followed through the course of reaction [83] (Scheme 31).



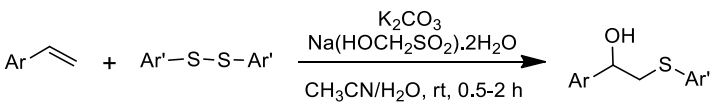
Scheme 31: NH_4I-promoted synthesis of *β*-alkoxy methyl sulfides.

Zou and co-workers carried out difunctionalization of alkenes by the reaction of aryl thiols with styrenes in presence of TBHP at room temperature without using any additive. Aerial oxygen was used as the only source of oxygen to afford hydroxyl sulfurization products in one-pot fashion in high yields [84] (Scheme 32).



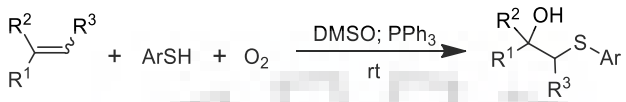
Scheme 32: *tert*-Butyl hydroperoxide mediated thiol−oxygen co-oxidation (TOCO) for hydroxysulfurization of styrenes.

Yadav and co-workers have developed a rongalite promoted synthesis of *β*-hydroxy sulfides from styrenes and disulfides under air at room temperature *via* a radical pathway leading to the desired product formation in good to excellent yields with high selectivity. Use of cheap promotor makes this protocol more economic [85] (Scheme 33).



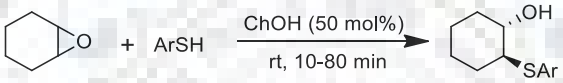
Scheme 33: Rongalite based aerobic hydroxysulfenylation of styrenes.

Wang *et al.* reported the synthesis of *β*-oxysulfoxides and *β*-hydroxy sulfides, the protocol provide switchable selectivity, scalable synthesis with a metal-free approach avoiding the use of any additive for the transformation. Mechanistic investigations were performed to get an insight of the reaction which explained the switchable selectivity of the presented work [86] (Scheme 34).



Scheme 34: Solvent enabled selective synthesis of *β*-oxysulfoxides and *β*-hydroxy sulfides.

Edrisi and co-workers studied the epoxides ring opening on treatment with aryl thiols in the presence of choline hydroxide, a biodegradable ionic liquid, which makes the protocol environmental friendly leading to the formation of *β*-hydroxy sulfides in excellent yields and short reaction time [87] (Scheme 35).



Scheme 35: Choline hydroxide mediated thiolysis of epoxides.

1.5. Synthesis of spirooxindoles

Oxindole moiety having spirocyclic system on C-3 position have a fascinating role in medicinal and natural products chemistry because of its presence in large number in bio-active scaffolds [88–102]. Therefore, it has been an important field of exploration in synthetic organic chemistry. Some of the recent examples involving construction of spirooxindolic systems are described here.

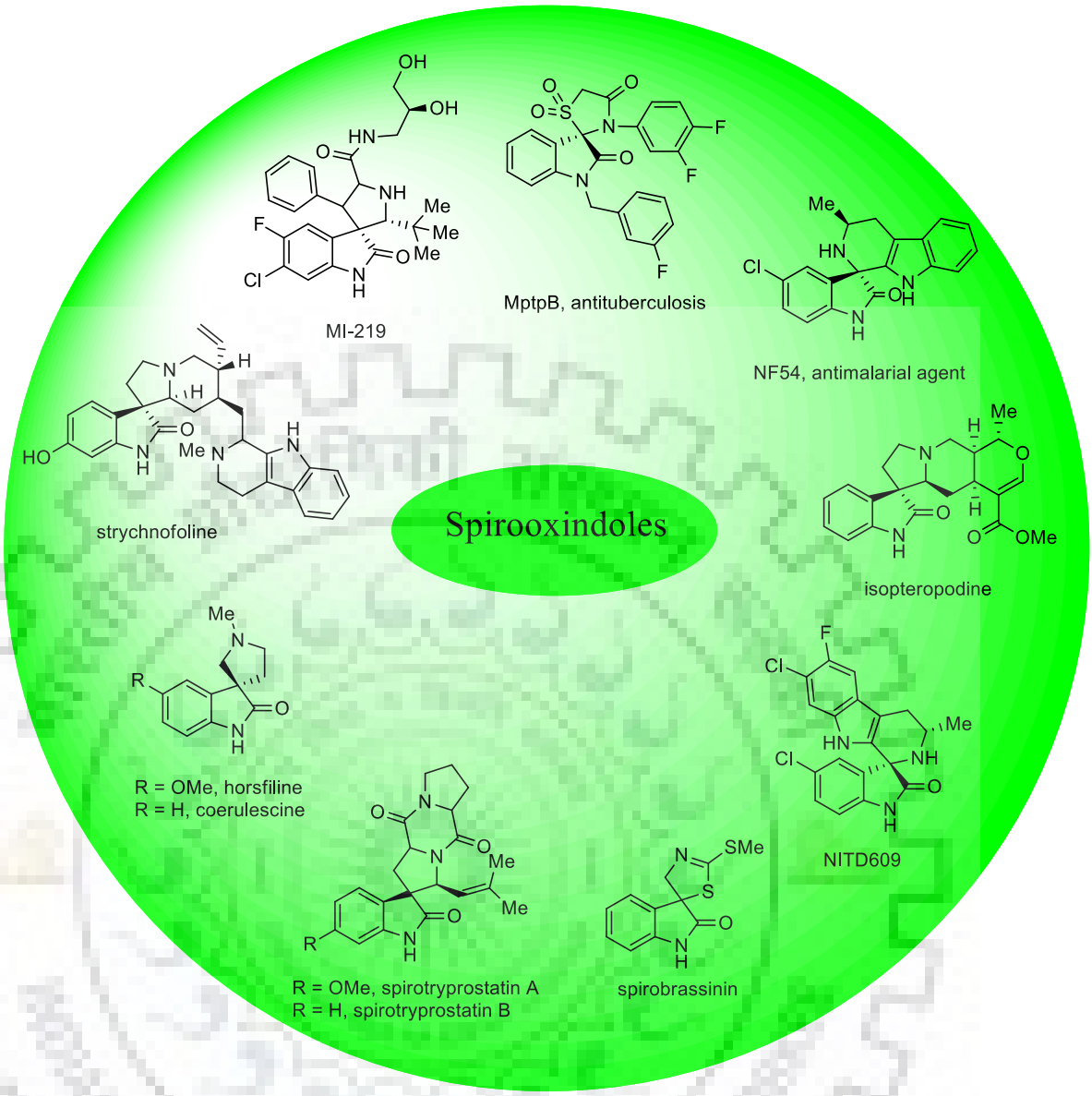
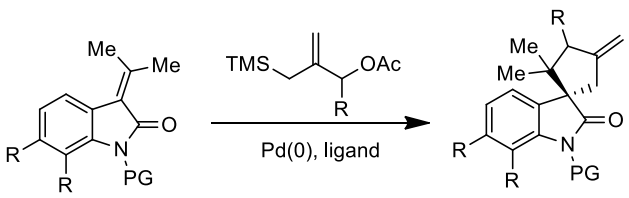


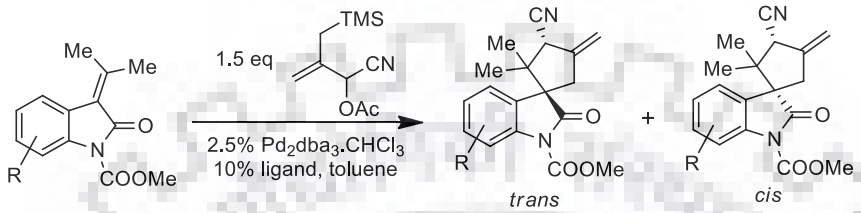
Figure 5: Some biologically important spirooxindoles.

Trost *et al*. disclosed rapid synthetic routes for the synthesis of spirocyclic oxindole alkaloids marcfortine B and marcfortine C through cycloadditions involving intramolecular Michael addition followed by radical cyclization. The reaction provides the spirooxindoles in excellent diastereo- and enantio-selectivity. Marcfortine B was synthesized in 25 steps and marcfortine C in 19 steps. A novel methodology for the functionalization of exocyclic olefin with an oxaziridine and a triethylaluminum promoted reduction of a nitrile selectively [103] (Scheme 36).



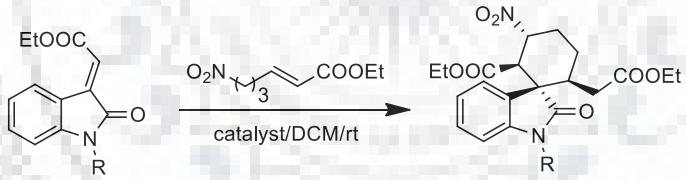
Scheme 36: Synthesis of marcfortine B and marcfortine C.

Silverman and co-workers reported [3 + 2] cycloaddition reaction for the synthesis of spirocyclic oxindolic cyclopentanes. The protocol works in the presence of palladium-catalyst with cyano-substituted Pd-TMM-complexes. Remarkably, different ligands were suggested to provide a set of complementary cycloadducts with opposite diastereoselectivity. The mild reaction conditions lead to the arrays of up to three stereo-centers in excellent diastereo- and enantio-selectivity [104] (Scheme 37).



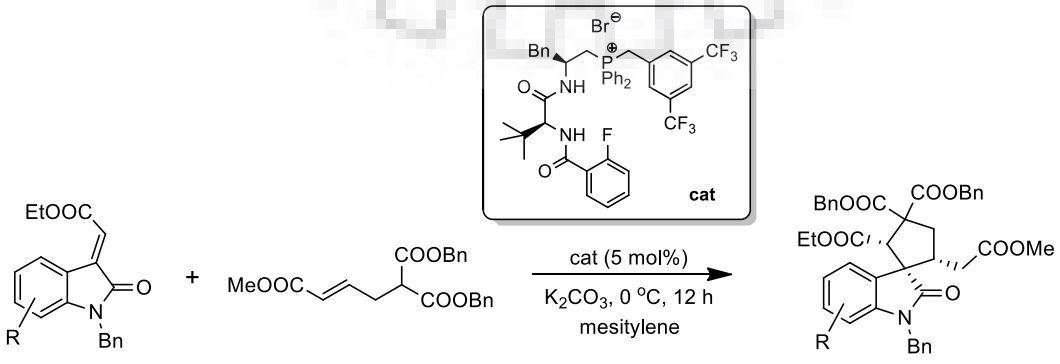
Scheme 37: Transition metal-catalyzed [3 + 2] cycloaddition to construct spirooxindoles.

Quintavalla and co-workers discovered the first ever synthesis of five- and six-membered *β*-nitro spirocarbocyclic oxindoles. Bifunctional thioureas were used to activate the reaction between 2-(2-oxoindolin-3-ylidene)acetic esters and nitroenoates in a Michael–Michael cascade fashion with a [4 + 2] or [3 + 2] spiroannulation for the formation of diversified polyfunctional spirocyclohexane derivatives with good yield and excellent diastereo and enantio-selectivity [105] (Scheme 38).



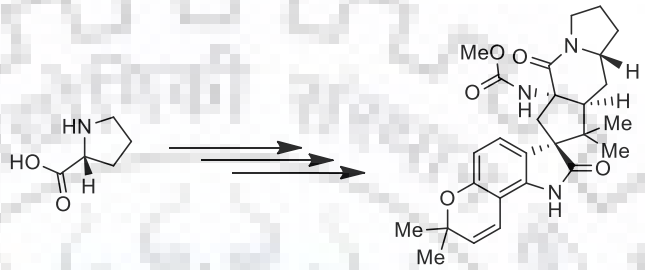
Scheme 38: Spiroannulations of 2-(2-oxoindolin-3-ylidene)acetic esters.

Shang and co-workers revealed chiral quaternary phosphonium salt as a novel catalyst to carry out a double Michael cascade reaction for the synthesis of spirocyclic oxindoles in good to excellent yields and high stereoselectivities [106] (Scheme 39).



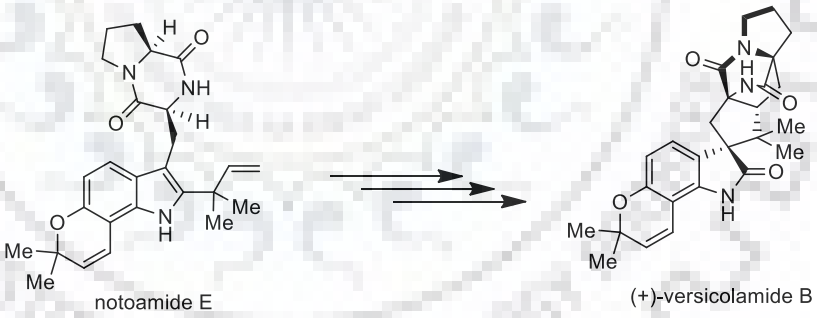
Scheme 39: Phosphonium salt catalyzed synthesis of spirooxindoles.

Sarpong and co-workers disclosed isolation and the total synthesis of prenylated indole alkaloid in their laboratory by following a disconnection approach. Starting the synthesis from a simple substrate *i.e.* D-proline and successfully accomplished the synthesis of desired *ent*-citrinalin B in 19 steps and cyclopiamine B in 21 steps. The biosynthetic consideration of the protocol brought highlights on the bicyclo[2.2.2]diazaoctane as an important precursor for the above mentioned transformation and established the structures of these metabolites [107] (Scheme 40).



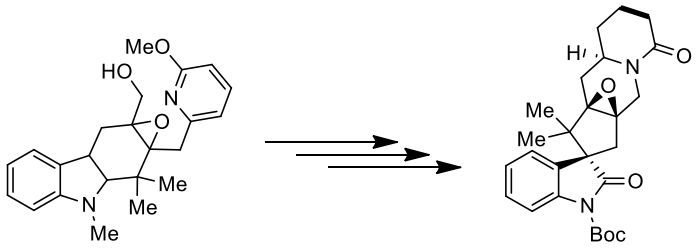
Scheme 40: Synthesis of citrinalin B intermediate.

Williams and co-workers carried out the total synthesis of each enantiomer of versicolamide B by developing the first ever experimental support for the biogenetic hypothesis that versicolamide B possibly arisen from IMDA reaction of an oxindolic substrate [108] (Scheme 41).



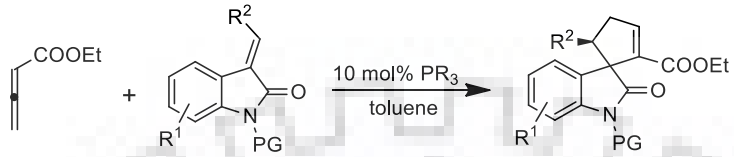
Scheme 41: Total synthesis of versicolamide B.

Mundal *et al*. established a strategy to construct the core of citrinadin natural products in racemic form by involving a methoxy pyridine alkylation, which evolved as an opportu-nity for the synthesis of fully substituted pentacyclic core of citrinadin [109] (Scheme 42).



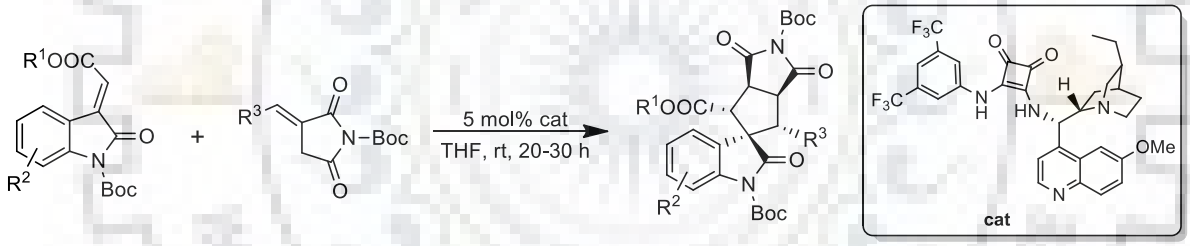
Scheme 42: Synthesis of the pentacyclic carbon skeleton of the citrinadin.

Marinetti and co-workers investigated phosphine based organocatalysts for the [3 + 2] cycloaddition of 2,3-butadienoate and (*E*)-3-benzylideneindolin-2-ones with excellent stereoselectivity to furnish spiroxindolic core containing two contiguous stereocentres, including one quaternary centre in good yield with high enantioselectivity [110] (Scheme 43).



Scheme 43: Phosphine mediated synthesis of spirooxindoles.

Zhao *et al*. successfully demonstrated bifunctional tertiary amine–squaramide catalysed chiral synthesis of spirooxindoles and also showcased one-pot four-component reaction. Reaction underwent double Michael reactions in a cascade manner and generating the desired products with excellent diastereoselectivity and enantioselectivity [111] (Scheme 44).

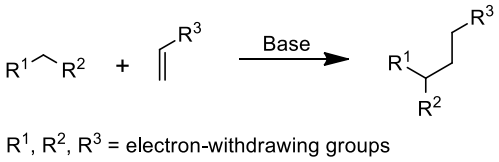


Scheme 44: Bifunctional squaramide-catalyzed synthesis of spirooxindoles.

1.6. Michael addition in organic synthesis

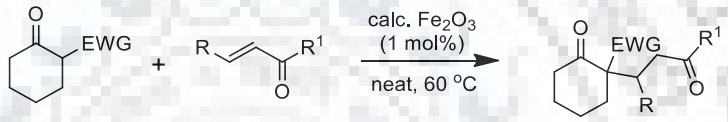
Michael reaction or Michael addition was first proposed by Arthur Michael in 1887. It is one of the most-frequently used methods for the construction of C–C bonds in organic chemistry. It involves the nucleophilic addition of carbanion or another nucleophile (commonly known as Michael donor) to an α,β-unsaturated compound [112]. There has been extensive use of Michael addition in carrying out important conversions. Matsunaga and co-workers disclosed the total synthesis of chimonanthine, folicanthine, and calycanthine [113]. In 2012, Liu *et al*. reported the total synthesis of (−)-chimonanthine, and in 2013, Yao's group revealed the total synthesis of lycopodium alkaloids [114,115]. Nagorny and co-workers displayed the total synthesis of cannogenol-3-O-α-L-rhamnoside

[116]. Many other reports are available in literature on the synthesis of target compounds that were achieved by employing Michael addition concept.



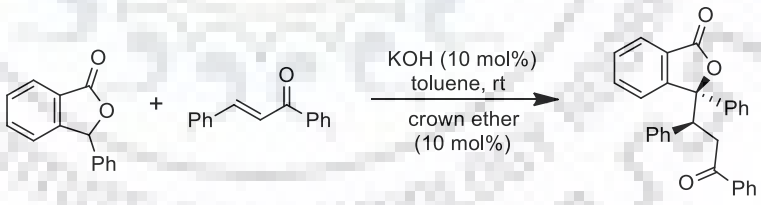
Scheme 45: General Michael addition reaction.

Jebari *et al*. described the synthesis of several iron oxides nanoparticles and used them as catalyst to access C–C bond formation through Michael addition of 1,3-dicarbonyl compounds onto methyl vinyl ketone under neat conditions. On optimization, they found potential catalytic activity as 1 mol% loading was sufficient to furnish the desired products in good to excellent yields [117] (Scheme 46).



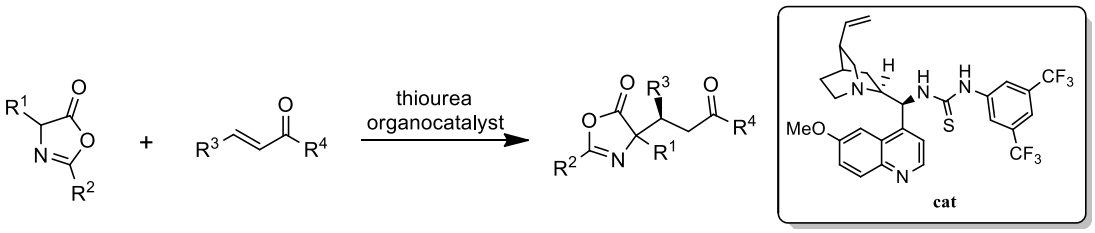
Scheme 46: Fe_2O_3-catalyzed Michael addition between keto ester and vinyl ketones.

Sala and co-workers demonstrated the first arylogous Michael addition of 3-aryl phthalides with chalcones in the presence of catalytic amount of KOH or K_3PO_4 and dibenzo-18-crown-6. The reaction proceeds under mild conditions to generate single diastereomers nearly in all cases in good to high yields [118] (Scheme 47).



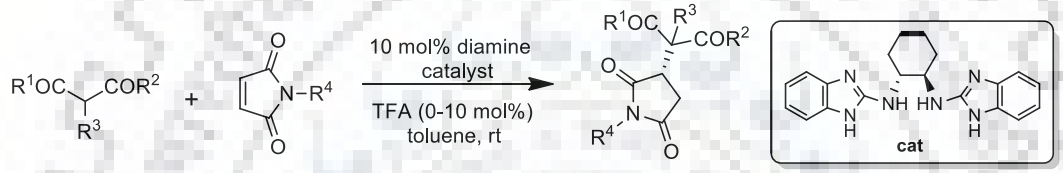
Scheme 47: Crown ether catalysed synthesis of 3,3-disubstituted phthalides.

Zhang *et al*. showcased quinine-derived bifunctional thiourea tertiary amine as a catalyst to carry out Michael addition of azalactones to *o*-hydroxychalcone derivatives. The protocol followed C-2 regioselectivity leading to the formation of pseudooxazol-5-one derivatives with all-carbon quaternary stereogenic centers in moderate to good yields with excellent diastereoselectivity and enantioselectivity. To understand the mechanism of the reaction and prediction of the transition state during the course of reaction, circular dichroism (CD) spectroscopy and density functional theory (DFT) were used [119] (Scheme 48).



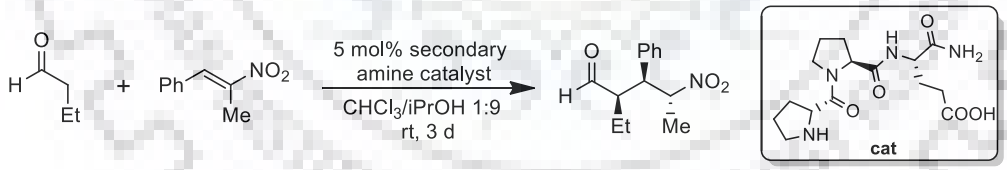
Scheme 48: Stereoselective Michael addition of azalactones on chalcones.

Najera and co-workers discovered a novel recyclable chiral 2-aminobenzimidazole catalyst to perform enantioselective conjugate addition of different 1,3-dicarbonyl compounds to maleimide and *N*-substituted maleimides to furnish various Michael adducts. In addition to the broad synthetic scope, the reaction provides excellent yields and enantioselectivity when executed on gram scale at room temperature [120] (Scheme 49).



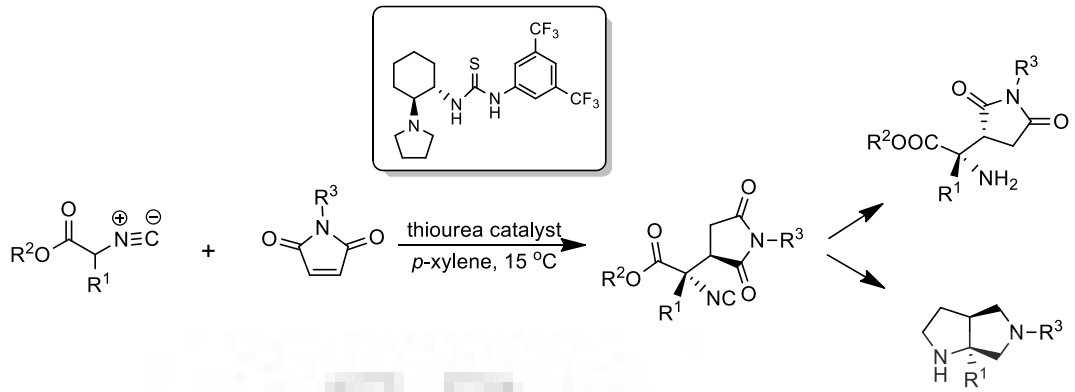
Scheme 49: Synthesis of α-branched succinimides.

Wennemers and co-workers displayed highly chemo-selective synthesis of γ-nitroaldehydes in the presence of peptidic catalysts from aldehydes and substituted nitrostyrenes. Low catalyst loading and the investigations through mechanistic studies clarify the role of peptide catalysis in providing the high yield with excellent stereoselectivities [121] (Scheme 50).



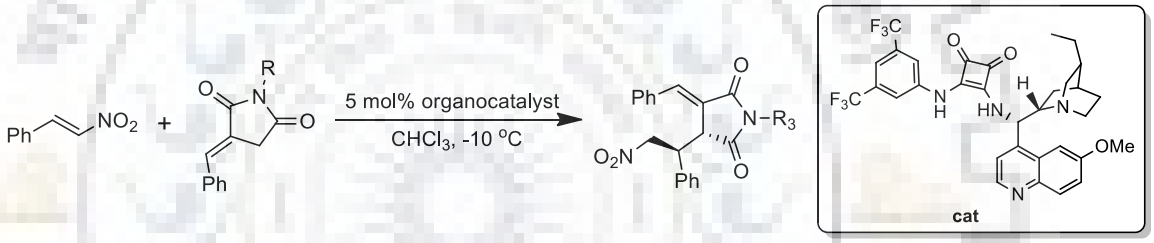
Scheme 50: Peptide catalysed synthesis of γ-nitroaldehydes.

Wang and co-workers demonstrated the synthesis of various chiral succinimide derivatives having adjacent quaternary and tertiary stereogenic-centers in the presence of organocatalyst, further transformation of the product led to the synthesis of h5-HT1d receptor agonist scaffolds in excellent selectivity and good to excellent yields [122] (Scheme 51).



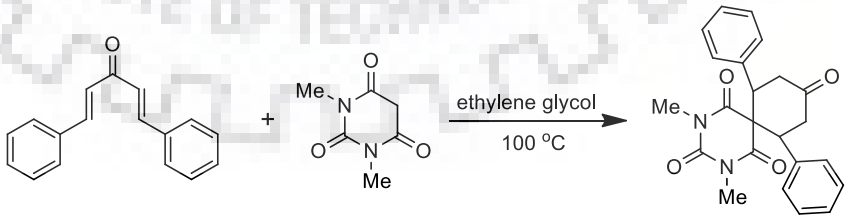
Scheme 51: Organocatalytic synthesis of chiral succinimide derivatives.

Du and co-workers displayed asymmetric Michael addition of *α*-alkylidene succinimides with nitrostyrenes to access functionalized succinimides in good to excellent yields. Presence of chiral squaramide organocatalyst made the protocol highly selective leading to excellent diastereo- and enantio-selectivities under mild reaction conditions on gram scale as well [123] (Scheme 52).



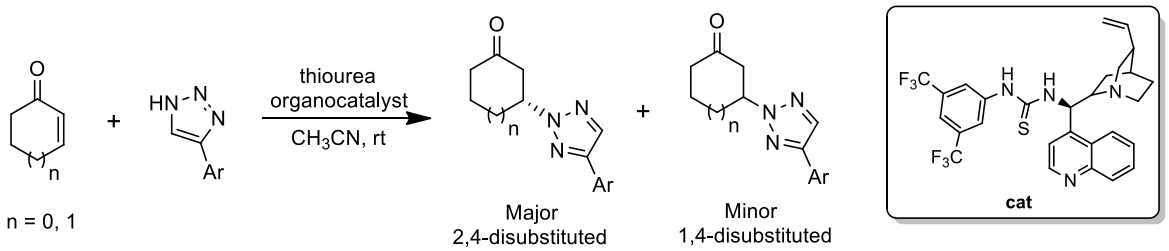
Scheme 52: Bifunctional squaramide-catalyzed catalysed synthesis of functionalized succinimides.

Khurana and co-workers utilized active methylene compounds for double Michael addition of 1,5-diaryl-1,4-pentadien-3-one in ethylene glycol in catalysts-free environment to synthesis diazaspiro compounds. The reaction worked smoothly with *N*,*N*-dimethyl barbituric acid, barbituric acid, thio-barbituric acid and *N*,*N*-diphenylthiobarbituric acid at 100 °C and provided all the products in good yields [124] (Scheme 53).



Scheme 53: Catalyst-free synthesis of spiroheterocycles.

Our group reported the enantioselective synthesis of 2,4-disubstituted 1,2,3-triazoles as major products through the bifunctional thiourea organocatalysis from 4-aryl-*NH*-1,2,3-triazoles and cyclic enones. The presented protocol was N2 selective and all the products were produced in good yields [125] (Scheme 54).



Scheme 54: N2-Selective aza-Michael addition for the synthesis of 2,4-disubstituted triazoles.

1.7. Synthesis of biaryls

Biaryls are the privileged class of organic scaffolds because of their presence in the pharmaceuticals, ligands, natural products and organic materials [126–129]. It was reported in early 2010 that nearly 4.3% of all known drugs were found to have biaryls structure, which include antitumor, anti-inflammatory, antihypertensive, antifungal, and antirheumatic agents [130]. Furthermore, there have been reports in the literature supporting the interaction of drugs with the protein binding sites through the involvement of aromatic sites and hydrophobic residues, which makes them as important templates for the designing of new drugs [131–133].

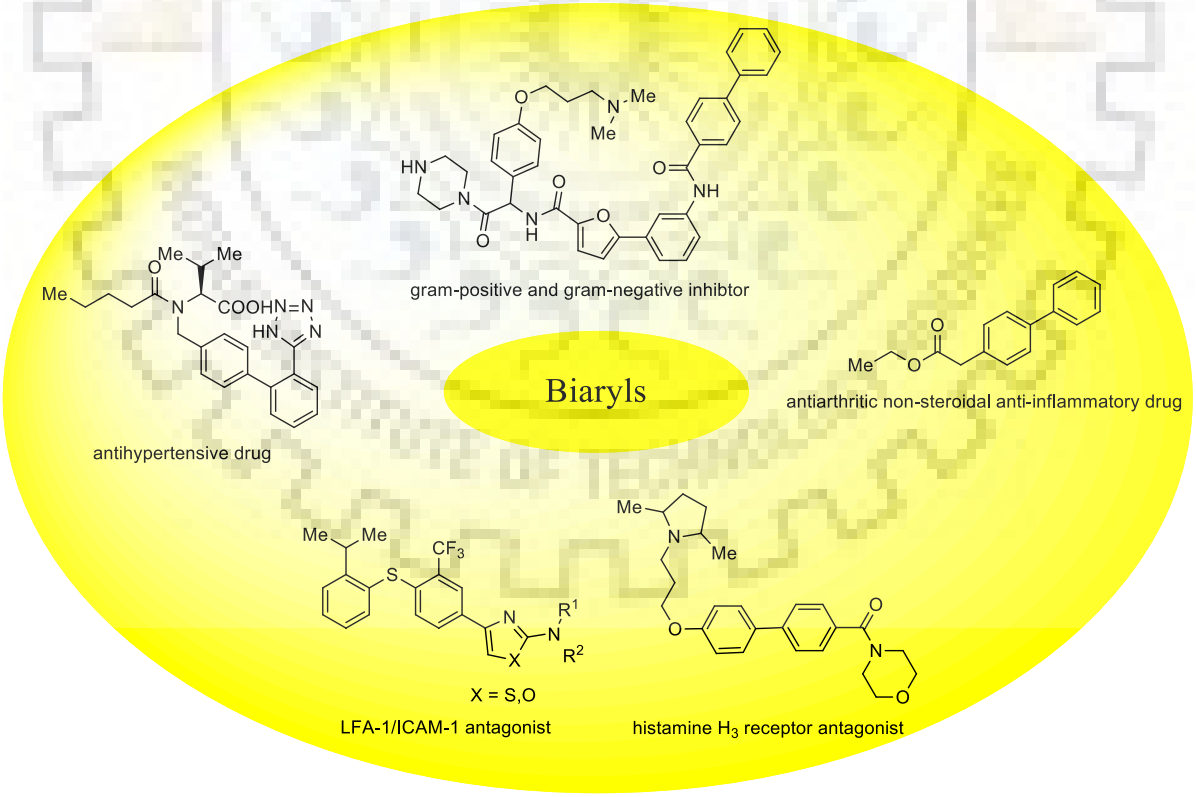
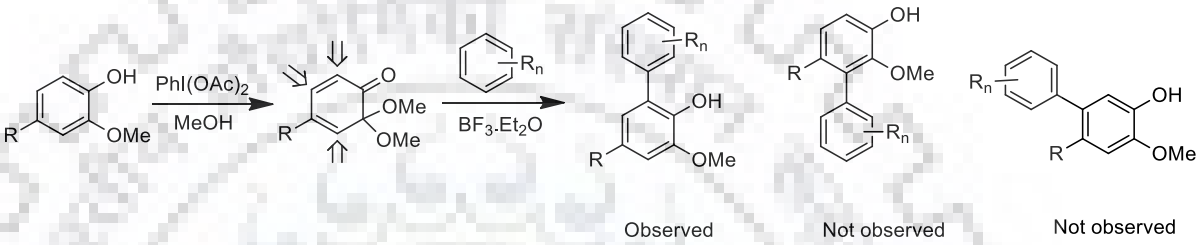


Figure 6: Structure of biaryl containing medicinally important scaffolds.

Numerous methods are available for the construction of biaryls using transition-metal catalyzed cross-coupling reactions. Negishi, Suzuki and Heck were awarded Nobel Prize in

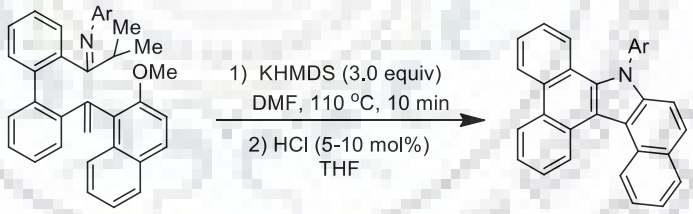
2010 for their well-known approaches which offer C–H arylation and the branch is continuously blooming which makes this area as an excellent opportunity to explore new ideas [134].

In 2013, our group disclosed a raid protocol for the synthesis of unsymmetrial biaryls by utilizing highly reactive *o*-benzoquinones. The presented strategy made available an alternative route to biaryls without any prefunctionalization of starting materials. Lewis acid activated protocol worked in an anti-Michael addition manner to furnish all the products in good to excellent yields [135] (Scheme 55).



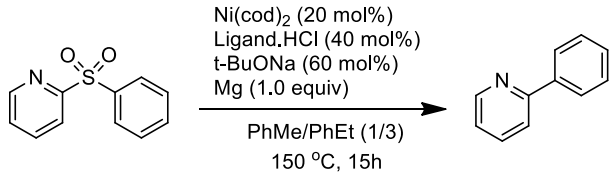
Scheme 55: Construction of unsymmetrical oxygenated biaryl.

Takasu and co-workers, in 2018, reported the synthesis of tribenzocarbazoles from azapropellanes. The reaction followed [2 + 2] cycloaddition pahway under the acidic conditions. Further the structural, electronic as well as optical properties of the products were analysed and the tribenzocarbazoles intermolecular packing were explained through X-ray crystallography [136] (Scheme 56).



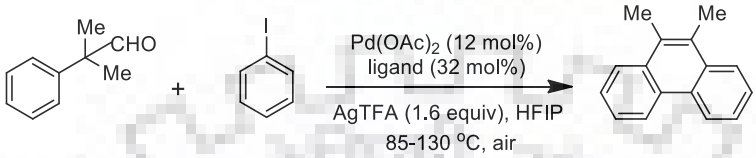
Scheme 56: Synthesis of tribenzocarbazoles.

Takahashi *et al*. revealed the biaryls formation *via* elimination of SO_2 from diarylsulfones. The protocol involves nickel-NHC catalysis through intramolecular desulfitative couplings. The reaction shows broad substrate scope and opens a new field for the exploration of sulfonyls under different catalytic systems to deliver new synthetic scaffolds [137] (Scheme 57).



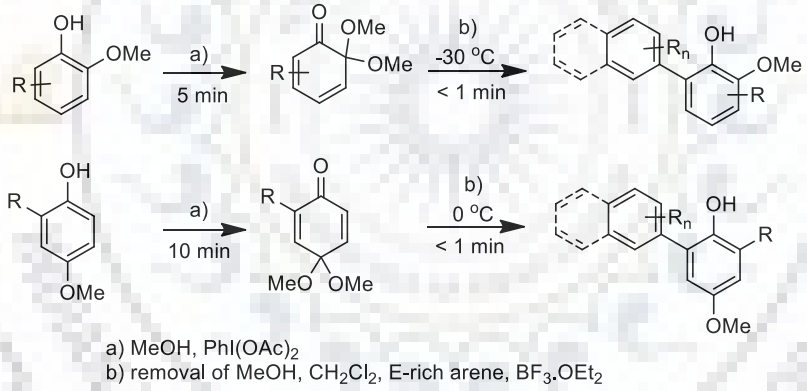
Scheme 57: Synthesis of biaryls *via* intramolecular desulfitative route.

Gou *et al*. displayed the synthesis of symmetrical and unsymmetrical phenanthrenes by utilizing palladium catalysis from iodobenzenes and benzylic aldehydes. The reaction underwent a series of C–H arylation, cyclization followed by dehydration and intramolecular 1,2-migration in a one-pot fashion. The reaction worked with a good tolerance of subsittuents and mechanistic investigation was performed to understand the course of reaction [138] (Scheme 58).



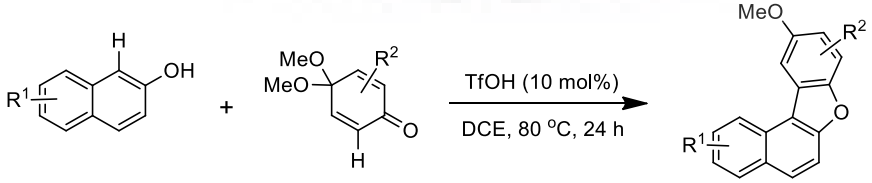
Scheme 58: Synthesis of functionalized phenanthrenes.

In 2017, our group disclosed the synthesis of oxygenated biaryls in a site-selective manner from electron-rich arenes and methoxyphenols. The reaction underwent dearomatization-rearomatization strategy to furnish highly selective unsymmetrical biaryls *via* Lewis acid activation. The protocol shows a broad substrate scope and the structure was confirmed by X-ray crystallography [139] (Scheme 59).



Scheme 59: Lewis acid promoted synthesis of oxygenated biaryls.

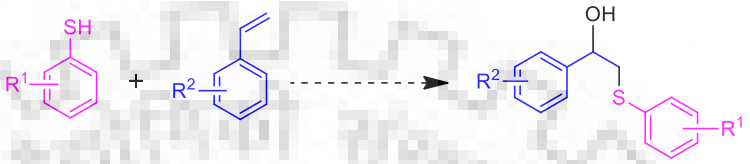
Biju and co-workers reported metal-free protocol to access naphtha[2,1-*b*]benzofuran derivatives from *β*-naphthols and quinone monoacetals. The reaction followed [3 + 3] annulation pathway to deliver the products in moderate to good yields under metal-free, Bronsted acid catalyzed conditions [140] (Scheme 60).



Scheme 60: Metal-free synthesis of naphtha[2,1-*b*]benzofurans.

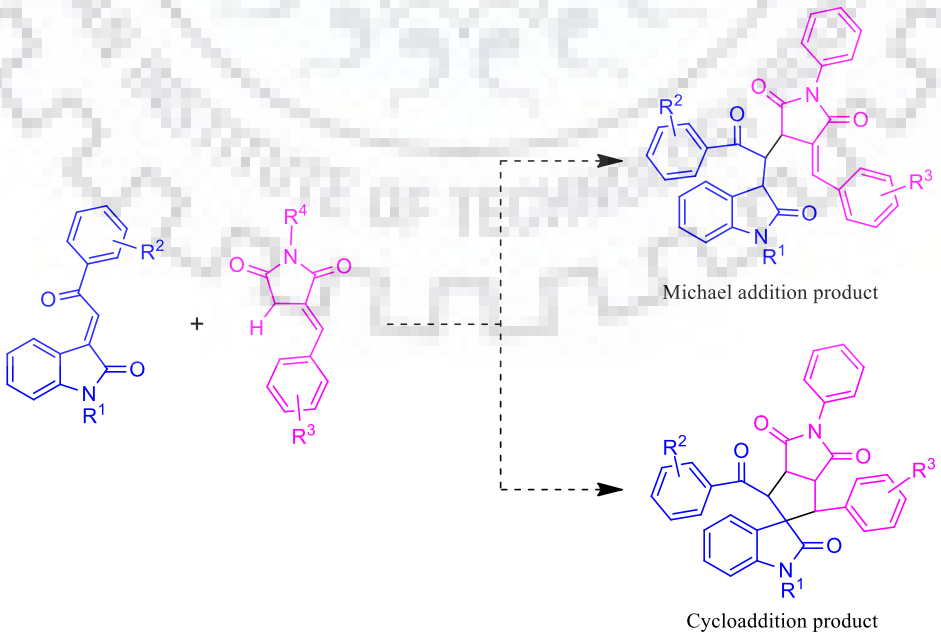
2.1. Objectives

- Synthesis of *β*-hydroxy sulfides has been a topic of interest in organic synthesis since decades. Various methods are known in literature for their synthesis by using metal catalysis or environmentally hazardous reagents. Our aim was to develop a protocol for easy access to *β*-hydroxy sulfides through environment friendly pathway by harnessing the reactivity of styrenes and thiophenols.

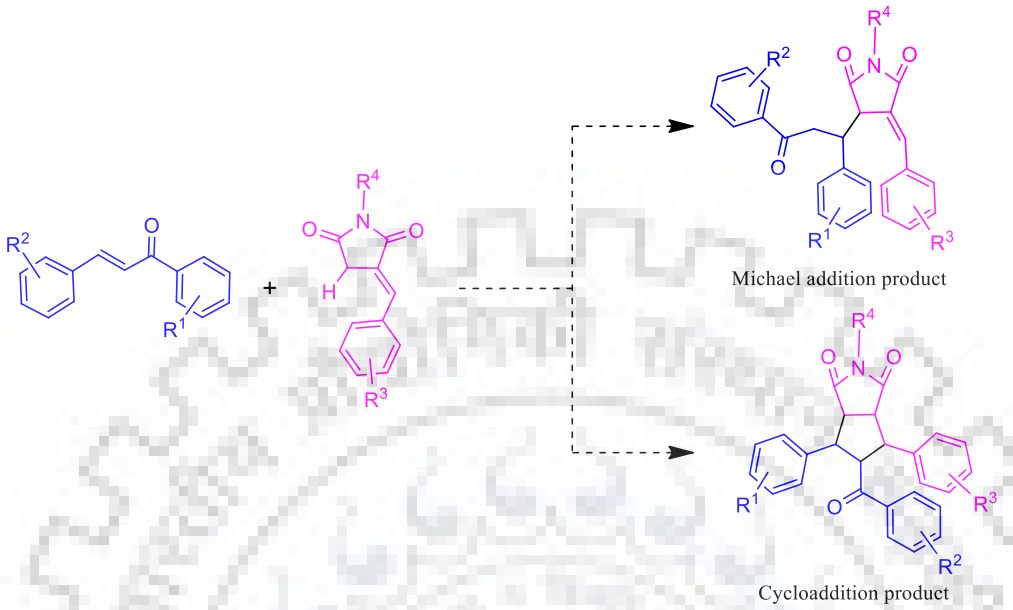


- Succinimides being important scaffolds having various applications in medicinal chemistry, attracted our attention to synthesis some important frameworks embraced with succinimide. Impressed by the structural diversity of 3-benzilidene succinimide unit as it can work as a donor as well as an acceptor, we were curious to explore its reactivity with various acceptors.

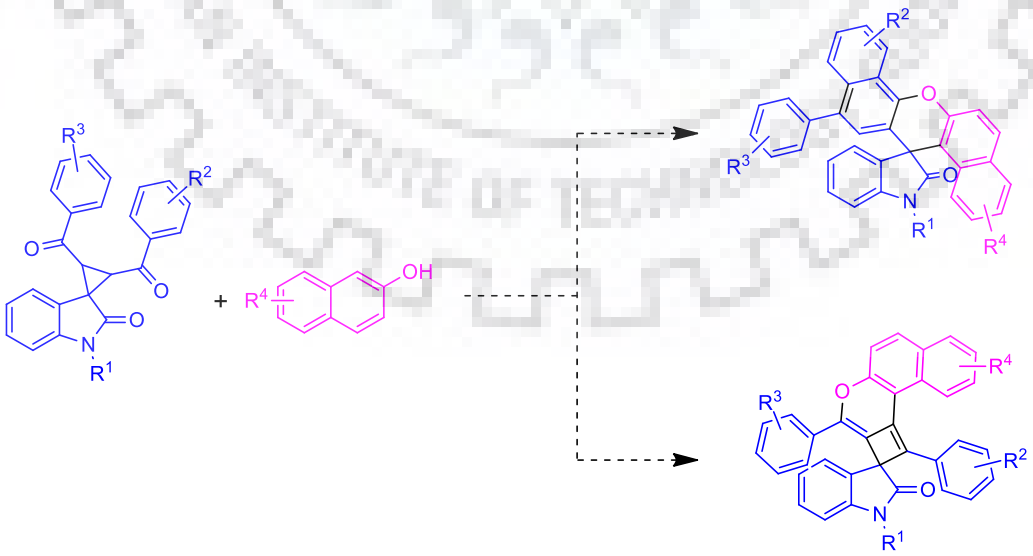
Inspired by enormous applications of oxindole moiety in medicinal chemistry and having wide literature support made us curious towards its exploration and to continue our research in this field, to invest some of our efforts in the synthesis of spirocyclic oxindole scaffolds which are known for their biological activities. Our aim was to provide an easy excess to spirooxindolic systems *via* simple protocol preferably obviating purification steps such as work-up, column chromatography and crystallization.



- Another objective was to explore the reactivity of 3-benzilidene succinimide with enone acceptors such as chalcones and to evaluate the competitive reaction pathways, *viz.* Michael addition *vs.* cycloaddition.



- Motivated by the magnificent reactivity profile of D-A cyclopropanes that have the potential to deliver profound scaffolds with wide biological profile, we were interested to utilize rarely used cyclopropanes containing multiple functional groups, which can be utilized through the course of reaction in a sequential manner as per their reactivity profile. However, it was not less than a challenge to bring this imagination down to a working protocol furnishing some interesting hybrid structures involving oxindoles.



2.2. Results and Discussion

This chapter deals with the detailed studies of the following:

2.2.1. Synthesis of substituted β-hydroxy sulfides

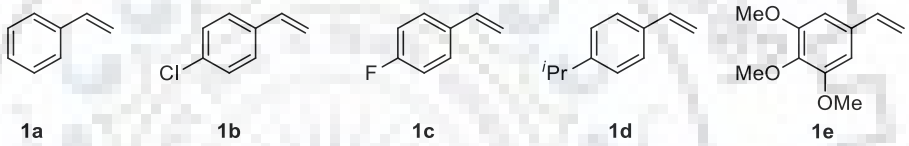
2.2.2. Synthesis of highly substituted spirooxindolic-cyclopentanes *via* [3 + 2]-cycloaddition reactions

2.2.3. Synthesis of benzylidene succinimide-tethered propanones *via* Michael addition reactions

2.2.4. Synthesis of highly conjugated xanthene-tethered unsymmetrical biarylic spirooxindoles *via* domino reactions

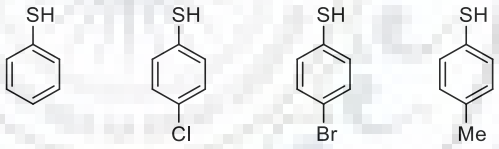
The starting materials are numbered as shown below to facilitate the discussion throughout the thesis:

Styrenes (1):



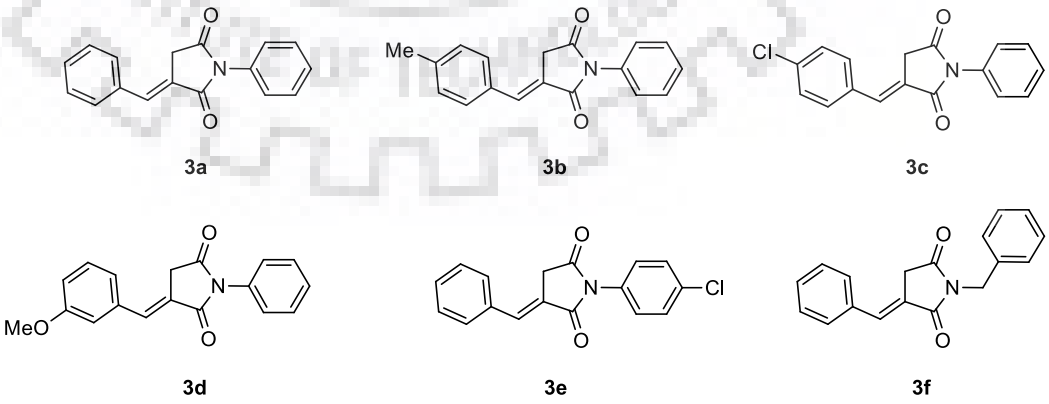
1a **1b** **1c** **1d** **1e**

Thiophenols (2):



2a **2b** **2c** **2d**

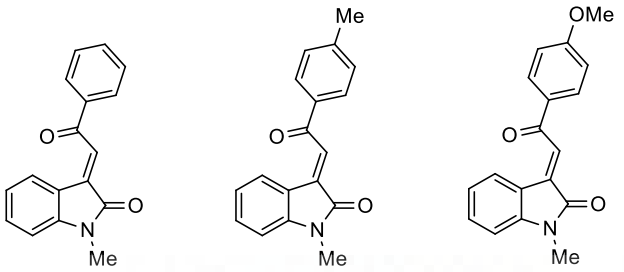
3-Benzylidene succinimides (3):



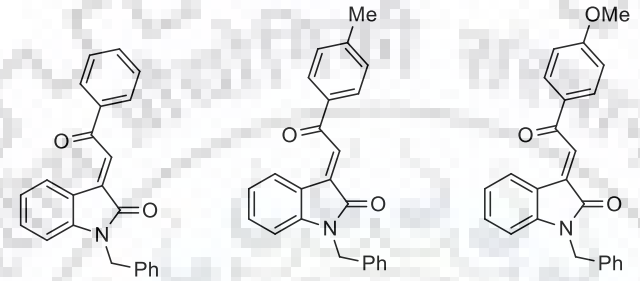
3a **3b** **3c**

3d **3e** **3f**

3-Ylidene oxindoles (4):

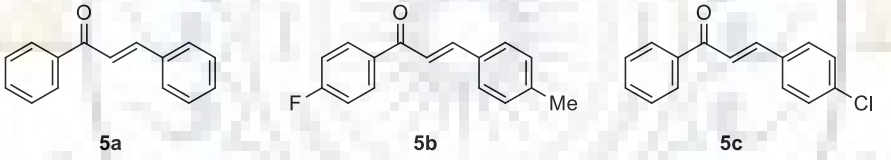


4a **4b** **4c**

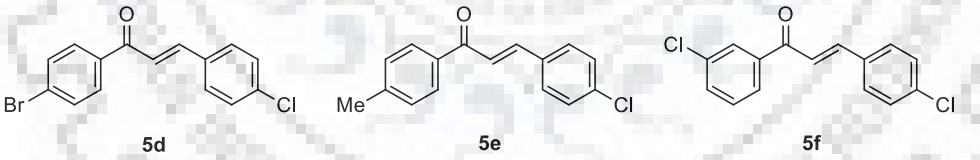


4d **4e** **4f**

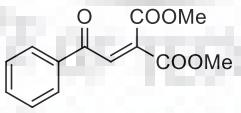
Chalcones and benzoylmethylidene malonate (5):



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

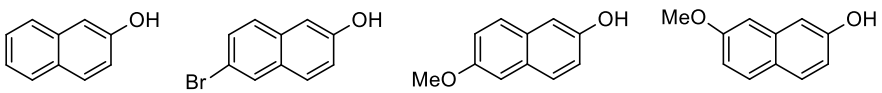


5d **5e** **5f**



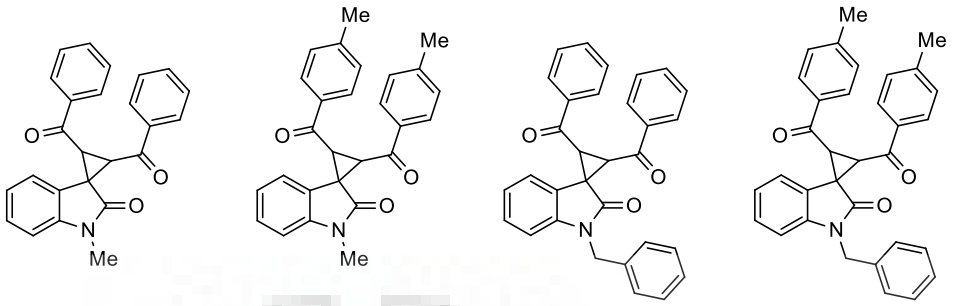
5g

***β*-Naphthols (6):**



6a **6b** **6c** **6d**

Spirocyclic cyclopropanes (7):



7a **7b** **7c** **7d**

2.2.1. Synthesis of substituted β-hydroxy sulfides

Carbon–heteroatom bond formation has a great importance in synthetic organic chemistry because of its presence in many natural products. Consequently, it has attracted much attention in recent times [141]. Various methods have been developed for the synthesis of C–X bonds. However, some protocols involve transition metals, expensive reagents or additives and therefore this process is still under exploration to develop environment friendly and affordable strategies for the construction of these bonds [142,143].

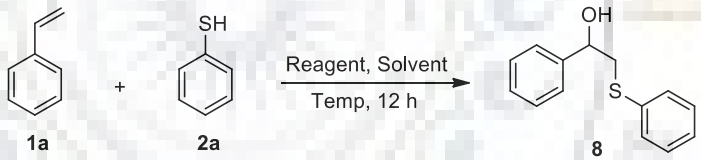
Over the last few years, bisfunctionalization methodologies such as alkoxythiolation, hydroxylthiolation, acetoxythiolation, sulfamination and disulfidation have been performed successfully [144–157]. The generation of bisfunctionality in a single step is itself a challenging task in synthetic organic chemistry. Further, sulfide functionalization raises its importance as it is present in numerous natural compounds [158–161]. Sulfur-containing organic compounds have various applications in the area of medicinal chemistry for their antibiotic, antioxidant, calcium channel antagonist, antimicrobial, anti-inflammatory, antitumor, and anti-HIV activities [162,163]. β-Hydroxy sulfides act as precursors in the synthesis of compounds having biological importance such as pharmacophores including bexarotene, tamoxifen, iso-combretastin (iso CA-4), ratanhine, and in the synthesis of β-hydroxy sulfoxides which can be obtained by the oxidation of β-hydroxy sulfides using conventional oxidising agents [85,164–173]. β-Hydroxy sulfides are important building blocks for the synthesis of thioketones, allylic alcohols, cyclic sulfides, benzothiazepines, benzoxathiepines and many other highly functionalized organic scaffolds specially in the synthesis of Leukoterin LTC4 and LTD4 [75,76].

Several reports are available in literature for the construction of β-hydroxy sulfides, which can be divided into two categories on the basis of the reactants used: i) styrenes and disulfides/thiols, and ii) epoxides and disulfides/thiols. Most of them are associated with some drawbacks such as use of toxic metals or solvents. Movassagh *et. al*. synthesized β-hydroxy sulfides using styrenes and disulfides by employing zinc/aluminium chloride as a promoter under oxygen [80]. Singh *et. al*. synthesized β-hydroxy sulfides using silver nitrate catalyst in DMF [82]. Later Chandrasekaran and co-workers reported the synthesis of β-hydroxy sulfides with rongalite, potassium carbonate in DMF and Lanke *et. al*. synthesized β-hydroxy sulfides using amberlyst-15 in toluene [81,174]. Use of iodine as a catalyst in oxidation reactions is one of the upcoming advances of the recent time in terms of environmental sustainability and cost effectiveness [175–178]. As iodine is environmentally

benign, we envisaged that it would provide us a green path towards the synthesis of *β*-hydroxy sulfides.

Initially the reaction was carried out with styrene (**1a**) and thiophenol (**2a**) as model substrates in DMSO at room temperature and 80 °C (Table 1, entry 1). However, no reaction was observed under these conditions. When **1a** and **2a** were treated in the presence of iodine at room temperature the reactants were recovered (entry 2). Later the reaction was performed with 50 mol% of iodine in DMSO at 80 °C. To our delight *β*-hydroxysulfide **8** was obtained in 51% yield (entry 3). When we performed the reaction of thiophenol with excess of styrene (2 equiv.), **3a** was obtained in 90% yield (entry 5). After that we screened different reagents such as potassium iodide, diacetoxyiodobenzene (DIB), *N*-chlorosuccinimide and molecular iodine. When reaction was carried out in the presence of KI and DIB, no reaction was observed (entries 6 and 7), while in the presence of NCS, traces of product was observed (entry 8). To improve the yield of **8** further, the reaction was carried out by loading iodine with 1.0 and 0.25 equiv. and the product was in observed 92 and 75% yields, respectively (entries 9 and 10). To evaluate the effect of temperature on reaction, we carried out the

Table 1: Optimization of reaction conditions.[a]



Entry	Reagent (equiv.)	Solvent	Temp (°C)	Yield[b] (%)
1	-	DMSO	80	-
2	I_2 (0.5)	DMSO	rt	-
3[c]	I_2 (0.5)	DMSO	80	51
4[d]	I_2 (0.5)	DMSO	80	56
5	I_2 (0.5)	DMSO	80	90
6	KI (0.5)	DMSO	80	nr
7	DIB (0.5)	DMSO	80	nr
8	NCS (0.5)	DMSO	80	traces
9	I_2 (1.0)	DMSO	80	92
10	I_2 (0.25)	DMSO	80	75
11	I_2 (0.5)	DMSO	100	58

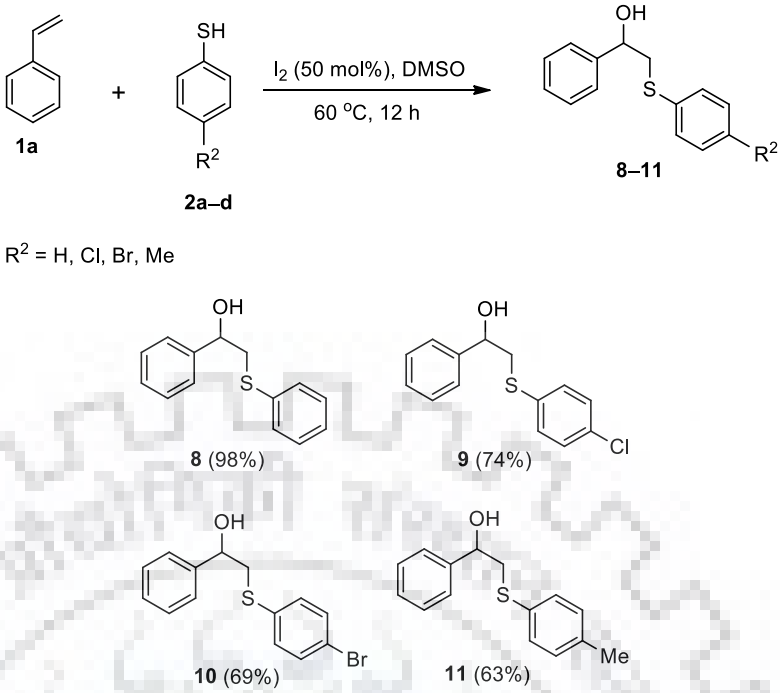
12	I_2 (0.5)	DMSO	60	98
13	I_2 (0.5)	DMSO	40	70
14	I_2 (0.5)	DMF	80	traces
15	I_2 (0.5)	ACN	80	traces
16	I_2 (0.5)	H_2O	80	nr

[a]All reactions were performed with **1a** (1.0 mmol), **2a** (0.5 mmol), reagent and solvent (2 mL) on heating. [b]Isolated yield. nr = no reaction. [c]**1a** (0.5 mmol) and **2a** (0.5 mmol) were used. [d]**1a** (0.5 mmol) and **2a** (1.0 mmol) were used.

reaction at different temperatures and we observed that product was obtained in diminished yield of 58% at 100 ^oC while at 60 ^oC, the product was isolated in slightly increased yield of 98% (entries 11 and 12). Further decrease of temperature of the reaction to 40 ^oC did not provide encouraging results (entry 13). Then we screened different solvents by using 0.5 equiv. of iodine and 1:2 equiv. of thiophenol and styrene, product was obtained in traces when DMF and ACN were used as solvents (entries 14 and 15). While no reaction was observed when H_2O was used as solvent (entry 16). Best results were obtained when the reaction was performed in DMSO. Thus the use of iodine (0.5 equiv.) in DMSO at 60 ^oC emerged as the optimal set of conditions for subsequent studies (entry 12).

With the optimized reaction conditions in hand, we investigated functional group compatibility and scope of the present iodine catalysed protocol for the synthesis of *β*-hydroxy sulfides using a variety of styrenes **1a**–**e**. It was noteworthy that the reaction demonstrated a wide tolerance for diverse substitutions like electron-withdrawing and electron-donating groups on styrenes. It was noticed that electronics properties on styrenes were less effective while influencing the productivity of the reaction.

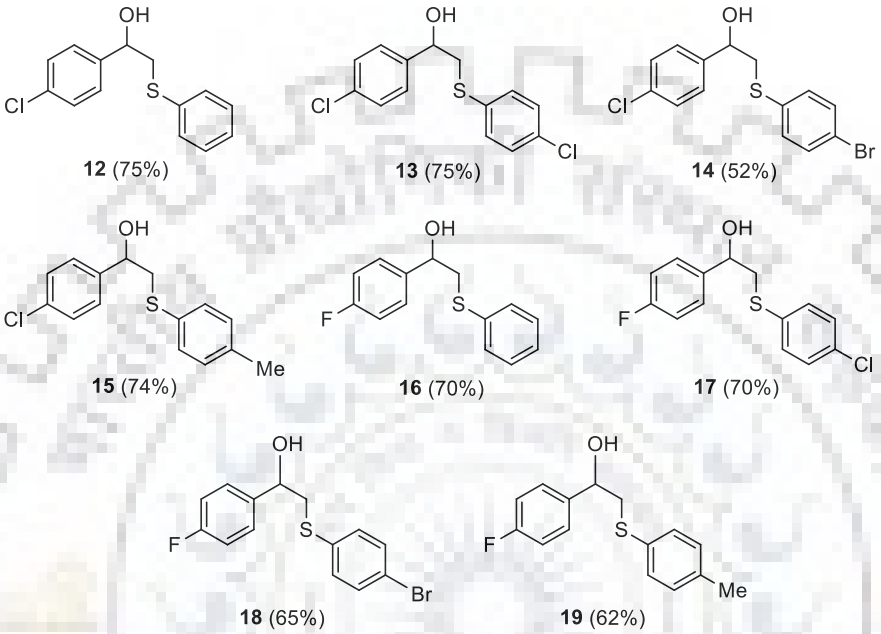
When the parent styrene was treated with differently substituted thiophenols **2a–d**, desired products **8–11** were furnished in 98, 74, 69 and 63%, respectively. The data suggests that electron-withdrawing groups on thiophenols facilitated the reaction, whereas electron-donating group on *para* position of thiophenol provided the corresponding *β*-hydroxy sulfide in 63% yield (Scheme 1).



Scheme 1: Reaction of styrene **1a** with thiophenols **2a–d**.

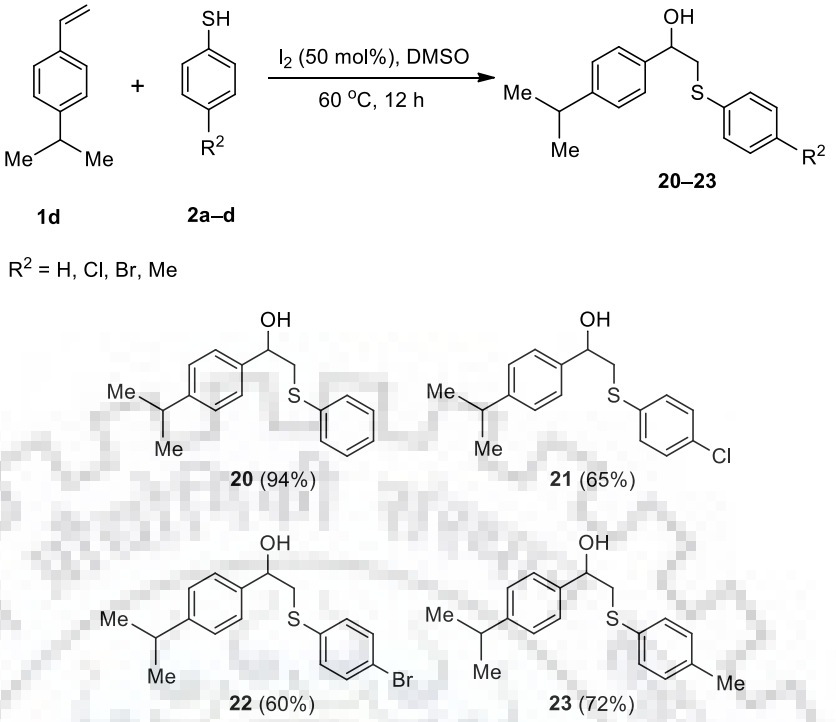
Next, we used styrenes having electron-withdrawing groups like chloro and fluoro on *para* position of styrene with various thiophenols **2a**–**d**. It was noticed the presence of EWG on styrenes affected the yields adversely. *p*-Chlorostyrene furnished the final products **12**–**15** in 75, 75, 52 and 74%; however, *p*-fluorostyrene provided the *β*-hydroxy sulfides **16**–**19** in 70, 70, 65, 62%, respectively. It is noteworthy to observe that fluorinated styrene having marginal negative influence on the yield of the products (Scheme 2).

R^1 = Cl, F
R^2 = H, Cl, Br, Me



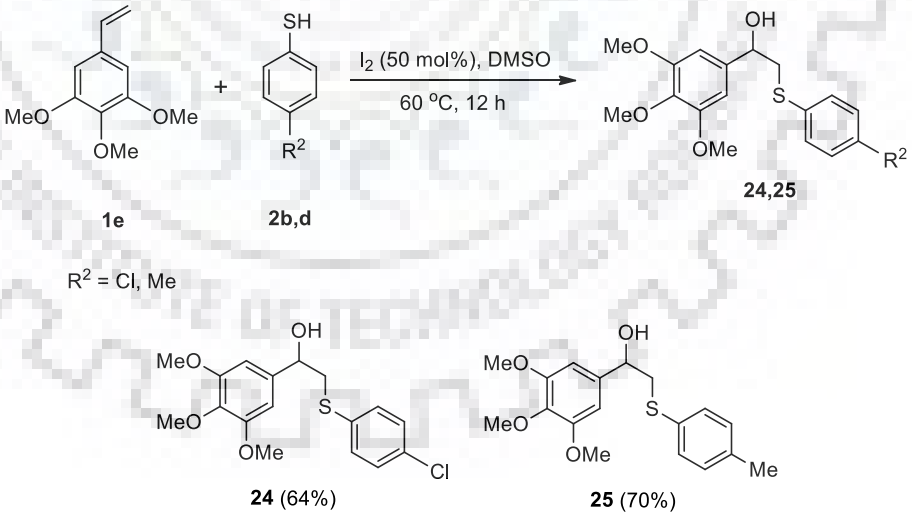
Scheme 2: Reaction of styrenes **1b**,**c** with thiophenols **2a–d**.

We investigated the compatibility of the reaction having bulky group like isopropyl on styrene with thiophenols **2a–d**. The reaction gave the product **20** in excellent yield of 94% with parent thiophenol. However, the reaction of **1d** with substituted thiophenols **2b–d** led to the formation of corresponding *β*-hydroxy sulfides **21**–**23** in substantially decreased yields (Scheme 3).



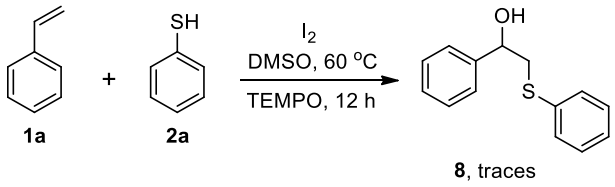
Scheme 3: Reaction of styrene **1d** with thiophenols **2a–d**.

To evaluate the effect of multisubstituted styrenes on the reaction, the styrene **1e** was reacted with thiophenols **2b,d**. The reaction did not show much influence as the products **24** and **25** were furnished in 64 and 70% yields which is in good co-relation with other *β*-hydroxy sulfides derived from these thiophenols with other styrenes (Scheme 4).



Scheme 4: Reaction of styrene **1e** with thiophenols **2b,d**.

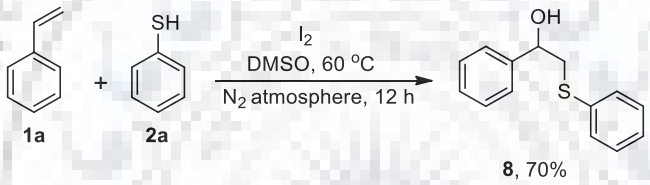
In order to understand the course of reaction, we performed the reaction in presence of TEMPO to have some clues about either ionic or radical mechanism was responsible for the reaction. It was observed that traces of products were observed on using three equiv.alents of TEMPO, clarifying the involvement of radical pathway (Scheme 5).



TEMPO (equiv.)	Yield
1.0	40%
3.0	traces

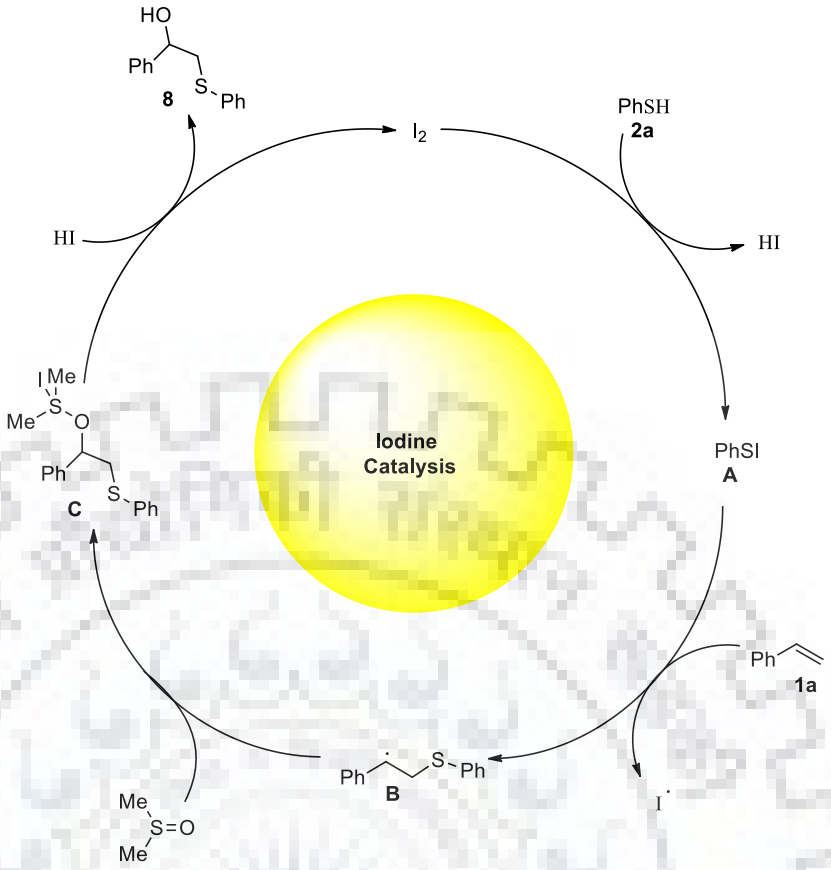
Scheme 5: Reaction of styrene **1a** with thiophenols (**2a**) in presence of TEMPO.

As none of the starting material having oxygen atom, we planned to investigate the source of oxygen in *β*-hydroxy sulfides. Thus we performed the reaction of **1a** and **2a** in the presence of I_2 in DMSO under nitrogen atmosphere and the *β*-hydroxy sulfide **8** was isolated in 70% yield eliminating the possibility of environmental oxygen to work as a source of oxidation and confirming the fact that DMSO is fulfilling the role as a solvent as well as oxidising agent in this reaction (Scheme 6).



Scheme 6: Reaction of styrene **1a** with **2a** thiophenols in N_2 atmosphere.

On the basis of our studies, a plausible reaction pathway for the bisfunctionalization of styrenes is illustrated in Scheme 7. Initially, the nucleophilic aryl thiol **2a** attacks the electrophilic iodine centre leading to the formation of intermediate ArS–I (A). The species ArS–I liberates ArS·, which reacts with electron-rich styrene **1a** to deliver a benzylic free radical intermediate B and iodine free radical. The presence of iodine free radical makes dimethylsulfoxide susceptible to attack at benzylic position of intermediate B leading to the generation of intermediate **C**. The attack of HI on **C** affords the desired *β*-hydroxy sulfide **8** and regenerates iodine. Though there is no direct evidence for the formation of ArS–I species, its formation from thiophenols is suggested in the literature [161] (Scheme 7).



Scheme 7: Plausible reaction mechanism for the formation of *β*-hydroxy sulfides.

2.2.2. Synthesis of highly substituted spirooxindolic-cyclopentanes *via* [3 + 2] cycloaddition reactions

Isatin and its derivatives are of great scientific interest in the family of nitrogen containing compounds because of their remarkable pharmacological profile [11,179–181]. Numerous efforts have been made by the researchers from time to time to synthesize these moieties [182–187]. In addition to this, cyclopentanes are a class of compounds endowed with decisive biological and pharmacological activities, such as antiviral, hepatitis B and significant antitumor activities [188,189]. Moreover, cyclopentane scaffolds can serve as intermediates in natural product synthesis and lead compound in the development of new drugs [190–194]. Owing to their wide spectrum of biological activity, the synthesis of cyclopentane derivatives attracted tremendous attention in the field of organic synthesis and construction of highly substituted derivatives have been an important concern for organic chemists since decades [195–198]. When the oxindole moiety is spirocyclized to cyclopentane, it upswings to a special class of biologically important natural alkaloids like notoamide A, cirinalins A, citrinadin B, cyclopiamine B, versicolamides C and could lead to the synthesis of highly stereocentric more fertile bioactive compounds [109,201–204] (Figure 1).

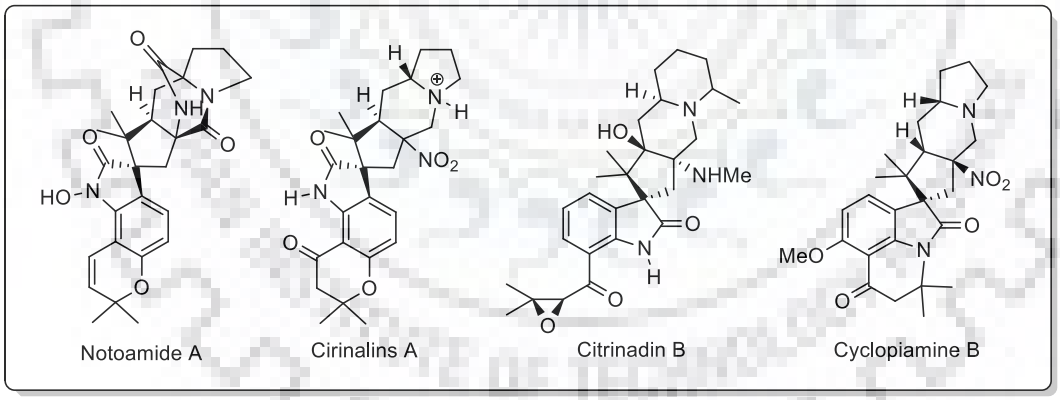


Figure 1: Biologically important spirooxindoles.

Owing to their stupendous properties in medicinal field, a number of attempts have been made towards the synthesis of spirooxindoles during the last decade. Some of the methods often require transition-metal catalysis, lengthy synthetic routes with prolonged reaction time and tedious isolation processes [205,206]. As a result, there exists high demand for the development of alternative user friendly, simple and environmentally benign approaches to synthesize more functionally-rich spirooxindoles from easily accessible materials. Since decades the [3 + 2] cycloaddition reaction has been considered as a major

tool to construct C−C bonds in many bioactive molecules and cycloaddition reactions of various dipolar compounds with isatin and its derivatives have attracted significant attention in recent years [111,207−215]. After literature survey we found 3-ylidine oxindoles as potent substrate for the reaction with 3-benzilidine *N*-phenylsuccinimides. However, there was a question about the regioselectivity of the reaction.

As per our hypothesis the proposed reaction could be accompanied by any of the two or both the products **26** and **26′** shown in figure 2 (Figure 2). However, in all the cases we ended up with a single product *i.e.* **26** with high purity as well as excellent diastereoselectivity. Regioselective initial attack on β-carbon of amide functionality in **4a** over α-position could be well explained by steric effect as the later (α-position) is relatively more hindered.

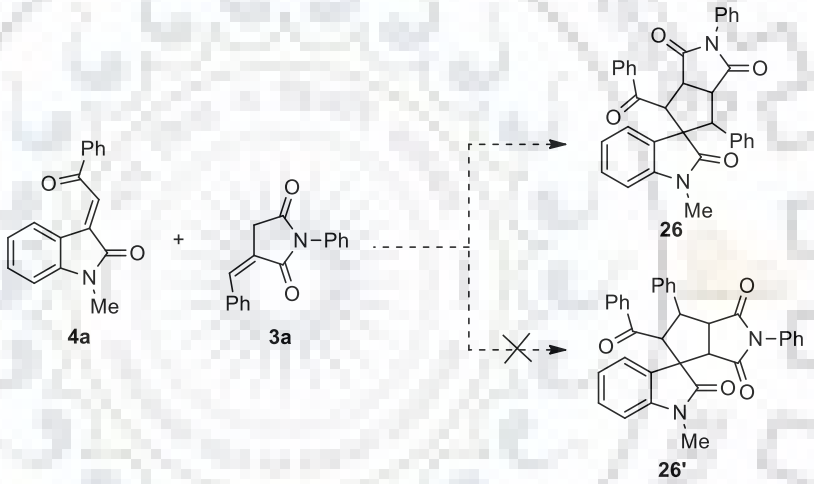
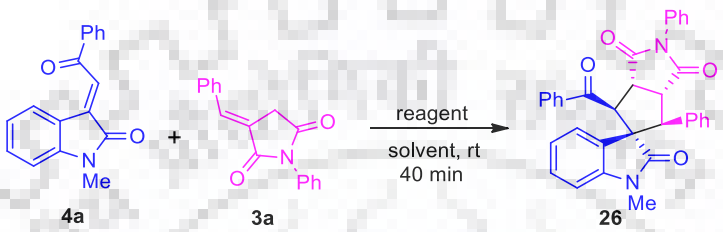


Figure 2: Working hypothesis for the synthesis of spirocyclic oxindoles.

To establish the optimum reaction conditions, we commenced our research by investigating the reaction of 3-ylidine *N*-methyloxindole **4a** and 3-benzilidine *N*-phenylsuccinimide (**3a**) as model substrates. When the reaction was performed in the presence of triethylamine in DCE at room temperature, no product was observed (Table 2, entry 1). To check the feasibility as per the mutual reactivity of the reactants, bases such as DIPEA, DABCO and K_2CO_3 were examined and it was observed that these bases were unable to drive the reaction (entries 2−4) whereas the reaction involving DBU furnished traces of **26** (entry 5). The spirooxindole **26** was obtained *via* [3 + 2] cyclization of 3-ylidine oxindole **4a** with 3-benzilidine succinimide **3a**. After screening of various bases, DBU was found to be promising base to furnish the product **26**. Subsequently, to assess the solvent effect, the reaction was studied by performing in different solvents (entries 6−10). EtOH was identified as the optimal solvent furnishing the spirooxindole **26** in 40 min in 60% yield

with 86:14 diastereoselectivity (entry 9). Encouraged by this promising result, we further varied the amount of DBU and found that on decreasing the amount of base to 50 mol% the product was obtained in an increased yield of 75% with very good diastereoselectivity (entry 11). When **4a** was treated with **3a** in the presence of 20 mol% of DBU, the reaction afforded spirooxindole **26** in 80% yield with 91:09 diastereoselectivity (entry 12). However, no appreciable variation in the yield of the product ensued by further diminishing the base to

Table 2: Optimization of reaction conditions.[a]



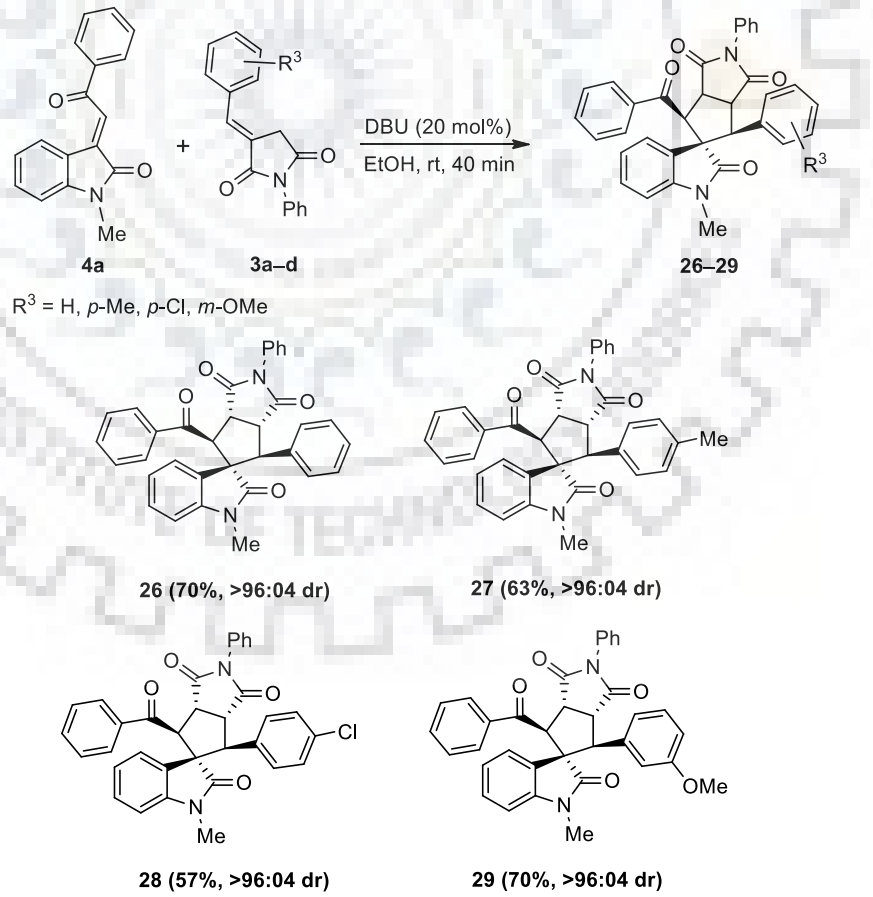
Entry	Reagent (equiv.)	Solvent	dr[b]	Yield[c] (%)
1	NEt_3	DCE	-	nr
2	DIPEA	DCE	-	nr
3	DABCO	DCE	-	nr
4	K_2CO_3	DCE	-	nr
5	DBU	DCE	-	traces
6	DBU	DCM	-	traces
7	DBU	Toluene	-	traces
8	DBU	MeOH	98:02	43
9	DBU	EtOH	86:14	60
10	DBU	IPA	93:07	28
11[d]	DBU	EtOH	90:10	75
12[e]	DBU	EtOH	91:09	80
13[f]	DBU	EtOH	93:07	71

[a]Reaction conditions: Unless otherwise specified, all reactions were carried out using **4a** (0.1 mmol), **3a** (0.1 mmol), and a reagent (0.1 mmol) in 2 mL solvent at room temperature for 40 min. [b]The dr was determined by ^{1}H NMR analysis of the crude product having **26** and its diastereomer. [c]Isolated yield of **26** and its diastereomer after column chromatography. nr: No reaction. [d]50 mol% of DBU was used. [e]20 mol% of DBU was used. [f]10 mol% of DBU was used.

10 mol% (entry 13). Thus, 20 mol% DBU in EtOH at room temperature was considered as the optimized reaction condition for the model reaction. Gratifyingly, when the crude reaction mixture was subjected to filtration followed by simple washing with ethanol, a single diastereomer **26** was isolated in 70% chemical yield.

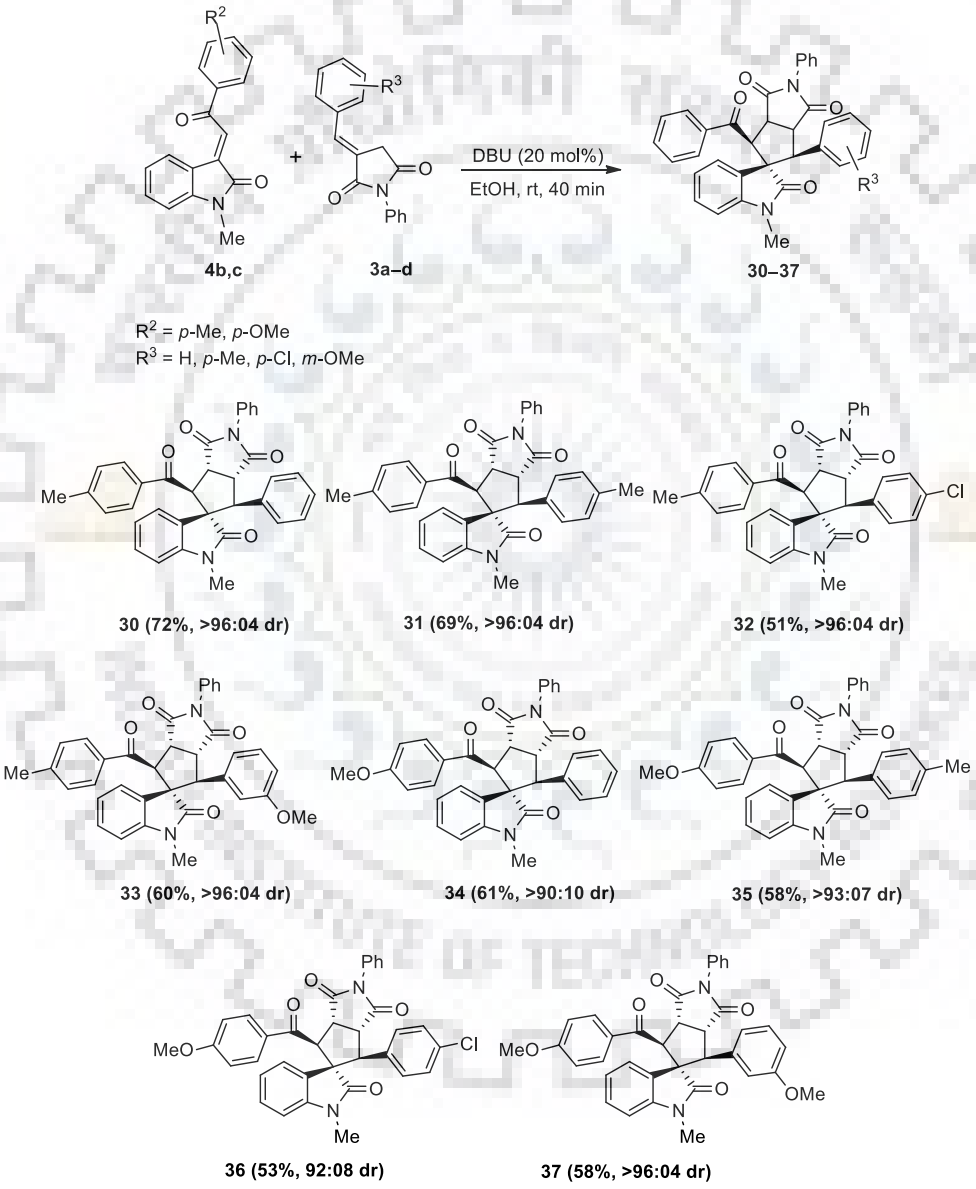
With the optimized reaction conditions in hand, we investigated functional group compatibility and scope of the present DBU catalysed protocol for the synthesis of spirooxindoles using a variety of 3-ylidine oxindoles **4a–c**. It was noteworthy that the reaction demonstrated a good tolerance for electron-donating groups on 3-ylidine oxindoles.

When the unsubstituted/parent 3-ylidine oxindoles **4a** was treated with differently substituted 3-benzilidine succinimides **3a–d**, the cyclized products **26–29** were furnished in 70, 63, 57 and 70% yield, respectively, with diastereoselectivity up to >99%. The pattern was showing electron-donating groups on 3-benzilidine succinimides facilitate the reaction, whereas electron-withdrawing group on 3-benzilidine succinimides produced the product **28** in relatively reduced yield (Scheme 8).



Scheme 8: Reaction of 3-ylidine *N*-methyl oxindole **4a** with 3-benzilidine succinimides **3a–d**.

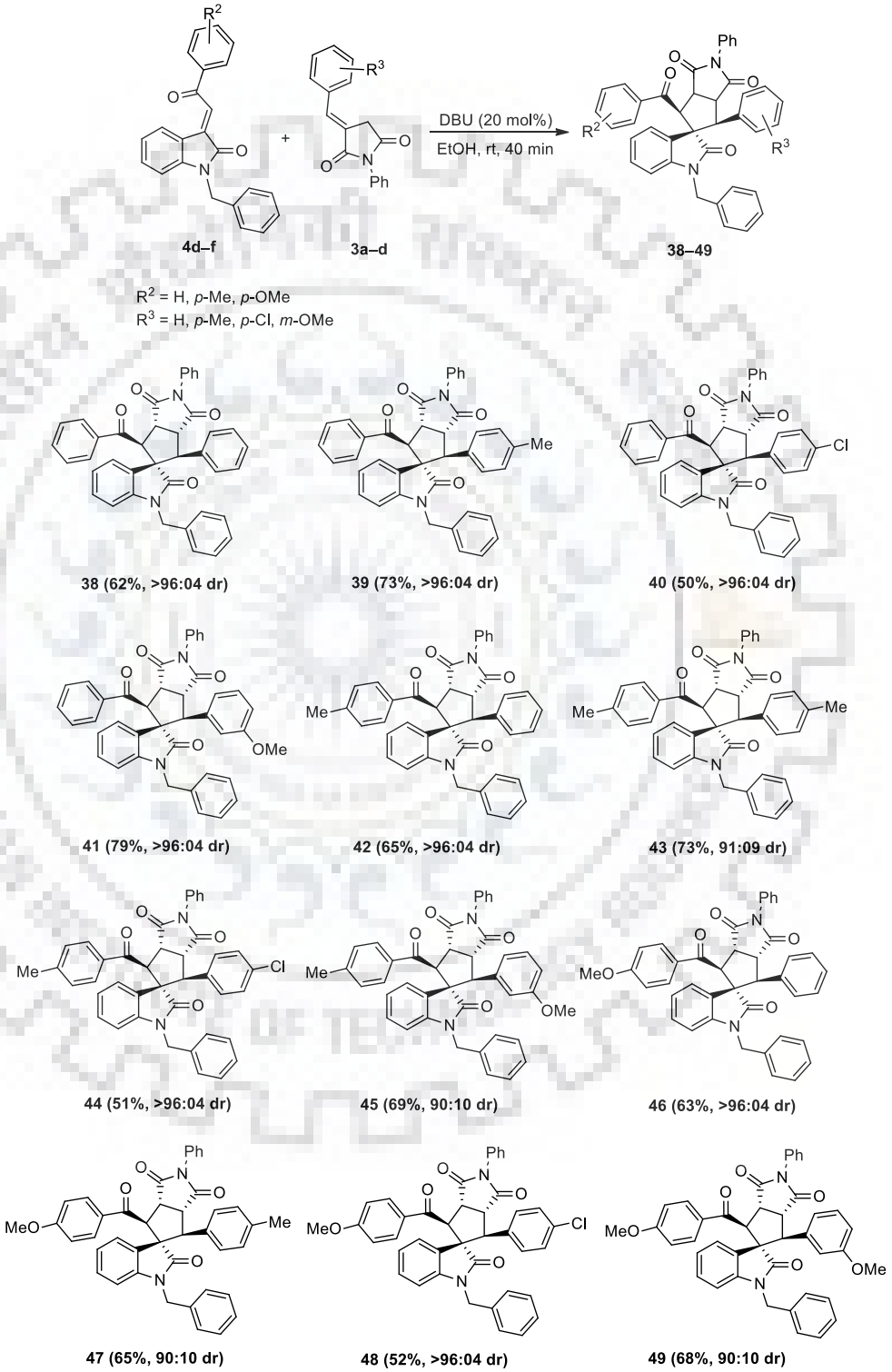
Next, we carried out reaction using 3-ylidine *N*-methyl oxindoles having electron-donating groups such as methyl and methoxy on various 3-benzilidine succinimides **3a–d**, marginal decrease in the yield was noticed in the presence of EDG on 3-ylidine *N*-methyl oxindole. 4-Methyl substituted 3-ylidine *N*-methyl oxindole **4b** furnished the corresponding products **30**–**33** in 72, 69, 51 and 60% yields; however, 4-methoxy substituted 3-ylidine *N*-methyl oxindole **4c** provided the cycloaddition products **34**–**37** in 61, 58, 53 and 58% yields with excellent diastereoselectivity (Scheme 9).



Scheme 9: Reaction of 3-ylidine *N*-methyl oxindoles **4b,c** with 3-benzilidine succinimides **3a–d**.

We tested the applicability of the present methodology for 3-ylidine oxindoles with bulky protecting group to ascertain its effect on stereochemical outcome of the reaction.

When *N*-benzyl protected oxindoles **4d–f** were used in the reaction, no significant changes in yields and diastereoselectivity of the products were noticed. The reactions proceeded smoothly to furnish the desired products **38–49** in 50–79% yield with excellent diastereoselectivity (Scheme 10).



Scheme 10: Reaction of 3-ylidine *N*-benzyl oxindole **4d–f** with 3-benzilidine succinimides **3a–d**.

NMR studies of 26:

The structures of spiroxindoles were confirmed by detailed spectral analysis obtained from ^{1}H and ^{13}C NMR, and HRMS experiments of isolated products. For instance, in the ^{1}H NMR of **26**, the protons H_a and H_d appear as doublets at δ 4.10 and 4.90 ppm, respectively, and the protons H_b and H_c appear as doublet of doublets at δ 4.21 and 5.04 ppm, respectively (Figure 3).

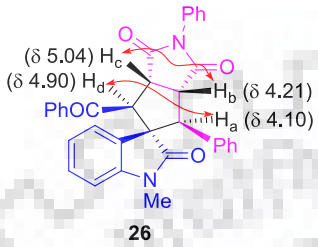
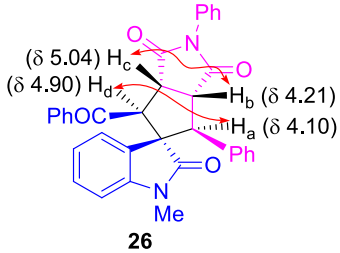


Figure 3: Selected ^{1}H NMR chemical shifts (ppm) and NOE correlations in **26**.

The connectivity of the protons that are coupled with each other and between protons and carbons of **26** was identified by two-dimensional ^{1}H–^{1}H COSY and ^{1}H–^{13}C COSY experiments, respectively (Figures 4 and 5). To gain more insight into the stereochemistry of these products and to understand the spatial correlation between H_a, H_d, H_c and H_d protons, we performed NOESY experiment on cyclized product **26**. The presence of correlation between the protons 'H_a and H_d'and 'H_b and H_c' and the absence of correlation between 'H_a and H_c', and 'H_b and H_d' establishes the depicted geometry (Figure 7). The correlation between the proton H_d and benzoyl carbonyl in HMBC spectrum ascertains their germinal relationship unambiguously (Figure 6, Table 3). The results obtained from NMR studies were further confirmed by single crystal X-ray analysis of compound **26** (Figure 8).

Table 3: Proton–proton and proton–carbon connectivity in **26**.

Cycloaddition adduct	^{1}H-^{1}H COSY	^{1}H-^{13}C COSY	δ (ppm)	HMBC	NOESY
	H_a - H_b	C_a	59.2	H_a - C_b, C_e	H_a - H_b
	H_b - H_c	C_b	48.1	H_b - C_a	H_a - H_d
	H_c - H_d	C_c	45.3	H_c - C_d	H_b - H_c
	-	C_d	56.5	H_d - C_c, C_e	H_c - H_d

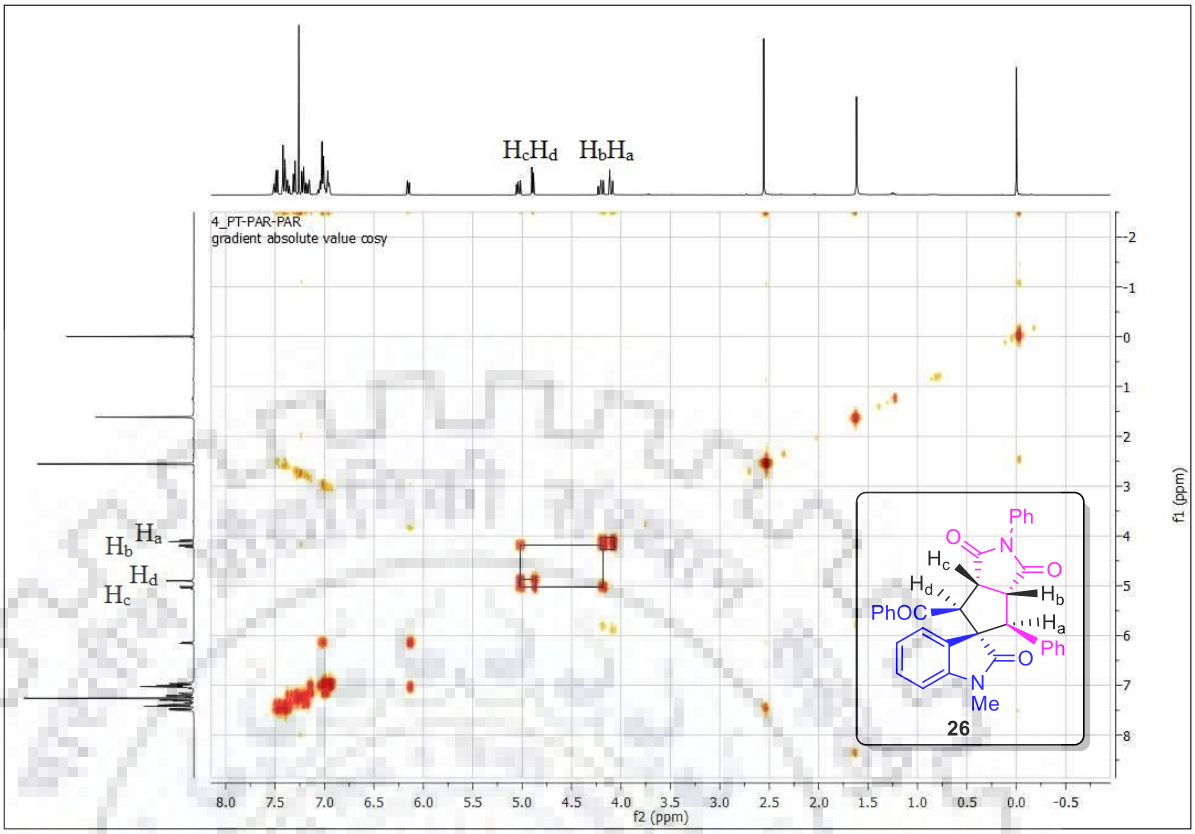


Figure 4: $^{1}H–^{1}H$ COSY spectrum of **26**.

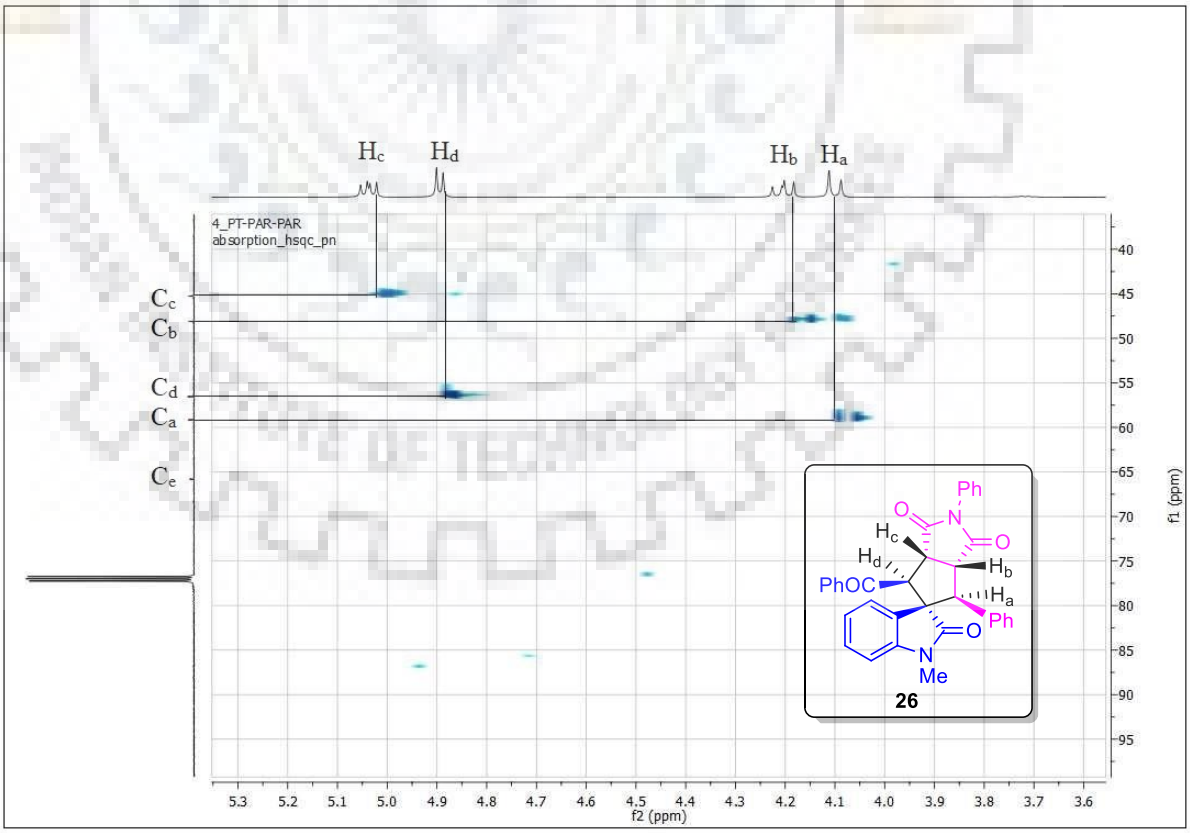


Figure 5: $^{1}H–^{13}C$ (HSQC) COSY spectrum of **26**.

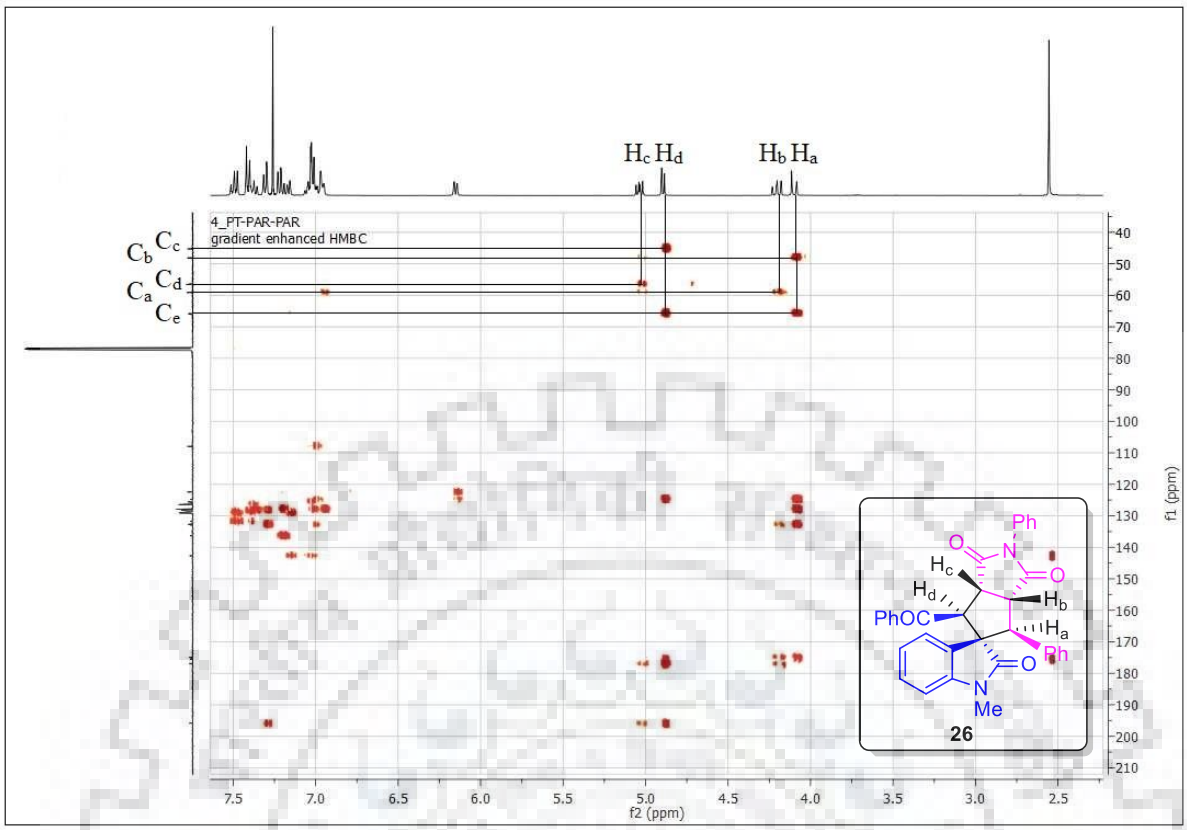


Figure 6: $^{1}H–^{13}C$ (HMBC) COSY spectrum of **26**.

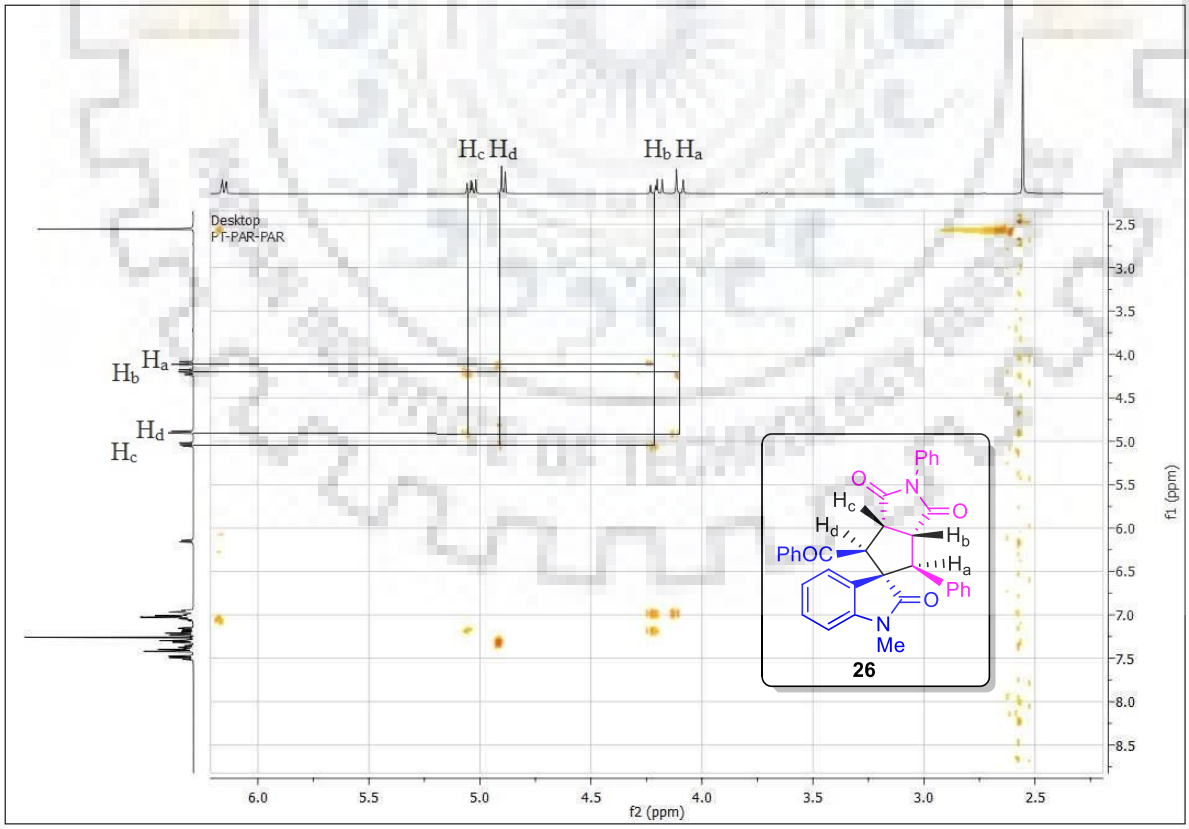
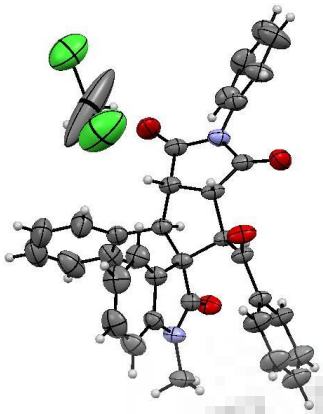
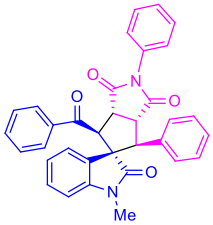


Figure 7: $^{1}H–^{1}H$ NOESY spectrum of **26**.





26

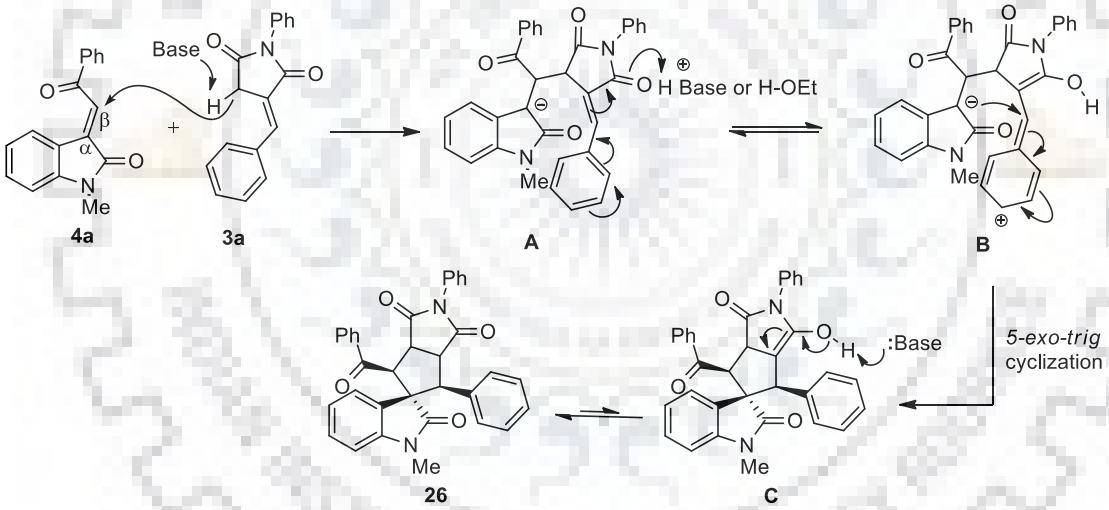
Figure 8: ORTEP representation of crystal structure of **26** [216].

Table 4: Crystallographic data for spirooxindole **26**.

Empirical formula	$C_{35}H_{28}Cl_2N_2O_4$
Formula weight	611.49
Temperature	296(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P -1
Unit cell dimensions:	
a (Å)	11.156(5)
b (Å)	11.456(5)
c (Å)	13.201(6)
α (deg.)	100.51(2)
β (deg.)	108.58(2)
γ (deg.)	100.45(2)
Volume ($Å^3$)	1519.5(11)
Z	30
Calculated density (mg/m^3)	3.735
Absorption coefficient	2.804 mm^{-1}
F(000)	1680
Theta range for data collection	1.684 to 28.697 deg.
Reflections collected/unique	25896/7505 [R(int) = 0.0356]
Completeness to theta = 25.242	99.0 %
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	7505 / 0 / 390
Goodness-of-fit on F^2	1.474

Final R indices [I>2sigma(I)]	R1 = 0.1081, wR2 = 0.3387
R indices (all data)	R1 = 0.1441, wR2 = 0.3861
Largest diff. peak and hole	1.397 and -1.137e.Å^{-3}

The plausible mechanism for the formation of spirooxindole is depicted in Scheme 11. Firstly, the anion generated from 3-benzylidene *N*-phenylsuccinimide (**3a**) by the abstraction of proton with DBU, attacks on β-carbon of amide functionality in **4a** as α-position is relatively more hindered and produces anion **A**. The carbanion **A**, being benzylic and α- to carbonyl is highly stabilized and acts as soft nucleophile. The aromatic ring of benzylidene moiety may participate in resonance to benzyl carbonium ion centre that facilitates *5-exo-trig* cyclization at a soft electrophilic centre of **B** leading to tetracyclic system **C**. The hydroxyenamine **C** tautomerises to more stable imide **26**. The excellent diastereoselectivity realised in the reactions of 3-benzilidine succinimides with the enones studied may be attributed to the presence of steric bulk in the vicinity of reacting sites.



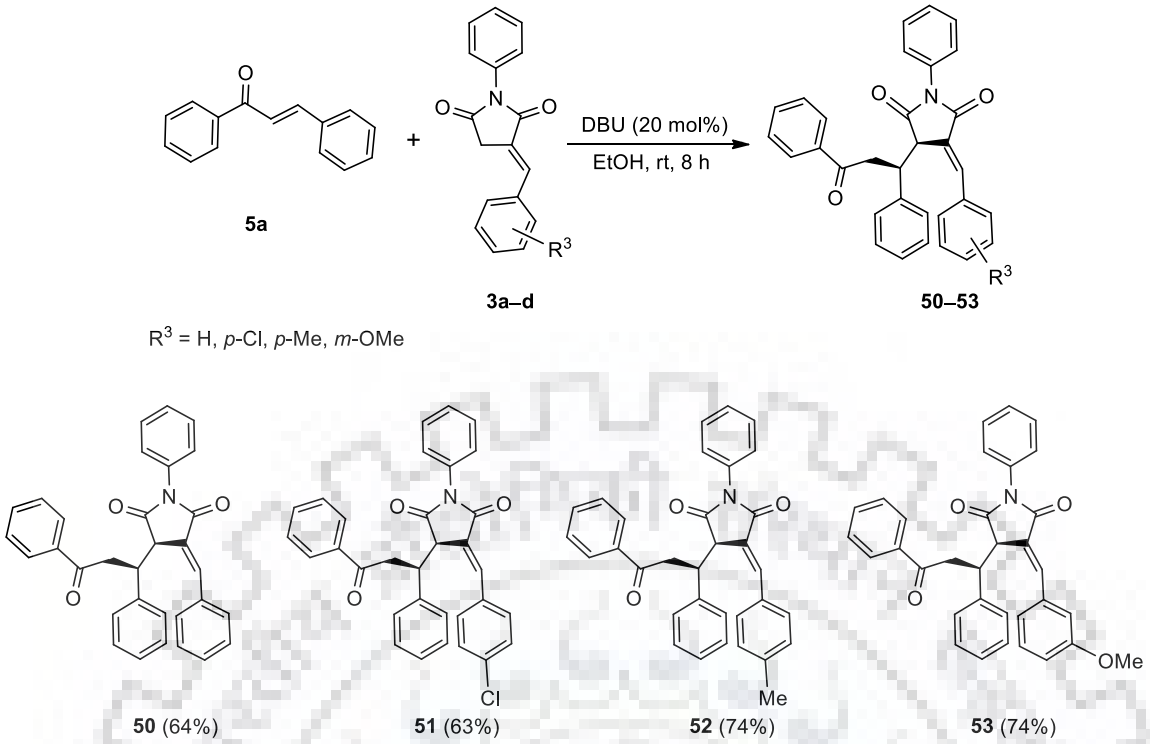
Scheme 11: Plausible reaction mechanism for the formation of spirooxindole **26**.

2.2.3. Synthesis of benzylidene succinimide-tethered propanones *via* Michael addition reactions

The functionalization of allylic center has always been an important concern to organic chemists as it is having a great contribution in synthesis of various biologically active molecules [217–220]. And Michael addition is an important tool to achieve C–C bond formation in economically favourable way by using the processes that are reasonably simple [117, 118, 221–224]. The use of Michael addition in organic synthesis is constantly increasing because it allows the chemists to synthesize a wide range of complex molecules including natural products and biologically active compounds such as pharmaceuticals and agrochemicals [119,225–229]. The construction of molecules with two and more stereocenters in a steteroselective manner through catalysis has attracted continuous attention in recent years because of their presence in various natural products [230–233].

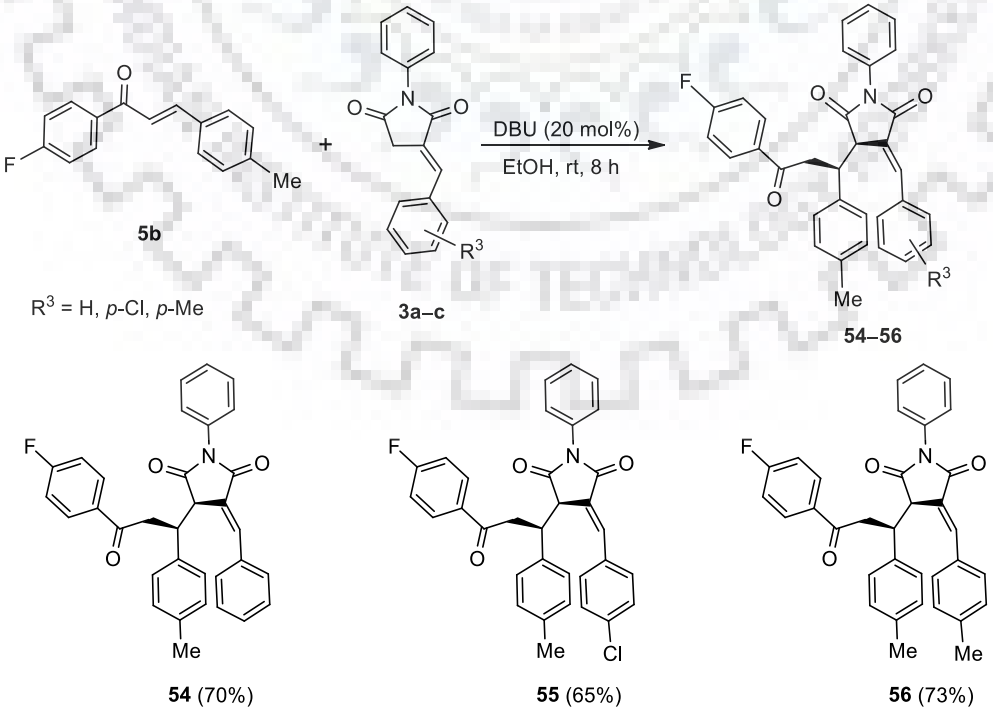
Succinimide and derivatives are of great scientific interest in the family of nitrogen containing compounds because of their remarkable pharmacological profile. These compounds are reported to have various biological activities such as anticoagulant, insecticidal, anthelminthic, hypnotic, antifungal, phytoalexin, and HIV protease inhibition [234–238]. Numerous efforts have been made by the researchers from time to time to synthesize these moieties. There are many reports in the literature where maleimide being used as Michael acceptor and brought out succinimide as a part of the final product [120,122,239–242]. However there are just a few literature reports known when 3-benzylidene succinimides being used either in cycloaddtion reactions or as a Michael donor. To the best of our knowledge, there are no reports known so far on their reactions with chalcones [111,123,243–244]. This made us curious, as chalcones are one of the most privileged compounds known for their unique contribution in organic synthesis and medicinal world [246–256]. Being motivated by these inputs, we tried to perform addition of 3-benzylidene succinimides on chalcones.

At the outset, we carried out the reactions of parent chalcone **5a** with differentially substituted 3-benzilidine *N*-phenyl succinimides **3a–d**. The reaction furnished Michael adducts **52** and **53** in good yield when benzilidine succinimides containing electron-donating groups in comparison to electron-withdrawing groups (**3b** furnished the product **51** in 63% yield, Scheme 12).



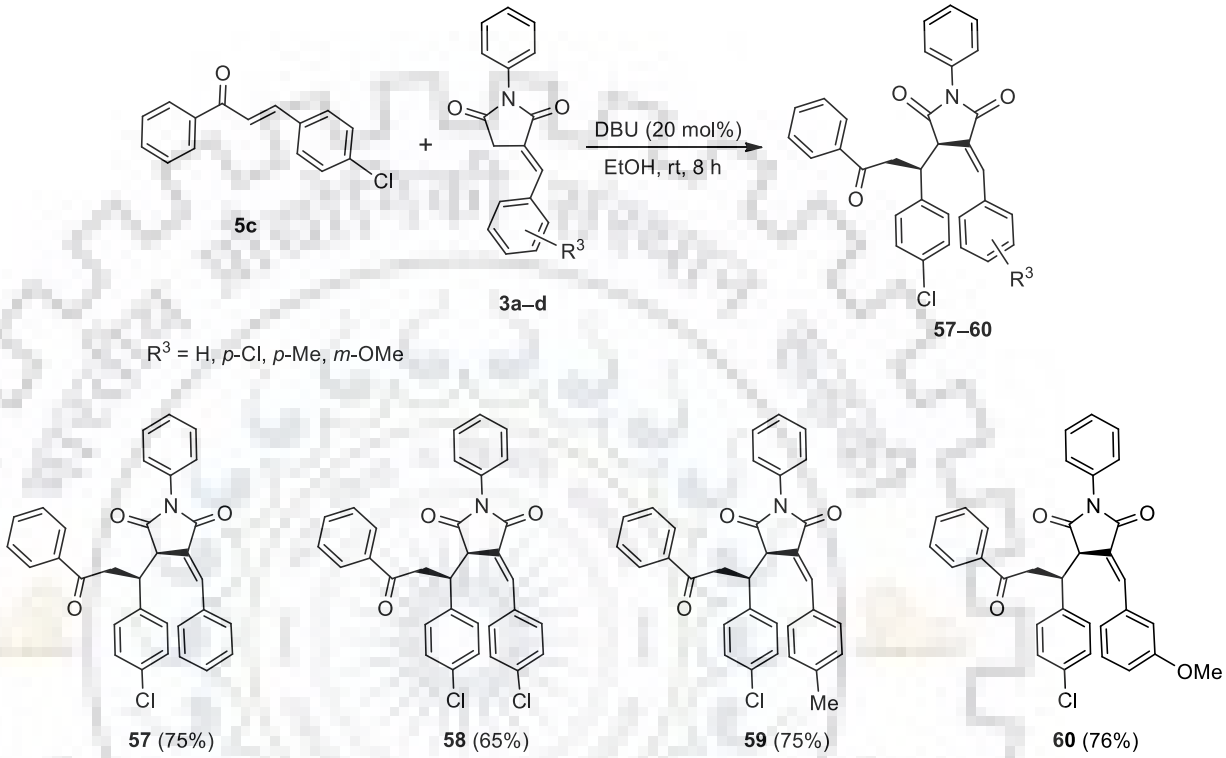
Scheme 12: Reaction of chalcone **5a** with 3-benzilidine succinimides **3a–d**.

When the chalcone **5b** was treated with 3-benzilidine succinimides **3a–c** the products **54–56** were obtained in 70, 65 and 63%, respectively, clearly showing favourable electronic conditions with electron-donating groups over electron-withdrawing groups on succinimides (Scheme 13).



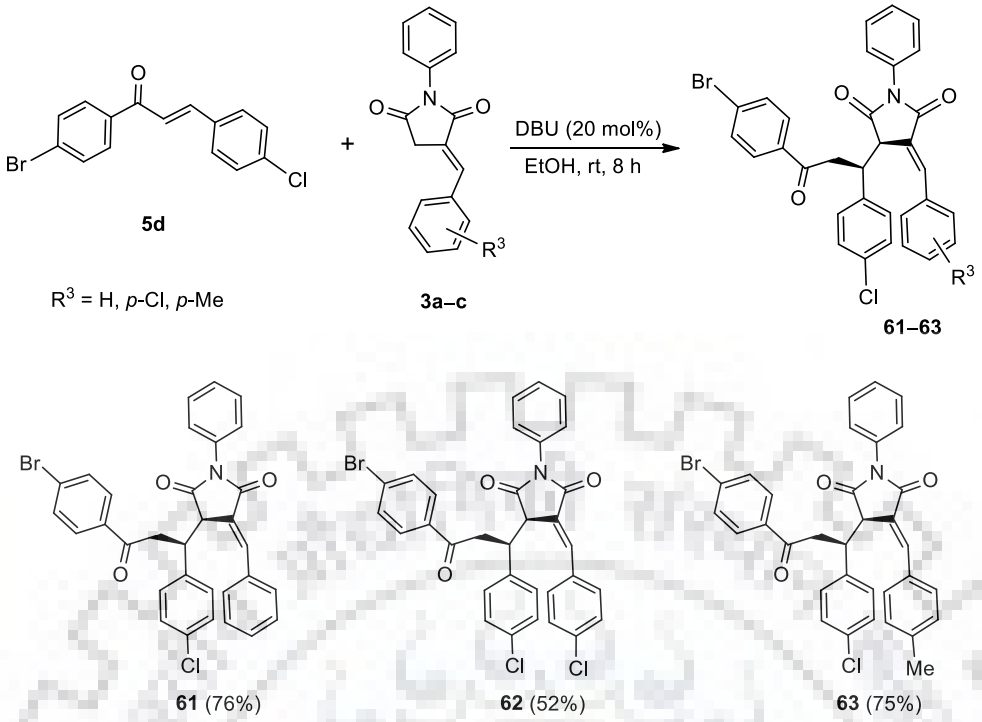
Scheme 13: Reaction of chalcone **5b** with 3-benzilidine succinimides **3a–c**.

To expand the scope of the reaction, chalcone **5a** was treated with 3-benzylidine succinimides **3a–d**. As shown in Scheme 14. Notably, the donors **3b–d** bearing 4-chloro, 4-methyl and 3-methoxy groups on the benzylidine moiety could also be well tolerated. It was observed that EDG on benzylidine favoured the reaction by furnishing addition products **59** and **60** in 75 and 76% yields as compared to EWG to afford **58** in 65% yield (Scheme 14).



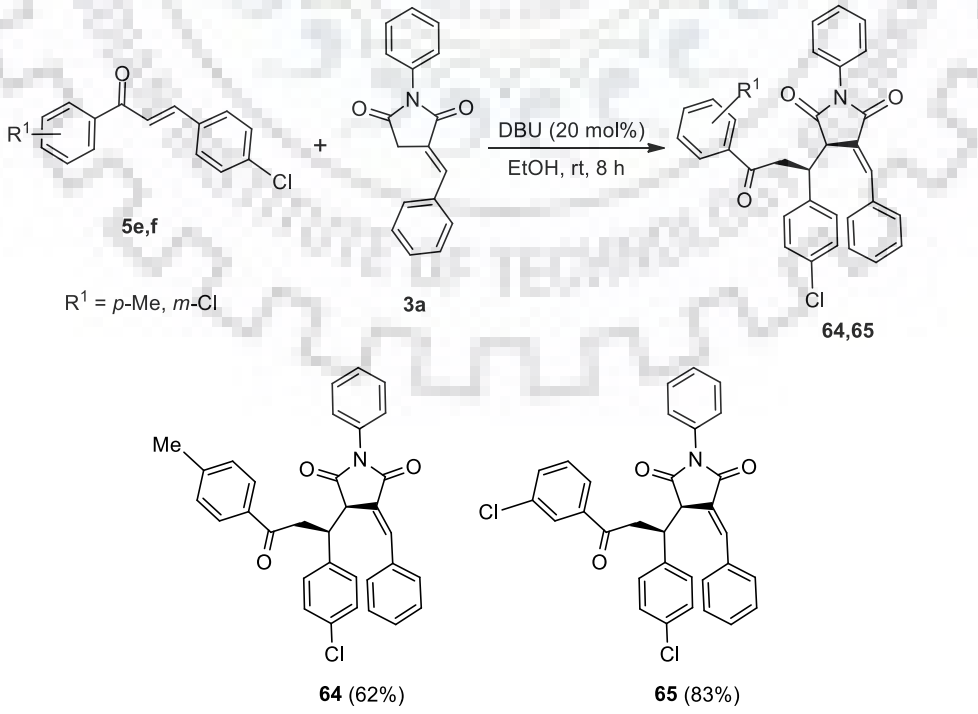
Scheme 14: Reaction of chalcone **5c** with 3-benzilidine succinimides **3a–d**.

Interestingly, when dihaloginated chalcone **5d** was reacted with 3-benzilidine succinimides **3a–c** under the optimized reaction conditions to provide the corresponding Michael adducts **61–63** in 76, 52 and 75% yields, respectively (Scheme 15).



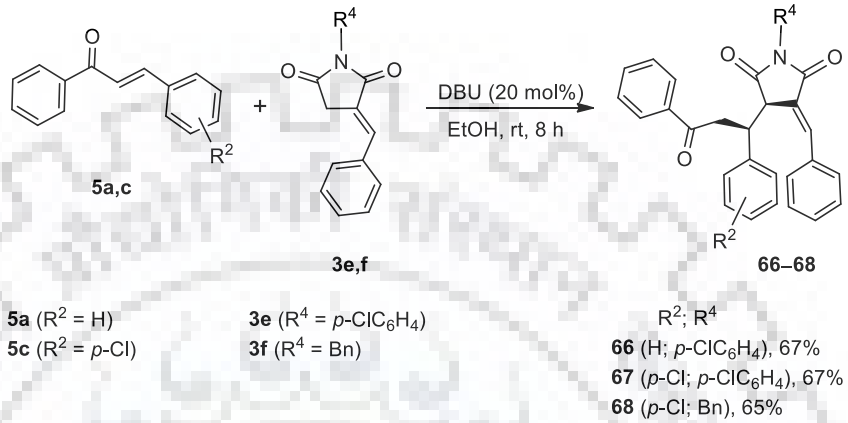
Scheme 15: Reaction of chalcone **5d** with 3-benzilidine succinimides **3a–c**.

Then we explored the scope of *N*-aryl benzylidine succinamide **3a** with chalcone derivatives **5e** and **5f**. The reaction proceeded smoothly under the optimized reaction conditions to provide the corresponding Michael adducts **64** and **65** in 62 and 83% yields, clearly showing the presence of *m*-chloro substituent on **5f** affected the yield significantly (Scheme 16).



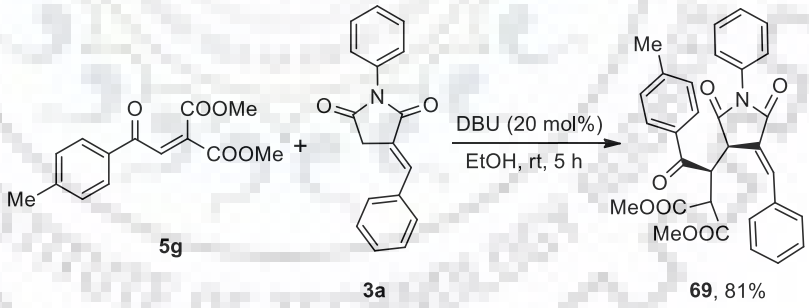
Scheme 16: Reaction of chalcone **5e,f** with 3-benzilidine succinimides **3a**.

On finding a good response of the reaction for various substrates, we thought of testing the presented protocol by changing the phenyl protection of succinimide with substituted phenyl(*p*-Cl) **3e** and benzyl groups **3f** with chalcones **5a,c**. Gratifyingly both the variations worked good and furnished the Michael adducts **66**–**68** in 67, 67 and 65% yields with excellent diastereoselectivity (Scheme 17).



Scheme 17: Reaction of chalcone **5a,c** with 3-benzilidine succinimides **3e,f**.

Further, we extended the scope of this protocol to benzoylmethylidene malonate **5g**. To our delight, the reaction of 3-benzylidine succinimide **3a** with **5g** showed good compatibility and produced Michael adduct **69** in 81% yield with excellent diastereoselectivity (Scheme 18).



Scheme 18: Reaction of benzoylmethylidene malonate **5g** with 3-benzilidine succinimide **3a**.

NMR studies of 51:

The structure of Michael adducts were confirmed by detailed analysis obtained from ^{1}H and ^{13}C NMR, and HRMS spectral data of isolated products. For instance, in the ^{1}H NMR of Michael adduct **51**, the protons H_a and $H_{a'}$ appear at δ 3.27 and 4.68 ppm, respectively, each as doublet of doublets and the proton H_b appears at δ 4.14 as doublet of triplet and the proton H_c appears at 4.51 ppm as doublet of doublet (Figure 9).

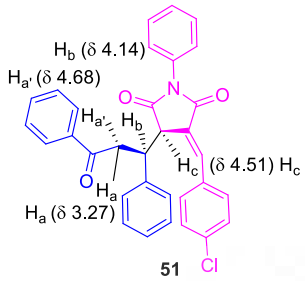
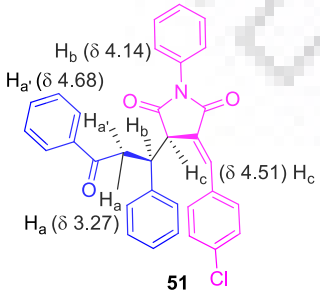


Figure 9: Selected ^{1}H NMR chemical shifts (ppm) in **51**.

The connectivity of the protons that are coupled with each other and between protons and carbons of Michael adduct **51** was identified by two-dimensional ^{1}H–^{1}H COSY and ^{1}H–^{13}C COSY experiments, respectively (Figures 10 and 11). To gain better insight on the stereochemistry of these products through the spatial correlation between H_a, $H_{a'}$, H_b and H_c protons, we performed NOESY experiment of Michael adduct **51**. The presence of correlation between the protons 'H_a and H_b', 'H_a and $H_{a'}$', 'H_b and H_c' and 'H_b and $H_{a'}$', the absence of correlation between 'H_a and H_c' establishes the geometry depicted in Figure 9. The results obtained from NMR studies were further confirmed by the single crystal X-ray analysis of compound **57** (Figure 14).

Table 5: Proton–proton and proton–carbon connectivity in **51.**

Michael adduct	^{1}H-^{1}H COSY	^{1}H-^{13}C COSY	**δ** (ppm)	HMBC	NOESY
	H_a - $H_{a'}$	C_a	39.9	H_a - C_b, C_c	H_a - H_b
	H_a - H_b	C_b	39.0	H_b - C_a, C_c	H_a - $H_{a'}$
	H_b - H_c	C_c	46.1	H_c – C_b	H_b - H_c
	H_b - $H_{a'}$	-	-	$H_{a'}$ - C_b, C_c	H_b - $H_{a'}$
	-	-	-	-	H_c - $H_{a'}$

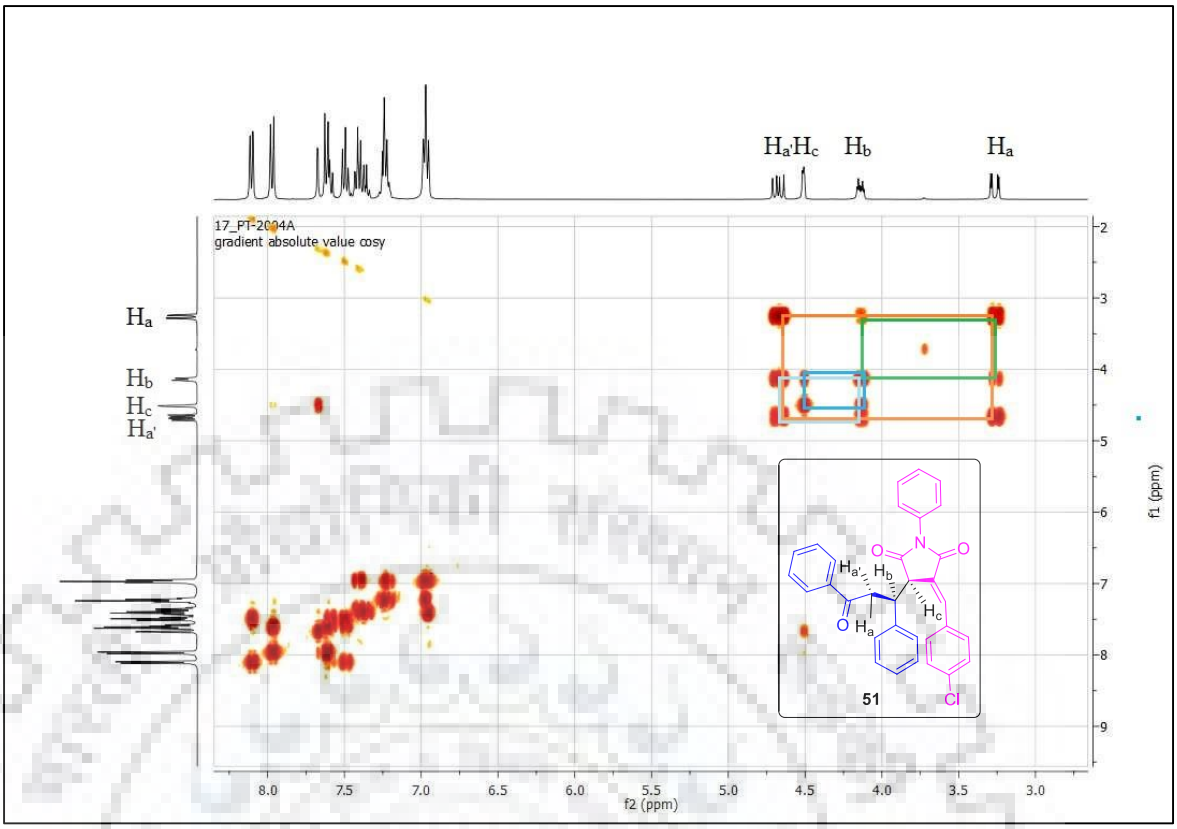


Figure 10: $^{1}H–^{1}H$ COSY spectrum of **51**.

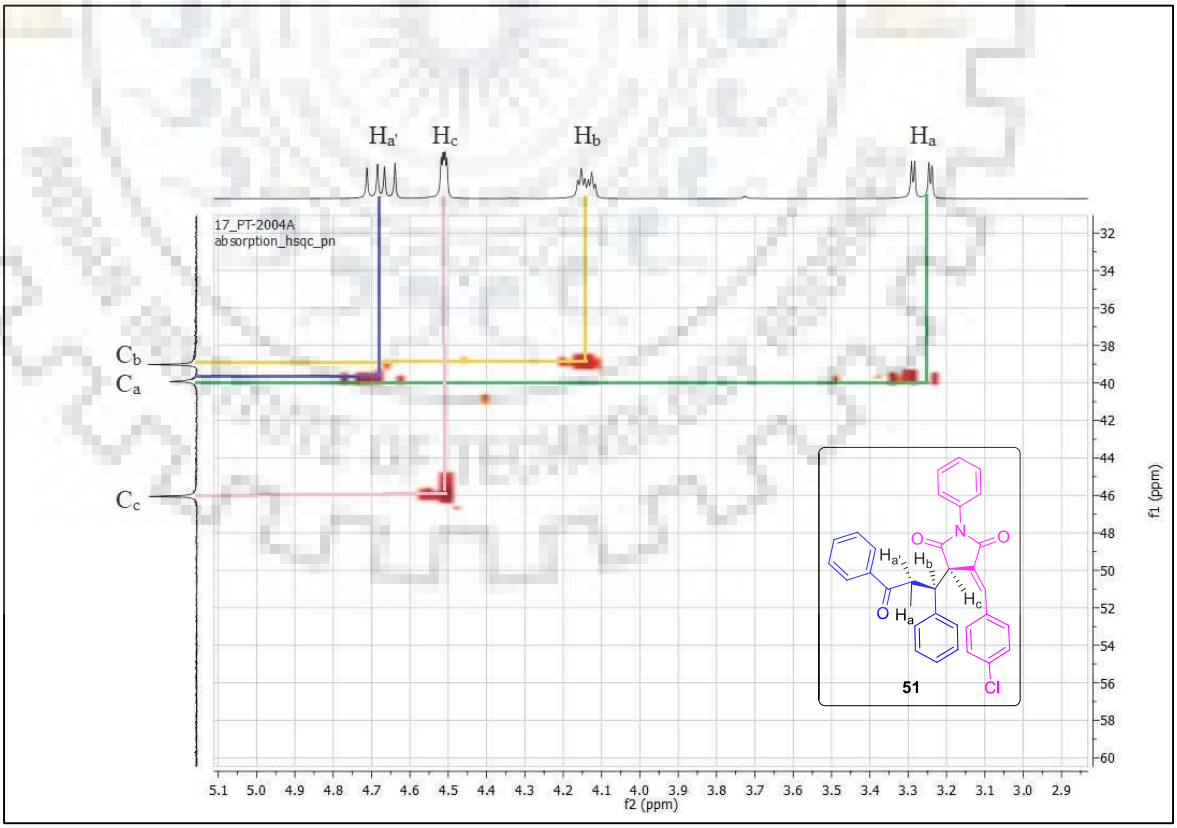


Figure 11: $^{1}H–^{13}C$ (HSQC) COSY spectrum of **51**.

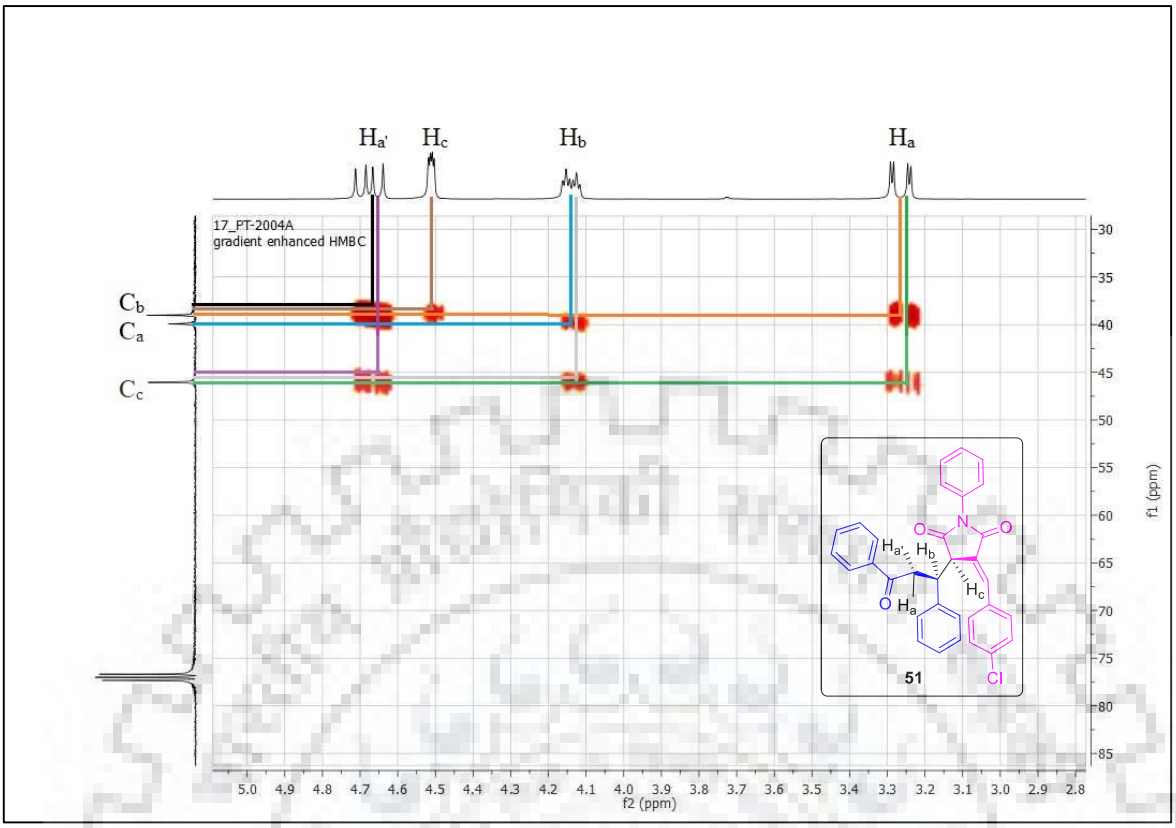


Figure 12: $^{1}H–^{13}C$ (HMBC) COSY spectrum of **51**.

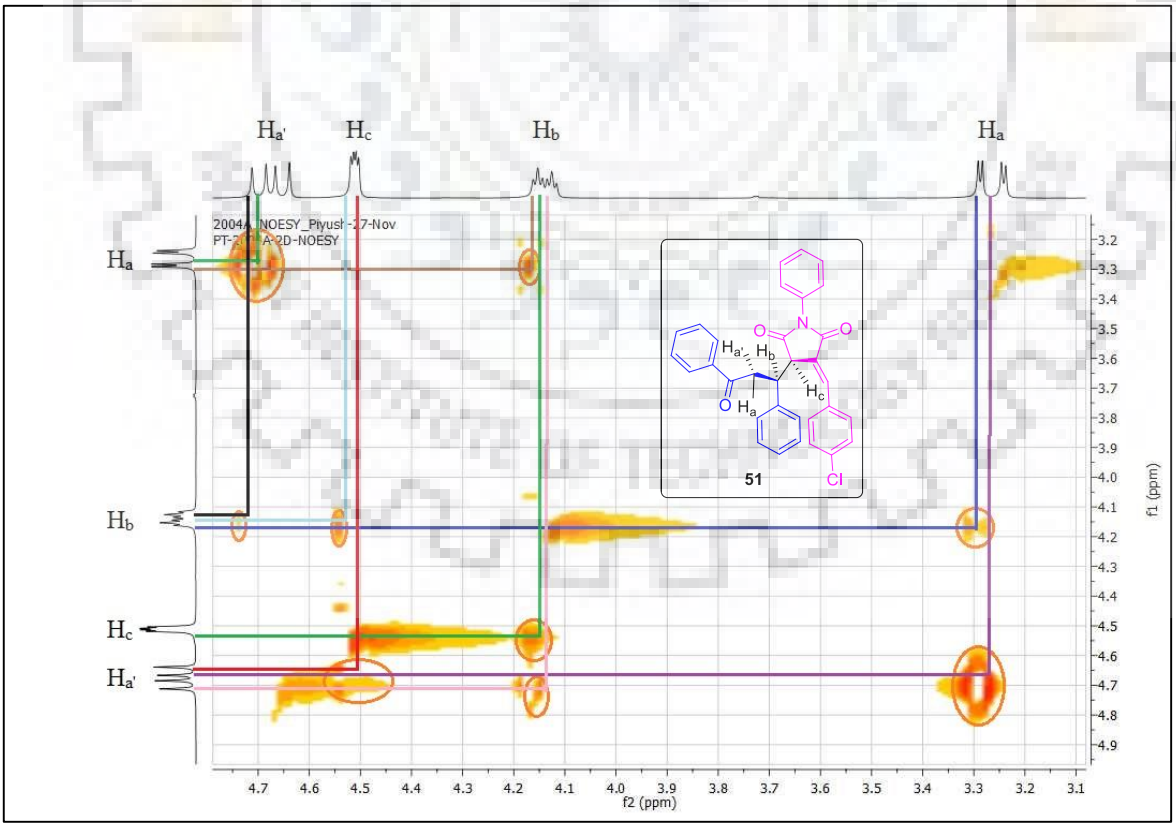
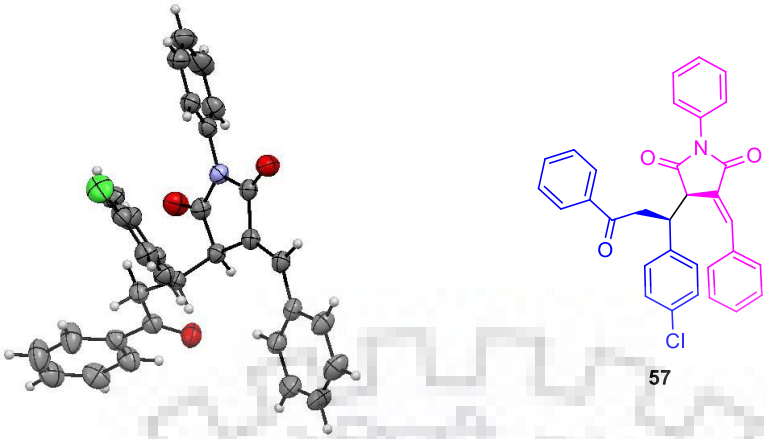


Figure 13: $^{1}H–^{1}H$ NOESY spectrum of **51**.



57

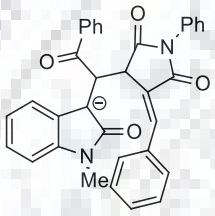
Figure 14: ORTEP representation of crystal structure of **57** [257].

Table 6: Crystallographic data for **57**.

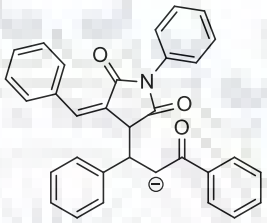
Empirical formula	$C_{32}H_{24}ClNO_3$
Formula weight	505.97
Temperature	296(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P-1
Unit cell dimensions:	
a (Å)	10.6788(6)
b (Å)	11.5046(3)
c (Å)	12.2981(3)
α (deg.)	114.4170(10)
β (deg.)	103.953(2)
γ (deg.)	96.855(2)
Volume ($Å^3$)	1293.50(9)
Z	17
Calculated density (mg/m^3)	1.713
Absorption coefficient	0.975 mm^{-1}
F(000)	663
Theta range for data collection	1.92 to 28.350 deg.
Reflections collected/unique	20574/6421 [R(int) = 0.0253]
Completeness to theta = 28.35°	99.3 %
Refinement method	Full-matrix least-square on F^2

Data/ restraints/ parameters	6421/ 0/ 335
Goodness-of-fit on F^2	1.052
Final R indices [I>2sigma(I)]	R1 = 0.0480, wR2 = 0.1407
R indices (all data)	R1 = 0.0740, wR2 = 0.1803
Largest diff. peak and hole	0.460 and –0.389 e.$Å^{-3}$

In the case of chalcone **4** or benzoylmethylidene malonate **6a**, the enolate arising from Michael addition is relatively 'hard' (less stabilized than amide enolates formed from 3-ylidene oxindoles) and therefore gets easily protonated (hard electrophile) rather than taking part in second Michael addition for the cyclization with a soft centre and Michael adduct is obtained as final entity.



(Amide enolate)



(Ketone enolate)

2.2.4. Synthesis of highly conjugated xanthene-tethered unsymmetrical biarylic spirooxindoles *via* domino reactions

Synthesis of biaryls has been admired as an important strategy in recent years because of frequent occurance of these units in many natural products and pharmaceuticals, further it extends the conjugation which makes them an integral part of organic conductors, light emitting diodes and fluorescent molecules [139,140,258–265]. Coupling the aryl moieties enriched with specific groups have been a traditional cross-coupling strategy known for the synthesis of biaryls [266–274]. While, C–H activation provides modern approach to biaryls, intromolecular construction of aromatic units leading to the formation of unsymmetrical biaryls provides a fascinating path to access structurally important scaffolds [11,136,275–278]. In addition to this oxindoles and spirooxindoles cores are privileged heterocyclic scaffolds which can be frequently found in numerous biologically and pharmacological active molecules and exhibit many properties including anticancer, anticonvulsant, anti-depressant, antibacterial, antifungal, antioxidant and antiviral activities. Hence, efforts have been made towards the exploration of productive methodologies for the synthesis of compounds having such moieties [109,201,275–284]. Moreover, It has been observed that xanthene and its derivatives came up as interesting moieties to be explored recently because of their special structural features which contribute towards medicinal, dye industries and in catalysis [64,285–293].

Donor–acceptor (D–A) cyclopropanes have attracted considerable interest as versatile synthetic intermediates for useful organic transformations, including enantioselective catalysis and annulation reactions, which are being driven by the inherent angle strain, and intrinsic torsional strain reconcile in such a fashion to provide substituent-controlled C–C bond polarization/cleavage [60,62,69,294–298]. This has provided impetus to research directed towards the development of practical, efficient, and convenient use of these reactive moieties [63,299,300]. With the wish to contribute to this continuously flourishing field of D–A cyclopropanes, several synthetic chemists started investigating their reactions [62–64]. In 2016, Biju and co-workers reported that Lewis acid activated D–A cyclopropanes react with β-naphthols to form naphthalene-fused cyclopentanes *via* a highly selective dehydrative [3 + 2] cyclopentannulatio [65]. (Figure 1) Usually there are four types of D-A cyclopropanes reported in literature, type (i) and (ii) have been explored to a good extent and still under consideration [67,69], whereas type (iii) and (iv) have not been explored much till date (Figure 15). Keeping this thing in mind, we envisioned the reaction

of spirooxindoles embedded cyclopropanes [type (ii), as unique substrate] with *β*-naphthols. Gratifyingly, the reaction underwent in a domino ring-opening cyclization (DROC) pathway and delivered hybrid structure enriched with important scafolds such as biaryl, xanthene and spirooxindole. The beauty of the work lies in its state of art working pattern, as the spirocyclic-cyclopropanes irrigated with two ketonic functional groups as acceptors and each of them contributes selectively to make the approach realistic by furnishing the highly conjugated spirooxindolic-xanthenes tathered unsymmetrical biaryls in a one-pot manner.

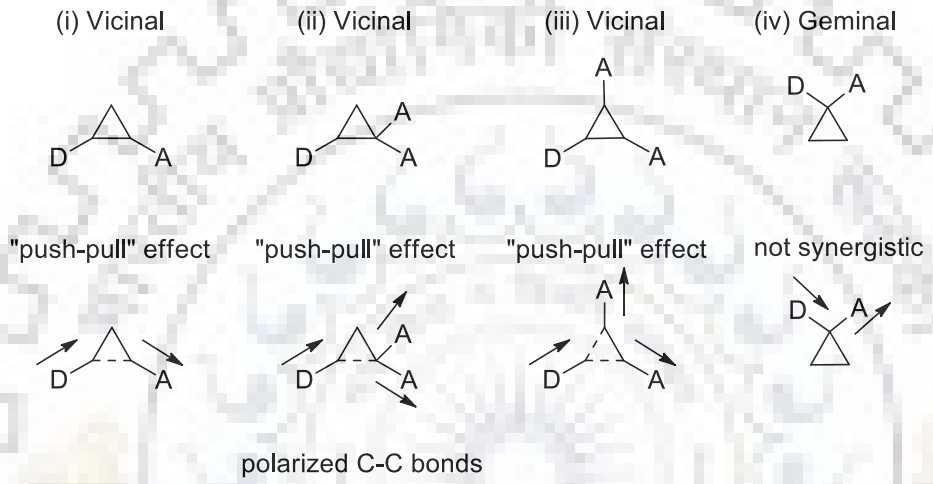
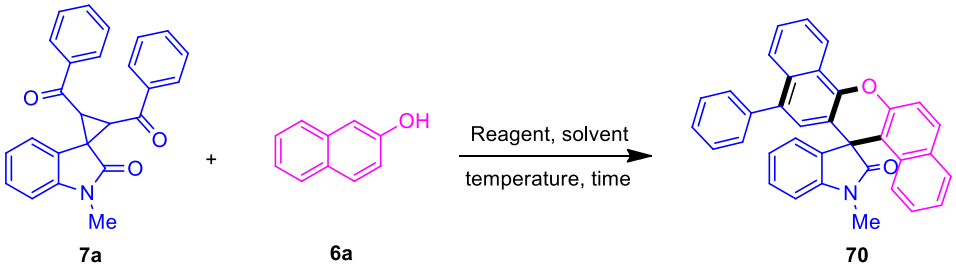


Figure 15: Types of donor-acceptor (D-A) cyclopropanes.

At the outset of our studies, we chose spirocyclic cyclopropane **7a** and *β*-naphthol (**6a**) as model substrates to optimize the conditions for the anticipated domino ring opening cyclization. As a starting point, the reaction was carried out in dichloroethane at 80 ^{o}C for 24 h. When most of the commonly used Lewis acids either did not work or just furnished small amounts of polycyclic product **70** (Table 7, entries 1–3), $BF_3.OEt_2$ delivered spirooxindole **70** in moderate yield (entry 4). Motivated by the outcome, we investigated the reaction with various reagents. The replacement of $BF_3.OEt_2$ with various Brønsted acids such as TFA, $MeSO_3H$, *p*-TSA·H_2O, 2,4-DNB, H_2SO_4, HCl and CF_3SO_3H demonstrated CF_3SO_3H as a motivating entity to move ahead (entries 5−11). We further checked the performance of the reaction with a series of solvents. In polar protic solvents like ethanol, only traces of the product were obtained whereas on using polar aprotic solvent such as DMF and ACN no reaction occurred (entries 12−14). When we used toluene as solvent, the reaction furnished 49% of spirooxindole **70** (entry 15). Notably, we concluded DCE as the suitable solvent for the reaction, thereafter we tried to vary the equiv.alents of CF_3SO_3H. On reducing the reagent to 0.5 equiv., the polycycle **70** was obtained in a reduced

Table 7: Optimization of reaction conditions.[a]



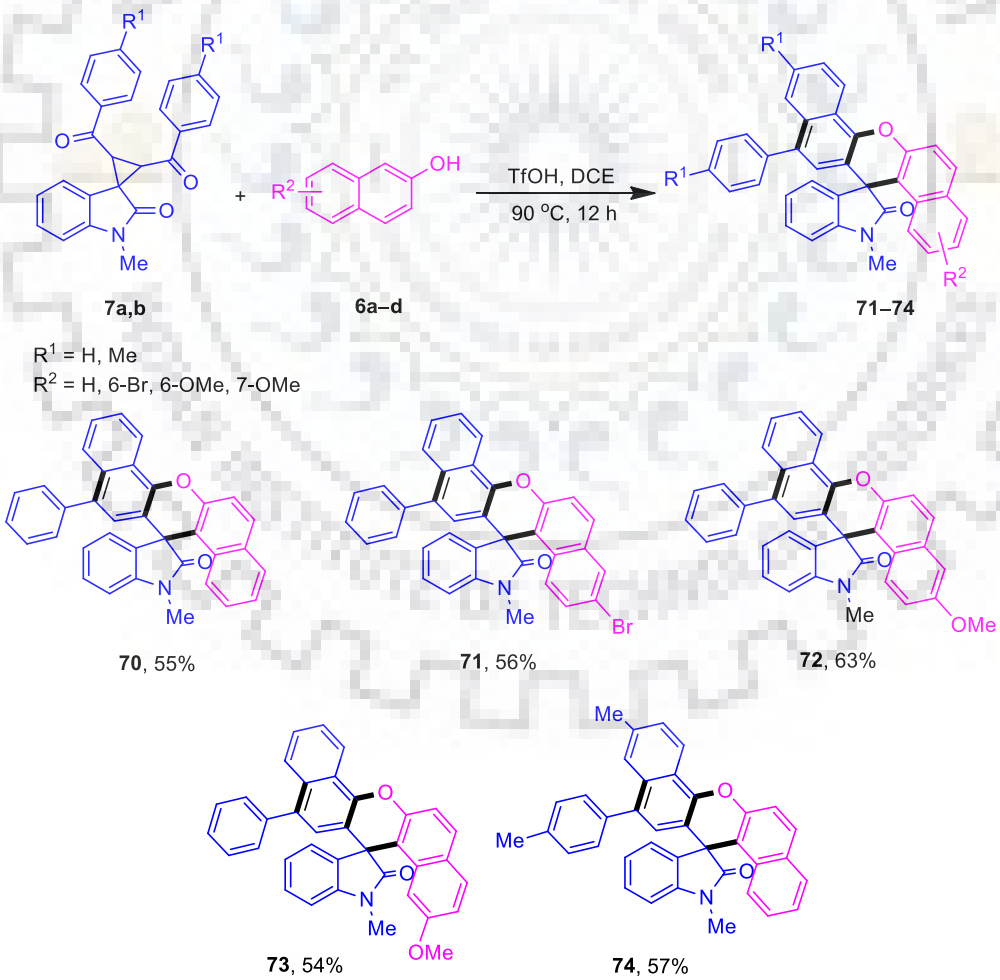
7a **6a** **70**

Entry	Reagent (equiv.)	Solvent	Temp (°C)	Yield [b] (%)
1	$AlCl_3$ (1.0)	DCE	80	nr
2	$ZnCl_2$ (1.0)	DCE	80	nr
3	$FeCl_3$ (1.0)	DCE	80	10
4	$BF_3.OEt_2$ (1.0)	DCE	80	40
5	TFA (1.0)	DCE	80	nr
6	$MeSO_3H$ (1.0)	DCE	80	15
7	$PTSA.H_2O$ (1.0)	DCE	80	traces
8	2,4-DNB (1.0)	DCE	80	nr
9	H_2SO_4 (1.0)	DCE	80	traces
10	HCl (1.0)	DCE	80	tr
11	CF_3SO_3H (1.0)	DCE	80	52
12	CF_3SO_3H (1.0)	EtOH	80	traces
13	CF_3SO_3H (1.0)	DMF	80	nr
14	CF_3SO_3H (1.0)	ACN	80	nr
15	CF_3SO_3H (1.0)	Toluene	80	49
16	CF_3SO_3H (1.0)	HFIP	80	45
17[c]	CF_3SO_3H (0.5)	DCE	80	38
18[d]	CF_3SO_3H (1.2)	DCE	80	50
19[e]	CF_3SO_3H (1.0)	DCE	60	nr
20[f]	CF_3SO_3H (1.0)	DCE	90	55
21[f]	CF_3SO_3H (1.0)	DCE	100	52

[a]Reaction conditions: Unless otherwise specified, all reactions were carried out with **7a** (0.1 mmol), **6a** (0.1 mmol), and triflic acid (0.1 mmol) in 2 mL of solvent for 24 h. [b]Isolated yield of **3a**. [c]0.5 mmol of triflic acid was used. [d]1.2 mmol of triflic acid was used. [e]reaction time 48 h. [f]reaction time 12 h.

yield of 38% (entry 17). No improvement was observed when 1.2 equiv. of CF_3SO_3H were used (entry 18). To know the effect of temperature, the reaction was performed at 60 °C; however, the starting materials were intact. On increasing the temperature to 90 °C, the product 70 was obtained in an increased yield of 55%; however, further increment in the temperature to 100 °C was not supportive (entries 20 and 21). Thus, with 1.0 equiv. of CF_3SO_3H, the reaction of spirocyclic cyclopropane **7a** and *β*-naphthol (**6a)** at 90 °C provided the polycyclic spirooxindole **70** in optimum yield of 55% in 12 h (entry 20).

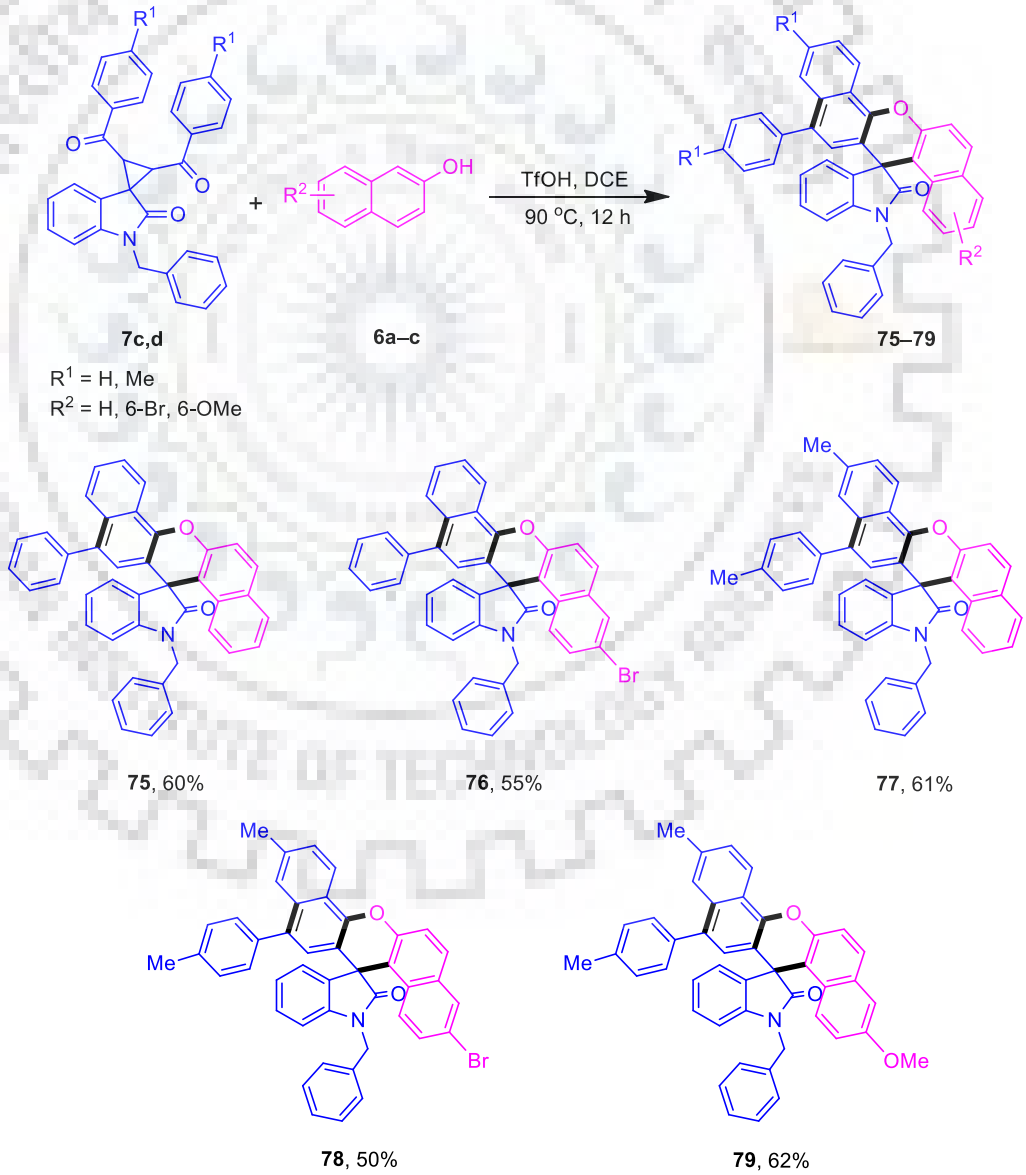
With the optimized reaction conditions in hand, we proceeded to explore the scope of triflic acid mediated protocol for the synthesis of xanthene-tethered biarylic spirooxindoles from cyclopropanes **7a–d** and *β*-naphthols **6a–d**. The reaction proceeded smoothly in highly regioselective manner to afford the polycyclic systems **70–79** in good yield. When the unsubstituted/parent *N*-methyl spirooxindolic cyclopropane **7a** was treated with various substituted *β*-naphthols **6a–d**, the domino adducts **70–73** were obtained in 55, 56, 63, and



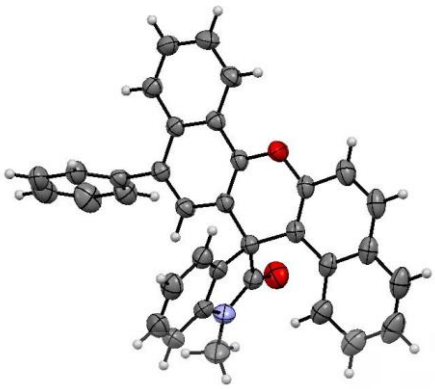
Scheme 19. Synthesis of xanthene-tethered biarylic spirooxindoles from *N*-methyl protected spirooxindolic cyclopropanes **7a,b**.

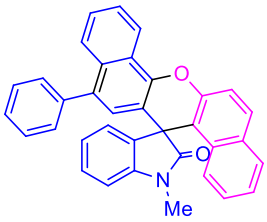
54% yields, respectively. On performing the reaction between *p*-methyl substituted cyclopropane **7b** and 2-naphthol, the product **74** was furnished in 57% yield (Scheme 19).

We tested the applicability of the present methodology for spirooxindolic cyclopropanes with bulky protecting group to ascertain its effect on the feasibility of the reaction. When *N*-benzyl protected spirooxindolic cyclopropanes were used in the reaction, no significant changes were noticed in the reaction. The reaction proceeded smoothly and the desired products **75**–**79** were obtained in 54–63% yield (Scheme 20). The structures of spiroxindoles hybrids obtained from spectral analysis of ^{1}H, ^{13}C NMR, and HRMS experiments of isolated products. The structure of compound **70** was further confirmed by its single crystal X-ray analysis (Figure 16).



Scheme 20: Synthesis of xanthene-tethered biarylic spirooxindoles from *N*-benzyl protected spirooxindolic cyclopropanes **7c,d**.





70

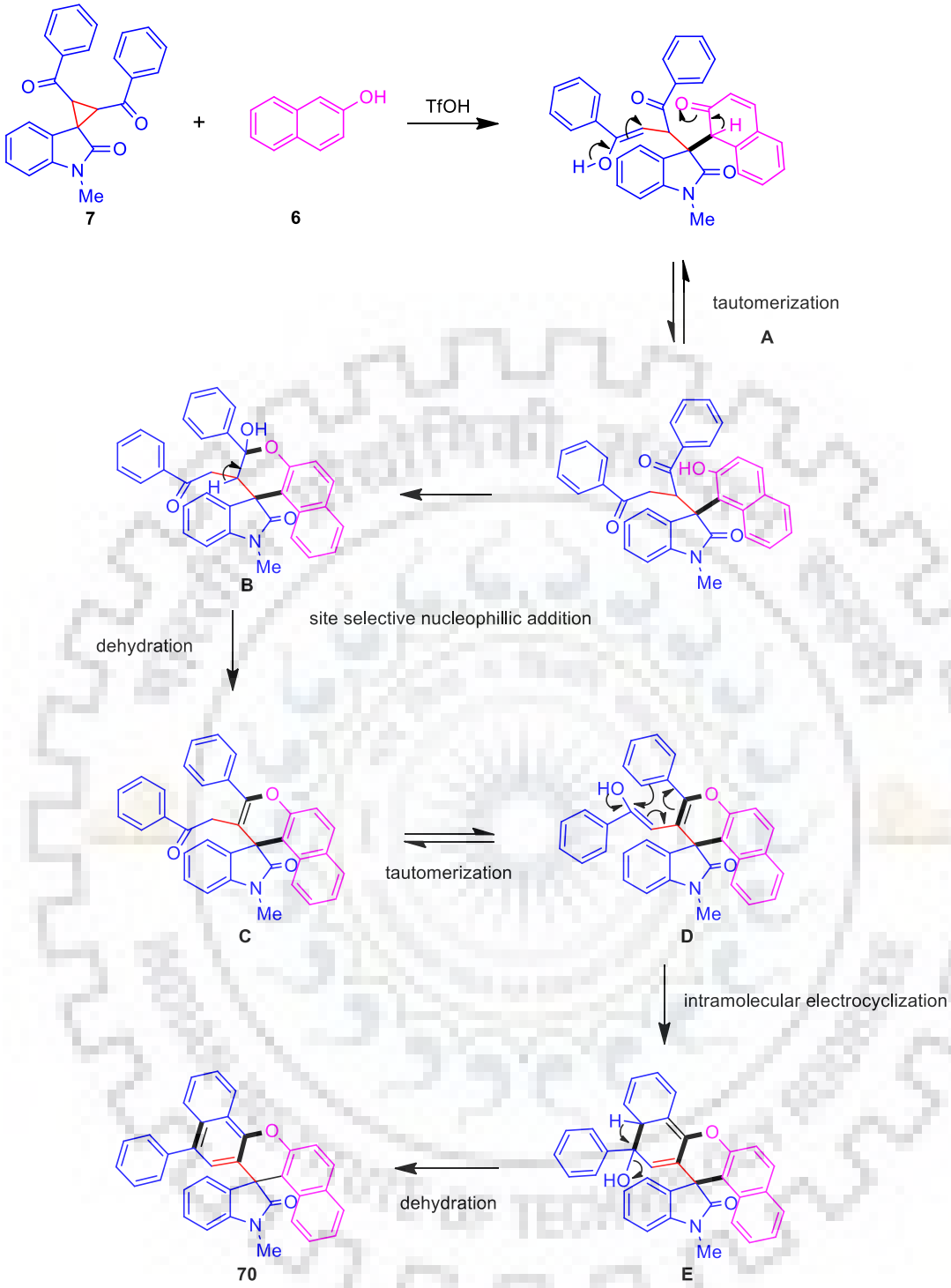
Figure 16: ORTEP representation of crystal structure of **70** [301].

Table 8: Crystallographic data for **70**.

Empirical formula	$C_{35}H_{23}NO_2$
Formula weight	489.17
Temperature	296(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P -1
Unit cell dimensions:	
a (Å)	10.764(3) Å alpha = 89.898(17) deg.
b (Å)	13.718(3)
c (Å)	18.089(5)
α (deg.)	89.898(17)
β (deg.)	89.092(15)
γ (deg.)	68.084(14)
Volume ($Å^3$)	2477.7(12)
Z	4
Calculated density (Mg/m^3)	1.442
Absorption coefficient	0.081 mm^{-1}

F(000)	1100
Theta range for data collection	1.126 to 28.480 deg.
Limiting indices	$-13\leq h\leq 14$, $-18\leq k\leq 18$, $-24\leq l\leq 24$
Reflections collected/unique	26324/12277 [R(int) = 0.0419]
Completeness to theta = 25.242 deg.	99.7 %
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	12277 / 0 / 688
Goodness-of-fit on F^2	1.005
Final R indices [I>2 sigma(I)]	R1 = 0.0604, wR2 = 0.1348
R indices (all data)	R1 = 0.1379, wR2 = 0.1958
Extinction coefficient	0.0254(18)
Largest diff. peak and hole	0.459 and -0.489 e.$Å^{-3}$

A plausible mechanism for this transformation is illustrated in Scheme 21. Initially triflic acid activates the cyclopropane **7a**, through polarization enhancement of C–C bonds of cyclopropane which triggers the Friedel–Crafts reaction with *β*-naphthol to generate the intermediate **A**, followed by an intramolcular nucleophilic attack of hydroxyl oxygen to one of the carbonyl groups selectively to form cyclized (six membered ring formation over seven membered) intermediate **B**. Then elimination of a water molecule from **B** leads to the formation of **C**. Intermediate **C** undergoes keto-enol tautomerization to **D**, which undergoes an intramolecular electrocyclization reaction followed by dehydration to generate the desired product **70**.



Scheme 21: Plausible reaction mechanism for the formation of xanthene-tethered biarylic spirooxindole **70**.

2.3. Conclusions

We have demonstrated metal-free regioselective stratigies for the synthesis biologically important scaffolds containing *β*-hydroxysulfides, highly diastereoselective synthesis of spirooxindoles and benzylidene succinimide-tethered propanones.

Iodine-catalysed regioselective synthesis of β-hydroxy sulfides

A metal-free, and environment benign iodine-catalysed protocol has been described for the regioselective synthesis of *β*-hydroxysulfides in good to excellent yields from easily accessible styrenes and thiophenols. The method involves C–S and C–O bonds formation in one-pot manner by utilizing DMSO as solvent as well as oxidant.

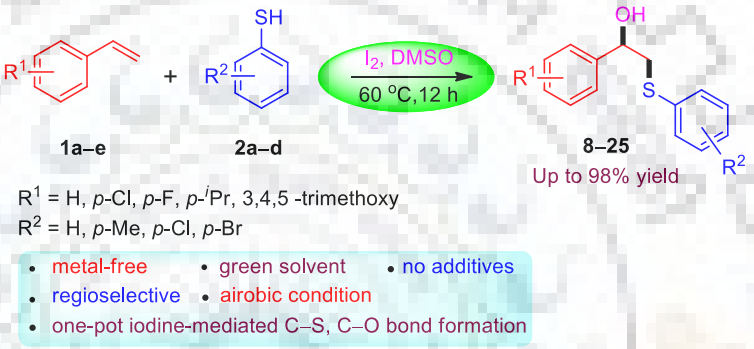


Figure 19: Synthesis of *β*-hydroxy sulfides from styrenes and thiophenols *via* free radical reaction.

DBU-Catalyzed highly diastereoselective synthesis of substituted spirooxindoles via a formal [3 + 2] cycloaddition of 3-ylideneoxindoles with 3-benzylidene succinimides

We have developed a metal-free, DBU catalyzed protocol for the regioselective synthesis of spirooxindoles incorporated with highly substituted functionally-rich cyclopentanes consisting of five consecutive stereocenters including one quaternary centre in good yield up to 79% with excellent diastereoselectivity up to >99%. The reaction proceeds through a formal [3 + 2] cycloaddition of 3-ylideneoxindoles with 3-benzilidine succinimides under mild conditions to furnish the title scaffolds by simple filtration followed by washing with ethanol.

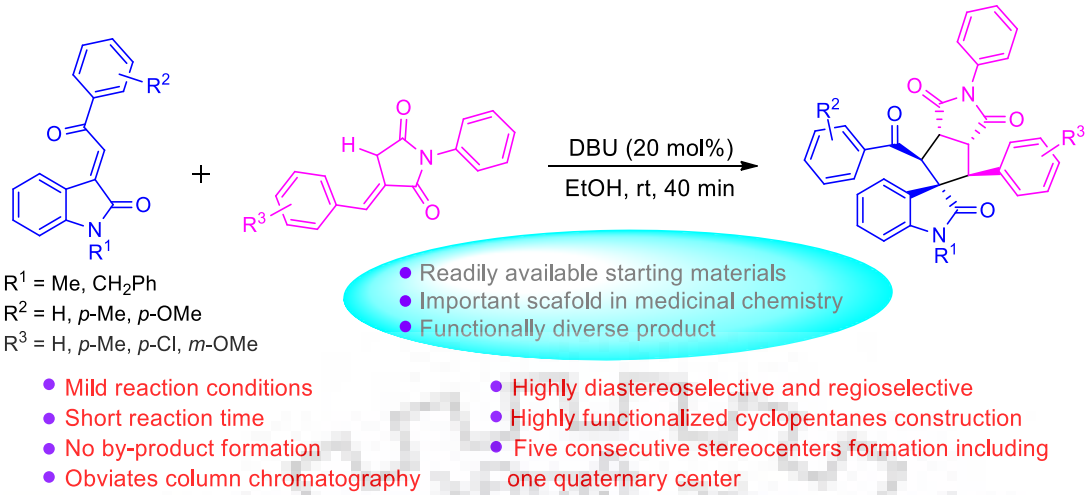


Figure 20: Synthesis of substituted spirooxindoles from 3-ylideneoxindoles with 3-benzylidene succinimides.

A DBU catalysed approach to achieve highly diastereoselective Michael type allylic addition of 3-benzylidene succinimides on chalcones

An efficient Michael addition approach for the synthesis of benzylidene succinimide-tethered propanones have been developed. The DBU-promoted strategy allowed us to access the title compounds in highly regeoselective pathway from easily accessible precursors. The products were isolated by filtration followed by simple washing with ethanol. The protocol displayed a good functional group tolerance.

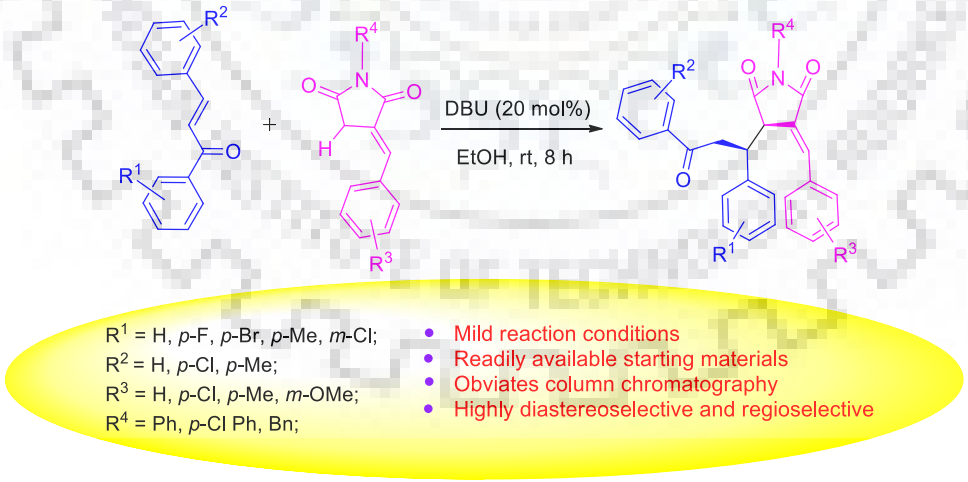


Figure 21: Synthesis of benzylidene succinimide-tethered propanones from 3-benzylidene succinimides and chalcones.

Bronsted acid mediated domino ring opening cyclization: Access to xanthene-tethered biarylic spirooxindoles from spirooxindolic D–A cyclopropanes

Triflic-acid mediated reactions of less-explored spirocyclic donor–acceptor (D–A) cyclopropanes with *β*-naphthols are demonstrated. The protocol underwent domino ring opening cyclization (DROC) approach involving nucleophillic ring opening/nucleophhillic addition/electrocyclization reactions in a sequential manner to furnish the highly conjugated biaryl-xanthene-spirooxindoles hybrid with one quaternary carbon atom regioselectivly. The presented approach involves generation of three C–C and one C–O bond formation in a single step in an atom economical way.

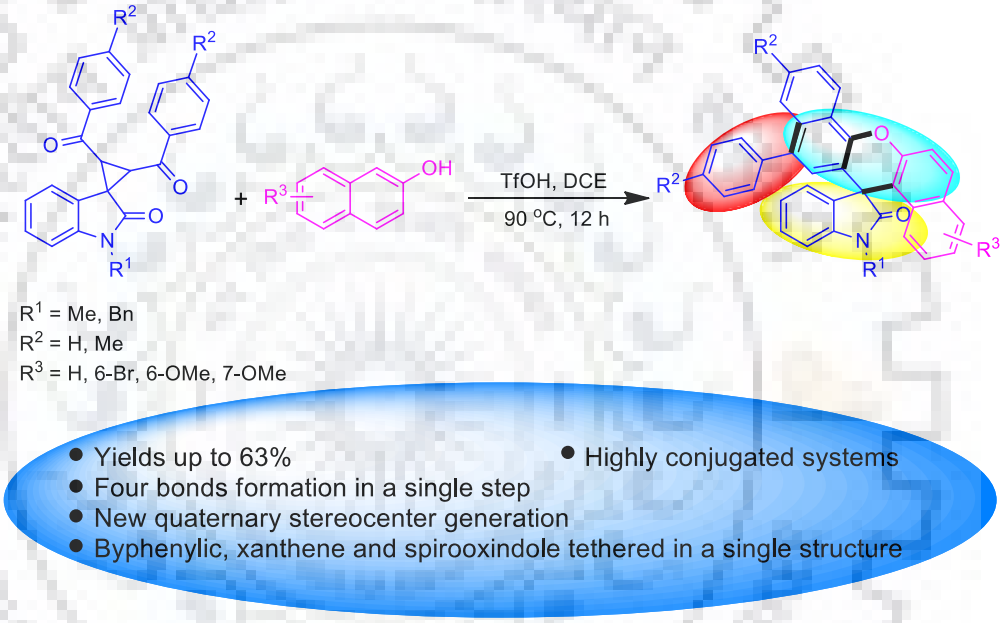


Figure 22: Synthesis of xanthene-tethered biarylic spirooxindoles from spirooxindolic donor-acceptor cyclopropanes and *β*-naphthols.

3.1. General Remarks

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

3.1.1. Solvents

The solvents for anhydrous reactions were dried and purified according to standard methods whenever needed.

Acetonitrile	:	Distilled over P_2O_5
CH_2Cl_2	:	Distilled over P_2O_5
EtOH	:	Distilled from magnesium cake
MeOH	:	Distilled from magnesium cake

3.1.2. Chemicals

The chemicals were purchased from the companies Sigma-Aldrich, Alfa-Aesar, Avra, Hi-media and S. D. Fine chemicals at the highest purity grade available and were used without further purification, unless otherwise stated.

3.1.3. Chromatographic methods

Thin Layer Chromatography

Thin layer chromatography was performed on Merck pre-coated 0.25 mm silica gel plates (60F254) using UV light as visualizing agent and/or iodine as developing agent.

Column Chromatography

Purification by gravity column chromatography was carried out on glass column using silica gel with 100–200 mesh.

3.1.4. Determination of the physical properties of the synthesized compounds

Melting Points

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

IR Spectroscopy

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

^{1}H NMR Spectroscopy

^{1}H NMR Spectra were recorded on Brüker AMX-500 instrument (500 MHz) or JEOL ECX-400-II spectrometer (400 MHz). Chemical shifts are given in ppm relative to tetramethylsilane (δ 0.00 ppm). Spectra were referenced to the solvent residual peak (from $CDCl_3$, δ 7.26 ppm) or with tetramethylsilane (TMS, δ 0.00 ppm) as the internal standard. Coupling patterns are described by the following abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), quintet (quint), dt (doublet of triplet), td (triplet of doublet), dd (doublet of doublet), m (multiplet), br (broad). Coupling constants are given in Hertz (Hz).

^{13}C NMR Spectroscopy

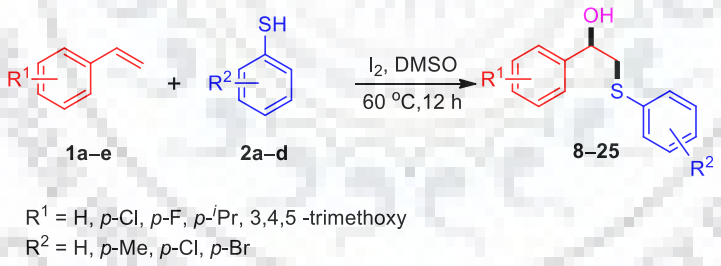
^{13}C NMR Spectra were recorded on Brüker AMX-500 spectrometer (125 MHz) or JEOL ECX-400-II spectrometer (100 MHz). Chemical shifts are given in ppm units and were determined by comparison with solvent peaks (from $CDCl_3$, δ 77.0 ppm).

Mass Spectroscopy

High resolution mass spectra (HRMS) were recorded on Brüker micrOTOF™-Q II mass spectrometer using electron spray ionization (ESI–MS).

3.2. Synthetic procedures

3.2.1 General procedure for the Synthesis of *β*-hydroxy sulfide derivatives:

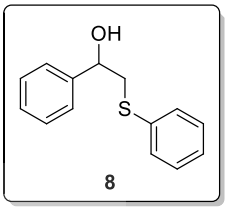


Mixture of a styrene **1**[302] (0.6 mmol), thiophenol **2** (0.3 mmol) and iodine (0.15 mmol) in DMSO (2 mL) was taken in a 10 mL round bottom flask and stirred at 60 °C for 12 h. After completion of the reaction as judged by TLC, iodine was quenched by saturated solution of sodiumthiosulphate and the product was extracted with ethyl acetate (3×10 mL). The combined organic phase was dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. The resulting crude product was purified by silica gel chromatography using a mixture of hexanes/ethyl acetate (4:1) as eluent to afford an analytically pure products **8-25**.

1-Phenyl-2-(phenylthio)ethanol (8):

Yield: 0.068 g (98%) as yellow oil.

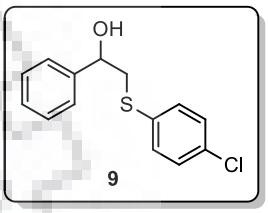
IR (KBr): ν_{max} 3445, 2925, 1583, 1404, 1330, 1121, 738, 700 cm^{-1}.



^{1}H NMR (400 MHz, $CDCl_3$):δ 7.38 (d, *J* = 7.6 Hz, 2H), 7.32−7.26 (m, 7H), 7.22−7.20 (m, 1H), 4.68 (dd, *J* = 3.6, 9.2 Hz, 1H), 3.27 (dd, *J* = 3.6, 13.6 Hz, 1H), 3.07 (dd, *J* = 9.2, 13.6 Hz, 1H), 2.98 (s, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 142.1, 134.9, 130.1, 129.1, 128.5, 127.9, 126.7, 125.8, 71.6, 43.9 ppm.

2-(4-Chlorophenylthio)-1-phenylethanol (9):



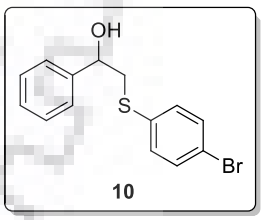
Yield: 0.059 (74%) as yellow oil.

IR (KBr): ν_{max} 3425, 2924, 1584, 1476, 1405, 1095, 1011, 700 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35−7.25 (m, 9H), 4.71 (dd, *J* = 3.2, 8.8 Hz, 1H), 3.27 (dd, *J* = 3.6, 13.6 Hz, 1H), 3.10 (dd, *J* = 9.2, 14.0 Hz, 1H), 2.80 (s, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 141.9, 133.5, 132.8, 131.4, 129.2, 128.6, 128.1, 125.8, 71.8, 44.0 ppm.

2-(4-Bromophenylthio)-1-phenylethanol (10):



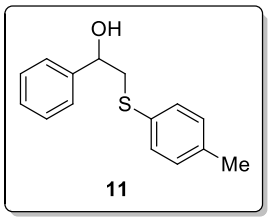
Yield: 0.064 g (69%) as yellow oil.

IR (KBr): ν_{max} 3427, 2922, 1582, 1473, 1387, 1090, 1063, 699 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (d, *J* = 8.8 Hz, 2H), 7.37−7.29 (m, 5H), 7.25 (d, *J* = 8.4 Hz, 2H), 4.71 (dd, *J* = 3.6, 9.2 Hz, 1H), 3.26 (dd, *J* = 3.6, 13.6 Hz, 1H), 3.10 (dd, *J* = 9.2, 13.6 Hz, 1H), 2.79 (s, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 141.9, 132.1, 132.0, 131.6, 131.5, 128.6, 128.1, 125.8, 120.6, 71.8, 43.8 ppm.

1-Phenyl-2-(*p*-tolylthio)ethanol (11):



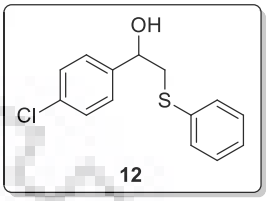
Yield: 0.046 (63%) as yellow oil.

IR (KBr): ν_{max} 3420, 2923, 1584, 1493, 1404, 805, 700 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35−7.24 (m, 7H), 7.13 (d, *J* = 8.0 Hz, 2H), 4.66 (d, *J* = 9.6 Hz, 1H), 3.27 (dd, *J* = 3.2, 13.6 Hz, 1H), 3.02 (dd, *J* = 9.6, 14.0 Hz, 1H), 2.96−2.95 (m, 1H), 2.34 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 142.1, 137.1, 131.0, 130.8, 129.9, 128.5, 127.9, 125.8, 71.4, 44.8, 21.0 ppm.

1-(4-Chlorophenyl)-2-(phenylthio)ethanol (12):



12

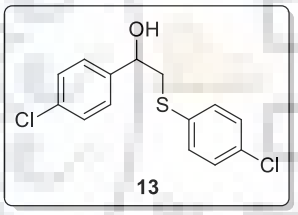
Yield: 0.59 g (75%) as yellow oil.

IR (KBr): ν_{max} 3430, 2923, 1583, 1487, 1405, 1090, 830, 741, 692 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (d, *J* = 8.0 Hz, 2H), 7.33–7.23 (m, 7H), 4.67 (dd, *J* = 3.6, 9.6 Hz, 1H), 3.27 (dd, *J* = 3.6, 13.6 Hz, 1H), 3.03(dd, *J* = 9.2, 13.6, 1H), 2.96(s, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 140.5, 134.4, 133.6, 130.4, 129.2, 128.6, 127.2, 127.0, 70.9, 44.1 ppm.

1-(4-Chlorophenyl)-2-(4-chlorophenylthio)ethanol (13):



13

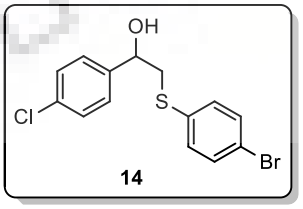
Yield: 0.067 g (75%) as yellow oil.

IR (KBr): ν_{max} 3423, 2923, 1593, 1477, 1406, 1094, 1012, 817, 490 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34−7.26 (m, 8H), 4.68 (d, *J* = 9.2 Hz, 1H), 3.23 (dd, *J* = 3.6, 14.0 Hz, 1H), 3.05 (dd, *J* = 9.2, 14.0 Hz, 1H), 2.85 (s, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 140.4, 133.8, 133.1, 133.0, 131.7, 129.3, 128.7, 127.2, 71.0, 44.2 ppm.

2-(4-Bromophenylthio)-1-(4-chlorophenyl)ethanol (14):



14

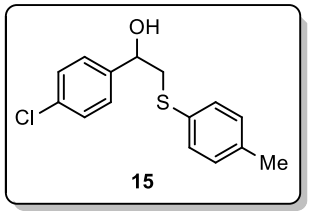
Yield: 0.062 g (60%) as yellow oil.

IR (KBr): ν_{max} 3428, 2926, 1636, 1585, 1404, 1121, 697 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.8 Hz, 2H), 7.27−7.23 (m, 4H), 4.68 (dd, *J* = 4.0, 9.2 Hz, 1H), 3.23 (dd, *J* = 4.0, 14.0 Hz, 1H), 3.05 (dd, *J* = 9.2, 13.6 Hz, 1H), 2.91 (s, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 140.4, 133.9, 133.7, 132.2, 131.7, 128.7, 127.2, 120.9, 71.0, 43.9 ppm.

1-(4-Chlorophenyl)-2-(*p*-tolylthio)ethanol (15):



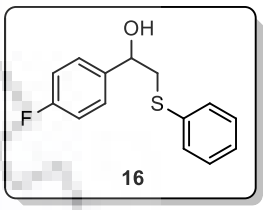
Yield: 0.062 g (74%) as yellow oil.

IR (KBr): ν_{max} 3425, 2920, 1586, 1492, 1405, 1089, 803 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34−7.25 (m, 6H), 7.13 (d, *J* = 8.0 Hz, 2H), 4.63 (dd, *J* = 2.8, 9.6 Hz, 1H), 3.22 (dd, *J* = 3.6, 14.0 Hz, 1H), 3.0−2.94 (m, 2H), 2.34 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 140.6, 137.4, 133.5, 131.3, 130.5, 130.0, 128.6, 127.2, 70.7, 44.9, 21.1 ppm.

1-(4-Fluorophenyl)-2-(phenylthio)ethanol (16):



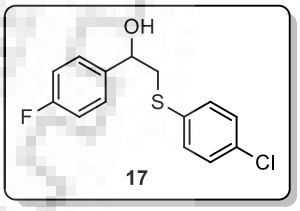
Yield: 0.052 g (70%) as yellow oil.

IR (KBr): ν_{max}3419, 3070, 2923, 1604, 1510, 1479, 1223, 1060, 742, 692 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (d, *J* = 7.6 Hz, 2H), 7.33−7.29 (m, 4H), 7.26−7.22 (m, 1H), 7.03 (t, *J* = 8.8 Hz, 2H), 4.69 (d, *J* = 8.4 Hz, 1H), 3.28 (dd, *J* = 4.0, 14.0 Hz, 1H), 3.05 (dd, *J* = 9.6, 14.0 Hz, 1H), 2.92 (s, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 162.4(d), 137.8(d), 134.6, 129.8(d), 127.5(d), 126.9, 115.4(d), 71.0, 44.1 ppm.

2-(4-Chlorophenylthio)-1-(4-fluorophenyl)ethanol (17):



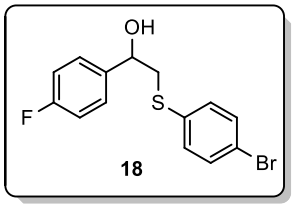
Yield: 0.059 g (70%) as yellow oil.

IR (KBr): ν_{max} 3419, 2925, 1603, 1510, 1476, 1404, 1225, 1096, 1011, 836 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33−7.26 (m, 6H), 7.02 (t, *J* = 8.4 Hz, 2H), 4.68 (dd, *J* = 3.6, 8.8 Hz, 1H), 3.23 (dd, *J* = 4.0, 14.0 Hz, 1H), 3.06 (dd, *J* = 9.2, 14.0 Hz, 1H), 2.88 (s, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 162.4 (d), 137.7 (d), 133.1 (d), 130.4 (d), 127.5 (d), 115.4 (d), 71.1, 44.1 ppm.

2-(4-Bromophenylthio)-1-(4-fluorophenyl)ethanol (18):



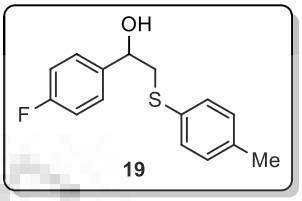
Yield: 0.064 g (65%) as yellow oil.

IR (KBr): ν_{max} 3423, 2923, 1604, 1510, 1473, 1407, 1092, 1008, 565 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (d, *J* = 8.4 Hz, 2H), 7.3 (dd, *J* = 6.0, 8.4 Hz, 2H), 7.25 (d, *J* = 8.4 Hz, 2H), 7.02 (t, *J* = 8.8 Hz, 2H), 4.69 (dd, *J* = 4.0, 9.2 Hz, 1H), 3.23 (dd, *J* = 4.0, 14.0 Hz, 1H), 3.06 (dd, *J* = 9.2, 14.0 Hz, 1H), 2.87 (s, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 162.5 (d), 137.8, 134.2, 132.1 (d), 127.7 (d), 120.9, 115.6 (d), 71.3, 44.0 ppm.

1-(4-Fluorophenyl)-2-(*p*-tolylthio)ethanol (19):



19

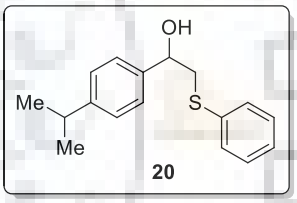
Yield: 0.049 g (62%) as yellow oil.

IR (KBr): ν_{max} 3424, 2923, 1604, 1510, 1224, 1157, 491 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33−7.25 (m, 4H), 7.13 (d, *J* = 8.0 Hz, 2H), 7.01 (t, *J* = 8.8 Hz, 2H), 4.64 (dd, *J* = 2.8, 9.2 Hz, 1H), 3.22 (dd, *J* = 3.2, 13.6 Hz, 1H), 3.02−2.96 (m, 2H), 2.33 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 162.3 (d), 137.9, 137.3, 131.2, 130.6, 130.0, 127.5 (d), 115.3 (d), 70.8, 44.9, 21.0 ppm.

1-(4-Isopropylphenyl)-2-(phenylthio)ethanol (20):



20

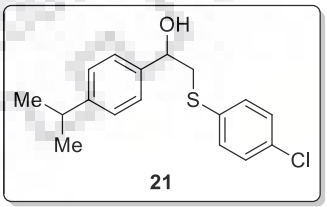
Yield: 0.77 g (94%) as yellow oil.

IR (KBr): ν_{max} 3435, 2960, 1584, 1056, 741 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, *J* = 7.6 Hz, 2H), 7.31−7.19 (m, 7H), 4.70 (d, *J* = 9.2 Hz, 1H), 3.31 (dd, *J* = 3.6, 13.6 Hz, 1H), 3.11 (dd, *J* = 9.6, 14.0 Hz, 1H), 2.94−2.84 (m, 2H), 1.24 (d, *J* = 6.8 Hz, 6H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 148.7, 139.5, 135.0, 130.0, 129.1, 126.6, 126.6, 125.8, 71.5, 43.7, 33.8, 24.0 ppm.

2-(4-Chlorophenylthio)-1-(4-isopropylphenyl)ethanol (21):



21

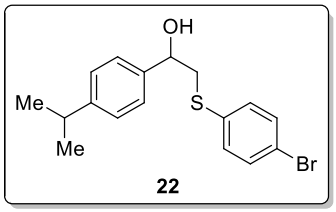
Yield: 0.060 g (65%) as yellow oil.

IR (KBr): ν_{max} 3420, 2960, 2925, 1582, 1476, 1406, 1096, 1012, 815, 564, 491 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32−7.29 (m, 2H), 7.26−7.24 (m, 4H), 7.21−7.19 (m, 2H), 4.70 (dd, *J* = 3.6, 8.8Hz, 1H), 3.26 (dd, *J* = 4.0, 13.6 Hz, 1H), 3.12 (dd, *J* = 8.8, 13.6 Hz, 1H), 2.89 (sep, *J* = 6.8 Hz, 1H), 2.71 (s,1H), 1.24 (d, *J* = 6.8 Hz, 6H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 148.9, 139.3, 133.7, 132.6, 131.3, 129.2, 126.6, 125.9, 71.8, 43.8, 33.8, 23.9 ppm.

2-(4-Bromophenylthio)-1-(4-isopropylphenyl)ethanol (22):



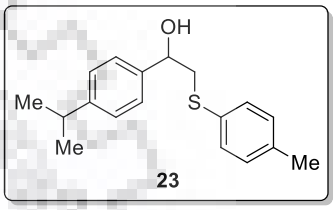
Yield: 0.063 (60%) as yellow oil.

IR (KBr): ν_{max} 3420, 2960, 2925, 1583, 1472, 1091, 1065, 568 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (d, *J* = 9.2 Hz, 2H), 7.26−7.18 (m, 6H), 4.69 (dd, *J* = 4.0, 9.2 Hz, 1H), 3.25 (dd, *J* = 4.0, 14.0 Hz, 1H), 3.12 (dd, *J* = 8.8, 13.6 Hz, 1H), 2.89 (Sep, *J* = 6.8 Hz, 1H), 2.77 (s, 1H), 1.23 (d, *J* = 6.8 Hz, 6H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 148.8, 139.3, 134.5, 132.0, 131.4, 126.6, 125.8, 120.4, 71.8, 43.5, 33.8, 23.9 ppm.

1-(4-Isopropylphenyl)-2-(*p*-tolylthio)ethanol (23):



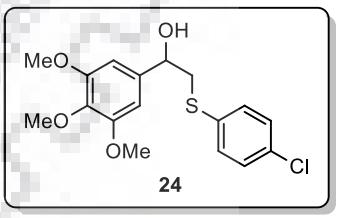
Yield: 0.062 g (72%) as yellow oil.

IR (KBr): ν_{max} 3423, 2959, 2924, 1584, 1493, 11405, 836, 805 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (d, *J* = 8.0 Hz, 2H), 7.25 (d, *J* = 8.0, 2H), 7.19 (d, *J* = 8.4 Hz, 2H), 7.11 (d, *J* = 8.0 Hz, 2H), 4.65 (dd, *J* = 3.2, 9.2 Hz, 1H), 3.26 (dd, *J* = 3.6, 14.0 Hz, 1H), 3.04 (dd, *J* = 9.6, 14.0 Hz, 1H), 2.88 (sep, *J* = 6.8 Hz, 2H), 2.32 (s, 3H), 1.23 (d, *J*= 6.8 Hz, 6H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 148.6, 139.5, 136.9, 131.1, 130.9, 129.9, 126.5, 125.8, 71.4, 44.5, 33.8, 23.9, 21.0 ppm.

2-((4-Chlorophenyl)thio)-1-(3,4,5-trimethoxyphenyl)ethanol (24):

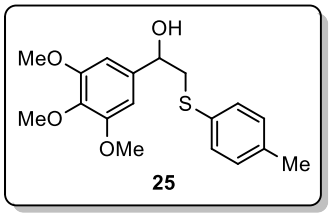


Yield: 0.068 (64%) as yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 (d, *J* = 8.4 Hz, 1H), 7.27 d, *J* = 8.4 Hz, 1H), 6.55 (s, 2H), 4.66 (dd, *J* = 3.6, 8.8 Hz, 1H), 3.85 (s, 6H), 3.83 (s, 3H), 3.26 (dd, *J* = 4.0, 13.6 Hz, 1H), 3.12 (dd, *J* = 8.8, 13.6 Hz, 1H), 2.83 (s, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 153.3, 137.7, 137.6, 133.5, 132.8, 131.6, 129.2, 102.8, 72.1, 60.8, 56.1, 44.0 ppm.

2-(*p*-Tolylthio)-1-(3,4,5-trimethoxyphenyl)ethanol (25):



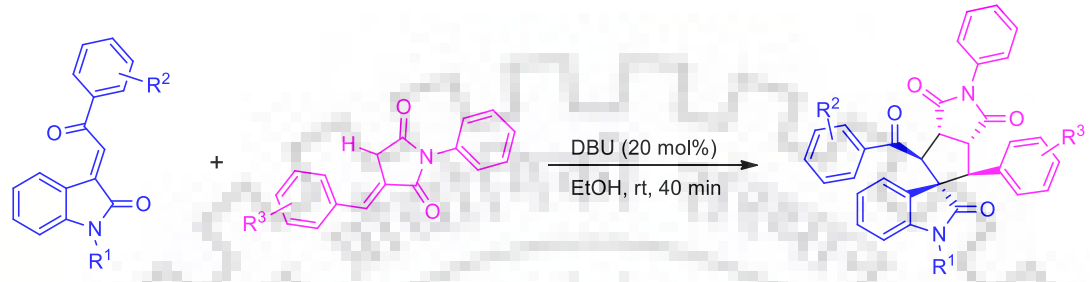
Yield: 0.070 g (70%) as yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 7.6 Hz, 2H), 6.55 (s, 2H), 4.62 (dd, *J* = 3.6, 9.2 Hz, 1H),

3.84 (s, 6H), 3.82 (s, 3H), 3.26 (dd, *J* = 3.6, 13.6 Hz, 1H), 3.05 (dd, *J* = 9.2, 13.6 Hz, 2H), 2.34 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 153.2, 137.9, 137.9, 137.4, 137.1, 131.0, 129.8, 102.7, 71.7, 60.7, 56.0, 44.6, 21.0 ppm.

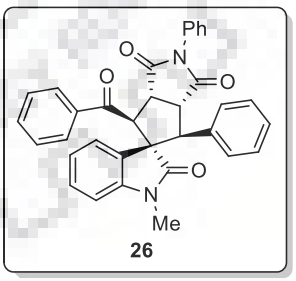
3.2.2. General procedure for the synthesis of 26-49:



R^1 = Me, CH_2Ph
R^2 = H, *p*-Me, *p*-OMe
R^3 = H, *p*-Me, *p*-Cl, *m*-OMe

To a stirred solution of 3-ylidene oxindole[303] derivative (**4**, 0.1 mmol) in 2 mL of EtOH was added benzylidene-1-phenylpyrrolidine-2,5-dione[304] (**3**, 0.1 mmol). Then DBU (0.05 mmol) was added, and the mixture was allowed to stir at room temperature for 40 min. After completion of the reaction as judged by TLC, the product started to settle down on the basement of the round bottom flask, reaction contents were filtered off. The product was afforded in good yield and excellent diastereoselectivity by simply washing with EtOH followed by drying.

(3a*S,3'*S**,4*S**,6*S**,6a*R**)-4-Benzoyl-1'-methyl-2,6-diphenyl-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1,2',3(2*H*)-trione (26):**



26

Yield: 0.037 g (70%) as white solid.

MP: 258–260 °C.

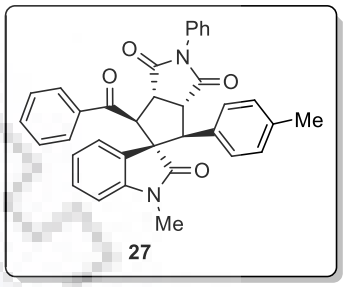
IR (KBr) ν_{max}: 3134, 1779, 1715, 1705, 1677, 1611, 1598, 1496, 1471, 1449, 1400, 1384, 1235, 1153, 1138, 1099, 763, 753, 717, 698, 691, 645, 617, 595, 515, 488 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.56 (s, 3H), 4.1 (d, *J* = 9.6 Hz, 1H), 4.21 (dd, *J* = 7.6, 9.6 Hz, 1H), 4.90 (d, *J* = 5.2 Hz, 1H), 5.04 (dd, *J* = 5.6, 7.6 Hz, 1H), 6.15 (d, *J* = 5.6 Hz, 1H), 6.95–6.97 (m, 2H), 6.10–7.06 (m, 5H), 7.16 (dd, *J* = 0.8, 5.6 Hz, 1H), 7.21 (t, *J* = 6.4 Hz, 2H), 7.31 (d, *J* = 5.6 Hz, 2H), 7.37 (t, *J* = 6.0 Hz, 1H), 7.40 (d, *J* = 6.4 Hz, 3H), 7.49 (t, *J* = 6.0 Hz, 2H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 25.9, 45.3, 48.1, 56.5, 59.15, 65.8, 107.9, 122.5, 124.8, 125.6, 126.4, 127.9, 127.9, 127.9, 128.2, 128.6, 129.0, 129.1, 131.8, 132.7, 132.9, 136.3, 142.8, 175.0, 175.5, 177.0, 195.9 ppm.

HRMS (ESI): *m/z* calcd for $C_{34}H_{27}N_2O_4$ $[M + H]^+$: 527.1965; found 527.1978.

(3a*S,3'*S**,4*S**,6*S**,6a*R**)-4-Benzoyl-1'-methyl-2-phenyl-6-(*p*-tolyl)-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1,2',3(2*H*)-trione (27):**



27

Yield: 0.034 g (63%) as off white solid.

MP: 269–271 °C.

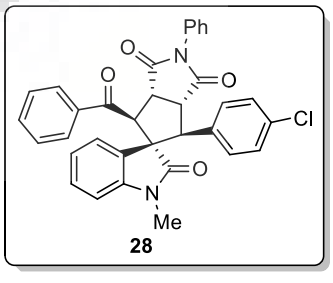
IR (KBr) ν_{max}: 3135, 1778, 1708, 1676, 1610, 1494, 1400, 1384, 1190, 1137, 1112, 1097, 907, 758, 749, 728, 691, 655, 645, 602 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.13 (s, 3H), 2.56 (s, 3H), 4.06 (d, *J* = 12.0 Hz, 1H), 4.17 (dd, *J* = 9.2, 12.0 Hz, 1H), 5.02 (dd, *J* = 6.8, 9.2 Hz, 1H), 6.16–6.18 (m, 1H), 6.83 (q, *J* = 8.4, 5.2 Hz, 4H), 7.0–7.08 (m, 2H), 7.15–7.23 (m, 3H), 7.28–7.30 (m, 2H), 7.35–7.41 (m, 4H), 7.47–7.51 (m, 2H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 21.0, 25.9, 45.2, 48.3, 56.6, 58.9, 65.7, 108.0, 122.4, 124.9, 125.6, 126.4, 127.8, 127.9, 128.1, 128.5, 128.7, 128.9, 129.1, 129.8, 131.8, 132.7, 136.3, 137.5, 142.8, 175.0, 175.6, 177.0, 195.9 ppm.

HRMS (ESI): *m/z* calcd for $C_{35}H_{29}N_2O_4$ $[M + H]^+$: 541.2122; found 541.2145.

(3a*S,3'*S**,4*S**,6*S**,6a*R**)-4-Benzoyl-6-(4-chlorophenyl)-1'-methyl-2-phenyl-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1,2',3(2*H*)-trione (28):**



28

Yield: 0.032 g (57%) as off white solid.

MP: 221–223 °C.

IR (KBr) ν_{max}: 3133, 1779, 1715, 1708, 1679, 1610, 1494, 1470, 1451, 1400, 1384, 1289, 1257, 1191, 1138, 1094, 905, 751, 737, 730, 722, 692, 655, 646, 614, 600 cm^{-1}.

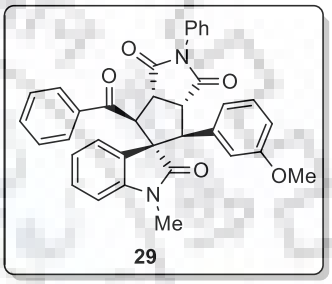
^{1}H NMR (400 MHz, $CDCl_3$): δ 2.57 (s, 3H), 4.06 (d, *J* = 12.0 Hz, 1H), 4.13 (dd, *J* = 9.2, 12.0 Hz, 1H), 4.87 (d, *J* = 6.4 Hz, 1H), 5.04 (dd, 6.8, 9.2 Hz, 1H), 6.20 (d, *J* = 7.6 Hz, 1H),

6.90 (d, *J* = 8.8 Hz, 2H), 6.99–7.04 (m, 3H), 7.08 (td, *J* = 1.2, 7.6 Hz, 1H), 7.15 (dd, *J* = 0.8, 7.6 Hz, 1H), 7.19–7.23 (m, 2H), 7.27–7.30 (m, 2H), 7.36–7.43 (m, 4H), 7.50 (t, *J* = 7.6 Hz, 2H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 25.9, 45.1, 48.2, 56.5, 58.3, 65.6, 108.2, 122.6, 124.4, 125.4, 126.4, 128.0, 128.1, 128.2, 128.6, 129.1, 129.2, 129.3, 131.5, 131.6, 132.8, 133.8, 136.2, 142.7, 174.8, 175.3, 176.8, 195.7 ppm.

HRMS (ESI): *m/z* calcd for $C_{34}H_{25}ClN_2O_4Na$ $[M + Na]^+$: 583.1395; found 583.1397.

(3a*S,3'*S**,4*S**,6*S**,6a*R**)-4-Benzoyl-6-(3-methoxyphenyl)-1'-methyl-2-phenyl-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1,2',3(2*H*)-trione (29):**



29

Yield: 0.039 g (70%) as white solid.

MP: 244–245 °C.

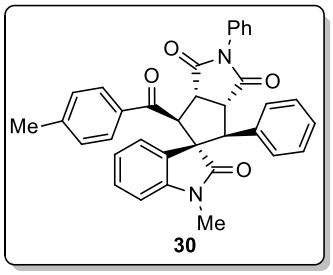
IR (KBr) ν_{max}: 3134, 1778, 1715, 1675, 1610, 1493, 1400, 1385, 1190, 1137, 1101, 757, 732, 692, 655, 644, 603 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.56 (s, 3H), 3.55 (s, 3H), 4.07 (d, *J* = 12.0 Hz, 1H), 4.17 (dd, *J* = 9.2, 11.6 Hz, 1H), 4.88 (d, *J* = 6.8 Hz, 1H), 5.03 (dd, *J* = 6.8, 9.2 Hz, 1H), 6.18–6.20 (m, 1H), 6.47 (t, *J* = 2.0 Hz, 1H), 6.57–6.60 (m, 2H), 6.94 (t, *J* = 8.0 Hz, 1H), 7.0–7.04 (m, 1H), 7.08 (td, *J* = 1.6, 7.6 Hz, 1H), 7.15–7.18 (m, 1H), 7.21 (t, *J* = 8.0 Hz, 2H), 7.29–7.31 (m, 2H), 7.36–7.42 (m, 4H), 7.48–7.51 (m, 2H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 25.9, 45.2, 48.3, 55.0, 56.6, 59.0, 65.7, 108.1, 113.1, 113.9, 120.6, 122.4, 124.8, 125.6, 126.4, 127.9, 128.1, 128.6, 128.9, 129.0, 129.1, 129.2, 131.7, 132.8, 134.4, 136.3, 142.8, 159.0, 174.9, 175.5, 176.9, 195.8 ppm.

HRMS (ESI): *m/z* calcd for $C_{35}H_{29}N_2O_5$ $[M + H]^+$: 557.2071; found 557.2082.

(3a*S,3'*S**,4*S**,6*S**,6a*R**)-1'-Methyl-4-(4-methylbenzoyl)-2,6-diphenyl-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1,2',3(2*H*)-trione (30):**



30

Yield: 0.039 g (72%) as off white solid.

MP: 233–235 °C.

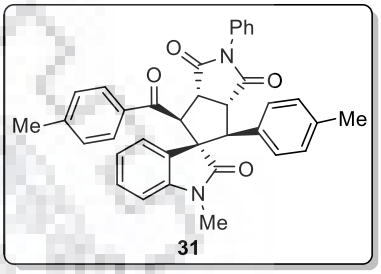
^{1}H NMR (400 MHz, $CDCl_3$): δ 2.29 (s, 3H), 2.58 (s, 3H), 4.10 (d, *J* = 12.0 Hz, 1H), 4.21 (dd, *J* = 9.6, 12.0 Hz, 1H), 4.88 (d, *J*

= 6.8 Hz, 1H), 5.04 (dd, *J* = 6.8, 9.2 Hz, 1H), 6.16–6.18(m, 1), 6.95–7.06 (m, 9H), 7.16–7.19 (m, 1H), 7.25 (s, 1H), 7.26 (d, *J* = 2.4 Hz, 1H), 7.37–7.41 (m, 3H), 7.47–7.50 (m, 2H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 21.5, 25.9, 45.3, 48.1, 56.2, 59.1, 65.9, 107.9, 122.4, 124.7, 125.6, 126.4, 127.8, 127.9, 127.9, 128.3, 128.5, 128.6, 128.9, 129.1, 131.7, 132.9, 133.6, 142.7, 143.7, 175.1, 175.5, 177.0, 195.2 ppm.

HRMS (ESI): *m/z* calcd for $C_{35}H_{29}N_2O_4$ $[M + H]^+$: 541.2122, found: 541.2119.

(3a*S,3'*S**,4*S**,6*S**,6a*R**)-1'-Methyl-4-(4-methylbenzoyl)-2-phenyl-6-(*p*-tolyl)-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1,2',3(2*H*)-trione (31):**



31

Yield: 0.038 g (69%) as off white solid.

MP: 263–266 °C.

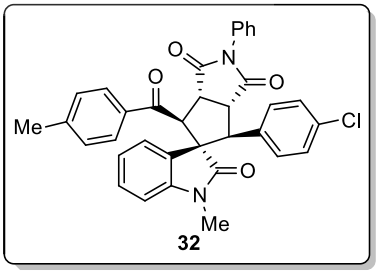
IR (KBr) ν_{max}: 3134, 1778, 1714, 1668, 1611, 1495, 1471, 1400, 1384, 1286, 1240, 1186, 1155, 1136, 1097, 825, 725, 710, 690, 655, 617, 597, 518, 495 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.13 (s, 3H), 2.29 (s, 3H), 2.59 (s, 3H), 4.06 (d, *J* = 9.6 Hz, 1H), 4.16 (dd, *J* = 7.6, 9.6 Hz, 1H), 4.86 (d, *J* = 5.2 Hz, 1H), 5.01 (dd, *J* = 5.2, 7.2 Hz, 1H), 6.20 (d, *J* = 6.0 Hz, 1H), 6.83 (q, *J* = 6.4 Hz, 4H), 6.99–7.07 (m, 4H), 7.17 (d, *J* = 5.6 Hz, 1H), 7.24 (s, 2H), 7.38–7.41 (m, 3H), 7.47–7.50 (m, 2H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 21.0, 21.5, 25.9, 45.3, 48.3, 56.4, 59.0, 65.9, 108.0, 122.4, 124.9, 125.7, 126.4, 127.8, 128.4, 128.5, 128.6, 128.7, 128.8, 129.1, 129.9, 131.8, 133.7, 137.4, 142.8, 143.6, 175.1, 175.6, 177.0, 195.3 ppm.

HRMS (ESI): *m/z* calcd for $C_{36}H_{31}N_2O_4$ $[M + H]^+$: 555.2278, found: 555.2281.

(3a*R,3'*S**,4*S**,6*S**,6a*S**)-4-(4-Chlorophenyl)-1'-methyl-6-(4-methylbenzoyl)-2-phenyl-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1,2',3(2*H*)-trione (32):**



32

Yield: 0.029 g (51%) as off white solid.

MP: 238–240 °C.

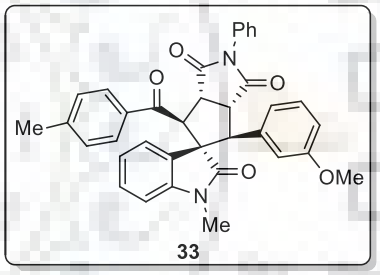
IR (KBr) ν_{max}: 3133, 1778, 1716, 1703, 1679, 1609, 1494, 1470, 1400, 1384, 1290, 1256, 1189, 1138, 1092, 909, 833, 780, 751, 740, 729, 655, 645, 616, 603, 527, 495 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.30 (s, 3H), 2.60 (s, 3H), 4.05 (d, *J* = 12.0 Hz, 1H), 4.13 (dd, *J* = 9.2, 11.6 Hz, 1H), 4.86 (d, *J* = 6.8 Hz, 1H), 5.03 (dd, 6.8, 9.2 Hz, 1H), 6.23 (d, *J* = 7.6 Hz, 1H), 6.90 (d, *J* = 8.8 Hz, 2H), 6.99–7.03 (m, 5H), 7.08 (td, *J* = 1.2, 7.6 Hz, 1H), 7.16 (d, *J* = 7.6 Hz, 1H), 7.24 (d, *J* = 8.4 Hz, 2H), 7.39–7.42 (m, 3H), 7.49 (t, *J* = 7.6 Hz, 2H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 21.5, 26.0, 45.2, 48.2, 56.3, 58.4, 65.754, 108.2, 122.6, 124.4, 125.5, 126.4, 128.2, 128.3, 128.6, 128.6, 129.1, 129.1, 129.3, 131.6, 133.6, 133.8, 142.7, 143.8, 174.9, 175.3, 176.8, 195.0 ppm.

HRMS (ESI): *m/z* calcd for $C_{35}H_{28}ClN_2O_4$ $[M + H]^+$: 575.1732, found: 575.1731.

(3a*R,3'*S**,4*S**,6*S**,6a*S**)-4-(3-Methoxyphenyl)-1'-methyl-6-(4-methylbenzoyl)-2-phenyl-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[c]pyrrole-5,3'-indoline]-1,2',3(2*H*)-trione (33):**



33

Yield: 0.034 g (60%) as off white solid.

MP: 250–251 °C.

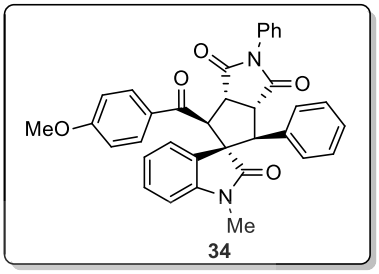
IR (KBr) ν_{max}: 3138, 1775, 1703, 1677, 1609, 1494, 1400, 1385, 1137, 1123, 750, 689, 656, 644, 603 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.29 (s, 3H), 2.59 (s, 3H), 3.56 (s, 3H), 4.07 (d, *J* = 11.6 Hz, 1H), 4.16 (dd, *J* = 9.2, 11.6 Hz, 1H), 4.86 (d, *J* = 6.8 Hz, 1H), 5.03 (dd, *J* = 6.8, 9.2 Hz, 1H), 6.21 (d, *J* = 8.0 Hz, 1H), 6.47 (s, 1H), 6.57–6.59 (m, 2H), 6.94 (t, *J* = 8.0 Hz, 1H), 7.0–7.08 (m, 5H), 7.18 (d, *J* = 7.2 Hz, 1H), 7.24 (s, 1H), 7.38–7.42 (m, 3H), 7.47–7.51 (m, 2H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 21.5, 25.9, 45.3, 48.3, 55.0, 56.3, 59.0, 65.8, 108.0, 113.1, 113.9, 120.6, 122.4, 124.8, 125.6, 126.4, 128.3, 128.5, 128.6, 128.9, 128.9, 129.1, 131.7, 133.6, 134.5, 142.8, 143.7, 159.0, 175.0, 175.5, 177.0, 195.2 ppm.

HRMS (ESI): *m/z* calcd for $C_{36}H_{31}N_2O_5$ $[M + H]^+$: 571.2227, found: 571.2224.

(3a*S,3'*S**,4*S**,6*S**,6a*R**)-4-(4-Methoxybenzoyl)-1'-methyl-2,6-diphenyl-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1,2',3(2*H*)-trione (34):**



34

Yield: 0.034 g (61%) as off white solid.

MP: 158–159 °C.

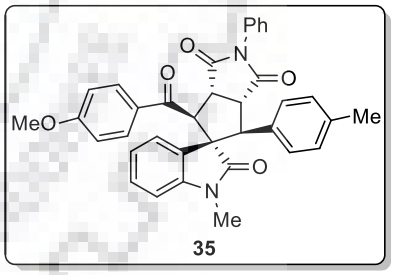
IR (KBr) ν_{max}: 3135, 1716, 1702, 1678, 1601, 1400, 1385, 1138, 1123, 749, 732, 656, 644, 603 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.65 (s, 3H), 3.78 (s, 3H), 4.10 (d, *J* = 12.0 Hz, 1H), 4.21 (dd, *J* = 9.2, 12.0 Hz, 1H), 4.87 (d, *J* = 6.8 Hz, 1H), 5.05 (dd, *J* = 6.8, 9.6 Hz, 1H), 6.19–6.22 (m, 1H), 6.72 (d, *J* = 8.8 Hz, 2H), 6.95–6.99 (m, 2H), 6.99–7.06 (m, 5H), 7.18–7.20 (m, 1H), 7.33–7.43 (m, 5H), 7.47–7.53 (m, 2H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 26.0, 45.5, 48.1, 55.4, 55.7, 59.3, 66.1, 107.9, 113.2, 122.4, 124.7, 125.7, 126.4, 127.9, 127.9, 128.5, 128.8, 128.9, 129.1, 130.7, 131.7, 132.9, 142.6, 163.4, 175.1, 175.7, 177.1, 193.7 ppm.

HRMS (ESI): *m/z* calcd for $C_{35}H_{29}N_2O_5$ $[M + H]^+$: 557.2071, found: 557.2059.

(3a*S,3'*S**,4*S**,6*S**,6a*R**)-4-(4-Methoxybenzoyl)-1'-methyl-2-phenyl-6-(*p*-tolyl)-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1,2',3(2*H*)-trione (35):**



35

Yield: 0.33 g (58%) as off white solid.

MP: 277–279 °C.

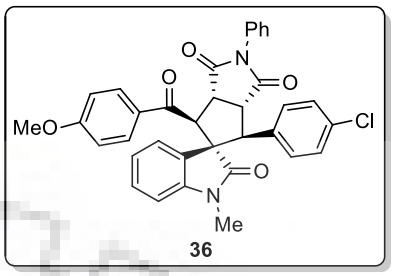
IR (KBr) ν_{max}: 3133, 1779, 1716, 1670, 1599, 1574, 1494, 1470, 1400, 1384, 1169, 1136, 1114, 750, 713, 692, 656, 604, 517 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.13 (s, 3H), 2.66 (s, 3H), 3.78 (s, 3H), 4.06 (d, *J* = 12.0 Hz, 1H), 4.16 (dd, *J* = 9.2, 12.0 Hz, 1H), 4.85 (d, *J* = 6.4 Hz, 1H), 5.02 (dd, *J* = 6.8, 9.2 Hz, 1H), 6.23 (d, *J* = 7.2 Hz, 1H), 6.72 (d, *J* = 8.8 Hz, 2H), 6.83 (dd, *J* = 8.4, 12.8 Hz, 4H), 6.99–7.07 (m, 2H), 7.19 (d, *J* = 7.2 Hz, 1H), 7.29 (d, *J* = 7.6, 1H), 7.39–7.42 (m, 4H), 7.46–7.50 (m, 2H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 21.0, 26.0, 45.5, 48.3, 55.4, 55.9, 59.1, 66.1, 107.9, 113.2, 122.4, 124.9, 125.7, 126.4, 127.8, 128.5, 128.6, 128.8, 129.0, 129.9, 130.7, 131.8, 137.4, 142.7, 175.1, 175.8, 177.1, 193.7 ppm.

HRMS (ESI): *m/z* calcd for $C_{36}H_{31}N_2O_5$ $[M + H]^+$: 571.2227, found: 571.2231.

(3a*R,3'*S**,4*S**,6*S**,6a*S**)-4-(4-Chlorophenyl)-6-(4-methoxybenzoyl)-1'-methyl-2-phenyl-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1,2',3(2*H*)-trione (36):**



36

Yield: 0.031 g (53%) as off white solid.

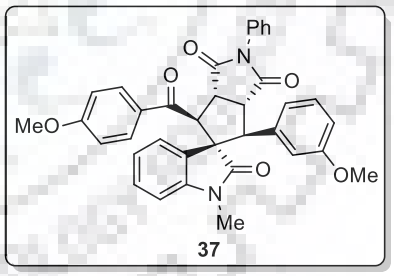
MP: 293–294 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.67 (s, 3H), 3.79 (s, 3H), 4.05 (d, *J* = 12.0 Hz, 1H), 4.13 (dd, *J* = 9.2, 12.0 Hz, 1H), 4.85 (d, *J* = 6.4 Hz, 1H), 5.05 (dd, *J* = 6.8, 9.2 Hz, 1H), 6.26 (d, *J* = 8.0 Hz, 1H), 6.72 (d, *J* = 8.8 Hz, 2H), 6.91 (d, *J* = 8.4 Hz, 2H), 6.99–7.10 (m, 4H), 7.18 (d, *J* = 7.2 Hz, 1H), 7.39–7.42 (m, 4H), 7.47–7.51 (m, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 26.1, 45.4, 48.3, 55.4, 55.8, 58.6, 66.0, 108.2, 113.3, 122.6, 124.4, 125.6, 126.4, 128.2, 128.6, 128.9, 129.1, 129.3, 130.7, 131.7, 133.8, 142.6, 163.5, 174.9, 175.5, 176.9, 193.5 ppm.

HRMS (ESI): *m/z* calcd for $C_{35}H_{28}ClN_2O_5$ $[M + H]^+$: 591.1681, found: 591.1683.

(3a*S,3'*S**,4*S**,6*S**,6a*R**)-4-(4-Methoxybenzoyl)-6-(3-methoxyphenyl)-1'-methyl-2-phenyl-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1,2',3(2*H*)-trione (37):**



37

Yield: 0.034 g (58%) as off white solid.

MP: 201–204 °C.

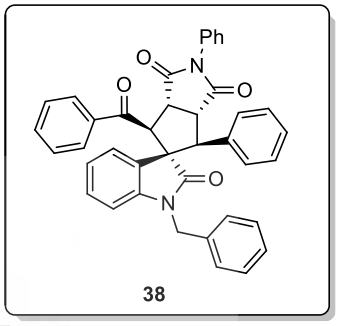
IR (KBr) ν_{max}: 3133, 1779, 1716, 1671, 1601, 1493, 1400, 1384, 1246, 1172, 1136, 1099, 750, 712, 693, 655, 604, 486 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.66 (s, 3H), 3.56 (s, 3H), 3.78 (s, 3H), 4.07 (d, *J* = 12.0 Hz, 1H), 4.17 (dd, *J* = 9.2, 12.0 Hz, 1H), 4.85 (d, *J* = 6.8 Hz, 1H), 5.04 (dd, *J* = 6.8, 9.6 Hz, 1H), 6.24 (d, *J* = 7.6 Hz, 1H), 6.47 (t, *J* = 2.0 Hz, 1H), 6.58 (dd, *J* = 2.0, 8.4 Hz, 2H), 6.71 (d, *J* = 8.8 Hz, 2H), 6.94 (t, *J* = 7.6 Hz, 1H), 6.99–7.08 (m, 2H), 7.19 (dd, *J* = 1.2, 7.2 Hz, 1H), 7.37–7.43 (m, 5H), 7.47–7.51 (m, 2H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 26.0, 45.5, 48.3, 55.0, 55.4, 55.9, 59.2, 66.0, 108.0, 113.1, 113.2, 113.9, 120.6, 122.4, 124.8, 125.7, 126.4, 128.5, 128.9, 129.1, 130.7, 131.7, 134.5, 142.7, 159.0, 163.4, 175.0, 175.7, 177.0, 193.6 ppm.

HRMS (ESI): *m/z* calcd for $C_{36}H_{31}N_2O_6$ $[M + H]^+$: 587.2177, found: 587.2194.

(3a*S,3'*S**,4*S**,6*S**,6a*R**)-4-Benzoyl-1'-benzyl-2,6-diphenyl-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1,2',3(2*H*)-trione (38):**



38

Yield: 0.037 g (62%) as white solid.

MP: 247–249 °C.

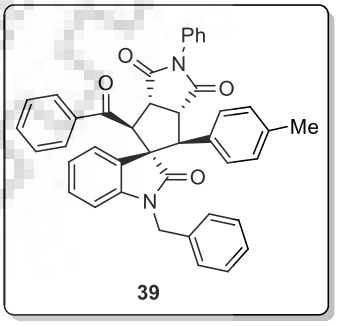
IR (KBr) ν_{max}: 3134, 1782, 1720, 1707, 1680, 1610, 1496, 1466, 1400, 1384, 1156, 1124, 1105, 745, 716, 690, 656, 615, 303 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.75 (d, *J* = 16.4 Hz, 1H), 4.11–4.19 (m, 2H), 4.69 (d, *J* = 16.0 Hz, 1H), 4.98 (d, *J* = 6.8 Hz, 1H), 5.08 (dd, *J* = 7.2, 9.2 Hz, 1H), 5.96 (d, *J* = 8.0 Hz, 1H), 6.37 (d, *J* = 7.6 Hz, 2H), 6.93–7.06 (m, 8H), 7.09–7.15 (m, 2H), 7.25 (s, 1H), 7.27–7.28 (m, 2H), 7.39–7.46 (m, 6H), 7.47–7.52 (m, 2H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 43.5, 45.4, 48.7, 56.4, 59.9, 65.9, 109.4, 122.5, 124.6, 125.8, 126.2, 126.4, 127.2, 128.1, 128.1, 128.2, 128.3, 128.5, 128.6, 129.1, 129.1, 131.7, 132.8, 133.0, 134.2, 136.3, 142.2, 174.9, 175.5, 176.9, 195.7 ppm.

HRMS (ESI): *m/z* calcd for $C_{40}H_{31}N_2O_4$ $[M + H]^+$: 603.2278, found: 603.2276.

(3a*S,3'*S**,4*S**,6*S**,6a*R**)-4-Benzoyl-1'-benzyl-2-phenyl-6-(*p*-tolyl)-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1,2',3(2*H*)-trione (39):**



39

Yield: 0.045 g (73%) as off white solid.

MP: 292–295 °C.

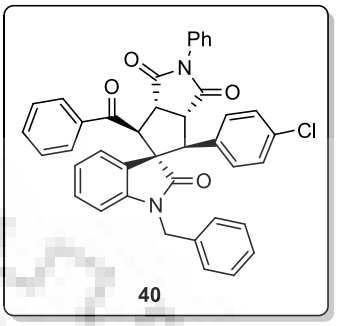
IR (KBr) ν_{max}: 3136, 1778, 1716, 1684, 1612, 1495, 1400, 1385, 1148, 1118, 755, 693, 656, 643, 603, 518 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.21 (s, 3H), 3.71 (d, *J* = 16.0 Hz, 1H), 4.07–4.17 (m, 2H), 4.74 (d, *J* = 16.0 Hz, 1H), 4.96 (d, *J* = 6.8 Hz, 1H), 5.06 (dd, *J* = 6.8, 8.4 Hz, 1H), 5.97 (d, *J* = 7.6 Hz, 1H), 6.38 (d, *J* = 7.6 Hz, 2H), 6.84 (s, 4H), 6.94–7.05 (m, 5H), 7.09–7.12 (m, 1H), 7.24 (s, 1H), 7.27 (s, 1H), 7.38–7.52 (m, 8H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 21.1, 43.4, 45.4, 48.9, 56.5, 59.7, 65.8, 109.4, 122.5, 124.8, 125.8, 126.2, 126.4, 127.2, 128.1, 128.3, 128.3, 128.4, 128.5, 128.9, 129.0, 129.1, 129.7, 131.8, 132.9, 134.3, 136.3, 137.7, 142.2, 174.9, 175.5, 176.9, 195.8 ppm.

HRMS (ESI): *m/z* calcd for $C_{41}H_{33}N_2O_4$ $[M + H]^+$: 617.2435, found: 617.2438.

(3a*S,3'*S**,4*S**,6*S**,6a*R**)-4-Benzoyl-1'-benzyl-6-(4-chlorophenyl)-2-phenyl-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1,2',3(2*H*)-trione (40):**



40

Yield: 0.032 g (50%) as off white solid.

MP: 252–254 °C.

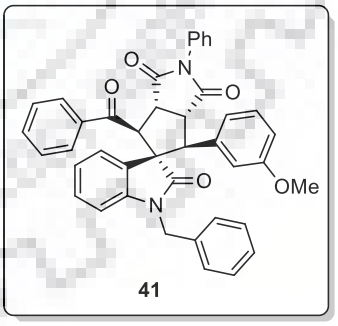
IR (KBr) ν_{max}: 3137, 1777, 1715, 1687, 1612, 1495, 1400, 1385, 1113, 757, 692, 656, 645, 603, 524 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.74 (d, *J* = 16.0 Hz, 1H), 4.05–4.14 (m, 2H), 4.72 (d, *J* = 16.4 Hz, 1H), 4.95 (d, *J* = 6.8 Hz, 1H), 5.08 (t, *J* = 7.2 Hz, 1H), 6.03 (d, *J* = 7.6 Hz, 1H), 6.38 (d, *J* = 7.2 Hz, 2H), 6.88 (d, *J* = 8.4 Hz, 2H), 6.97–7.03 (m, 3H), 7.07 (t, *J* = 7.2 Hz, 3H), 7.15 (t, *J* = 7.6 Hz, 1H), 7.24 (s, 1H), 7.28 (s, 2H), 7.38–7.44 (m, 5H), 7.46–7.52 (m, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 43.4, 45.3, 48.8, 56.3, 59.2, 65.7, 109.6, 122.7, 124.3, 125.7, 126.2, 126.4, 127.4, 128.1, 128.3, 128.4, 128.5, 128.7, 129.1, 129.8, 131.4, 131.6, 133.0, 134.1, 134.1, 136.2, 142.2, 174.7, 175.2, 176.7, 195.5 ppm.

HRMS (ESI): *m/z* calcd for $C_{40}H_{30}ClN_2O_4$ $[M + H]^+$: 637.1889, found: 637.1887.

(3a*S,3'*S**,4*S**,6*S**,6a*R**)-4-Benzoyl-1'-benzyl-6-(3-methoxyphenyl)-2-phenyl-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1,2',3(2*H*)-trione (41):**



41

Yield: 0.050 g (79%) as off white solid.

MP: 236–239 °C.

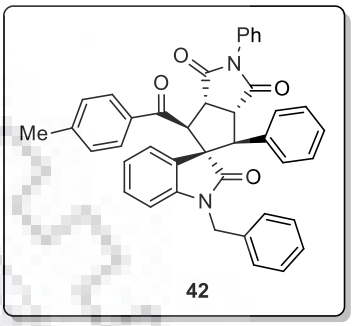
IR (KBr) ν_{max}: 3135, 1778, 1716, 1683, 1611, 1488, 1400, 1385, 1193, 1108, 750, 690, 655, 644, 603, 486 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.48 (d, *J* = 16.0 Hz, 1H), 4.10 (d, *J* = 12.0 Hz, 1H), 4.16 (dd, *J* = 9.2, 12.4 Hz, 1H), 4.74 (d, *J* = 16.0 Hz, 1H), 4.97 (d, *J* = 6.8 Hz, 1H), 5.08 (dd, *J* = 6.8, 8.8 Hz, 1H), 5.98 (d, *J* = 7.6 Hz, 1H), 6.37 (d, *J* = 7.6 Hz, 2H), 6.47 (t, *J* = 1.6 Hz, 1H), 6.60 (d, *J* = 7.6 Hz, 1H), 6.70 (dd, *J* = 2.4, 8.4 Hz, 1H), 6.94–7.06 (m, 5H), 7.11 (t, *J* = 7.6 Hz, 1H), 7.28 (d, *J* = 7.6 Hz, 2H), 7.39–7.44 (m, 5H), 7.46–7.52 (m, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 43.4, 45.3, 48.9, 54.9, 56.4, 59.8, 65.7, 109.4, 113.3, 114.4, 121.1, 122.5, 124.7, 125.7, 126.0, 126.4, 127.2, 128.1, 128.3, 128.5, 128.6, 129.1, 129.2, 131.7, 133.0, 134.1, 134.2, 136.2, 142.2, 159.1, 174.8, 175.4, 176.9, 195.7 ppm.

HRMS (ESI): *m/z* calcd for $C_{41}H_{33}N_2O_5$ $[M + H]^+$: 633.2384, found: 633.2390.

(3a*S,3'*S**,4*S**,6*S**,6a*R**)-1'-Benzyl-4-(4-methylbenzoyl)-2,6-diphenyl-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1,2',3(2*H*)-trione (42):**



42

Yield: 0.040 g (65%) as white solid.

MP: 149–151 °C.

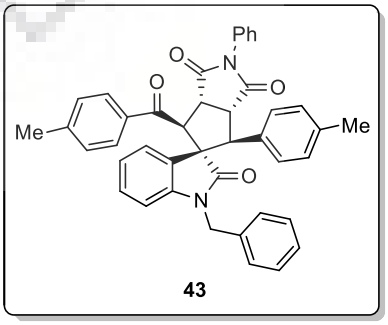
IR (KBr) ν_{max}: 3134, 1717, 1673, 1637, 1400, 1385, 1192, 1123, 750, 656, 644, 603 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.35 (s, 3H), 3.91 (d, *J* = 16.0 Hz, 1H), 4.12 (d, *J* = 12.0 Hz, 1H), 4.19 (dd, *J* = 9.2, 12.4 Hz, 1H), 4.63 (d, *J* = 16.0 Hz, 1H), 4.98 (d, *J* = 6.8 Hz, 1H), 5.07 (dd, *J* = 6.8, 8.8 Hz, 1H), 5.99 (d, *J* = 7.6 Hz, 1H), 6.39 (d, *J* = 7.6 Hz, 2H), 6.93–7.04 (m, 7H), 7.05–7.15 (m, 5H), 7.28 (d, *J* = 7.2, 1H), 7.38–7.42 (m, 5H), 7.48–7.52 (m, 2H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6, 43.5, 45.6, 48.7, 55.9, 60.0, 66.0, 109.4, 122.5, 124.6, 125.9, 126.2, 126.4, 127.2, 128.1, 128.1, 128.4, 128.6, 128.9, 129.1, 131.8, 132.9, 133.6, 134.3, 142.1, 144.0, 175.0, 175.5, 176.910, 194.9 ppm.

HRMS (ESI): *m/z* calcd for $C_{41}H_{33}N_2O_4$ $[M + H]^+$: 617.2435, found: 617.2437.

(3a*S,3'*S**,4*S**,6*S**,6a*R**)-1'-Benzyl-4-(4-methylbenzoyl)-2-phenyl-6-(*p*-tolyl)-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1,2',3(2*H*)-trione (43):**



43

Yield: 0.046 g (73%) as off white solid.

MP: 241–243 °C.

IR (KBr) ν_{max}: 3138, 1781, 1718, 1715, 1609, 1402, 1384, 1125, 1101, 758, 743, 722, 695, 656, 613, 598 cm^{-1}.

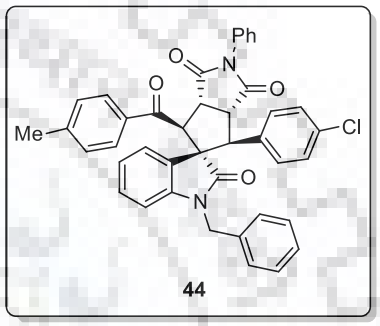
^{1}H NMR (400 MHz, $CDCl_3$): δ 2.2 (s, 3H), 2.35 (s, 3H), 3.86 (d, *J* = 16.0 Hz, 1H), 4.09 (d, *J* = 12.0 Hz, 1H), 4.15 (dd, *J* = 8.8, 12.0 Hz, 1H), 4.70 (d, *J* = 16.0 Hz, 1H), 4.96 (d, *J* = 6.8 Hz, 1H), 5.07 (dd, *J* = 7.2, 8.8 Hz, 1H), 5.99 (d, *J* = 7.6 Hz, 1H), 6.39 (d, *J* = 7.6 Hz, 2H),

6.85 (s, 4H), 6.94–7.03 (m, 4H), 7.05–7.13 (m, 3H), 7.28 (d, *J* = 7.2 Hz, 1H), 7.36–7.42 (m, 5H), 7.47–7.51 (m, 2H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 21.1, 21.6, 43.4, 45.5, 48.9, 56.0, 59.8, 66.0, 109.4, 122.4, 124.8, 125.9, 126.2, 126.4, 127.1, 128.3, 128.5, 128.6, 128.8, 128.9, 128.9, 129.1, 129.8, 131.8, 133.6, 134.3, 137.7, 142.1, 143.9, 175.0, 175.5, 177.0, 195.0 ppm.

HRMS (ESI): *m/z* calcd for $C_{42}H_{35}N_2O_4$ $[M + H]^+$: 631.2591, found: 631.2614.

(3a*R,3'*S**,4*S**,6*S**,6a*S**)-1'-Benzyl-4-(4-chlorophenyl)-6-(4-methylbenzoyl)-2-phenyl-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1,2',3(2*H*)-trione (44):**



44

Yield: 0.033 g (51%) as orange solid.

MP: 239–241 ºC.

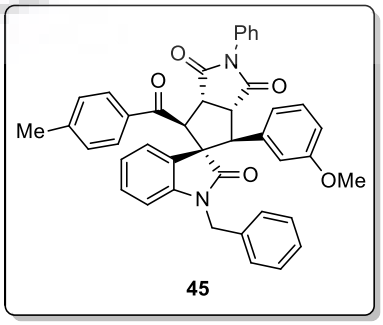
IR (KBr) ν_{max}: 3135, 1780, 1715, 1678, 1610, 1494, 1467, 1400, 1385, 1189, 1112, 748, 656, 644, 603 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.35 (s, 3H), 3.89 (d, *J* = 16.0 Hz, 1H), 4.05–4.13 (m, 2H), 4.68 (d, *J* = 16.0 Hz, 1H), 4.95 (d, *J* = 6.8 Hz, 1H), 5.05–5.09 (m, 1H), 6.05 (d, *J* = 7.6 Hz, 1H), 6.40 (d, *J* = 7.6 Hz, 2H), 6.88 (d, *J* = 8.8 Hz, 2H), 6.97–7.09 (m, 8H), 7.15 (t, *J* = 7.2 Hz, 1H), 7.27 (s, 1H), 7.36–7.42 (m, 5H), 7.48–7.52 (m, 2H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6, 43.5, 45.5, 48.8, 55.9, 59.3, 65.8, 109.5, 122.6, 124.3, 125.8, 126.2, 126.4, 127.4, 128.4, 128.5, 128.6, 128.6, 128.9, 129.1, 129.3, 129.8, 131.5, 131.7, 133.5, 134.1, 134.1, 142.1, 144.1, 174.8, 175.2, 176.7, 194.7 ppm.

HRMS (ESI): *m/z* calcd for $C_{41}H_{32}ClN_2O_4$ $[M + H]^+$: 651.2045, found: 651.2063.

(3a*R,3'*S**,4*S**,6*S**,6a*S**)-1'-Benzyl-4-(3-methoxyphenyl)-6-(4-methylbenzoyl)-2-phenyl-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1,2',3(2*H*)-trione (45):**



45

Yield: 0.045 g (69%) as off white solid.

MP: 215–218 ºC.

IR (KBr) ν_{max}: 3135, 1717, 1677, 1633, 1620, 1400, 1385, 1192, 1123, 749, 656, 644, 603 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.35 (s, 3H), 3.49 (s, 3H), 3.87 (d, *J* = 16.4 Hz, 1H), 4.09 (d, *J* = 12.0 Hz, 1H), 4.15 (dd, *J* = 8.8, 12.0 Hz, 1H), 4.68 (d, *J* = 16.4 Hz, 1H), 4.96 (d, *J* = 6.8 Hz, 1H), 5.07 (dd, *J* = 6.8, 8.8 Hz, 1H), 6.01 (d, *J* = 7.6 Hz, 1H), 6.39 (d, *J* = 7.2 Hz, 2H), 6.46 (t, *J* = 2.0 Hz, 1H), 6.59 (d, *J* = 8.0 Hz, 1H), 6.69 (dd, *J* = 2.4, 8.4 Hz, 1H), 6.95–7.04 (m, 5H), 7.07–7.13 (m, 3H), 7.29 (d, *J* = 7.2 Hz, 1H), 7.40 (dd, *J* = 8.4, 16.0 Hz, 5H), 7.48–7.52 (m, 2H) ppm.

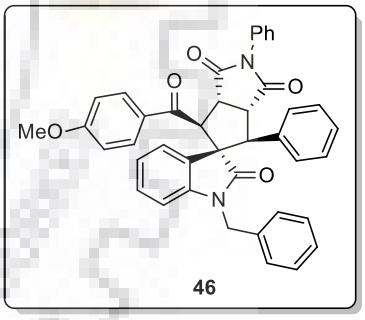
^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6, 43.5, 45.5, 48.9, 55.0, 56.0, 60.0, 65.9, 109.5, 113.3, 114.5, 121.1, 122.4, 124.8, 125.9, 126.1, 126.4, 127.2, 128.5, 128.6, 128.6, 128.9, 129.0, 129.1, 129.1, 131.8, 133.6, 134.3, 134.4, 142.2, 144.0, 159.2, 174.9, 175.5, 176.9, 194.9 ppm.

HRMS (ESI): *m/z* calcd for $C_{42}H_{35}N_2O_5$ $[M + H]^+$: 647.2540, found: 647.2544.

(3a*S,3'*S**,4*S**,6*S**,6a*R**)-1'-Benzyl-4-(4-methoxybenzoyl)-2,6-diphenyl-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1,2',3(2*H*)-trione (46):**

Yield: 0.040 g (63%) as off white solid.

MP: 241–244 °C.



46

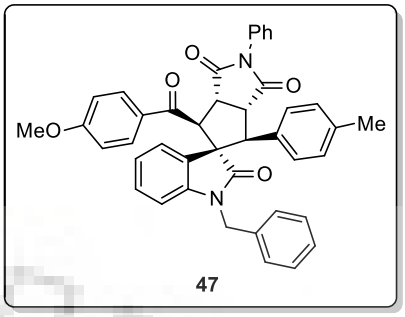
IR (KBr) ν_{max}: 3137, 1781, 1716, 1663, 1598, 1495, 1467, 1455, 1400, 1384, 1244, 1171, 1155, 1123, 842, 749, 698, 656, 615, 603, 582, 512 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.81 (s, 3H), 4.07–4.14 (m, 2H), 4.20 (dd, *J* = 8.8, 12.0 Hz, 1H), 4.61 (d, *J* = 16.4 Hz, 1H), 4.98 (d, *J* = 6.8 Hz, 1H), 5.10 (dd, *J* = 7.2, 8.8 Hz, 1H), 6.01 (d, *J* = 8.0 Hz, 1H), 6.37 (d, *J* = 7.6 Hz, 2H), 6.77 (d, *J* = 8.8 Hz, 2H), 6.93–6.98 (m, 3H), 7.0–7.06 (m, 5H), 7.12 (dd, *J* = 7.6, 16.8 Hz, 2H), 7.30 (d, *J* = 7.6 Hz, 1H), 7.38–7.42 (m, 3H), 7.48–7.55 (m, 4H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 43.5, 45.7, 48.6, 55.3, 55.5, 60.1, 66.2, 109.3, 113.5, 122.5, 124.5, 125.9, 126.1, 126.4, 127.2, 128.1, 128.1, 128.4, 128.5, 128.6, 128.8, 128.9, 129.1, 130.9, 131.7, 132.8, 134.2, 141.9, 163.6, 175.0, 175.5, 177.0, 193.4 ppm.

HRMS (ESI): *m/z* calcd for $C_{41}H_{33}N_2O_5$ $[M + H]^+$: 633.2384, found: 633.2401.

(3a*S,3'*S**,4*S**,6*S**,6a*R**)-1'-Benzyl-4-(4-methoxybenzoyl)-2-phenyl-6-(*p*-tolyl)-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1,2',3(2*H*)-trione (47):**



47

Yield: 0.042 g (65%) as off white solid.

MP: 258–260 ºC.

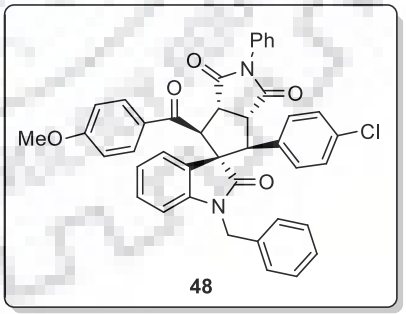
IR (KBr) ν_{max}: 3136, 1779, 1716, 1669, 1597, 1489, 1400, 1385, 1239, 1171, 1115, 831, 757, 695, 656, 603 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.21 (s, 3H), 3.81 (s, 3H), 4.04 (d, *J* = 16.0 Hz, 1H), 4.09 (s, 1H), 4.15 (dd, *J* = 9.2, 12.0 Hz, 1H), 4.67 (d, *J* = 16.0 Hz, 1H), 4.95 (d, *J* = 6.8 Hz, 1H), 5.07 (dd, *J* = 7.2, 9.2 Hz, 1H), 6.03 (d, *J* = 8.0 Hz, 1H), 6.39 (d, *J* = 7.2 Hz, 2H), 6.76 (d, *J* = 8.8 Hz, 2H), 6.84 (s, 4H), 6.93–7.05(m, 4H), 7.09–7.13 (m, 1H), 7.29 (d, *J* = 7.2 Hz, 1H), 7.38–7.42 (m, 3H), 7.47–7.54 (m, 4H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 21.1, 43.4, 45.6, 48.8, 55.4, 55.5, 59.9, 66.1, 109.3, 113.4, 122.4, 124.7, 125.9, 126.2, 126.4, 127.2, 128.3, 128.3, 128.5, 128.9, 129.1, 129.7, 130.9, 131.7, 134.3, 137.7, 142.0, 163.6, 175.0, 175.6, 177.1, 193.5 ppm.

HRMS (ESI): *m/z* calcd for $C_{42}H_{35}N_2O_5$ $[M + H]^+$: 647.2540, found: 647.2541.

(3a*R,3'*S**,4*S**,6*S**,6a*S**)-1'-Benzyl-4-(4-chlorophenyl)-6-(4-methoxybenzoyl)-2-phenyl-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1,2',3(2*H*)-trione (48):**



48

Yield: 0.035 g (52%) as off white solid.

MP: 240–242 ºC.

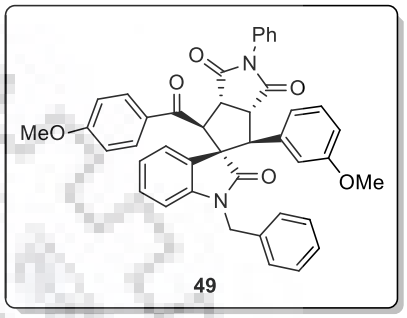
IR (KBr) ν_{max}: 3136, 1779, 1717, 1669, 1598, 1494, 1467, 1311, 1267, 1241, 1171, 1112, 1093, 1017, 837, 758, 694, 656, 616, 603, 590, 524 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.81 (s, 3H), 4.05–4.13 (m, 3H), 4.66 (d, *J* = 12.8 Hz, 1H), 4.95 (d, *J* = 5.6, 1H), 5.09 (dd, *J* = 5.6, 6.8 Hz, 1H), 6.08 (d, *J* = 6.0 Hz, 1H), 6.4 (d, *J* = 6.0 Hz, 2H), 6.77 (d, *J* = 6.8 Hz, 2H), 6.88 (d, *J* = 6.8 Hz, 2H), 6.97–7.01 (m, 3H), 7.05 (dd, *J* = 5.6, 11.6 Hz, 3H), 7.15 (t, *J* = 6.0 Hz, 1H), 7.29 (d, *J* = 6.0 Hz, 1H), 7.39–7.42 (m, 3H), 7.48–7.54 (m, 4H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 43.5, 45.7, 48.8, 55.4, 55.5, 59.5, 66.0, 109.5, 113.5, 122.6, 124.3, 125.9, 126.2, 126.4, 127.4, 128.4, 128.5, 128.6, 128.8, 129.1, 129.2, 129.7, 130.9, 131.5, 131.7, 134.1, 134.2, 142.1, 163.7, 174.8, 175.4, 176.8, 193.2 ppm.

HRMS (ESI): *m/z* calcd for $C_{41}H_{31}ClN_2O_5Na$ [M + Na]+: 689.1814, found: 689.1814.

(3a*S,3'*S**,4*S**,6*S**,6a*R**)-1'-Benzyl-4-(4-methoxybenzoyl)-6-(3-methoxyphenyl)-2-phenyl-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1,2',3(2*H*)-trione (49):**



49

Yield: 0.045 g (68%) as off white solid.

MP: 247–249 °C.

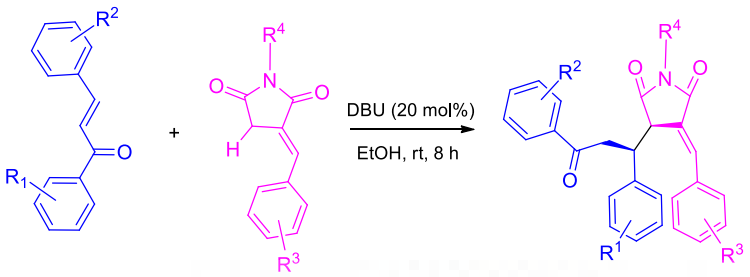
IR (KBr) ν_{max}: 3133, 1778, 1714, 1675, 1599, 1489, 1467, 1400, 1384, 1243, 1172, 1119, 758, 747, 695, 656, 604 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.49 (s, 3H), 3.81 (s, 3H), 4.03–4.18 (m, 3H), 4.66 (d, *J* = 16.0 Hz, 1H), 4.96 (d, *J* = 6.8 Hz, 1H), 5.09 (dd, *J* = 7.2, 9.2 Hz, 1H), 6.04 (d, *J* = 7.6 Hz, 1H), 6.38 (d, *J* = 7.2 Hz, 2H), 6.45 (t, *J* = 2.0 Hz, 1H), 6.59 (d, *J* = 8.0 Hz, 1H), 6.69 (dd, *J* = 2.4, 8.4 Hz, 1H), 6.77 (d, *J* = 8.8 Hz, 2H), 6.94–7.06 (m, 5H), 7.11 (t, *J* = 7.2 Hz, 1H), 7.31 (d, *J* = 7.6 Hz, 1H), 7.41 (d, *J* = 8.0 Hz, 3H), 7.49 (d, *J* = 7.2 Hz, 2H), 7.54 (d, *J* = 9.2 Hz, 2H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 43.5, 45.6, 48.9, 55.0, 55.4, 55.5, 60.1, 66.1, 109.4, 113.2, 113.5, 114.4, 121.0, 122.5, 124.7, 125.9, 126.0, 126.4, 127.2, 128.5, 128.6, 128.9, 129.0, 129.1, 130.9, 134.2, 134.3, 142.1, 159.1, 163.6, 174.9, 175.5, 177.0, 193.4 ppm.

HRMS (ESI): *m/z* calcd for $C_{42}H_{35}N_2O_6$ $[M + H]^+$: 663.2490, found: 663.2489.

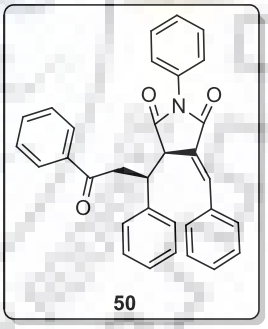
3.2.3. General procedure for the synthesis of 50-69:



R^1 = H, *p*-F, *p*-Br, *p*-Me, *m*-Cl;
R^2 = H, *p*-Cl, *p*-Me;
R^3 = H, *p*-Cl, *p*-Me, *m*-OMe;
R^4 = Ph, *p*-Cl Ph, Bn;

To a stirred solution of chalcone[305] derivative **5** (0.1 mmol) in 2 mL of EtOH was added benzylidene-1-phenylpyrrolidine-2,5-dione **3** (0.1 mmol). Then DBU (0.02 mmol) was added, and the mixture was allowed to stir at room temperature for 8 h (5 h in case of **69**). After completion of the reaction as judged by TLC, the product started to settle down in the round bottom flask. Then the reaction contents were filtered off, washed with EtOH and dried under vacuum.

(*R,*E*)-3-Benzylidene-4-((*S**)-3-oxo-1,3-diphenylpropyl)-1-phenylpyrrolidine-2,5-dione (50):**



Yield: 0.030 g (64%) as off white solid.

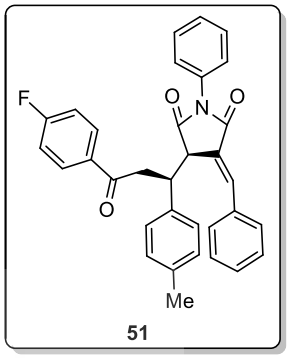
MP: 171–174 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.33 (dd, *J* = 4.0, 18.4 Hz, 1H), 4.19 (dt, *J* = 4.4, 11.2 Hz, 1H), 4.55 (dd, *J* = 2.0, 4.4 Hz, 1H), 4.61 (dd, *J* = 10.4, 18.0 Hz, 1H), 6.96–7.0 (m, 5H), 7.19–7.26 (m, 3H), 7.34–7.74 (m, 7H), 7.97–7.99 (m, 2H), 8.09–8.12 (m, 4H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 39.1, 40.0, 46.3, 126.5, 126.8, 127.8, 128.2, 128.2, 128.3, 128.5, 128.5, 128.7, 129.0, 129.3, 130.5, 131.0, 131.7, 133.3, 136.5, 137.1, 138.4, 169.4, 175.5, 199.2 ppm.

HRMS (ESI): *m/z* calcd for $C_{32}H_{25}KNO_3$ $[M+K]^+$: 510.1466, found: 510.1461.

(*R,*E*)-3-(4-Chlorobenzylidene)-4-((*S**)-3-oxo-1,3-diphenylpropyl)-1-phenylpyrrolidine-2,5-dione (51):**



51

Yield: 0.032 g (63%) as off white solid.

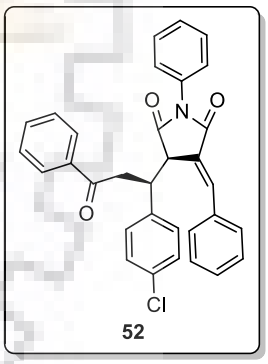
MP: 215–218 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.27 (dd, *J* = 3.6, 18.4 Hz, 1H), 4.14 (dt, *J* = 3.6, 11.2 Hz, 1H), 4.51 (dd, *J* = 2.0, 4.0 Hz, 1H), 4.68 (dd, *J* = 10.8, 18.0 Hz, 1H), 6.95–6.99 (m, 4H), 7.20–7.28 (m, 3H), 7.34–7.43 (m, 3H), 7.50 (t, *J* = 7.6 Hz, 2H), 7.58–7.63 (m, 3H), 7.68 (d, *J* = 2.0 Hz, 1H), 7.97 (d, *J* = 8.8 Hz, 2H), 8.09–8.12 (m, 2H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 39.0, 39.9, 46.1, 126.4, 127.3, 127.9, 128.2, 128.2, 128.2, 128.3, 128.5, 128.6, 128.7, 129.0, 129.6, 131.6, 131.7, 132.2, 132.3, 132.3, 133.4, 134.9, 135.0, 135.0, 135.1, 136.6, 137.0, 138.2, 169.3, 175.3, 199.4 ppm.

HRMS (ESI): *m/z* calcd for $C_{32}H_{24}ClNO_3Na$ $[M+Na]^+$: 528.1337, found: 528.1359.

(*R,*E*)-3-(4-Methylbenzylidene)-4-((*S**)-3-oxo-1,3-diphenylpropyl)-1-phenylpyrrolidine-2,5-dione (52):**



52

Yield: 0.036 g (74%) as off white solid.

MP: 235–238 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 2.48 (s, 3H), 3.34 (dd, *J* = 3.5, 18.0 Hz, 1H), 4.23 (dt, *J* = 4.0, 10.5 Hz, 1H), 4.51 (m, 1H), 4.62 (dd, *J* = 10.5, 18.0 Hz, 1H), 6.97–7.0 (m, 4H), 7.21–7.26 (m, 3H), 7.35 (t, *J* = 7.5 Hz, 1H), 7.42 (dd, *J* = 8.0, 18.0 Hz, 4H), 7.49 (t, *J* = 7.5 Hz, 2H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.71 (d, *J* = 1.0 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 2H), 8.12 (d, *J* = 7.5 Hz, 2H) ppm.

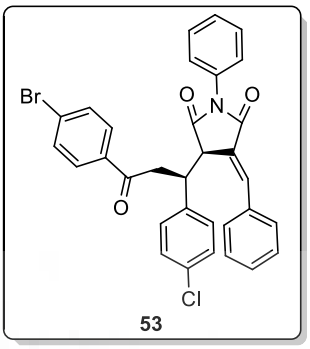
^{13}C NMR (125 MHz, $CDCl_3$): δ 21.6, 39.0, 40.1, 46.4, 125.7, 126.5, 127.8, 128.2, 128.4, 128.4, 128.5, 128.7, 129.0, 130.1, 130.6, 131.1, 131.8, 133.3, 136.5, 137.3, 138.5, 141.1, 169.6, 175.6, 199.3 ppm.

HRMS (ESI): *m/z* calcd for $C_{33}H_{31}N_2O_3$ $[M+NH_4]^+$: 503.2329, found: 503.2335.

(*R,*E*)-3-(3-Methoxybenzylidene)-4-((*S**)-3-oxo-1,3-diphenylpropyl)-1-phenylpyrrolidine-2,5-dione (53):**

Yield: 0.037 g (74%) as white solid.

MP: 95–98 °C.



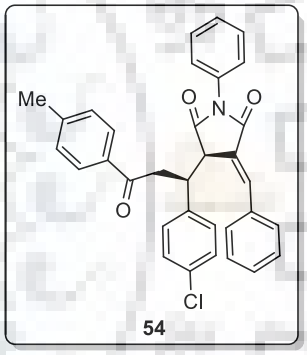
53

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.38 (dd, *J* = 4.4, 18.4 Hz, 1H), 3.99 (s, 3H), 4.19 (dt, *J* = 4.4, 10.0 Hz, 1H), 4.53 (dd, *J* = 10.4, 18.0 Hz, 1H), 4.59 (dd, *J* = 2.0, 4.0 Hz, 1H), 6.98–7.01 (m, 4H), 7.07 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.20–7.25 (m, 3H), 7.34–7.44 (m, 4H), 7.46–7.50 (m, 2H), 7.53–7.63 (m, 3H), 7.70 (d, *J* = 2.0 Hz, 1H), 8.07–8.09 (m, 2H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 39.3, 40.1, 46.1, 55.6, 115.9, 116.6, 123.0, 126.4, 127.1, 127.8, 128.2, 128.3, 128.4, 128.6, 129.0, 130.3, 131.7, 133.3, 134.7, 136.5, 137.1, 138.4, 160.1, 169.3, 175.5, 199.0 ppm.

HRMS (ESI): *m/z* calcd for $C_{33}H_{27}NO_4K$ $[M+K]^+$: 540.1566, found: 540.1570.

(*R,*E*)-3-Benzylidene-4-((*S**)-3-(4-fluorophenyl)-3-oxo-1-(*p*-tolyl)propyl)-1-phenylpyrrolidine-2,5-dione (54):**



54

Yield: 0.035 g (70%) as off white solid.

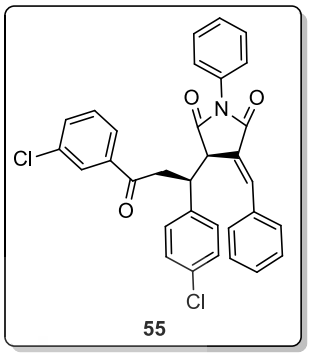
MP: 163–165 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 2.29 (s, 3H), 3.25 (dd, *J* = 4.0, 18.0 Hz, 1H), 4.15 (dt, *J* = 4.0, 10.5 Hz, 1H), 4.50–4.57 (m, 2H), 6.85 (d, *J* = 7.5 Hz, 2H), 7.01 (t, *J* = 5.6 Hz, 1H), 7.15 (t, *J* = 7.2 Hz, 2H), 7.37 (t, *J* = 7.5 Hz, 1H), 7.42–7.45 (m, 2H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.63 (t, *J* = 7.5 Hz, 2H), 7.73 (d, *J* = 1.5 Hz, 1H), 7.96 (d, *J* = 8.0 Hz, 2H), 8.14 (dd, *J* = 5.5, 9.0 Hz, 2H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 21.0, 38.7, 40.1, 46.2, 115.7, 115.8, 126.5, 126.9, 128.1, 128.5, 129.0, 129.1, 129.3, 130.5, 130.9, 130.9, 131.7, 133.4, 133.6, 133.6, 135.2, 136.4, 137.5, 164.9, 166.9, 169.5, 175.7, 197.7 ppm.

HRMS (ESI): *m/z* calcd for $C_{33}H_{26}FNO_3Na$ $[M+Na]^+$: 526.1789, found: 526.1807.

(*R,*E*)-3-(4-Chlorobenzylidene)-4-((*S**)-3-(4-fluorophenyl)-3-oxo-1-(*p*-tolyl)propyl)-1-phenylpyrrolidine-2,5-dione (55):**



55

Yield: 0.035 g (65%) as off white solid.

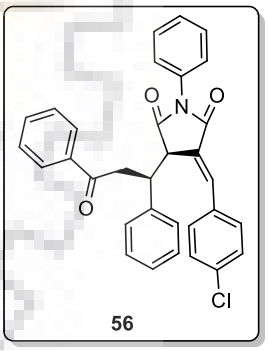
MP: 176–179 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.30 (s, 3H), 3.19 (dd, *J* = 3.2, 18.0 Hz, 1H), 4.10 (dt, *J* = 3.6, 10.8 Hz, 1H), 4.48 (dd, *J* = 2.0, 4.0 Hz, 1H), 4.62 (dd, *J* = 10.8, 18.0 Hz, 1H), 6.85 (d, *J* = 8.0 Hz, 2H), 6.98–7.04 (m, 4H), 7.16 (t, *J* = 8.8 Hz, 2H), 7.35–7.40 (m, 1H), 7.41–7.46 (m, 2H), 7.62 (d, *J* = 8.4 Hz, 2H), 7.67 (d, *J* = 2.0 Hz, 1H), 7.95 (d, *J* = 8.4 Hz, 2H), 8.11–8.16 (m, 2H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 21.0, 38.6, 40.0, 45.9, 115.7, 115.9, 126.4, 127.3, 128.1, 128.6, 129.1, 129.2, 129.6, 130.8, 130.9, 131.6, 131.7, 132.2, 133.4, 133.5, 135.0, 135.0, 136.6, 137.7, 164.6, 167.2, 169.3, 175.5, 197.9 ppm.

HRMS (ESI): *m/z* calcd for $C_{33}H_{25}ClFNO_3Na$ $[M+Na]^+$: 560.1399, found: 560.1396.

(*R,*E*)-3-((*S**)-3-(4-Fluorophenyl)-3-oxo-1-(*p*-tolyl)propyl)-4-(4-methylbenzylidene)-1-phenylpyrrolidine-2,5-dione (56):**



56

Yield: 0.038 g (73%) as white solid.

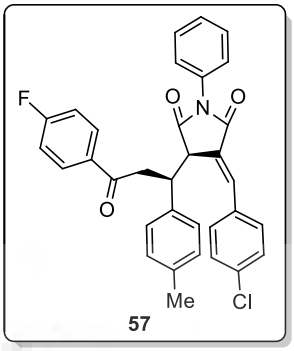
MP: 195–198 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.29 (s, 3H), 2.48 (s, 3H), 3.26 (dd, *J* = 4.0, 18.0 Hz, 1H), 4.18 (dt, *J* = 4.0, 10.4 Hz, 1H), 4.46 (dd, *J* = 2.0, 4.0 Hz, 1H), 4.56 (dd, *J* = 10.4, 17.6 Hz, 1H), 6.86 (d, *J* = 8.0 Hz, 2H), 6.99–7.03 (m, 4H), 7.16 (t, *J* = 8.4 Hz, 2H), 7.34–7.39 (m, 1H), 7.43 (t, *J* = 7.6 Hz, 4H), 7.70 (d, *J* = 1.6 Hz, 1H), 7.86 (d, *J* = 8.0 Hz, 2H), 8.13–8.17 (m, 2H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 21.0, 21.6, 38.6, 40.1, 46.3, 115.6, 115.9, 125.7, 125.7, 126.5, 128.2, 128.5, 129.0, 129.1, 130.0, 130.6, 130.9, 131.0, 131.0, 131.8, 133.7, 135.3, 136.5, 137.5, 141.1, 164.6, 167.2, 169.6, 175.8, 197.8 ppm.

HRMS (ESI): *m/z* calcd for $C_{34}H_{28}FNO_3K$ $[M+K]^+$: 556.1685, found: 556.1687.

(*R,*E*)-3-Benzylidene-4-((*S**)-1-(4-chlorophenyl)-3-oxo-3-phenylpropyl)-1-phenylpyrrolidine-2,5-dione (57):**



57

Yield: 0.038 g (75%) as off white solid.

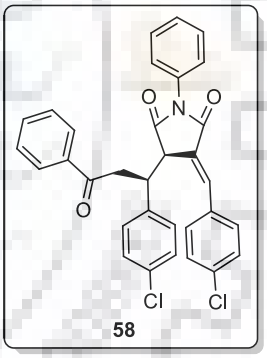
MP: 164–167 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 3.31 (dd, *J* = 3.5, 18.0 Hz, 1H), 4.17–4.19 (m, 1H), 4.52–4.58 (m, 2H), 6.91 (d, *J* = 8.0 Hz, 2H), 7.01 (d, *J* = 7.5 Hz, 2H), 7.19 (d, *J* = 8.0 Hz, 2H), 7.37–7.65 (m, 9H), 7.76 (s, 1H), 7.95 (d, *J* = 7.5 Hz, 2H), 8.09 (d, *J* = 8.0 Hz, 2H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 38.4, 40.1, 46.1, 126.3, 126.4, 128.2, 128.6, 128.6, 128.7, 129.1, 129.4, 129.6, 130.7, 130.9, 131.6, 133.2, 133.4, 133.7, 136.8, 137.0, 137.0,169.2, 175.4, 198.8 ppm.

HRMS (ESI): *m/z* calcd for $C_{32}H_{24}ClNO_3Na$ $[M+Na]^+$: 528.1337, found: 528.1339.

(*R,*E*)-3-(4-Chlorobenzylidene)-4-((*S**)-1-(4-chlorophenyl)-3-oxo-3-phenylpropyl)-1-phenylpyrrolidine-2,5-dione (58):**



58

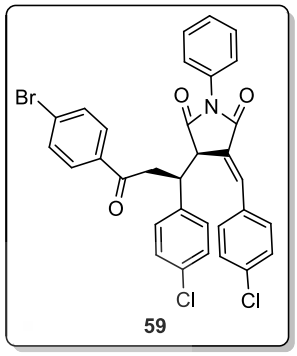
Yield: 0.035 g (65%) as off white solid.

MP: 173–176 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.24 (dd, *J* = 3.6, 18.0 Hz, 1H), 4.13 (dt, *J* = 4.0, 10.8 Hz, 1H), 4.51 (dd, *J* = 2.0, 4.0 Hz, 1H), 4.63 (dd, *J* = 10.8, 18.4 Hz, 1H), 6.91 (d, *J* = 8.8 Hz, 2H), 6.97–7.0 (m, 2H), 7.20 (d, *J* = 8.8 Hz, 2H), 7.36–7.40 (m, 1H), 7.43–7.46 (m, 2H), 7.50 (t, *J* = 7.6 Hz, 2H), 7.58–7.63 (m, 3H), 7.70 (d, *J* = 2.0 Hz, 1H), 7.95 (d, *J* = 8.4 Hz, 2H), 8.08–8.10 (m, 2H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 38.4, 39.9, 45.9, 126.3, 127.0, 128.2, 128.7, 128.7, 128.8, 129.1, 129.6, 129.7, 131.5, 131.6, 132.2, 133.5, 133.9, 135.3, 136.9, 136.9, 169.1, 175.2, 199.0 ppm.

(*R,*E*)-3-((*S**)-1-(4-Chlorophenyl)-3-oxo-3-phenylpropyl)-4-(4-methylbenzylidene)-1-phenylpyrrolidine-2,5-dione (59):**



59

Yield: 0.039 g (75%) as white solid.

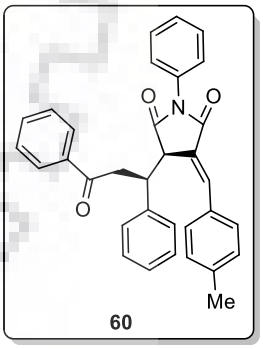
MP: 178–181 ºC.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.47 (s, 3H), 3.32 (dd, *J* = 4.0, 18.0 Hz, 1H), 4.21 (dt, *J* = 4.0, 10.4 Hz, 1H), 4.50 (dd, *J* = 2.0, 4.0 Hz, 1H), 4.56 (dd, *J* = 10.4, 18.0 Hz, 1H), 6.91 (d, *J* = 8.4 Hz, 2H), 6.98–7.01 (m, 2H), 7.19 (d, *J* = 8.4 Hz, 2H), 7.37 (t, *J* = 7.2 Hz, 1H), 7.42–7.46 (m, 4H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.60 (t, *J* = 7.2 Hz, 1H), 7.73 (d, *J* = 2.0, 1H), 7.85 (d, *J* = 8.0 Hz, 2H), 8.08–8.11 (m, 2H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 21.6, 38.3, 40.0, 46.2, 125.2, 126.4, 128.2, 128.6, 128.7, 129.1, 129.7, 130.1, 130.4, 131.0, 131.7, 133.4, 133.7, 136.8, 137.0, 141.3, 169.4, 175.4, 198.9 ppm.

HRMS (ESI): *m/z* calcd for $C_{33}H_{30}ClN_2O_3$ $[M+NH_4]^+$: 537.1939, found: 537.1973.

(*R,*E*)-3-((*S**)-1-(4-Chlorophenyl)-3-oxo-3-phenylpropyl)-4-(3-methoxybenzylidene)-1-phenylpyrrolidine-2,5-dione (60):**



60

Yield: 0.041 g (76%) as white solid.

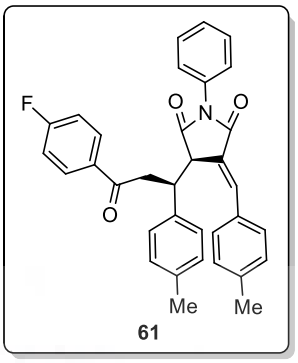
MP: 134–137 ºC.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.36 (dd, *J* = 4.4, 18.0 Hz, 1H), 3.98 (s, 3H), 4.15–4.20 (m, 1H), 4.47 (dd, *J* = 10.0, 18.0 Hz, 1H), 4.58 (dd, *J* = 2.0, 4.0 Hz, 1H), 6.91 (d, *J* = 8.4 Hz, 2H), 7.01–7.03 (m, 2H), 7.06–7.09 (m, 1H), 7.19 (d, *J* = 8.4 Hz, 2H), 7.34–7.40 (m, 2H), 7.43–7.50 (m, 4H), 7.53–7.61 (m, 3H), 7.72 (d, *J* = 2.0 Hz, 1H), 8.05–8.07 (m, 2H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 38.6, 40.1, 46.0, 55.6, 115.8, 116.6, 123.0, 126.3, 126.7, 128.2, 128.6, 128.7, 129.1, 129.6, 130.4, 131.5, 133.4, 133.7, 134.5, 136.9, 136.9, 137.0, 160.1, 169.2, 175.4, 198.7 ppm.

HRMS (ESI): *m/z* calcd for $C_{33}H_{26}ClNO_4$ $[M]^+$: 535.1545, found: 535.1559.

(*R,*E*)-3-Benzylidene-4-((*S**)-3-(4-bromophenyl)-1-(4-chlorophenyl)-3-oxopropyl)-1-phenylpyrrolidine-2,5-dione (61):**



61

Yield: 0.044 g (76%) as off white solid.

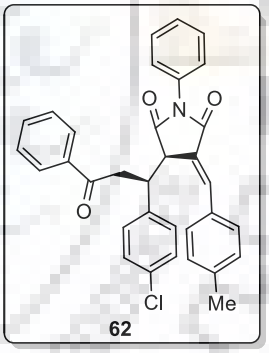
MP: 98–101 ºC.

^{1}H NMR (500 MHz, $CDCl_3$): δ 3.25 (dd, *J* = 4.0, 18.0 Hz, 1H), 4.16 (dt, *J* = 4.0, 10.0 Hz, 1H), 4.48–4.54 (m, 2H), 6.88 (d, *J* = 8.5 Hz, 2H), 7.01 (d, *J* = 7.5 Hz, 2H), 7.19 (d, *J* = 8.0 Hz, 2H), 7.39 (t, *J* = 7.5 Hz, 1H), 7.43–7.46 (m, 2H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.62–7.65 (m, 4H), 7.75 (d, *J* = 1.5 Hz, 1H), 7.93–7.96 (m, 4H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 38.3, 40.0, 46.0, 126.3, 128.7, 128.7, 129.1, 129.4, 129.6, 129.7, 130.7, 130.9, 131.5, 132.0, 133.2, 133.8, 135.7, 136.8, 136.9, 169.2, 175.4, 197.9 ppm.

HRMS (ESI): *m/z* calcd for $C_{32}H_{23}BrClNO_3Na$ $[M+Na]^+$: 606.0442, found: 606.047.

(*R,*E*)-3-((*S**)-3-(4-Bromophenyl)-1-(4-chlorophenyl)-3-oxopropyl)-4-(4-chlorobenzylidene)-1-phenylpyrrolidine-2,5-dione (62):**



62

Yield: 0.032 g (52%) as off white solid.

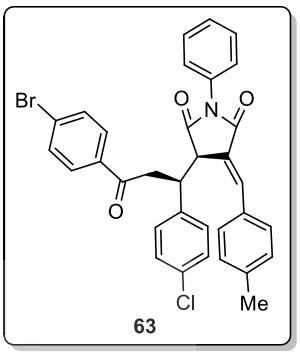
MP: 173–175 ºC.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.18 (dd, *J* = 3.6, 18.4 Hz, 1H), 4.11 (dt, *J* = 3.6, 10.8 Hz, 1H), 4.48 (dd, *J* = 2.0, 4.0 Hz, 1H), 4.58 (dd, *J* = 10.8, 18.0 Hz, 1H), 6.88 (d, *J* = 8.4 Hz, 2H), 6.98–7.0 (m, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 7.36–7.41 (m, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.63 (t, *J* = 8.4 Hz, 4H), 7.69 (d, *J* = 2.0 Hz, 1H), 7.94 (t, *J* = 8.4 Hz, 4H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 38.3, 39.9, 45.8, 126.3, 126.8, 128.7, 128.8, 128.8, 129.2, 129.6, 129.7, 131.4, 131.5, 132.1, 132.2, 133.9, 135.4, 135.4, 135.6, 136.6, 136.9, 169.0, 175.2, 198.0 ppm.

HRMS (ESI): *m/z* calcd for $C_{32}H_{22}BrCl_2NO_3K$ $[M+K]^+$: 655.9792, found: 655.9775.

(*R,*E*)-3-((*S**)-3-(4-Bromophenyl)-1-(4-chlorophenyl)-3-oxopropyl)-4-(4-methylbenzylidene)-1-phenylpyrrolidine-2,5-dione (63):**



63

Yield: 0.045 g (75%) as off white solid.

MP: 177–180 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.48 (s, 3H), 3.26 (dd, *J* = 4.4, 18.0 Hz, 1H), 4.19 (dt, *J* = 4.0, 10.0 Hz, 1H), 4.46–4.55 (m, 2H), 6.89 (d, *J* = 8.4 Hz, 2H), 6.99–7.01 (m, 2H), 7.18 (d, *J* = 8.8 Hz, 2H), 7.38 (t, *J* = 7.6 Hz, 1H), 7.42–7.46 (m, 4H), 7.63 (d, *J* = 8.8 Hz, 2H), 7.72 (d, *J* = 1.6 Hz, 1H), 7.83 (d, *J* = 8.4 Hz, 2H), 7.96 (d, *J* = 8.8 Hz, 2H) ppm.

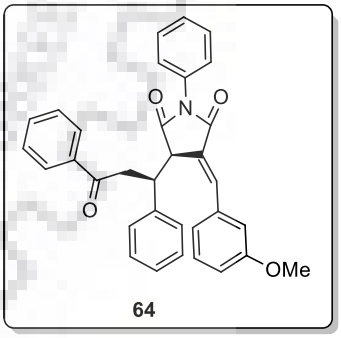
^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6, 38.2, 40.0, 46.0, 125.1, 126.3, 128.6, 128.6, 128.7, 129.1, 129.6, 129.7, 129.7, 129.8, 130.1, 130.4, 131.0, 131.0, 131.6, 132.0, 132.0, 133.8, 135.7, 136.8, 136.9, 141.4, 169.3, 175.4, 198.0 ppm.

HRMS (ESI): *m/z* calcd for $C_{33}H_{25}BrClNO_3$ $[M]^+$: 597.0701, found: 597.4141.

(*R,*E*)-3-Benzylidene-4-((*S**)-1-(4-chlorophenyl)-3-oxo-3-(*p*-tolyl)propyl)-1-phenylpyrrolidine-2,5-dione (64):**

Yield: 0.032 g (62%) as off white solid.

MP: 134–137 °C.



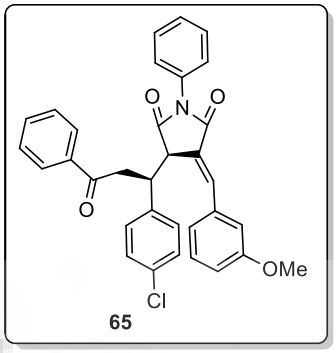
64

^{1}H NMR (500 MHz, $CDCl_3$): δ 2.42 (s, 3H), 3.28 (dd, *J* = 4.0, 17.5 Hz, 1H), 4.17 (dt, *J* = 4.0, 10.0 Hz, 1H), 4.49–4.54 (m, 2H), 6.91 (d, *J* = 8.5 Hz, 2H), 7.0 (d, *J* = 7.5 Hz, 2H), 7.19 (d, *J* = 8.5 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.38 (t, *J* = 7.5 Hz, 1H), 7.43–7.46 (m, 2H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.63 (t, *J* = 8.0 Hz, 2H), 7.75 (d, *J* = 2.0 Hz, 1H), 7.95 (d, *J* = 7.5 Hz, 2H), 7.99 (d, *J* = 8.5 Hz, 2H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 21.7, 38.5, 39.9, 46.2, 126.3, 126.5, 128.3, 128.6, 128.6, 129.1, 129.3, 129.4, 129.6, 130.6, 130.9, 131.6, 133.2, 133.7, 134.5, 136.8, 137.1, 144.3, 169.3, 175.3, 198.4 ppm.

HRMS (ESI): *m/z* calcd for $C_{33}H_{26}ClNO_3Na$ $[M+Na]^+$: 542.1493, found: 542.1500.

(*R,*E*)-3-Benzylidene-4-((*S**)-3-(3-chlorophenyl)-1-(4-chlorophenyl)-3-oxopropyl)-1-phenylpyrrolidine-2,5-dione (65):**



65

Yield: 0.045 g (83%) as off white solid.

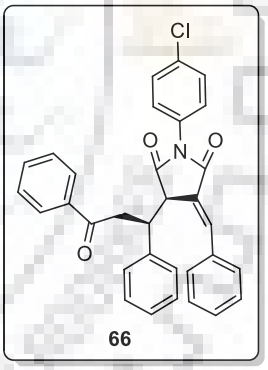
MP: 175–178 ºC.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.27 (dd, *J* = 4.0, 18.0 Hz, 1H), 4.16 (dt, *J* = 4.0, 10.0 Hz, 1H), 4.49–4.56 (m, 2H), 6.89 (d, *J* = 8.4 Hz, 2H), 7.0–7.02 (m, 2H), 7.19 (d, *J* = 8.4 Hz, 2H), 7.37–7.47 (m, 4H), 7.55 (q, *J* = 7.6 Hz, 2H), 7.64 (t, *J* = 7.6 Hz, 2H), 7.76 (d, *J* = 2.0 Hz, 1H), 7.94–7.97 (m, 3H), 8.04 (t, *J* = 2.0 Hz, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 38.2, 40.2, 45.9, 126.3, 126.3, 128.2, 128.3, 128.7, 128.7, 129.1, 129.4, 129.6, 130.1, 130.7, 130.9, 131.5, 133.2, 133.4, 133.8, 135.1, 136.7, 136.9, 138.4, 169.2, 175.4, 197.6 ppm.

HRMS (ESI): *m/z* calcd for $C_{32}H_{27}Cl_2N_2O_3$ $[M+NH_4]^+$: 557.1393, found: 557.1395.

(*R*,*E)-3-Benzylidene-1-(4-chlorophenyl)-4-((*S**)-3-oxo-1,3-diphenylpropyl)pyrrolidine-2,5-dione (66):**



66

Yield: 0.034 g (67%) as off white solid.

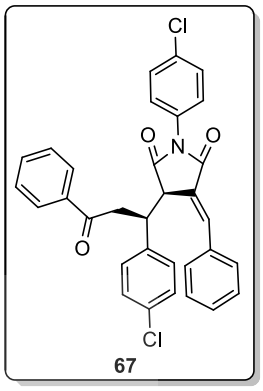
MP: 169–172 ºC.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.34 (dd, *J* = 4.0, 18.0 Hz, 1H), 4.17 (dt, *J* = 3.6, 10.4 Hz, 1H), 4.53–4.61 (m, 2H), 6.93 (d, *J* = 8.8 Hz, 2H), 6.97 (dd, *J* = 1.6, 8.0 Hz, 2H), 7.19–7.24 (m, 3H), 7.38 (d, *J* = 8.4 Hz, 2H), 7.48–7.54 (m, 3H), 7.58–7.65 (m, 3H), 7.74 (d, *J* = 2.0 Hz, 1H), 7.98 (d, *J* = 7.6 Hz, 2H), 8.09–8.11 (m, 2H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 39.2, 39.9, 46.4, 126.5, 127.7, 127.9, 128.2, 128.3, 128.5, 128.7, 129.2, 129.3, 130.1, 130.7, 131.0, 133.2, 133.4, 134.3, 136.9, 137.1, 138.3, 169.2, 175.3, 199.2 ppm.

HRMS (ESI): *m/z* calcd for $C_{32}H_{24}ClNO_3Na$ $[M+Na]^+$: 528.1337, found: 528.1364.

(*R*,*E)-3-Benzylidene-1-(4-chlorophenyl)-4-((*S**)-1-(4-chlorophenyl)-3-oxo-3-phenylpropyl)pyrrolidine-2,5-dione (67):**



67

Yield: 0.036 g (67%) as off white solid.

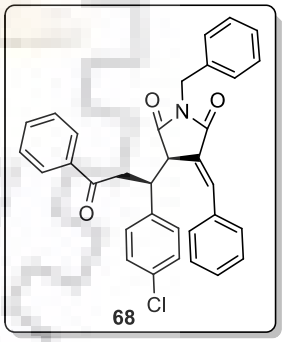
MP: 162–165 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.32 (dd, *J* = 4.0, 18.0 Hz, 1H), 4.16 (dt, *J* = 4.0, 10.4 Hz, 1H), 4.48–4.55 (m, 2H), 6.89 (d, *J* = 8.4 Hz, 2H), 6.96 (d, *J* = 8.8 Hz, 2H), 7.18 (d, *J* = 8.4 Hz, 2H), 7.41 (d, *J* = 8.8 Hz, 2H), 7.48–7.55 (m, 3H), 7.58–7.65 (m, 3H), 7.76 (d, *J* = 2.0 Hz, 1H), 7.95 (d, *J* = 7.6 Hz, 2H), 8.07–8.09 (m, 2H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 38.5, 39.9, 46.2, 126.1, 127.5, 128.2, 128.6, 128.8, 129.3, 129.4, 129.6, 130.0, 130.8, 131.0, 133.0, 133.5, 133.8, 134.1, 134.5, 136.9, 137.0, 137.2, 169.0, 175.1, 198.8 ppm.

HRMS (ESI): *m/z* calcd for $C_{32}H_{24}Cl_2NO_3$ $[M+H]^+$: 540.1128, found: 540.1117.

(*R*,*E)-1-Benzyl-3-benzylidene-4-((*S**)-1-(4-chlorophenyl)-3-oxo-3-phenylpropyl)pyrrolidine-2,5-dione (68):**



68

Yield: 0.034 g (65%) as off white solid.

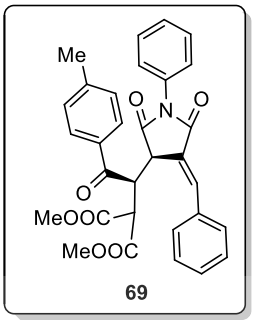
MP: 144–146 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.24 (dd, *J* = 4.4, 18.4 Hz, 1H), 4.03 (dt, *J* = 4.4, 10.4 Hz, 1H), 4.38 (dd, *J* = 2.4, 4.0 Hz, 1H), 4.44–4.64 (m, 3H), 6.57 (d, *J* = 8.4 Hz, 2H), 6.78 (d, *J* = 8.4 Hz, 2H), 7.20–7.22 (m, 2H), 7.29–7.31 (m, 3H), 7.46–7.52 (m, 3H), 7.57–7.62 (m, 3H), 7.67 (d, *J* = 2.0 Hz, 1H), 7.87 (d, *J* = 7.2 Hz, 2H), 8.05–8.07 (m, 2H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 37.6, 40.2, 42.3, 45.7, 126.6, 127.9, 128.1, 128.4, 128.6, 128.7, 129.0, 129.2, 129.2, 130.4, 130.7, 133.1, 133.2, 133.4, 135.4, 136.1, 136.6, 137.0, 170.0, 176.0, 198.8 ppm.

HRMS (ESI): *m/z* calcd for $C_{33}H_{27}ClNO_3$ $[M+H]^+$: 520.1674, found: 520.1701.

Dimethyl 2-((*S)-1-((*R*,*E**)-4-benzylidene-2,5-dioxo-1-phenylpyrrolidin-3-yl)-2-oxo-2-(*p*-tolyl)ethyl)malonate (69):**



69

Yield: 0.043 g (81%) as white solid.

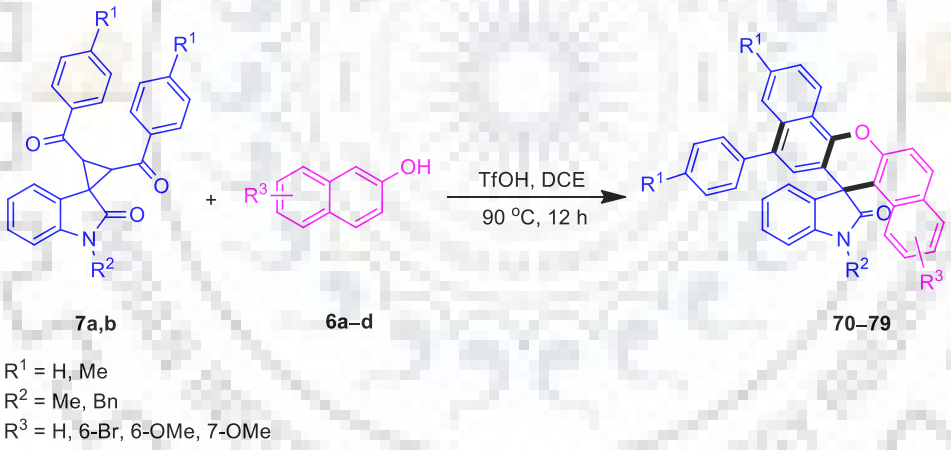
MP: 197–200 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.31 (s, 3H), 3.24 (s, 3H), 3.89 (s, 3H), 4.55 (dd, *J* = 2.4, 4.8 Hz, 1H), 4.77 (d, *J* = 11.6 Hz, 1H), 5.05 (dd, *J* = 4.8, 11.6 Hz, 1H), 6.94 (d, *J* = 8.0 Hz, 2H), 7.17 (d, *J* = 8.4 Hz, 2H), 7.40–7.44 (m, 1H), 7.48–7.62 (m, 10H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6, 41.6, 42.7, 51.7, 52.6, 53.1, 125.7, 126.8, 128.5, 128.6, 129.1, 129.1, 129.2, 130.4, 130.6, 132.1, 133.2, 133.9, 136.9, 144.7, 168.3, 168.8, 169.1, 174.7, 198.5 ppm.

HRMS (ESI): *m/z* calcd for $C_{31}H_{27}NO_7Na$ $[M+Na]^+$: 548.1680, found: 548.1696.

3.2.4. General procedure for the synthesis of 70–79:

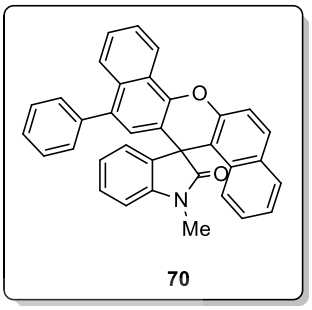


7a,b 6a–d 70–79

R^1 = H, Me
R^2 = Me, Bn
R^3 = H, 6-Br, 6-OMe, 7-OMe

To a mixture of spirooxindolic cyclopropane[298] **7** (0.1 mmol) and *β*-naphthol **6** (0.1 mmol) in 2 mL of DCE, was added TfOH (0.1 mmol) and the contents were stirred at 90 °C for 12 h. The reaction was monitored by TLC. After completion of the reaction, the mixture was concentrated under reduced pressure, the crude product was purified by column chromatography on silica gel using 10−15% ethyl acetate in hexanes to afford xanthene-tethered biarylic spirooxindole (**70**−**79**) as a solid.

1'-Methyl-12-phenylspiro[dibenzo[*a,h*]xanthene-14,3'-indolin]-2'-one (70):



70

Yield: 0.027 g (55%) as off white solid.

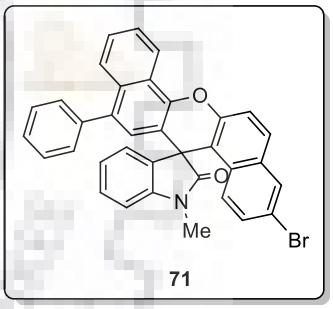
MP: 288–291 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.49 (s, 3H), 6.62 (s, 1H), 6.95 (td, *J* = 0.8, 7.2 Hz, 1H), 6.98–7.03 (m, 2H), 7.09 (d, *J* = 8.0 Hz, 1H), 7.17–7.21 (m, 1H), 7.28–7.32 (m, 3H), 7.34 (td, *J* = 1.6, 7.6 Hz, 1H), 7.38–7.44 (m, 3H), 7.46–7.50 (m, 1H), 7.60–7.65 (m, 2H), 7.75–7.81 (m, 2H), 7.90 (d, *J* = 8.8 Hz, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 27.0, 52.44, 108.72, 110.7, 114.0, 118.5, 122.0, 122.6, 123.4, 124.0, 124.2, 124.3, 125.1, 125.8, 126.2, 127.0, 127.1, 127.2, 128.2, 128.9, 129.2, 130.2, 130.7, 131.4, 131.5, 131.9, 136.0, 137.8, 140.1, 142.4, 149.8, 178.8 ppm.

HRMS (ESI): *m/z* calcd for $C_{35}H_{23}NO_2Na$ $[M+Na]^+$: 512.1621, found: 512.1618.

3-Bromo-1'-methyl-12-phenylspiro[dibenzo[*a,h*]xanthene-14,3'-indolin]-2'-one (71):



71

Yield: 0.032 g (56%) as off white solid.

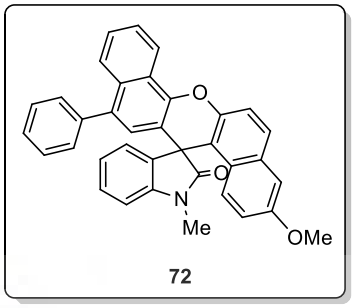
MP: 287–289 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.48 (s, 3H), 6.60 (s, 1H), 6.88 (d, *J* = 9.2 Hz, 1H), 6.94–7.0 (m, 2H), 7.09 (d, *J* = 8.0 Hz, 1H), 7.26–7.29 (m, 3H), 7.34–7.44 (m, 4H), 7.46–7.50 (m, 1H), 7.61–7.65 (m, 2H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.81 (d, *J* = 8.8 Hz, 1H), 7.94 (d, *J* = 2.0 Hz, 1H), 8.59 (d, *J* = 8.0 Hz, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 27.0, 52.3, 108.8, 111.1, 113.8, 118.0, 119.7, 121.9, 123.3, 124.2, 124.3, 124.3, 125.1, 125.8, 126.4, 127.1, 127.2, 128.2, 129.1, 130.0, 130.2, 130.2, 130.4, 131.0, 132.0, 132.6, 136.3, 137.4, 140.0, 142.4, 143.8, 150.0, 178.5 ppm.

HRMS (ESI): *m/z* calcd for $C_{35}H_{22}BrNO_2Na$ $[M+Na]^+$: 590.0726, found: 590.0745.

3-Methoxy-1'-methyl-12-phenylspiro[dibenzo[*a,h*]xanthene-14,3'-indolin]-2'-one (72):



72

Yield: 0.033 g (63%) as off white solid.

MP: 289–291 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.48 (s, 3H), 3.84 (s, 3H), 6.61 (s, 1H), 6.85-6.88 (m, 1H), 6.91 (s, 1H), 6.93–7.0 (m, 3H), 7.08 (d, *J* = 7.6 Hz, 1H), 7.13 (d, *J* = 2.8 HZ, 1H), 7.29 (d, *J* = 7.6 Hz, 2H), 7.32–7.43 (m, 5H), 7.45–7.49 (m, 1H), 7.57–7.64 (m, 2H), 7.75–7.81 (m, 2H), 8.60 (d, *J* = 8.4 Hz, 1H) ppm.

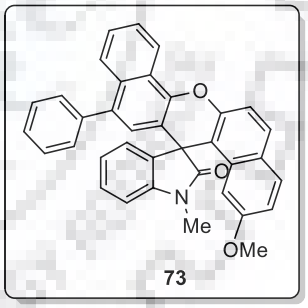
^{13}C NMR (100 MHz, $CDCl_3$): δ 26.9, 52.5, 55.2, 108.0, 108.7, 110.9, 113.9, 118.9, 119.1, 122.0, 123.5, 124.0, 124.0, 124.3, 125.1, 125.7, 126.2, 126.4, 126.9, 127.1, 128.1, 128.9, 129.7, 130.2, 131.9, 132.6, 135.8, 137.8, 140.2, 142.4, 144.0, 148.3, 156.1, 178.8 ppm.

HRMS (ESI): *m/z* calcd for $C_{36}H_{26}NO_3$ $[M+H]^+$: 520.1907, found: 520.2231.

2-Methoxy-1'-methyl-12-phenylspiro[dibenzo[*a,h*]xanthene-14,3'-indolin]-2'-one (73):

Yield: 0.028 g (54%) as brown solid.

MP: 269–271 °C.



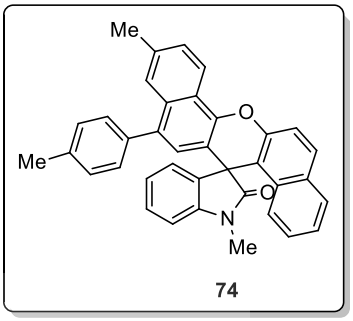
73

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.41 (s, 3H), 3.49 (s, 3H), 6.36 (d, *J* = 2.0 Hz, 1H), 6.61 (s, 1H), 6.94 (dd, *J* = 2.4, 9.2 Hz, 1H), 7.0 (td, *J* = 0.8, 7.2 Hz, 1H), 7.04–7.09 (m, 2H), 7.30 (d, *J* = 6.0 Hz, 2H), 7.33–7.44 (m, 4H), 7.46–7.51 (m, 2H), 7.61–7.65 (m, 1H), 7.68 (d, *J* = 8.8 Hz, 1H), 7.77 (d, *J* = 8.4 Hz, 1H), 7.82 (d, *J* = 8.8 Hz, 1H), 8.62 (d, *J* = 8.0 Hz, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 26.8, 52.5, 54.7, 102.1, 108.3, 109.8, 113.8, 115.9, 115.9, 116.5, 116.5, 122.1, 123.5, 124.2, 124.3, 124.4, 125.3, 125.7, 126.2, 126.5, 127.0, 127.1, 128.2, 128.8, ppm.

HRMS (ESI): *m/z* calcd for $C_{36}H_{26}NO_3$ $[M+H]^+$: 520.1907, found: 520.1921.

1',10-Dimethyl-12-(*p*-tolyl)spiro[dibenzo[*a,h*]xanthene-14,3'-indolin]-2'-one (74):



74

Yield: 0.030 g (57%) as off white solid.

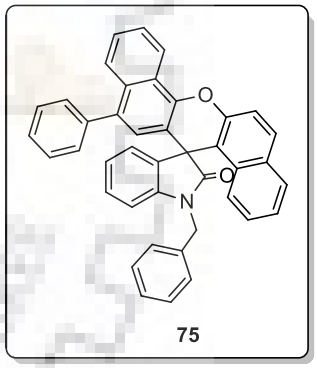
MP: 241–243 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.43 (d, *J* = 4.0 Hz, 6H), 3.48 (s, 3H), 6.57 (s, 1H), 6.91–7.02 (m, 3H), 7.06–7.10 (m,1H), 7.17–7.24 (m, 5H), 7.29–7.35 (m, 2H), 7.45 (d, *J* = 8.4 Hz, 1H), 7.53 (s, 1H), 7.60 (d, *J* = 8.8 Hz, 1H), 7.79 (d, *J* = 8.4 Hz, 1H), 7.88 (d, *J* = 8.8 Hz, 1H), 8.48 (d, *J* = 8.4 Hz, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 21.2, 21.9, 52.4, 108.7, 110.8, 113.2, 118.5, 121.9, 122.5, 122.6, 123.5, 124.0, 124.1, 124.9, 125.1, 127.2, 128.3, 128.8,128.9, 129.1, 130.1, 130.9, 131.3, 131.6, 132.2, 135.4, 136.7, 136.7, 137.4, 137.8, 142.5, 143.8, 149.9, 178.9 ppm.

HRMS (ESI): *m/z* calcd for $C_{37}H_{27}NO_2$ $[M]^+$: 517.2036, found: 517.2030.

1'-Benzyl-12-phenylspiro[dibenzo[*a,h*]xanthene-14,3'-indolin]-2'-one (75):



75

Yield: 0.034 g (60%) as off white solid.

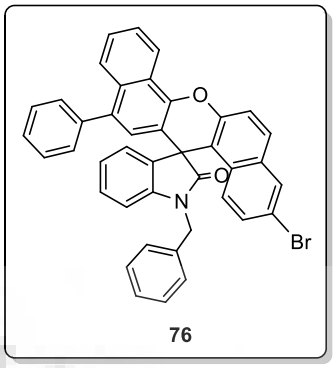
MP: 208–211 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.13 (dd, *J* = 14.8, 36.4 Hz, 2H), 6.66 (s, 1H), 6.90 (t, *J* = 7.2 Hz, 1H), 6.97–7.01 (m, 3H), 7.07 (d, *J* = 8.0 Hz, 1H), 7.24–7.25 (m, 5H), 7.28–7.30 (m, 2H), 7.39–7.42 (m, 3H), 7.47–7.51 (m, 3H), 7.63 (t, *J* = 8.8 Hz, 2H), 7.79 (d, *J* = 8.0 Hz, 2H), 7.91 (d, *J* = 8.8 Hz, 1H), 8.62 (d, *J* = 8.4 Hz, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 44.8, 52.3, 96.1, 109.6, 110.6, 114.0, 118.5, 118.5, 122.0, 123.1, 123.6, 124.0, 124.2, 124.4, 125.2, 125.8, 126.3, 127.0, 127.1, 127.1, 128.0, 128.2, 128.5, 128.7, 128.8, 129.1, 130.1, 131.0, 131.4, 131.5, 131.9, 135.7, 136.0, 137.8, 140.0, 141.7, 143.8, 149.9, 178.6 ppm.

HRMS (ESI): *m/z* calcd for $C_{41}H_{28}NO_2$ $[M+H]^+$: 566.2115, found: 566.2661.

1'-Benzyl-3-bromo-12-phenylspiro[dibenzo[*a*,*h*]xanthene-14,3'-indolin]-2'-one (76):



76

Yield: 0.035 g (55%) as off white solid.

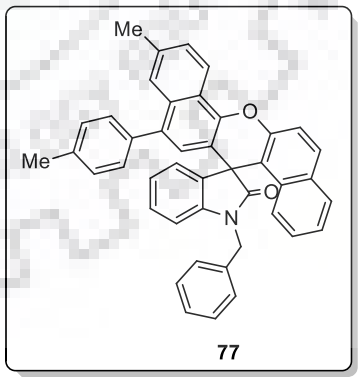
MP: 289–292 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.11 (dd, *J* = 15.2, 32.4 Hz, 2H), 6.63 (s, 1H), 6.83 (d, *J* = 9.2 Hz, 1H), 6.90–6.98 (m, 2H), 7.04 (dd, *J* = 2.0, 9.2 Hz, 1H), 7.09 (d, *J* = 8.0 Hz, 1H), 7.23–7.25 (m, 3H), 7.27–7.31 (m, 3H), 7.39–7.42 (m, 3H), 7.47–7.51 (m, 3H), 7.62–7.66 (m, 2H), 7.78–7.82 (m, 2H), 7.94 (d, *J* = 2.0 Hz, 1H), 8.60 (d, *J* = 8.0 Hz, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 44.8, 52.2, 109.7, 111.0, 113.8, 118.0, 119.7, 122.0, 123.4, 124.1, 124.3, 124.9, 125.2, 125.8, 126.4, 127.1, 128.1, 128.2, 128.5, 128.9, 129.0, 130.0, 130.1, 130.1, 130.3, 130.9, 131.9, 132.6, 135.5, 136.2, 137.5, 139.9, 141.6, 143.7, 150.0, 178.3 ppm.

HRMS (ESI): *m/z* calcd for $C_{41}H_{27}BrNO_2$ $[M+H]^+$: 644.1220, found: 644.1767.

1'-Benzyl-10-methyl-12-(*p*-tolyl)spiro[dibenzo[*a*,*h*]xanthene-14,3'-indolin]-2'-one (77):



77

Yield: 0.036 g (61%) as pale yellow solid.

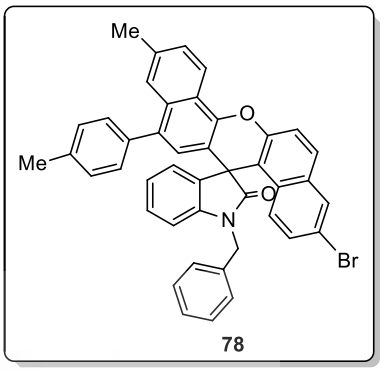
MP: 154–157 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.45 (s, 6H), 5.12 (s, 2H), 6.60 (s, 1H), 6.89 (td, *J* = 0.8, 7.6 Hz, 1H), 6.96–7.01 (m, 4H), 7.06 (d, *J* = 7.6 Hz, 1H), 7.13 (d, *J* = 7.2 Hz, 2H), 7.21–7.23 (m, 3H), 7.27–7.29 (m, 3H), 7.46 (dd, *J* = 1.2, 8.4 Hz, 1H), 7.50–7.52 (m, 2H), 7.57 (s, 1H), 7.61 (d, *J* = 8.8 Hz, 1H), 7.79 (d, *J* = 8.4 Hz, 1H), 7.89 (d, *J* = 9.2 Hz, 1H), 8.49 (d, *J* = 8.8 Hz, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 21.2, 21.9, 44.8, 52.3, 109.5, 110.6, 113.1, 118.5, 121.9, 122.5, 123.2, 123.6, 123.9, 124.1, 124.9, 125.2, 127.0, 127.9, 128.3, 128.5, 128.6, 128.8, 128.9, 129.0, 130.0, 130.9, 131.3, 131.6, 132.2, 135.3, 135.7, 136.6, 136.8, 137.3, 137.8, 141.7, 143.7, 149.9, 178.7 ppm.

HRMS (ESI): *m/z* calcd for $C_{36}H_{26}NO_3$ $[M+H]^+$: 632.1986, found: 632.2004.

1'-Benzyl-3-bromo-10-methyl-12-(*p*-tolyl)spiro[dibenzo[*a*,*h*]xanthene-14,3'-indolin]-2'-one (78):



Yield: 0.034 g (50%) as off white solid.

MP: 290–293 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.44 (s, 6H), 5.10 (s, 2H), 6.57 (s, 1H), 6.81 (d, *J* = 9.2 Hz, 1H), 6.88–6.96 (m, 2H), 7.02 (dd, *J* = 2.4, 9.2 Hz, 1H), 7.07 (d, *J* = 8.0 Hz, 1H), 7.13 (d, *J* = 7.6 Hz, 2H), 7.21–7.25 (m, 3H), 7.27–7.34 (m, 3H), 7.45–7.50 (m, 3H), 7.57 (s, 1H), 7.62 (d, *J* = 9.2 Hz, 1H), 7.79 (d, *J* = 8.8 Hz, 1H), 7.93 (d, *J* = 2.0 Hz, 1H), 8.47 (d, *J* = 8.8 Hz, 1H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 21.2, 21.9, 44.8, 52.2, 109.6, 111.1, 113.0, 117.9, 119.7, 121.8, 122.4, 123.5, 124.1, 124.9, 125.2, 128.1, 128.4, 128.6, 128.9, 129.9, 130.0, 130.2, 130.9, 132.2, 132.6, 132.6, 135.6, 135.6, 136.7, 136.9, 137.2, 137.5,141.7, 143.6, 150.1, 178.4 ppm.

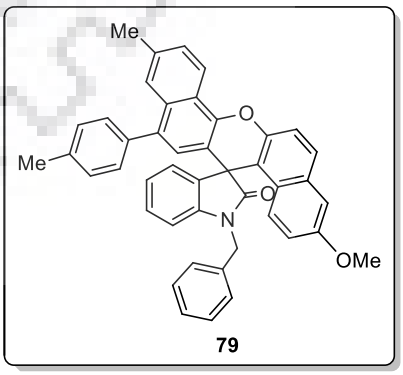
HRMS (ESI): *m/z* calcd for $C_{43}H_{30}BrNO_2Na$ $[M+Na]^+$: 694.1352, found: 694.1444.

1'-Benzyl-3-methoxy-10-methyl-12-(*p*-tolyl)spiro[dibenzo[*a*,*h*]xanthene-14,3'-indolin]-2'-one (79):

Yield: 0.038 g (62%) as off white solid.

MP: 235–238 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.44 (s, 6H), 3.84 (s, 3H), 5.11 (d, *J* = 3.6 Hz, 2H), 6.58 (s, 1H), 6.64 (dd, *J* = 2.8, 9.2 Hz, 1H), 6.85–6.91 (m, 2H), 6.95–6.97 (m, 1H), 7.05 (d, *J* = 8.0 Hz, 1H), 7.12–7.14 (m, 3H), 7.21–7.25 (m, 4H), 7.28–7.31 (m, 2H), 7.45 (dd, *J* = 1.6, 8.4 Hz, 1H), 7.49–7.51 (m, 2H), 7.56–7.59 (m, 2H), 7.78 (d, *J* = 8.8 Hz, 1H), 8.48 (d, *J* = 8.4 Hz, 1H) ppm.



^{13}C NMR (100 MHz, $CDCl_3$): δ 21.2, 21.9, 44.8, 52.3, 55.2, 96.1, 107.9, 109.5, 110.9, 113.0, 118.8, 118.9, 121.9, 122.5, 123.7, 123.9, 124.6, 124.9, 125.2, 126.5, 127.9, 128.2, 128.6, 128.6, 128.9, 129.6, 130.0, 132.2, 132.6, 135.2, 135.7, 136.6, 136.7, 137.4, 137.9, 141.7, 143.9, 148.5, 156.1, 178.7 ppm.

HRMS (ESI): *m/z* calcd for $C_{44}H_{33}NO_3Na$ $[M+Na]^+$: 646.2353, found: 646.2938.

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NMR Spectra for Selected Compounds

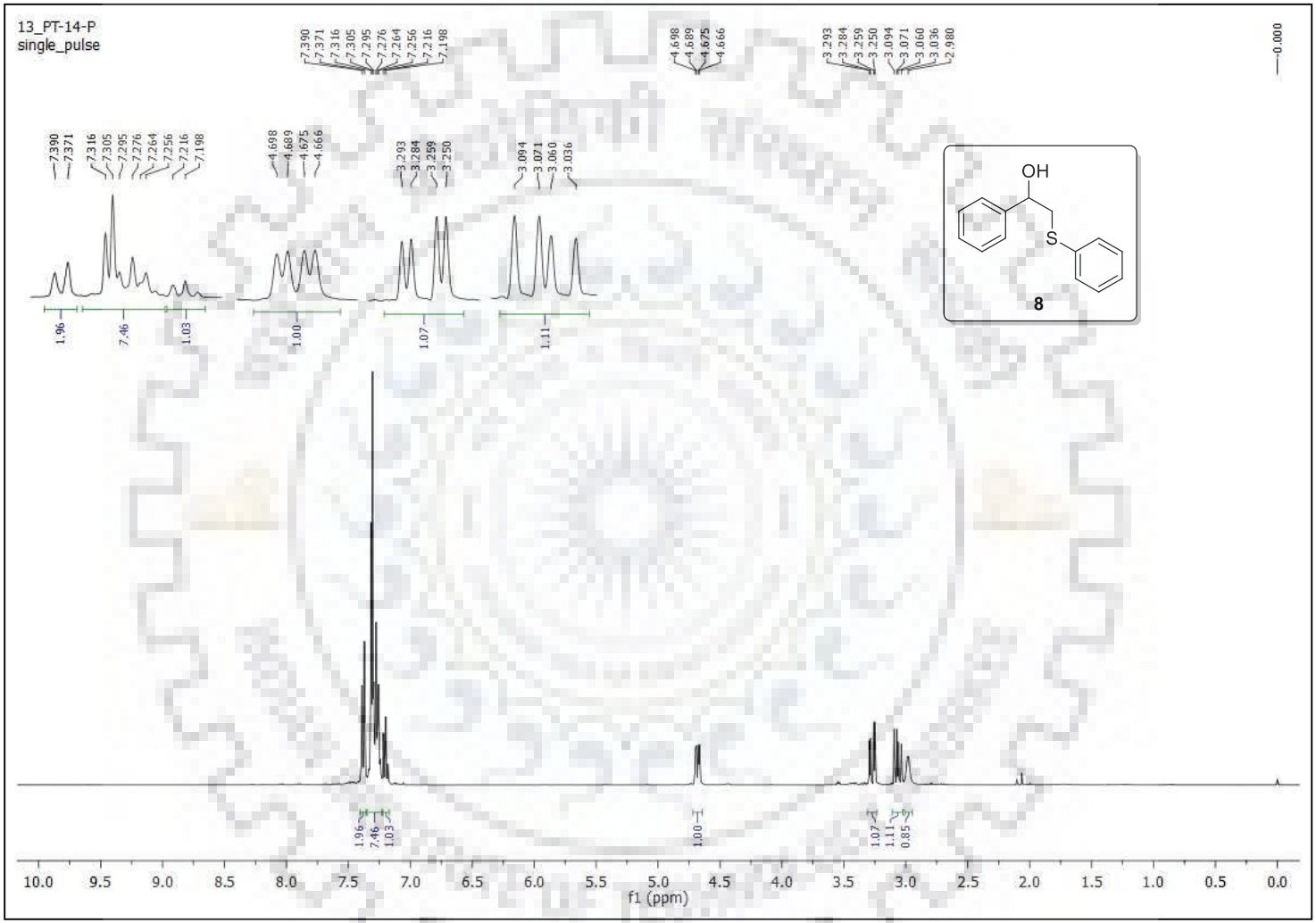


Figure S-1: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **8**.

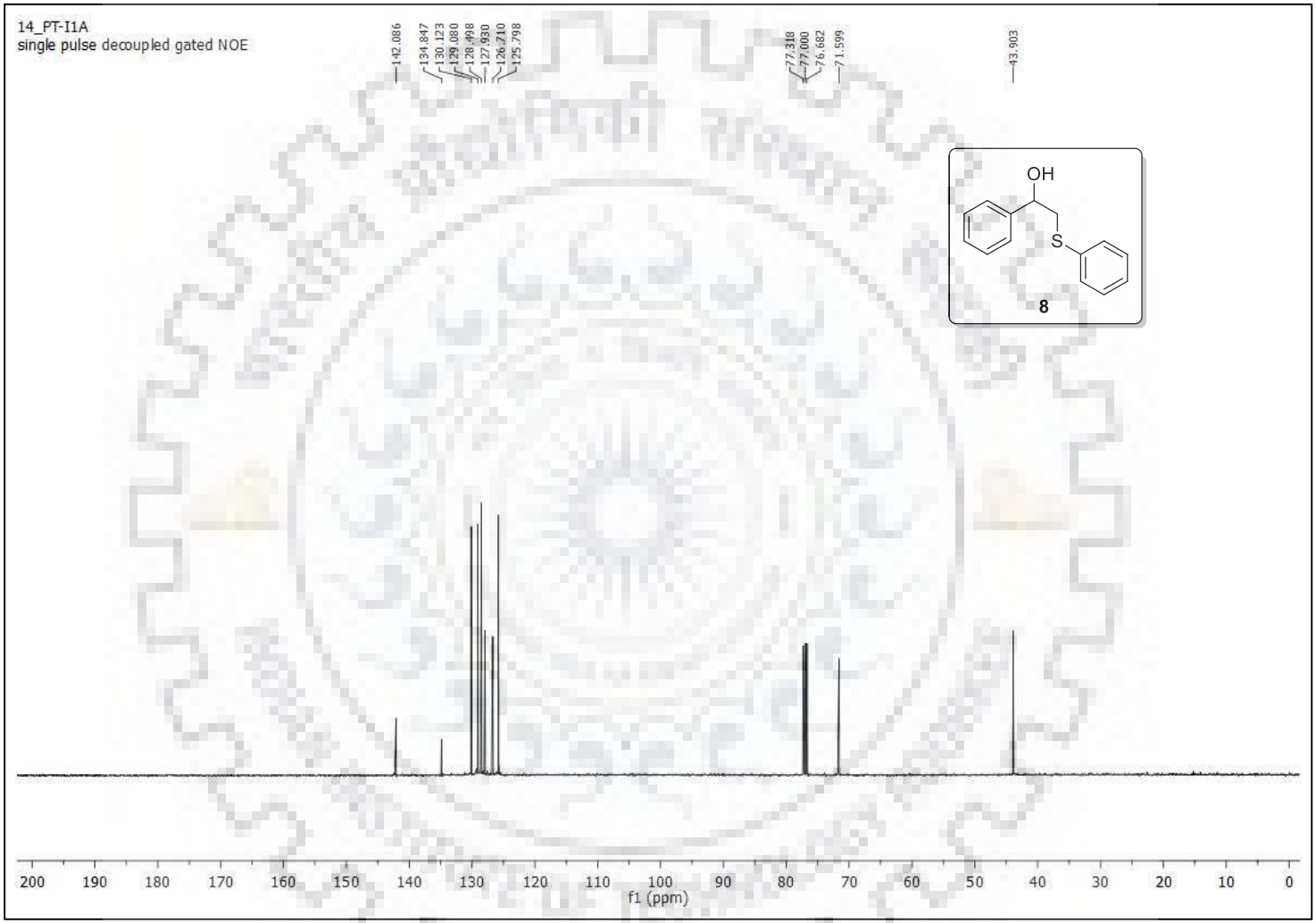


Figure S-2: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **8**.

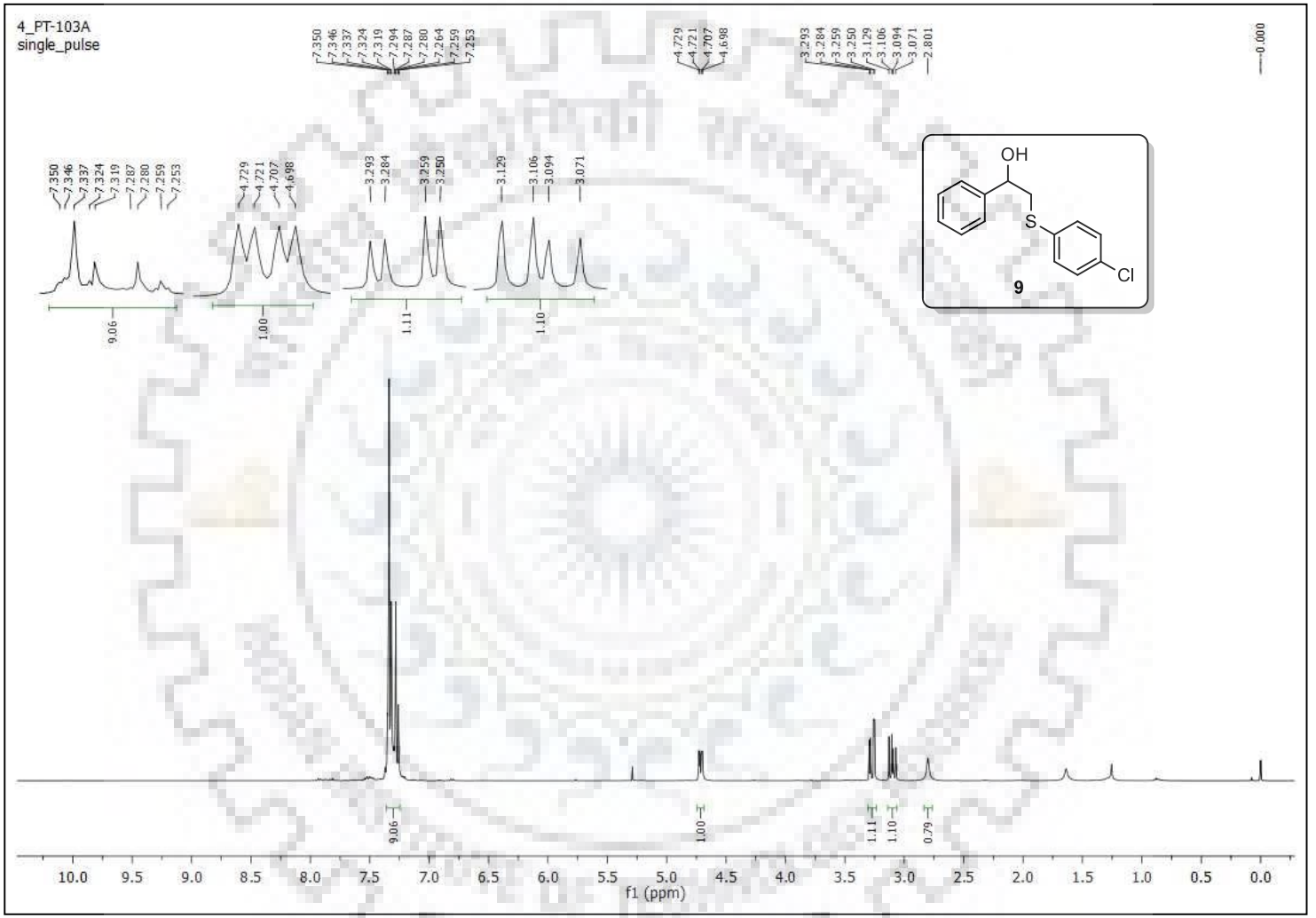


Figure S-3: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **9**.

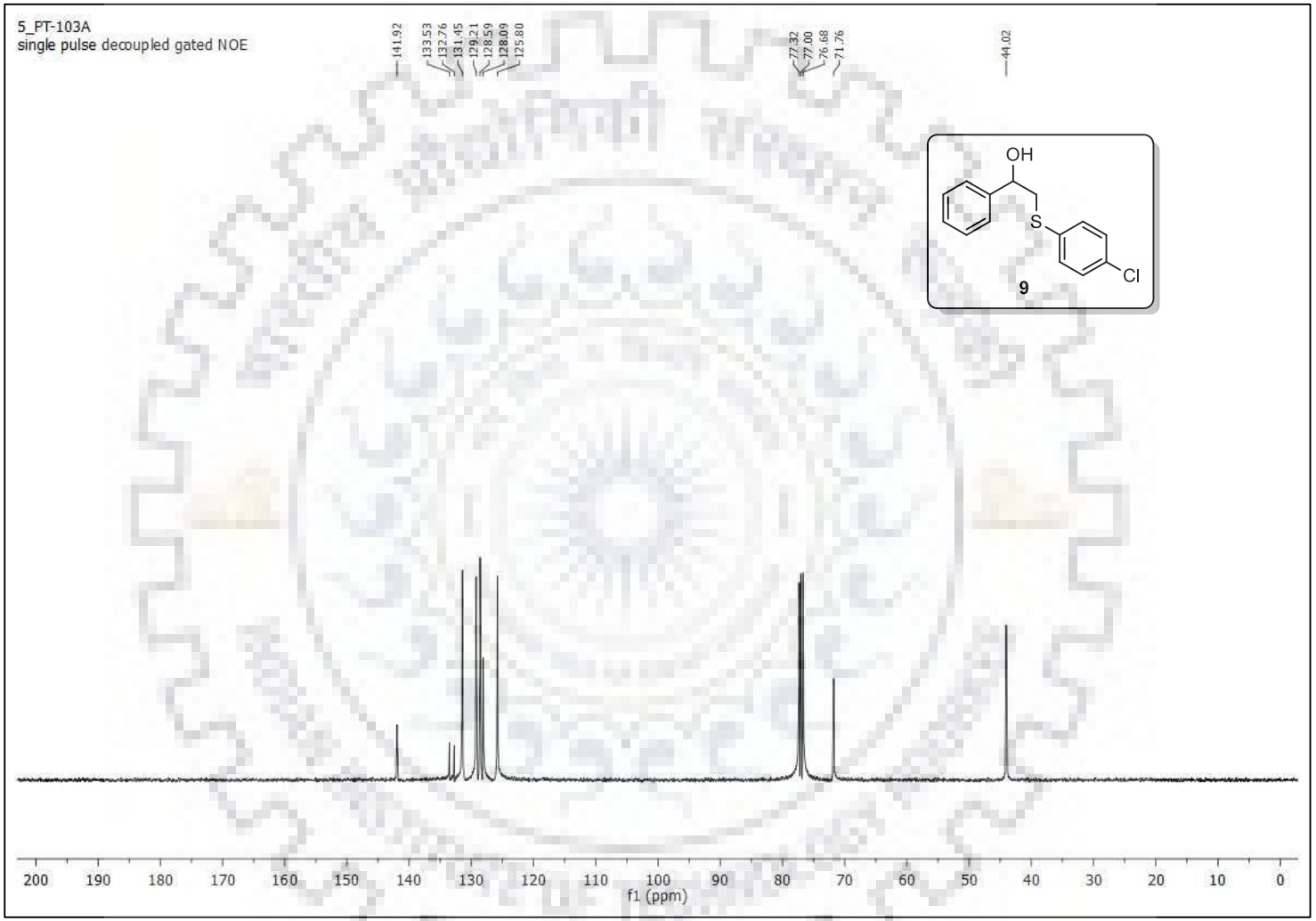


Figure S-4: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **9**.

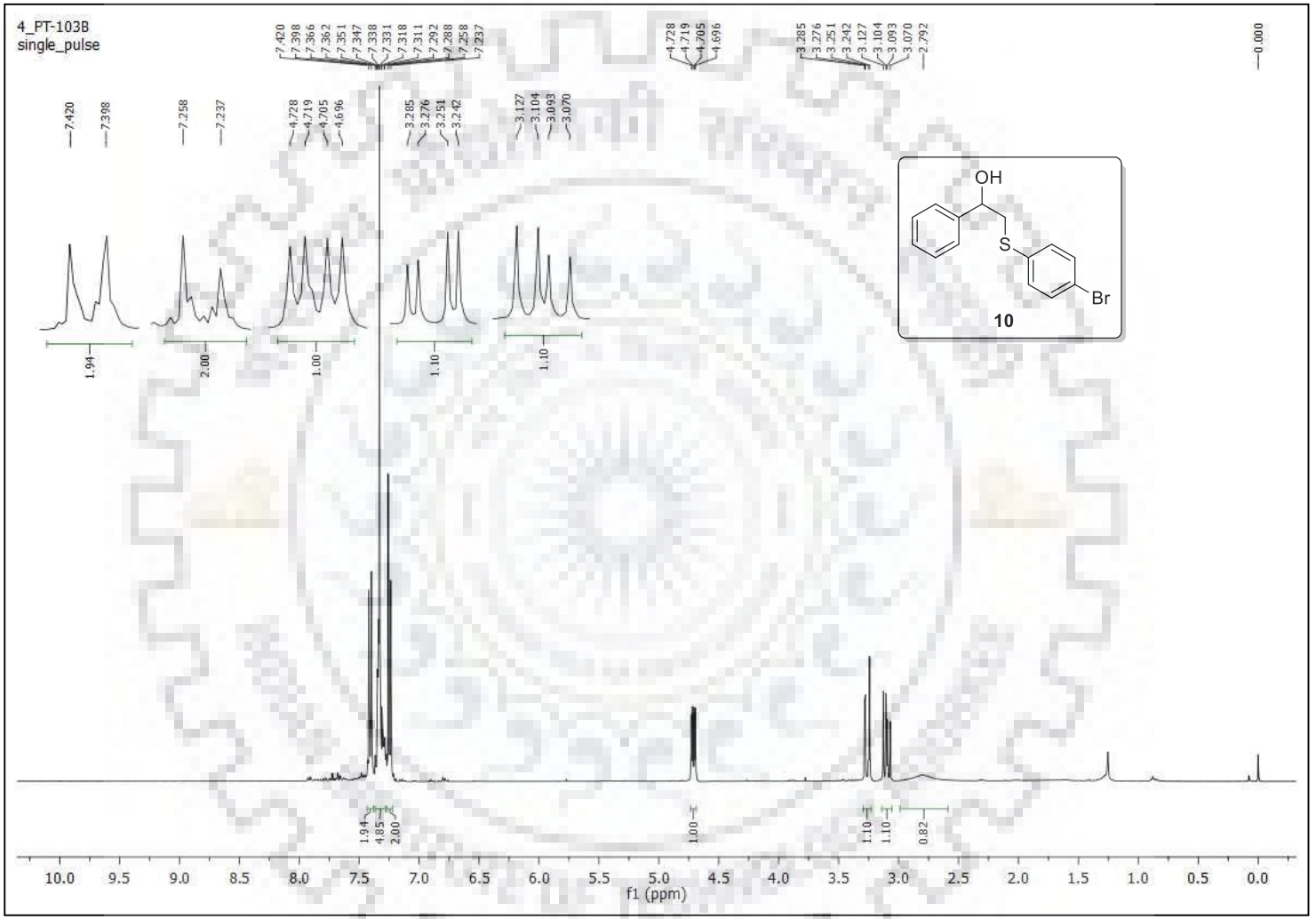


Figure S-5: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **10**.

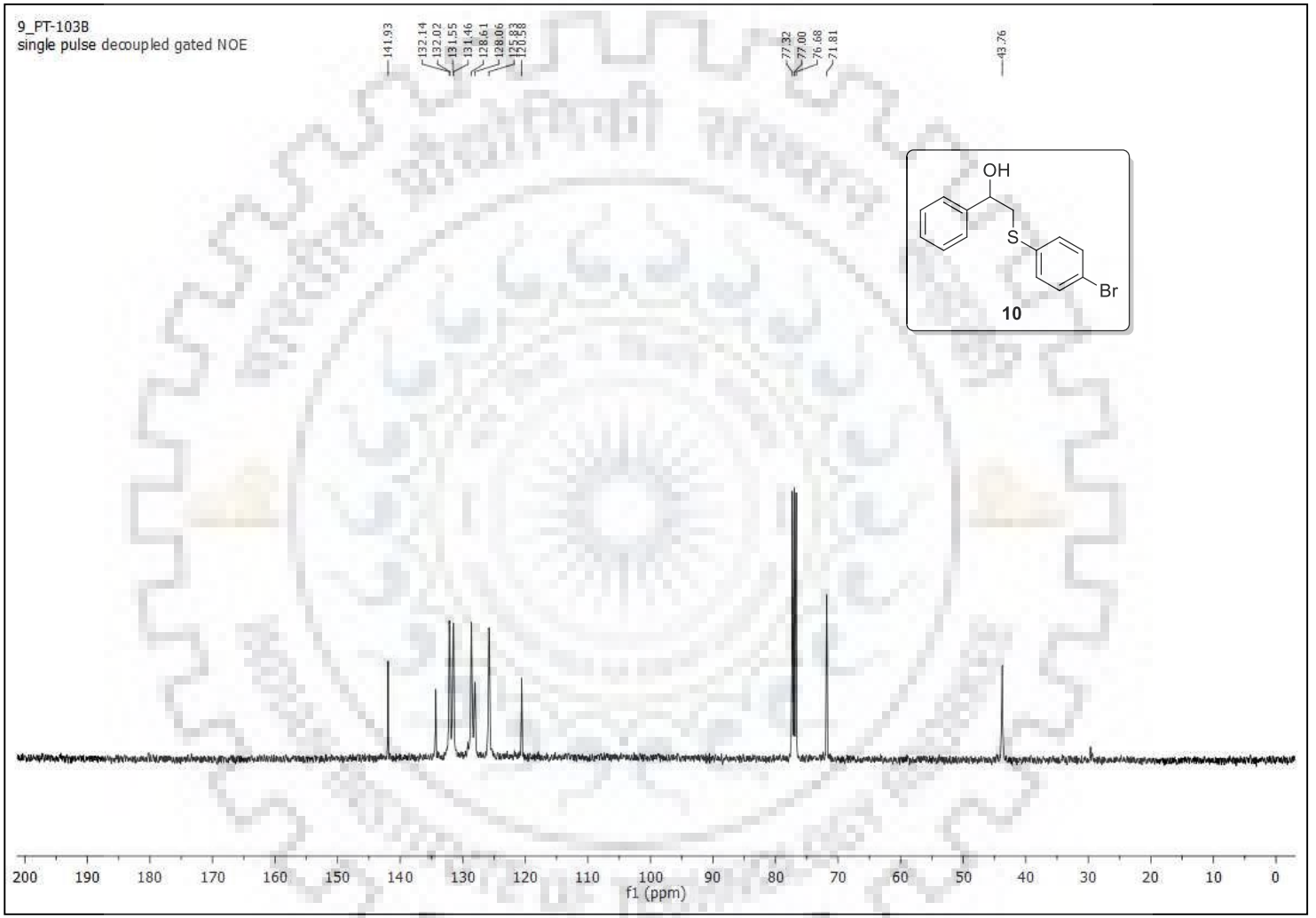


Figure S-6: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **10**.

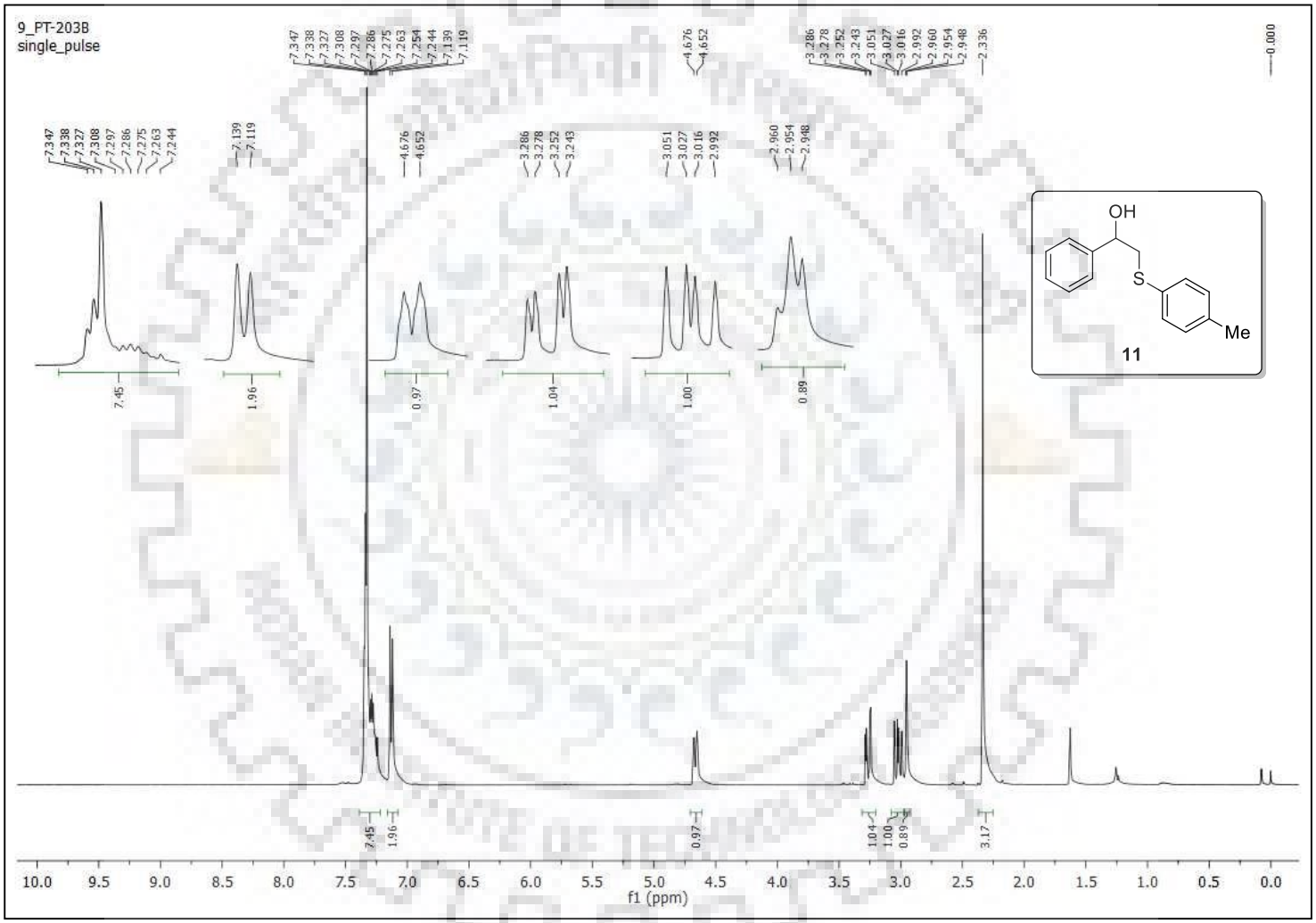


Figure S-7: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **11**.

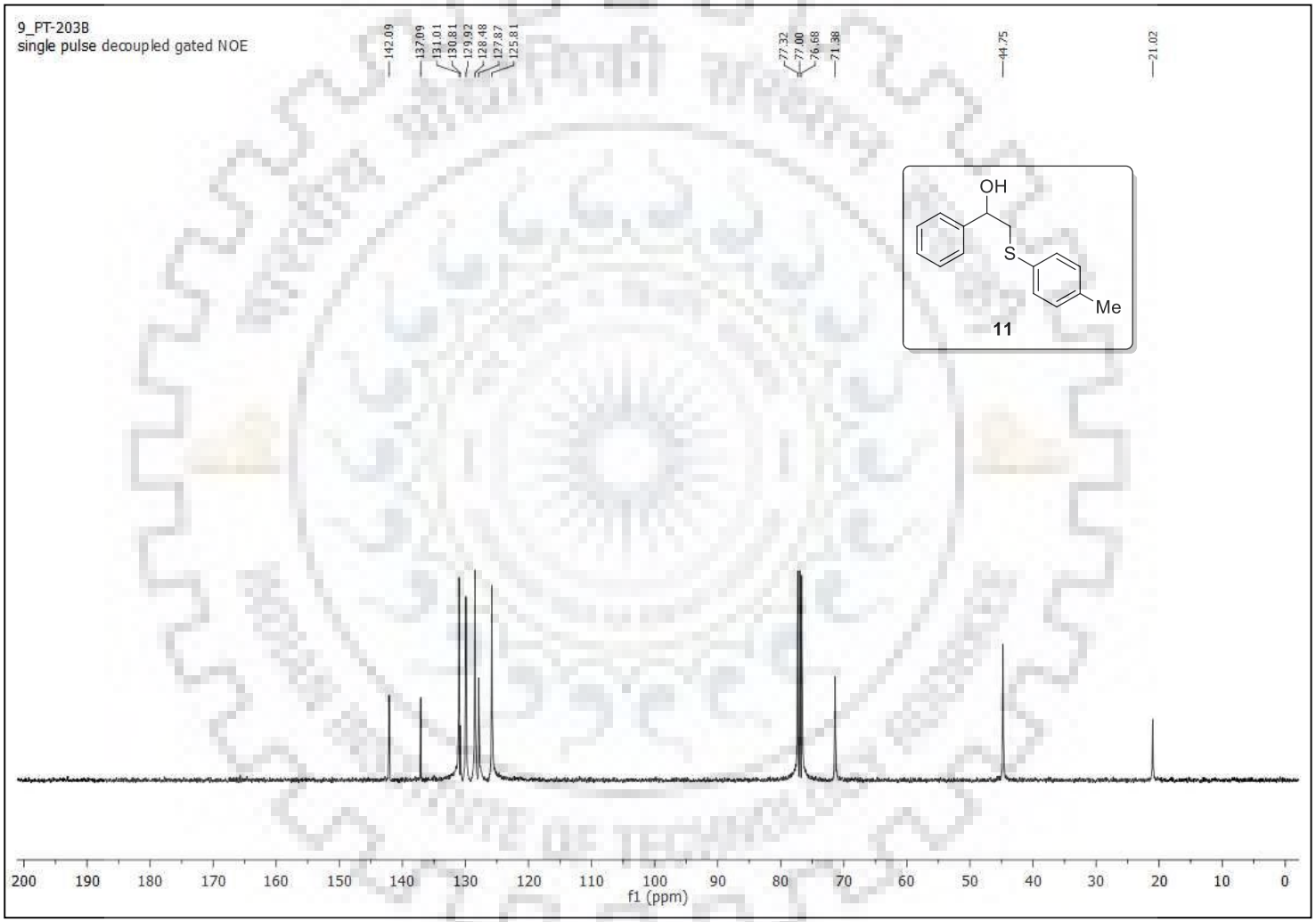


Figure S-8: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **11**.

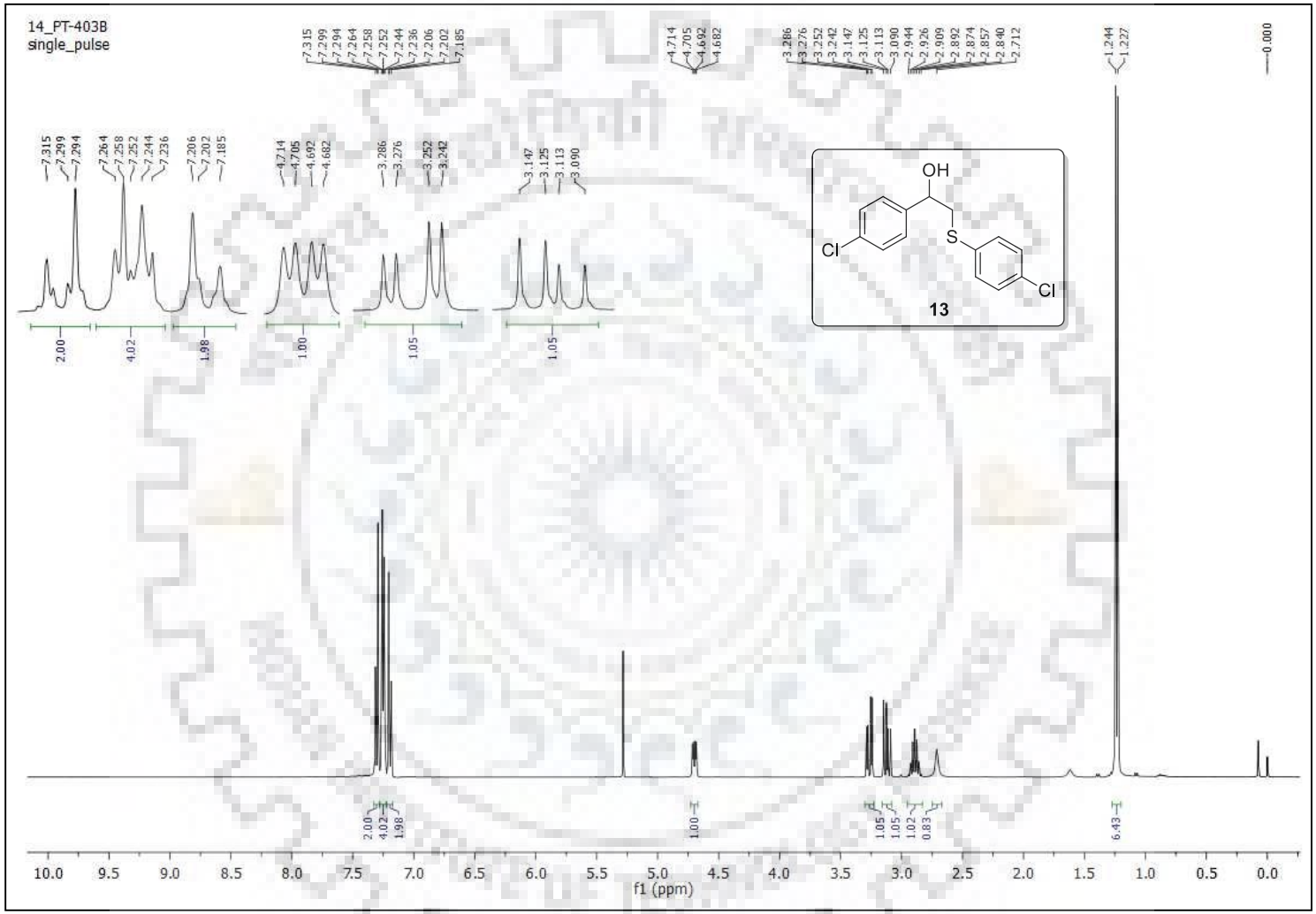


Figure S-9: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **13**.

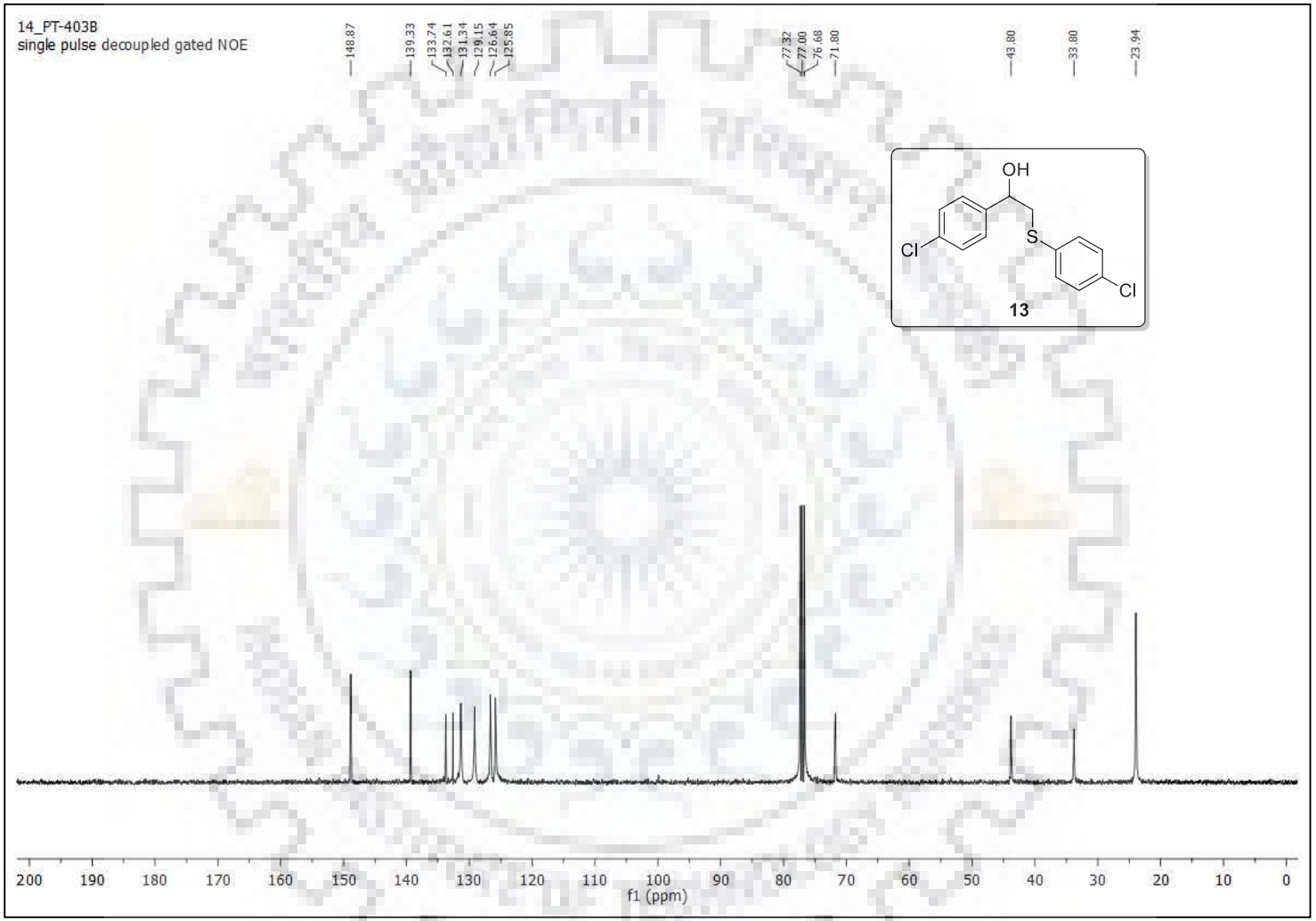


Figure S-10: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **13**.

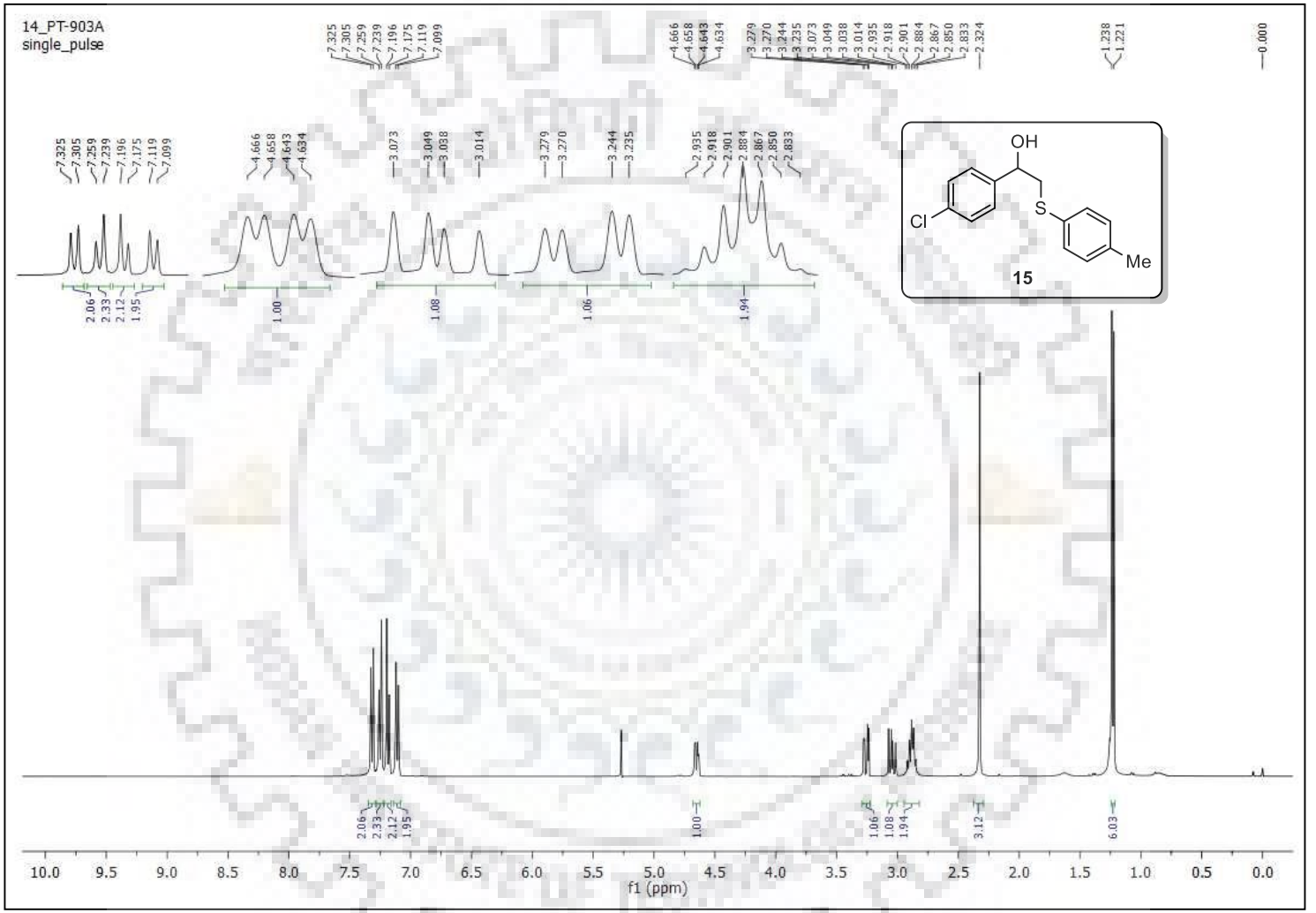


Figure S-11: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **15**.

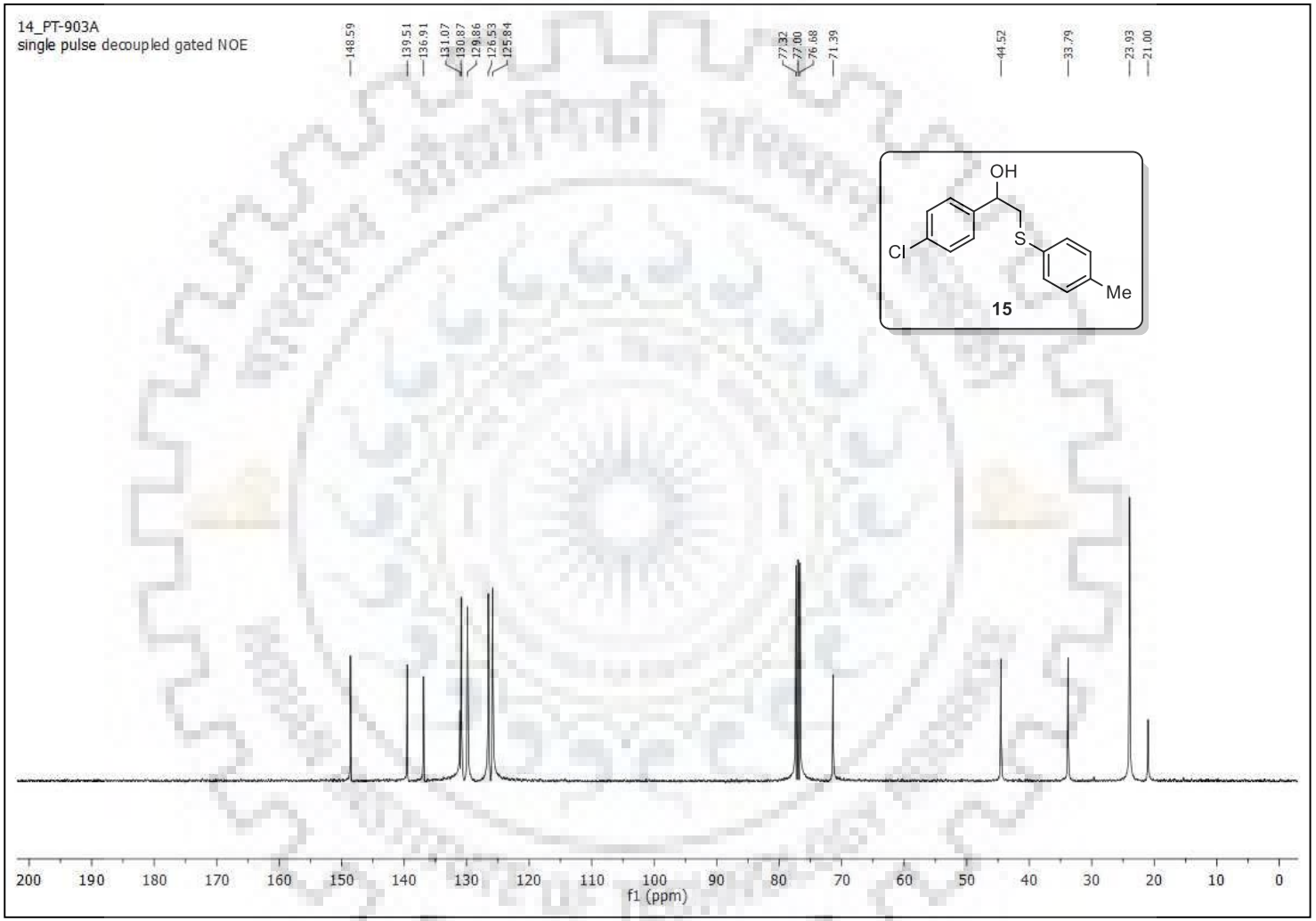


Figure S-12: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **15**.

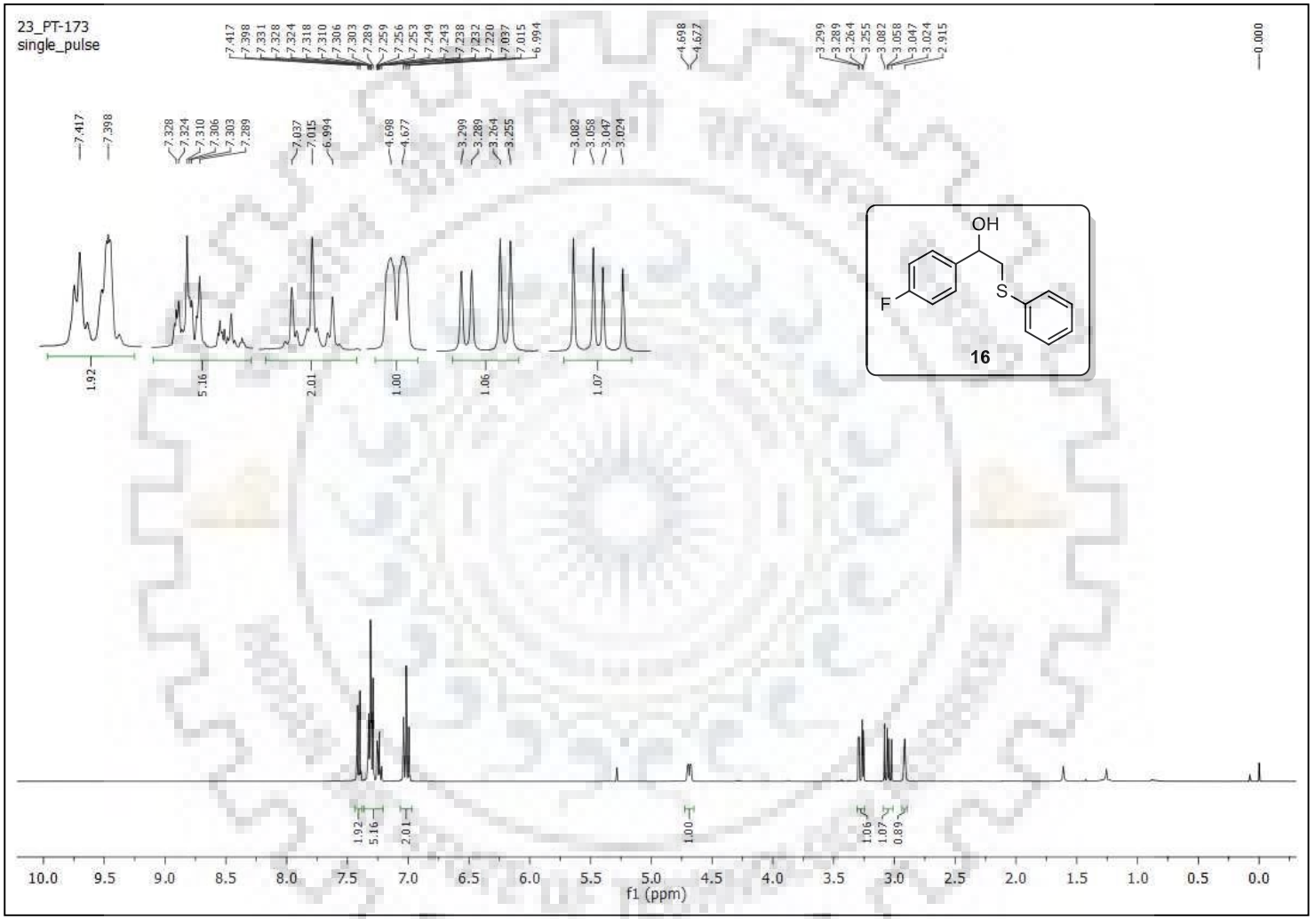


Figure S-13: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **16**.

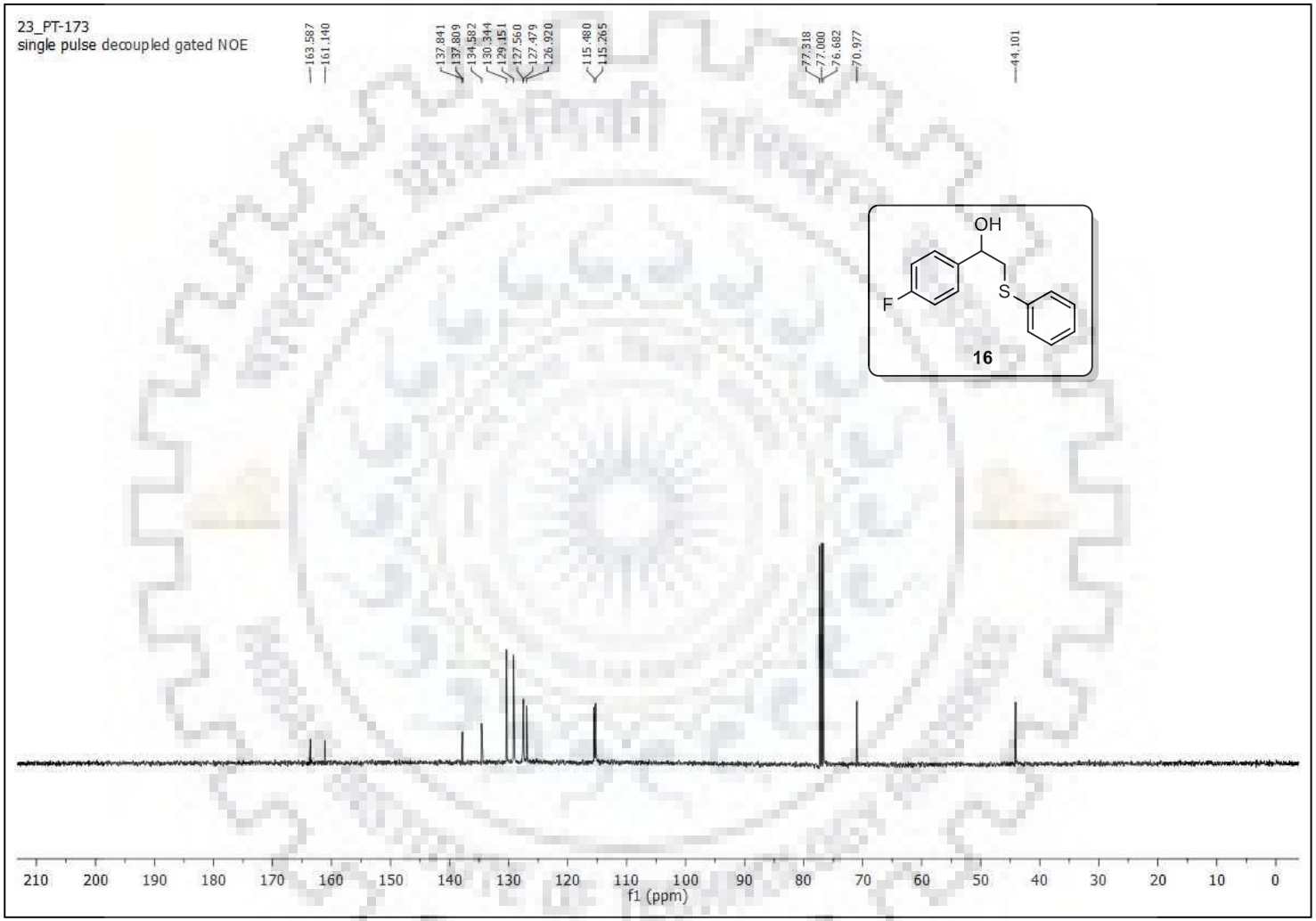


Figure S-14: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **16**.

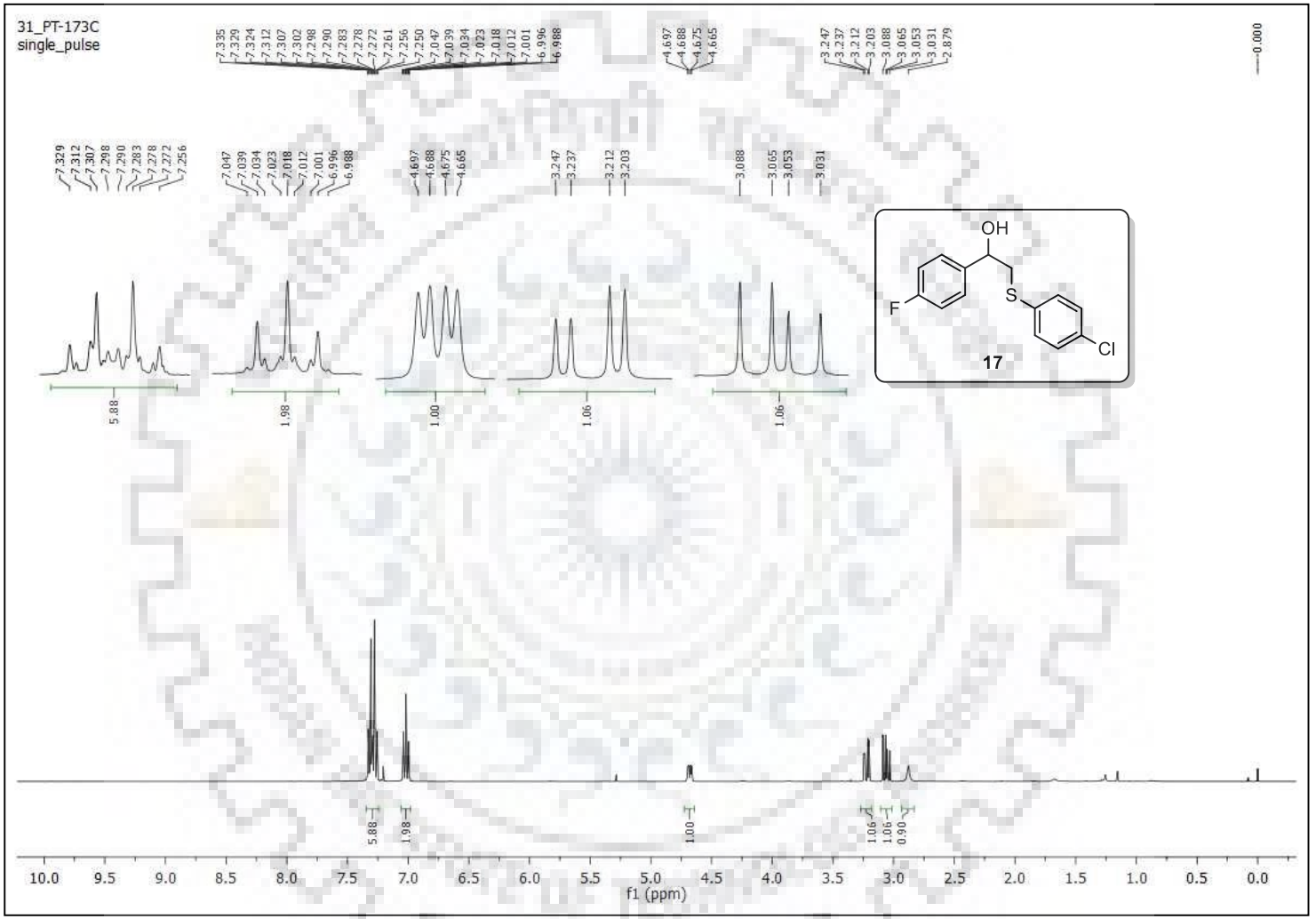


Figure S-15: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **17**.

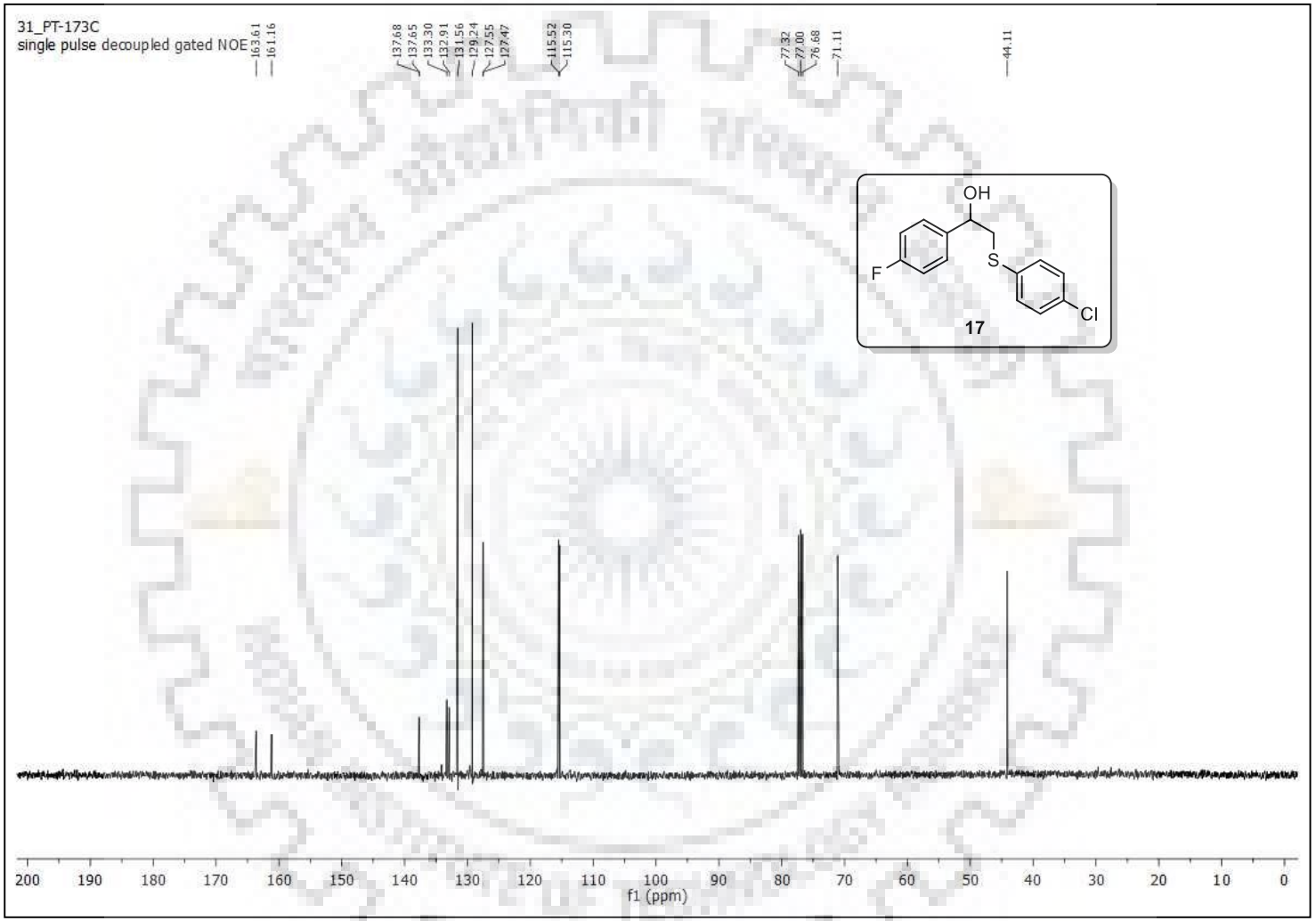


Figure S-16: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **17**.

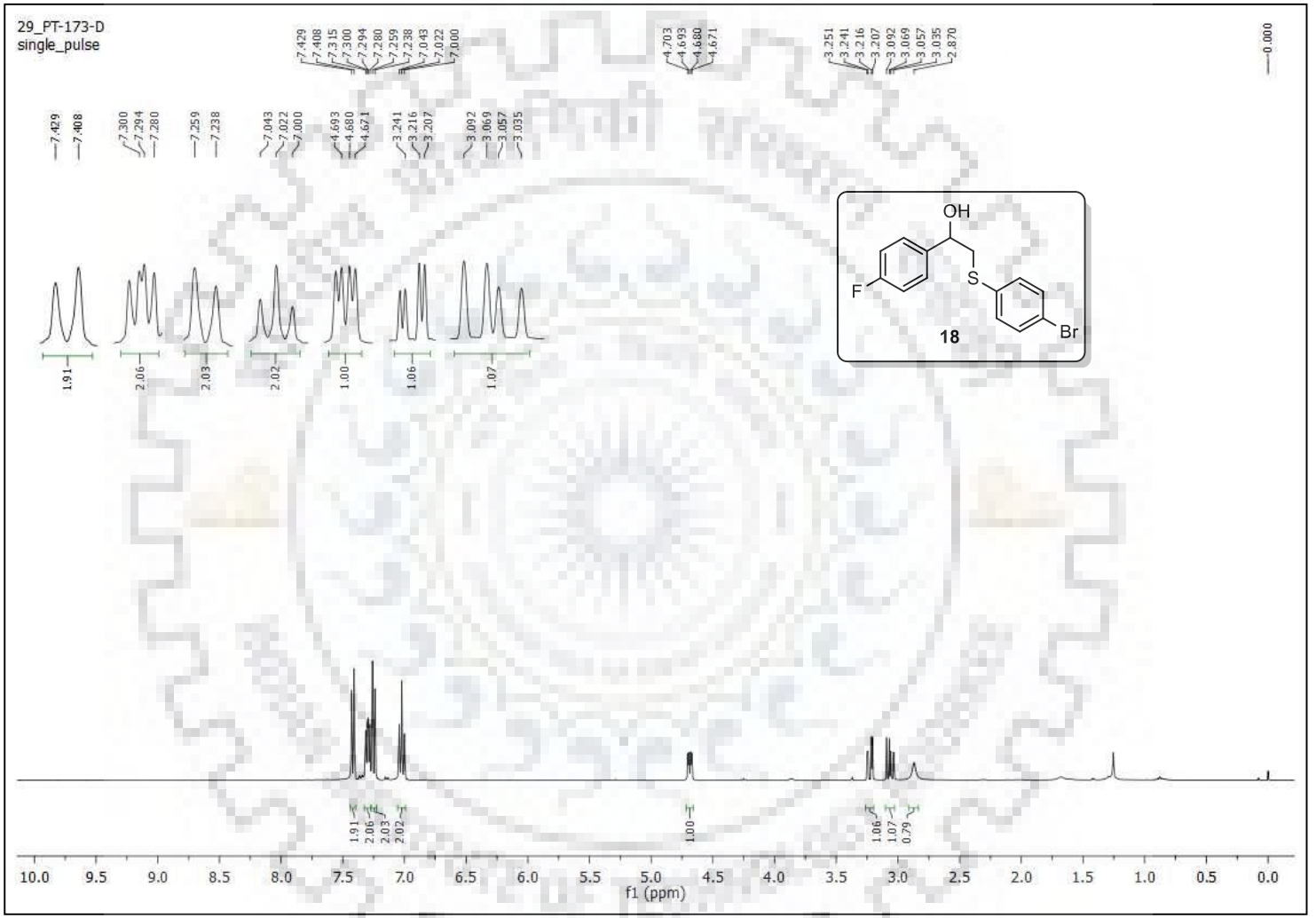


Figure S-17: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **18**.

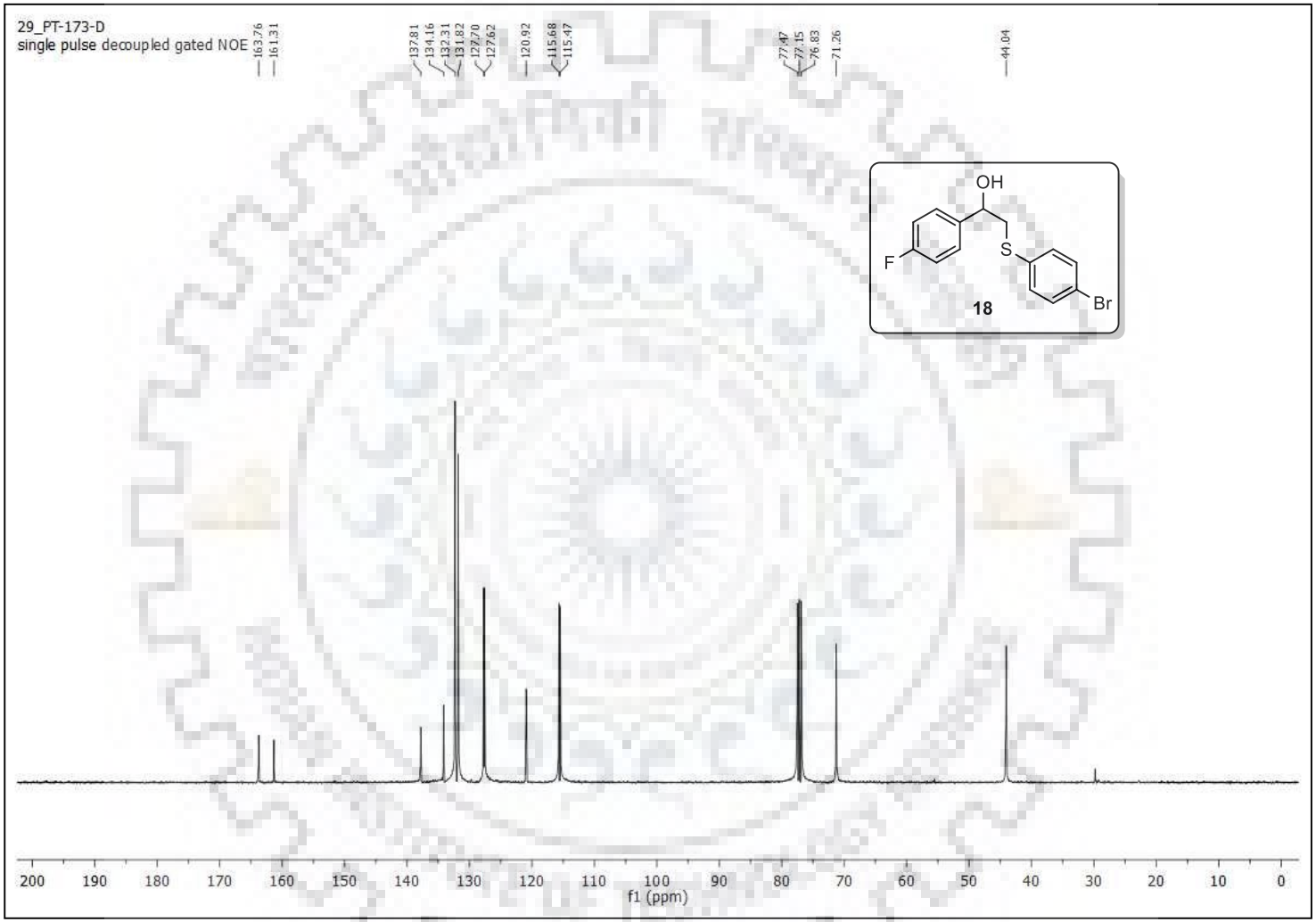


Figure S-18: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **18**.

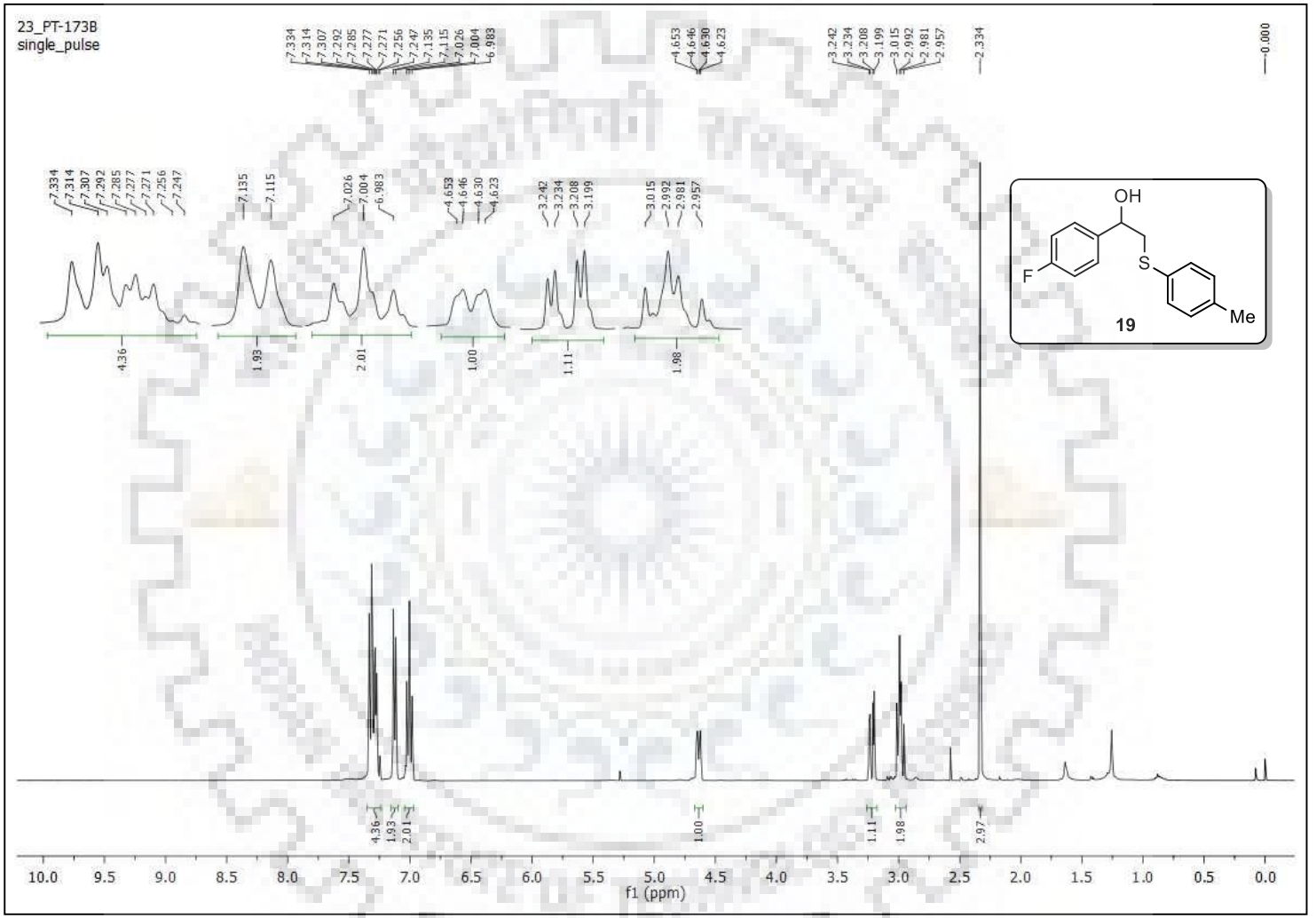


Figure S-19: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **19**.

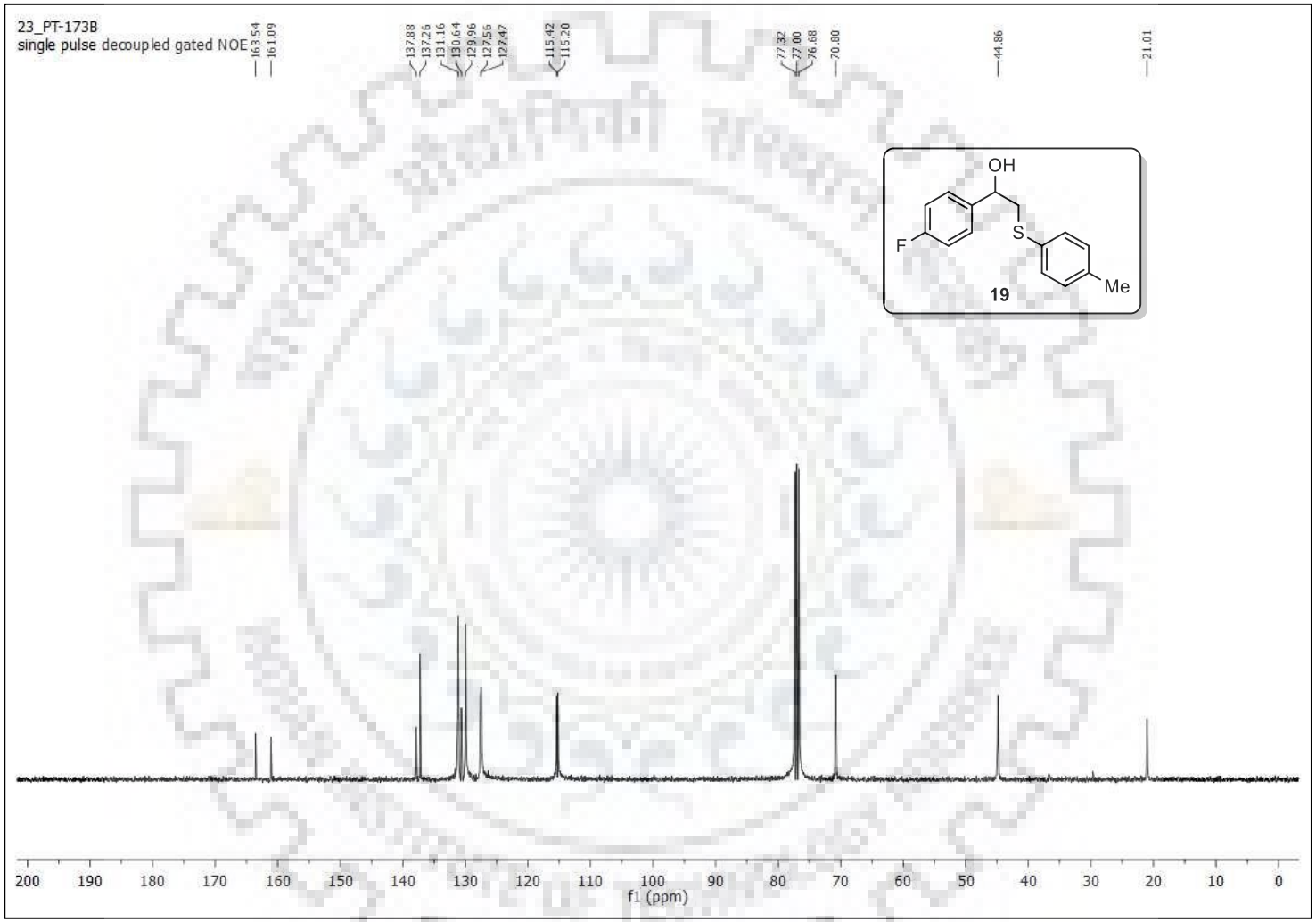


Figure S-20: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **19**.

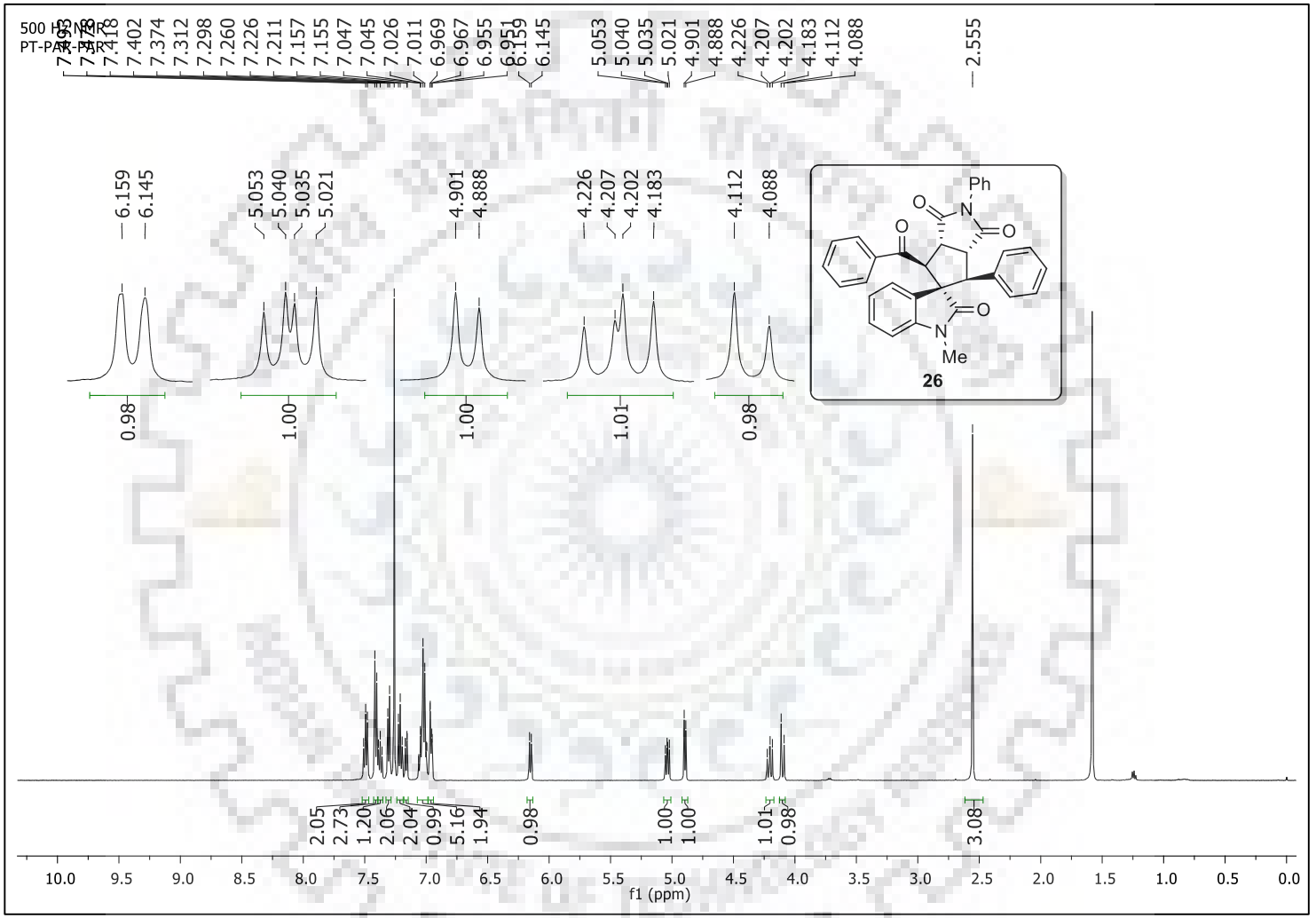


Figure S-21: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **26**.

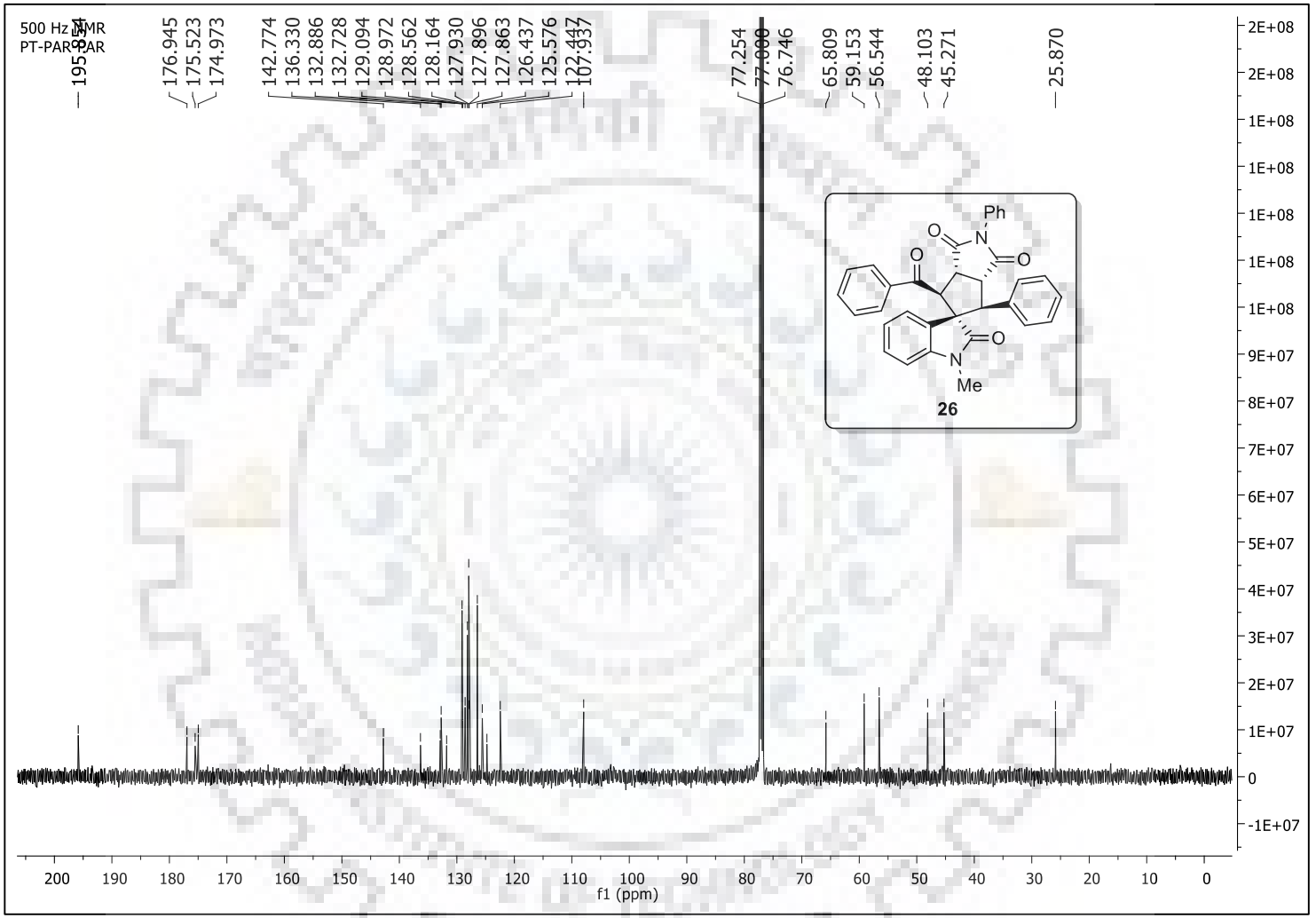


Figure S-22: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **26**.

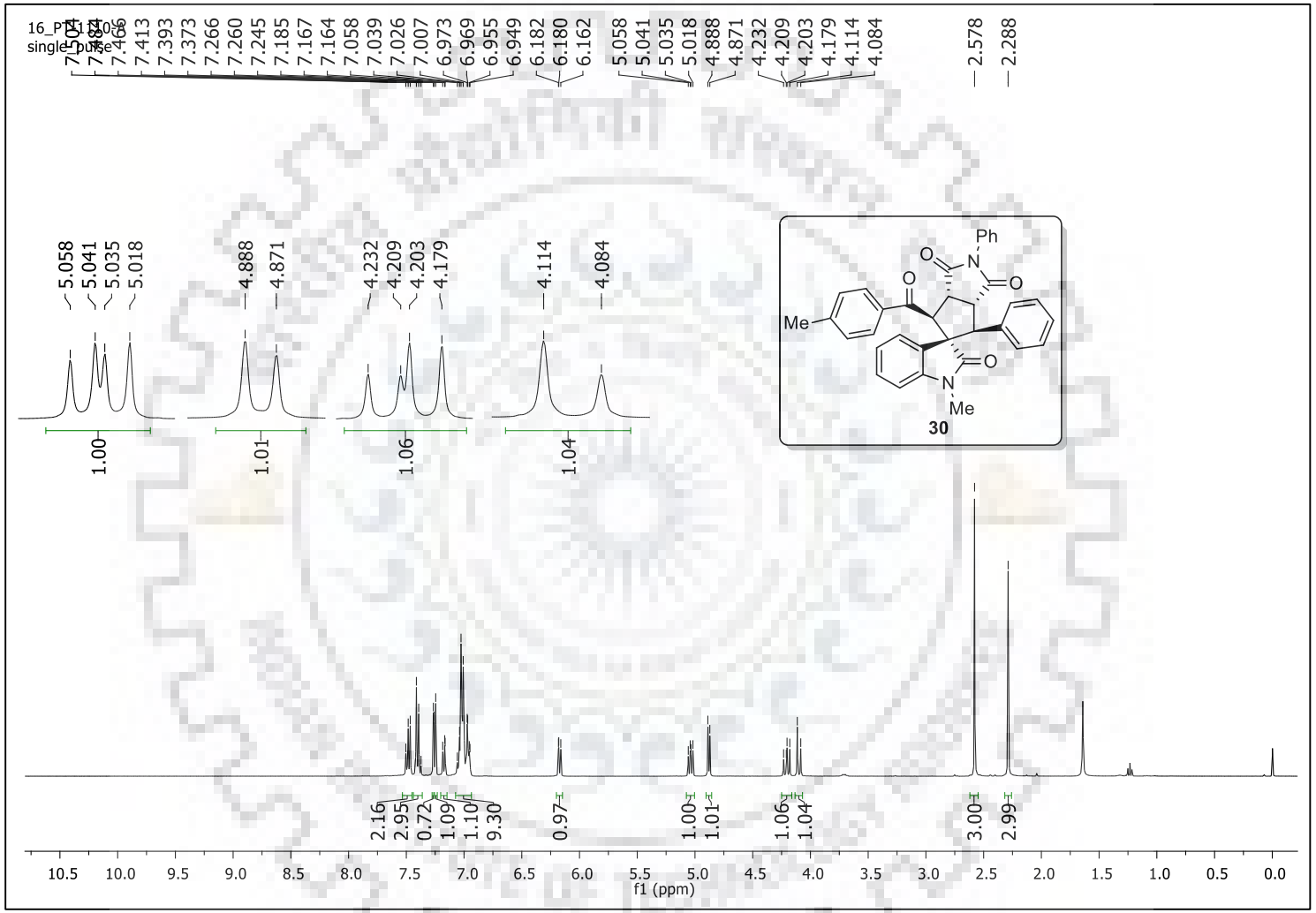


Figure S-23: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **30**.

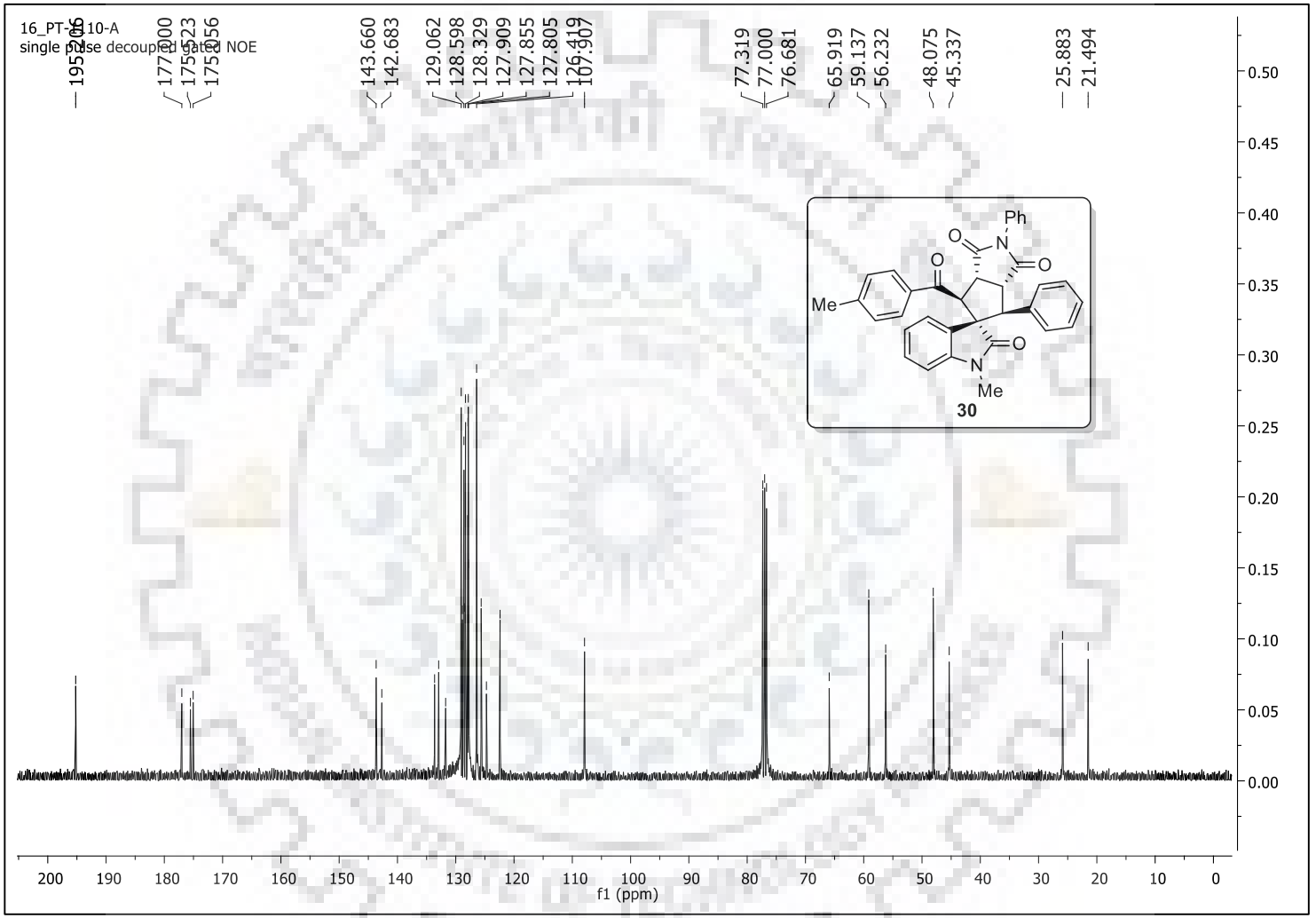


Figure S-24: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **30**.

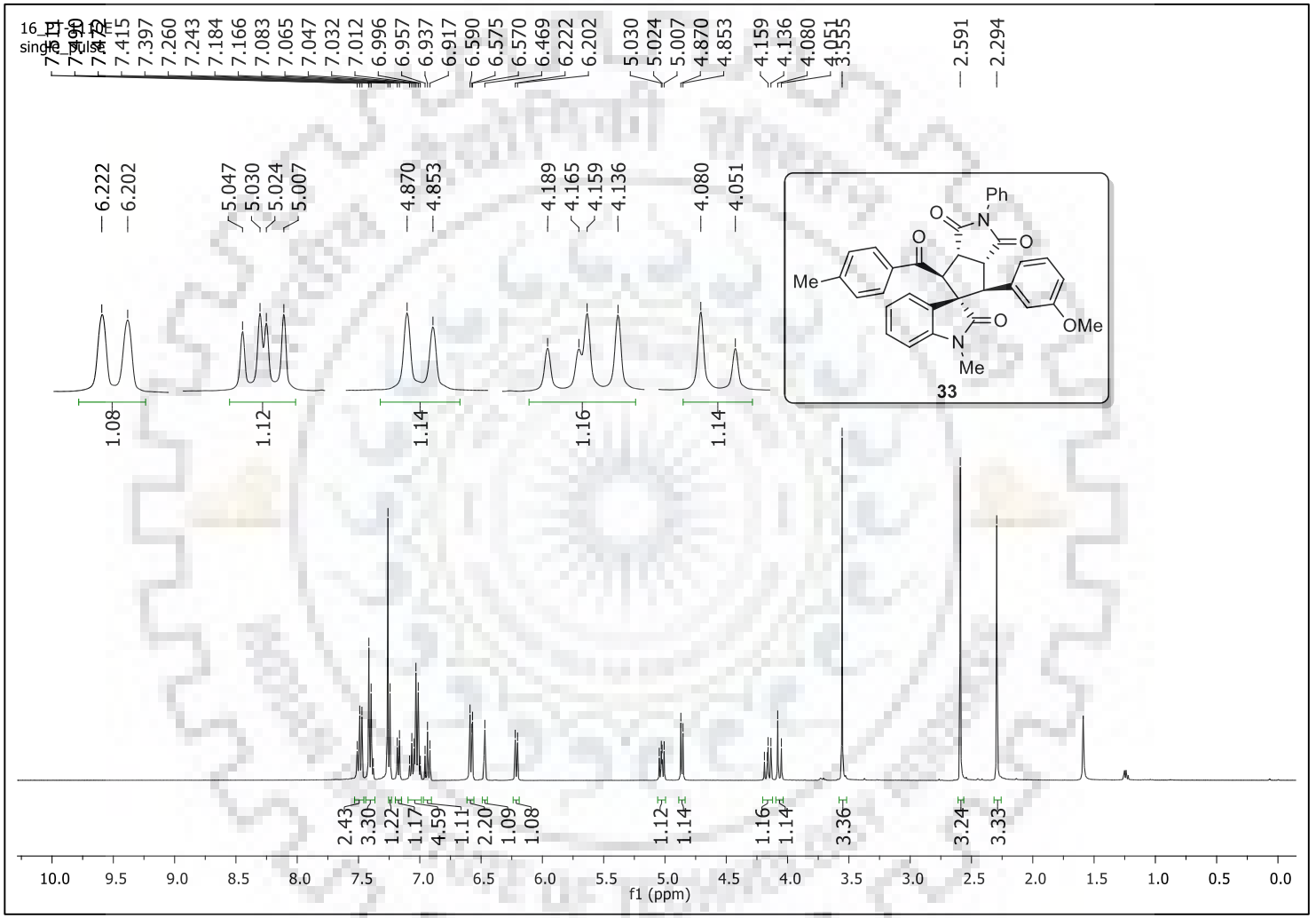


Figure S-25: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **33**.

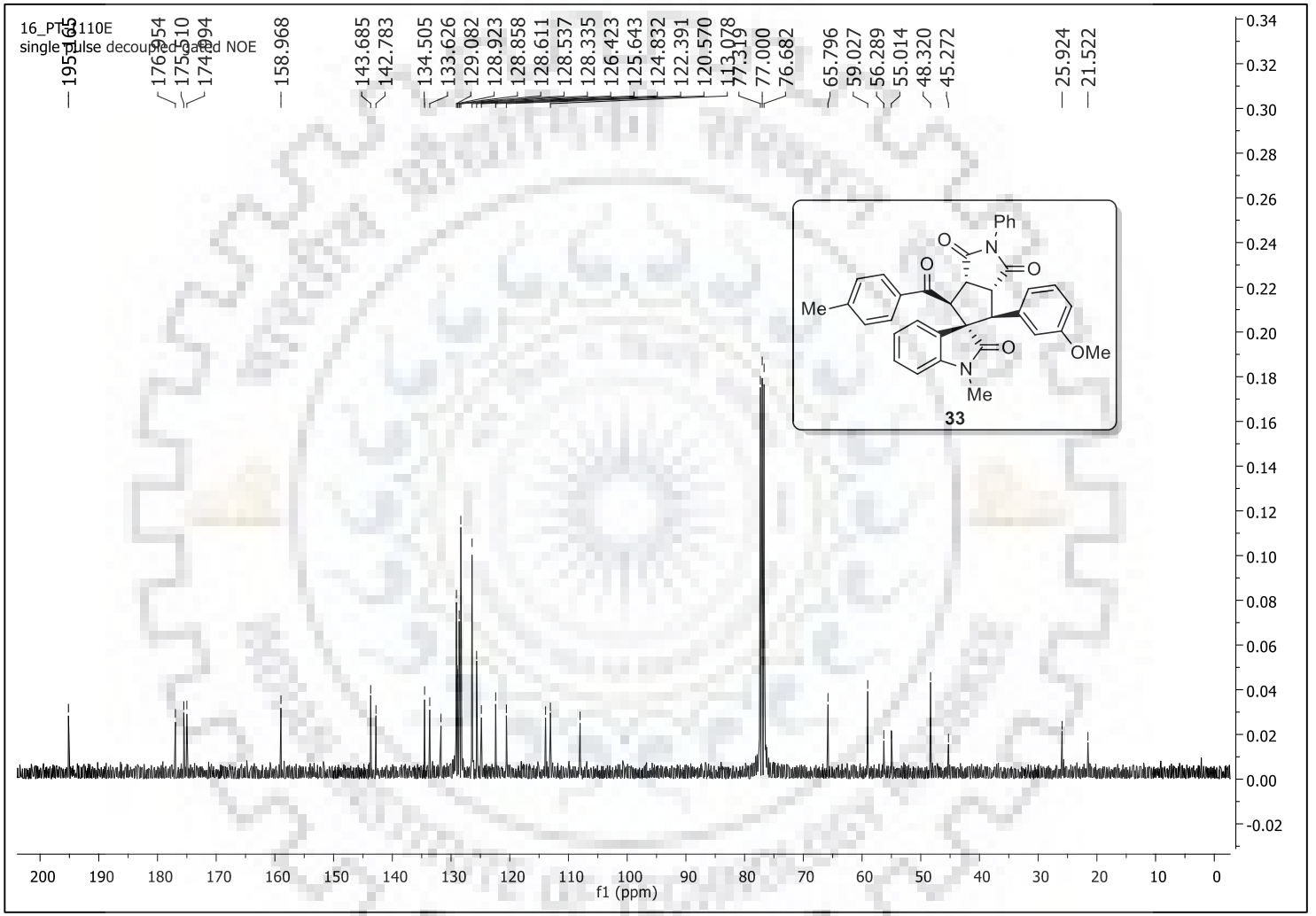


Figure S-26: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **33**.

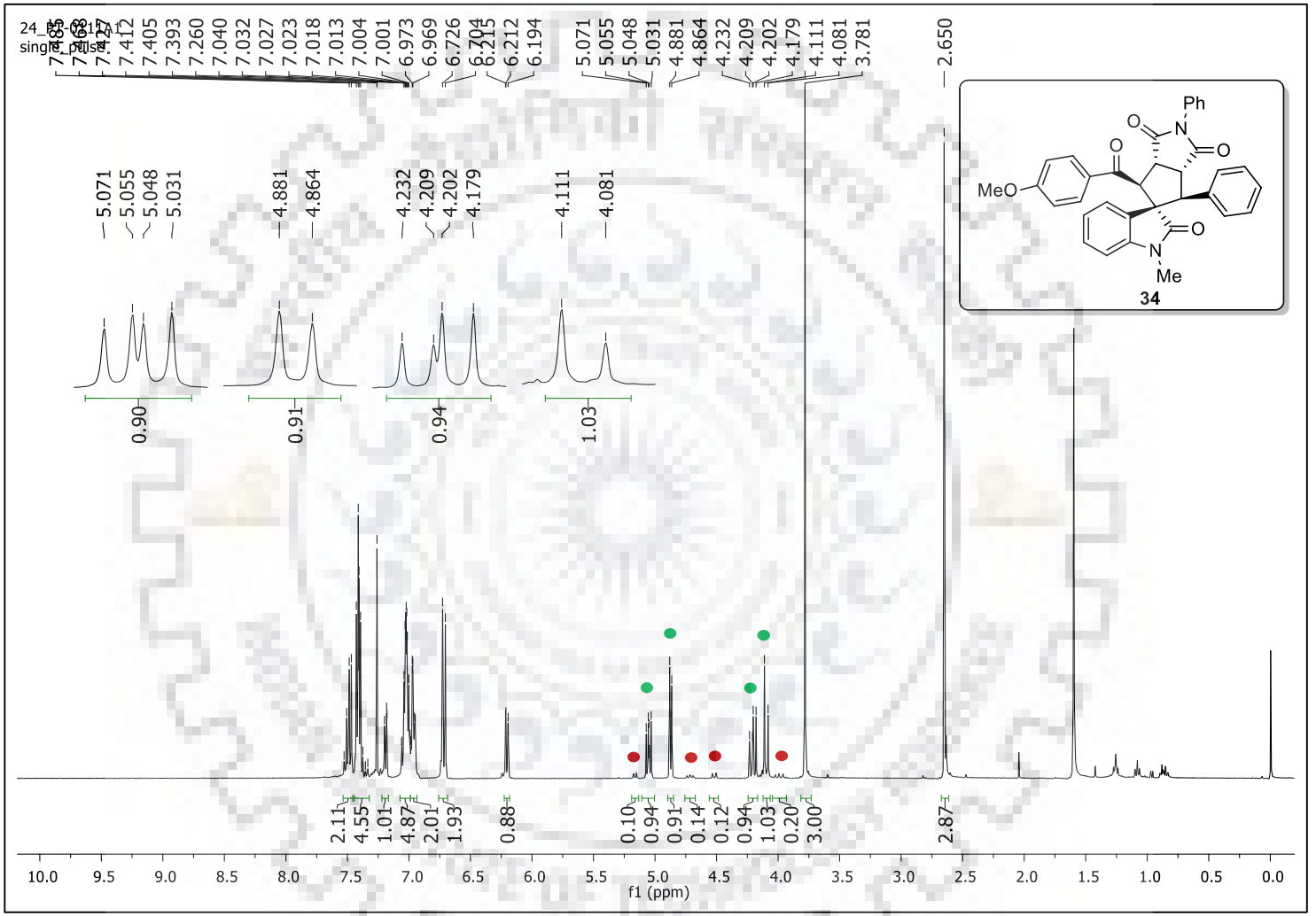


Figure S-27: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **34**.

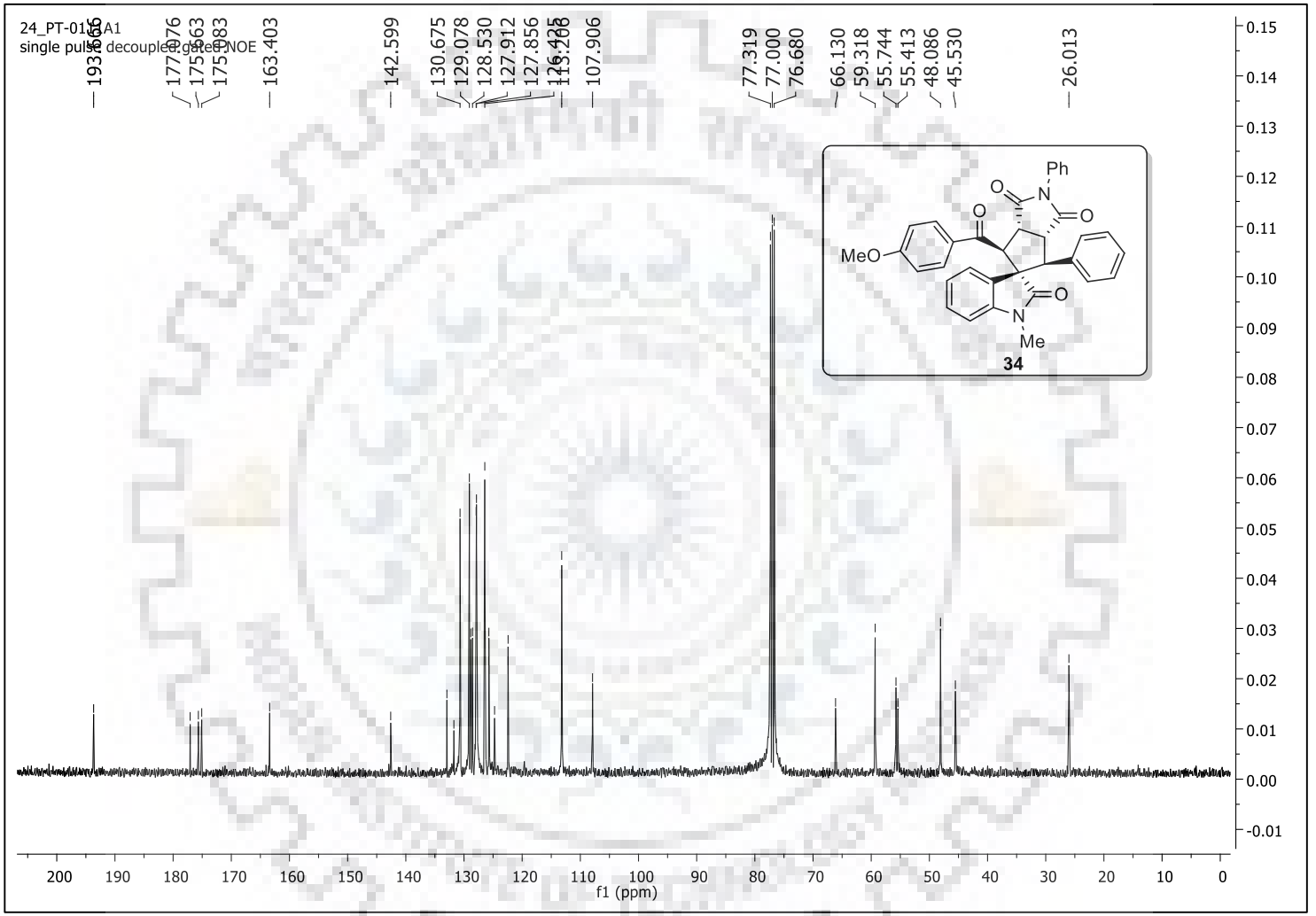


Figure S-28: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **34**.

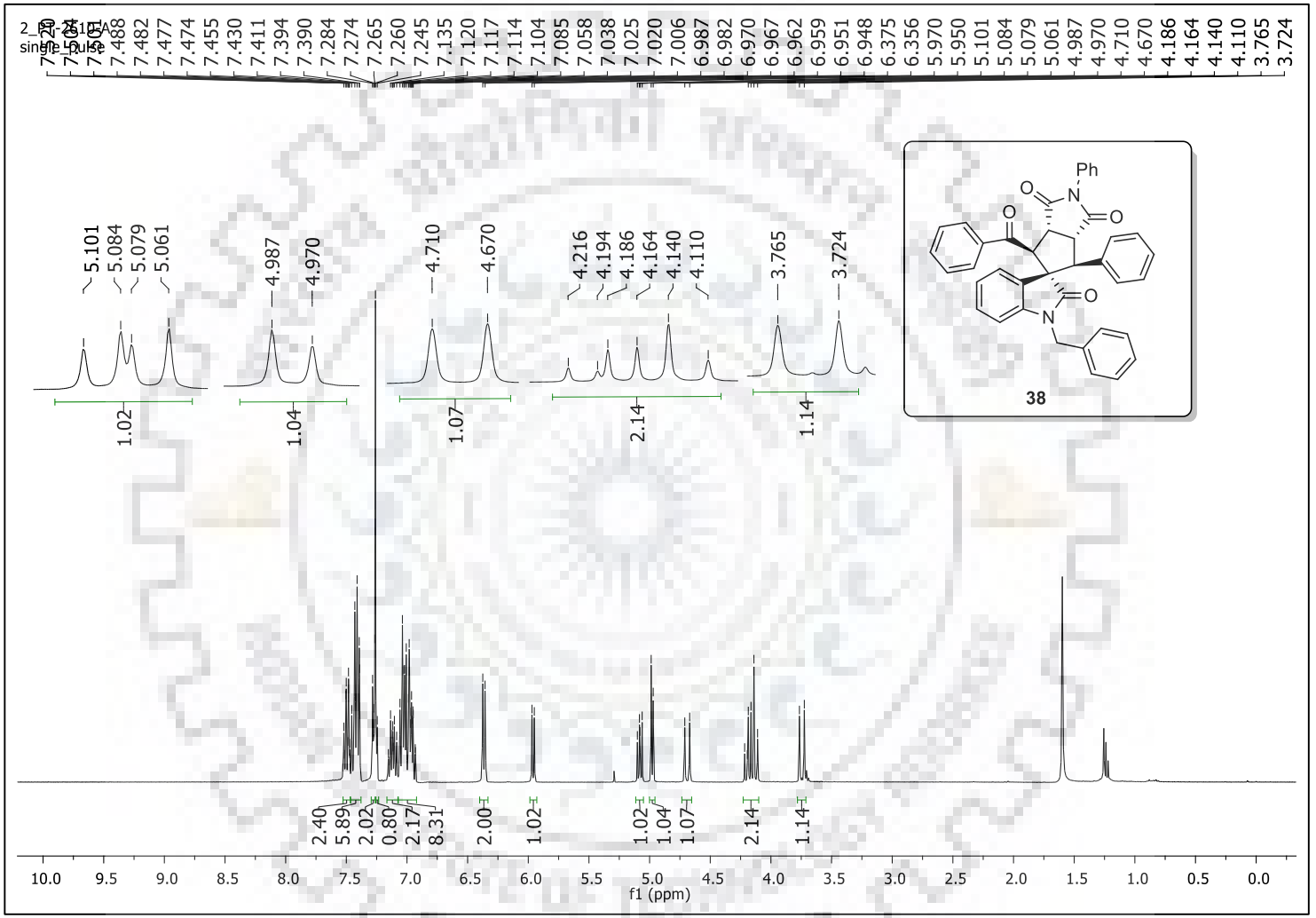


Figure S-29: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **38**.

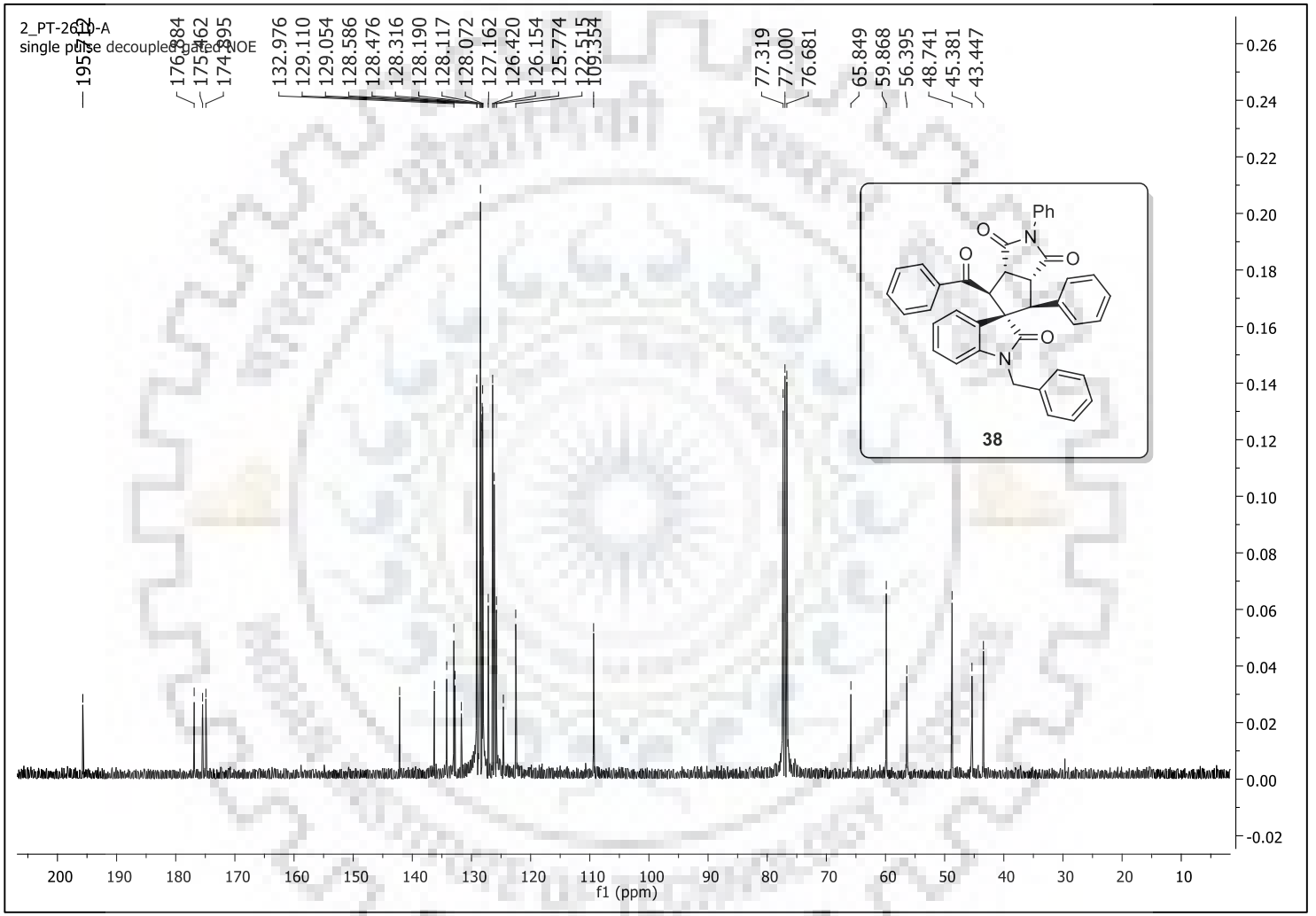


Figure S-30: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **38**.

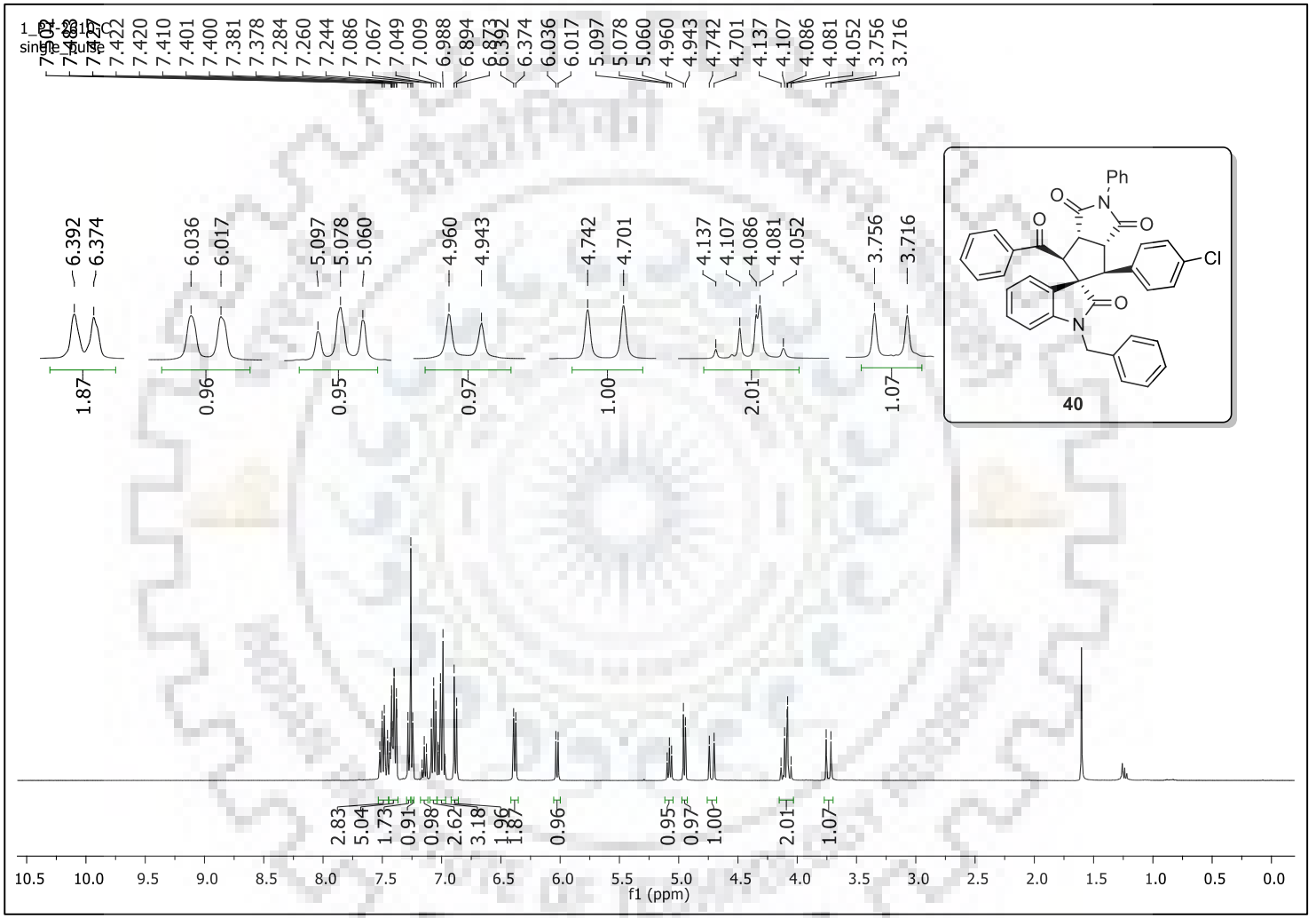


Figure S-31: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **40**.

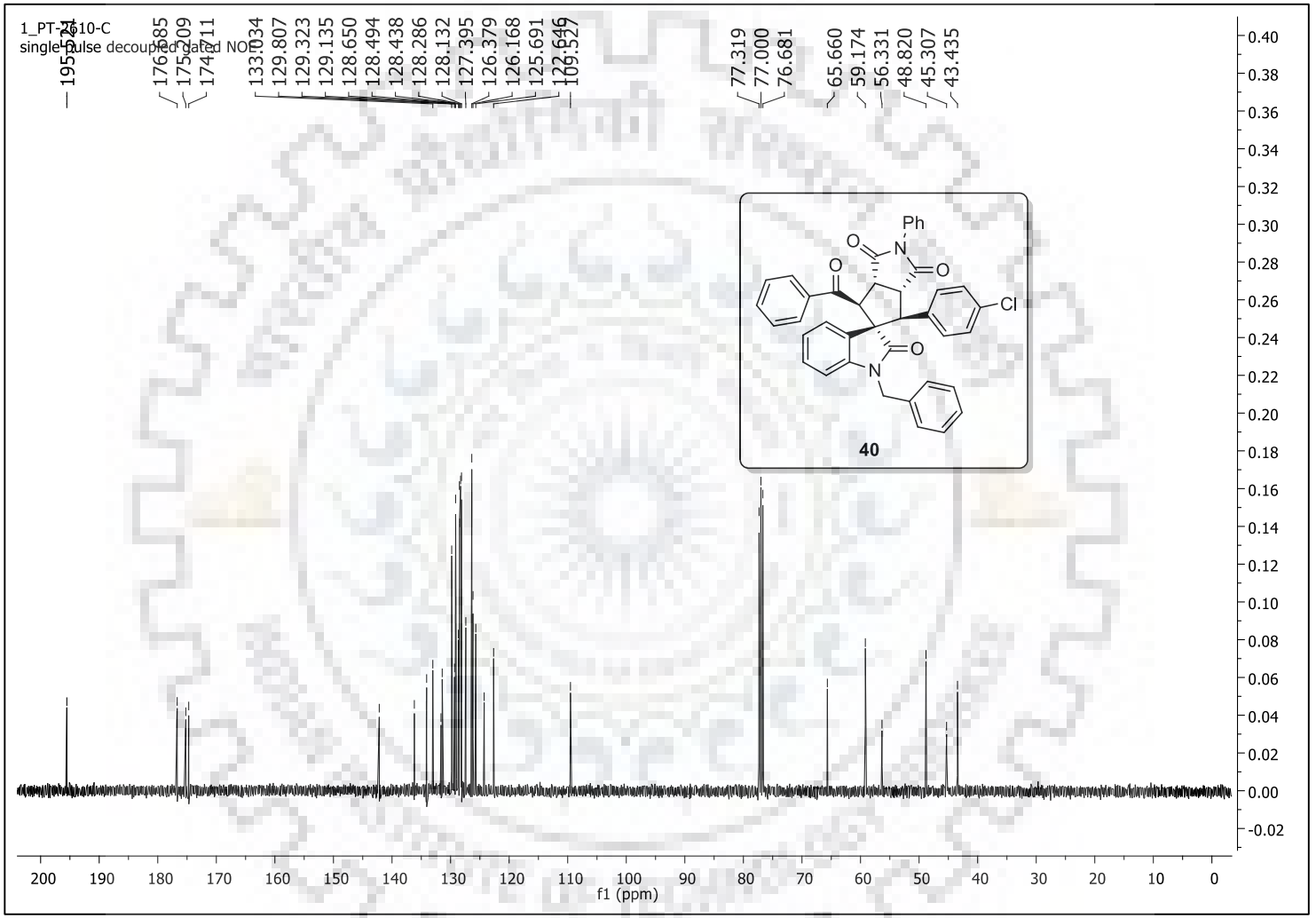


Figure S-32: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **40**.

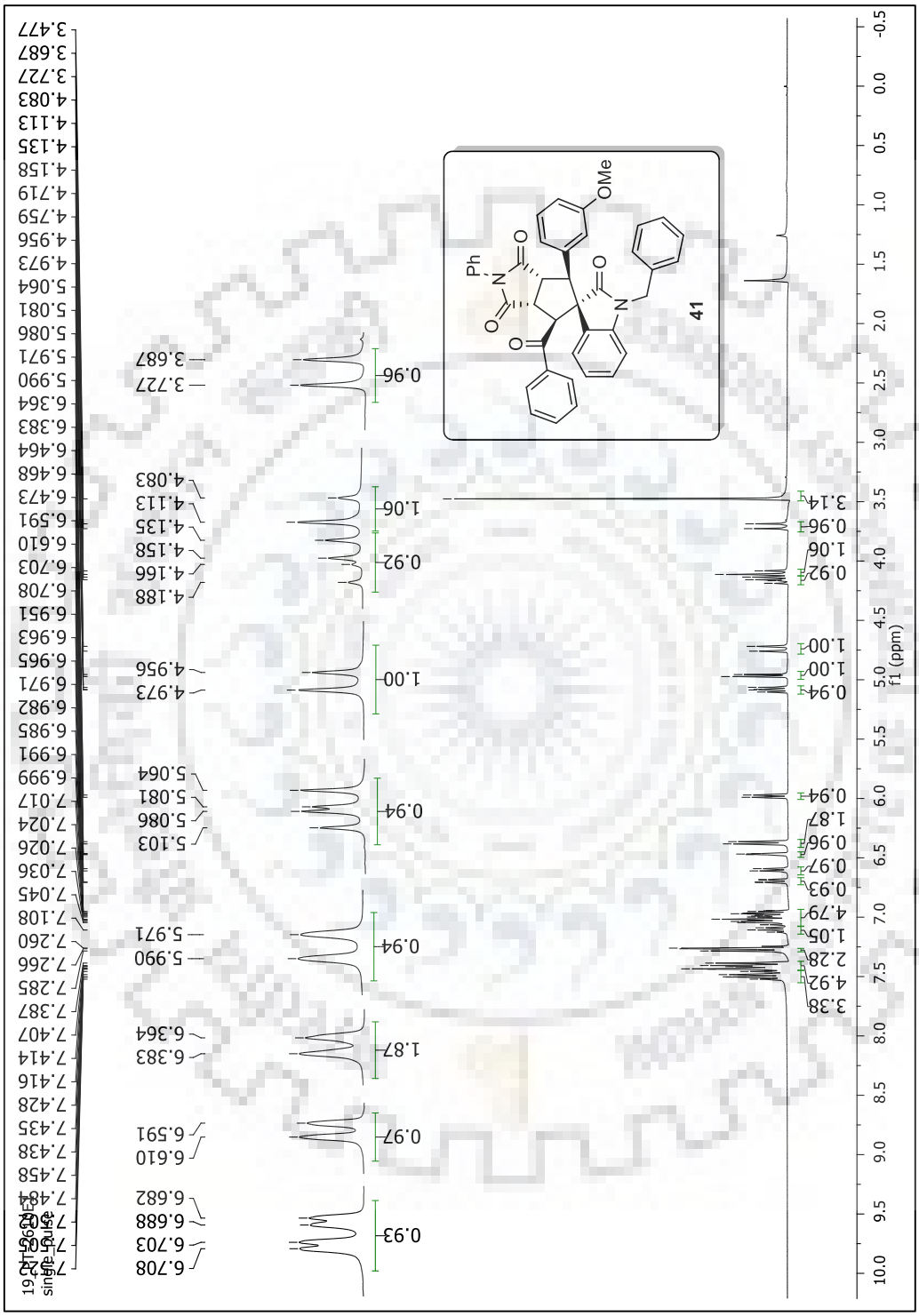
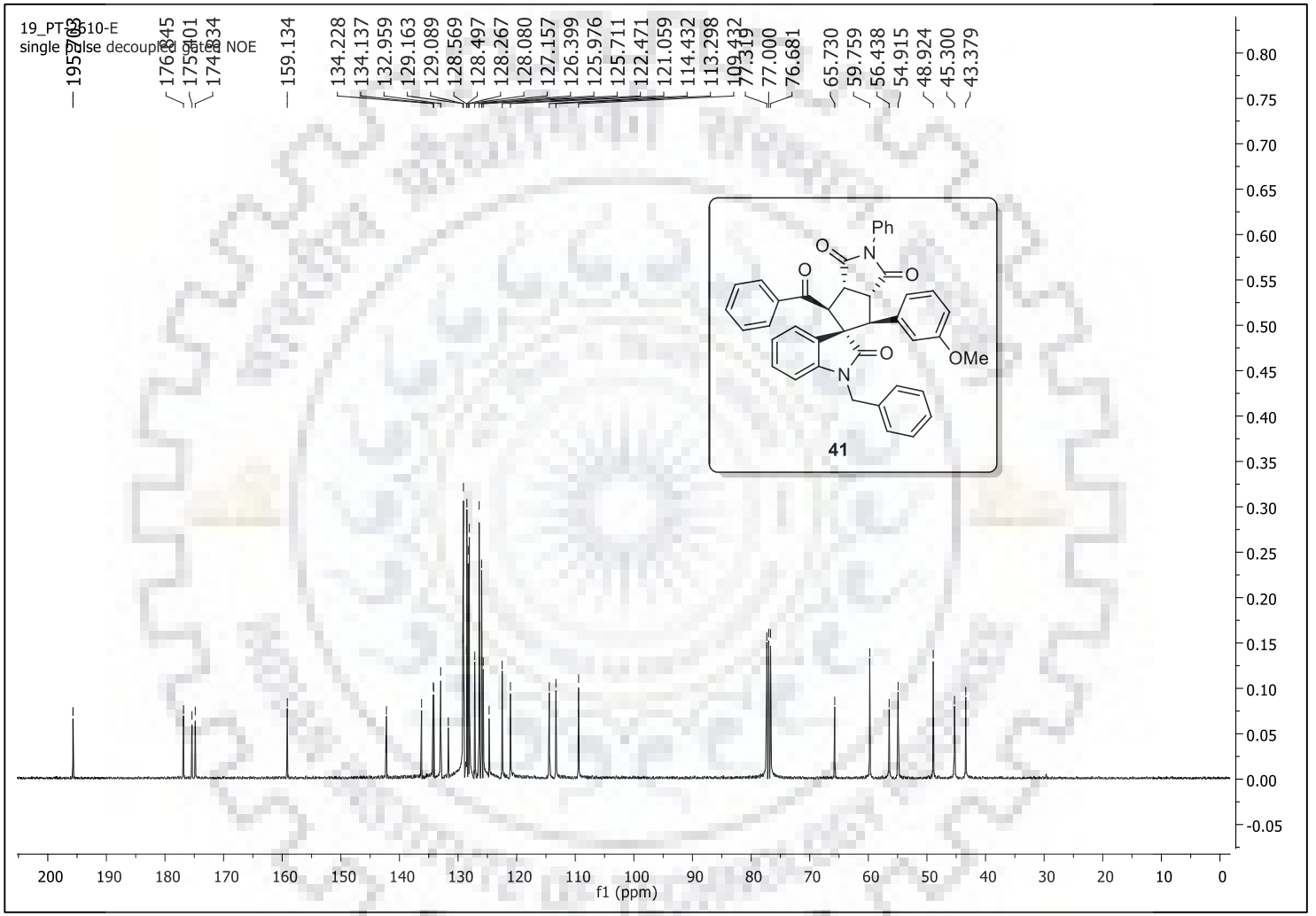


Figure S-33: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **41**.



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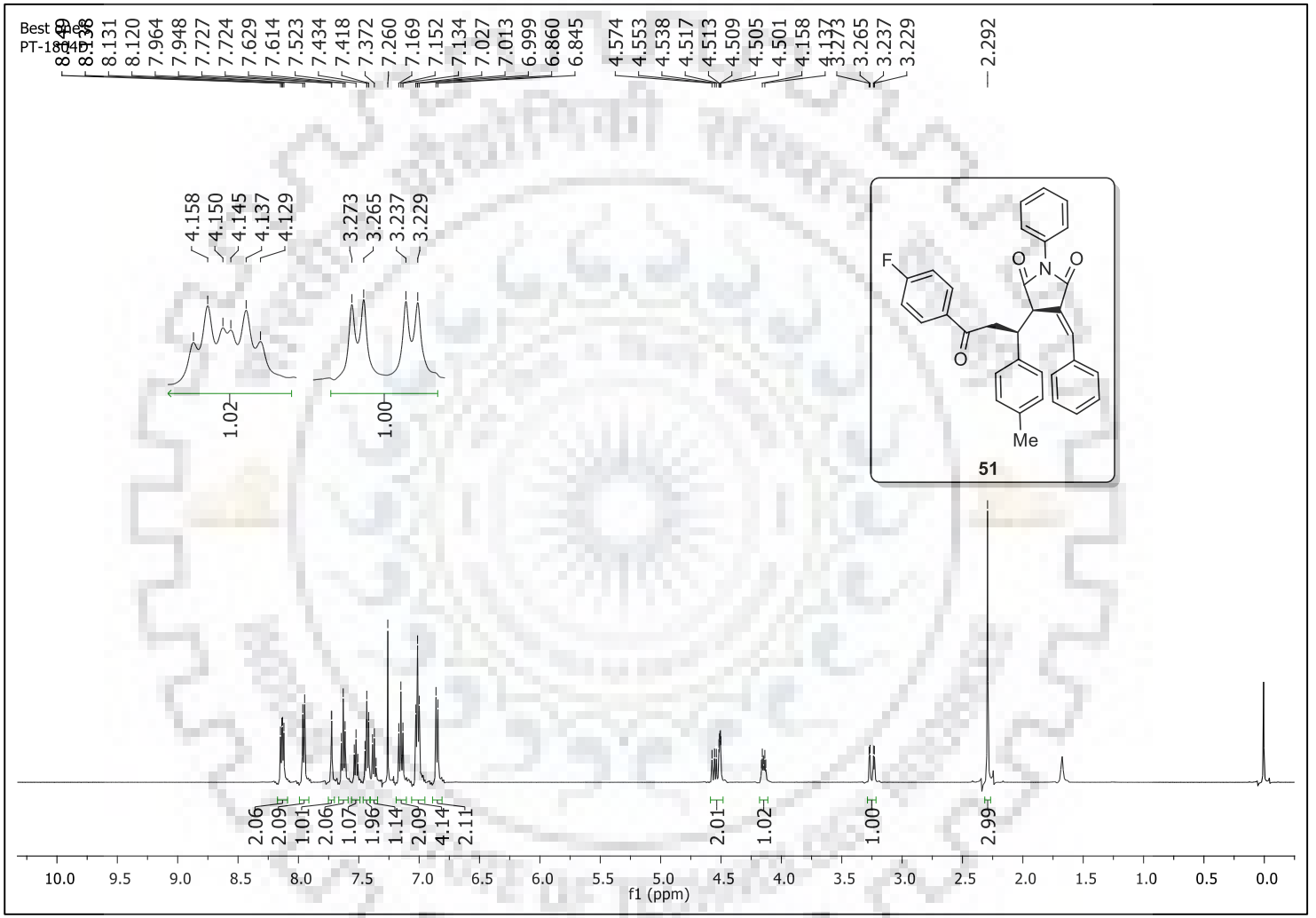


Figure S-35: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **51**.

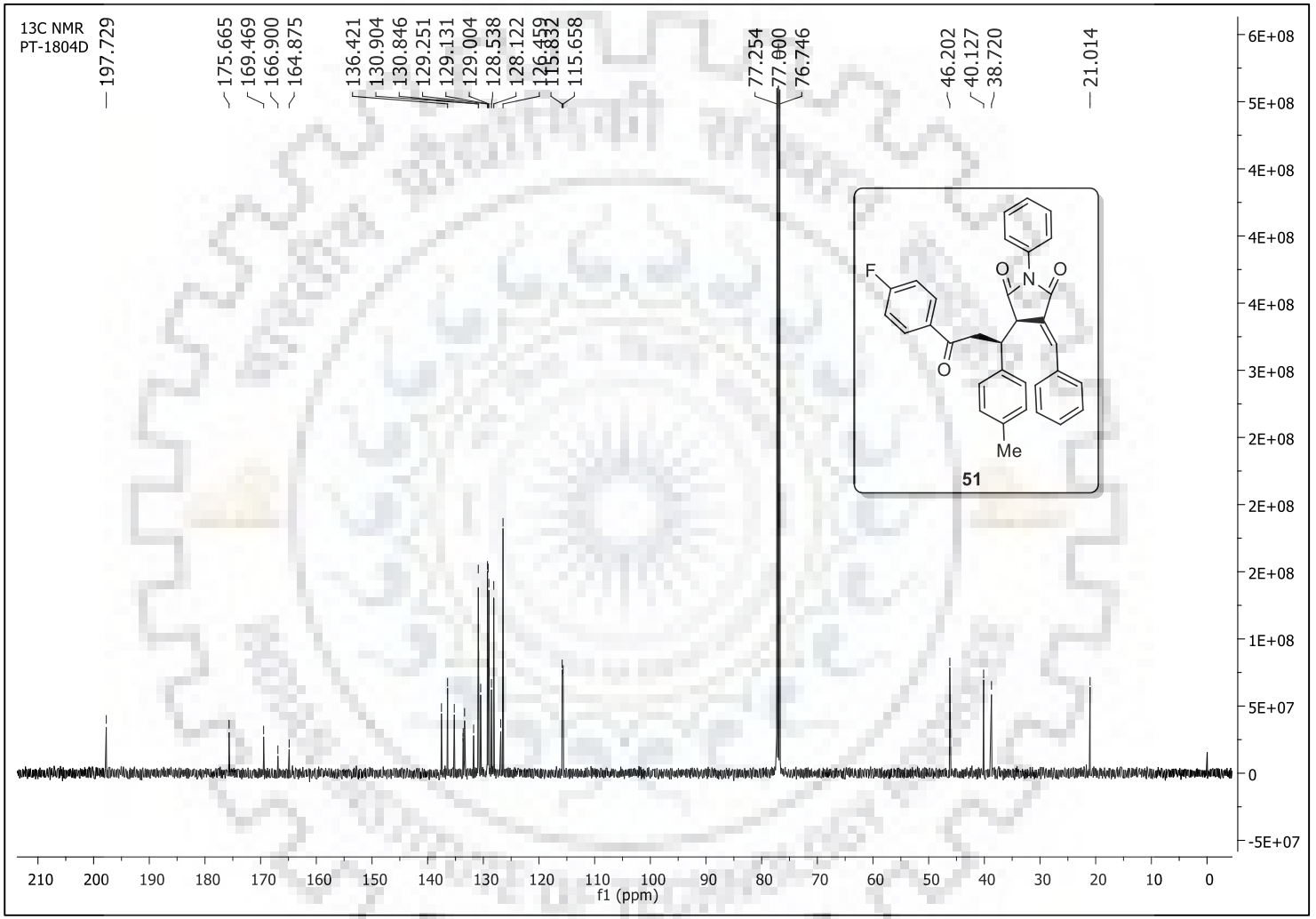


Figure S-36: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **51**.

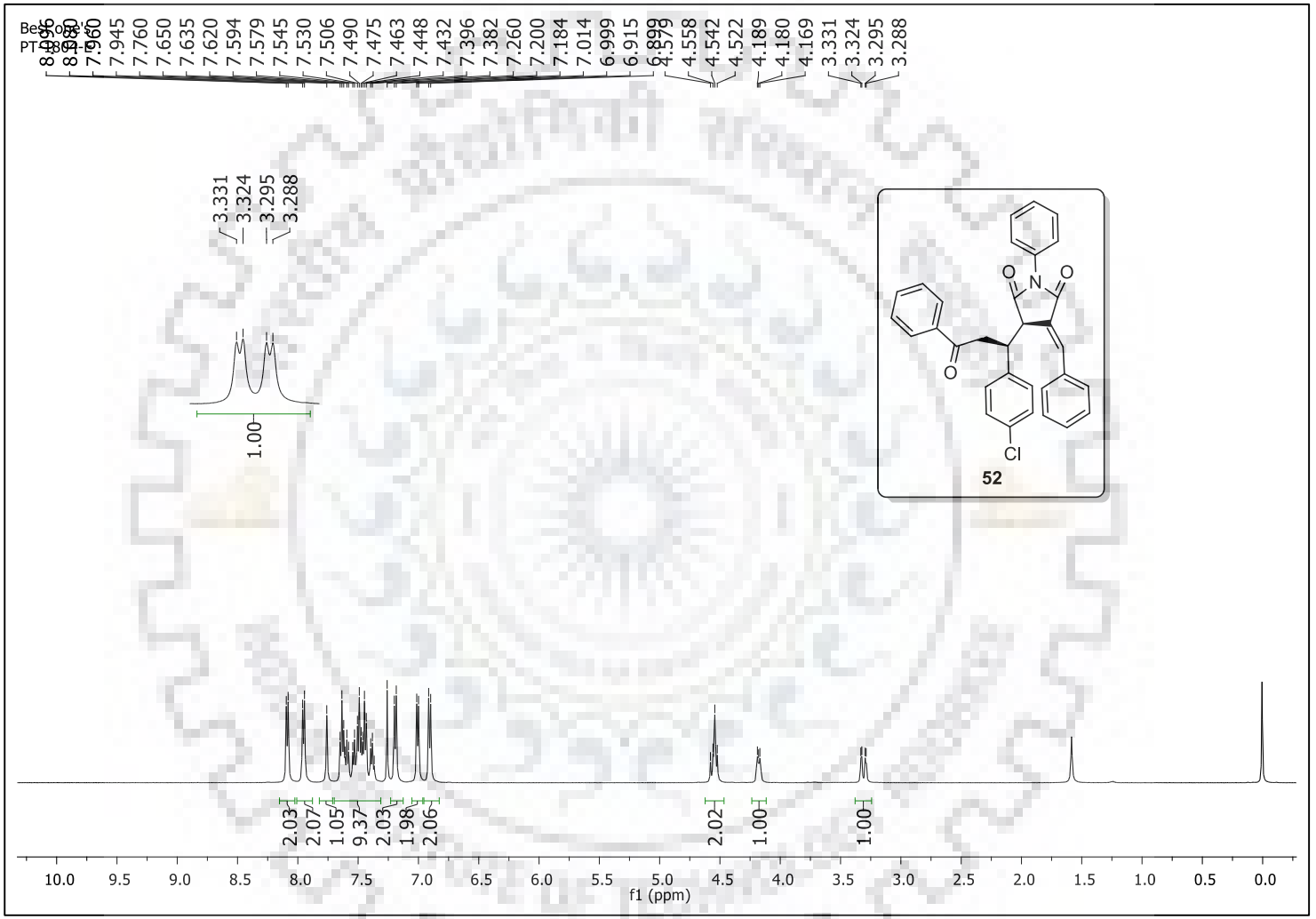


Figure S-37: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **52**.

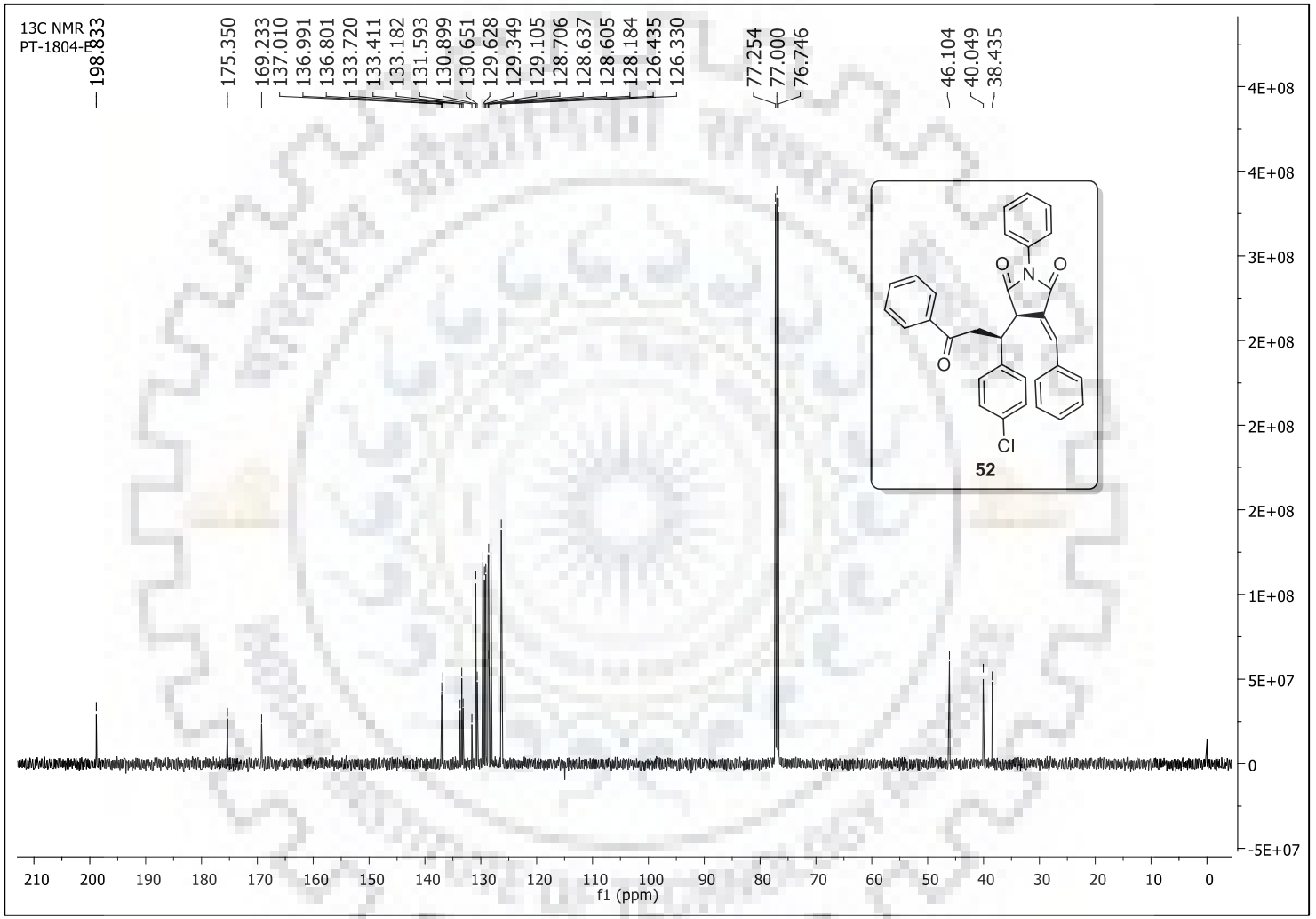


Figure S-38: ^{13}C NMR (125 MHz, $CDCl_3$) Spectrum of **52**.

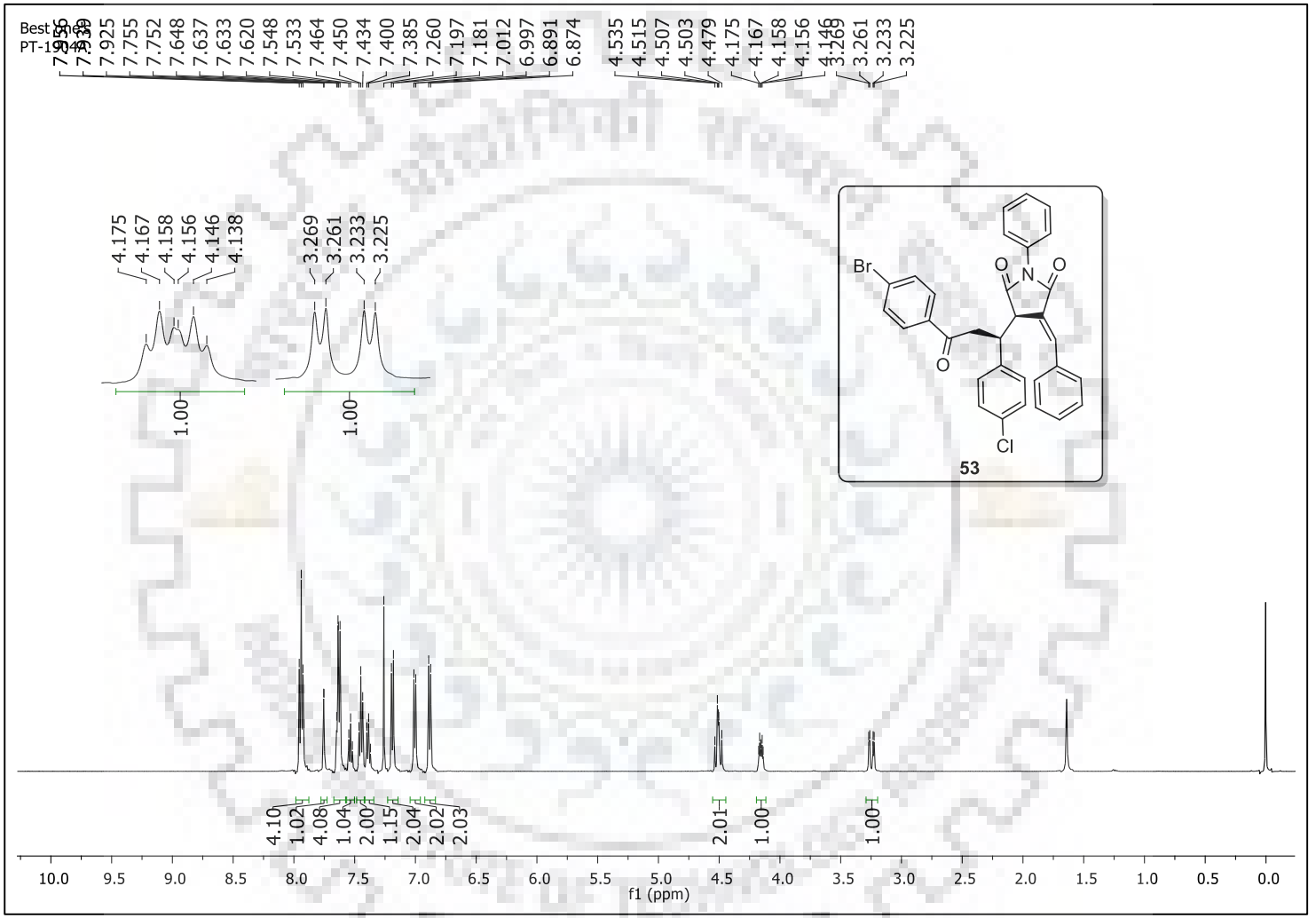


Figure S-39: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **53**.

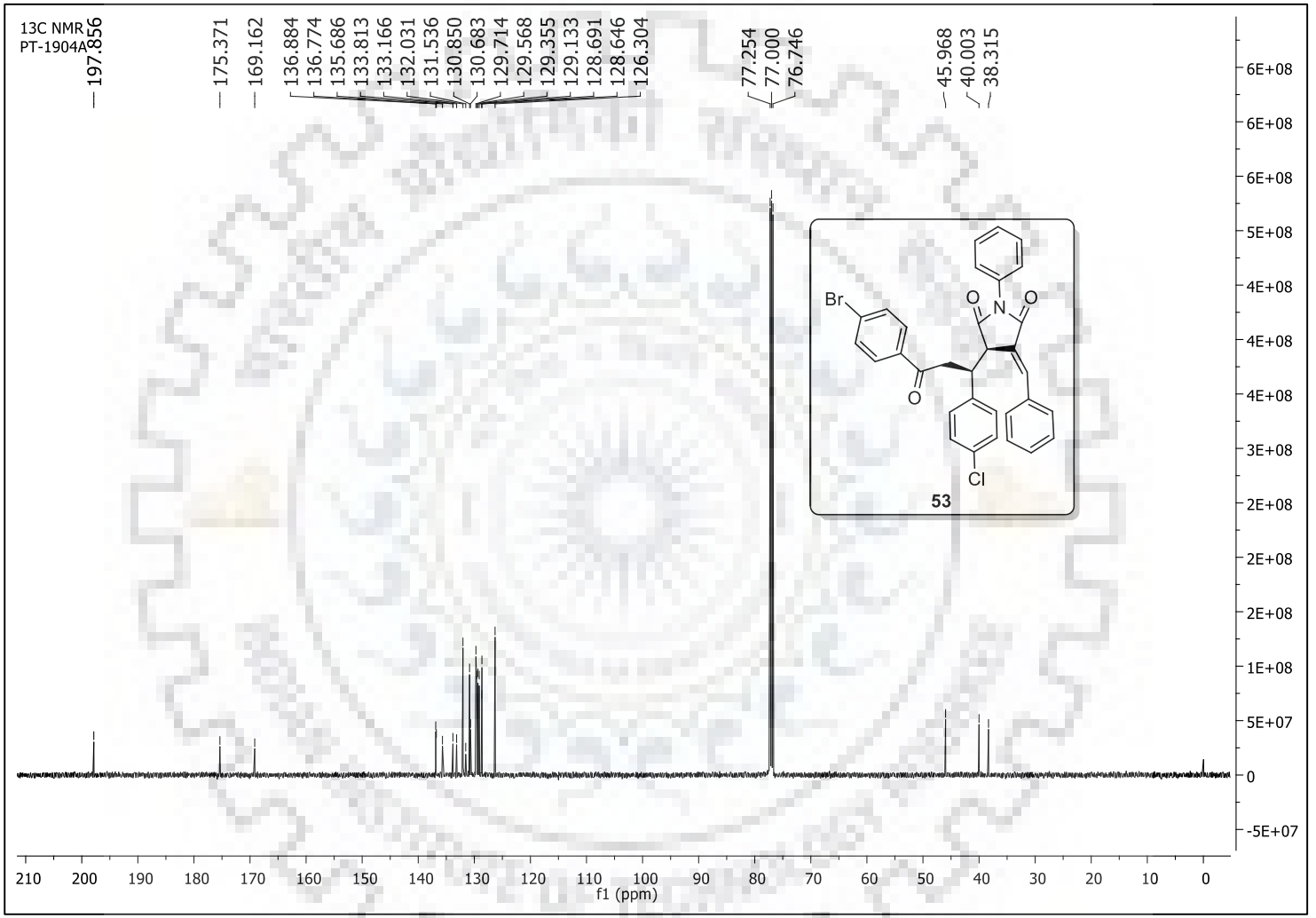


Figure S-40: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **53**.

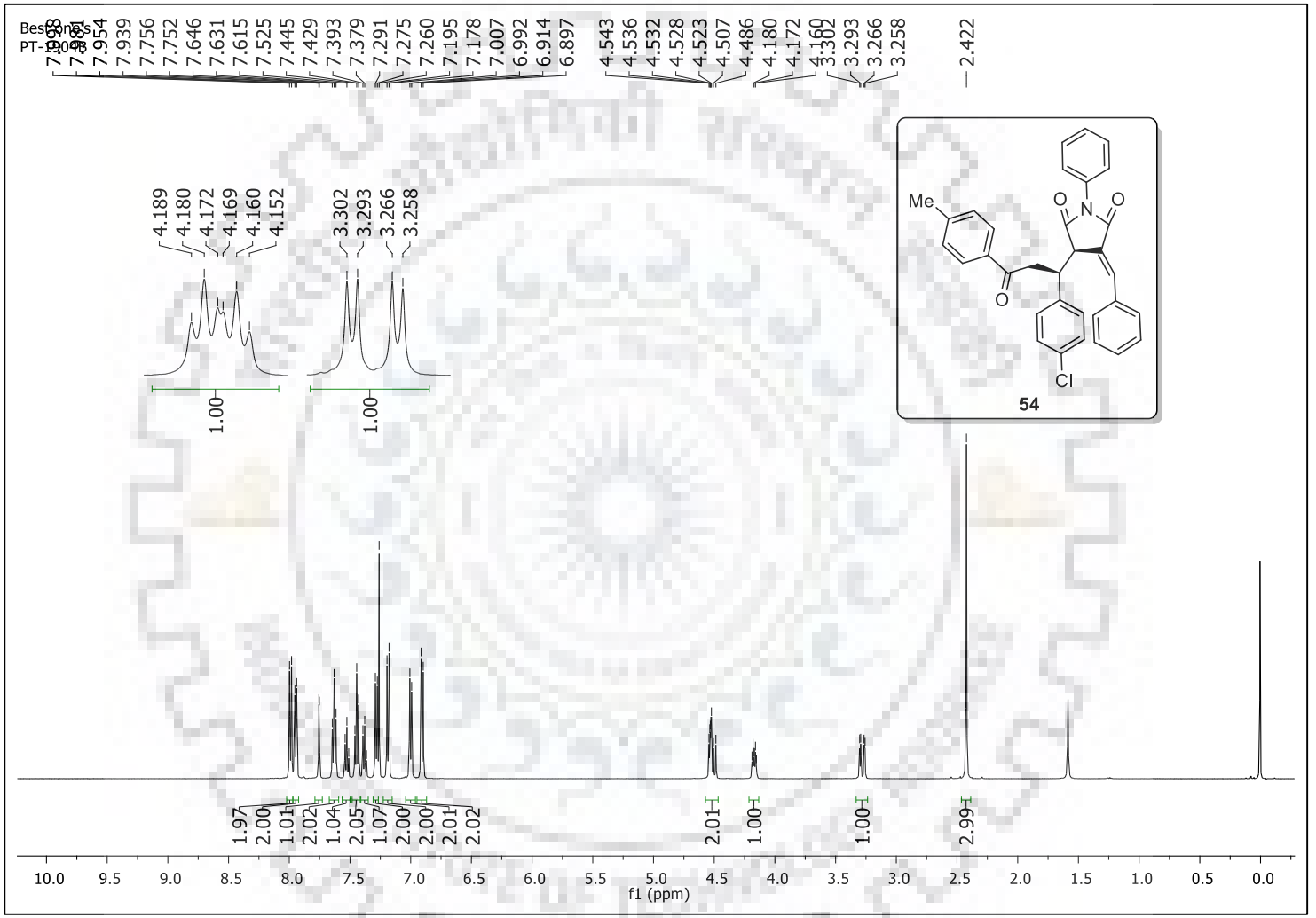


Figure S-41: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **54**.

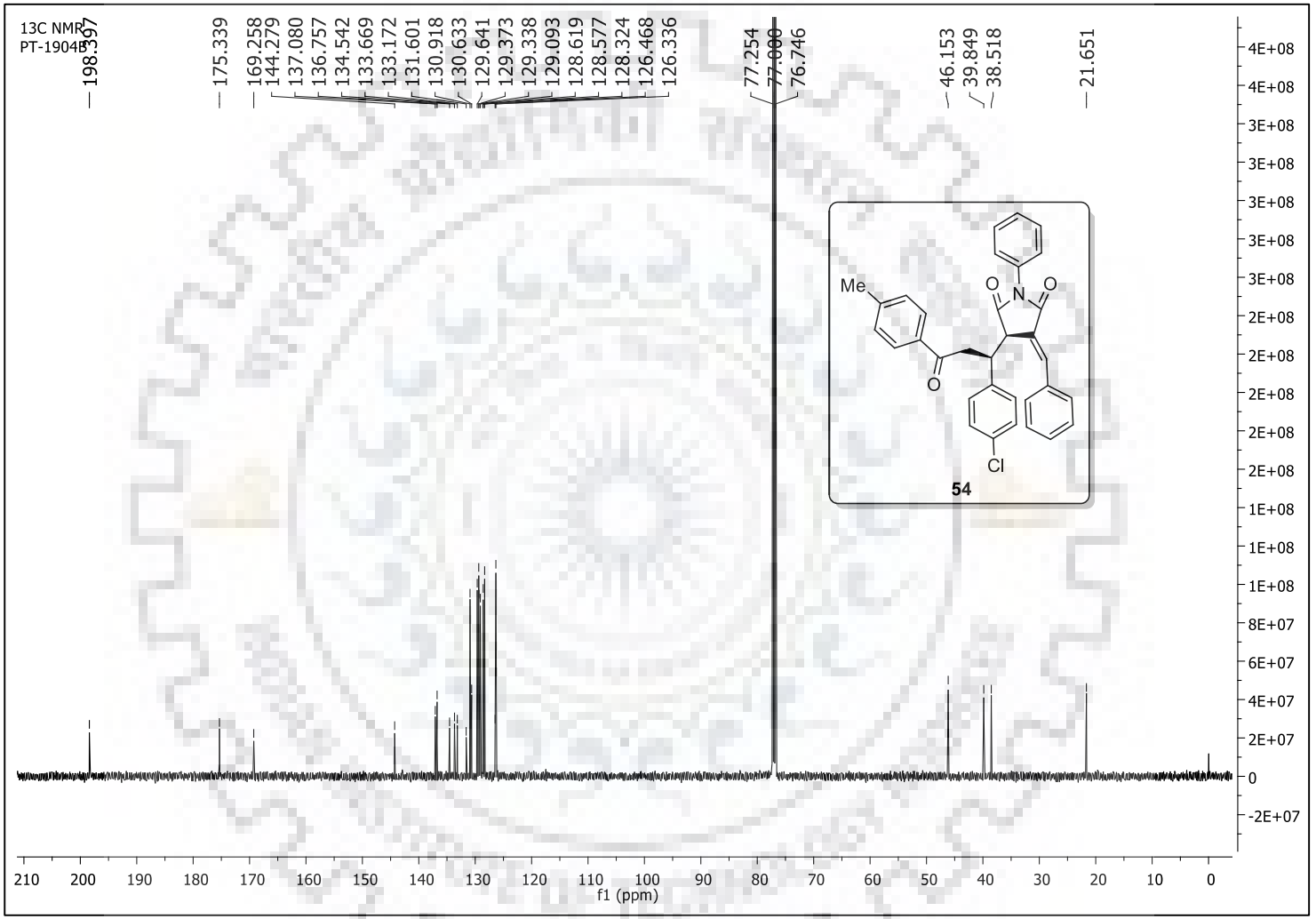


Figure S-42: ^{13}C NMR (125 MHz, $CDCl_3$) Spectrum of **54**.

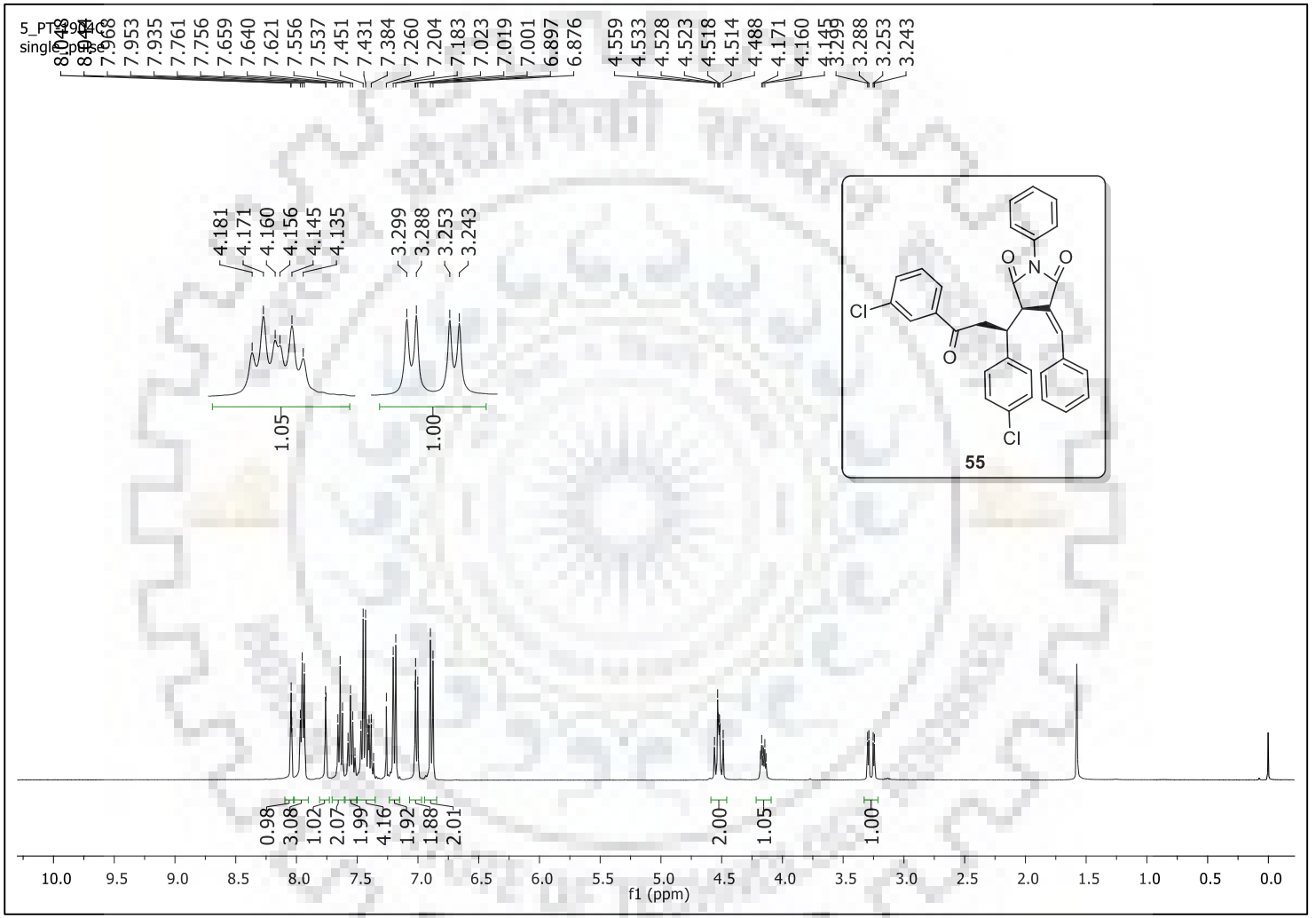


Figure S-43: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **55**.

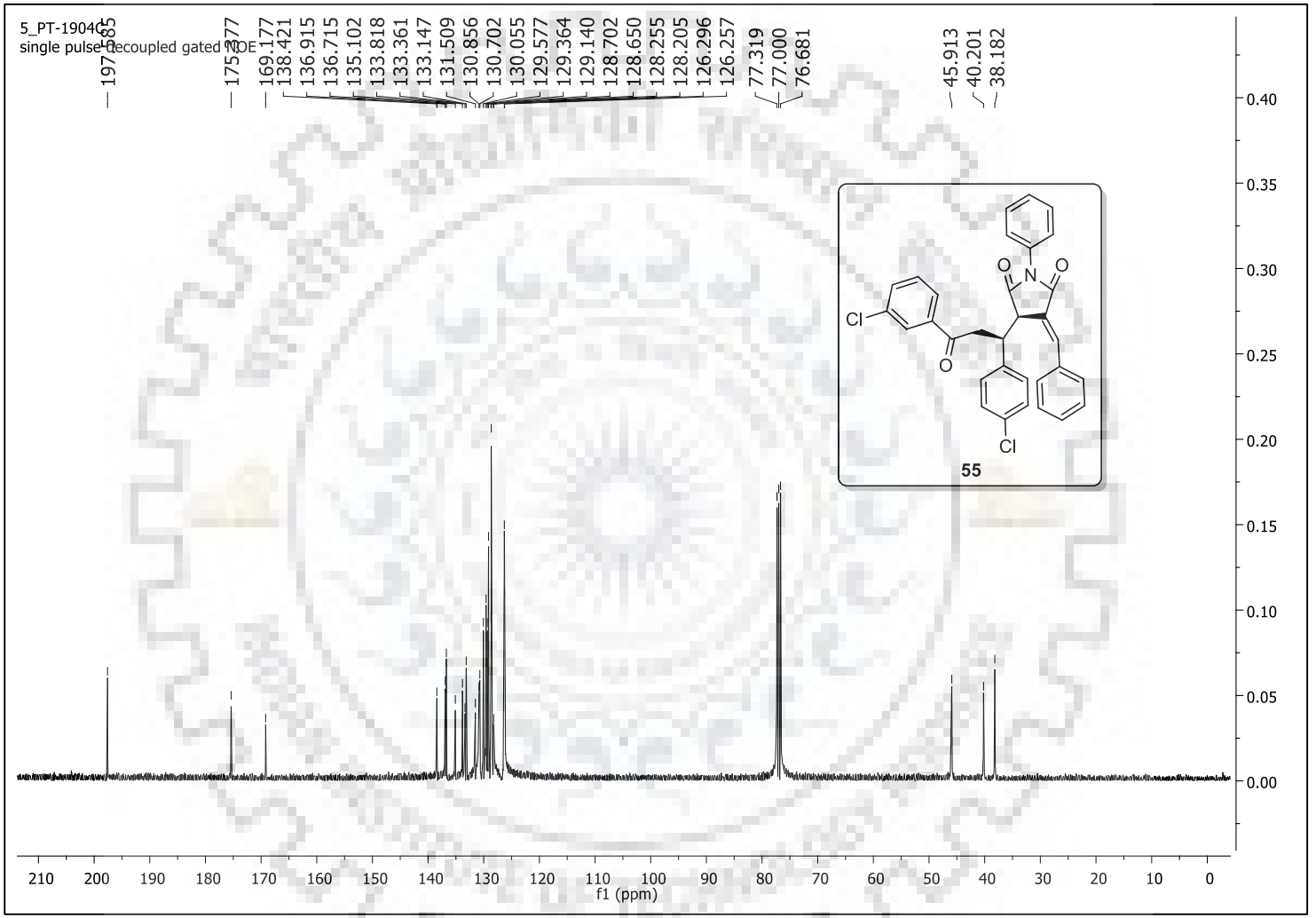


Figure S-44: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **55**.

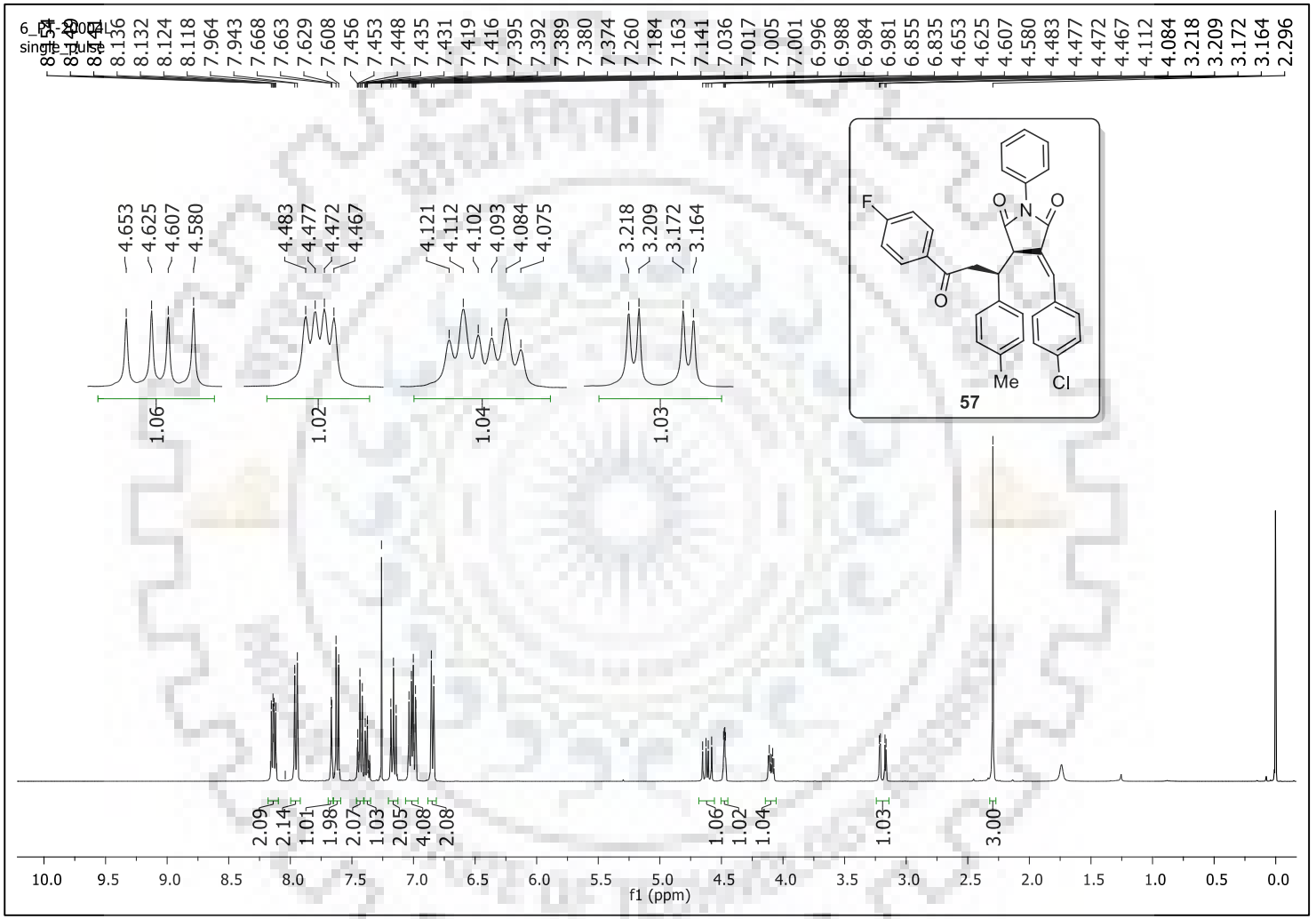


Figure S-45: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **57**.

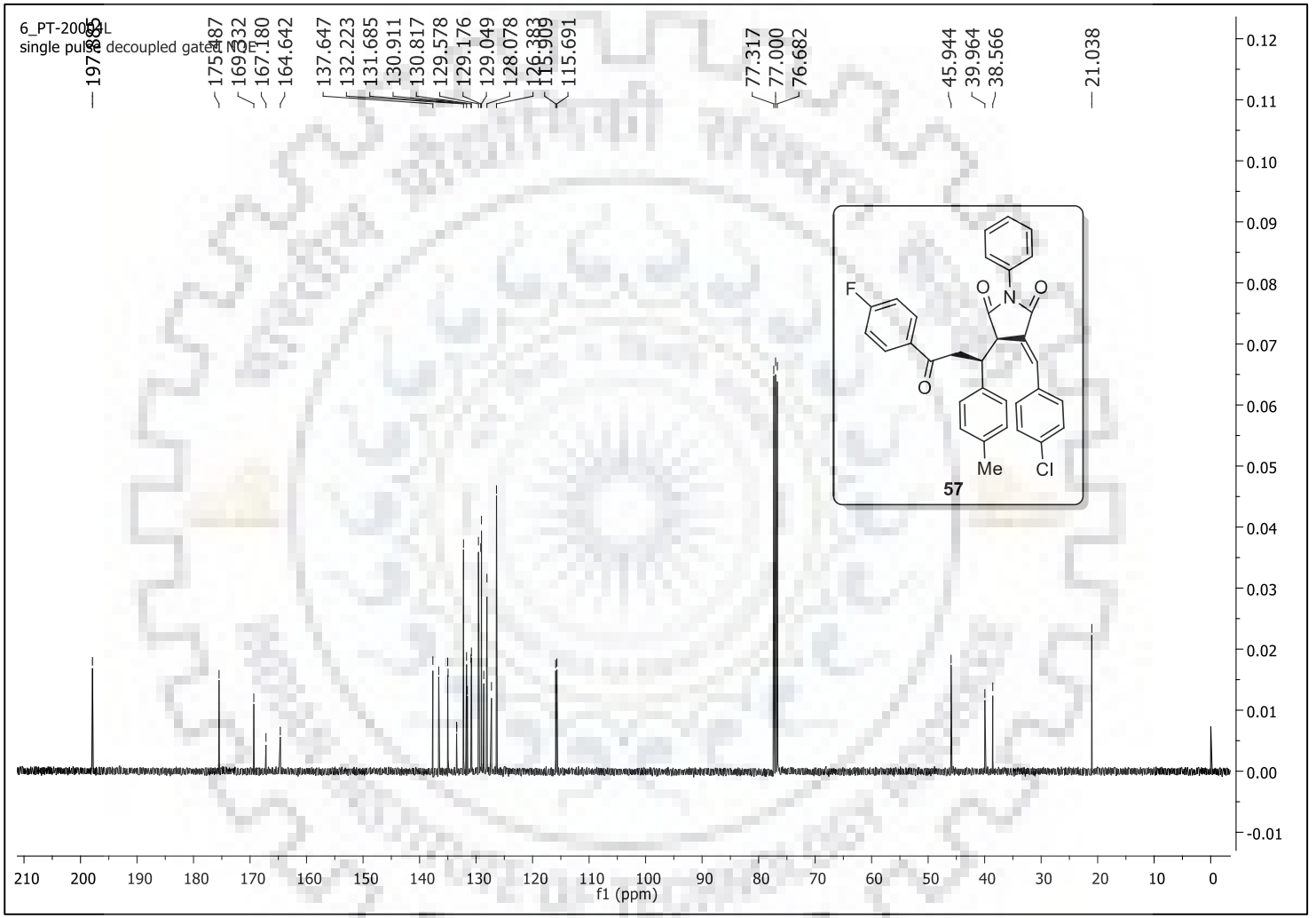


Figure S-46: ^{13}C NMR (125 MHz, $CDCl_3$) Spectrum of **57**.

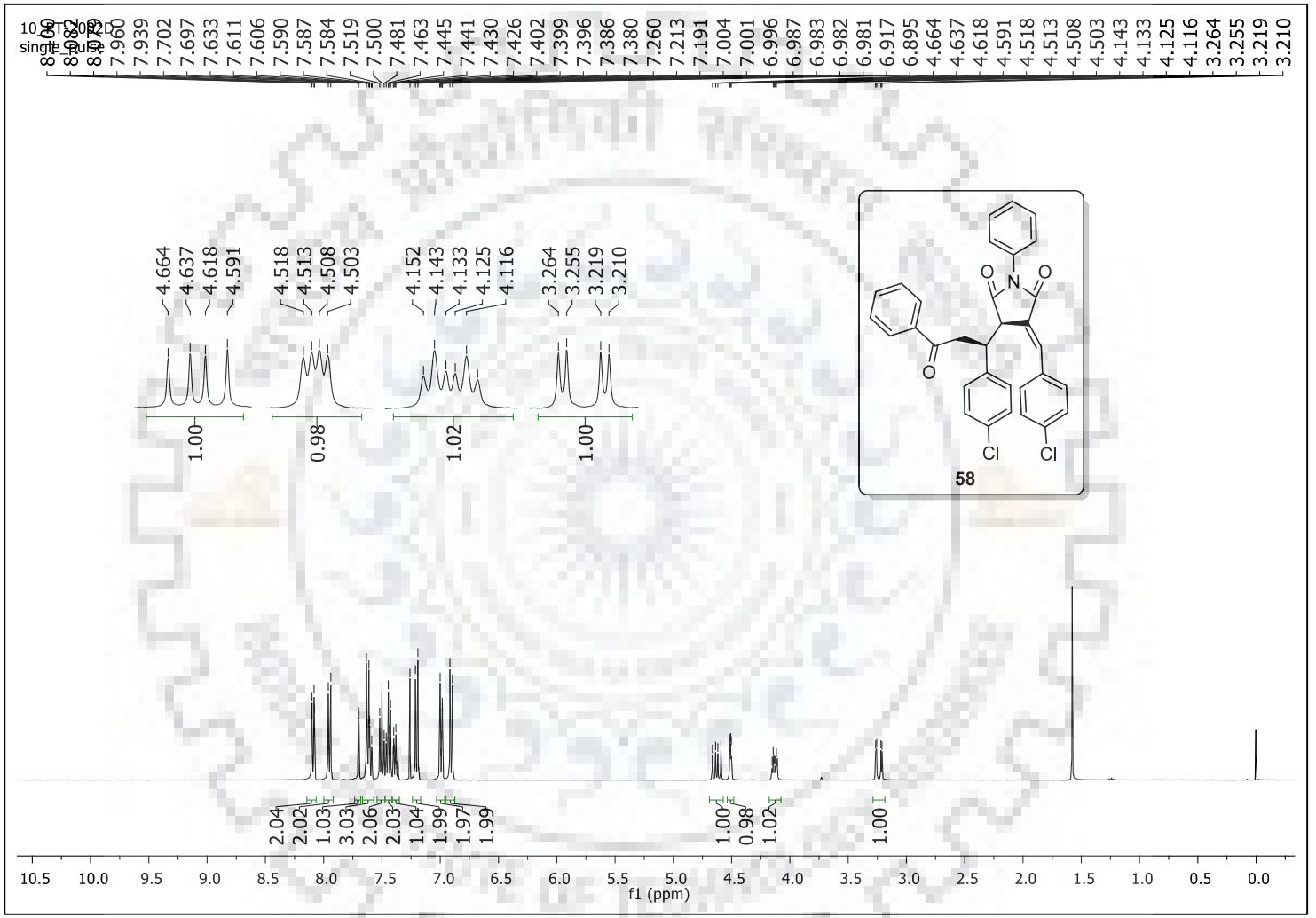


Figure S-47: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **58**.

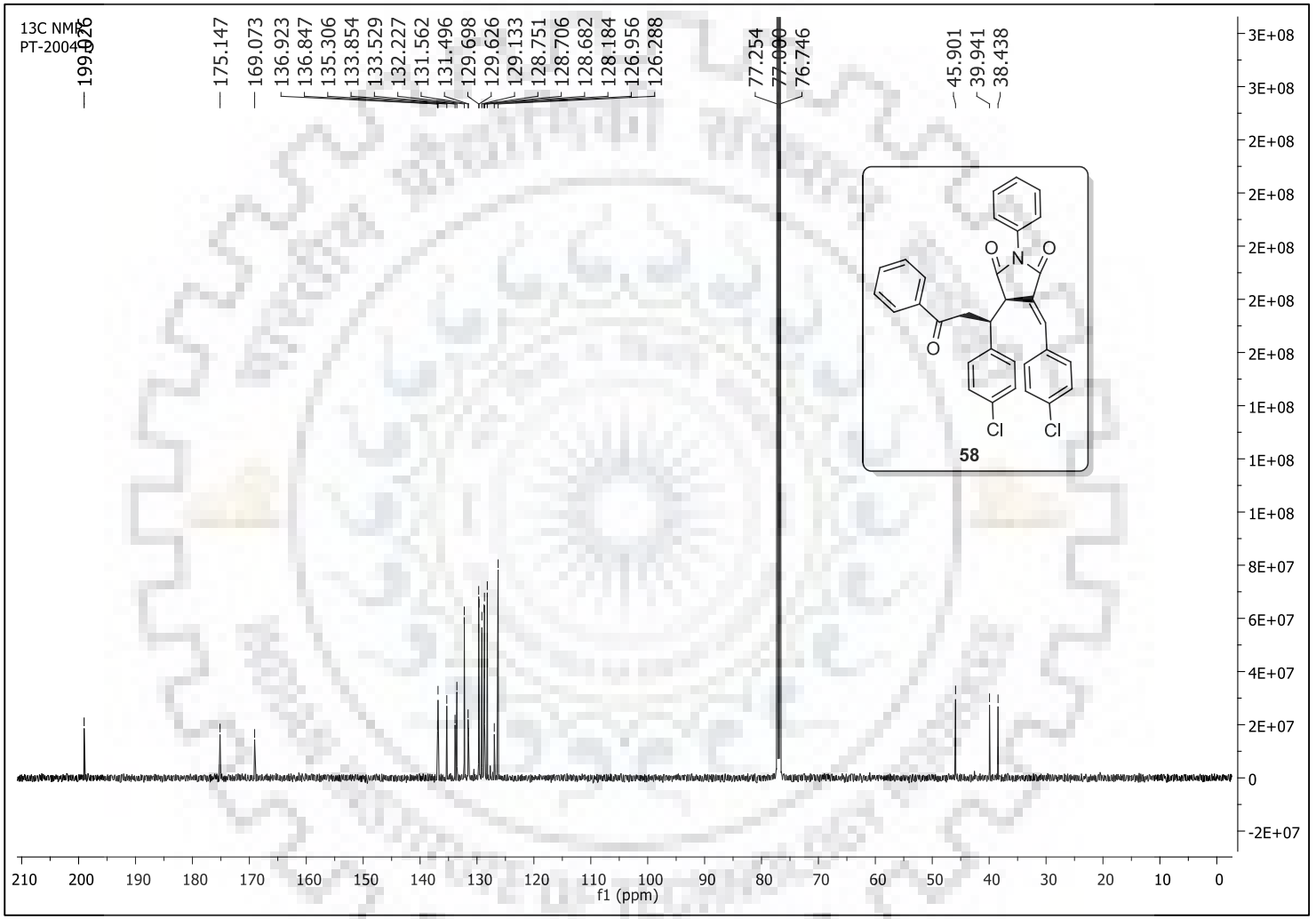


Figure S-48: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **58**.

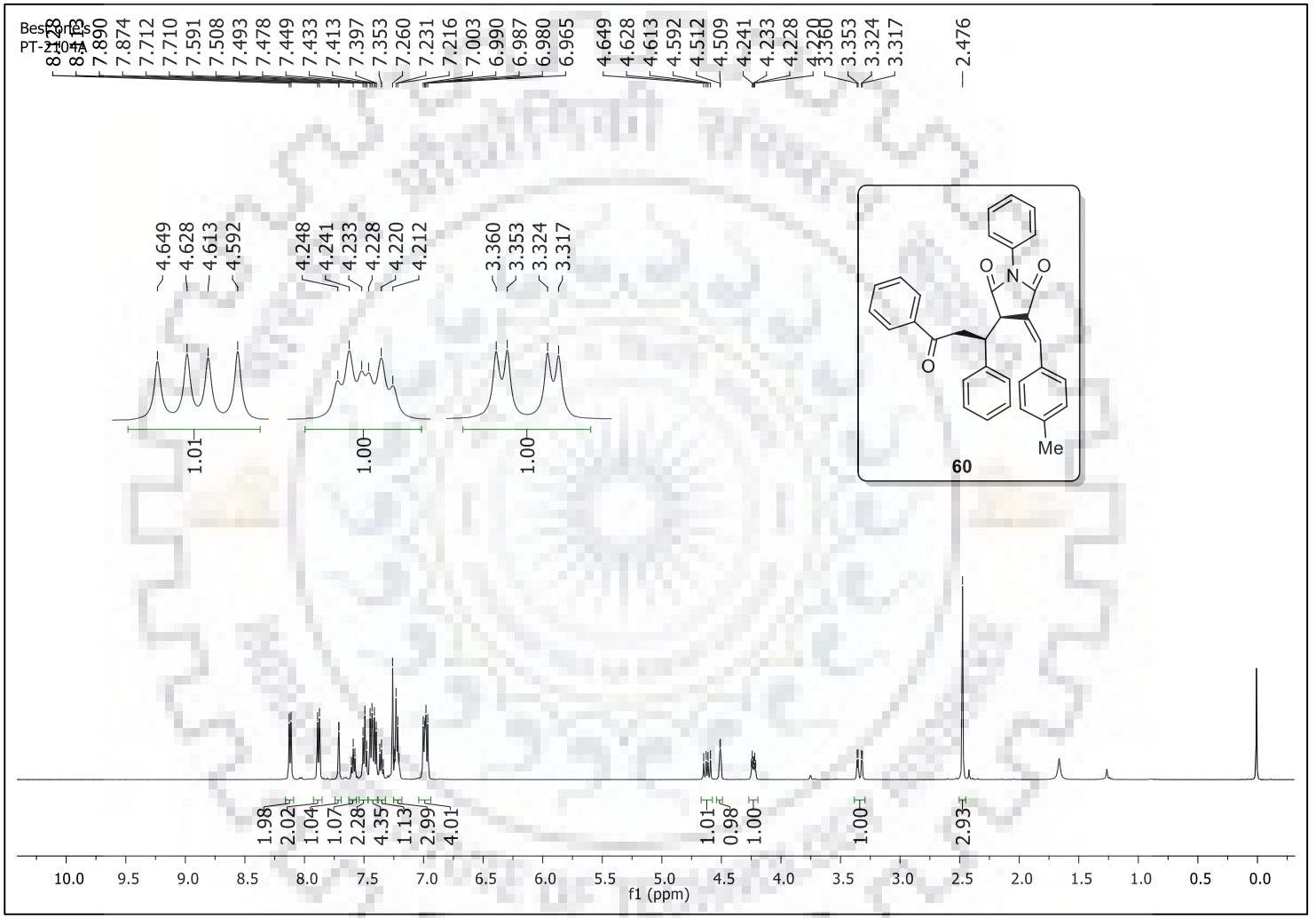


Figure S-49: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **60**.

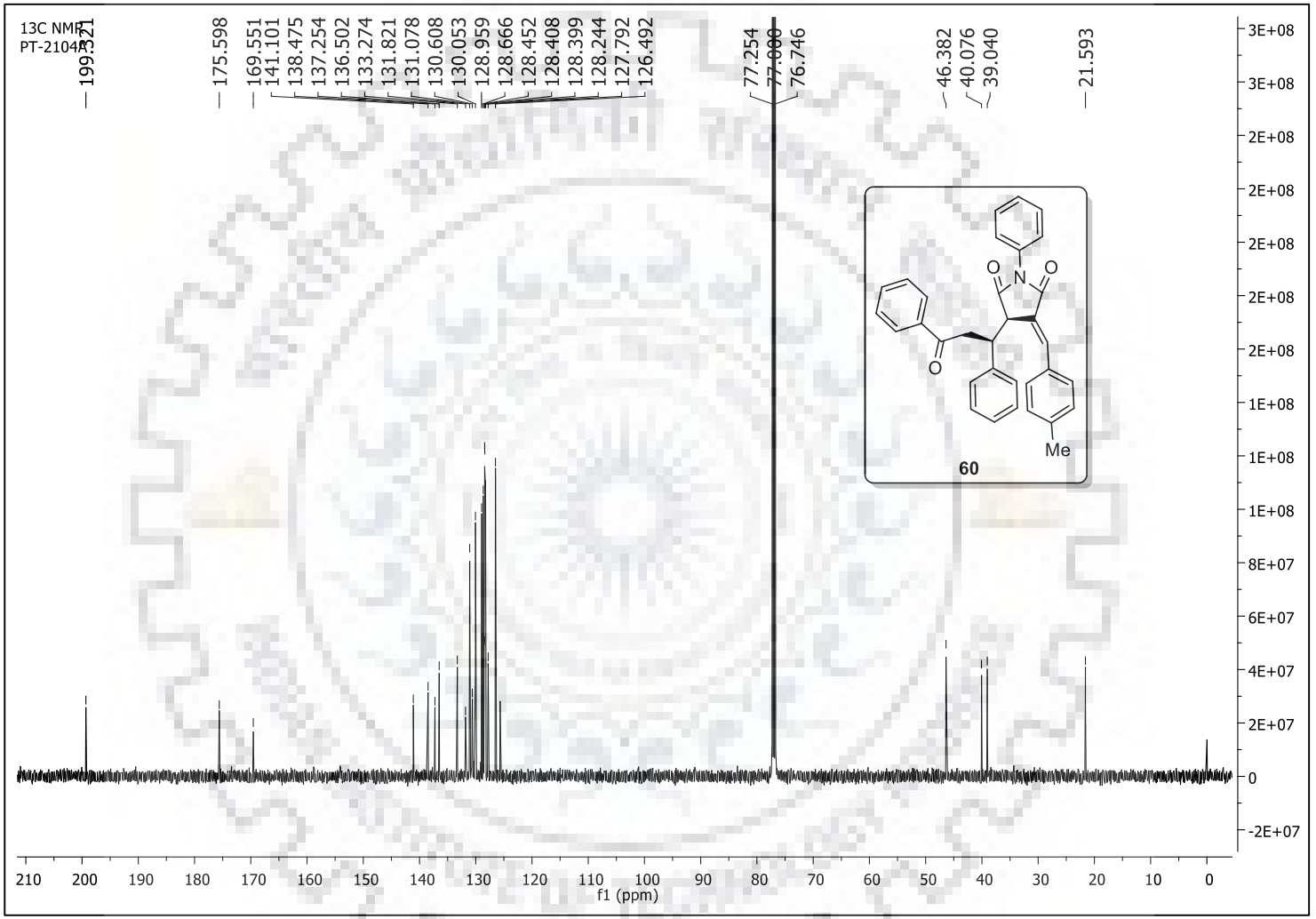


Figure S-50: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **60**.

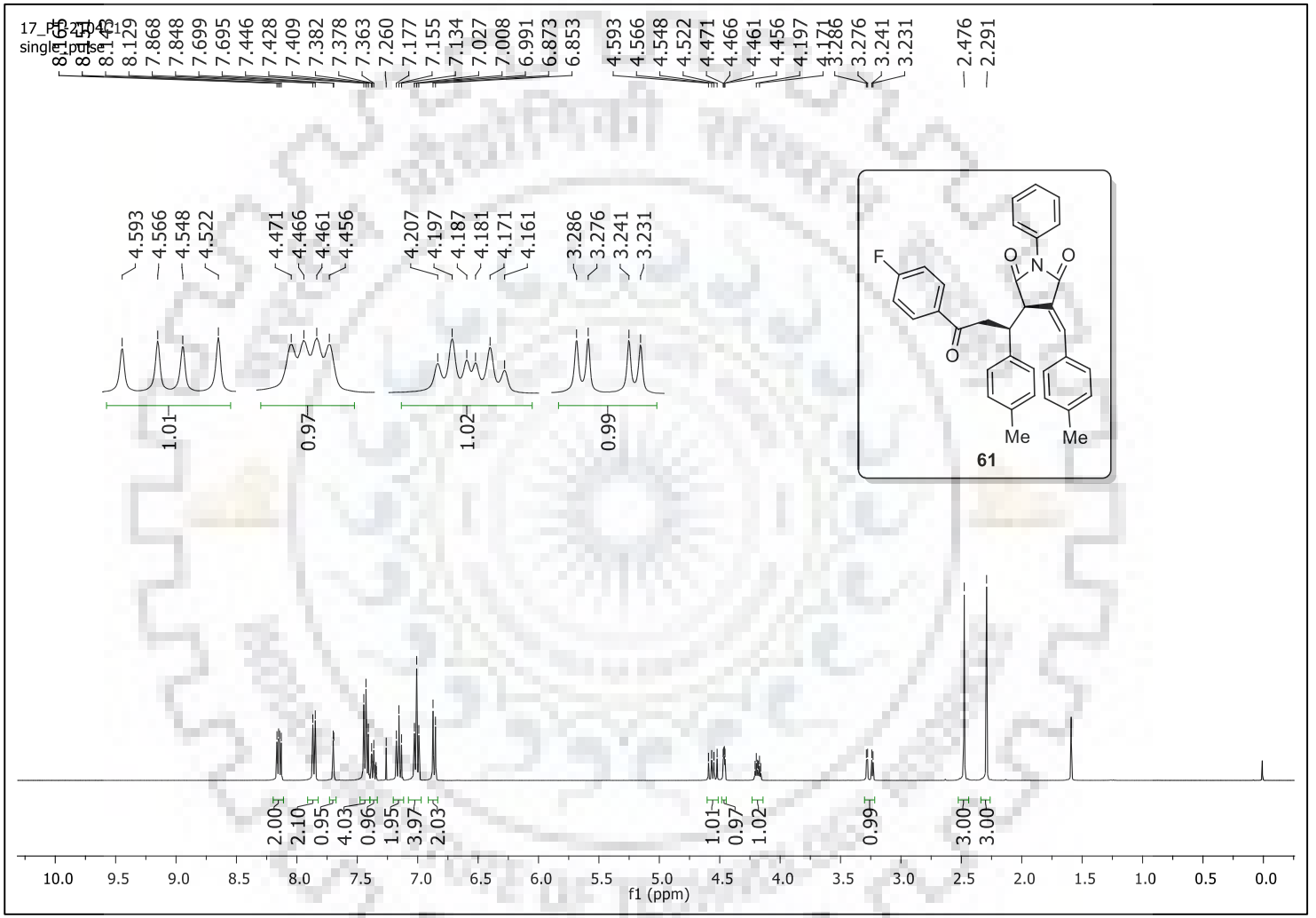


Figure S-51: ^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of **61**.

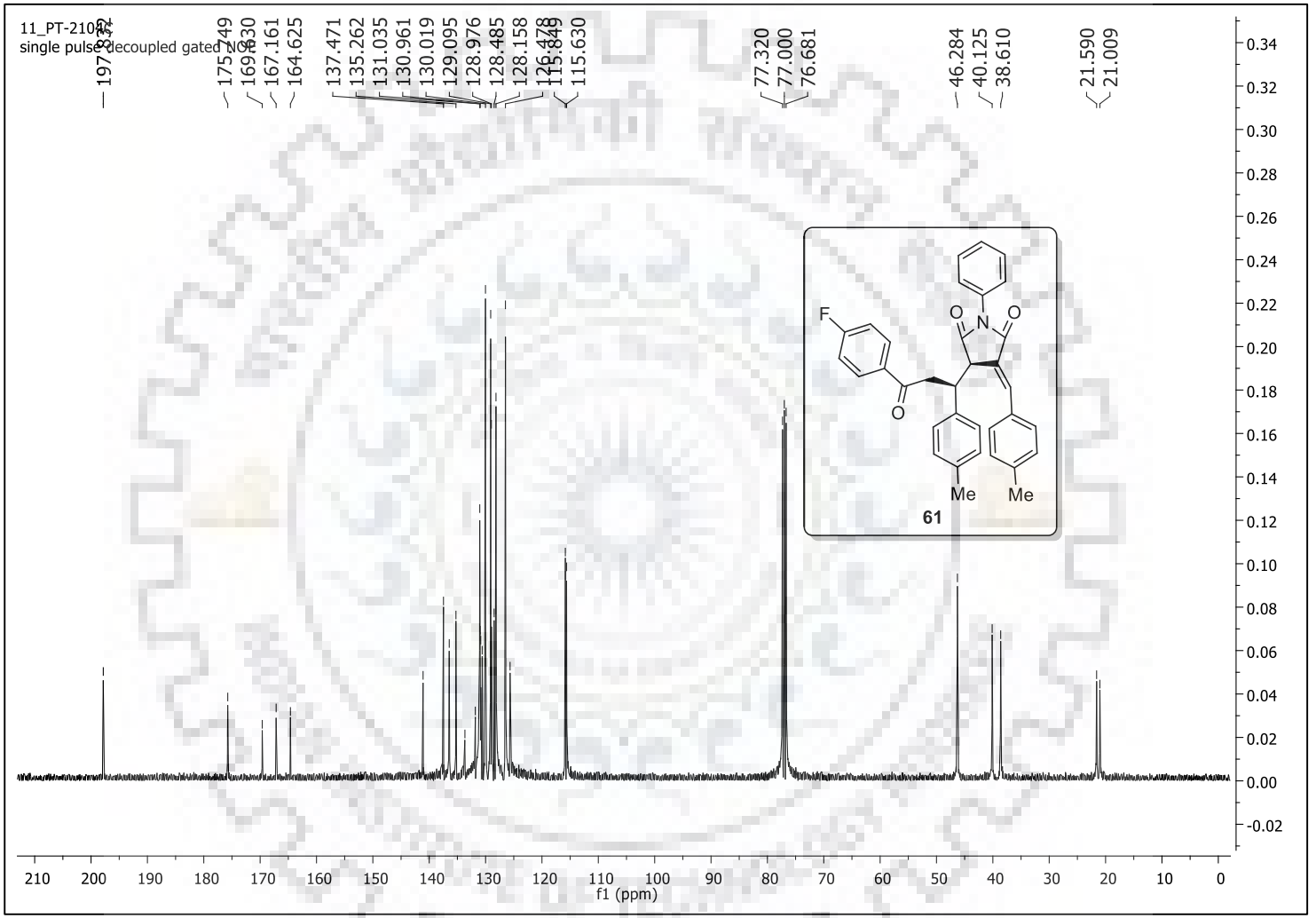


Figure S-52: ^{13}C NMR (125 MHz, $CDCl_3$) Spectrum of **61**.

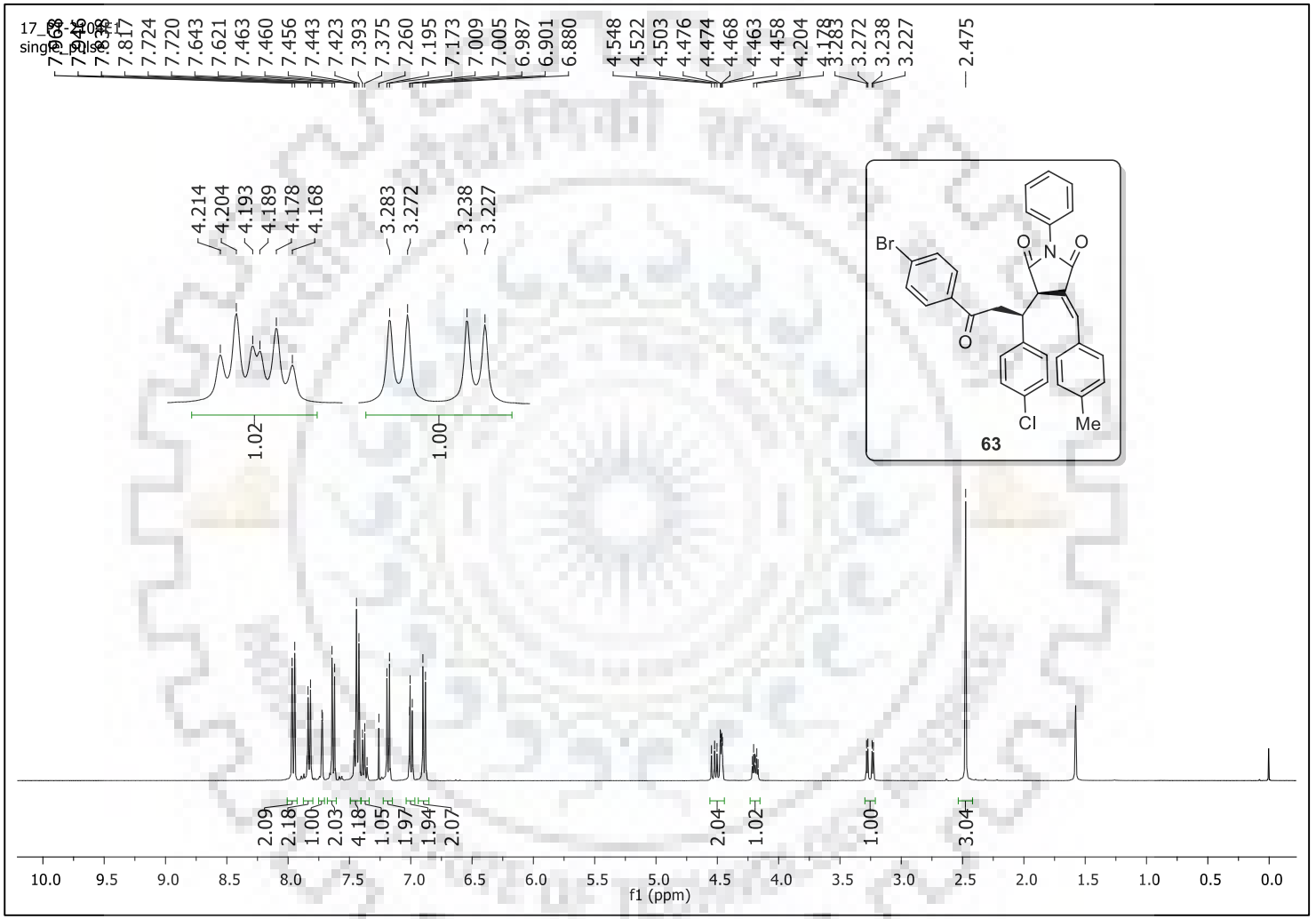


Figure S-53: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **63**.

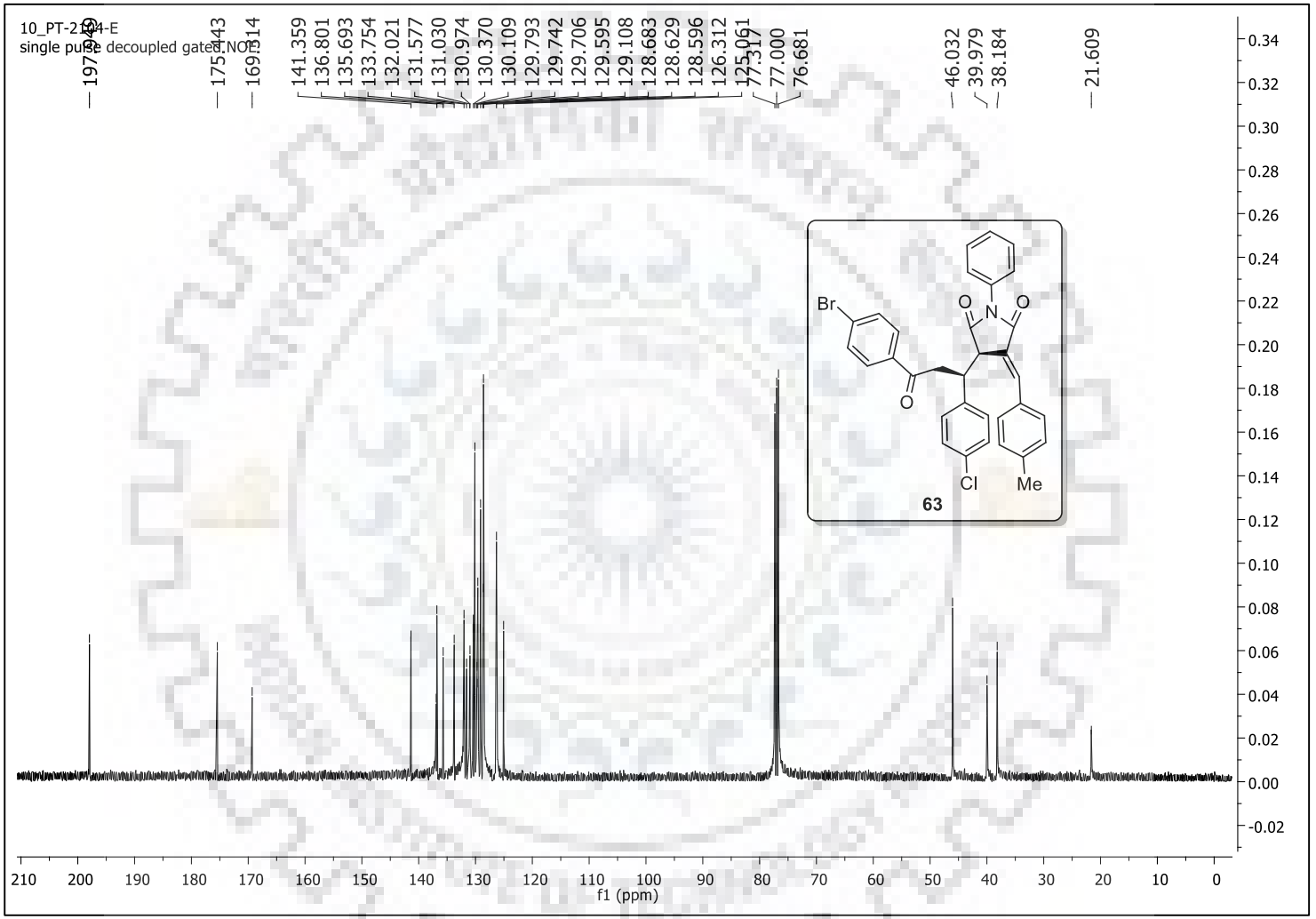


Figure S-54: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **63**.

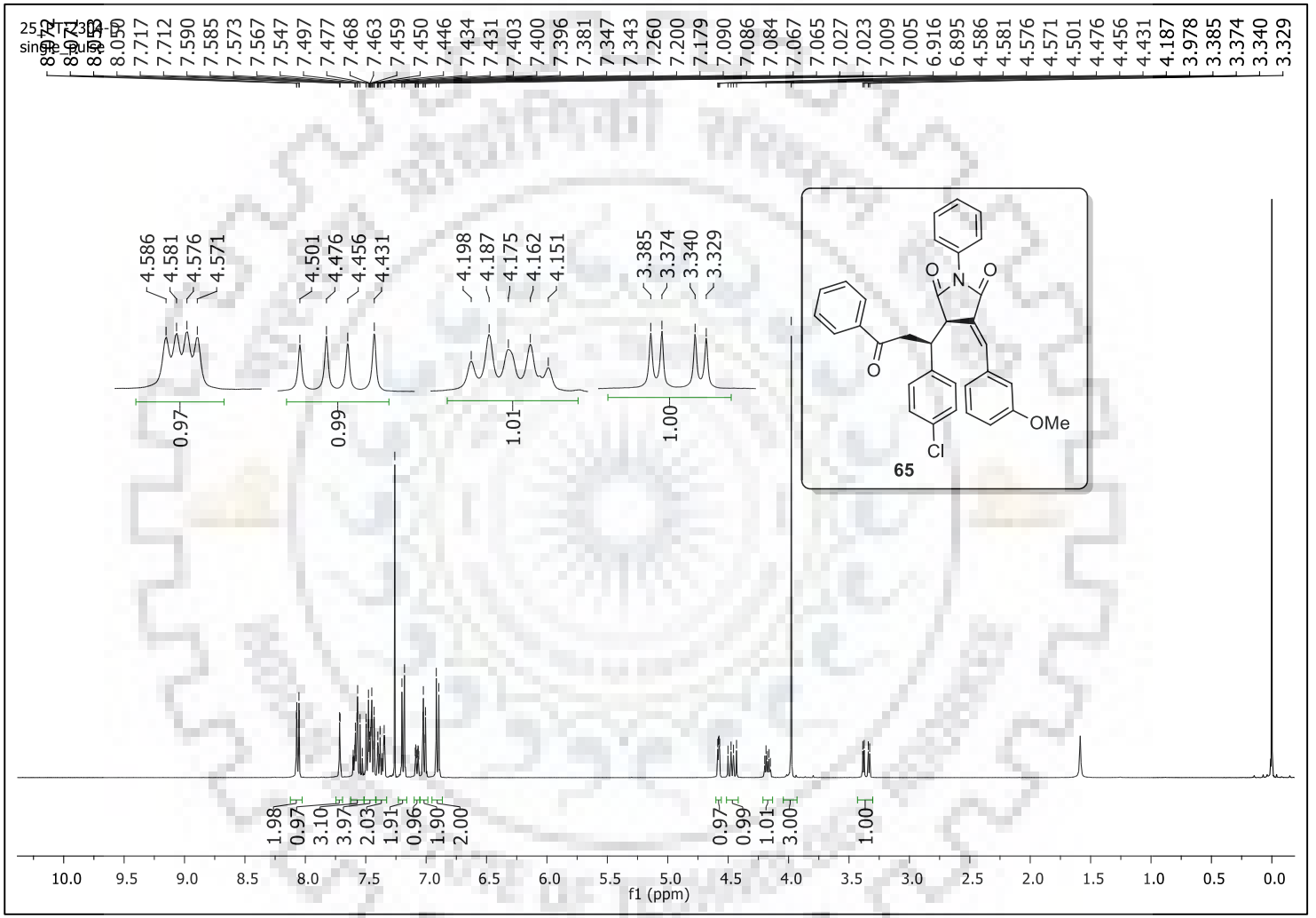


Figure S-55: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **65**.

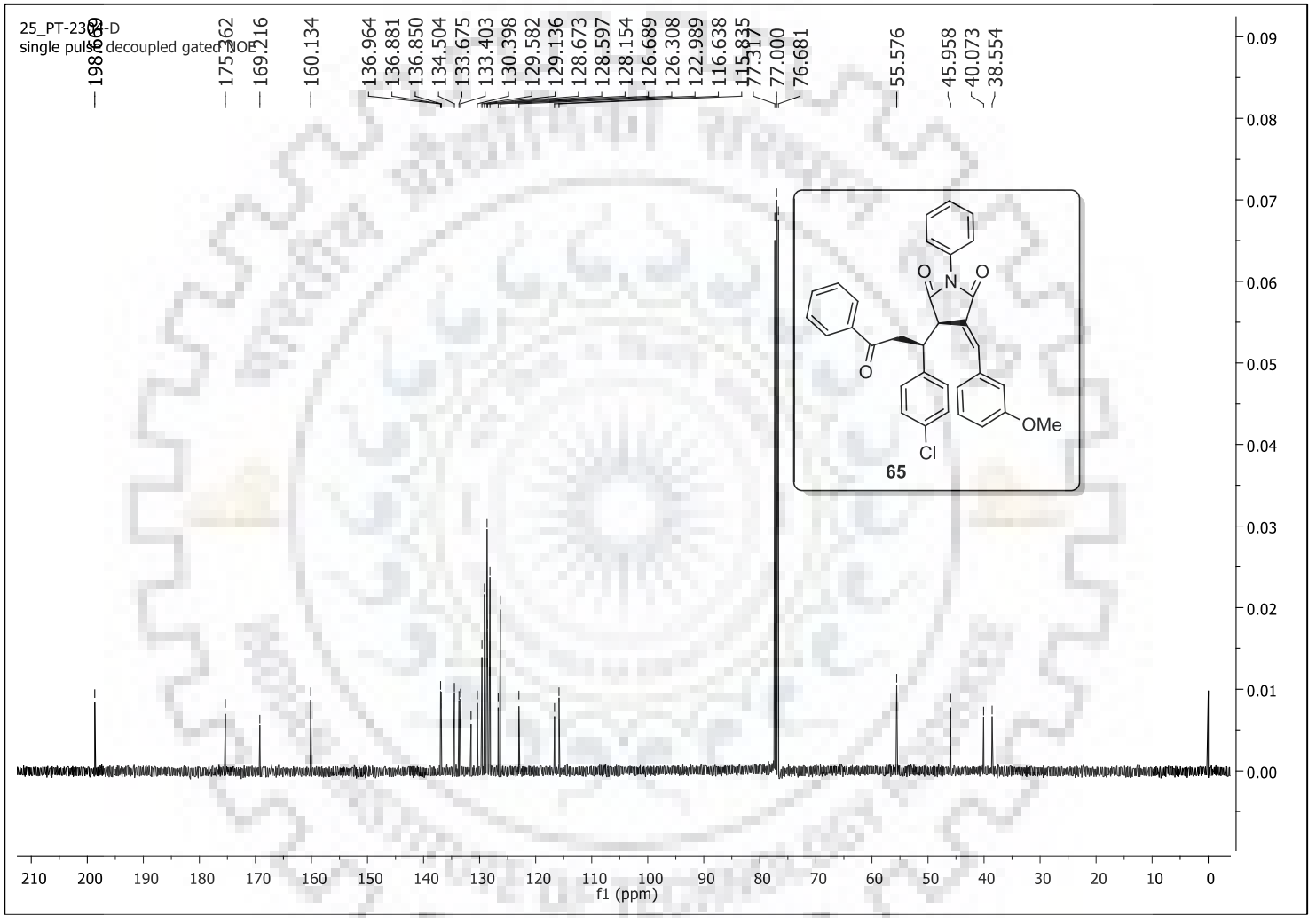


Figure S-56: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **65**.

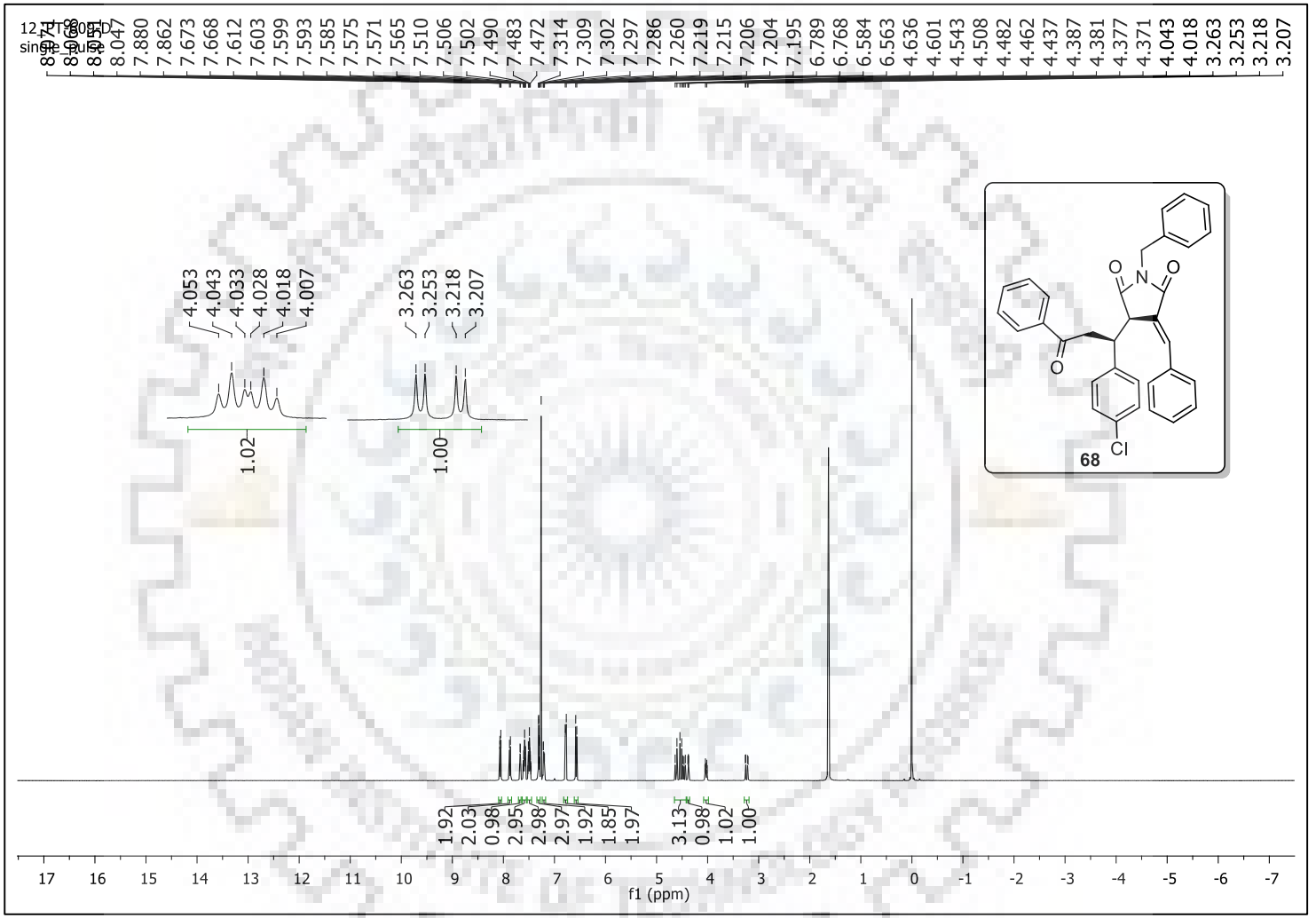


Figure S-57: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **68**.

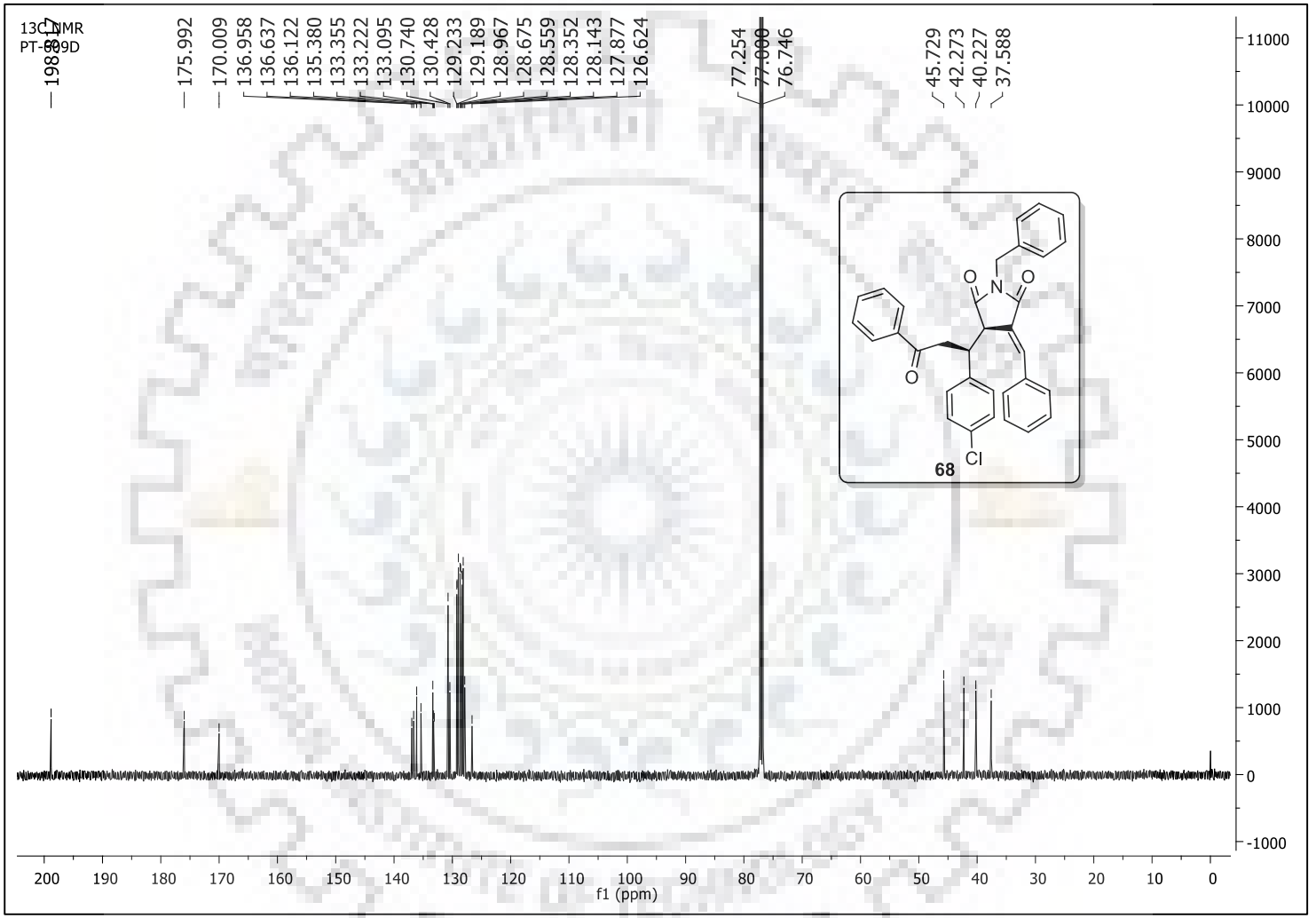


Figure S-58: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **68**.

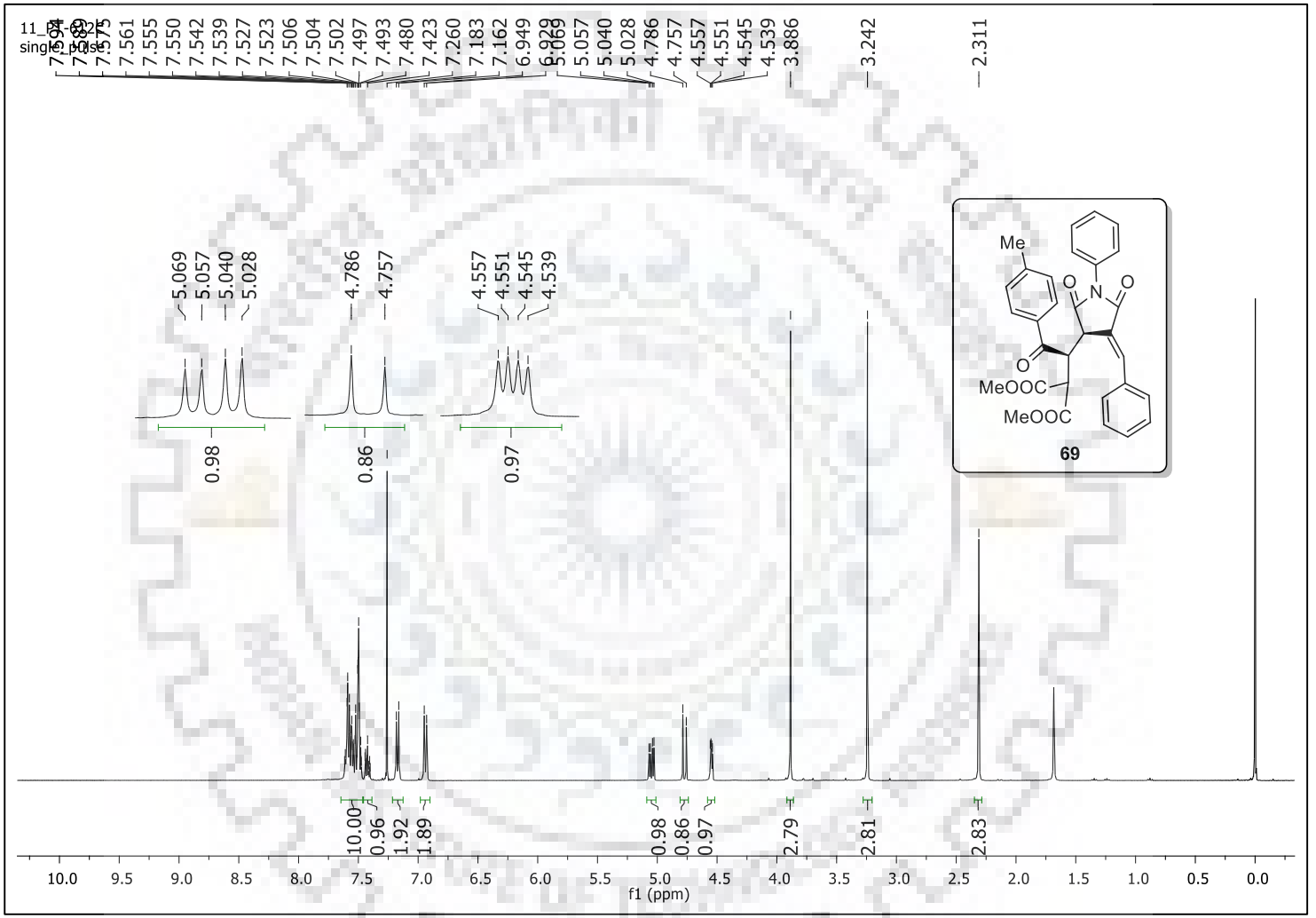


Figure S-59: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **69**.

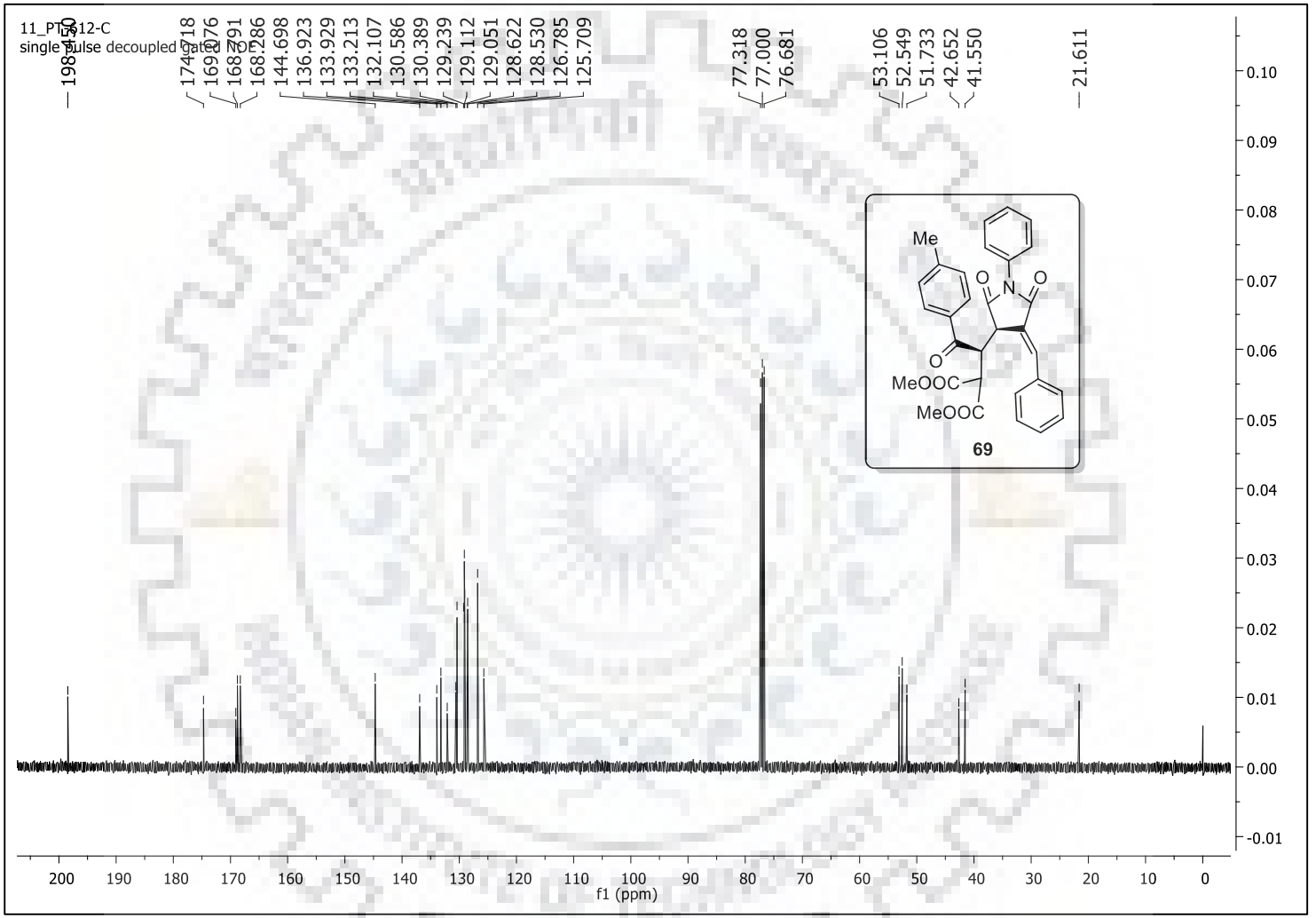


Figure S-60: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **69**.

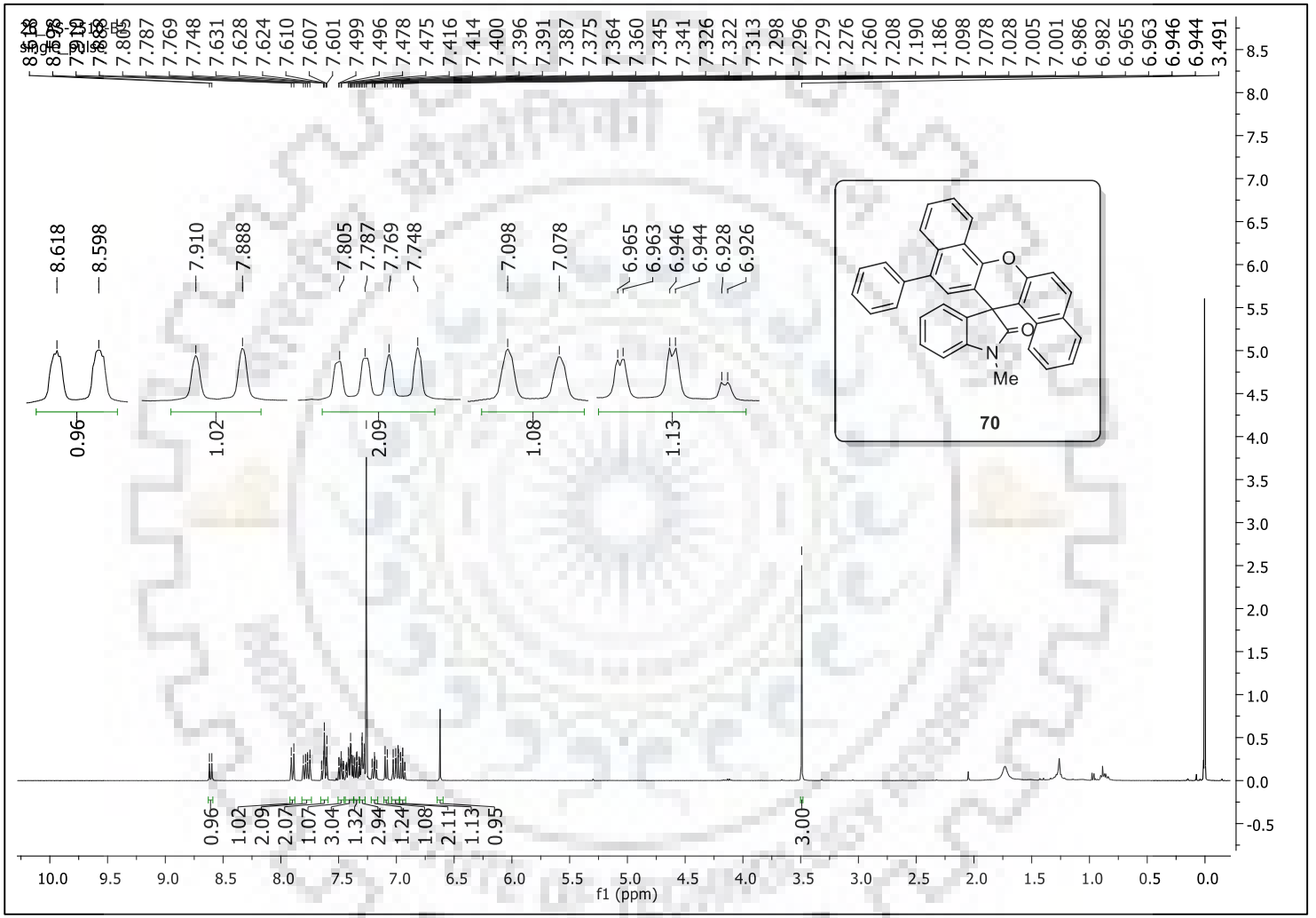


Figure S-61: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **70**.

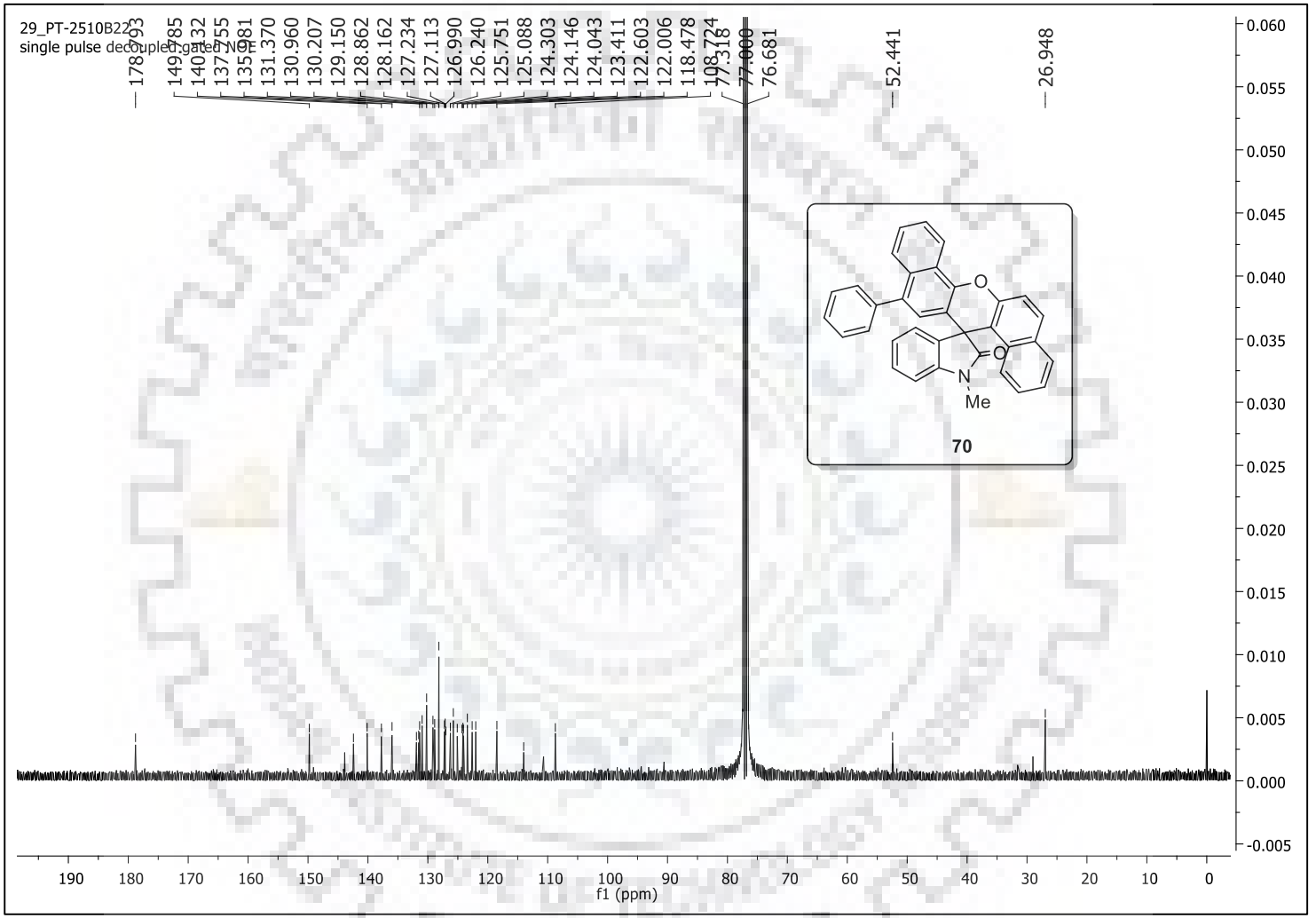


Figure S-62: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **70**.

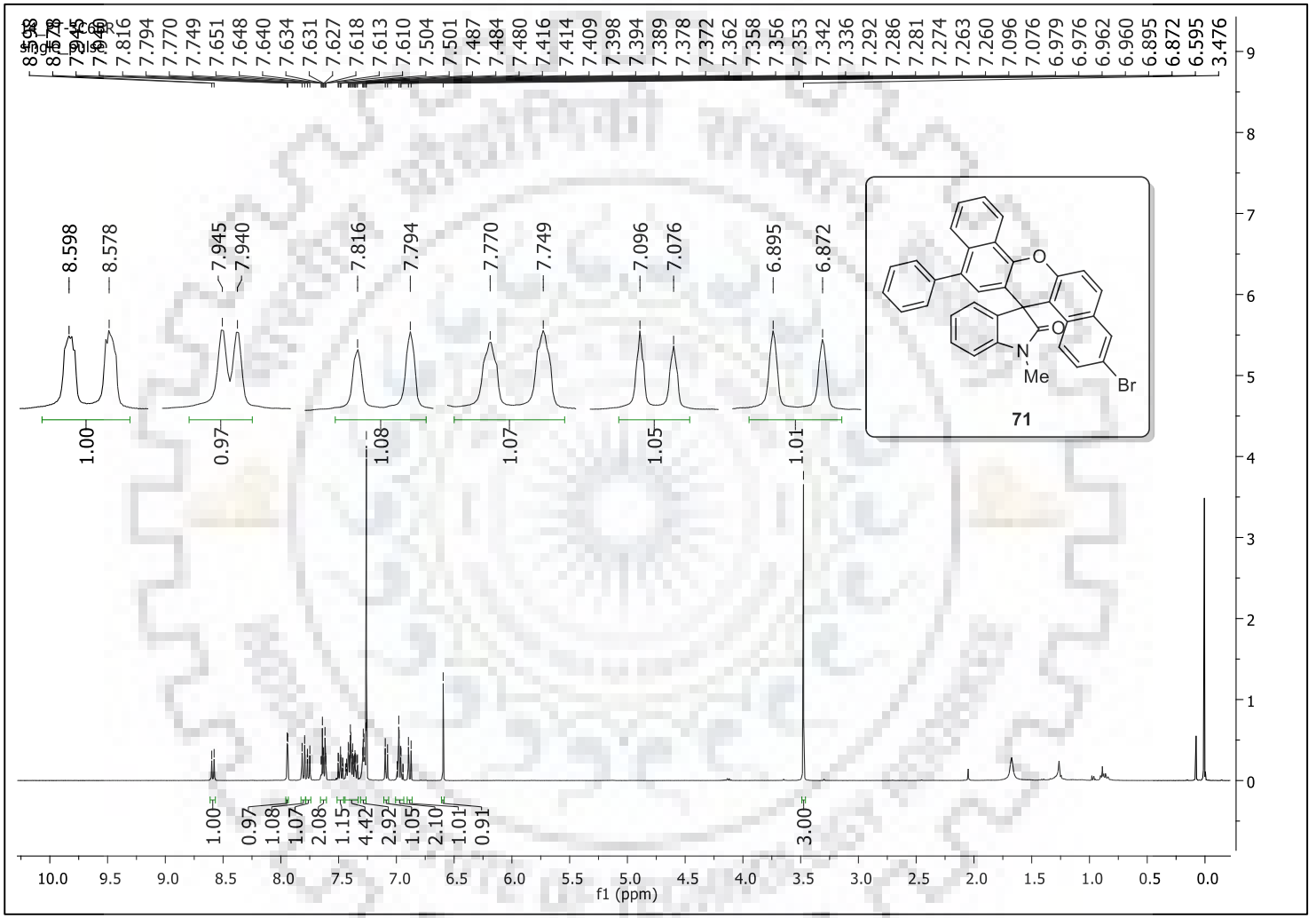


Figure S-63: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **71**.

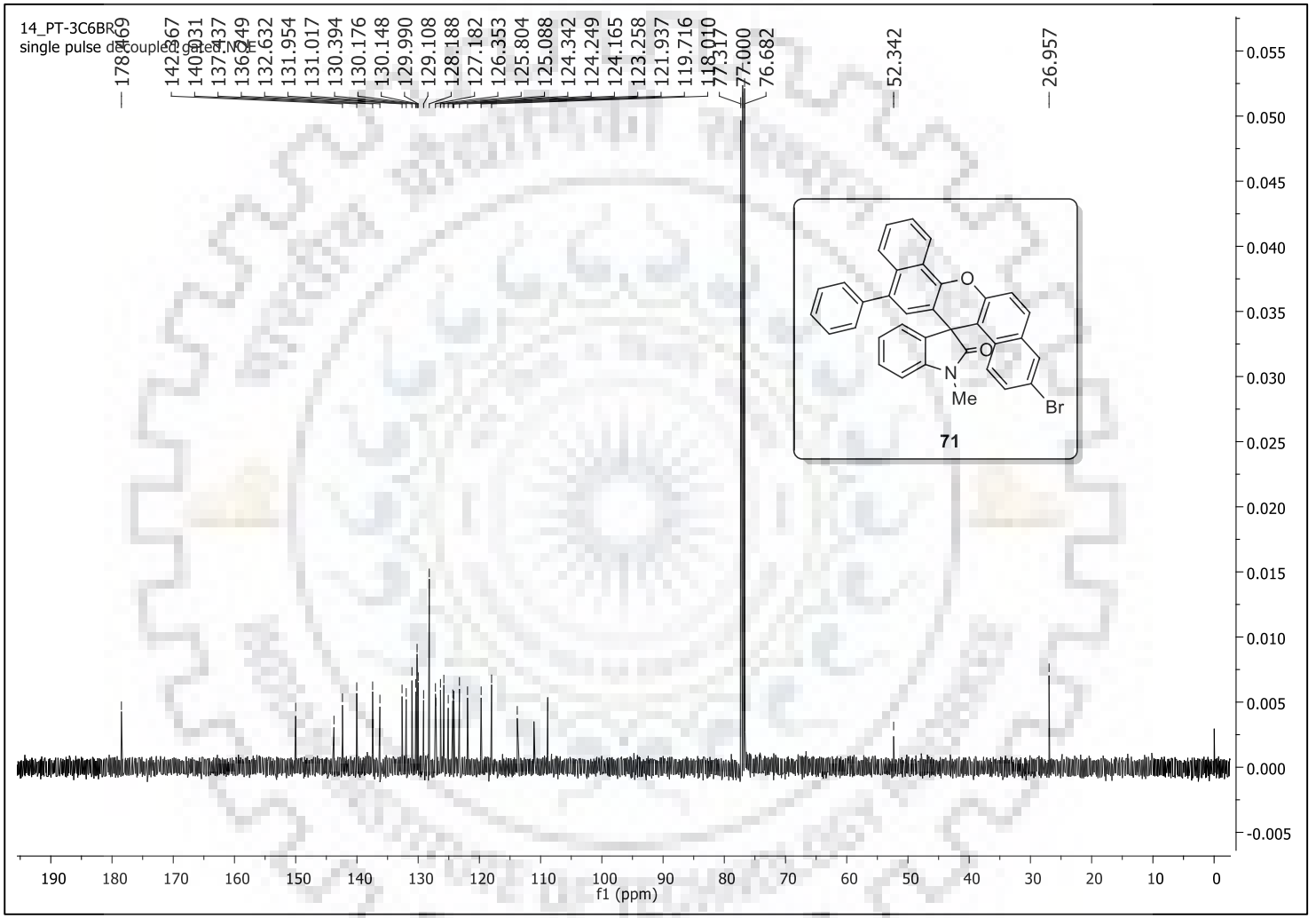


Figure S-64: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **71**.

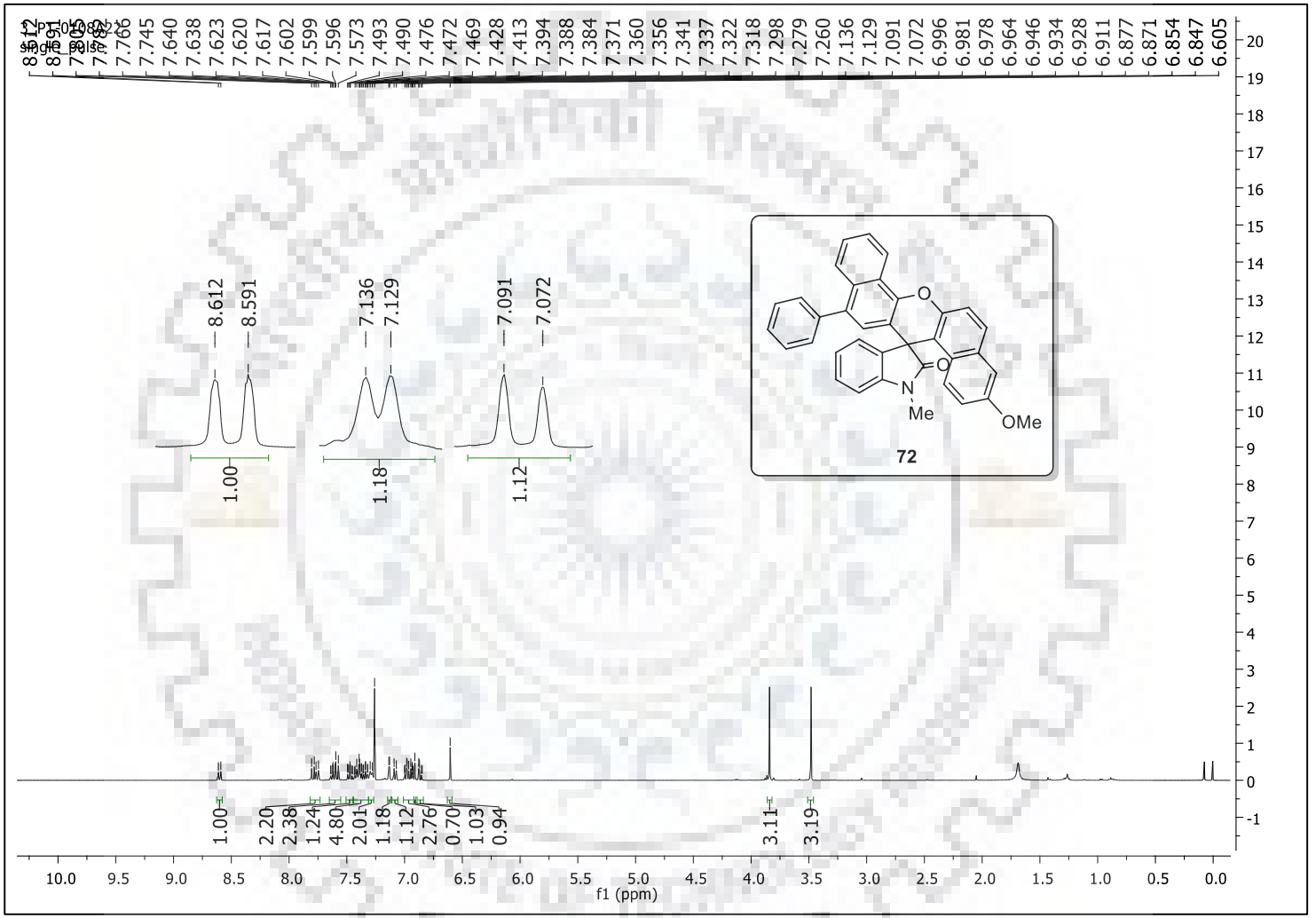


Figure S-65: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **72**.

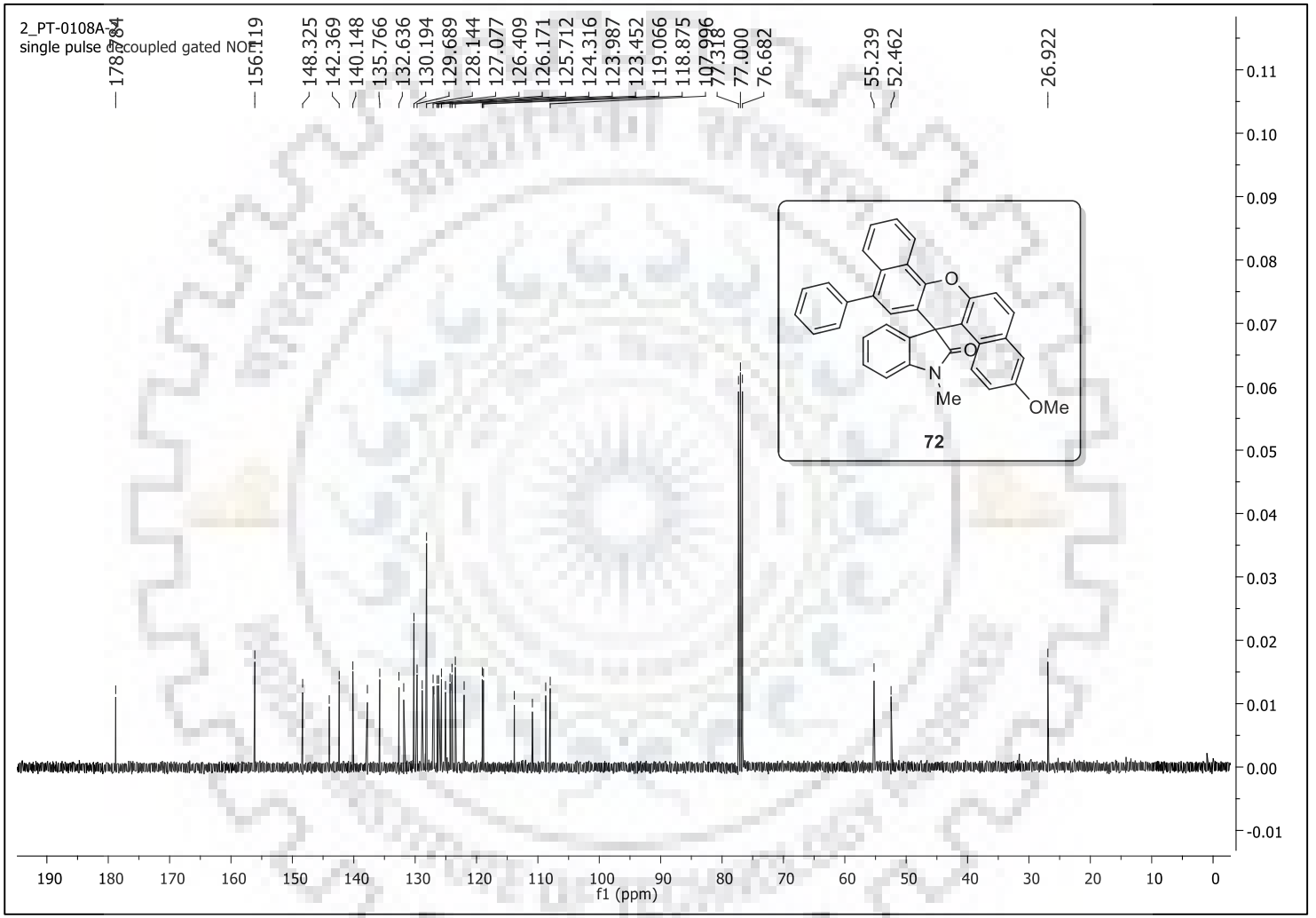


Figure S-66: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **72**.

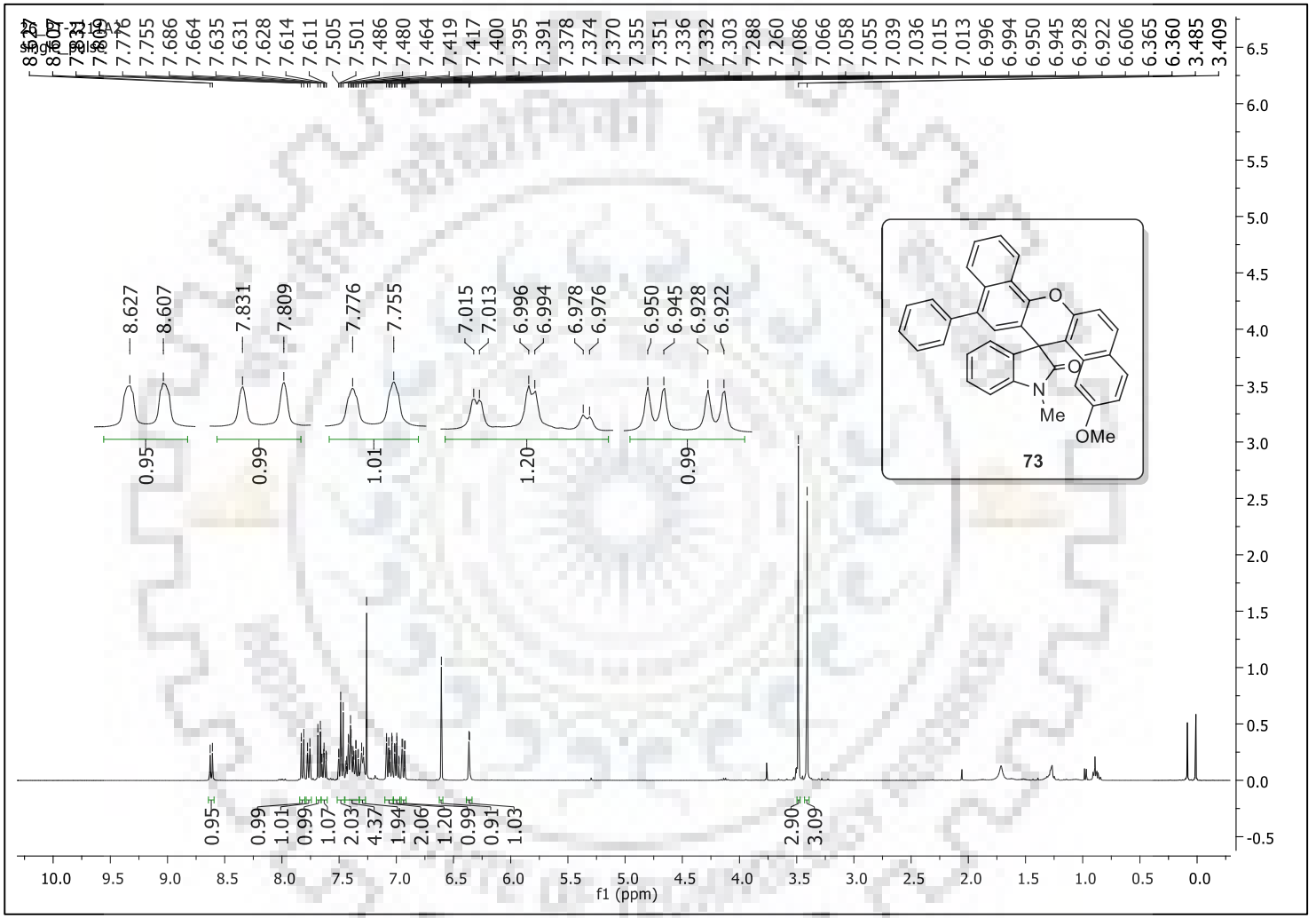


Figure S-67: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **73**.

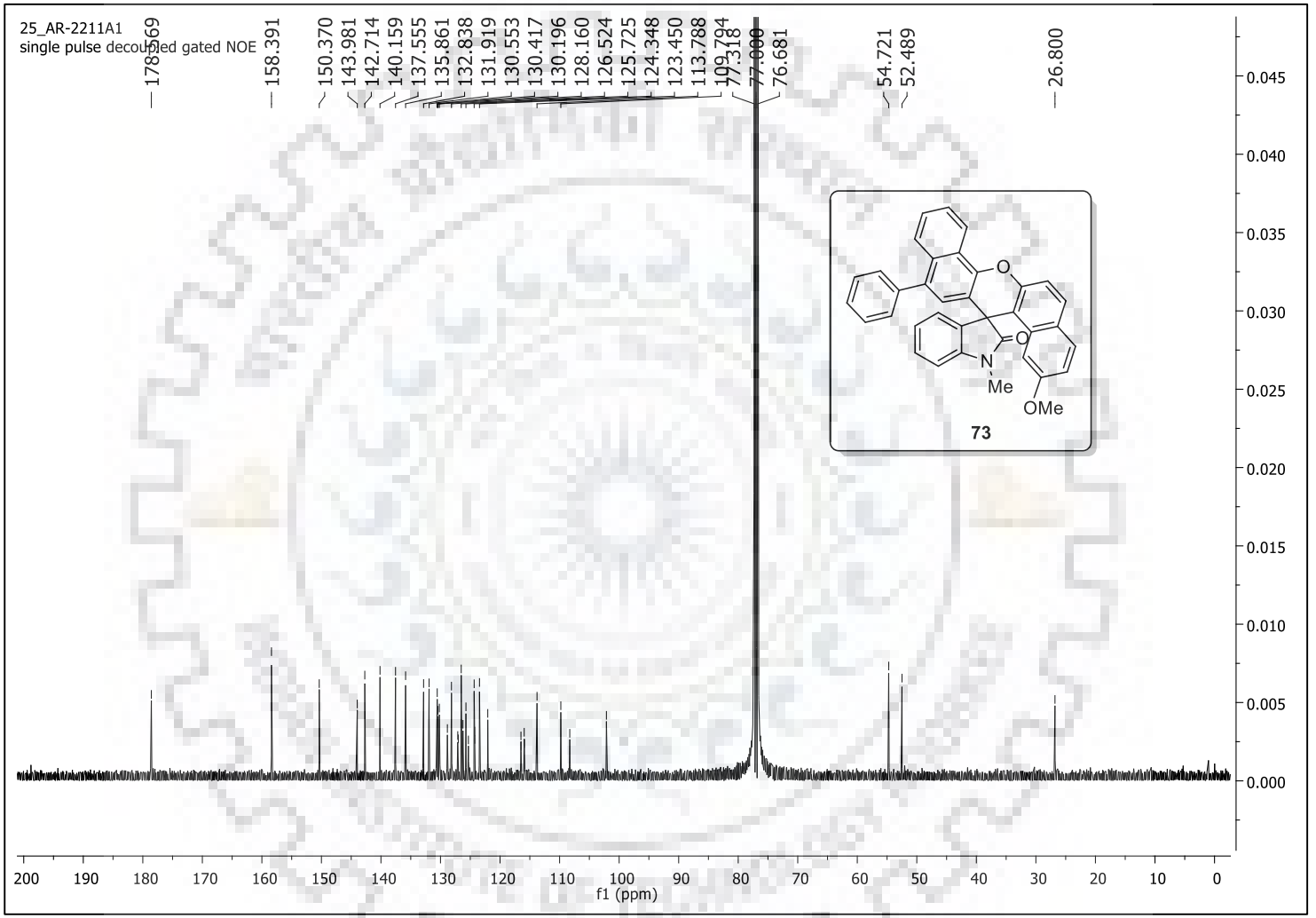


Figure S-68: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **73**.

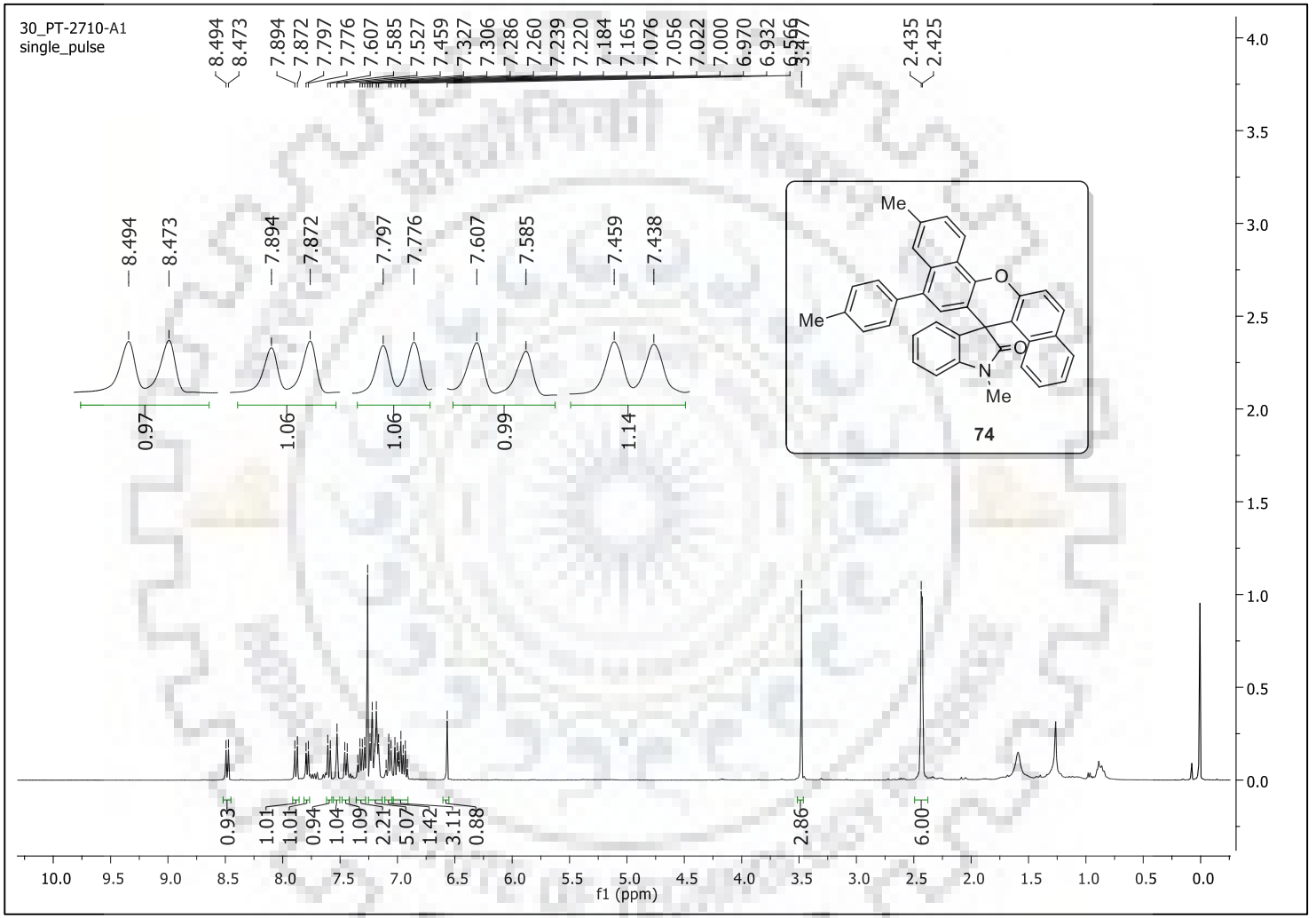


Figure S-69: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **74**.

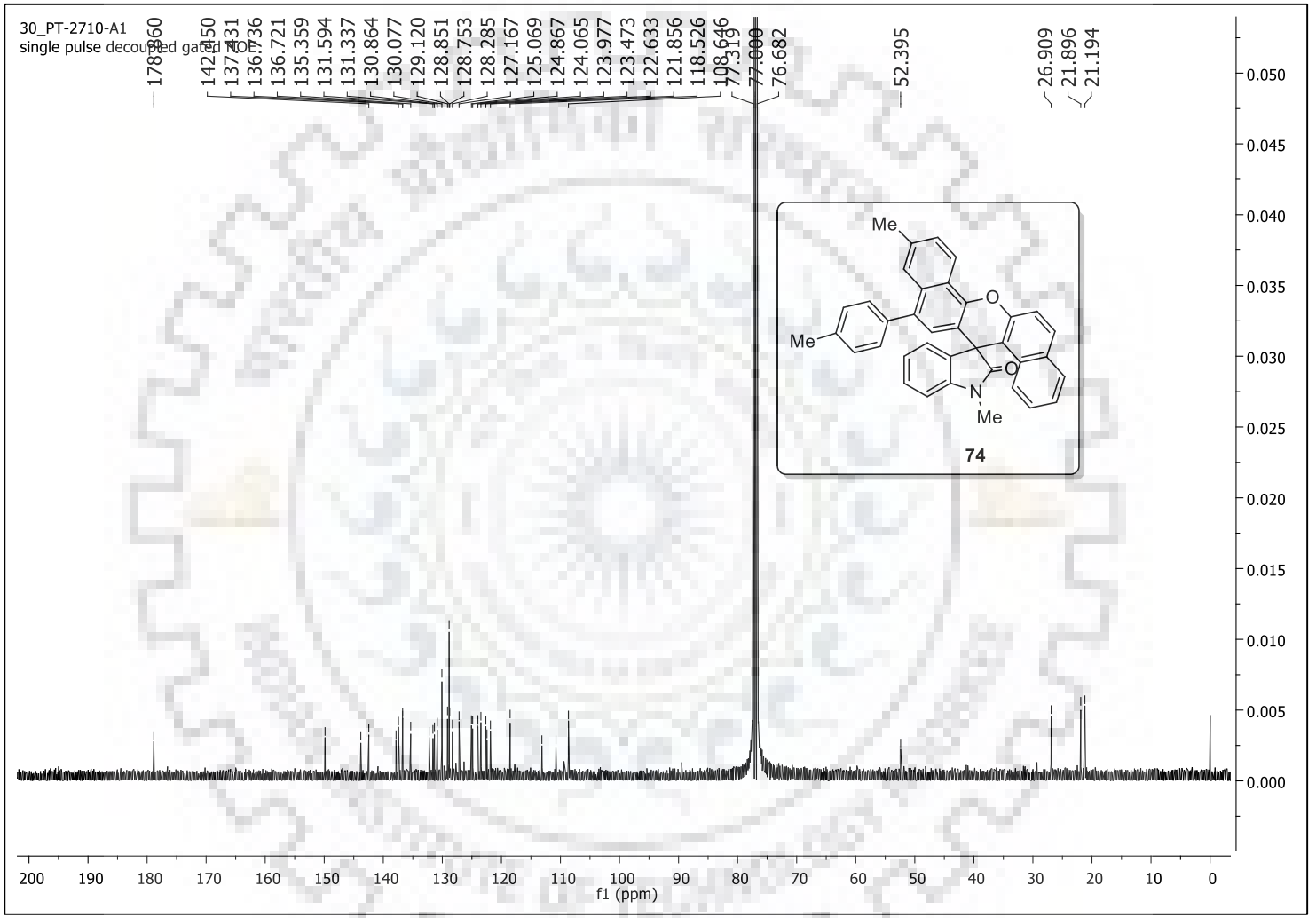


Figure S-70: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **74**.

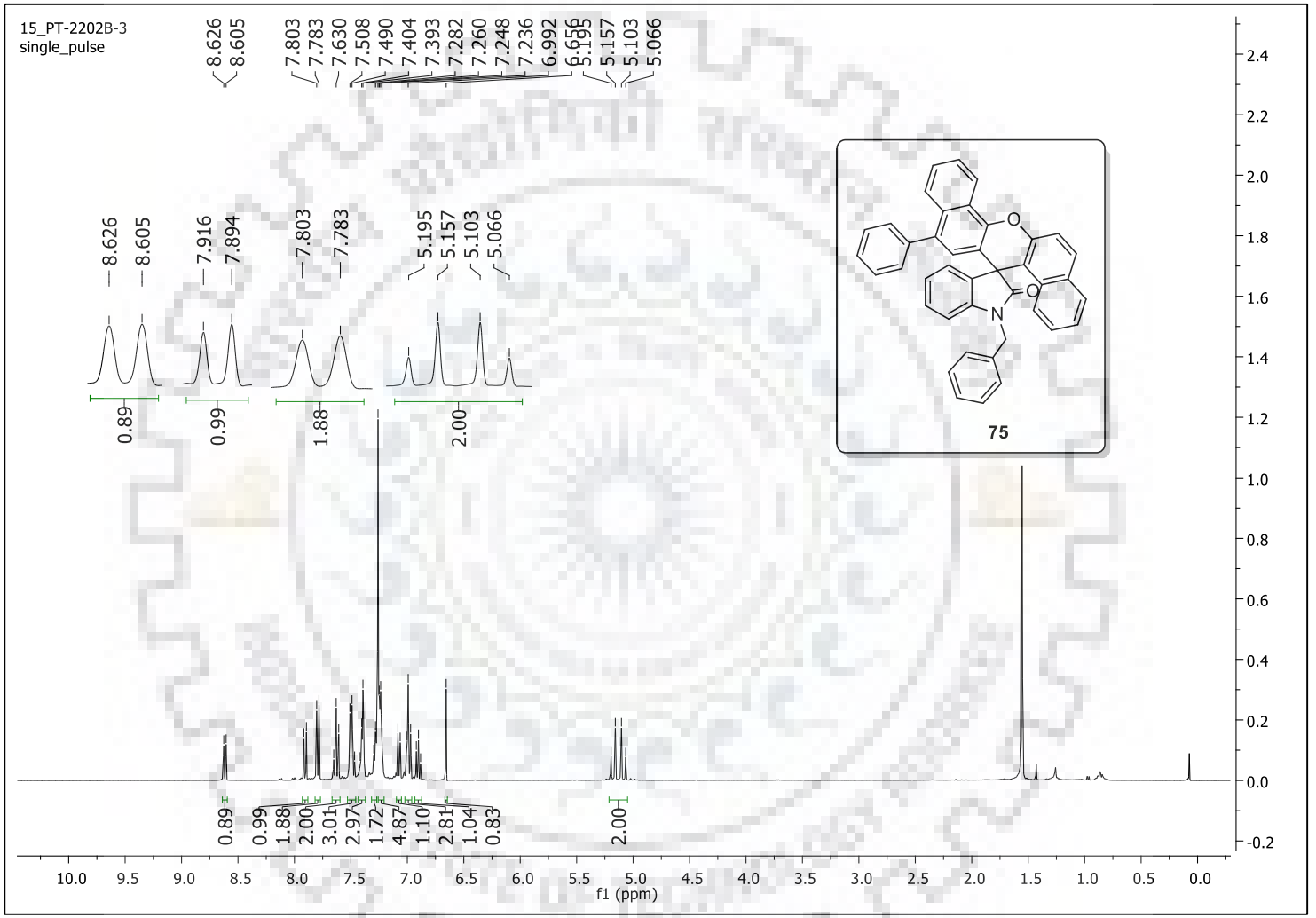


Figure S-71: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **75**.

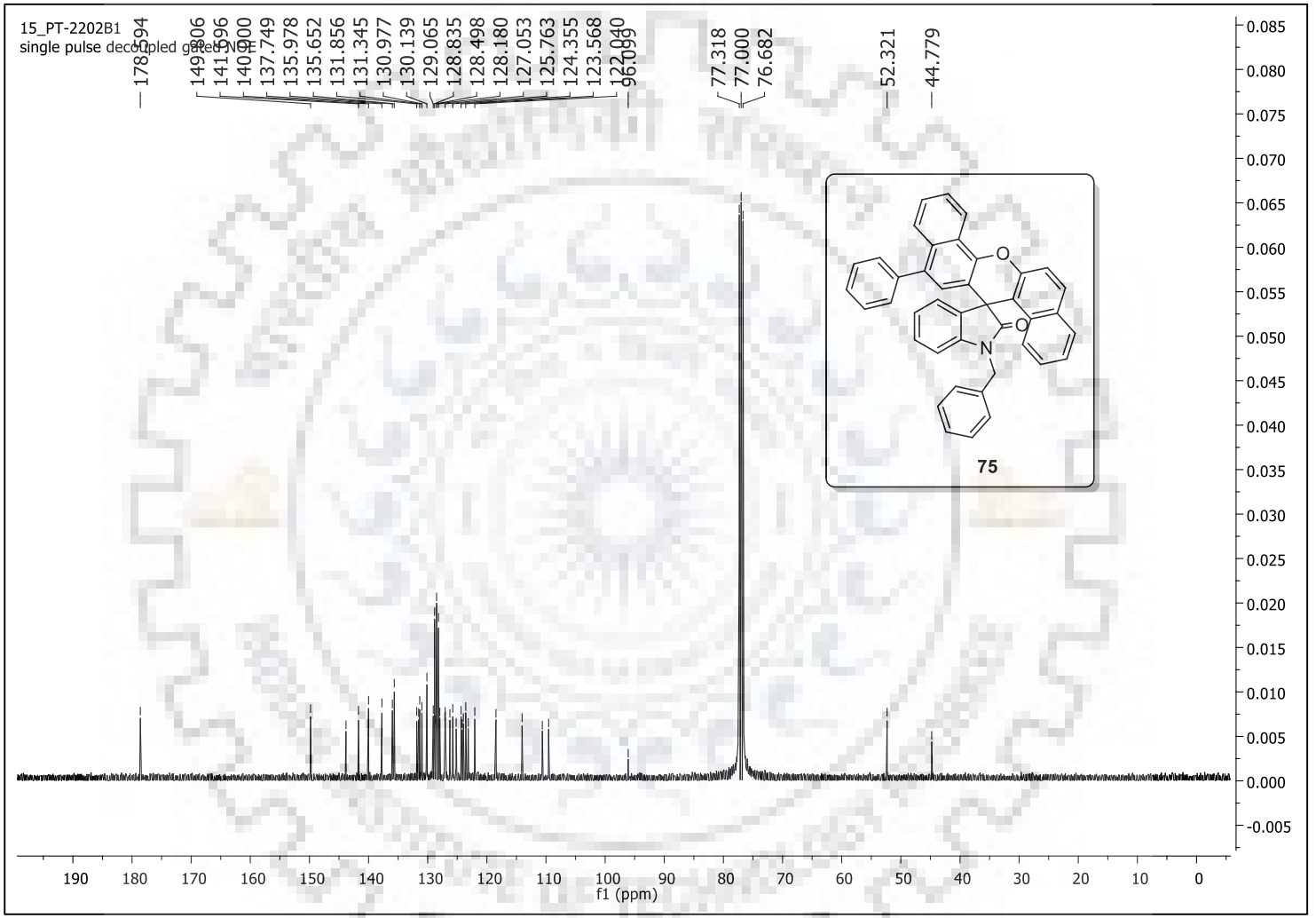


Figure S-72: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **75**.

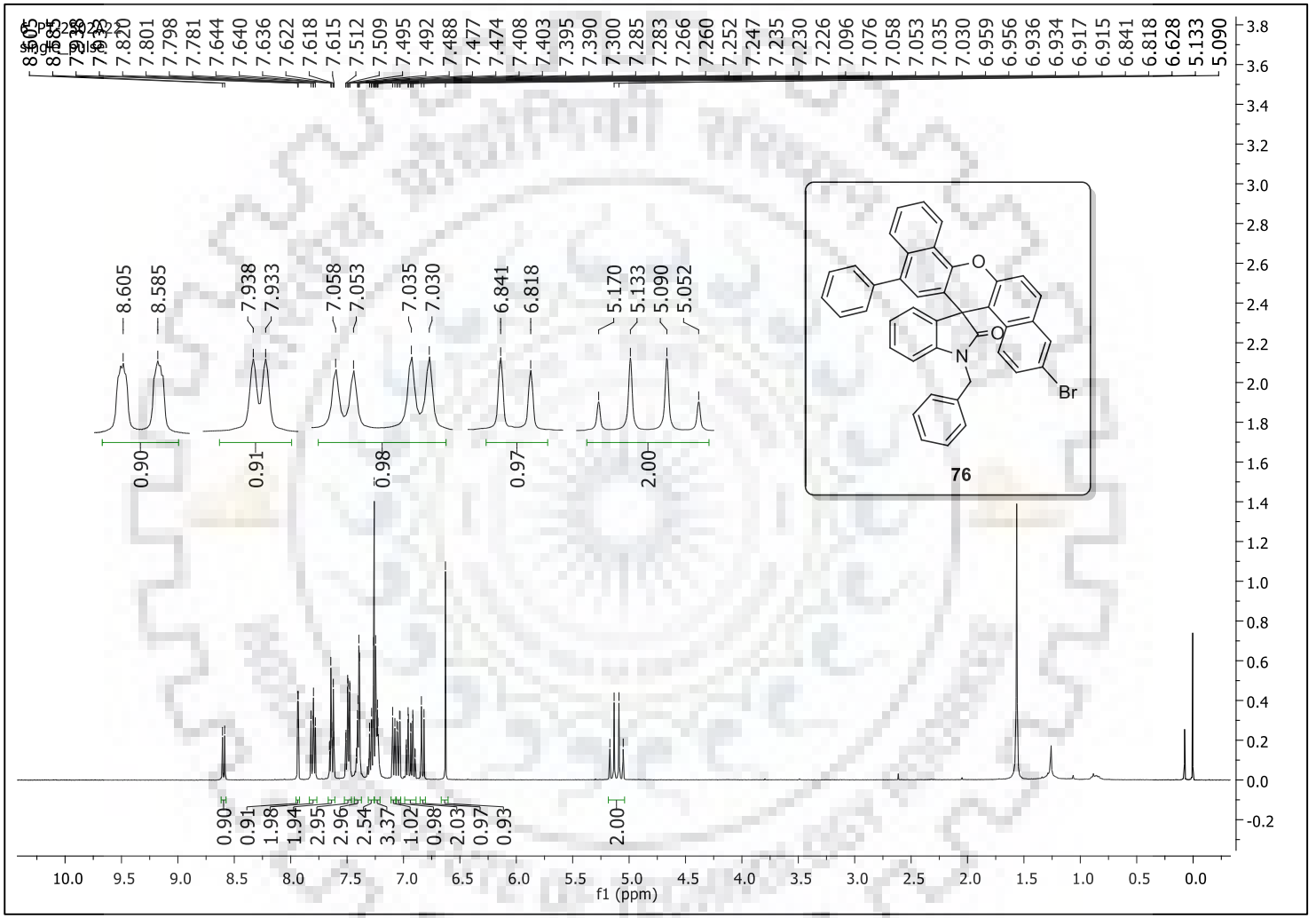


Figure S-73: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **76**.

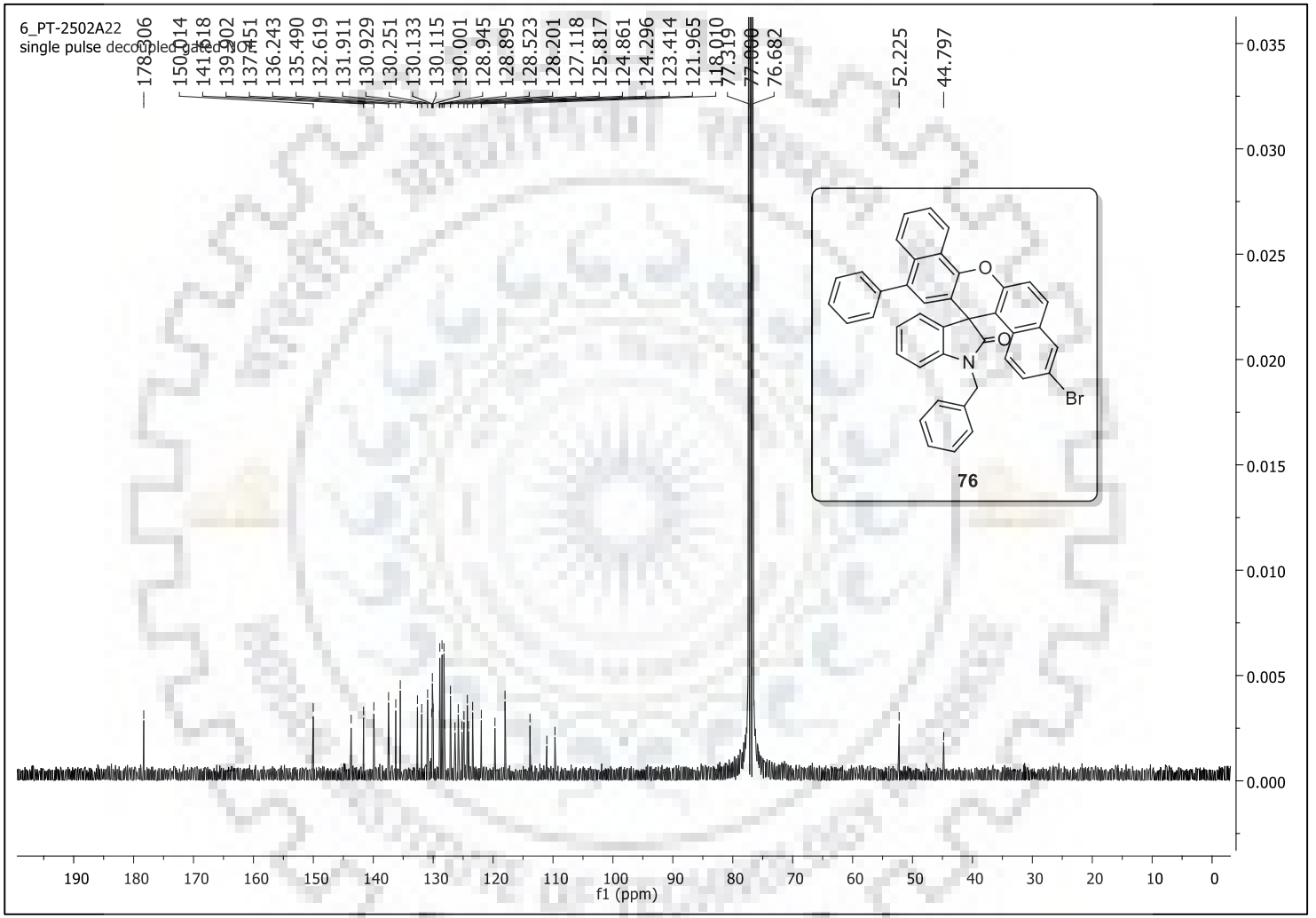


Figure S-74: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **76**.

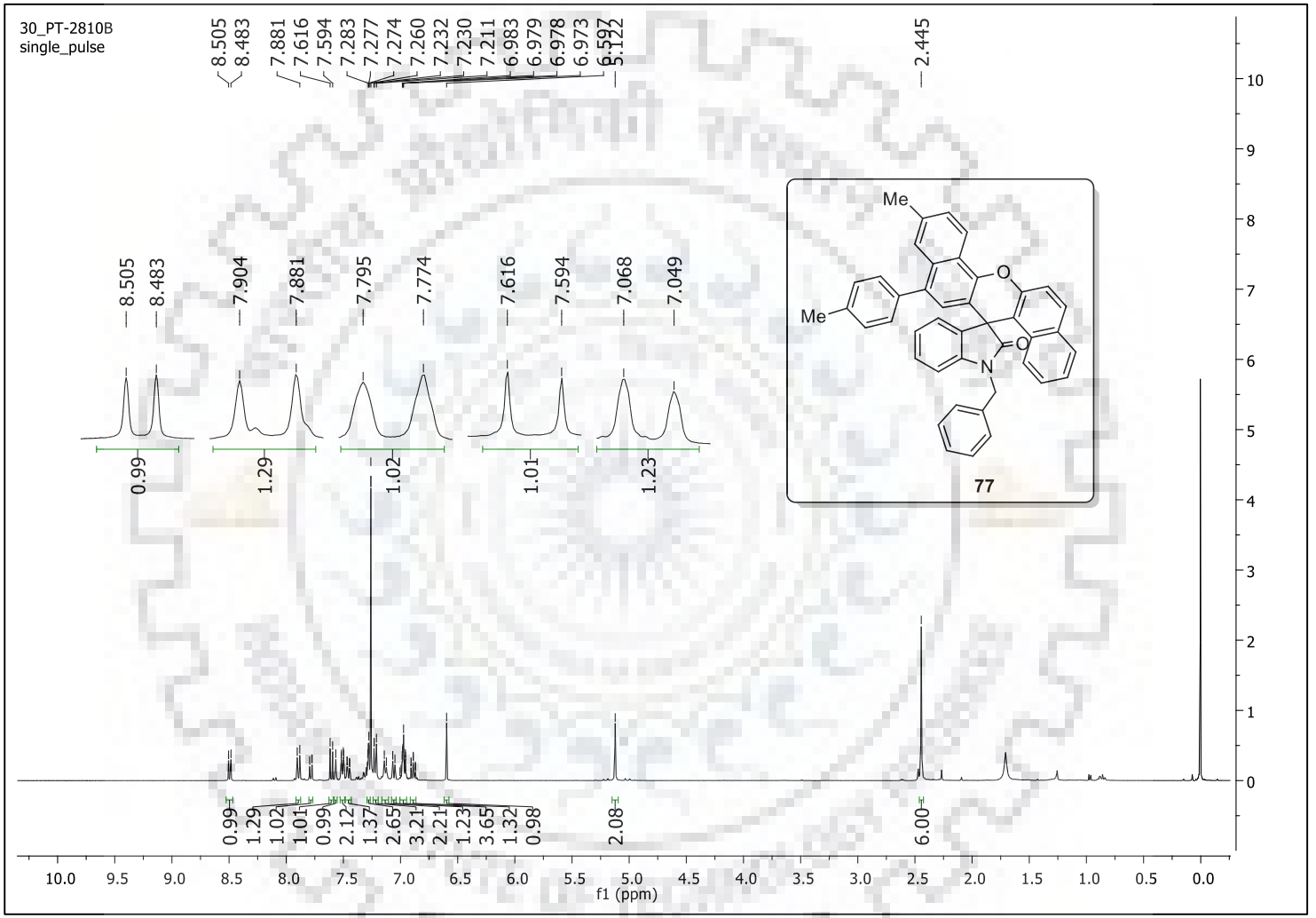


Figure S-75: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **77**.

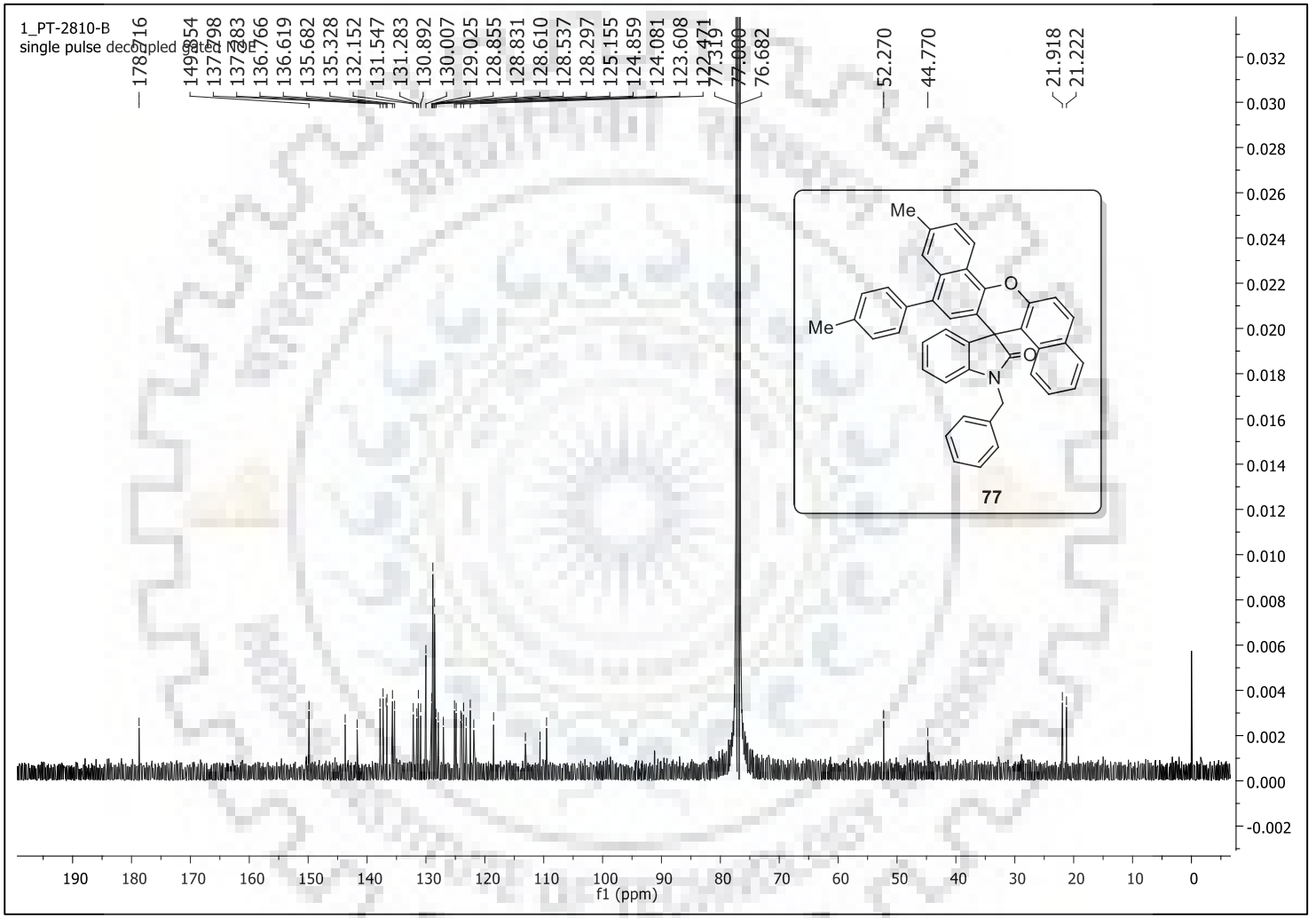


Figure S-76: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **77**.

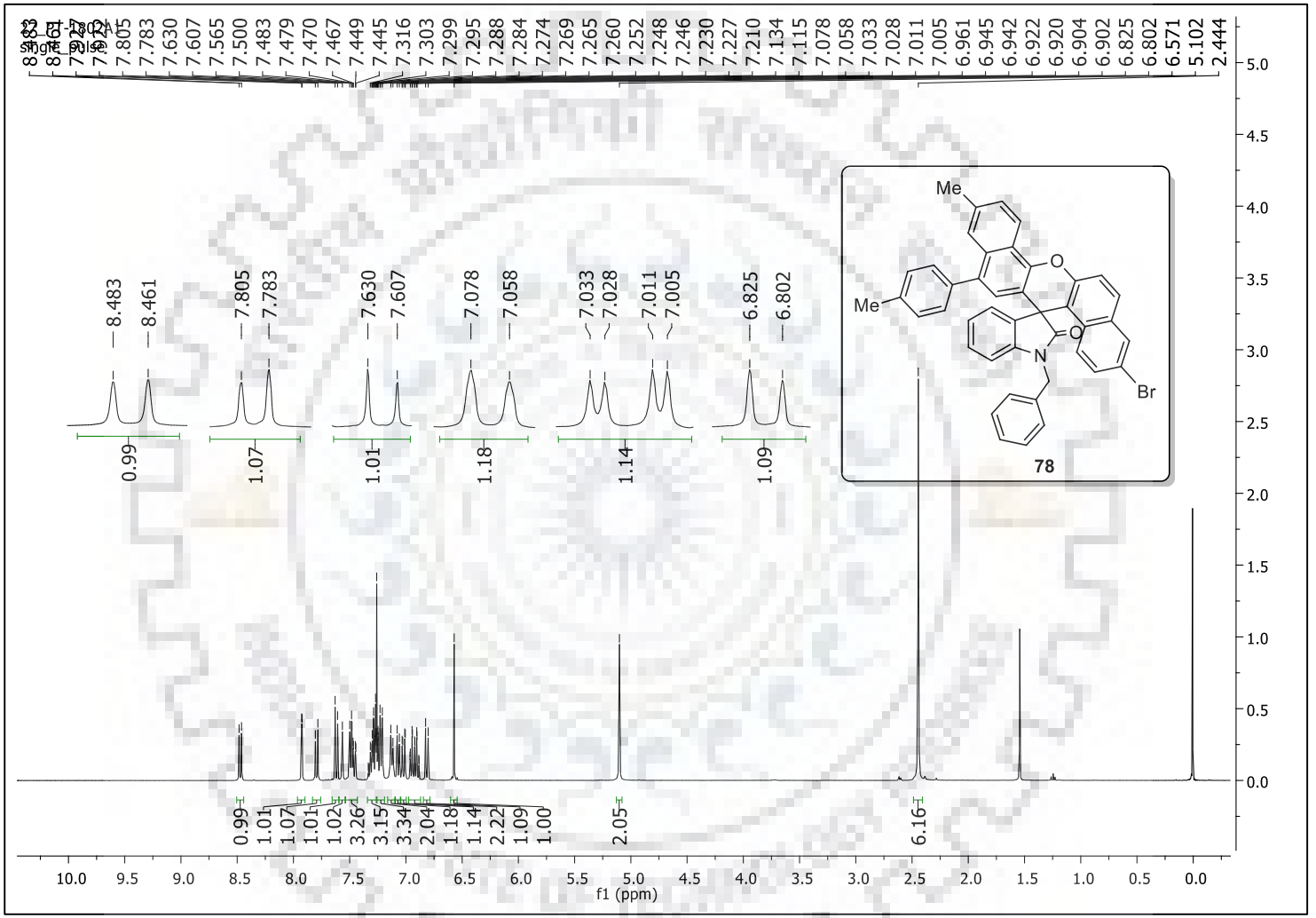


Figure S-77: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **78**.

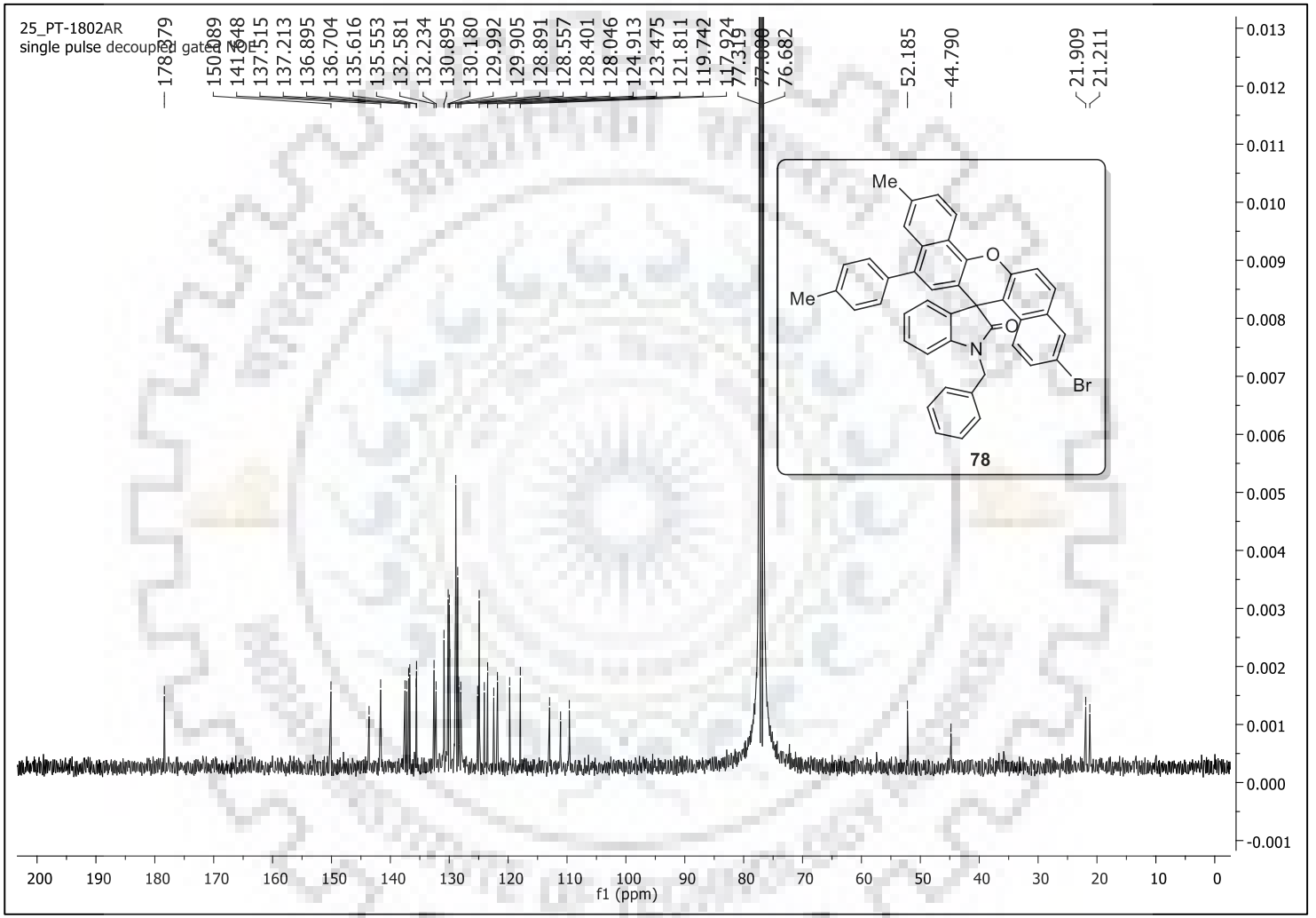


Figure S-78: ^{13}C NMR (100 MHz, $CDCl_3$) Spectrum of **78**.

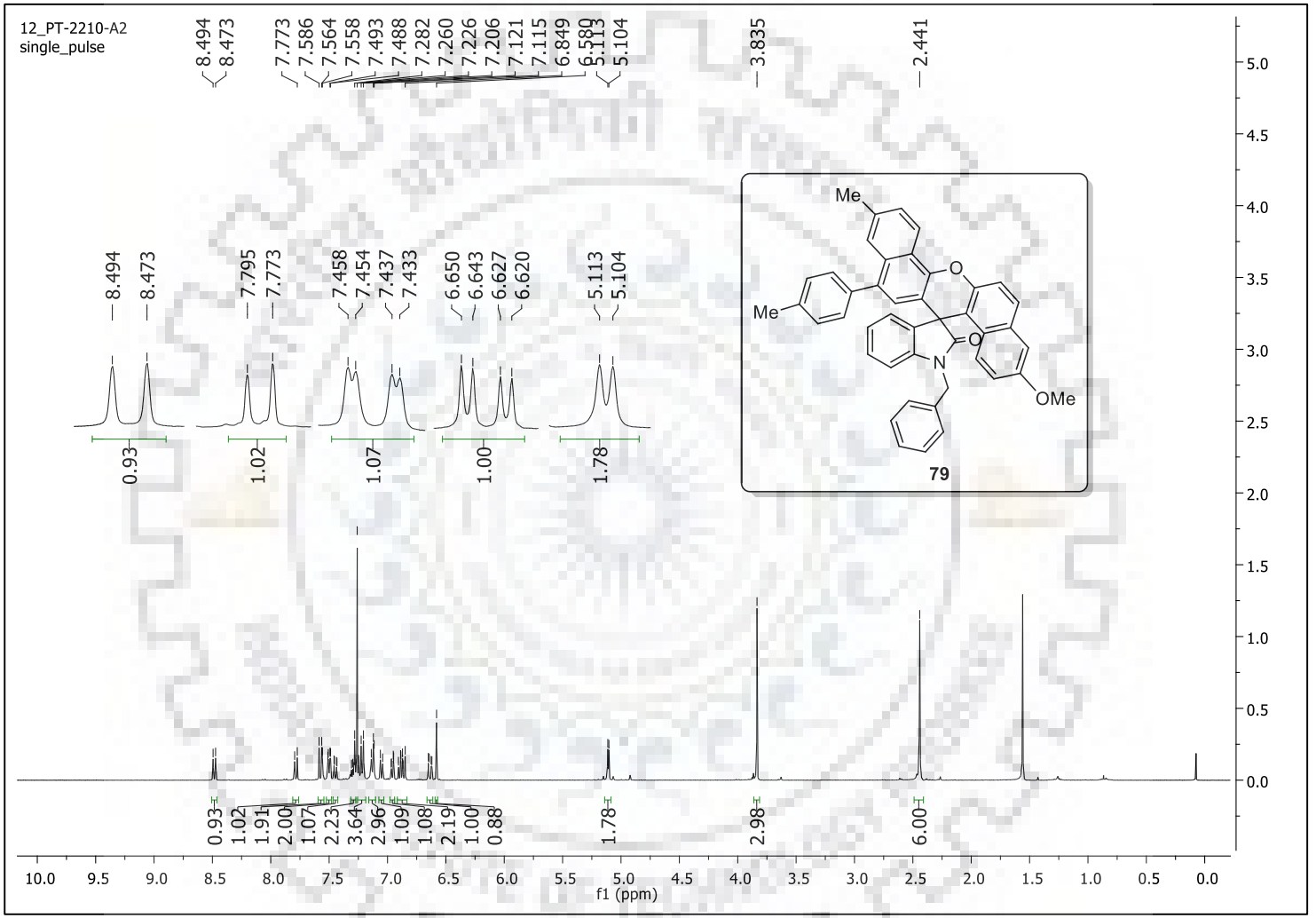


Figure S-79: ^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of **79**.

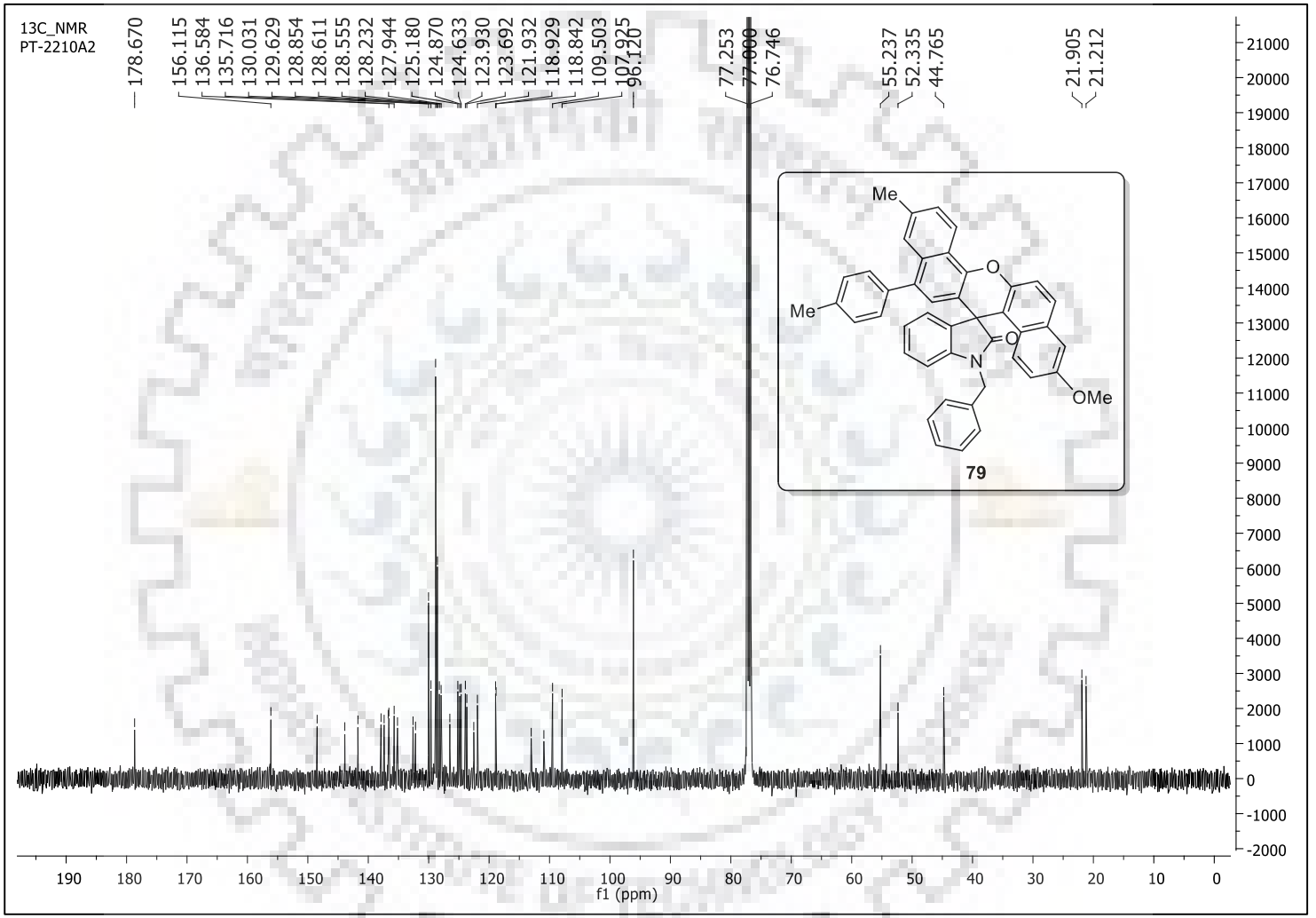
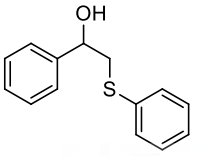


Figure S-80: ^{13}C NMR (125 MHz, $CDCl_3$) Spectrum of **79**.

Structures of compounds synthesized



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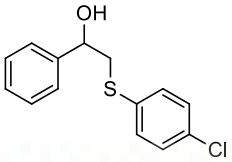

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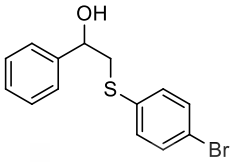

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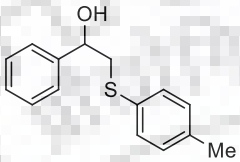

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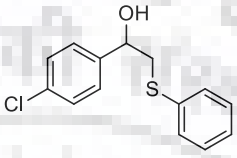

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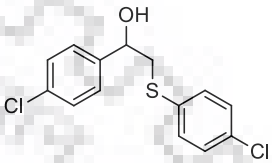

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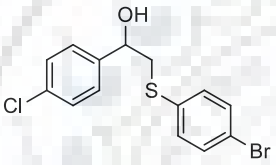

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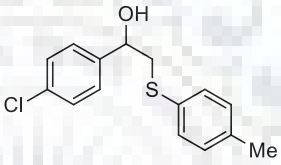

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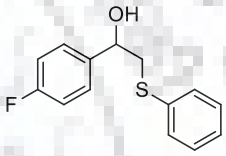

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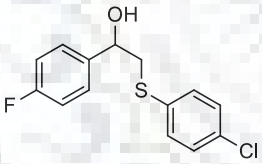

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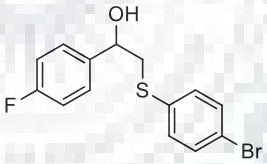

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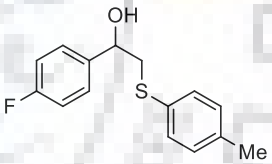

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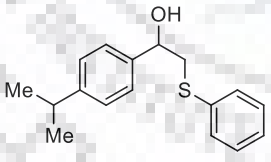

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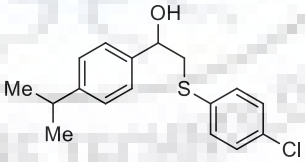

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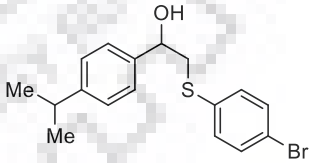

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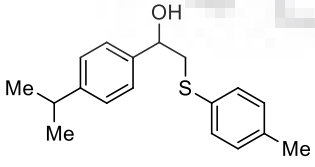

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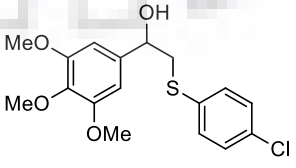

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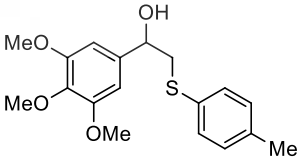

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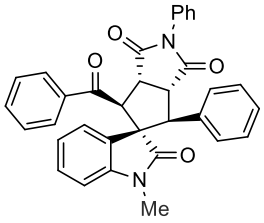

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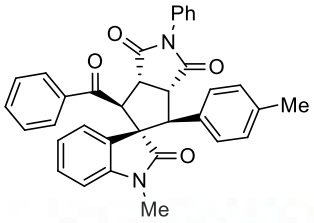

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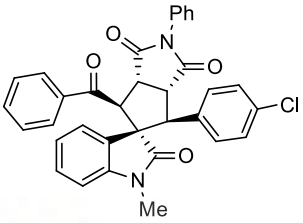

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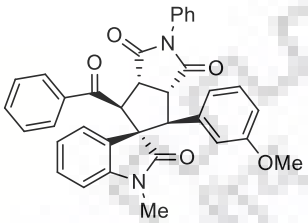

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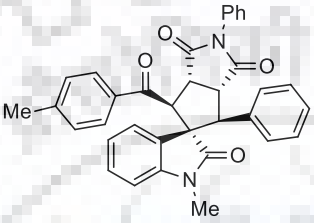

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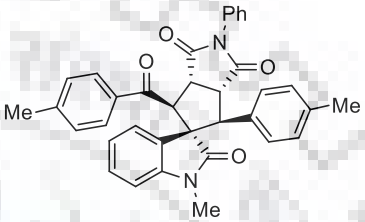

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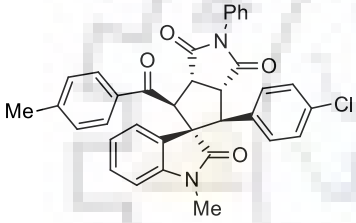

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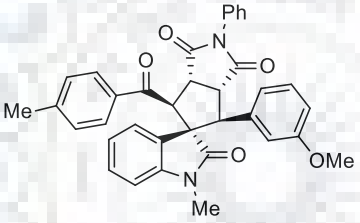

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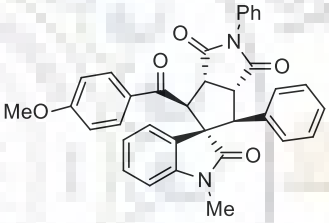

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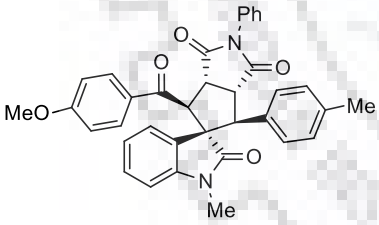

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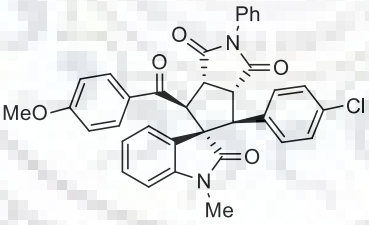

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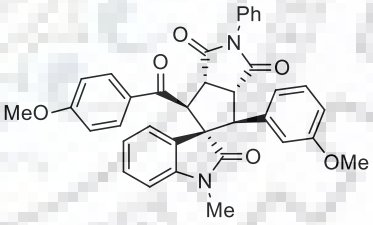

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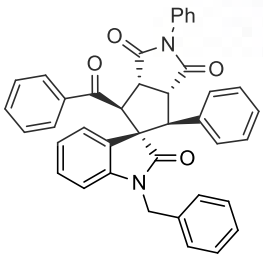

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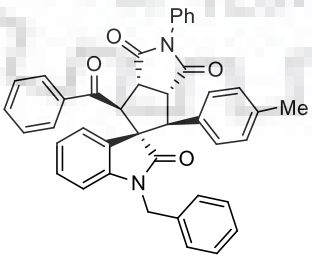

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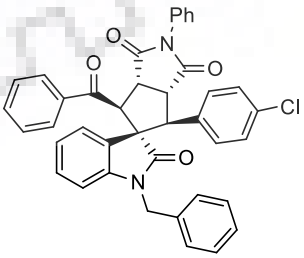

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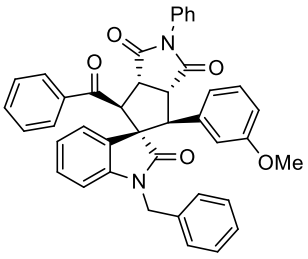

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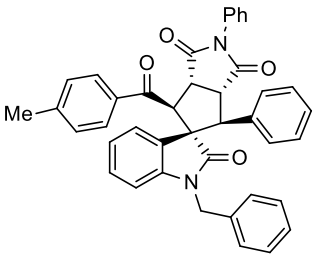

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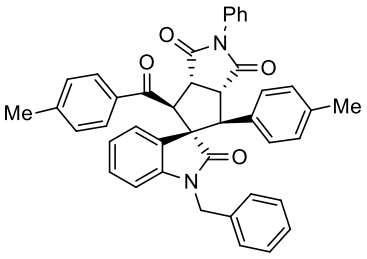

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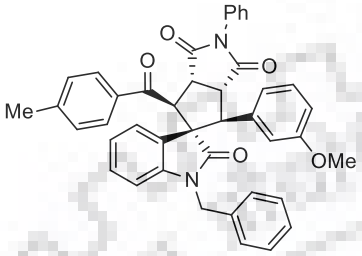

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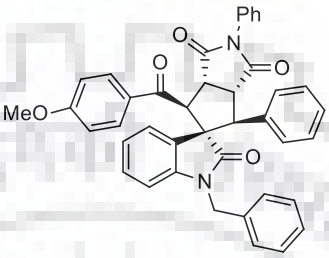

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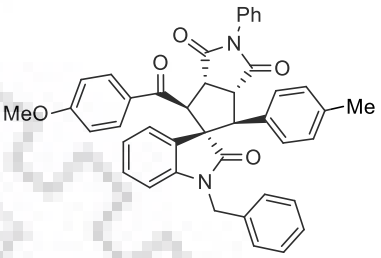

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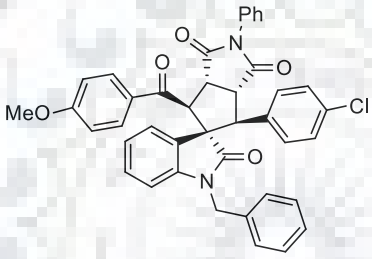

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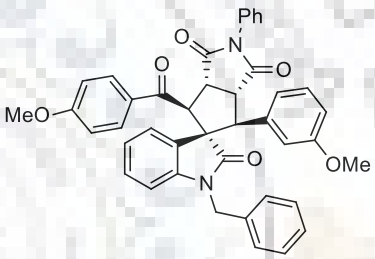

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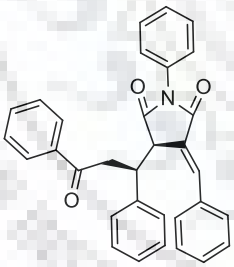

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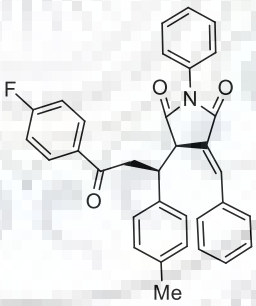

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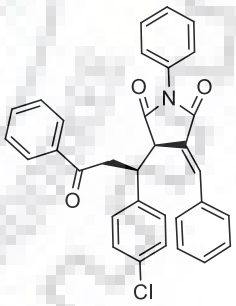

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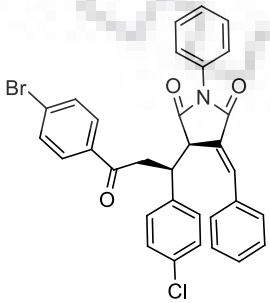

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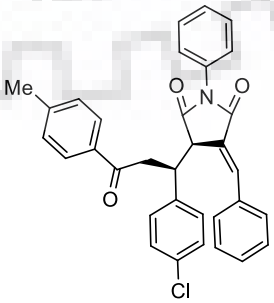

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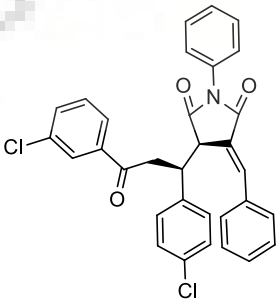

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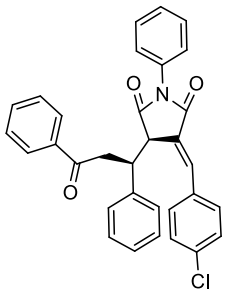

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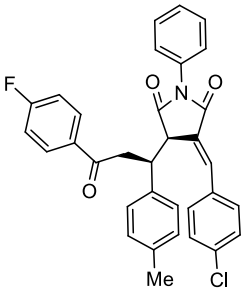

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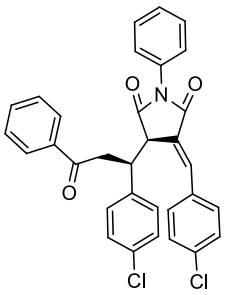

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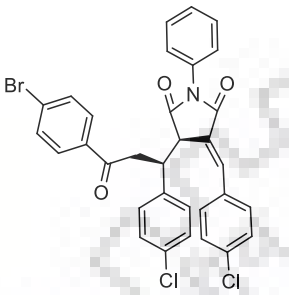

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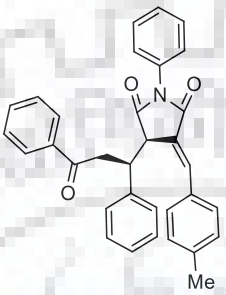

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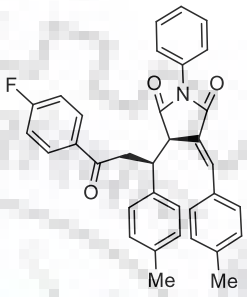

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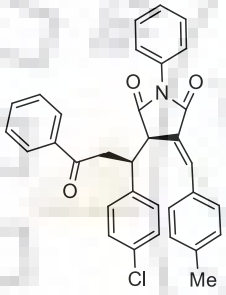

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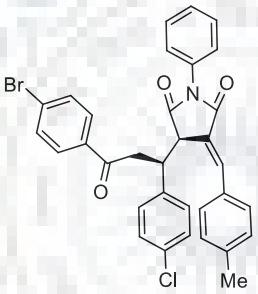

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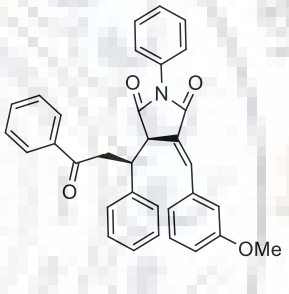

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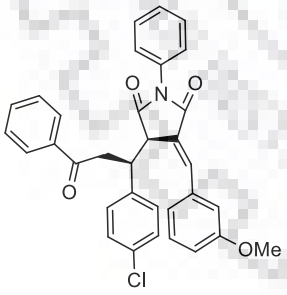

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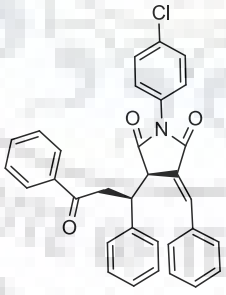

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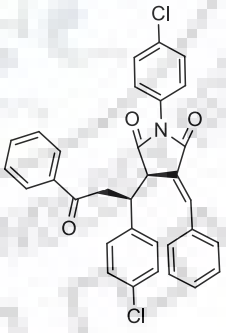

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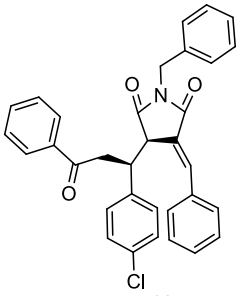

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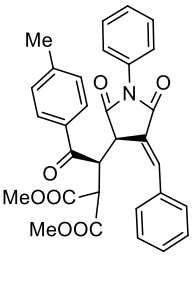

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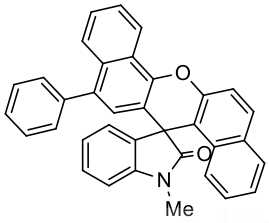

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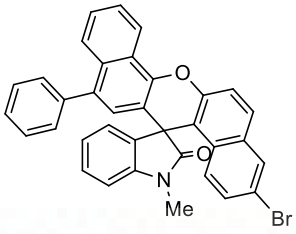

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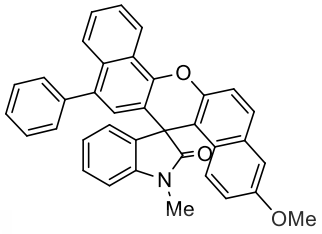

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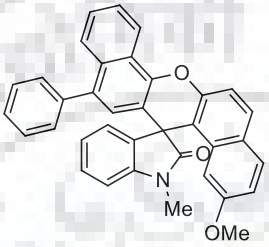

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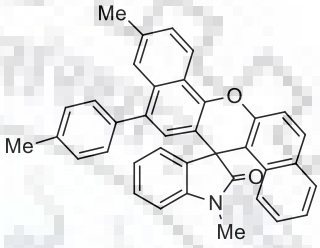

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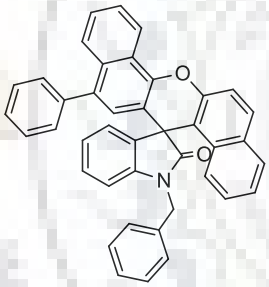

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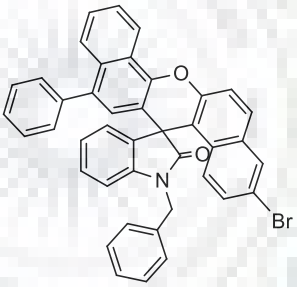

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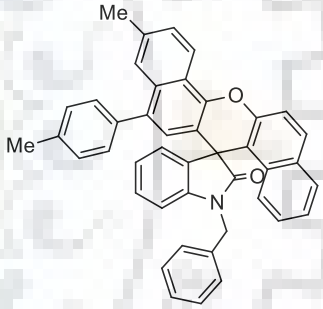

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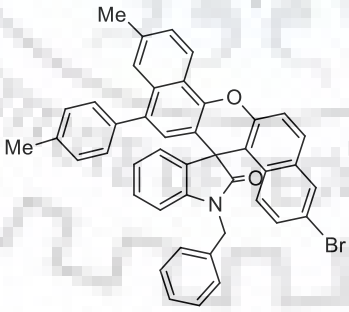

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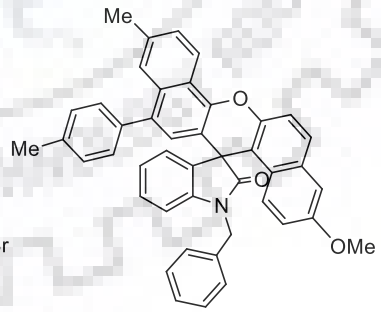

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List of publications

1 Iodine-catalysed regioselective synthesis of *β*-hydroxy sulfides.
Tehri, P.; Aegurula, B.; Peddinti, R. K.
Tetrahedron Lett. **2017**, *58*, 2062.

2 DBU-catalyzed [3 + 2] cycloaddition and Michael addition reactions of 3-benzylidene succinimides with 3-ylidene oxindoles and chalcones.
Tehri, P.; Peddinti, R. K.
Org. Biomol. Chem. **2019**, *17*, 3964.

3 Bronsted acid mediated domino approach: Access to xanthene-tethered unsymmetrical biarylic spirooxindoles from spirooxindolic donor-acceptor cyclopropanes.
Tehri, P.; Peddinti, R. K.
Manuscript under preparation.

Conferences attended

1 Poster Presentation in "CRSI 2017, 21st National symposium in chemistry" held at CSIR-Indian Institute of Chemical Technology (IICT), Hyderabad during July 14th –16th, 2017.

2 Attended "CFOS 2017, National symposium in organic chemistry" held at Indian Institute of Technology (IIT) Roorkee, Roorkee during 22nd–24th December, 2017.

3 Poster Presentation in "XIV J-NOST 2018, National conference for organic chemistry research scholars" held at CSIR-Indian Institute of Chemical Technology (IICT), Hyderabad during Nov 28th – Dec 1th, 2018.

4 Poster Presentation in "OMSRI 2018, National conference in organic chemistry" held at Indian Institute of Technology (IIT) Roorkee, Roorkee during 22nd–24th December, 2017.