SYNTHESIS OF HETEROCYCLES & CARBOCYCLES USING BAYLIS-HILLMAN ADDUCTS AND SYNTHESIS OF INDENE-SPIRO-OXINDOLES USING TANDEM PRINS AND FRIEDEL-CRAFTS REACTIONS

KANUMURI RAMESH REDDY

SCHOOL OF CHEMISTRY

UNIVERSITY OF HYDERABAD

HYDERABAD–500 046

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KANUMURI RAMESH REDDY

SCHOOL OF CHEMISTRY

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ABBREVIATIONS

Ac	acetyl
AcOH	acetic acid
AIBN	azobisisobutyronitrile
aq.	aqueous
BINOL	1,1′-bi-2-naphthol
Bp	boiling point
Bu	butyl
Bt	benzotriazole
t-Bu or Bu^t	*tertiar*y butyl
cat.	catalyst
*m*CPBA	*meta*-chloroperbenzoic acid
DABCO	1,4-diazabicyclo(2.2.2)octane
DBU	1,8-diazabicyclo(5.4.0)undec-7-ene
DCC	1,3-dicyclohexylcarbodiimide
DCE	1,2-dichloroethane
DCM	dichloromethane
DMAP	dimethylaminopyridine
DME	ethylene glycol dimethyl ether

DMF	*N*,*N*-dimethylformamide
DMSO	dimethyl sulfoxide
dr	diastereomeric ratio
Eq.	equation
equv.	equivalent(s)
Et	ethyl
EWG	electron withdrawing group
Hex	hexyl
HMT	hexamethylenetetramine
3-HQD	3-hydroxyquinuclidine
LAH	lithium aluminum hydride
LDA	lithium diisopropylamide
Me	methyl
Mp	melting point
MVK	methyl vinyl ketone
NBS	*N*-bromosuccinimide
NMM	*N*-methylmorpholine
PAP	polymer bound 4-(*N*-benzyl-*N*-methylamino)pyridine
Ph	phenyl
i-pr	isopropyl

pr	propyl
PTA	1,3,5-triaza-7-phosphaadamantane
rt	room temperature
TBAI	tetrabutylammonium iodide
TFAA	trifluoroacetic anhydride
THF	tetrahydrofuran
TMEDA	tetramethylethylenediamine
TMG	1,1,3,3-tetramethylguanidine
TMPDA	1,1,3,3-tetramethylpropane-1,3-diamine

ABSTRACT

The Baylis-Hillman reaction is a three component atom economy carbon-carbon bond forming reaction. It involves the coupling of α-position of an activated alkene with an electrophile under the influence of a catalyst or catalytic system providing interesting classes of densely functionalized molecules, which have been used in various organic synthetic transformation methodologies and also in synthesis of various natural products and bio-active molecules. Our research group has been working on this fascinating reaction for the last several years with a view to expand the scope of the applications of Baylis-Hillman adducts in organic synthesis.

This thesis deals with the synthesis of heterocycles and carbocycles using the Baylis-Hillman adducts and synthesis of indene-spiro-oxindoles using the Prins-Friedel-Crafts reactions and consists of three chapters 1) Introduction 2) Objectives, Results & Discussion and 3) Experimental. The first chapter i.e., Introduction presents a brief literature survey on the developments of Baylis-Hillman reaction and also on the application of the Baylis-Hillman adducts in the synthetic organic chemistry.

The second chapter deals with the objectives, results & discussion. With a view to study the application of Baylis-Hillman adducts for the synthesis of heterocyclic & carbocyclic molecules and with a view to develop a simple synthesis of spiro-oxindoles *via* the tandem

Prins and Friedel-Crafts reactions we have undertaken a research program with following objectives.

1) To develop a simple and one-pot synthesis of benzo[*b*][1,8]naphthyridones from the Baylis-Hillman adducts.
2) To develop a simple facile and multi-step one-pot synthesis of quinoline derivatives from the Baylis-Hillman acetates.
3) To develop a simple synthesis of bicyclic frameworks containing benzocycloheptane moiety and tetracyclic carbocyclic framework containing 6,7,6,6 ring systems from the Baylis-Hillman acetates.
4) Our objective also includes the development of simple and one-pot protocol for synthesis of indene-spirooxindoles involving construction of two carbon-carbon bonds *via* the tandem Prins and Friedel-Crafts reactions.

Simple and one-pot Synthesis of tri and tetracyclic frameworks containing [1,8]naphthyridin-2-one moiety from the Baylis-Hillman adducts

The 1,8-naphthyridine framework represents an important class of molecules which are found to possess interesting biological properties such as anti-inflammatory, anticancer, antibacterial, antitumour, antihypertensive, antiallergitic, antimalarials and also some of these derivatives are found to be potential diuretic agents.

We have developed a simple, facile and one-pot procedure for the synthesis benzo[*b*][1,8]naphthyidine-2-ones (**95a-j**) in 45-69% isolated yields (Eq.s 28, 29 & Table 2), from the Baylis-Hillman alcohols (**93a-e**).

We have also developed a simple protocol for obtaining tetracyclic framework containing benzo[*b*][1,8]naphthyridin-2-one derivatives (**95k,l**) in 51-59% isolated yields (Eq.s 31 & 32) from the Baylis-Hillman alcohols (**93f**).

Development of simple, facile and multi-step one-pot synthesis of substituted quinoline derivatives from the Baylis-Hillman acetates

The quinoline frame work represents an important class of molecules which are found to possess interesting biological properties such as antimalarial, antitumor, liver X receptor agonists for treatment of atherosclerosis hypotensive, allosteric enhancers of the adenosine A3 receptor, antifeedant, fingicidal.

Because of the importance of the quinoline derivatives in medicinal chemistry, development of simple and convenient methodologies for the synthesis of such frameworks represents an interesting and attractive endeavor in synthetic organic chemistry.

We have developed simple protocol for the transformation of acetates of the Baylis-Hillman adducts (**106a-d**) into variety of substituted quinoline derivatives (**109a-k**) in 54-

79% isolated yields (Scheme 53, Eq.s, 37, 39, 40 & Table 4), *via* the treatment with β-keto ester (**107a-c**) followed by reductive cyclization.

With a view to understand the generality of this reaction and also to synthesis of tricyclic system having the quinoline moiety we have transformed 4-acetoxy-3-methylenebutan-4-(2-nitronaphth-1-yl)-2-one (**106e**) into quinoline derivatives (**109l-n**) in 58-65% isolated yields (Eq.s 41-43).

Development of a simple synthesis of bicyclic and tetracyclic carbocyclic framework having 6,7 and 6,7,6,6 fused ring systems from the Baylis-Hillman acetates

Benzocycloheptane framework is well known to possess important biological activities such as antidepressants, anticonvulsants, psychotropicagents, anti-HIV-1, β-adrenergic agonist, estrogen receptors, human neuropeptide Y Y5 receptors, 5-HT_{1A} receptors in brain, estrogen receptor, and β-adrenergic agonist.

We have developed a simple synthesis of bicyclic carbocyclic (benzocycloheptane) framework (**128a-g**) in 61-75% isolated yields (Eq.s 47, 49, Table 8, Scheme 64) *via* the reaction of Baylis-Hillman acetate (**124a, 124c-e, 124g**) with β-keto esters (**125a-c**) followed by intramolecular Friedel-Crafts reaction. We have also applied the similar strategy for synthesis of tetracyclic carbocyclic framework containing 6,7,6,6 ring system (**131c-l**) in 56-81% isolated yields (Eq. 60, Table 10, Schemes 69, & 70) *via* the treatment

of Baylis-Hillman acetates (**124a**, **124c-f, 124h-l**) with β-keto esters (**129b-c**) followed by two intramolecular Friedel-Crafts reactions.

A simple and one pot protocol for synthesis of indene-spiro-oxindoles involving tandem Prins and Friedel-Crafts reactions

The spiro-oxindole framework represents an important structural organization present in a number of bioactive natural products such as elacomine, alstonisine, horsfiline, welwitindolinone A, spirotryprostatin A, tasmanine, coerulescine, surugatoxin. Indene and spiro-indene derivatives occupy a special place in organic and medicinal chemistry because these compounds are well known h5-HT6 serotonin receptors, oxytocin antagonists, estrogen receptor modulators, anti-proliferative agents, neurokininreceptors.

With a view that the oxindole derivatives containing indene framework connected through spiro-bridge, will be of medicinal importance we have developed a facile synthesis of 1*H*-indene-spiro-oxindoles derivatives (**155a-m**) in 61-90% isolated yields (Table 11 &12) *via* the reaction between isatins (**154a-f**), and 1,1-diarylethylenes (**153a-c**) in the presence of $TiCl_4$.

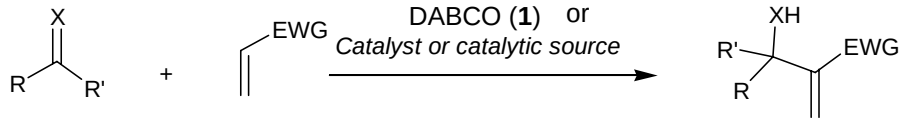
The third chapter provides detailed experimental procedures, physical constants like boiling point, melting point, IR, ^{1}H & ^{13}C NMR, mass (LC-MS) spectral data and elemental analysis.

INTRODUCTION

The formation of carbon-carbon bond is one of the most fundamental reactions in organic chemistry.[1,2] Recent developments in organic chemistry demand complete atom-economy in construction of carbon-carbon bonds as such reactions will be environment friendly. Various atom-economy carbon-carbon bond forming reactions, such as aldol reaction,[3] Diels-Alder reaction[4] and Michael reaction[5] have been developed and their applications have been well documented in the literature. The Baylis-Hillman reaction yet another atom economy carbon-carbon bond forming reaction which has become a popular carbon-carbon bond forming reaction in synthetic organic chemistry in recent years.[6-19]

The Baylis-Hillman Reaction

This is an essentially three component atom-economy carbon-carbon bond forming reaction involving the coupling of α-position of an activated alkene with carbon electrophile under the influence of a catalyst or catalytic system [commonly tertiary amine and particularly DABCO (**1**) (1,4-diazabicyclo[2.2.2]octane)], providing an interesting class of highly functionalized molecules (Eq.1).[6-19]



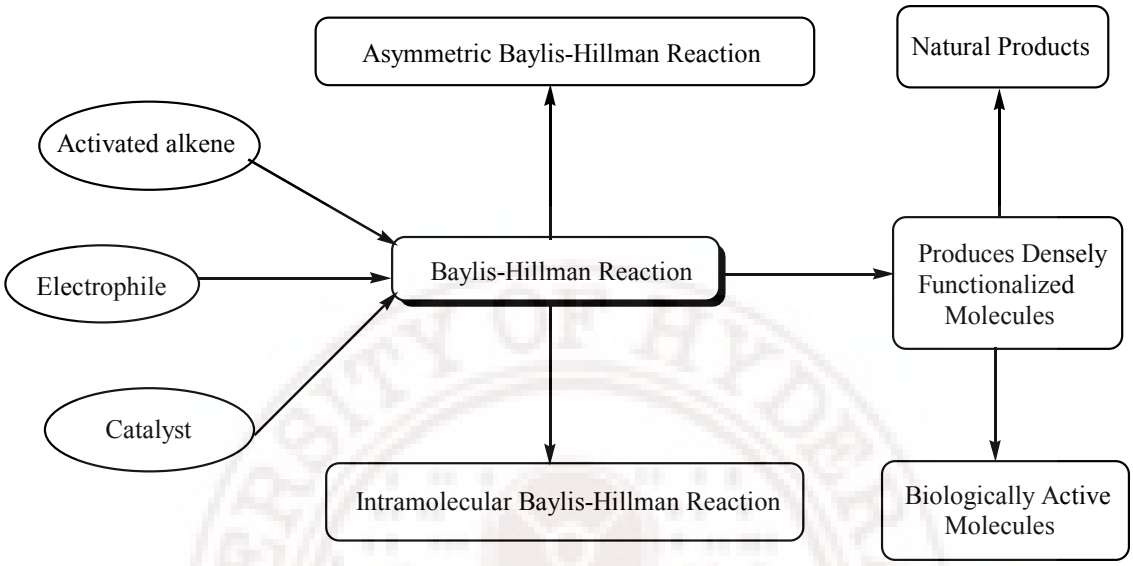
Eq. 1

EWG = Electron Withdrawing Group : COR, CHO, CN, COOR, $PO(OEt)_2$, SO_2Ph, SO_3Ph, SOPh
R' = alkyl, H, COOR
R = alkyl, aryl, heteroaryl
X = O, NCOOR, NTs, NSO_2Ph

During the last two decades Baylis-Hillman reaction has grown from almost unknown (patent) level to the stage of high popularity as evidenced by the large number of publications, five major reviews[8-12] and many mini reviews.[13-19] In fact Baylis-Hillman reaction has seen tremendous growth in terms of all the three essential components, that is, activated alkenes, electrophiles and catalyst or catalytic systems. There is also considerable progress in the development of asymmetric version of the Baylis-Hillman reaction based on the utility of chiral activated alkenes, chiral electrophiles and chiral catalysts. Significant progress has also been achieved in its intramolecular version. The Baylis-Hillman adducts, which contain a minimum of three functional groups in close proximity have been employed successfully in various organic transformation methodologies and in the synthesis of carbocyclic & heterocyclic molecules of medicinal importance.[11,12] All these developments have been presented pictorially in Fig. 1.

Since the major part of this thesis deals with the synthetic applications of the Baylis-Hillman adducts, this chapter presents the important developments of Baylis-Hillman reaction with respect to all the three essential components, its asymmetric version and intramolecular version. This chapter will also present the some of the recent and relevant applications of the Baylis-Hillman adducts in organic synthesis. Mechanism of this reaction is presented briefly at the end of this chapter.

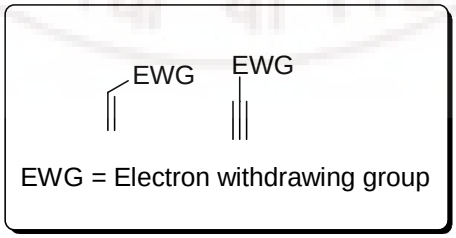
Fig. 1



ACIVATED ALKENES AND ALKYNES

Several activated alkenes and activated alkynes (see Fig. 2) have been successfully employed for coupling with various electrophiles under the influence of catalysts or catalytic systems to provide multifunctional molecules.

Fig. 2 Activated alkenes and activated alkynes

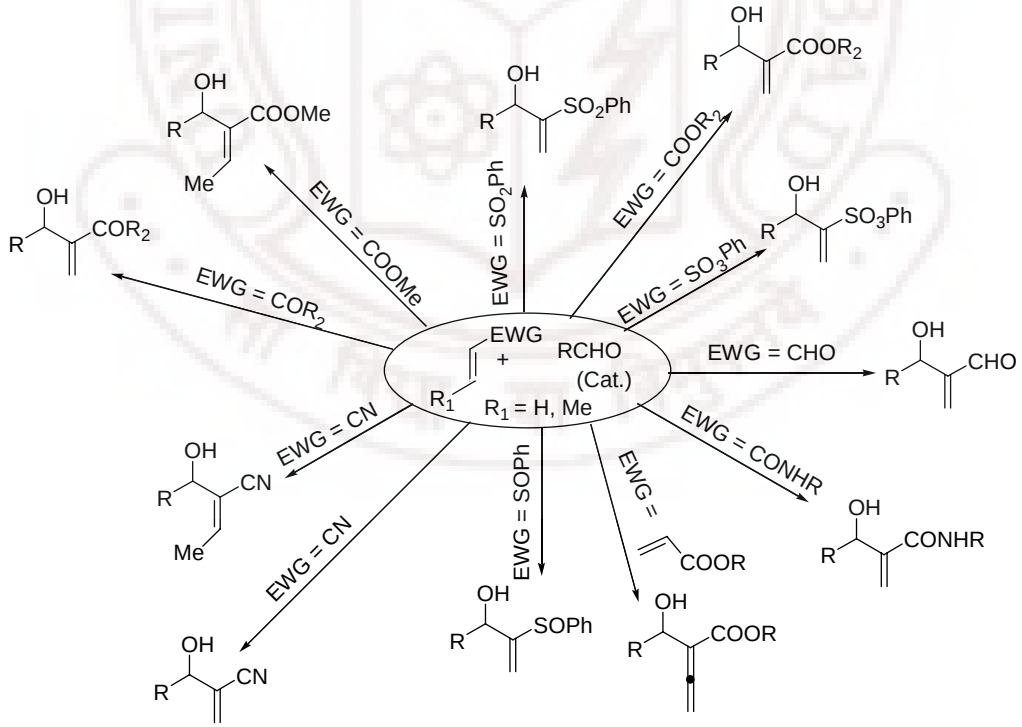


Earlier work

A large number of ethylene (alkenes) compounds having electron withdrawing groups such as ketones,[20-22] nitrile,[22,23] esters,[24-27] amide,[28] sulphones,[29] sulphonates,[30], sulphoxides[31], aldehyde[32] at the α-position, have been employed successfully for Baylis-Hillman coupling with number of electrophiles under the influence of a catalyst or catalytic system to provide the densely functionalized molecules (see Scheme 1). Also allenic esters,[33,34] crotonic esters[35] and crotononitrile[35] have been used as activated alkenes in the Baylis-Hillman coupling with various electrophiles (Scheme 1).

Acyclic activated alkens

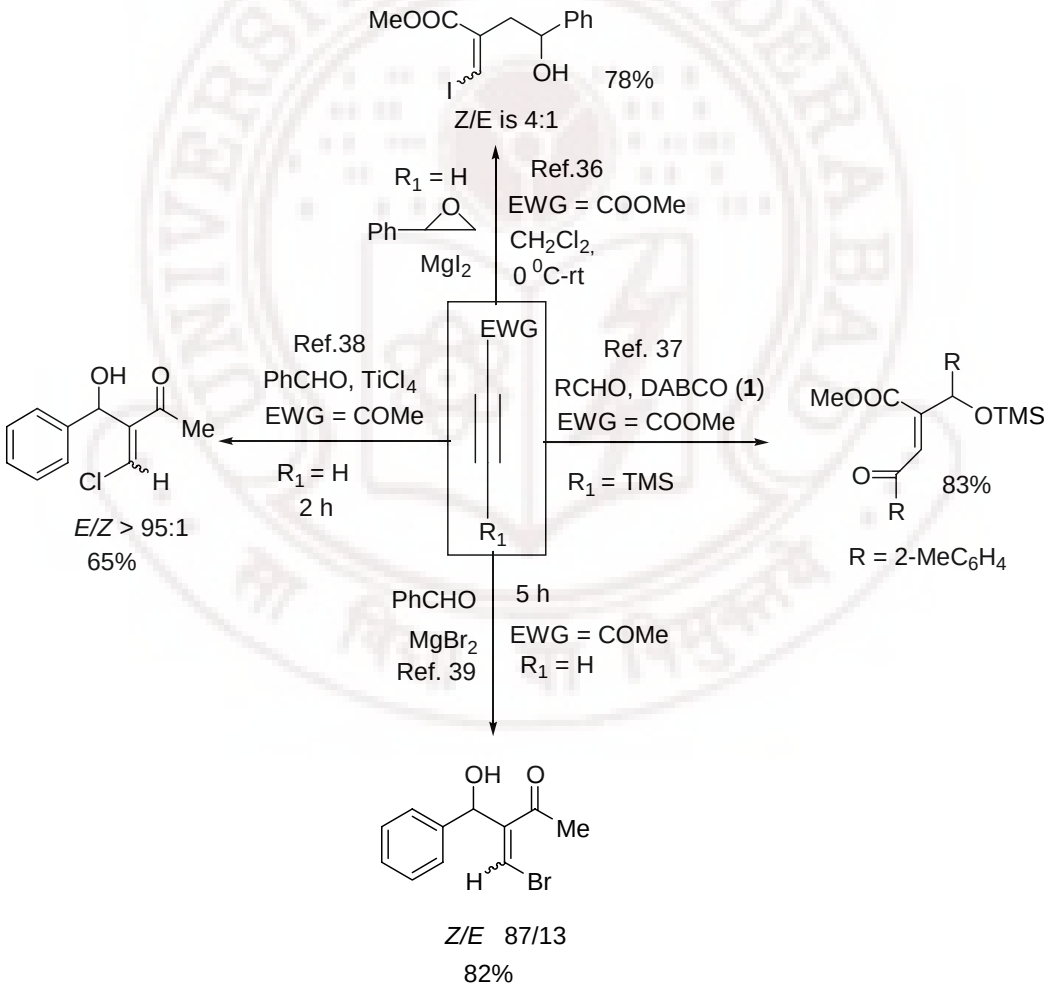
Scheme 1



Activated Alkynes

In addition to the activated alkenes,[11,12] activated alkynes such as methyl propiolate[36] methyl 3-trimethylsilylpropiolate,[37] but-3-yn-2-one [38,39] have also been used for Baylis-Hillman coupling with various electrophiles to provide the β-substitued Baylis-Hillman adducts (Scheme 2).

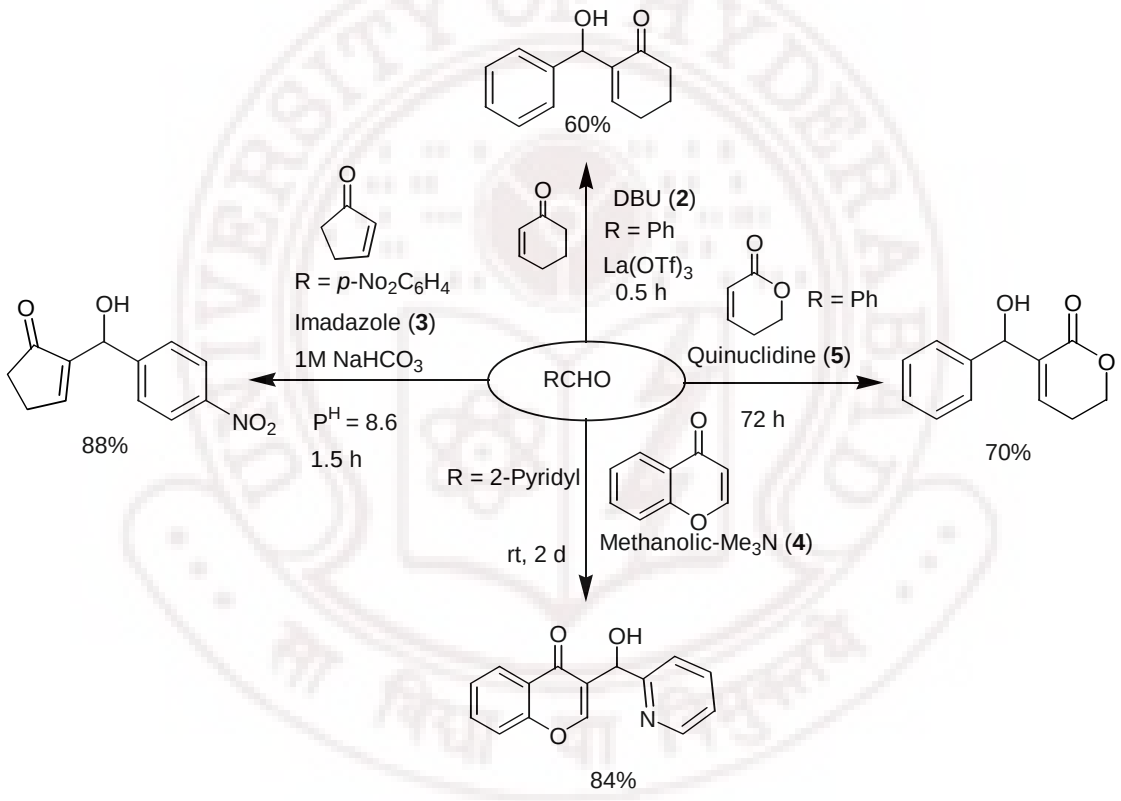
Scheme 2



Cyclic activated alkenes

Cyclic activated alkenes such as cyclohex-2-enone,[40] cyclopentenones,[41] chromones,[42] 5,6-dihydro-2*H*-pyran-2-one[43] *etc.* have also been used for coupling with aldehydes to provide densely functionalized compounds (Scheme 3).

Scheme 3

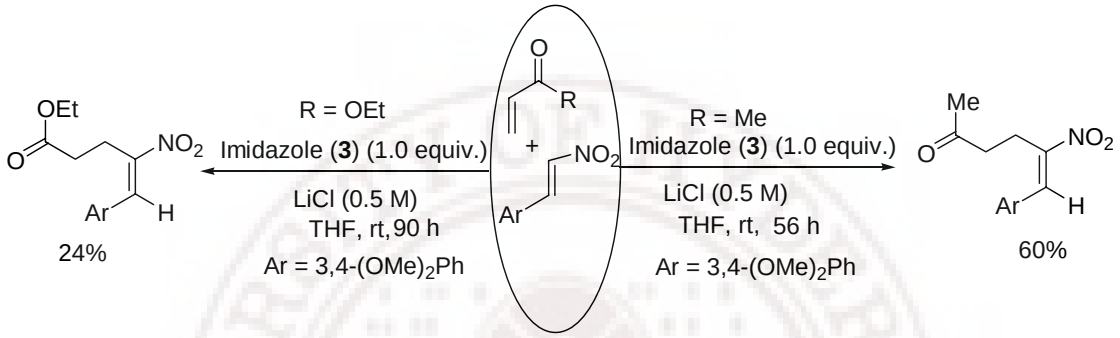


Recent developments

Namboothri and co-workers[44] have elegantly used β-arylnitroethylenes as activated alkenes for Baylis-Hillman coupling with methyl vinyl ketone and ethyl acrylate as electrophiles

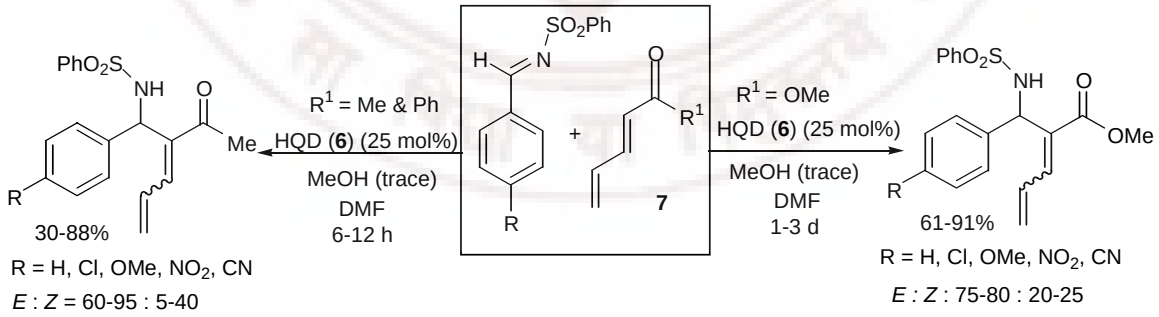
using imidazole / LiCl as catalytic system to provide the resulting adducts in moderate to good yields (Scheme 4).

Scheme 4



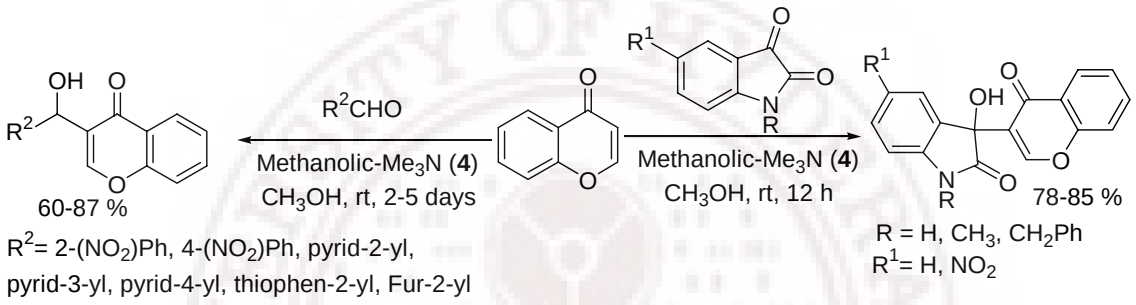
Back and co-workers[45] reported an interesting 3-hydroxyquinuclidine (3-HQD) (**6**) catalyzed Baylis-Hillman coupling of β-vinylic activated alkene (**7**), as an activated alkene, with aldimine derivatives to provide the resulting adducts as a mixture of *E/Z* isomers (Scheme 5).

Scheme 5



1-Benzopyran-4(4*H*)-one derivatives[42] have been successfully used as activated alkenes in the Baylis-Hillman coupling with various electrophiles, such as isatins and aldehydes under the influence of methanolic trimethyl amine (**4**) by our research group to provide the resulting products in good yields (Scheme 6).

Scheme 6



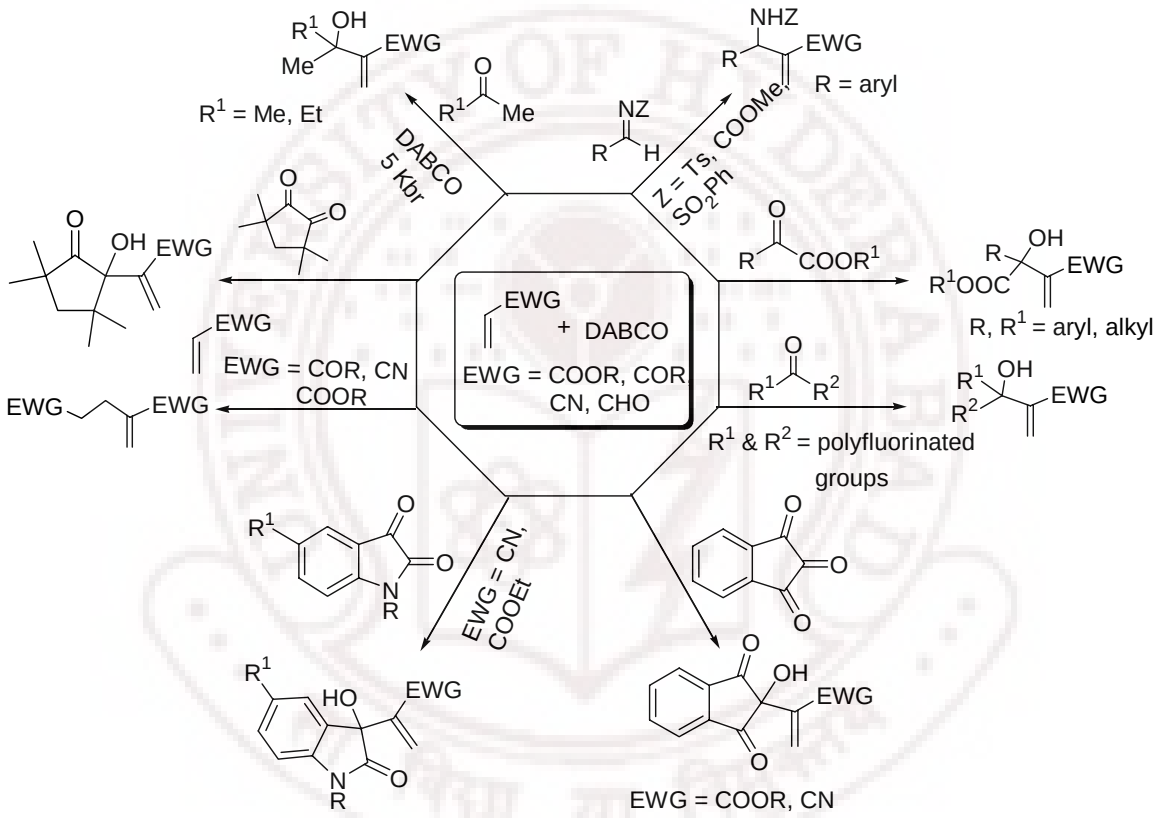
Electrophiles

Earlier developments

Although the aldehydes such as aliphatic, aromatic and heteroaromatic constitute a major portion of the electrophiles in Baylis-Hillman coupling with large number of activated alkenes to produce different kinds of densely functionalized molecules, various other electrophiles such as aldimines,[46-48] α-keto esters,[49-51] fluoroketones,[52] non-enolizable 1,2-diketones,[53] ninhydrin,[54,55] and isatin derivatives,[55,56] have also been successfully employed in this fascinating reaction for coupling with different activated alkenes. Also activated alkenes such as acrylonitrile, alkyl vinyl ketones, aryl vinyl ketones, aryl(alkyl) acrylates have also been employed as electrophiles [57-60] in the Baylis-Hillman reaction.

Simple ketones[61] such as 2-butanone and acetone, which are usually less reactive, have been employed as electrophiles at high pressure conditions (Scheme 7). Some of the relevant examples are presented in the Scheme 7.

Scheme 7

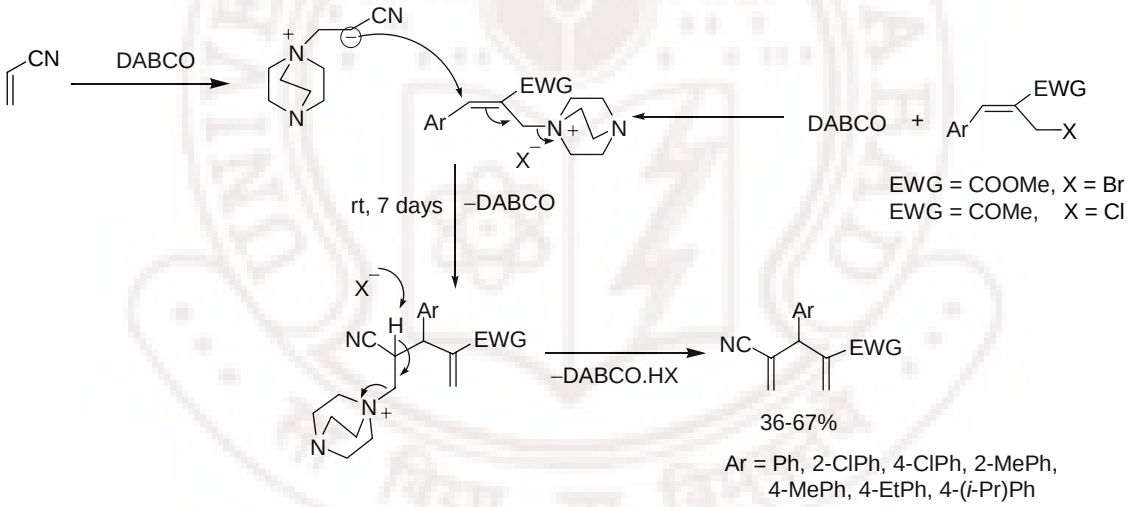


Recent developments

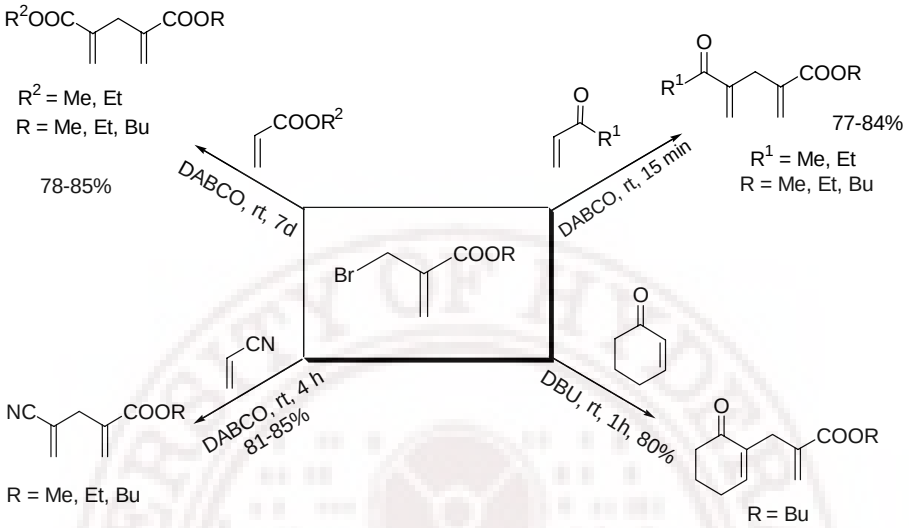
Our research group[62] has successfully employed, for the first time allyl bromides /allyl chlorides, derived from Baylis-Hillman adducts, as electrophiles in the Baylis-Hillman reaction with various activated alkenes. Thus the treatment of the Baylis-Hillman allyl

bromides/chlorides with acrylonitrile under the influence of DABCO provided the 3-substituted 1,4-pentadienes following the reaction sequence as described in Scheme 8. Subsequently our research group[63] has also reported a simple protocol for the synthesis of various 2,4-functionalized 1,4-pentadienes *via* the Baylis-Hillman coupling of allyl bromides derived from the alkyl 3-hydroxy-2-methylenepropanoates, as electrophiles with alkyl acrylates, acrylonitrile, alkyl vinyl ketones and cyclic enones following the reaction sequence as shown in Scheme 9.

Scheme 8

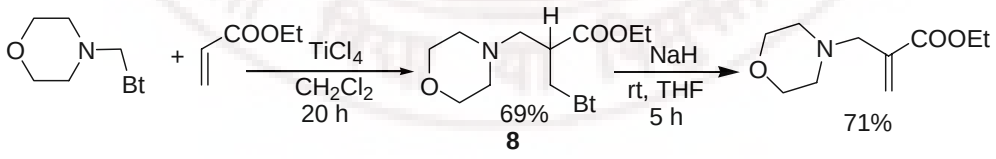


Scheme 9



Katritzky and co-workers,[64] successfully used substituted aminomethylbenzotriazoles as a electrophiles in coupling with ethyl acrylate under the influence of $TiCl_4$, to provide addition products (**8**), which on treatment with NaH provided the desired Baylis-Hillman products. One representative example is presented in Scheme 10.

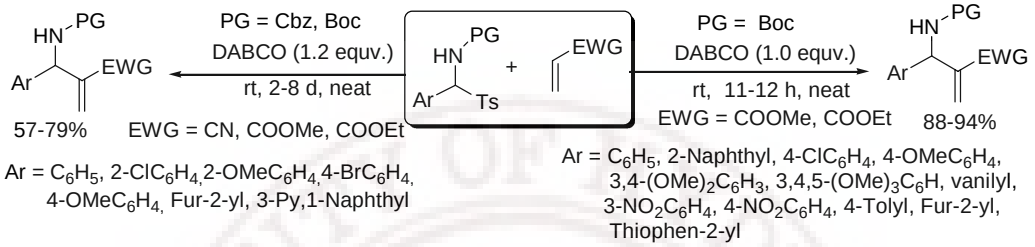
Scheme 10



N-Protected α-amino sulphones, have been, for the first time, used by Das and co-workers[65] as a electrophiles for coupling with alkyl acrylates under catalytical influence of

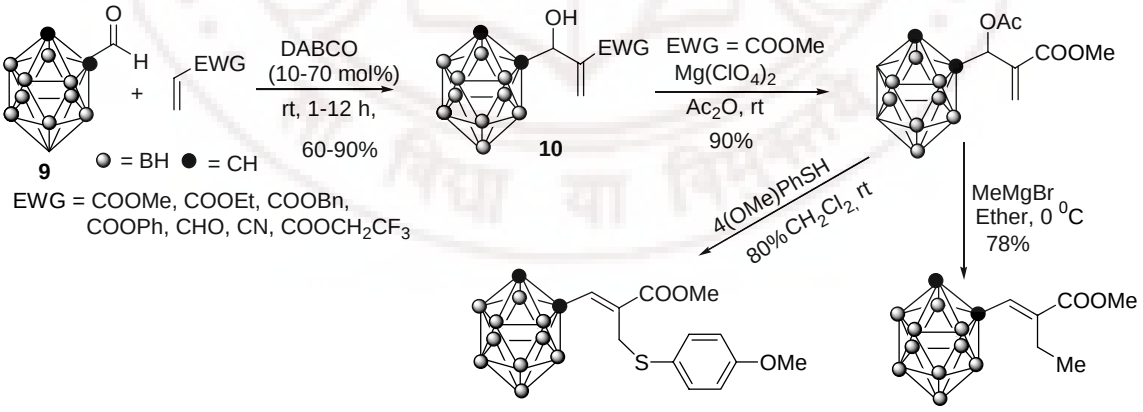
DABCO to afford Baylis-Hillman adducts (Scheme 11). Subsequently, Gajda[66] *et* al performed similar reaction strategy to obtain Morita-Baylis-Hillman adducts (Scheme 11).

Scheme 11



Reddy and co-workers[67] have successfully used carborane aldehyde (**9**) as electrophile in the Baylis-Hillman reaction with various activated alkenes to provide the corresponding alcohols in good to excellent yields (Scheme 12). These Baylis-Hillman adducts (**10**) have been transformed into various trisubstituted alkenes. Representative examples are shown in Scheme 12.

Scheme 12

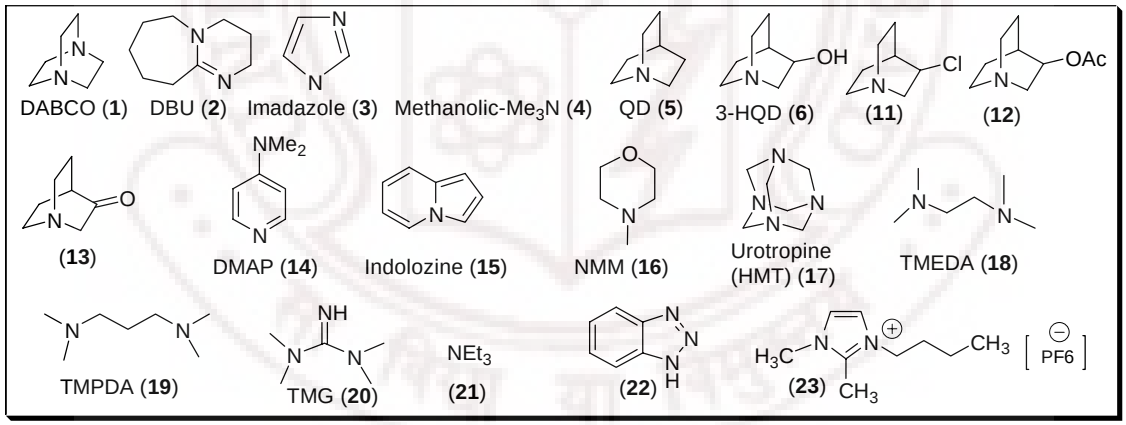


Catalysts

Earlier developments

Several *tert*-amines such as DABCO (**1**),[11] DBU (**2**),[40] imidazole (**3**),[41,44,68,69] methanolic-Me_3N (**4**),[42,70,71] quinuclidine (**5**),[43] 3-HQD (**6**),[43,72] 3-chloroquinuclidine (**11**),[43] 3-acetoxyoquinuclidine (**12**),[43,72] quinuclidinone (**13**),[43] DMAP (**14**),[73,74] indolizine (**15**),[6] NMM (**16**),[75] HMT (**17**),[75,76] TMEDA (**18**),[77] TMPDA (**19**),[78] TMG (**20**),[79,80] Et_3N (**21**),[35] benzotrizole (**22**)[81] have been successfully employed in various Baylis-Hillman reactions. Very recently, [bdmin][PF_6] ionic liquid (**23**)[82] has also been successfully employed as a catalyst for Baylis-Hillman reaction (Fig. 3).

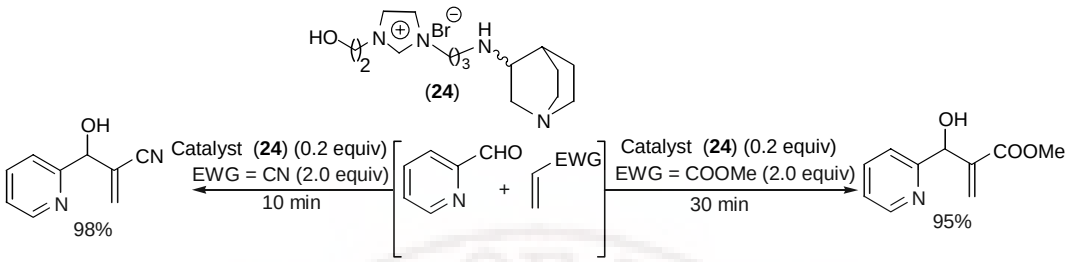
Fig. 3



Recent developments

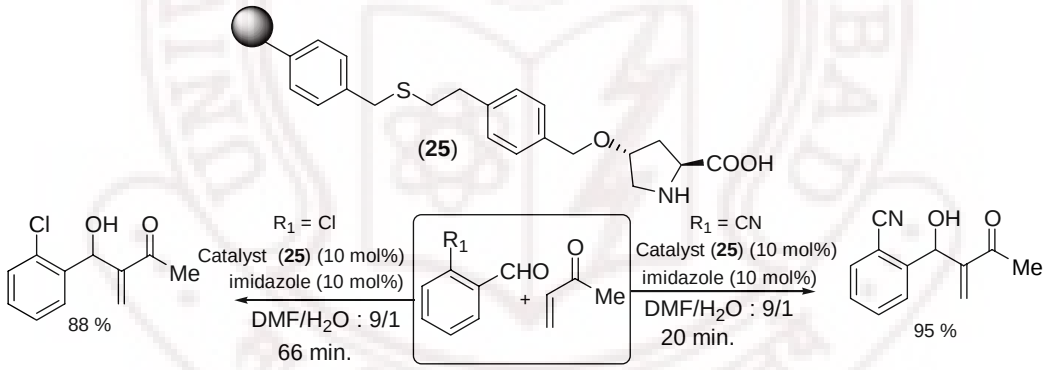
Cheng and co-workers[83] introduced hydroxy ionic liquid (HIL) (**24**) built on quinuclidine framework, as a novel catalyst for the Baylis-Hillman reaction as shown in Scheme 13. It is interesting to note that this catalyst (**24**) is recoverable and reusable.

Scheme 13



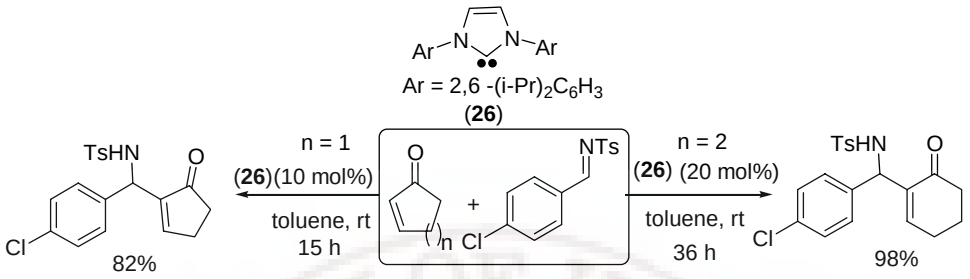
Gruttadauria and co-workers[84] used an interesting polystyrene-supported proline (**25**) as a recyclable catalyst for Baylis-Hillman reaction of various aldehydes with alkyl vinyl ketones (Scheme 14).

Scheme 14



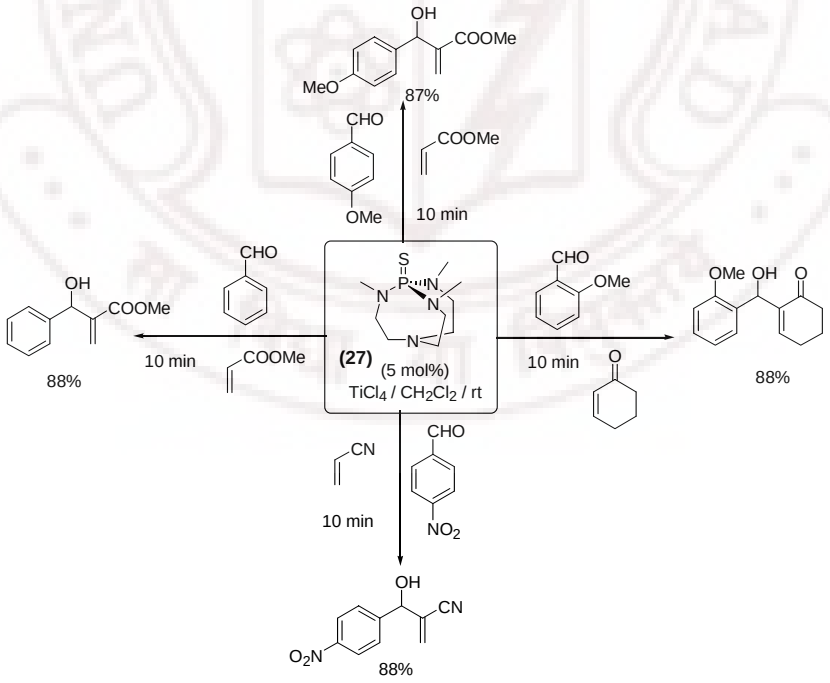
Ye and co-workers[85] for the first time employed N-heterocyclic carbenes (NHCs) (**26**) as efficient catalysts for Baylis-Hillman coupling between cyclic enones and N-tosylarylimines to provide the resulting adducts in good yields. Representative examples are presented in Scheme 15.

Scheme 15



Verkade and co-workers [86] used aza-phosphine catalyst (**27**) for Baylis-Hillman coupling of various aldehydes with cyclic and acyclic activated alkenes under the influence of $TiCl_4$ to provide the resulting Baylis-Hillman adducts in excellent yields at faster reaction rates (Scheme 16).

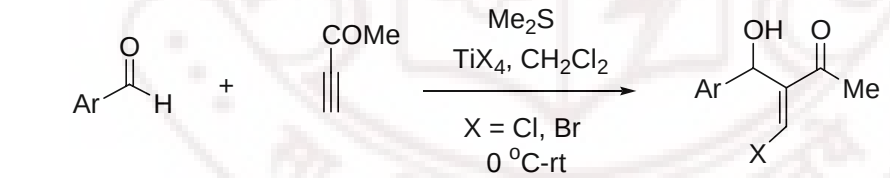
Scheme 16



NON-AMINE CATALYZED/MEDIATED BAYLIS-HILLMAN REACTIONS

Literature survey reveals that several catalysts such as alkyl (aryl) phosphines[87-90] and also metal complexes, $RhH(PPh_3)_4$,[91,92] $RuH_2(PPh_3)_4$[92,93] have been successfully employed for the coupling of activated alkenes with electrophiles. Combination of Lewis acids with bases, such as R_2S-$TiCl_4$,[11,94-96] R_2X-BF_3 (X = O, S),[97-98] $TiCl_4$-NR_3[99], $TiCl_4$-R_4NX[100,101] have also been successfully employed for obtaining the Baylis-Hillman adducts. Lewis acids such as $TiCl_4$,[102-104] Et_2AlI,[105] $MgBr_2$,[39] MgI_2[36] have also been used for performing the Baylis-Hillman reactions.

Kataoka and co-workers[103] reported the synthesis of β–halo-Baylis-Hillman adducts *via* the reaction between aldehydes and activated alkynes under the catalytic influence of dimethyl sulphide in presence of titanium halides (TiX_4) see Eq. 2.



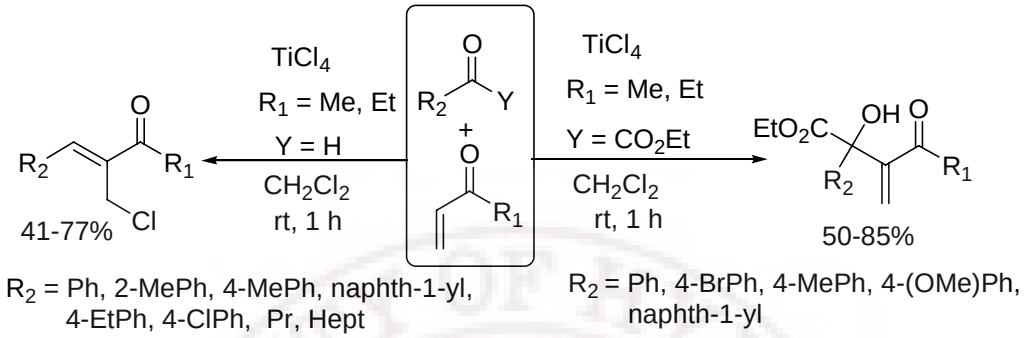
Ar = 4-(NO_2)Ph, 4-FPh, 4-(CF_3)Ph, 4-ClPh,

73-89%

Eq. 2

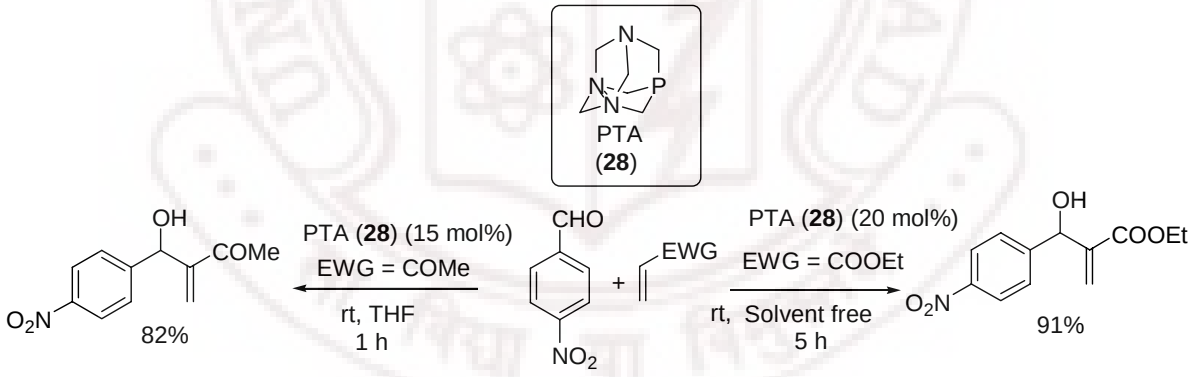
Later our research group[104] developed Lewis acid ($TiCl_4$) catalyzed Baylis-Hillman coupling of electrophiles such as α-keto esters, and aldehydes with alkyl vinyl ketones to provide the desired product and allyl halides respectively in moderate to good yields (Scheme 17).

Scheme 17

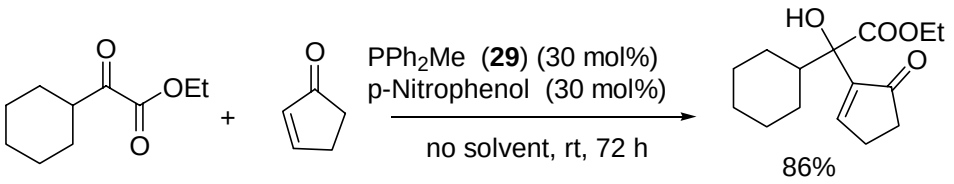


He and co-workers[106] used 1, 3, 5-triaza-7-phosphaadamantane (PTA) (**28**) as an efficient catalyst to promote the Baylis-Hillman reaction of alkyl acrylates and alkyl vinyl ketones with various aldehydes. Representative examples are described in Scheme 18.

Scheme 18



Shi and co-workers[107] successfully used PPh_2Me (**29**) as a catalyst for Baylis-Hillman coupling between cyclopentenone and α-keto esters providing the desired adducts. One representative example is presented in Eq. 3.



Eq. 3

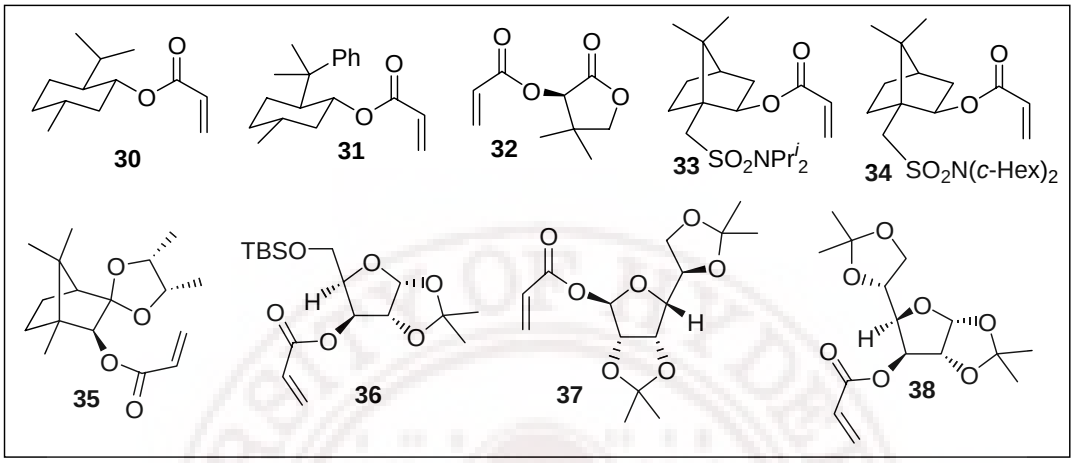
Asymmetric Baylis-Hillman reaction

Asymmetric version of the Baylis-Hillman reaction in the case of prochiral electrophiles in principle can be performed using chiral activated alkenes or chiral electrophiles or chiral catalysts or chiral additives or combination of some of these components in chiral form. Efforts have been directed in all these possibilities and considerable progress has been achieved in certain aspects.[11,13]

CHIRAL ACTIVATED ALKENES

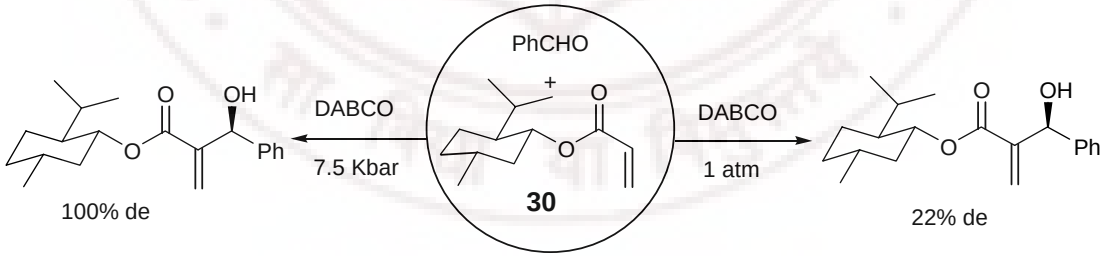
Chiral activated alkenes most generally, chiral acrylates and chiral amides have been employed for coupling with various electrophiles. A number of chiral acrylates, derived from various chiral auxiliaries such as cyclohexnol derivatives (**30, 31**),[108,109] (*R*)-(+)-pentolactone (**32**),[110-112] camphor derivatives (**33-35**),[113-115] and sugar derivatives (**36-38**)[116,117] (see Fig. 4) are successfully used in the Baylis-Hillman reaction with various electrophiles, to provide the resulting products in low to moderate diastereoselectivities.

Fig. 4



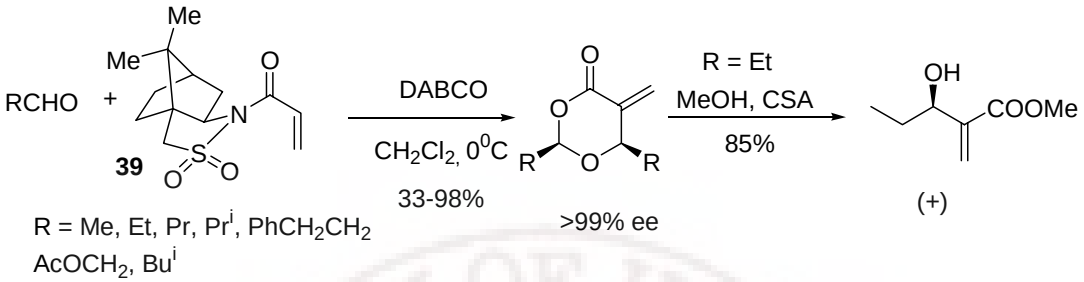
Gillbert[118] and co-workers described interesting effect of pressure on the enantioselectivity of the Baylis-Hillman reaction of benzaldehyde with (-)-menthyl acrylate (**30**) under the influence of DABCO. Thus high pressure (7.5 Kbar) provided 100% diastereoselectivity while normal pressure provided 22% diastereoselectivity only (Scheme 19).

Scheme 19

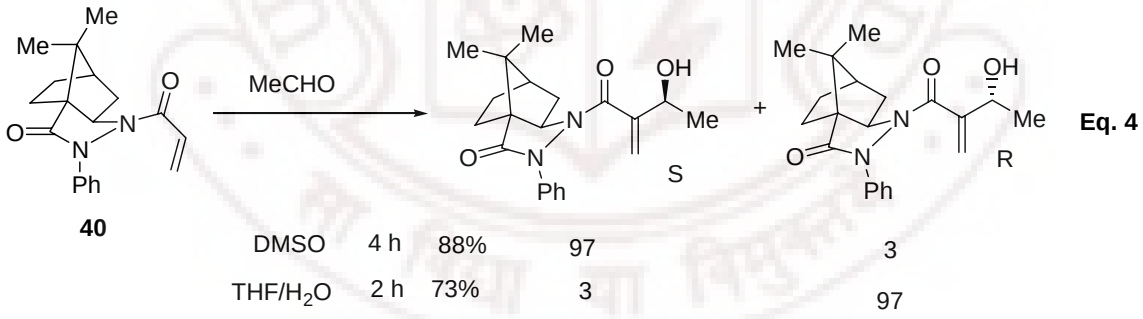


Leahy and coworkers[119] successfully used chiral acrylamide (**39**) as an activated alkene in the Baylis Hillman reaction with aldehydes to provide the resulting Baylis-Hillman adducts in excellent diastereoselectivities (Scheme 20).

Scheme 20



In the year 2000, Chen and co-workers[120], developed highly diastereoselective Baylis-Hillman reaction using chiral acryloylhydrazide (**40**) as a activated alkene for coupling with carbon electrophiles. They also found an interesting reversal of diastereoselectivity by changing the solvent from THF/H_2O to DMSO. One representative example is presented in Eq. 4.



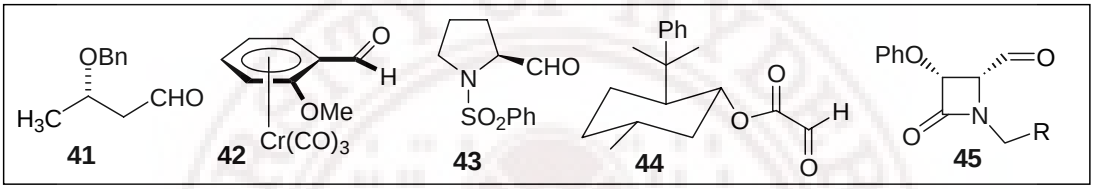
Eq. 4

CHIRAL ELECTROPHILES

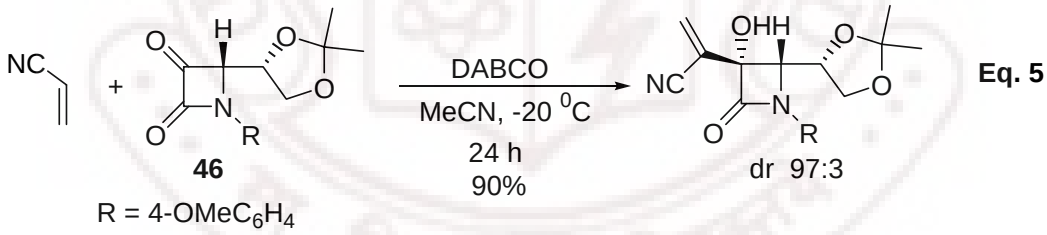
Several enantiopure aldehydes such as (*S*)-3-benzyloxybutyraldehyde (**41**),[121] enantio pure ortho substituted benzaldehyde tricarbonylchromimum complex (**42**)[122], N-phenylsulfonyl-

(*L*)-prolinal (**43**)[123], (-)-8-phenylmenthylglyoxylate (**44**)[124] enantiopure 1-alkenyl(alkynyl)-4-oxoazetidine-2-carbaldehydes (**45**)[125] (see Fig. 5) were used as chiral electrophiles for coupling with activated alkenes to provide the resulting adducts in moderate to good diastereoselectives.

Fig. 5

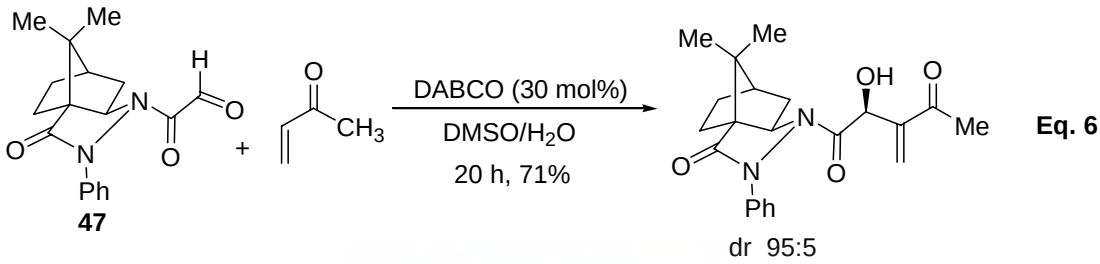


Alcaide and co-workers[126] successfully used chiral azetidine (**46**) as a chiral electrophile in the Baylis-Hillman reaction with acrylonitrile to provide the resulting Baylis-Hillman adducts in high diastereoselectivity. One representative example is presented in (Eq. 5).



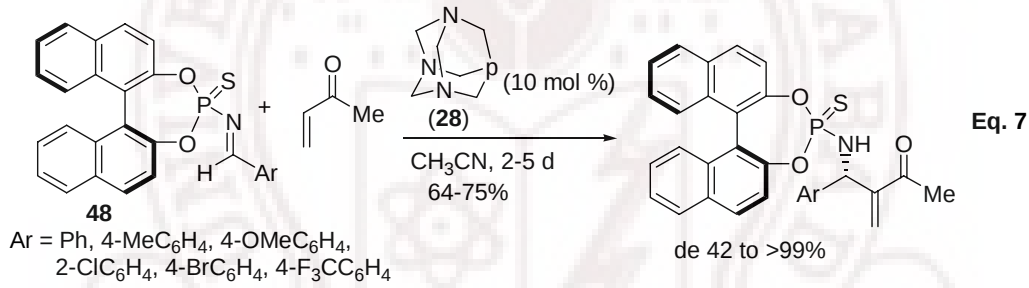
Eq. 5

Chen and pan have[127] used enantio pure N-glyoxyloyl camphorpyrazolidinone (**47**), as a chiral electrophile in the Baylis-Hillman reaction with various activated alkenes in presence of DABCO as a catalyst which provided the resulting adducts in high diastereoselectivity. One representative example is presented in Eq. 6.



Eq. 6

Recently, Zhou and co-workers[128] used chiral N-thiophosphorylimines containing (*S*)-binapthalene scaffold (**48**), as an electrophile for coupling with methyl vinyl ketone to afford the resulting Baylis-Hillman adducts in good yields and in moderate to excellent diastereoselectivities (Eq. 7).

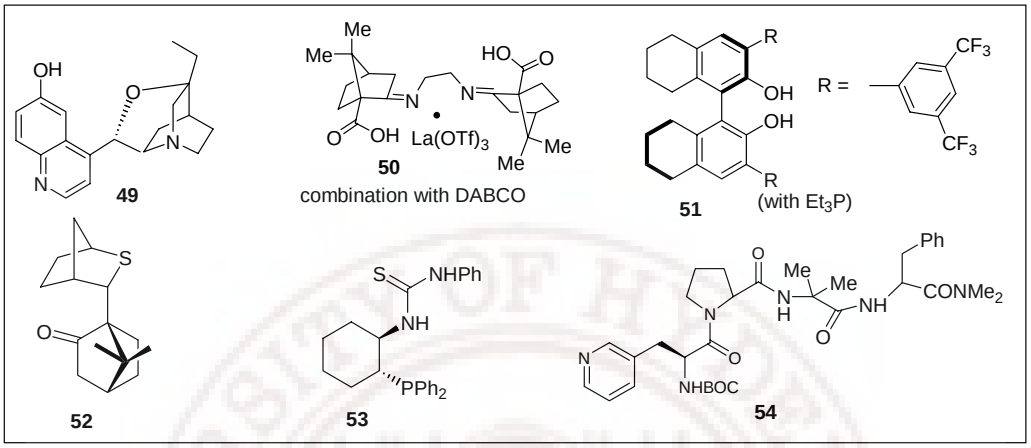


Eq. 7

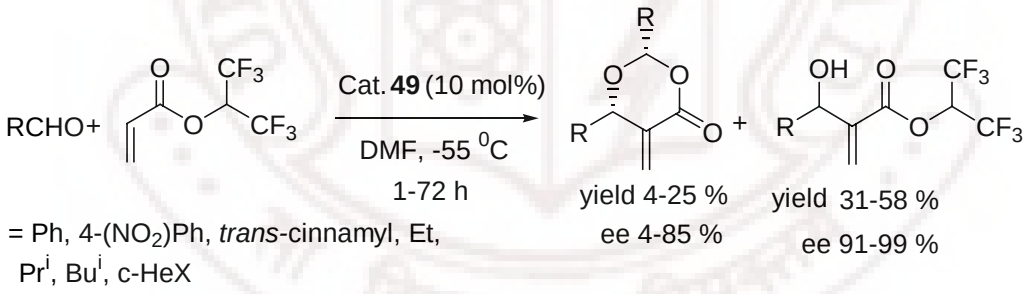
CHIRAL CATALYSTS

Development of appropriate chiral catalysts for various Baylis-Hillman reactions to provide the resulting adducts in high enantiomeric purities has been and continues to be challenging endeavor in asymmetric Baylis-Hillman reaction. Various catalysts have been developed for this purpose (Fig. 6).[129-134]

Fig. 6

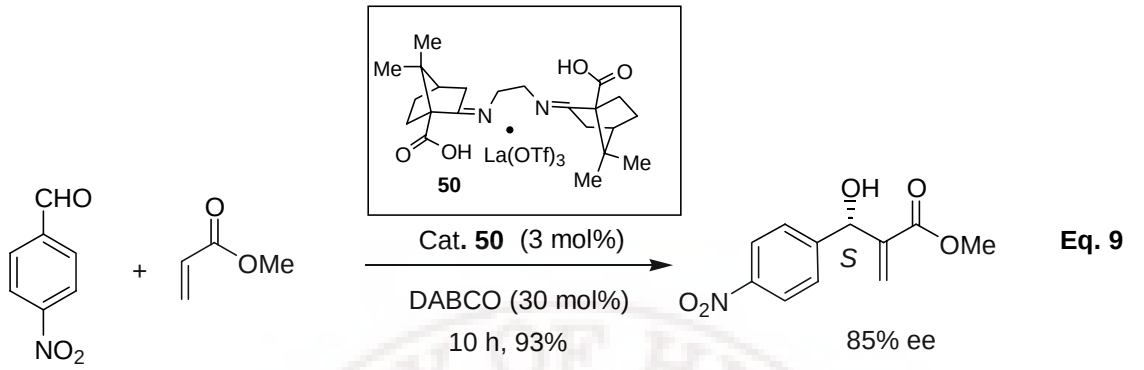


Hatakayema and co-workers[129] have been used the catalyst (**49**) for coupling of various electrophiles with 1,1,1,3,3,3-hexafluoroisopropyl acrylate to provide the resulting adducts in high enantiomeric purity up to 99 % see Eq. 8.



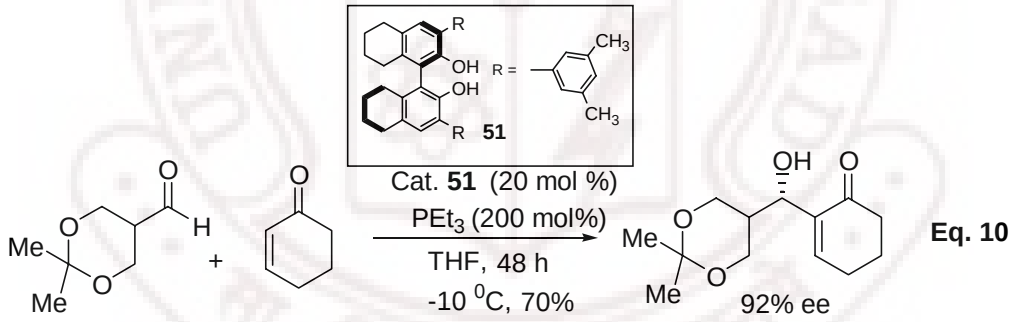
Eq. 8

Recently, Chen and co-workers[130] used a novel, camphor derived bidentate ligands (**50**) as additives for asymmetric Baylis-Hillman reaction between acrylates and various aldehydes under the catalytic influence of DABCO to obtain the resulting Baylis-Hillman adducts in 6-95% enantiomeric purities (Eq. 9).



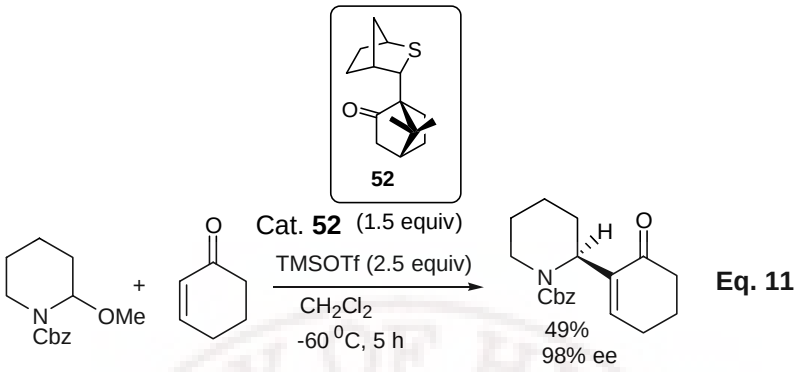
Eq. 9

Schaus and Mcdougal[131] reported highly enantioselective Baylis-Hillman reaction of 2,2-dimethyl-1,3-dioxane-5-carbaldehyde with various cyclic enones under the catalytic influence of Et_3P in presence of catalytic amount of chiral tetrahydro-BINOL (**51**). One representative example is presented in Eq. 10.



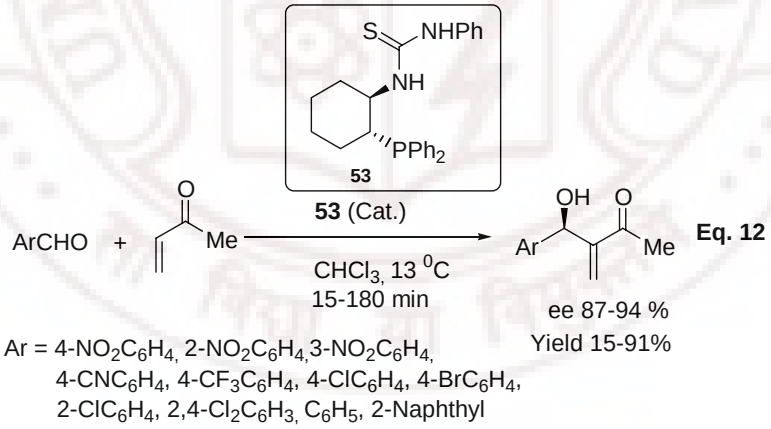
Eq. 10

Aggarwal and co-workers[132] have used chiral sulphide (**52**) as an efficient catalyst for asymmetric Baylis-Hillman reaction, between in situ generated iminium ions as electrophiles and cyclic enones (as activated alkenes) to provide the resulting adducts in high enantioselectivities. One representative example is presented in Eq. 11.



Eq. 11

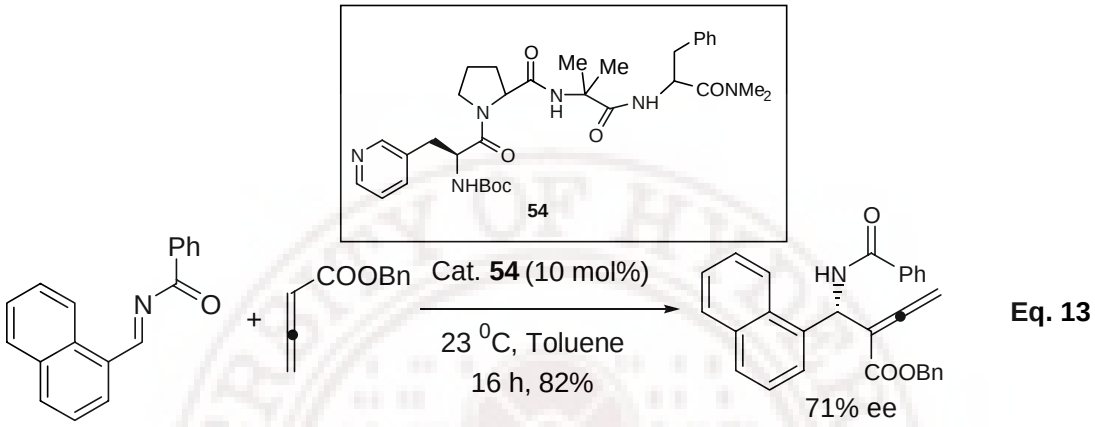
Very recently, Wu and co-workers[133] reported a highly enantioselective Baylis-Hillman reaction of methyl vinyl ketone with various aromatic aldehydes under the influence of chiral phosphinothiourea catalyst (**53**), derived from *trans*-2-amino-1-(diphenylphosphino)cyclohexane, to provide the resulting adducts in good to excellent enantiomeric purities (Eq.12).



Eq. 12

Very recently, Miller and co-workers[134] reported an asymmetric Baylis-Hillman reaction between N-acyl imines as electrophiles and allenoates as activated alkenes using

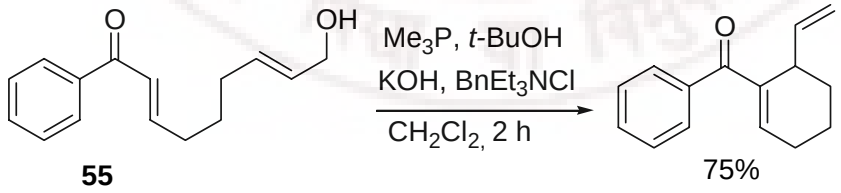
pyridylalanine (Pal)-peptide (**54**), as a catalyst. One representative example is presented in Eq. 13.



Eq. 13

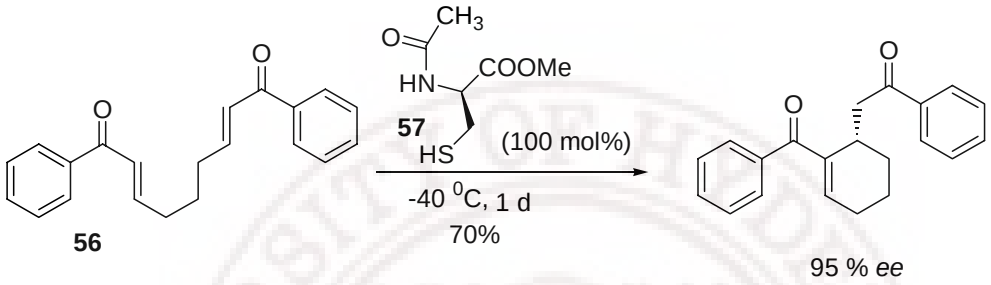
INTRAMOLECULAR BAYLIS-HILLMAN REACTION

In recent years intramolecular Baylis-Hillman reaction has received considerable attention from synthetic chemists.[11] Kraft and co-workers,[135] have described an interesting intramolecular Baylis-Hillman reaction of enone-allylic alcoholic system (**55**) under the catalytic influence of trimethylphosphine to provide carbocyclic framework in good yields. One representative example is mentioned in Eq. 14.



Eq. 14

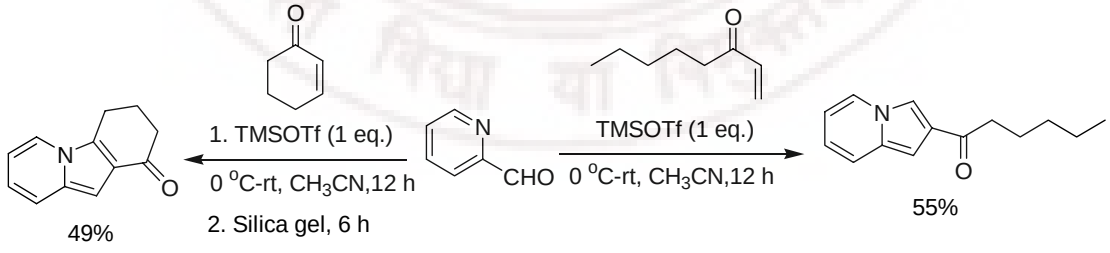
Very recently, Miller and Aroyan developed[136] an interesting, higly enantioselective intra-molecular Baylis-Hillman reaction of enone-enoe framework (**56**), under the influence of **57** as shown in Eq. 15.



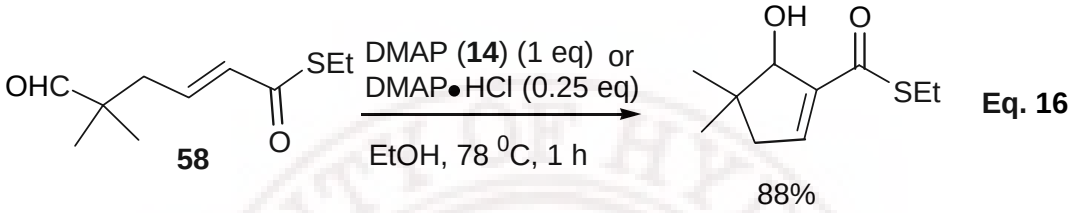
Eq. 15

Our research group[137] has developed for the first time electrophile induced Baylis-Hillman reaction between pyridine-2-carboxladehyde and activated alkenes under the influence of trimethylsilyl trifluoromethanesulfonate (TMSOTf), which actually involves intramolecular cyclization (Baylis-Hillman reaction) as the key step, leading to the formation of indolizine frameworks in one-pot operation. Representative examples are mentioned in Scheme 21.

Scheme 21



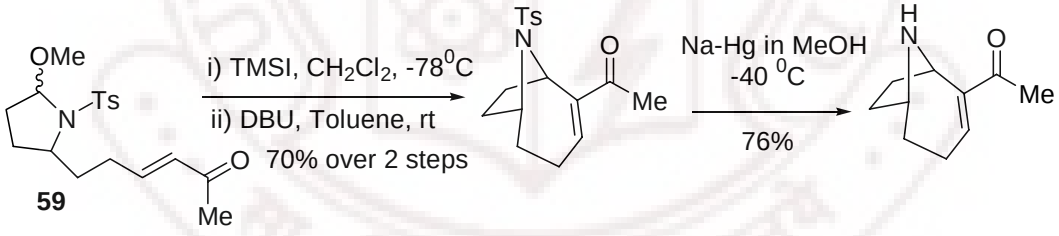
Keck and co-workers[138] described an intramolecular Baylis-Hillman reaction of α, β - unsaturated ester /thioester aldehyde systems (**58**) under the influence of DMAP (**14**), or DMAP**.**HCl in EtOH as a solvent (Eq. 16).



Eq. 16

Stockman and Roe[139] described the total synthesis of anatoxin & homoanatoxin, *via* interesting intramolecular Baylis-Hillman reaction of the substrate (**59**) as the key step following the reaction sequence as shown in Scheme 22.

Scheme 22

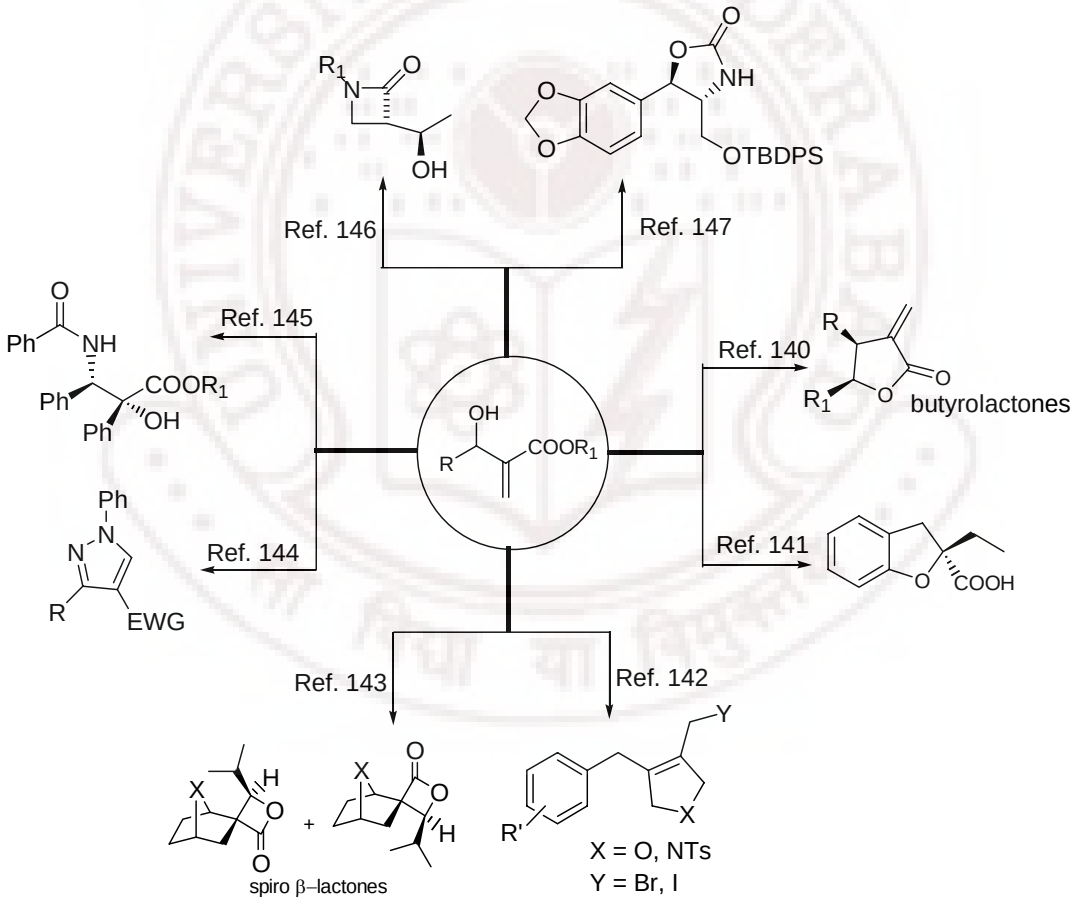


APPLICATIONS OF THE BAYLIS-HILLMAN ADDUCTS

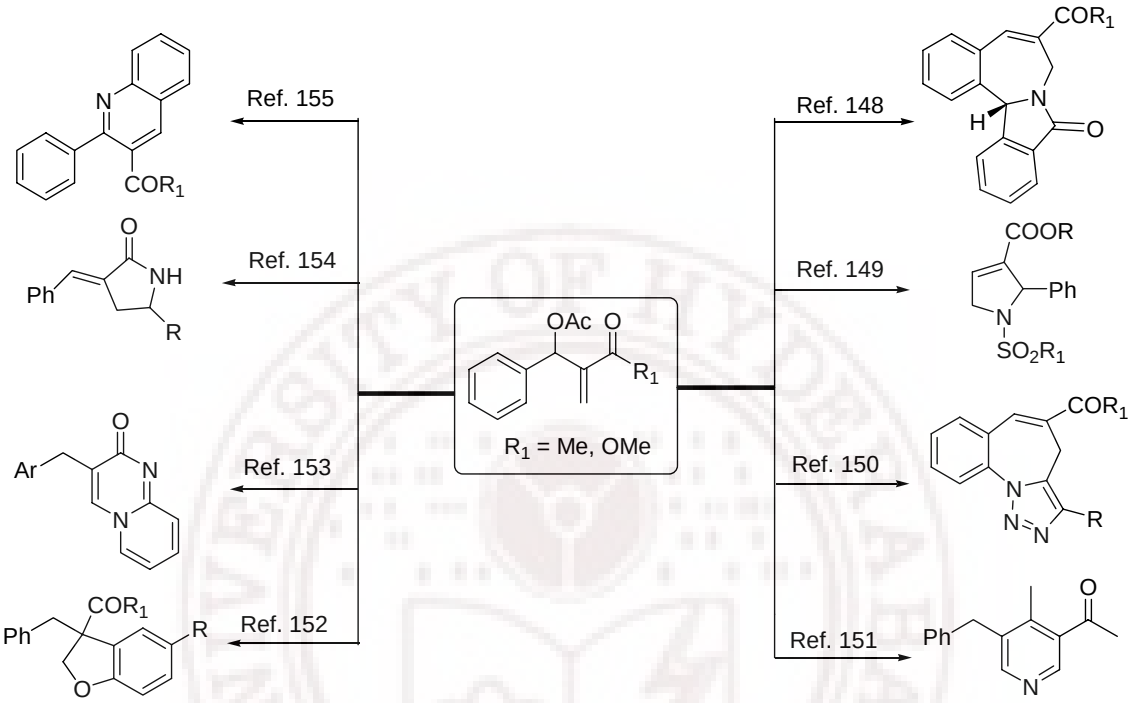
The Baylis-Hillman adducts have been employed in various organic transformation methodologies as they contain a minimum of three functional groups in close proximity.

Thus Baylis-Hillman adducts /acetates have been conveniently utilized as substrates for various organic reactions such as Diels-Alder reation, Heck reaction, Friedel-Crafts reaction, indium mediated reactions, photochemical reactions. Also some of these methodologies have successfully applied for synthesis of various biologically active molecules. Some of the these developments are presented in Scheme 23 and 24.

Scheme 23

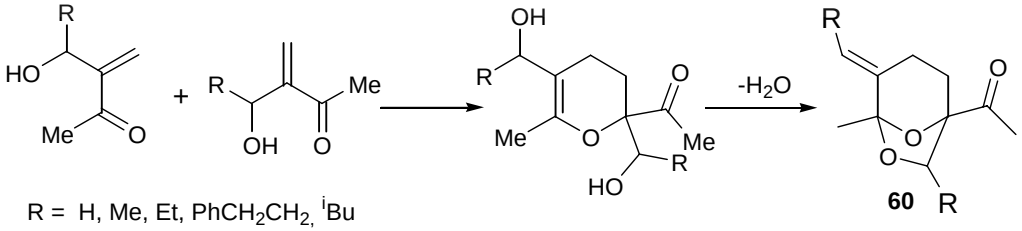


Scheme 24



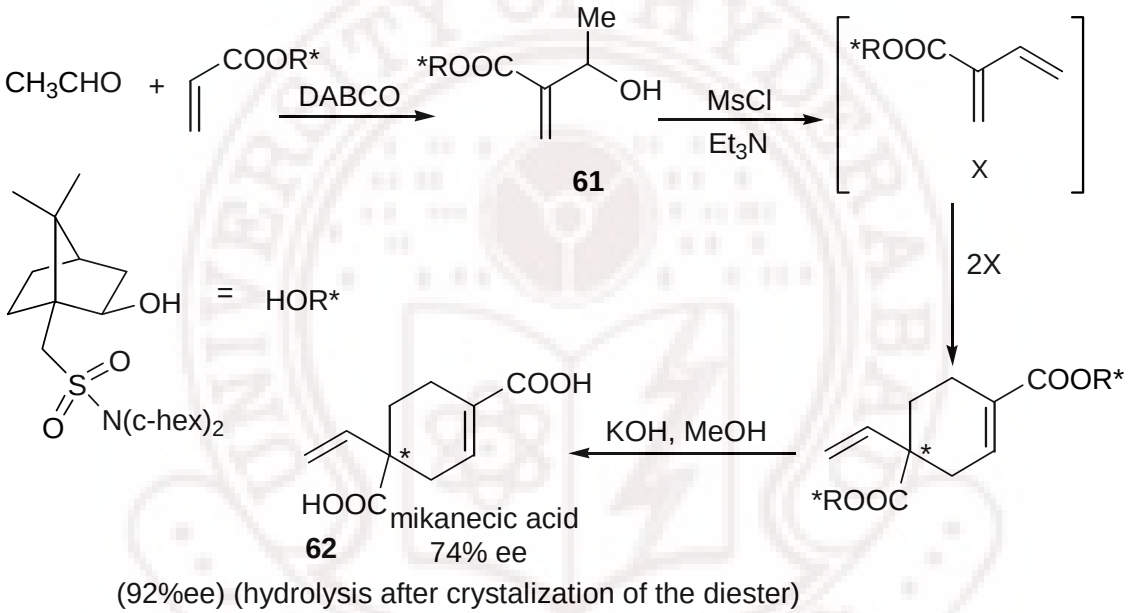
Hoffman and co-workers[156] reported an interesting synthesis of functionalized 6,8-dioxabicyclo[3.2.1]octane derivatives (**60**) (framework present in a number of pheromones) *via* Diels-Alder dimerization of Baylis-Hillman adducts, α-methylene-β-hydroxyalkanones (Scheme 25).

Scheme 25



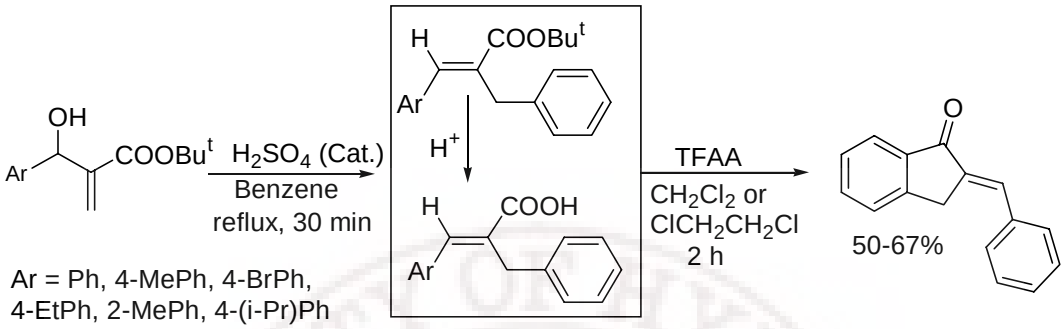
Our research group[114] has reported an interesting synthesis of enantiomerically enriched mikanecic acid (**62**), a terpene dicarboxylic acid having vinylic quarternary chiral center, from the Baylis-Hillman adduct (**61**) following the reaction sequence as described in Scheme 26.

Scheme 26



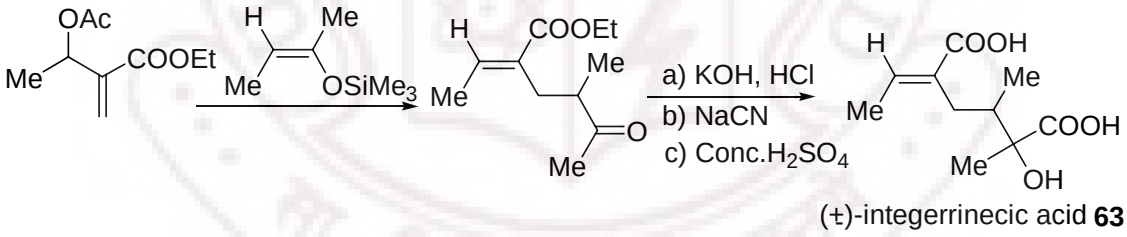
A simple and convenient methodology for synthesis of (*E*)-2-arylideneindan-1-ones *via* inter and intramolecular Friedel-Crafts reactions of the Baylis-Hillman adducts, obtained from *tert*-butyl acrylate and various aromatic aldehydes, according to Scheme 27 has been reported by our research group[157]

Scheme 27



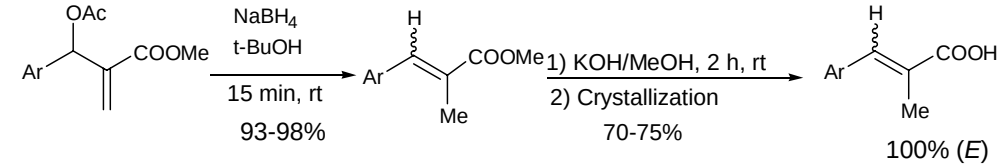
Drewes and co-workers [24] described an efficient synthesis of recemic integerrinecic acid (**63**) form the acetates of the Baylis-Hillman adduct (ethyl 3-acetoxy-2-methylenebutanoate) following the reaction sequence as shown in Scheme 28.

Scheme 28

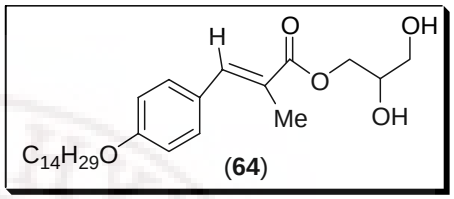


A simple and convenient synthesis of (*E*)-α-methylcinnamic acid derivatives *via* the nucleophilic addition of hydride ion from sodium borohydride, to the Baylis-Hillman acetates followed by hydrolysis, and crystallization (Scheme 29) has been developed by our research group.[158] This strategy has been extended to the synthesis of the precursors of the hypolipidemic active agent (**64**).

Scheme 29



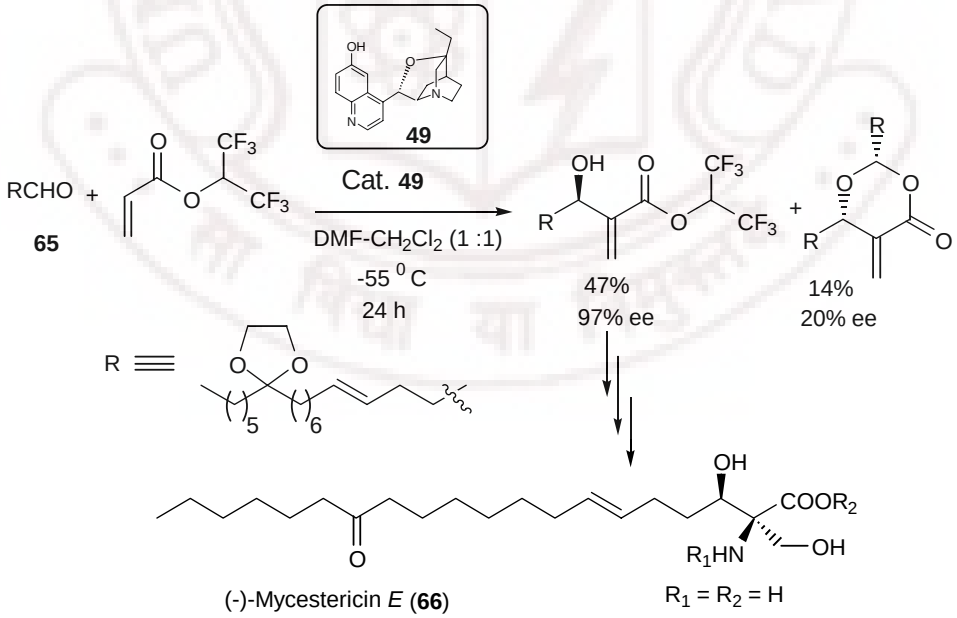
Ar = Ph, 4-ClPh, 4-(i-Pr)Ph, 4-MePh, 2,4-$(Cl)_2$Ph, naphth-1-yl, 4-(tetradecyloxy)Ph



(**64**)

Hatakeyama and co-workers[159] synthesized a potent immunosuppressive agent (-)-Mycestericin *E* (**66**) using the Baylis-Hillman adduct derived *via* the asymmetric Baylis-Hillman coupling of 1,1,1,3,3,3-hexafluoroisopropyl acrylate as a activated alkene with aldehydes (**65**) using the chiral catalyst (**49**) according to Scheme 30.

Scheme 30

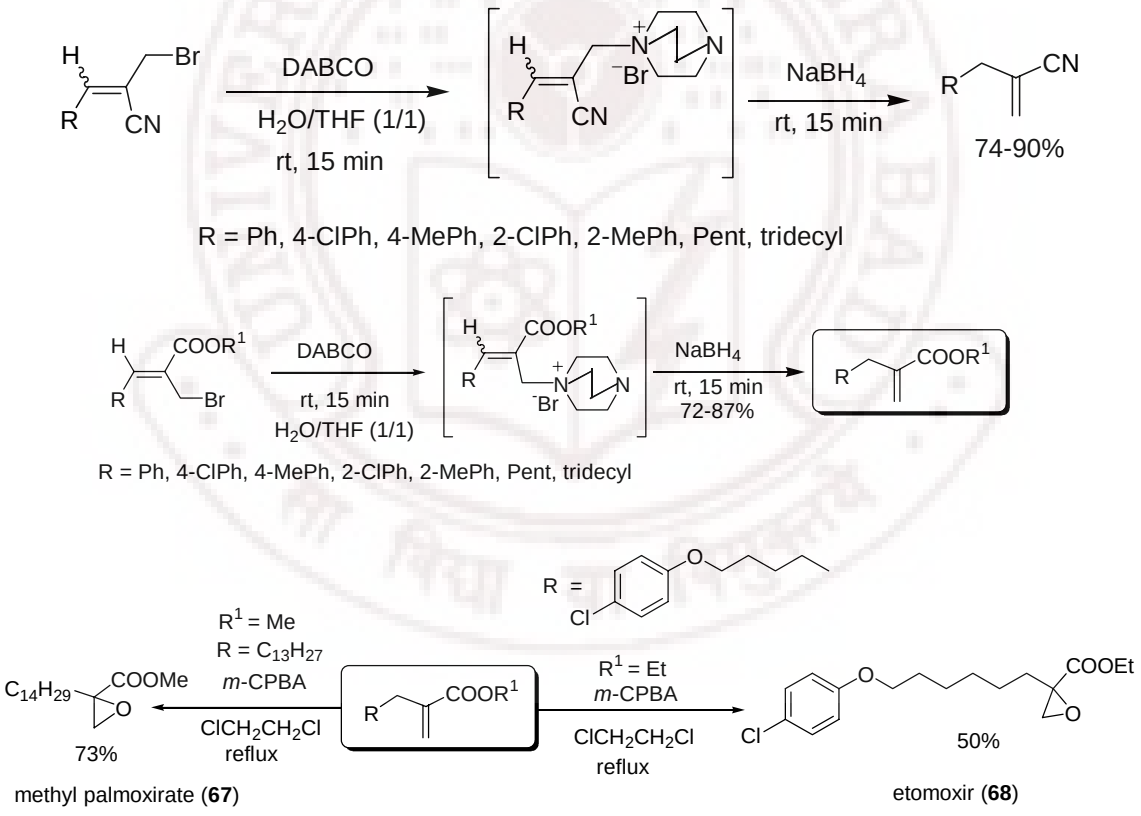


(-)-Mycestericin *E* (**66**)

$R_1 = R_2 = H$

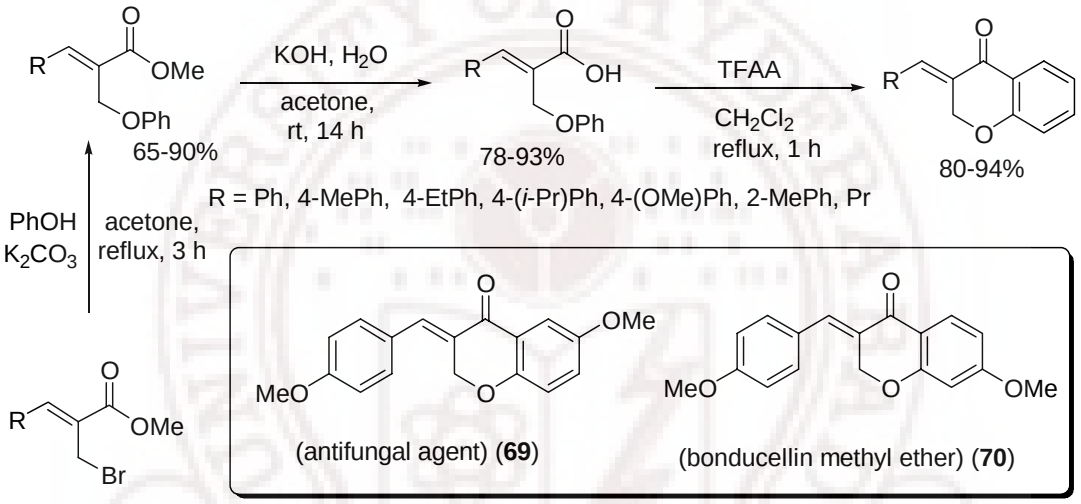
Very recently, our research group[160,161] described an expedient facile one-pot synthesis of 2-methylenealkanoates and alkanenitriles from the Baylis–Hillman bromides in aqueous media via the nucleophilic addition of hydride ion from $NaBH_4$ to in situ generated DABCO Baylis-Hillman allyl bromide salt in aqueous media (Scheme 31). This strategy has been extended for synthesis of two hypoglycemic agents methyl palmoxirate (**67**), and etomoxir (**68**).

Scheme 31



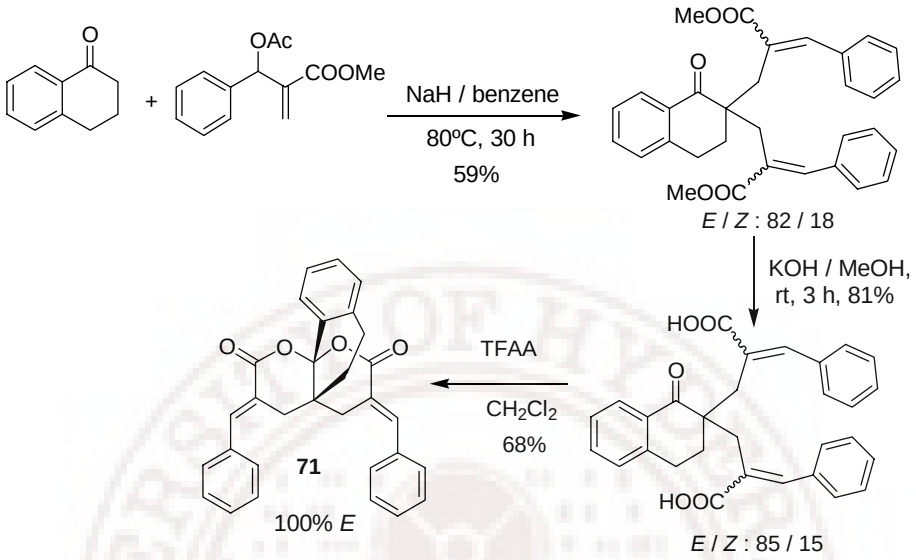
Our research group[162] conveniently, transformed the Baylis-Hillman bromides into 3-arylidene(alkylidene)chroman-4-ones following the reaction sequence as described in Scheme 32. This strategy has been conveniently extended to the synthesis of representative natural products such as antifungal agent (**69**), bonducellin methyl ether (**70**) (Scheme 32).

Scheme 32



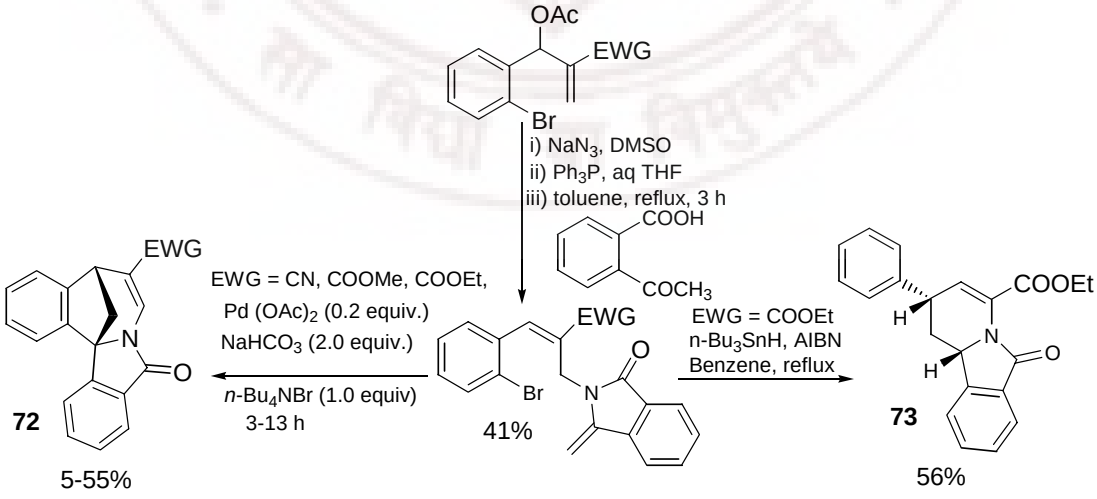
Our research group[163] developed the simple and convenient synthesis of functionalized [4. 4. 4] and [4 .4. 3] propellano-bislactones (**71**) from the Baylis-Hillman acetates following the reaction sequence as shown in Scheme 33 (involving bisalkylation, hydrolysis and lactonization steps). One example is presented in Scheme 33.

Scheme 33



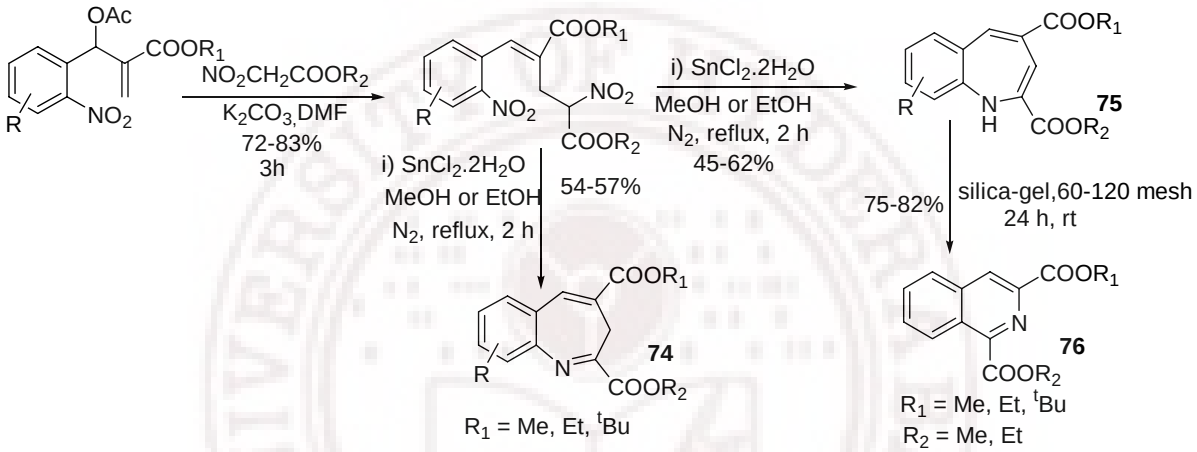
Kim and co-workers have[164,165] reported a facile synthesis of dihydropyrido[2,1-a]isoindoles **72** and **73** (*via* Heck reaction and radical cyclization as the key steps respectively) from the Baylis-Hillman acetates following the reaction sequence as shown in Scheme 34.

Scheme 34



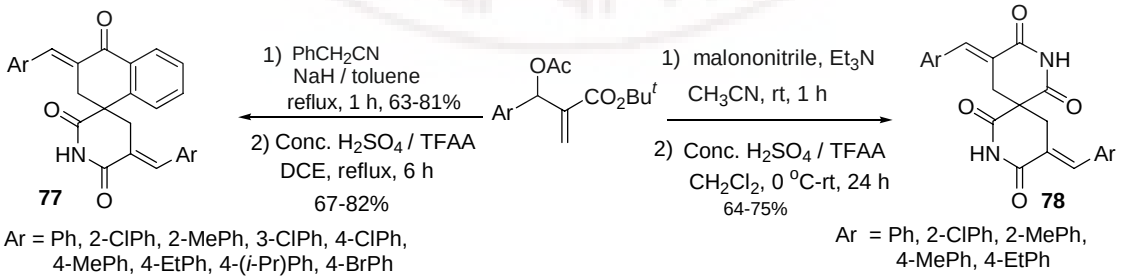
Recently, Batra and co-workers[166] reported the synthesis of 1*H*-and 3*H*-1-benzazepine derivatives (**74**, **75**) and quinoline derivatives (**76**) from the Baylis-Hillman acetates according to Scheme 35.

Scheme 35



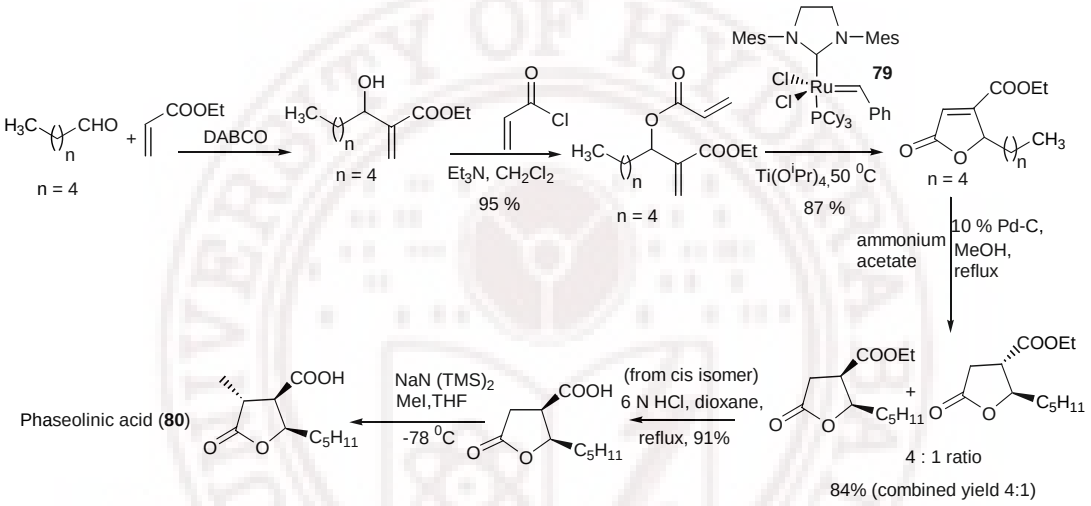
The Baylis-Hillman acetates were transformed into (*E*)-arylidine-tetralone-spiro-glutarimides (**77**) and di (*E*)-arylidine-spiro-bisglutarimides (**78**) by our research group[167]according to reaction sequence as shown in Scheme 36.

Scheme 36



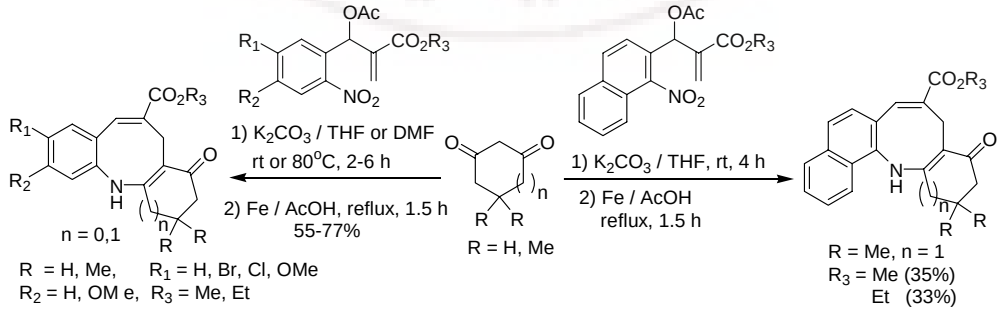
Recently, Selvakumar and co-workers [168] developed a facile methodology for synthesis of butenolides from the Baylis-Hillman adducts involving RCM as the key step using the Grubbs catalyst (**79**) according to Scheme 37. They have successfully applied this methodology for synthesis of phaseolinic acid (**80**).

Scheme 37



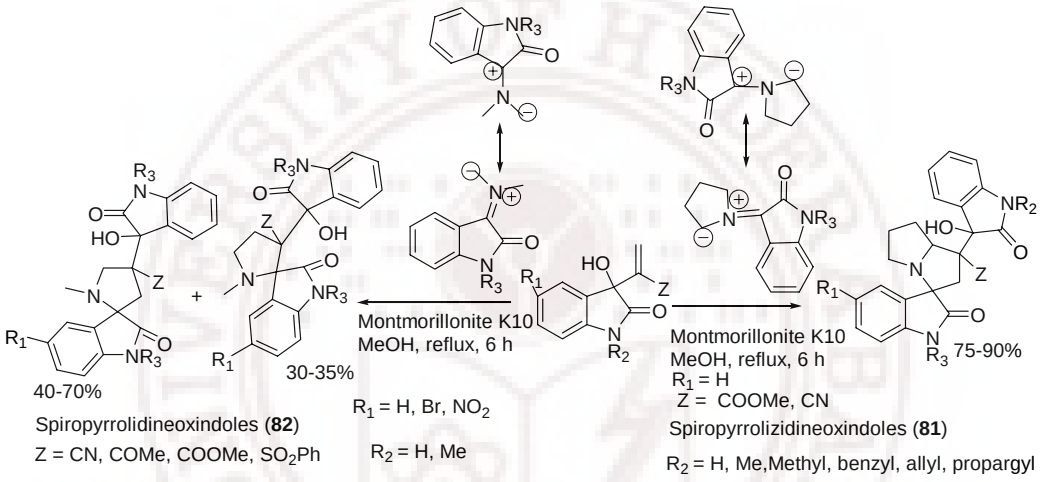
The Baylis-Hillman acetates have been conveniently transformed into tri-/tetracyclic framework containing azocine skeleton following the reaction sequence as described by our research group[169] (Scheme 38).

Scheme 38



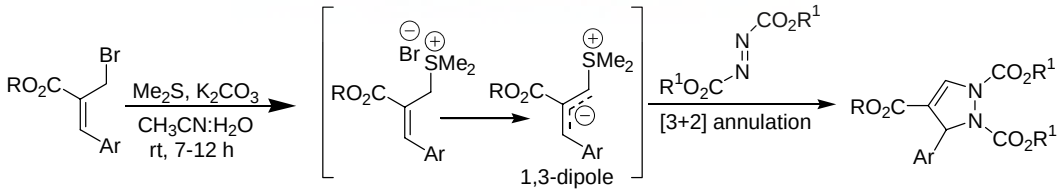
Recently, Shanmugam and co-workers[170] reported the synthesis of functionalized 3-spiropyrrolizidineoxindoles (**81**) and 3-spiropyrrolidineoxindoles (**82**) from the Baylis-Hillman adducts, derived from isatin and heteroaldehydes, involving [3+2] cycloaddition between azomethine ylides and Baylis-Hillman adducts as the key step (Scheme 39).

Scheme 39



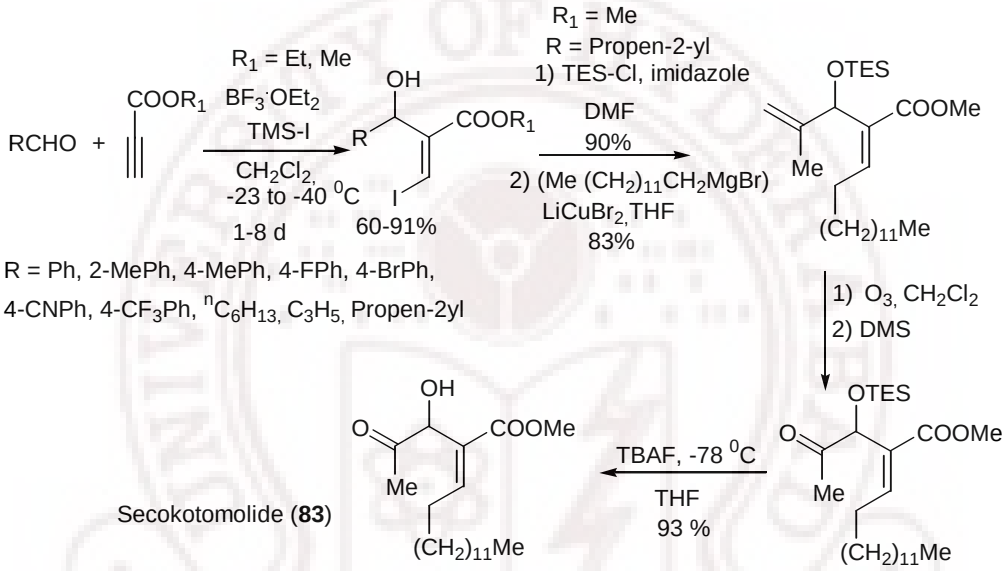
Very recently, our research group[171] has developed a facile synthesis of functionalized dihydropyrazole derivatives, from the Baylis-Hillman bromides in an operationally simple one-pot procedure *via* [3+2] annulation strategy, following the reaction sequence as shown in Scheme 40.

Scheme 40

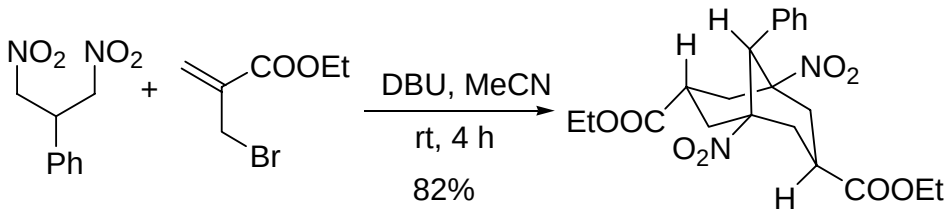


Recently, Ryu and co-workers[172] reported an interesting coupling of α, β-acetylinic esters with aldehydes under the influence of $BF_3.OEt_2$ and TMS-I to provide β-iodo Baylis-Hillman adducts and successfully utilized this methodology for synthesis of naturally occurring secokotomolide (**83**) (Scheme 41).

Scheme 41



Ethyl (2-bromomethyl)acrylate was transformed into bicyclo[3.2.1]nonane derivative *via* the treatment with 1, 3-dinitroalkanes in the presence of DBU by Ballini and co-workers.[173] This reaction is believed to proceed through domino process involving double alkylation and double Michael addition reactions (Eq. 17).



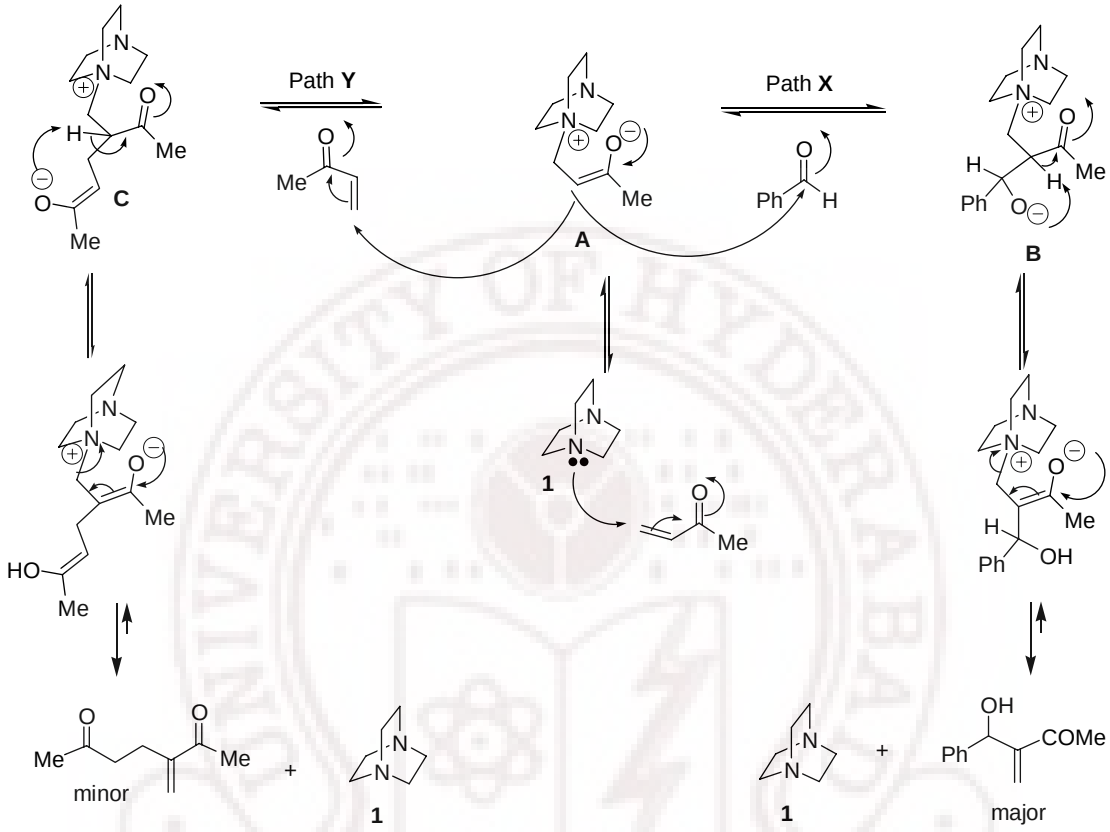
Eq. 17

MECHANISAM

Although the Baylis-Hillman reaction has seen tremendous progress in terms of its variations and applications its mechanism has been not bee completely understood because of the large number variations involved in all the three essential components. However, the most generally accepted mechanism[174-176] of this fascinating reaction is presented in the Scheme 42 by taking methyl vinyl ketone (as an activated alkene), and benzaldehyde (as an electrophile), under the catalytical influence of DABCO (as a catalyst) as a model case.

The first step of this Baylis-Hillman reaction is believed to involve the Michael type addition of DABCO, on to the activated alkene (methyl vinyl ketone) to generate zwitterionic enolate **A**, which then might add onto electrophile (benzaldehyde), *via* an aldol fashion leading to the formation of zwitterionic enolate **B** (path **X**). This zwitterionic species **B** might undergo proton migration and release the catalyst to provide the desired multi-functional molecules, usually called as the Baylis-Hillman alcohols (adducts). On the other hand if the activated alkene is more reactive such as methyl vinyl ketone, then there is a possibility of itself act as an electrophile leading to the formation of Micheal type dimer (Path **Y**) as a minor product as indicated in Scheme 42.

Scheme 42



OBJECTIVES, RESULTS AND DISCUSSION

From the preceding chapter it is clear that Baylis-Hillman reaction has become a very popular carbon-carbon bond forming reaction and the Baylis-Hillman adducts have been employed in various organic transformation methodologies and also in the synthesis of various biologically active molecules and natural products.[10-12] Our research group has been working for the last several years, on various aspects of the Baylis-Hillman reaction and has extensively used the Baylis-Hillman adducts in various organic transformations. In continuation of our interest in expanding the scope of Baylis-Hillman adducts as a novel source for organic transformations we have undertaken the thesis work with the following objectives.

OBJECTIVES

1) To develop a simple and one-pot synthesis of benzo[*b*][1,8]naphthyridones from the Baylis-Hillman adducts.

2) To develop a simple facile and multi-step, one-pot synthesis of quinoline derivatives from the Baylis-Hillman adducts.

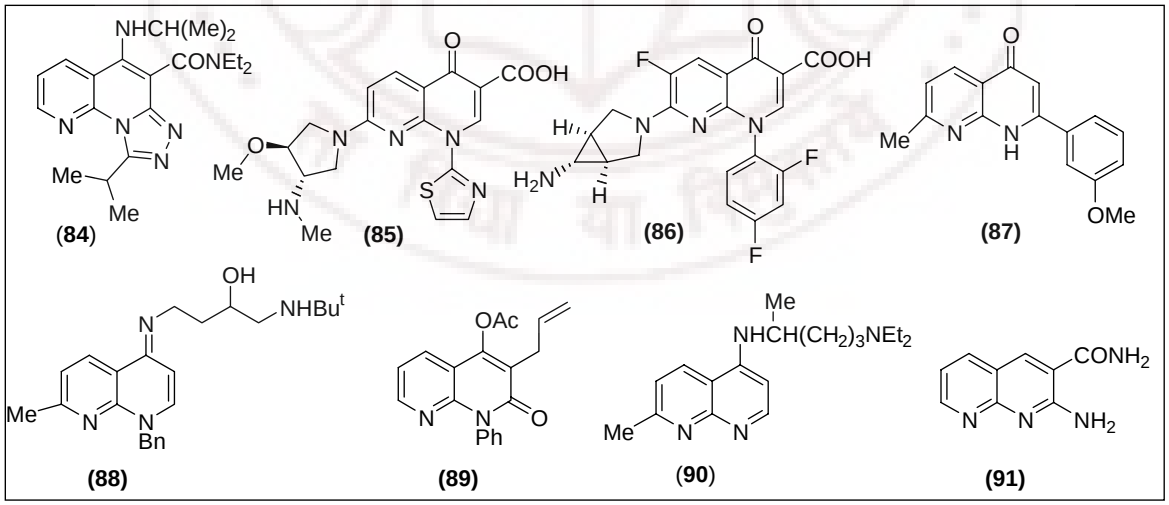
3) To dovelope a simple synthesis of bicyclic frameworks containing benzocycloheptane skeleton and tetracyclic-carbocyclic framework containing 6,7,6,6 ring systems from the Baylis-Hillman adducts.

4) Our objective also includes the developement of simple and one-pot protocol for synthesis of indene-spiro-oxindoles involving construction of two carbon-carbon bonds *via* tandem Prins and Friedel-Crafts reactions.

Simple and One-Pot Synthesis of Tri and Tetracyclic Frameworks Containing [1,8]naphthyridin-2-one Moiety from the Baylis-Hillman Adducts

The 1,8-naphthyridine framework represents an important class of molecules which are found to possess interesting biological properties such as anti-inflammatory (**84**),[177] anticancer (**85**),[178] antibacterial (**86**),[179] antitumour (**87**),[180] antihypertensive (**88**),[181] antiallergitic (**89**),[182] antimalarials (**90**),[183] and also they are found to be potential diuretic agents (**91**)[184] [see Fig. 7].

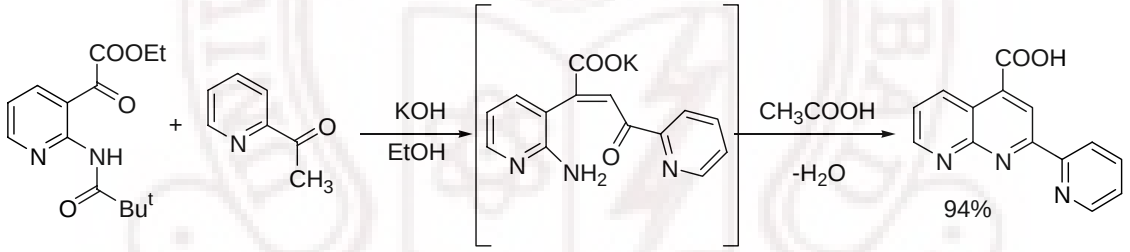
Fig. 7



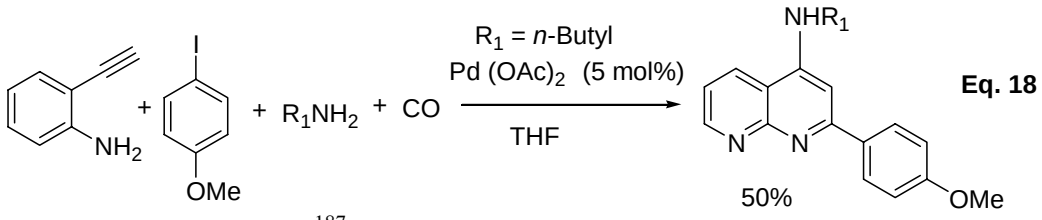
Therefore, there has been increasing interest in the development of facile methodologies for synthesis of [1,8]naphthyridine framework of medicinal relevance. Most of the known methodologies for synthesis of [1,8]naphthyridine framework employed either 2-amino-pyridine or 2-halopyridine derivatives as the key starting materials.

Thummel and co-workers[185] reported a facile synthesis of [1,8]naphthyridine derivatives *via* reaction between [2-(pivaloylamino)pyrid-3-yl]oxoacetic acid ethyl ester {which is prepared from 2-aminopyridine}and 2-acetylpyridine in the presence of ethanolic KOH followed by cyclization according to the reaction sequence as described in Scheme 43.

Scheme 43



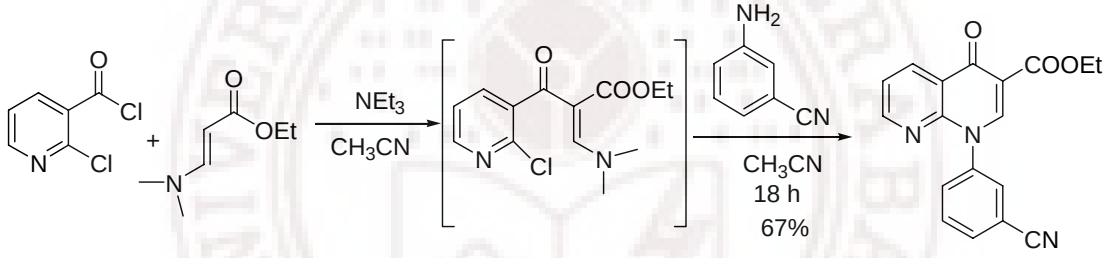
2-Aryl-4-amino[1,8]naphthyridenes derivatives were conveniently synthesized by Rossi and co-workers[186] *via* the palladium assisted multi-component reaction involving 2-ethynylarylamines, aryl iodides, and primary amines in presence of carbon monoxide as shown in Eq. 18.



Eq. 18

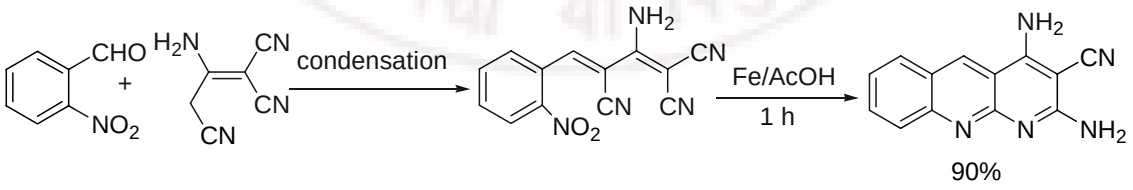
Springfield and co-workers[187] developed the synthesis of [1, 8]naphthyridines *via* the treatment of 2-chloronicotinoyl chloride with β-N,N-dimethylaminoacrylate followed by the reaction with a variety of amines. One such example is given in the Scheme 44.

Scheme 44

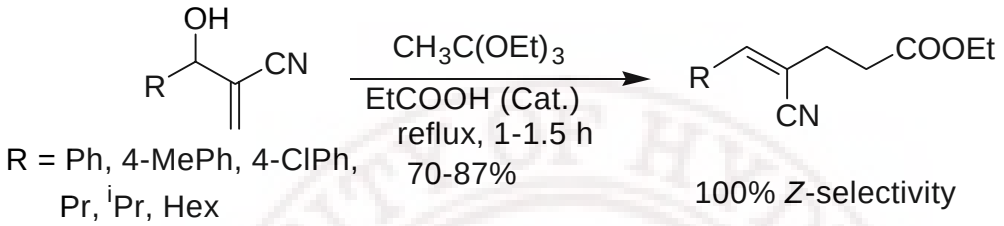


In 1963, Junek[188] reported an interesting synthesis of [1,8]naphthyridine framework *via* the condensation of 2-nitrobenzaldehyde derivatives with appropriate malononitrile derivative followed by reduction of the nitro group and subsequent cyclization (Scheme 45).

Scheme 45

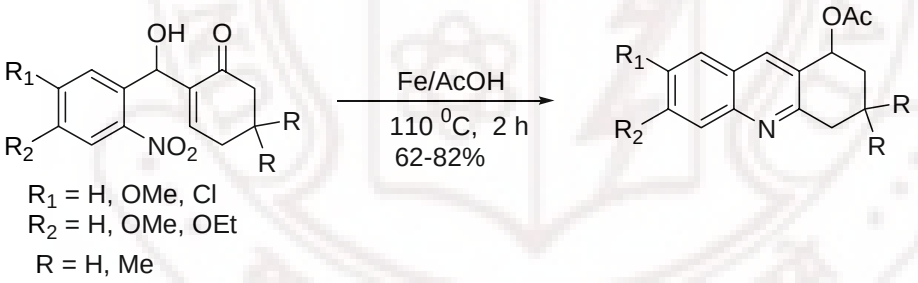


Our research group[189] few years ago, has described the Johnson-Claisen rearrangement of Baylis-Hillman alcohols, obtained from various aldehydes and acrylonitrile, providing 4-cynoalk-4-enoates with exclusive (*Z*)-selectivity in good yields (Eq. 19).



Eq. 19

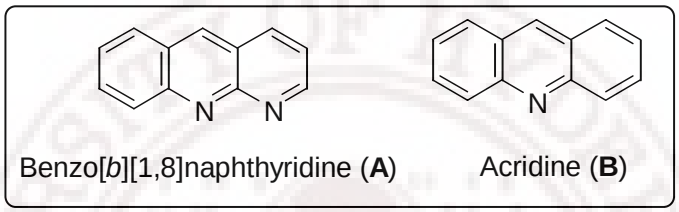
Recently, we have also developed a convenient methodology for facile transformation of Baylis-Hillman adducts, derived from 2-nitrobenzaldehydes and cyclohex-2-enones, into tetrahydroacridine derivatives (Eq. 20).[190]



Eq. 20

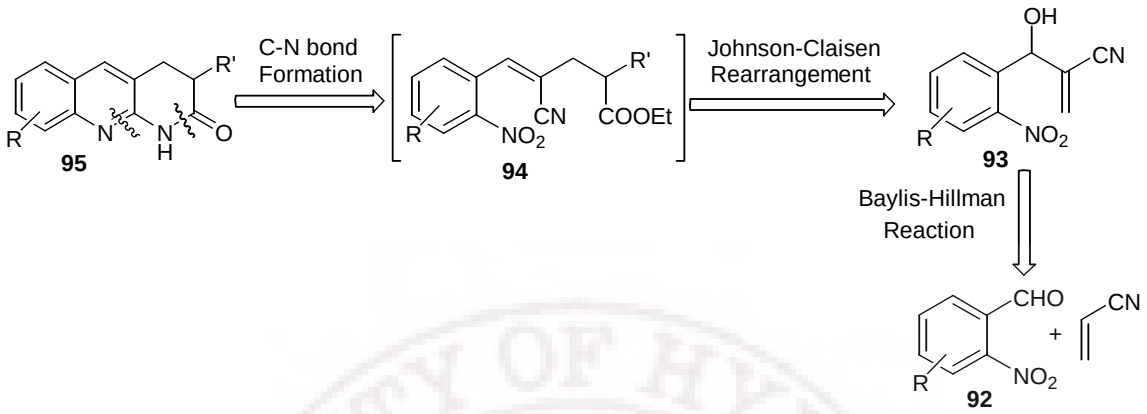
Since the benzo[*b*][1,8]naphthyridine moiety (**A**) is nothing but azaversion of acridine skelton (**B**) (Fig. 8), we became interested in developing a simple synthetic protocol for obtaining such derivatives from the Baylis-Hillman adducts.

Fig. 8 Benzo[*b*][1,8]naphthyridine (**A**) and acridine (**B**) frameworks.

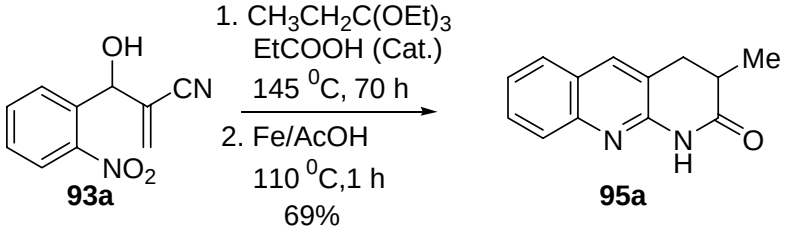


From our previous experience [154,163,167,169,190] on the synthesis of heterocyclic compounds using the Baylis-Hillman adducts it occurred to us that the trisubstituted alkenes (**94**) obtained *via* the Johnson-Claisen rearrangement of Baylis-Hillman alcohols (**93**) derived from 2-nitrobenzaldehydes (**92**) and acrylonitrile, could serve as appropriate synthons for the synthesis of benzonaphthyridin-2-one (**95**) framework through reductive cyclization protocol. It also occurred to us that all these steps, in principle, can be performed in one-pot operation as described in retrosynthetic strategy from the Baylis-Himan alcohols (Scheme 46).

Scheme 46 Retro-synthetic strategy

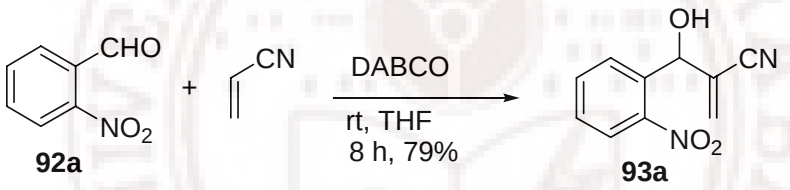


Accordingly, we have first selected 3-hydroxy-2-methylene-3-(2-nitrophenyl)propanenitrile (**93a**) as a substrate for the multi-step one-pot reaction sequence to obtain the desired benzo[*b*][1,8]naphthyridin-2-one derivative (**95a**). In this direction best result was obtained when 3-hydroxy-2-methylene-3-(2-nitrophenyl)propanenitrile (**93a**) (1 mmol) was treated with trietyl orthopropionate (1.25 mL) in the presence of catalytic amount of propanoic acid at reflux temperature for 70 h followed by the treatment of the resulting product (obtained after removal of excess triethyl orthopropionate under reduced pressure) with Fe (6 mmol) / AcOH (5 mL) at reflux temperature at 110 ^{0}C for 1 h thus providing the resulting 2,4-diaza-6-methyltricylo[8.4.0.0$^{3.8}$]tetradeca-1(10),2,8,11,13-pentaene-5-one (**95a**) in 69% isolated yield (Eq. 21). Structure of this molecule was confirmed by IR, ^{1}H NMR [for compound **95a** see Spectrum 1], ^{13}C NMR [for compound **95a** see Spectrum 2], mass spectral data and elemental analysis.



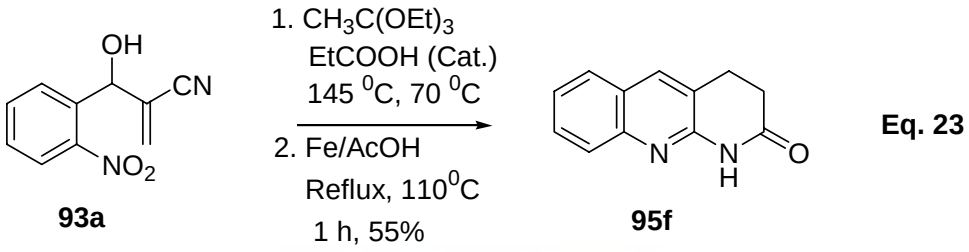
Eq. 21

Required 3-hydroxy-2-methylene-3-(2-nitrophenyl)propanenitrile (**93a**), was obtained *via* the Baylis-Hillman coupling of 2-nitrobenzaldehyde (**92a**) with acrylonitrile under the catalytical influence of DABCO (Eq. 22).



Eq. 22

Encouraged by this result and with a view to understand the generality of this reaction strategy we have selected triethyl orthoacetatae for Johnson-Claisen rearrangement step. Thus treatment of 3-hydroxy-2-methylene-3-(2-nitrophenyl)propanenitrile (**93a**) with triethyl orthoacetate (2.0 mL) in presence of propanoic acid (Cat.) for 70 h followed by reductive cyclization using Fe/AcOH for 1 h provided the desired product 2,4-diazatricyclo[8.4.0.0$^{3.8}$]tetradeca-1(10),2,8,11,13-pentaene-5-one (**95f**)$^{\cap}$ in 55% isolated yield (Eq. 23). Structure of this product was confirmed by IR, ^{1}H NMR, ^{13}C NMR, mass spectral data, mass and elemental analysis.

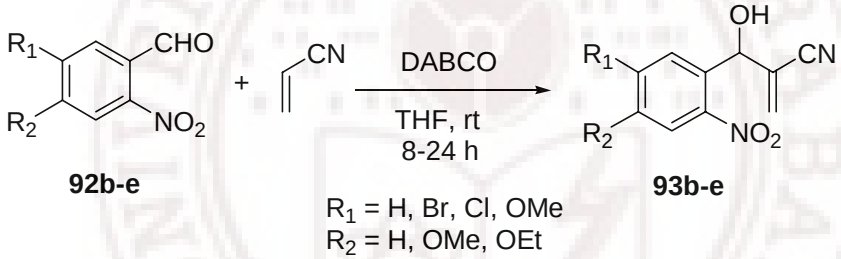


Eq. 23

With a view to understand the generality of this strategy we have prepared representative Baylis-Hillman adducts (**93b-e**) from various 2-nitrobenzaldehydes (**92b-e**) *via* the reaction with acrylonitrile in presence of DABCO (Eq. 24, Table 1).

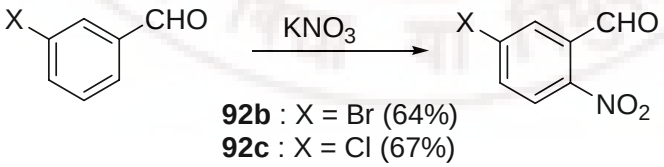
---

[n] For easy understanding and continuation we have numbered naphthyridin-2-one derivatives obtained from B. H. alcohols (**93a-e**) and triethyl orthopropionate as **95a-e** respectively and naphthyridin-2-one derivatives obtained from B. H. alcohols (**93a-e**) and triethyl orthoacetate as **97f-j** respectively.



Eq. 24

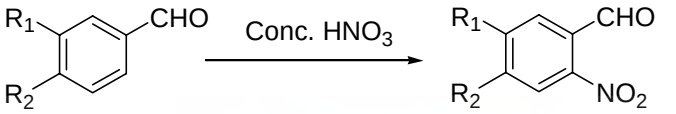
The required 5-bromo-2-nitrobenzaldehyde (**92b**), 5-chloro-2-nitrobenzaldehyde (**92c**) were prepared *via* the nitration of corresponding 3-bromobenzaldehyde and 3-chlorobenzaldehyde respectively, using KNO_3 as a reagent (Eq. 25).[191]



Eq. 25

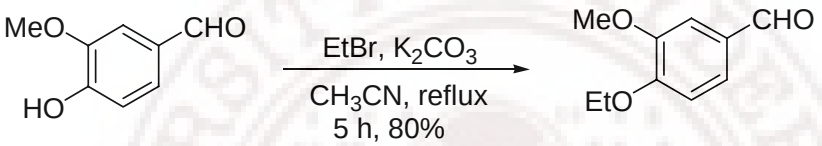
Required 4,5-dimethoxy-2-nitrobenzaldehyde (**92d**) and 4-ethoxy-5-methoxy-2-nitrobenzaldehyde (**92e**), were prepared *via* the nitration of 3,4-dimethoxybenzaldehyde, and 4-ethoxy-3-methoxybenzaldehyde respectively with conc. HNO_3 following the

literature procedure (Eq. 26).[192] 4-Ethoxy-3-methoxybenzaldehyde was prepared from vanillin following the reaction sequence as shown in Eq. 27.



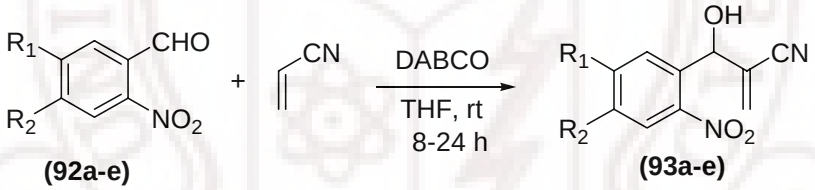
Eq. 26

92d : $R_1 = R_2 = OMe$ (52%)
92e : $R_1 = OMe$, $R_2 = OEt$ (27%)



Eq. 27

Table 1. Synthesis of 3-hydroxy-2-methylene-3-(2-nitrophenyl)propanenitrile derivatives (93a-e)[θ, a]



Aldehyde	R_1	R_2	Product[a]	Yield (%)[b,c]	M.P (^{0}C)
92a	H	H	**93a**	79	58-60
92b	Br	H	**93b**	74	88-90
92c	Cl	H	**93c**	65	58-60
92d	OMe	OMe	**93d**	62	–
92e	OMe	OEt	**93e**	64	98-100

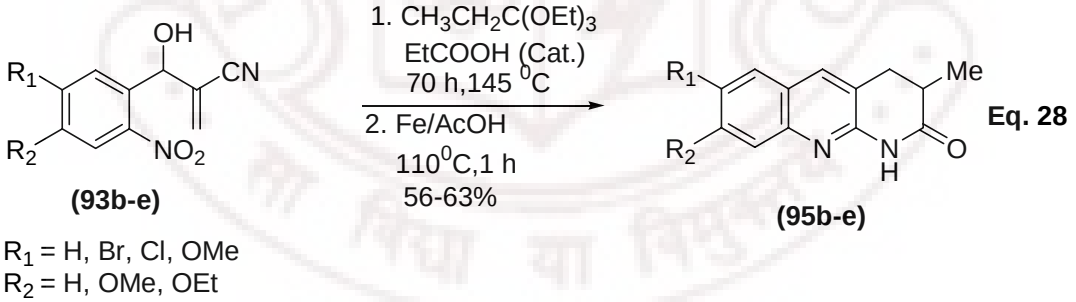
[a]All reactions were carried out on 50 mmol of various 2-nitrobenzaldehydes (**92a-e**) and acrylonitrile (75 mmol), in THF (50 mL) under the catalytic influence of DABCO (15 mol%) at room temperature.

[b]All the compounds (**93a-e**) were characterized by IR, ^{1}H NMR, and ^{13}C NMR spectral data.

[c]Yields are on aldehydes.

[θ]For continuity and better understanding we have numbered various 2-nitroarylaldehydes, Baylis-Hillman alcohols (obtained from acrylonitrile) and benzo[*b*][1,8]naphthyridines as **92**, **93** and **95** respectively.

The Baylis-Hillman alcohols (**93b-e**) were then subjected to Johnson-Claisen rearrangement with triethyl orthopropionate in presence of propanoic acid (catalytic amount) and the subsequent treatment of the resulting *insitu* product with Fe/AcOH provided the benzo[*b*][1,8]naphthyridin-2-one derivatives (**95b-e**) in 56-63% isolated yields (Eq. 28, Table 2). Structures of these compounds were in agreement with IR, ^{1}H NMR, ^{13}C NMR, mass spectral data and elemental analyses.

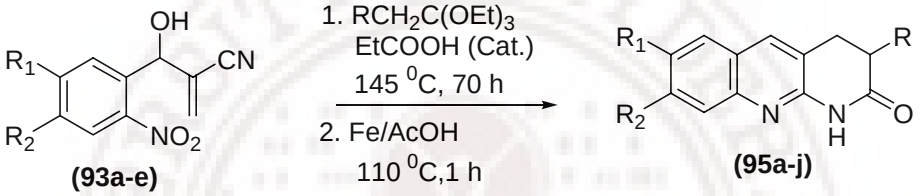


Eq. 28

We have then used triethyl orthoacetate for Johnson-Claisen rearrangement. Thus Johnson-Claisen rearrangement of Baylis-Hillman adducts (**93b-e**) with triethyl orthoacetate under the catalytical influence of propanoic acid (4 drops) followed by the treatment of *insitu* generated product with Fe/AcOH provided benzo[*b*][1,8]naphthyridin-

2-one derivatives (**95g-j**) in 45-58% isolated yields (Eq. 29, Table 2). Structures of these compounds were confirmed by IR, ^{1}H NMR [for compound **95j** see Spectrum 3], ^{13}C NMR, [for compound **95j** see Spectrum 4] mass spectral data and elemental analyses.

Table 2. Synthesis of benzo[*b*][1,8]naphthyridin-2-ones derivatives (95a-j)[a]

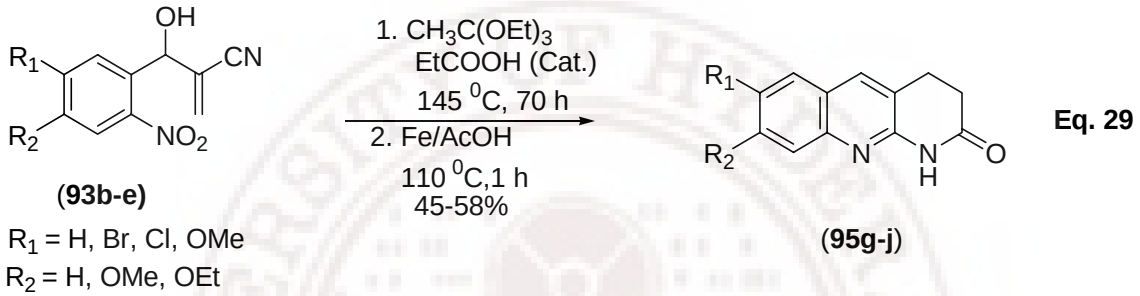


B.H. Alcohol	R_1	R_2	R	Product [a,b]	Yield[c]	M.p (^{0}C)
93a	H	H	Me	**95a**	69	212-214
93b	Br	H	Me	**95b**	56	215-217
93c	Cl	H	Me	**95c**	63	210-212 (dec.)
93d	OMe	OMe	Me	**95d**	60	236-238 (dec.)
93e	OMe	OEt	Me	**95e**	56	227-228 (dec.)
93a	H	H	H	**95f**	55	210-211 (dec.)
93b	Br	H	H	**95g**	45	248-249 (dec.)
93c	Cl	H	H	**95h**	58	246-248
93d	OMe	OMe	H	**95i**	48	234-236 (dec.)
93e	OMe	OEt	H	**95j**	49	247-248 (dec.)

[a] All reactions were carried out on 1 mmol scale of B. H. alcohols (**93a-e**) with triethyl orthopropionate (1.25 mL) or triethyl orthoacetate (2.0 mL), at 145 ^{0}C in the presence of propanoic acid (4 drops) and reductive cyclization was carried out with Fe/AcOH at 110 ^{0}C for 1 h.

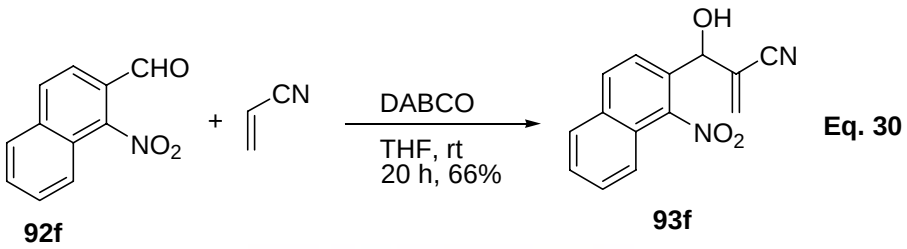
[b]All the compounds (**95a-j**) were obtained as a solids and gave satisfactory IR, ^{1}H NMR, ^{13}C NMR, mass spectral data and elemental analyses.

[c] Yields are based on B. H. alcohols.



Eq. 29

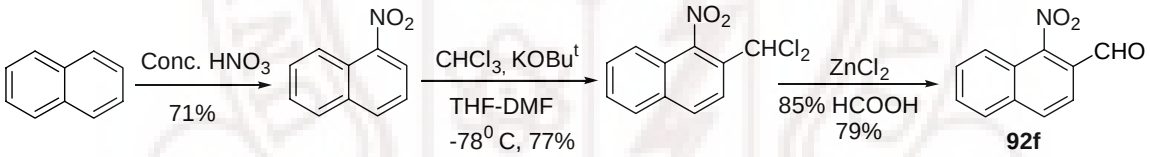
With a view to understand the generality of the reaction strategy and also to obtain tetracyclic system having benzo[*b*][1,8]naphthyridin-2-one framework we have then selected 3-hydroxy-2-methylene-3-(1-nitronaphth-2-yl)propanenitrile (**93f**) as a substrate for Johnson-Claisen rearrangement. Required 3-hydroxy-2-methylene-3-(1-nitronaphth-2-yl)propanenitrile **(93f)** was prepared *via* the Baylis-Hillman coupling of 1-nitro-2-naphthaldehyde (**92f**) with acrylonitrile under the catalytical influence of DABCO (Eq. 30).



92f **93f** **Eq. 30**

Required 1-nitro-2-naphthaldehyde (**92f**) was prepared according to Scheme 47 starting from naphthalene. Thus nitration of naphthalene provided α-nitronaphthalene in 71% isolated yield. Subsequent treatment with chloroform in presence of potassium *tert*-butoxide followed by hydrolysis using $ZnCl_2$ provided 1-nitro-2-naphthaldehyde (**92f**) in 79% isolated yield (Scheme 47)[193a,b]

Scheme 47

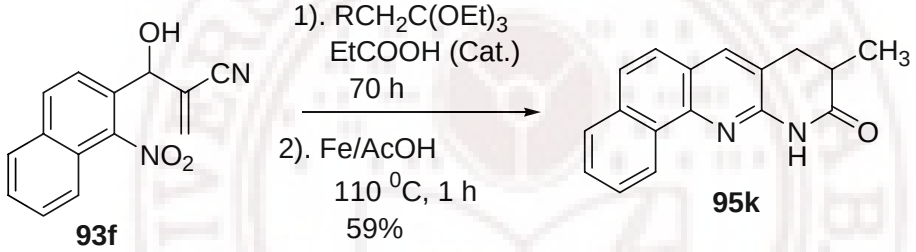


92f

We have then subjected 3-hydroxy-2-methylene-3-(1-nitronaphth-2-yl)propanenitrile (**93f**)[μ] to the reaction strategy as mentioned in Eq. 31. Thus treatment of 3-hydroxy-2-methylene-3-(1-nitronaphth-2-yl)propanenitrile (**93f**) with triethyl orthopropionate under Johnson-Claisen rearrangement conditions followed by reductive cyclization using Fe/AcOH afforded 3,5-diaza-7-methyltetracyclo[12.4.0.$0^{2,11}$.$0^{4,9}$]octadeca-1(14),2(11),3,-9,12,15,17-heptaene-6-one (**95k**) in 59% isolated yield (Eq. 31). Structure of this molecule

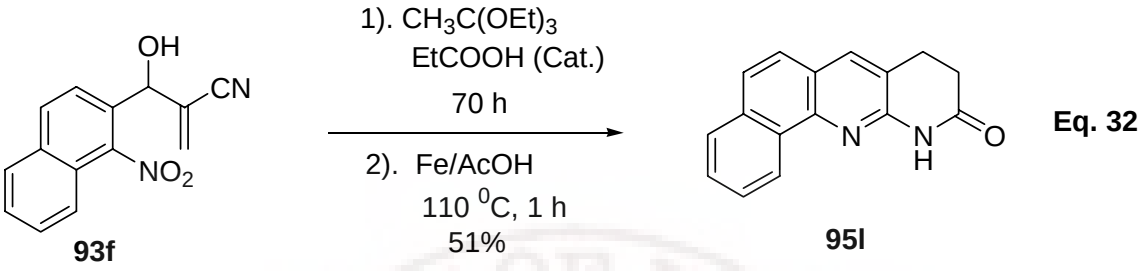
was confirmed by IR, ^{1}H NMR [for compound **95k** see Spectrum 5], ^{13}C NMR [for compound **95k** see Spectrum 6], mass spectral data and elemental analysis. The structure of this molecule was further confirmed by single crystal X-ray data (Table I). For ORTEP diagram see Fig. X1.

[µ]For continuaty and better understanding we have numbered 1-nitro-2-naphthaldehyde as **92f** and corresponding Baylis-Hillman alcohol (obtained from acrylonitrile) as **93f**. We have also numbered the corresponding benzo[*b*][1,8]naphthyridin-2-one derivatives obtained from **93f**, *via* the reaction with triethyl orthopropionate and triethyl orthoacetate as **95k** and **95l** respectively.



Eq. 31

Similarly, treatment of 3-hydroxy-2-methylene-3-(1-nitronaphth-2-yl)propanenitrile (**93f**) with triethylortho acetate (2.0 mL) in presence of propanoic acid (catalytical amount) followed treatment with Fe/AcOH at 110 ^{0}C for 1 h furnished the 3,5-diazatetracyclo[12.4.0.0^{2,11}.0^{4,9}]octadeca-1(14),2(11),3,9,12,15,17-heptaene-6-one **(95l)** in 51% isolated yield (Eq. 32). Structure of this molecule was in agreement with IR, ^{1}H NMR, ^{13}C NMR, mass spectral data and elemental analyses. Structure of this molecule (**95l)** was further confirmed by single crystal X-ray data analysis (Table II). For ORTEP diagram see Fig. X2.



93f **95l** **Eq. 32**

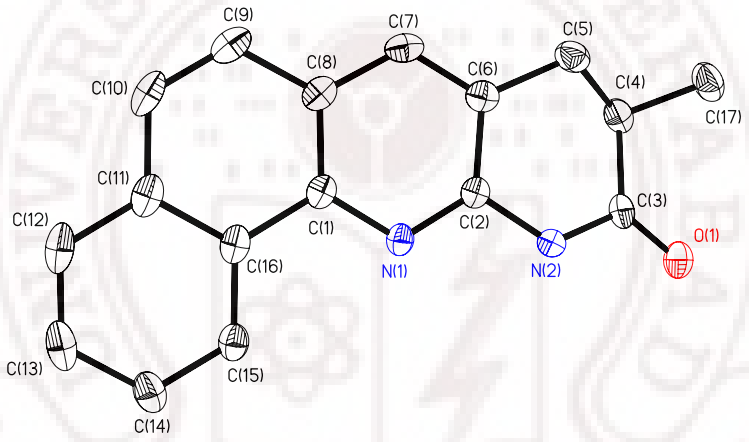


Fig. X1 ORTEP diagram of the compound **95k**
(hydrogen atoms were omitted for clarity)

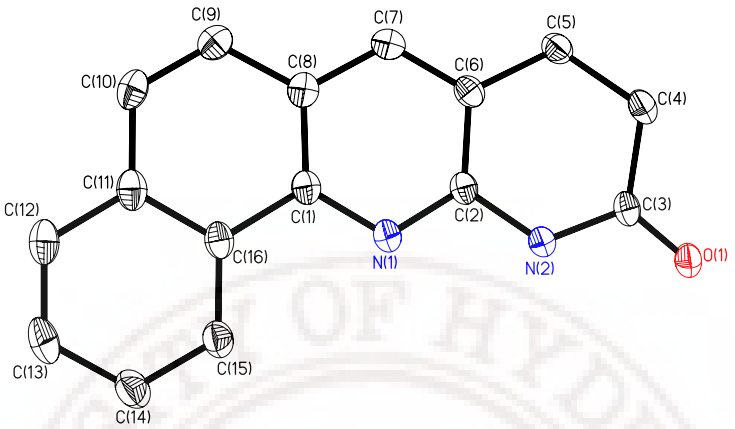


Fig. X2 ORTEP diagram of the compound **95l**
(hydrogen atoms were omitted for clarity)

Table I. Crystal data and structure refinement for 95k

Identification code	: **95k**
Empirical formula	: $C_{17}H_{14}N_2O$
Formula weight	: 262.30
Temperature	: 100(2) K
Wavelength	: 0.71073 Å
Crystal system	: Monoclinic
space group	: P 2(1)/c
Unit cell dimensions	: a = 15.2721(9) Å; α = 90 deg.
	: b = 12.3272(8) Å; β = 113.1960(10) deg.
	: c = 15.1619(9) Å; γ = 90 deg.
Volume	: 2623.7(3) $Å^3$
Z, Calculated density	: 8, 1.328 Mg/m^3
Absorption coefficient	: 0.084 mm^{-1}
F(000)	:1104

Crystal size	: 0.34 x 0.22 x 0.06 mm
Theta range for data collection	: 2.20 to 25.98 deg.
Limiting indices	:-18<=h<=18, -15<=k<=15, -18<=l<=18
Reflections collected / unique	: 26589 / 5129 [R(int) = 0.0496]
Completeness to theta = 25.98	: 99.7 %
Max. and min. transmission	: 0.9924 and 0.9580
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 5129 / 0 / 371
Goodness-of-fit on F^2	:1.020
Final R indices [I>2sigma(I)]	: R1 = 0.0438, wR2 = 0.1008
R indices (all data)	: R1 = 0.0644, wR2 = 0.1108
Largest diff. peak and hole	: 0.205 and -0.273 e. $Å^{-3}$

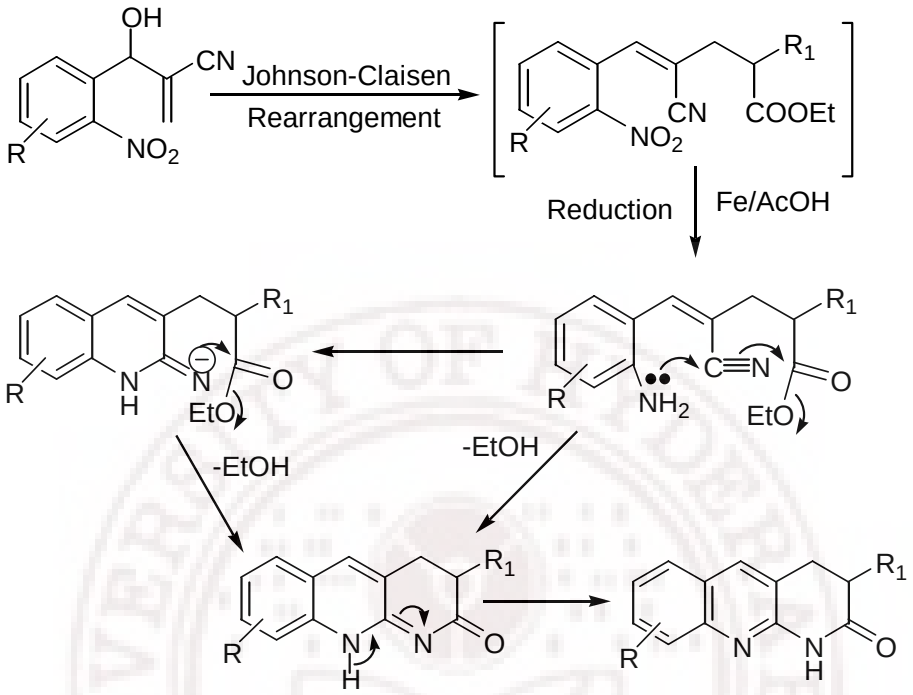
Table II Crystal data and structure refinement for 95l

Identification code	: **95l**
Empirical formula	: $C_{16}\ H_{12}\ N_2\ O$
Formula weight	: 248.28
Temperature	: 100(2) K
Wavelength	: 0.71073 Å
Crystal system	: Monoclinic
space group	: P2(1)/n
Unit cell dimensions	: a = 6.6279(3) Å; α = 90 deg.
	: b = 7.5251(4) Å; β = 96.0860(10) deg.
	: c = 23.1973(12) Å; γ = 90 deg.
Volume	: 1150.46(10) $Å^{-3}$
Z, Calculated density	: 4, 1.433 Mg/m^3
Absorption coefficient	: 0.128 mm^{-1}
F(000)	: 520

Crystal size	: 0.48 x 0.34 x 0.20 mm
Theta range for data collection	: 1.77 to 25.92 deg.
Limiting indices	: -8<=h<=8, -9<=k<=9, -28<=l<=28
Reflections collected / unique	: 11371 / 2239 [R(int) = 0.0378]
Completeness to theta = 25.92	:100.0 %
Max. and min. transmission	: 0.9748 and 0.9409
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 2239 / 0 / 176
Goodness-of-fit on F^2	: 1.081
Final R indices [I>2sigma(I)]	: R1 = 0.0426, wR2 = 0.1144
R indices (all data)	: R1 = 0.0453, wR2 = 0.1171
Largest diff. peak and hole	: 0.205 and -0.329 e. $Å^{-3}$

A plausible mechanism for this one-pot transformation of Baylis-Hillman alcohols derived from 2-nitrobenzaldehydes and acrylonitrile, into benzo[*b*][1,8]naphthyridin-2-one framework is presented in Scheme 48.

Scheme 48. Plausible mechanism for the synthesis of benzo[*b*][1,8]naphthyridone-2-one derivatives



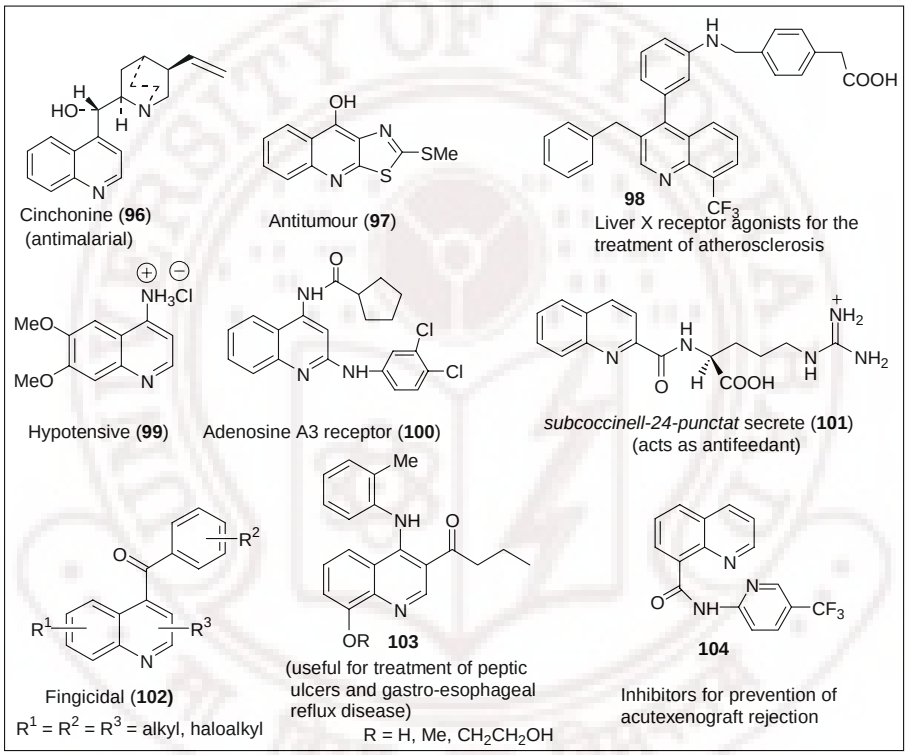
In conclusion, we have successfully developed a simple, facile and one-pot procedure for the synthesis of tri and tetracyclic heterocyclic systems containing benzo[*b*] [1,8]naphthyidine-2-one framework from the Baylis-Hillman alcohols, thus demonstrating the importance of Baylis-Hillman alcohols as valuable synthons for obtaining benzo[*b*][1,8]naphthyridin-2-one framework of medicinal relavence.

Development of simple, facile and multi-step one-pot synthesis of substituted quinoline derivatives from the Baylis-Hillman adducts

The quinoline framework represents an important class of molecules which are found to possess interesting biological properties such as antimalaria (**96**),[194] antitumor (**97**),[195] liver X receptor agonists for treatment of atherosclerosis (**98**),[196] hypotensive (**99**),[197] allosteric

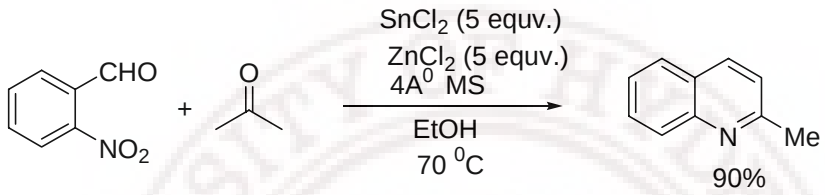
enhancers of the adenosine A3 receptor (**100**),[198] antifeedant (**101**),[194] fingicidal (**102**).[199] Some of the quinoline derivatives are also known to be useful in the treatment of peptic ulcers and also gastro-esophageal reflux disease (**103**),[200] inhibitors for prevention of acute xenograft rejection (**104**)[201] see Fig. 9.

Fig. 9



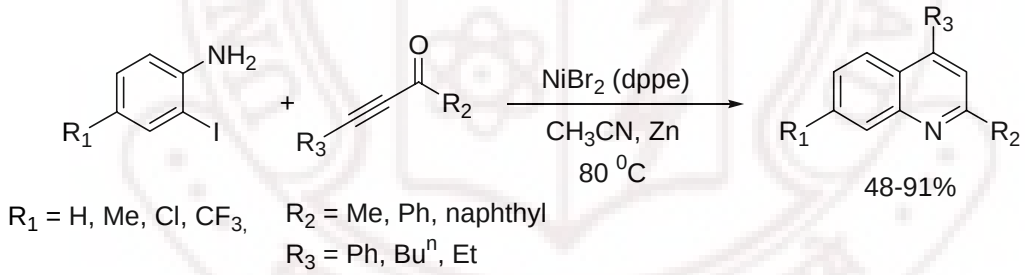
Due to the high importance of the quinoline derivatives in the medicinal chemistry there has been increasing interest to develop simple and convenient methodologies for obtaining quinoline frameworks. Some of the recent and relevant reports are presented in this section.

Miller and co-workers[202] developed an efficient, mild, high yielding one-pot synthesis (Friedlander synthesis), of quinoline derivatives *via* the reaction between 2-nitrobenzaldehyde and acetone derivatives using the combination of $SnCl_2$ and $ZnCl_2$. One representative example is presented in the Eq. 33.



Eq. 33

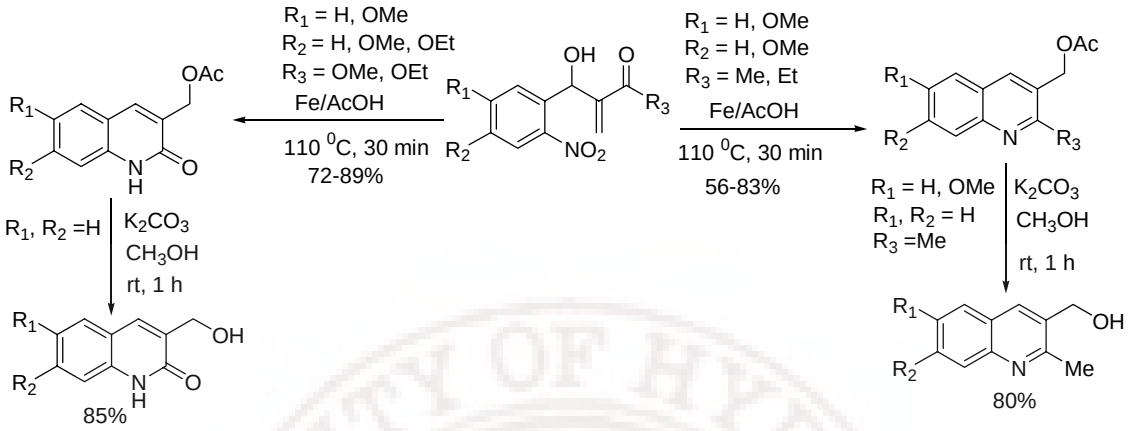
Cheng and co workers[203] developed an efficient nickel catalyzed reaction of 2-iodoanilines with alkynyl aryl (alkyl) ketones to provide the 2,4-disubstituted quinoline derivatives following the reaction sequence as described in Eq. 34.



Eq. 34

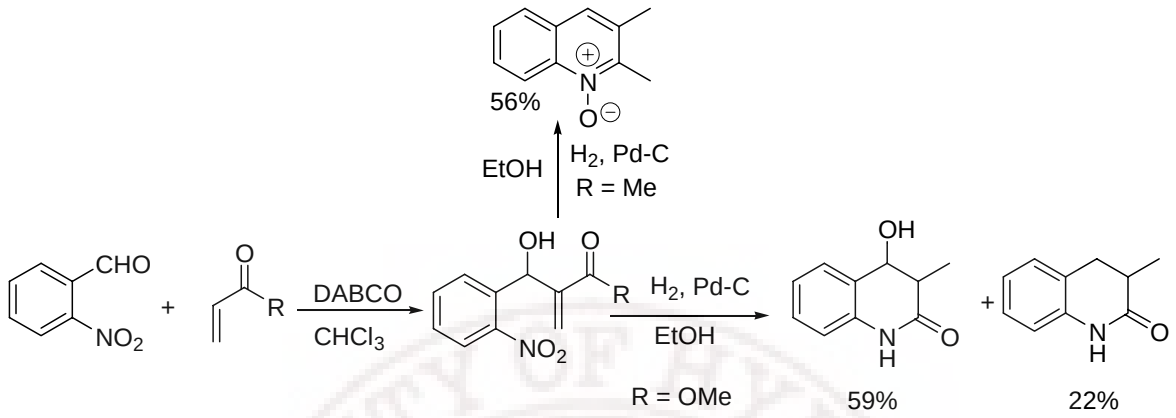
It is worth mentioning here that our research group[204] successfully transformed the Baylis-Hillman alcohols, derived from various 2-nitrobenzaldehydes and methyl acrylate, into substituted (1*H*)-quinoline-2-ones *via* reductive cyclization. Our research group[204] also transformed the Baylis-Hillman alcohols obtained from various 2-nitrobenzaldehydes and methyl (ethyl) vinyl ketones into substituted quinolines (Scheme 49).

Scheme 49



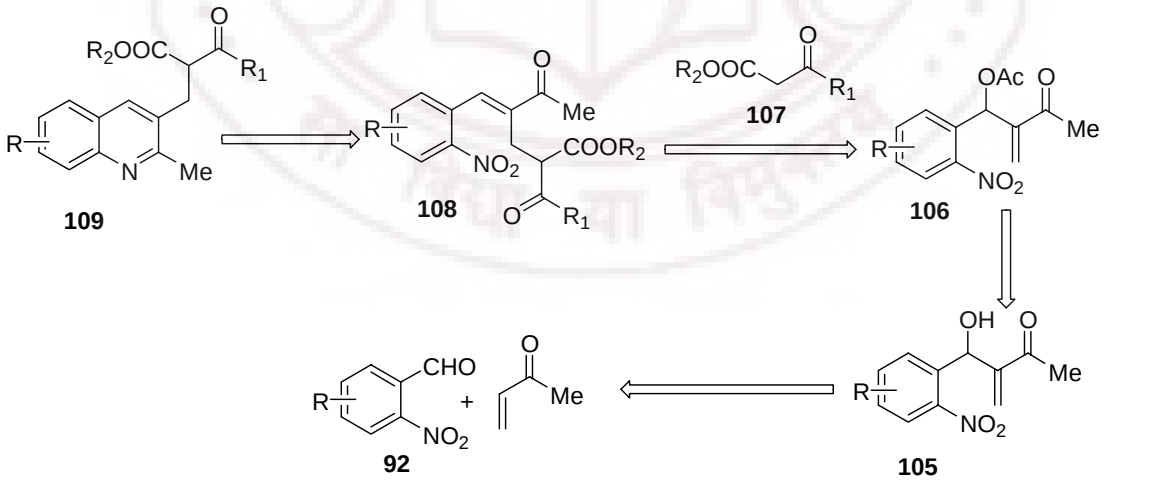
Kaye and co-workers[205] described the synthesis of quinoline derivatives *via* the hydrogenation of the Baylis-Hillman adducts obtained from various 2-ntrobenzaldehydes, and methyl vinyl ketone (or methyl acrylate) following the reaction sequence as described in Scheme 50.

Scheme 50



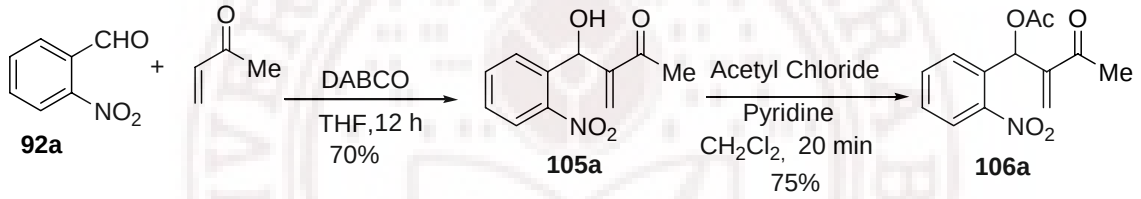
With a view to develop a facile methodology for synthesis of substituted quinoline derivatives we planned to alkylate the acetate of Baylis-Hillman alcohols derived from various 2-nitrobenzaldehydes and perform reductive cyclization to provide various substituted quinoline derivatives as described in retero synthetic strategy (Scheme 51).

Scheme 51 Retero-synthetic strategy

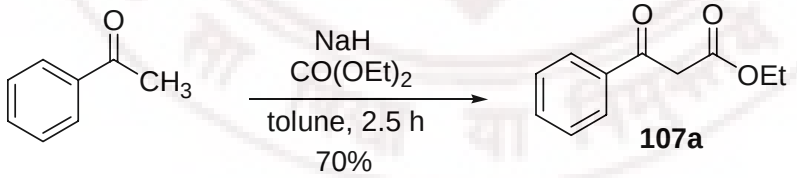


Accordingly, first we have selected 4-acetoxy-3-methylene-4-(2-nitrophenyl)butan-2-one (**106a**) for this study. The required 4-acetoxy-3-methylene-4-(2-nitrophenyl)butan-2-one (**106a**) was prepared following the reaction strategy as shown in Scheme 52. 4-Hydroxy-3-methylene-4-(2-nitrophenyl)butane-2-one (Baylis-Hillman alcohol) (**105a**) was obtained from 2-nitrobenzaldehyde (**92a**) and methyl vinyl ketone under the catalytic influence of DABCO as mentioned in Scheme 52.

Scheme 52



We have also selected ethyl 3-oxo-3-phenylpropionate (**107a**) as an alkylating agent. The required ethyl 3-oxo-3-phenylpropionate (**107a**) was prepared following the known method [206] as mentioned in Eq. 35.

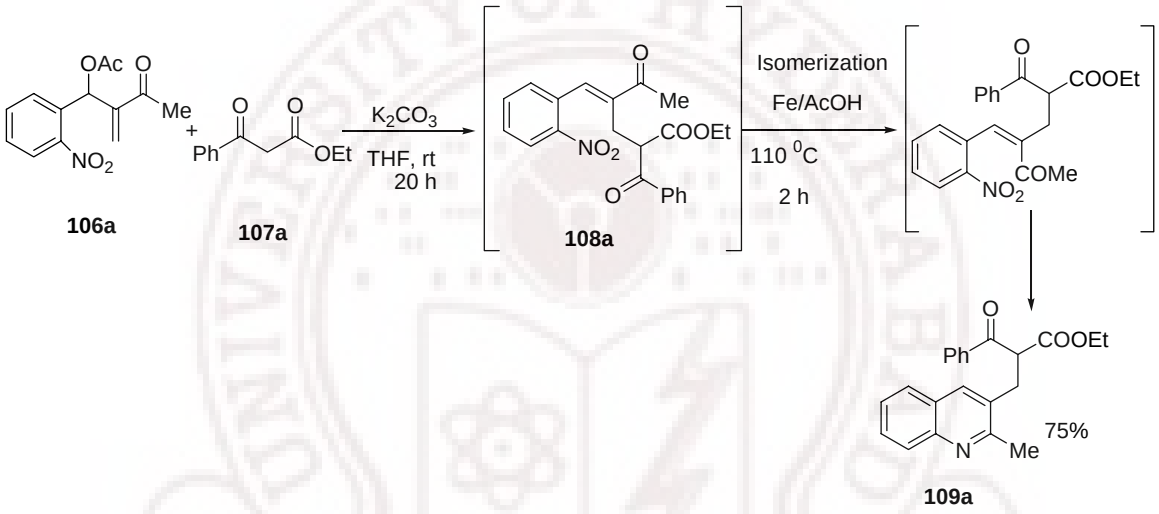


Eq. 35

We have then treated 4-acetoxy-3-methylene-4-(2-nitrophenyl)butan-2-one (**106a**) with ethyl 3-oxo-3-phenylpropionate (**107a**) under the influence of K_2CO_3 in THF at room temperature for 20 h (after the removal of THF at reduced pressure) and subjected the resulting product (**108a**) to the reductive cyclization using Fe/AcOH at 110 ^{0}C for 2 h to

provide 3-(2-ethoxycarbonyl-3-oxo-3-phenylpropyl)-2-methylquinoline (**109a**) in 75% isolated yield (Scheme 53). Structure of this molecule was in full agreement with IR, ^{1}H NMR [for compound **109a** see Spectrum 7], ^{13} C NMR [for compound **109a** see Spectrum 8], mass spectral data and elemental analysis.

Scheme 53

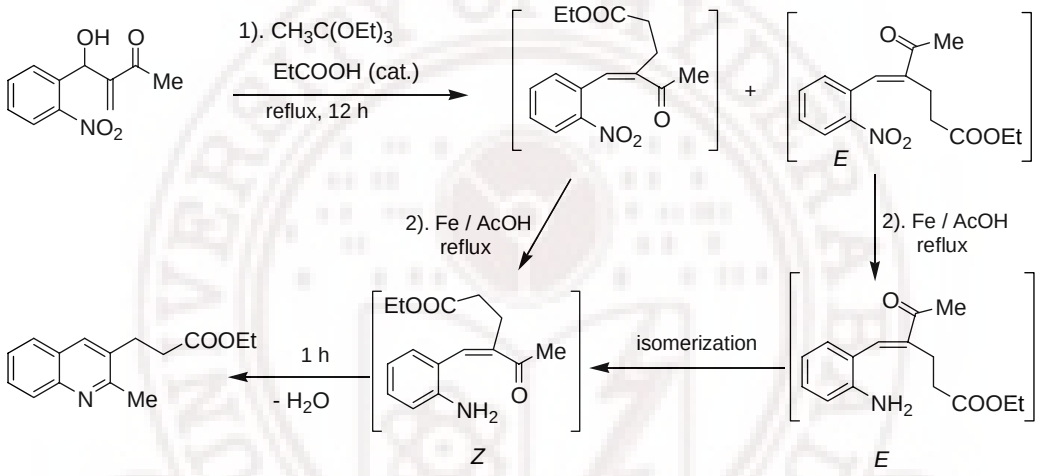


This is interesting reaction in the sense that in the first step, that is in the Michael type addition step, the resulting product **108a** had (*E*)-stereo chemistry (which became (*Z*) double bond in the final product) as determined by ^{1}H NMR spectral data. The structure of the compound was confirmed by IR, ^{13}C NMR, mass and elemental analysis. The structure was further confirmed by single crystal X-ray data (**108a**) (see Fig. X3, Table III). From these results it is clear that the (*E*) intermediate (**108a**) isomerized to *cis* compound in the

presence of Fe/AcOH to provide 3-(2-ethoxycarbonyl-3-oxo-3-phenylpropyl)-2-methylquinoline (**109a**).

It should be mentioned that similar kind of isomerization and cyclization reaction is already observed in our laboratory (Scheme 54).[207]

Scheme 54



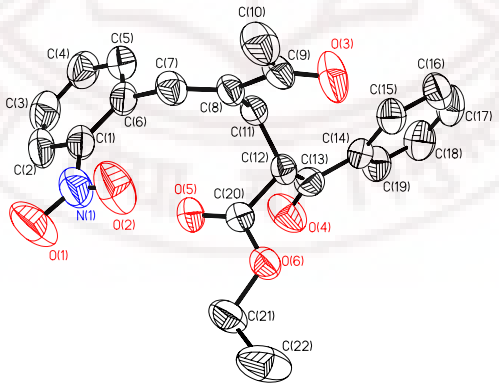


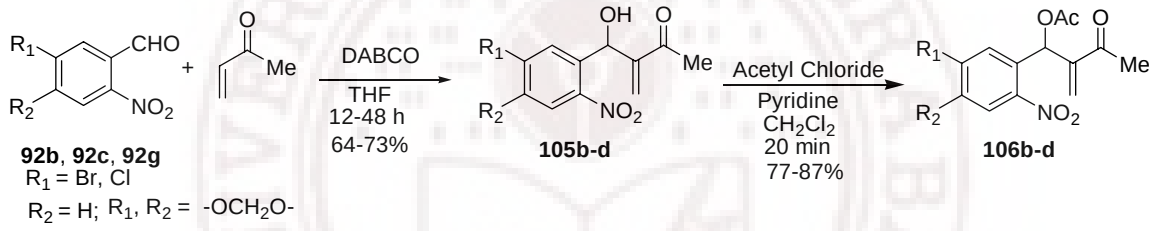
Fig. X3 ORTEP diagram of compound **108a**
(Hydrogen atoms were omitted for clarity)

Table III. Crystal data and structure refinement for 108a

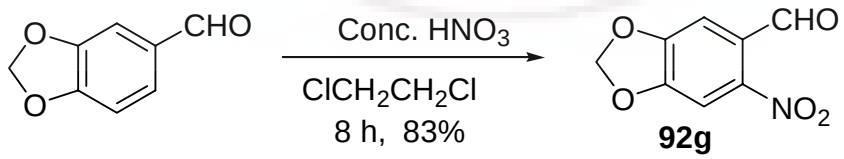
Identification code	: **108a**
Empirical formula	: $C_{22}H_{21}NO_6$
Formula weight	: 395.40
Temperature	: 298 K
Wavelength	: 0.71073 Å
Crystal system	: Orthorhombic
Space group	: Fdd2
Unit cell dimensions	: a = 22.652(3) Å; α = 90 deg.
	: b = 41.697(6) Å; β = 90 deg.
	: c = 8.4369(12) Å; γ = 90 deg.
Volume	: 7969(2) $Å^3$
Z, Calculated density	: 16, 1.318 Mg/m^3
Absorption coefficient	: 0.097 mm^{-1}
F(000)	: 3328
Crystal size	: 0.43 x 0.32 x 0.21 mm
Theta range for data collection	: 1.95 to 25.96 deg.
Limiting indices	: -27<=h<=27, -51<=k<=51, -10<=l<=10
Reflections collected / unique	: 20249 / 3894 [R(int) = 0.0551]
Completeness to theta = 25.96	:100.0 %
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 3894 / 1 / 264
Goodness-of-fit on F^2	: 0.967
Final R indices [I>2sigma(I)]	: R1 = 0.0503, wR2 = 0.0800
R indices (all data)	: R1 = 0.0817, wR2 = 0.0885
Absolute structure parameter	: 0.3(11)
Largest diff. peak and hole	: 0.148 and -0.132 $e.A^{-3}$

In order to understand the generality of this reaction we have prepared representative 4-acetoxy-3-methylene-4-(2-nitroaryl)butan-2-ones (**106b-d**) from corresponding 4-hydroxy-3-methylene-4-(2-nitroaryl)butane-2-ones (**105b-d**) following the reaction sequence as shown in Scheme 55. The required 4-hydroxy-3-methylene-4-(2-nitroaryl)butane-2-one derivatives (**105b-d**) were obtained *via* the Baylis-Hillman coupling between various 2-nitrobenzaldehyds (**92b**, **92c**, **92g**) and methyl vinyl ketone (Scheme 55, Table 3).

Scheme 55

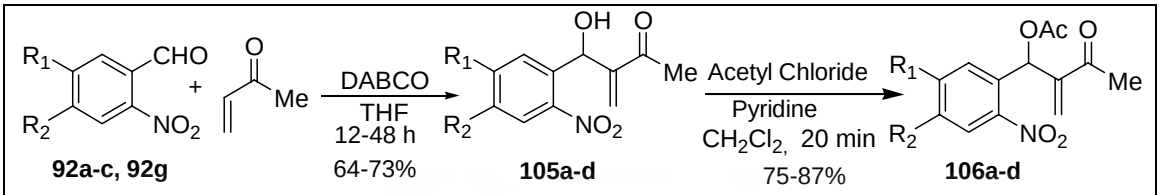


The 6-nitropiperonal (**92g**) was prepared from the piperonal using Conc. HNO_3 according to the literature procedure[208] (Eq. 36). Preparation of 5-bromo-2-nitrobenzaldehyde (**92b**) and 5-chloro-2-nitrobenzaldehyde (**92c**) was already represented in the previous section (Eq. 25).



Eq. 36

Table 3. **Synthesis of Baylis-Hillman alcohols (105a-d)[λ,a] and acetates (106a-d)[λ,b]**



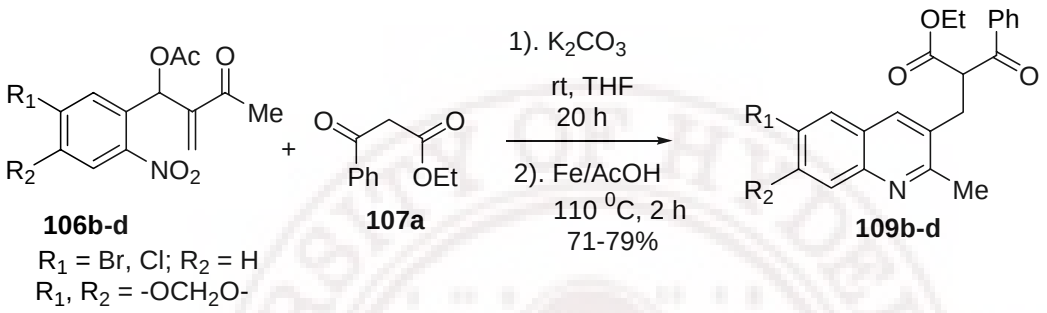
Aldehyde	R_1	R_2	B. H. Alcohol[e]	Yield (%)[c]	B. H. Acetate[e]	Yield (%)[d]
92a	H	H	**105a**	70	**106a**	75
92b	Br	H	**105b**	69	**106b**	77
92c	Cl	H	**105c**	73	**106c**	87
92g	-OCH_2O-		**105d**	64	**106d**	84

[a]All reactions were carried out on 20 mmol scale of various 2-nitrobenzaldehydes (**92a-c**, **92g**) with methyl vinyl ketone (20 mmol), under the catalytical influence of DABCO (15 mol%) at room temperature for 12-48 h. [b]All reactions were carried out on 10 mmol scale of B. H alcohols (**105a-d**) with 20 mmol of acetyl chloride under the influence of pyridine (20 mmol) in dichloromethane at room temperature for 20 min. [c]Yields are based on aldehydes. [d]Yields are based on B. H. alcohols. [e]All compounds (**105a-d** & **106a-d**) gave satisfactory IR, ^{1}H NMR, ^{13}C NMR spectral data.

[λ] For continuity and better understandings we have numbered Baylis-Hillman alcohols (derived from various 2-nitroarylaldehydes and methyl vinyl ketone), Baylis-Hillman acetates, and quinoline derivatives as **105**, **106** and **109** respectively. We have also numbered the B.H. alcohols derived from the aldehydes **92a, 92b, 92c, 92g** as **105a-d** respectively and the corresponding B.H. acetates as **106a-d** respectively.

We have then alkylated the Baylis-Hillman adducts (**106b-d**) with ethyl 3-oxo-3-phenylpropionate (**107a**), in presence of K_2CO_3 at room temperature and the subsequent

reductive cyclization provided the resulting quinoline derivatives (**109b-d**) in 71-79% isolated yields (Eq. 37, Table 4). Structures of these compounds were in agreement with IR, ^{1}H NMR, ^{13}C NMR, mass and elemental analyses.



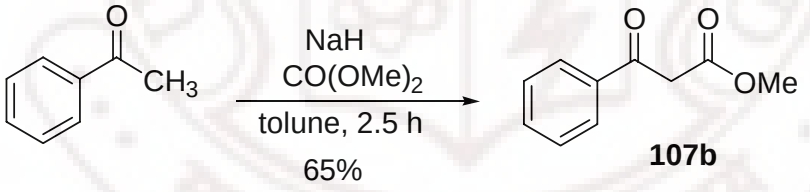
106b-d
R_1 = Br, Cl; R_2 = H
R_1, R_2 = -OCH_2O-

107a

109b-d

Eq. 37

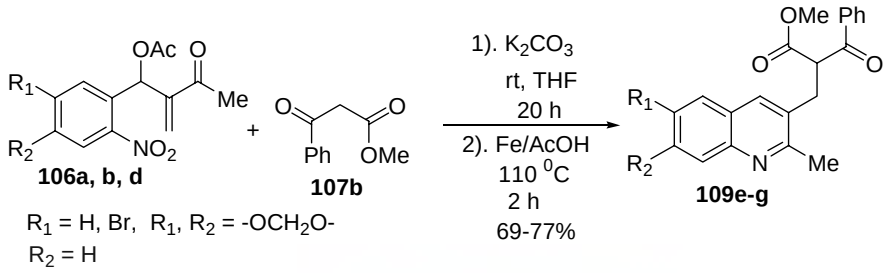
We have also examined methyl 3-oxo-3-phenylpropionate (**107b**) as alkylating agent. This compound (**107b**) was prepared according to the reaction sequence as described in Eq. 38.[206]



107b

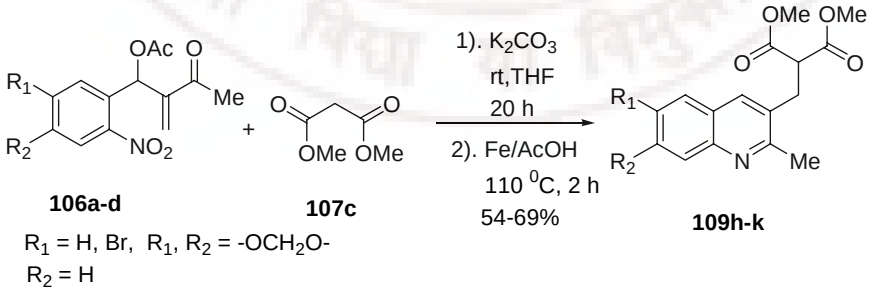
Eq 38

Treatment of Baylis-Hillman adducts (**106a,b,d**) with methyl 3-oxo-3-phenylpropionate (**107b**) in presence of K_2CO_3 at room temperature followed by reductive cyclization using Fe/AcOH provided the resulting quinoline derivatives (**109e-g**) in 69-77% isolated yield (Eq. 39, Table 4). Structures of these compounds were established by IR, ^{1}H NMR [for compound **109g** see Spectrum 9], ^{13}C NMR [for compound **109g** see Spectrum 10], mass spectral data and elemental analyses.



Eq. 39

With a view to understand the scope of this reaction we have selected dimethyl malonate (**107c**) as an alkylating gent. Thus alkylation of Baylis-Hillman acetates (**106a-d**) with dimethyl malonate (**107c**) and subsequent treatment of the resulting adducts with Fe/AcOH furnished the desired quinoline derivatives (**109h-k**) in 54-69% isolated yields (Eq. 40, Table 4). Structures of these compounds were in complete agreement with IR, ^{1}H NMR [for compound **109j** see Spectrum 11], ^{13}C NMR [for compound **109j** see Spectrum 12], mass spectral data and elemental analyses. Structure of the compounds **109h** and **109j** were further confirmed by single crystal X-ray data [for **109h, 109j** see Table IV & Table V respectively]. For ORTEP diagrams of compounds **109h** and **109j** see Fig. X4 and Fig. X5 respectively.



Eq 40

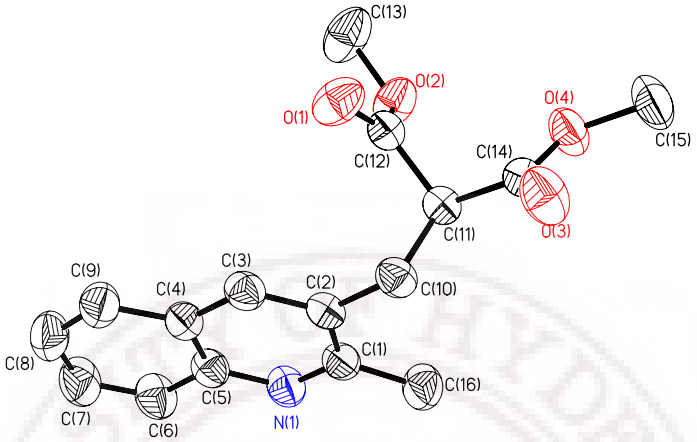


Fig. X4 ORTEP diagram of compound **109h**
(Hydrogen atoms were omitted for clarity)

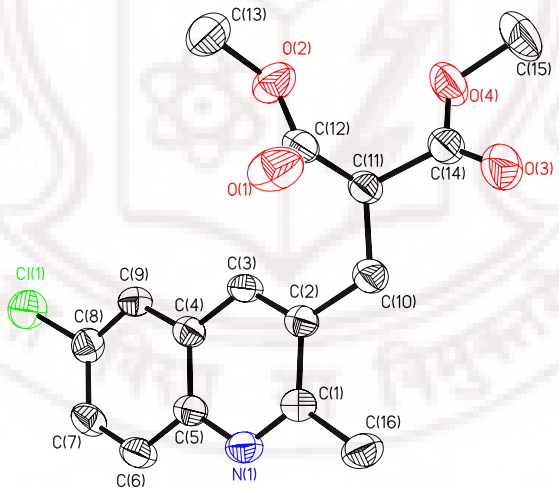


Fig. X5 ORTEP diagram of compound **109j**
(Hydrogen atoms were omitted for clarity)

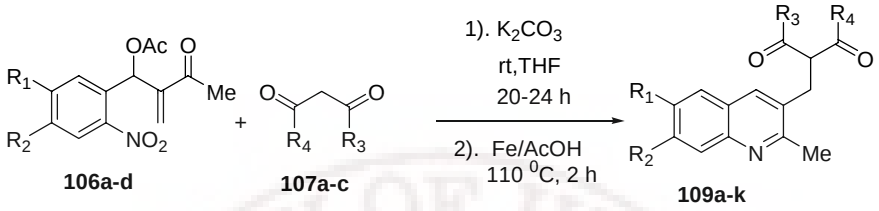
Table IV. Crystal data and structure refinement for 109h.

Identification code	: **109h**
Empirical formula	: $C_{16}\,H_{17}\,N\,O_4$
Formula weight	: 287.31
Temperature	: 298 K
Wavelength	: 0.71073 Å
Crystal system	: Monoclinic
Space group	: P2(1)/c
Unit cell dimensions	: a = 10.3544(19) Å; α = 90 deg.
	: b = 8.0020(15) Å; β = 94.051(3) deg.
	: c = 17.790(3) Å; γ = 90 deg.
Volume	: 1470.3(5) $Å^3$
Z, Calculated density	: 4, 1.293 Mg/m^3
Absorption coefficient	: 0.127 mm^{-1}
F(000)	: 608
Crystal size	: 0.42 x 0.38 x 0.38 mm
Theta range for data collection	: 1.97 to 25.90 deg.
Limiting indices	: -12<=h<=12, -9<=k<=9, -21<=l<=21
Reflections collected / unique	: 13559 / 2848 [R(int) = 0.0369]
Completeness to theta = 25.90	: 99.9 %
Max. and min. transmission	: 0.9534 and 0.9487
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 2848 / 0 / 193
Goodness-of-fit on F^2	: 1.096
Final R indices [I>2sigma(I)]	: R1 = 0.0480, wR2 = 0.1273
R indices (all data)	: R1 = 0.0534, wR2 = 0.1330
Largest diff. peak and hole	: 0.237 and -0.280 $e.A^{-3}$

Table V. Crystal data and structure refinement for 109j

Identification code	: **109j**
Empirical formula	: $C_{16}\ H_{16}\ Cl\ N\ O_4$
Formula weight	: 321.75
Temperature	: 298 K
Wavelength	: 0.71073 Å
Crystal system	: Monoclinic
Space group	: Cc
Unit cell dimensions	: a = 10.1003(11) Å; α = 90 deg.
	: b = 19.958(2) Å; β = 100.866(2) deg.
	: c = 7.6490(8) Å; γ = 90 deg.
Volume	: 1514.3(3) $Å^3$
Z, Calculated density	: 4, 1.411 Mg/m^3
Absorption coefficient	: 0.270 mm^{-1}
F(000)	: 672
Crystal size	: 0.43 x 0.08 x 0.06 mm
Theta range for data collection	: 2.04 to 25.93 deg.
Limiting indices	: -12<=h<=12, -24<=k<=24, -9<=l<=9
Reflections collected / unique	: 7690 / 2936 [R(int) = 0.0402]
Completeness to theta = 25.93	: 99.6 %
Max. and min. transmission	: 0.9435 and 0.6779
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 2936 / 2 / 202
Goodness-of-fit on F^2	: 0.982
Final R indices [I>2sigma(I)]	: R1 = 0.0350, wR2 = 0.0802
R indices (all data)	: R1 = 0.0383, wR2 = 0.0819
Absolute structure parameter	: -0.01(5)
Largest diff. peak and hole	: 0.172 and -0.204 e. $Å^{-3}$

Table 4. Synthesis of quinolines derivatives (109a-k) from the Baylis-Hillman adducts (106a-d)[a,*]



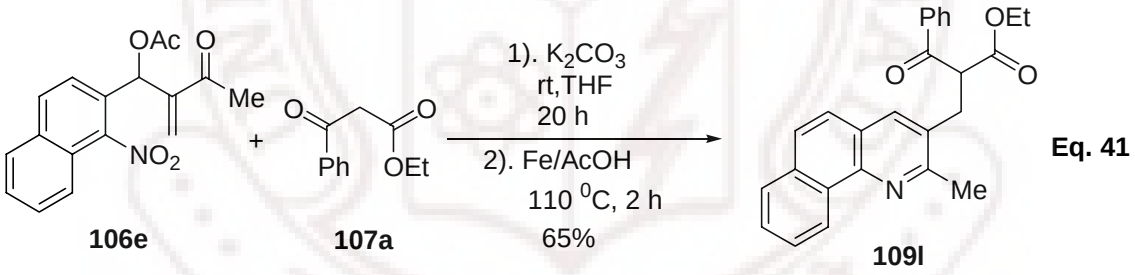
B. H. Acetate	R_1	R_2	R_3	R_4	Product[a]	Yield (%)[b]	M. P ^{0}C
106a	H	H	OEt	Ph	**109a**	75	55-57
106b	Br	H	OEt	Ph	**109b**	72	-
106c	Cl	H	OEt	Ph	**109c**	71	-
106d	-OCH_2O-		OEt	Ph	**109d**	79	119-121
106a	H	H	OMe	Ph	**109e**	77	98-100
106b	Br	H	OMe	Ph	**109f**	72	-
106d	-OCH_2O-		OMe	Ph	**109g**	69	136-138
106a	H	H	OMe	OMe	**109h**	69[c]	98-100
106b	Br	H	OMe	OMe	**109i**	60	117-119
106c	Cl	H	OMe	OMe	**109j**	54[c]	128-130
106d	-OCH_2O-		OMe	OMe	**109k**	61	88-90

[a]All reactions were carried out at on 1 mmol scale of Baylis-Hillman acetates (**106a-d**) with 1 mmol of ethyl 3-oxo-3-phenylpropionate (**107a**) or methyl 3-oxo-3-phenylpropionate (**107b**) or dimethyl malanoate (**107c**) in presence of K_2CO_3 and the reductive cyclization of the resulting product was carried using Fe/AcOH. [b]All the compounds (**109a-k**) gave satisfactory IR, ^{1}HNMR, ^{13}C NMR, mass spectral data and elemental analyses. [c] Structure of compounds **109h** & **109j** further confirmed by single X-ray data analysis.

*For continuity we have numbered quinoline derivatives derived from B .H. acetates (**106a-d**) *via* the reaction with **107a**, as **109a-d** respectively. Quinoline derivatives obtained *via* the reaction of B. H. acetates (**106a**, **106b**, **106d**) with **107b** as **109e-g** respectively. Quinoline derivatives obtained ***via*** the reaction of B. H. acetates (**106a-d**) with **107c** as **109h-k** respectively.

With a view to extend the scope of this strategy and also to obtain tricyclic heterocyclic compounds we have selected 4-acetoxy-3-methylene-4-(1-nitronaphth-2-yl)butan-2-one (**106e**) as a substrate.

Thus the treatment of 4-acetoxy-3-methylene-4-(1-nitronaphth-2-yl)-butan-2-one (**106e**) with ethyl 3-oxo-3-phenylpropionate (**107a**), in presence of K_2CO_3 and subsequent treatment with Fe/AcOH provided the 3-aza-5-(2-ethoxycarbonyl-3-oxo-3-phenylpropyl)-4-methyltricyclo(8.4.0.0^{2,7})tetradeca-1(10),2(7),3,5,8,11,13-heptaene (**109l**) in 65% isolated yield (Eq. 41). Structure of this compound was established by IR, ^{1}H NMR, ^{13}C NMR, mass spectral data and elemental analysis.

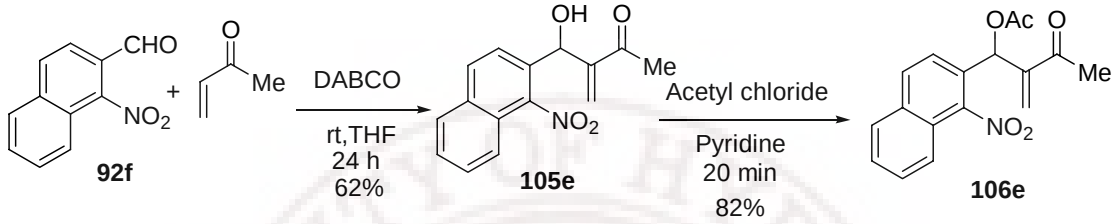


Eq. 41

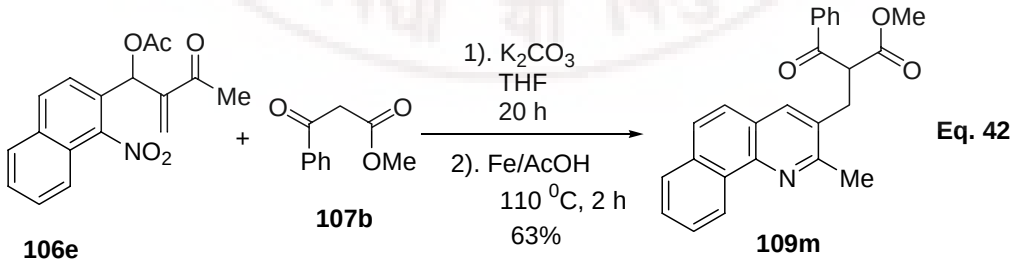
4-Acetoxy-3-methylene-4-(1-nitronaphth-2-yl)-butan-2-one (**106e**) was prepared *via* the acetylation of 4-hydroxy-3-methylene-4-(1-nitronaphth-2-yl)butane-2-one (**105e**) as mentioned in Scheme 56. The required 4-hydroxy-4-(1-nitronaphth-2-yl)-3-methylene-butane-2-one (**105e**) was prepared *via* the Baylis-Hillman coupling of 1-nitronaphalene-2-carboxaldehyde (**92f**) with methyl vinyl ketone under the influence of DABCO as

mentioned in Scheme 55. Preparation of 1-nitonaphthalene-2-carboxaldehyde (**92f**) was already mentioned in previous section Scheme 47.

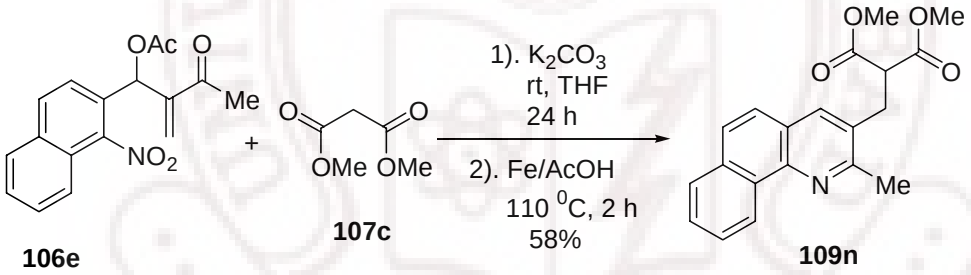
Scheme 56



Alkylation of 4-acetoxy-3-methylene-4-(1-nitronaphth-2-yl)-butanone (**106e**)**,** with methyl 3-oxo-3-phenylpropionate (**107b**) in presence of K_2CO_3 at room temperature followed by treatment with Fe/AcOH provided 3-aza-5-(2-methoxycarbonyl-3-oxo-3-phenylpropyl)-4-methyltricyclo(8.4.0.0^{2,7})tetradeca-1(10),2(7),3,5,8,11,13-heptaene (**109m**) in 63% isolated yield (Eq. 42). Structures of this compound was in confirmed by IR, ^{1}H NMR [for compound **109m** see Spectrum 13], ^{13}C NMR [for compound **109m** see Spectrum 14], mass spectral data and elemental analysis.



We have also treated the 4-acetoxy-3-methylene-4-(1-nitronaphth-2-yl)-butanone (**106e**) with dimethyl malonate (**107c**), in presence of K_2CO_3 at room temperature for 24 h and the treatment of the resulting product with Fe/AcOH for 2 h provided 3-aza-5-(2-methoxycarbonyl)-4-methyltricyclo(8.4.0.$0^{2,7}$)tetradeca-1(10),2(7),3,5,8,11,13-heptaene (**109n**) in 58% isolated yield (Eq. 43). Structures of this compound was full agreement with IR, ^{1}H NMR, ^{13}C NMR, mass spectral data and elemental analysis. Structure of this molecule was further confirmed by single crystal X-ray data analysis [Table VI]. For ORTEP diagram see Fig. X6. A plausible mechanism for the formation of quinoline derivatives from the B. H. acetates is described in Scheme 57.



Eq. 43

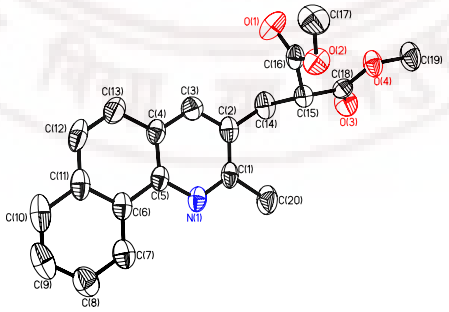
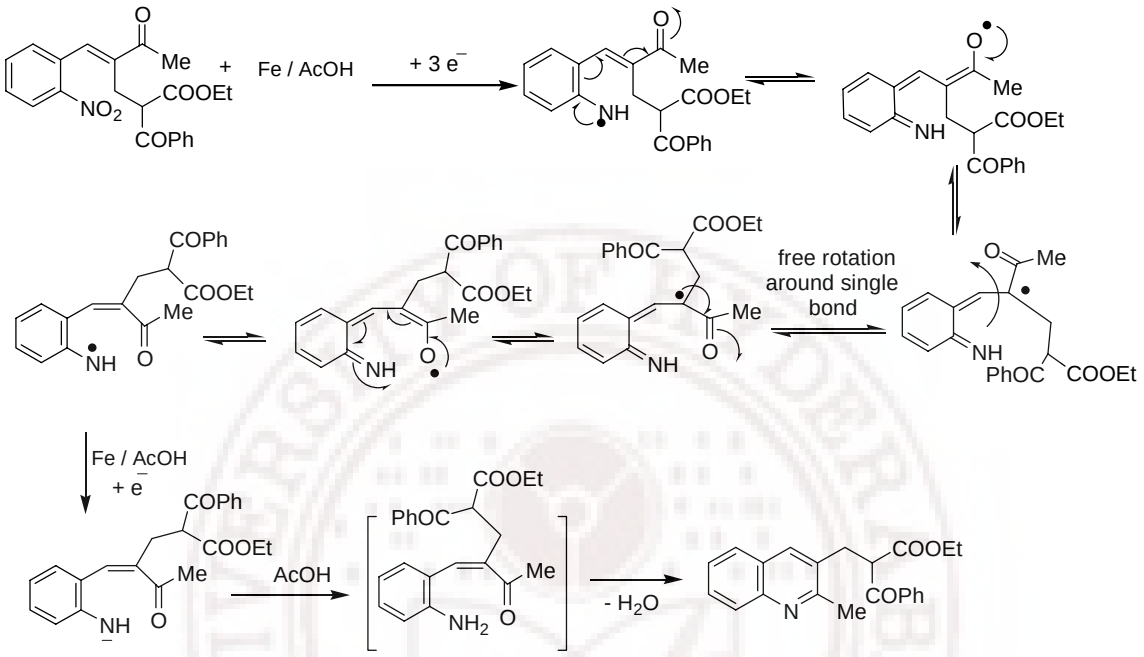


Fig. X6 ORTEP diagram of compound **109n**
(Hydrogen atoms were omitted for clarity)

Table VI. Crystal data and structure refinement for 109n

Identification code	: **109n**
Empirical formula	: C_{20} H_{19} N O_4
Formula weight	: 337.36
Temperature	: 298 K
Wavelength	: 0.71073 Å
Crystal system	: Monoclinic
Space group	: P 2(1)/c
Unit cell dimensions	: a = 4.8463(5) Å; α = 90 deg.
	: b = 17.4458(17) Å; β = 92.524(2) deg.
	: c = 20.110(2) Å; γ = 90 deg.
Volume	: 1698.6(3) $Å^3$
Z, Calculated density	: 4, 1.319 Mg/m^3
Absorption coefficient	: 0.092 mm^{-1}
F(000)	: 712
Crystal size	: 0.40 x 0.36 x 0.28 mm
Theta range for data collection	: 1.55 to 25.99 deg.
Limiting indices	: -5<=h<=5, -21<=k<=21, -24<=l<=24
Reflections collected / unique	: 16900 / 3307 [R(int) = 0.0866]
Completeness to theta = 25.99	: 99.9 %
Max. and min. transmission	: 0.9649 and 0.9504
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 3307 / 0 / 229
Goodness-of-fit on F^2	: 1.056
Final R indices [I>2sigma(I)]	: R1 = 0.0761, wR2 = 0.1535
R indices (all data)	: R1 = 0.1384, wR2 = 0.1780
Largest diff. peak and hole	: 0.205 and -0.234 e. $Å^{-3}$

Scheme 57 Plausible mechanism

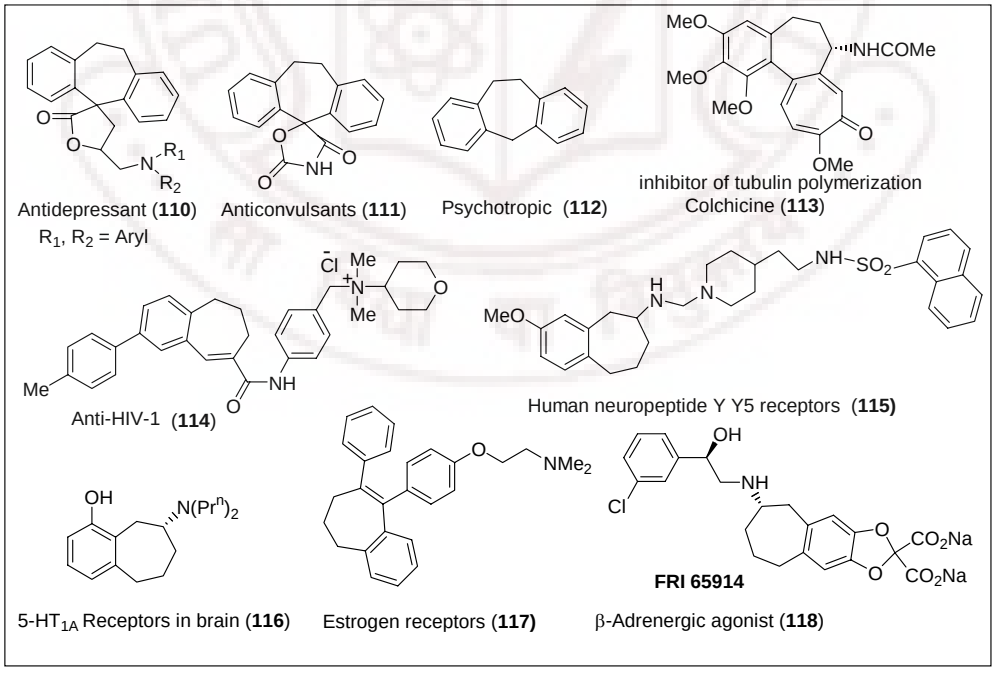


In conclusion we have developed simple and one-pot protocol for synthesis of substituted quinoline derivatives starting from the Baylis-Hillman acetates *via* the Michael addition reaction with various carbon nucleophiles followed by reductive cyclization using Fe/AcOH.

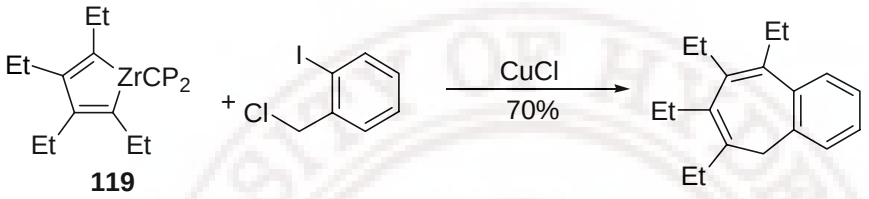
Development of a simple synthesis of bicyclic and tetracyclic carbocyclic framework having 6,7 and 6,7,6,6 fused ring systems from the Baylis-Hillman acetates

Benzocycloheptane framework is well known to possess important biological activities such as antidepressants (**110**),[209] anticonvulsants (**111**),[210] psychotropic agents (**112**)[211] colchicine (**113**),[212] anti-HIV-1 (**114**),[213] β-adrenergic agonist, estrogen receptors, Human neuropeptide Y Y5 receptors (**115**),[214] 5-HT_{1A} receptors in brain (**116**),[215] estrogen receptor (**117**),[216] β-adrenergic agonist (**118**),[217] (Fig. 10). Therefore development of simple and facile methodologies for the synthesis of benzocycloheptane derivatives is an important and attractive endeavor in synthetic organic chemistry.

Fig. 10

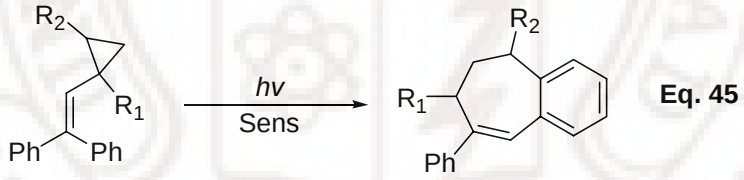


Some of the recent and relevant reports on the synthesis of benzocycloheptane derivatives are presented in this section. Takahashi and co-workers[218] developed an interesting copper catalyzed reaction of zirconacyclopentadienes (**119**) with 2-iodobenzylhalides to afford the benzocycloheptene derivatives. One such example is presented in the Eq. 44.



119 **Eq. 44**

Armesto and co-workers[219] developed a novel photochemical vinylcyclopropane rearrangement strategy for the synthesis of 6,7-dihydro-5*H*-benzocycloheptene framework (**120**), derivatives according to Eq. 45.



Eq. 45

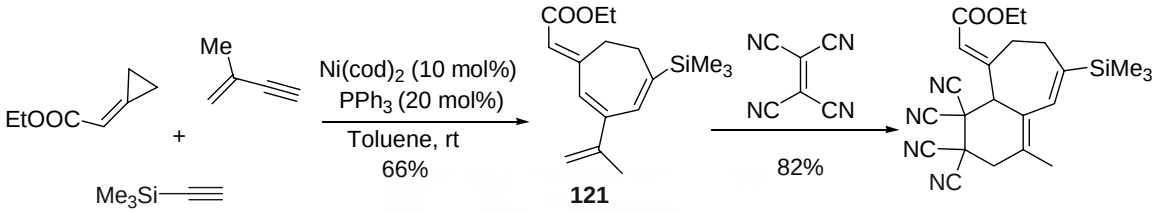
120

R_1 = COOR or C =N-OAc

R_2 = H, Me, Ph

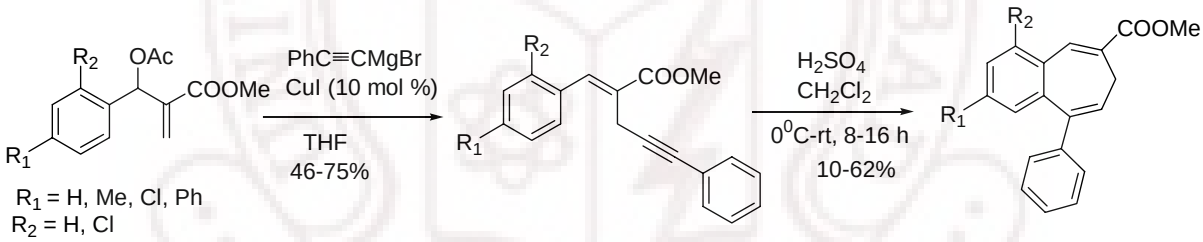
Saito and co-workers[220] have reported a facile synthesis of bicyclic system (containing cyclohexane moiety fused with cycloheptane skelton, that is, 6+7 fused ring system) *via* the Diels-Alder reaction of vinylcycloheptadiene derivative (**121)** (which in turn was prepared *via* the nickel catalyzed three component 3+2+2 cyclization) with dienophiles following the reaction sequence as shown in Scheme 58.

Scheme 58



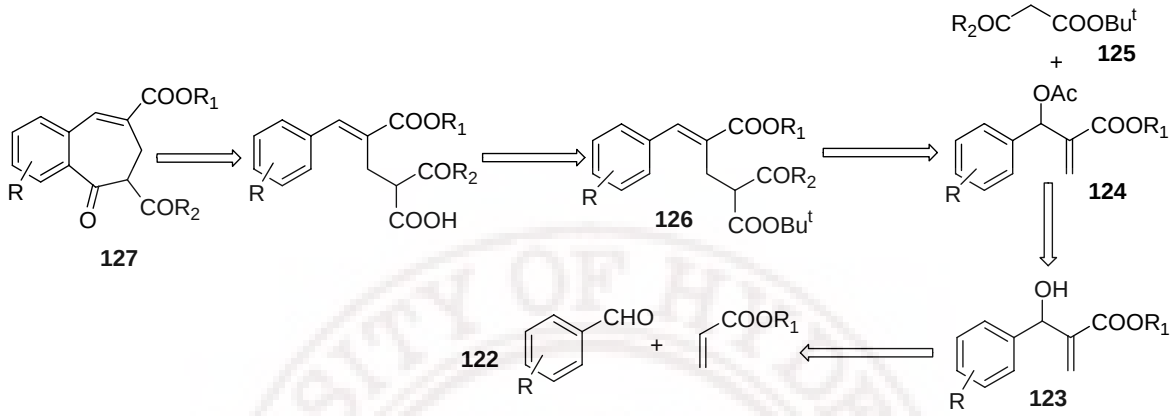
Kim and co-workers[221] reported an interesting synthesis of 9-phenyl-7*H*-benzocycloheptene-6-carboxylate derivatives from the Baylis-Hillman acetates *via* the treatment of with alkynylmagnisium bromide followed by the intramolecular Friedel-Crafts reaction according to Scheme 59.

Scheme 59

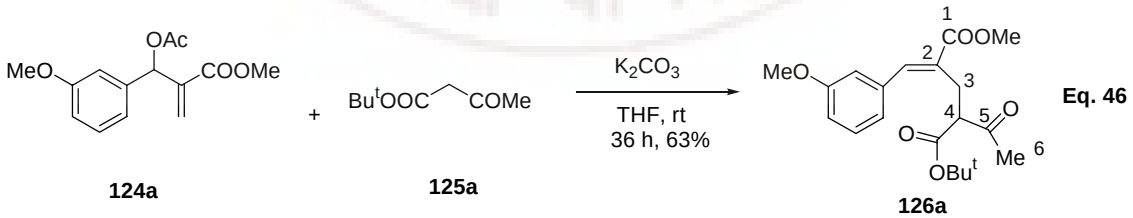


In continuation of our interest on the applications of Baylis-Hillman acetates for synthesis of carbocyclic[157] and heterocyclic molecules[137,153,167,169,171] we have undertaken the synthesis of bicyclic framework containing benzofused cycloheptaenone (**127**) moiety according to the retrosynthetic strategy as described in Scheme 60.

Scheme 60 Retero-synthetic strategy

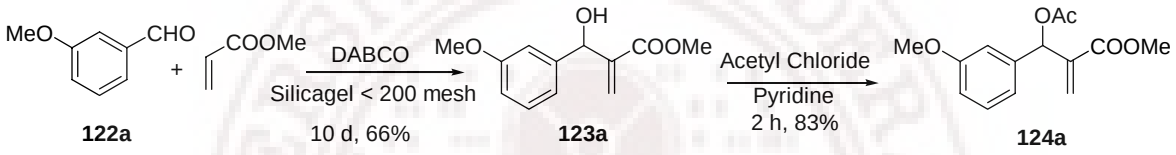


Accordingly, we have first selected methyl 3-acetoxy-3-(3-methoxyphenyl)-2-methylenepropanoate (**124a**), the Baylis-Hillman acetate, as a substrate for alkylation with *tert*-butyl acetoacetate (**125a**). Thus the treatment of methyl 3-acetoxy-3-(3-methoxyphenyl)-2-methylenepropanoate (**124a**) (3 mmol), with *tert*-butyl acetoacetate (**125a**) (3.3 mmol), in presence of K_2CO_3 (3 mmol) at room temperature for 36 h provided methyl 2-[(*E*)-(3-methoxybenzylidene)]-4-*tert*-butoxycarbonyl-5-oxo-hexanoate (**126a**), in 63% isolated yield (Eq. 46). Structure of this molecule was in established with the IR, ^{1}H NMR, ^{13}C NMR, mass spectral data and elemental analysis.



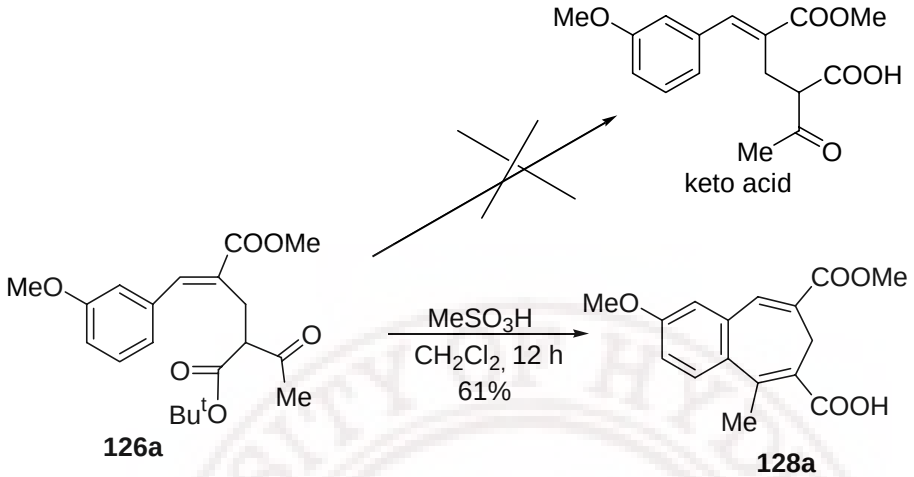
Required methyl 3-acetoxy-3-(3-methoxyphenyl)-2-methylenepropanoate (**124a**) was prepared *via* the acetylation of methyl 3-hydroxy-3-(3-methoxyphenyl)-2-methylen-epropanoate (**123a**) which in turn was prepared *via* the Baylis-Hillman coupling of 3-methoxybenzaldehyde (**122a**) with methyl acrylate in presence of DABCO following the procedure developed in our laboratory[222] (Scheme 61).

Scheme 61



122a **123a** **124a**

We have then treated methyl 2-[(*E*)-(3-methoxybenzylidene)]-4-*tert*-butoxycarbonyl-5-oxohexanoate (**126a**), (1 mmol) with methanesulfonic acid (4 mmol) in dichloromethane (3 mL), at room temperature for 12 h to provide 9-methoxy-5-methoxycarbonyl-2-methylbicyclo[5.4.0]undeca-1(7),2,5,8,10-pentaene-3-carboxylic acid (**128a**) in 61% isolated yield (Eq. 47). Structure of this molecule was established by IR, ^{1}H NMR, ^{13}C NMR, mass spectral data and elemental data. Structure of this molecule was further confirmed by single crystal X-ray data analysis [Table VII] (For ORTEP diagram see Fig. X7).



Eq. 47

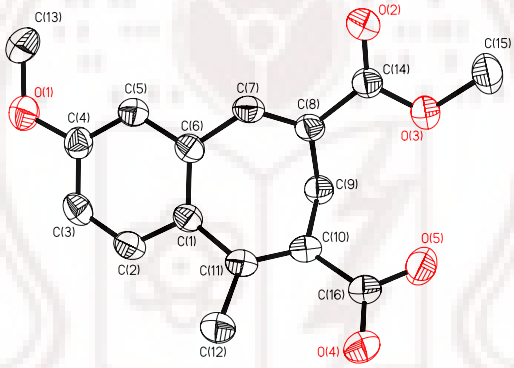
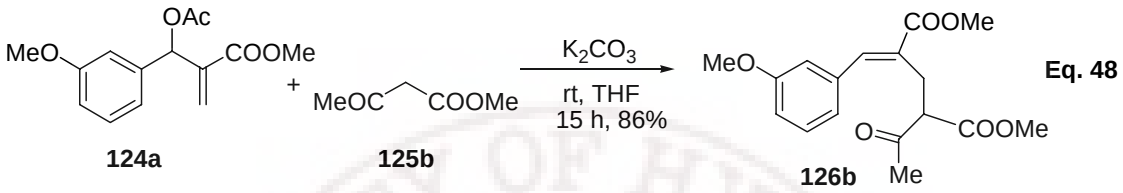


Fig. X7 ORTEP diagram of compound **128a**
(Hydrogen atoms were omitted for clarity)

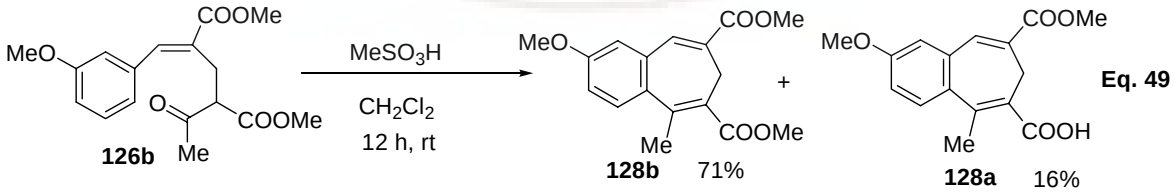
With a view to understand the applicability of this strategy to methyl acetoacetate (**125b**), as alkylating agent, we have treated methyl 3-acetoxy-3-(3-methoxyphenyl)-2-methylenepropanoaten (**124a**) (3 mmol), with methyl acetoacetate (**125b**) (3.3 mmol), in presence of K_2CO_3 (3 mmol) at room temperature which provided methyl 2-[(*E*)-(3-methoxybenzylidene)]-4-methoxycarbonyl-5-oxohexanoate (**126b**), in 86% isolated yield

(Eq. 48). Structure of this molecule was confirmed by IR, ^{1}H NMR, ^{13}C NMR, mass spectral data and elemental analysis.



124a **125b** **126b**

Treatment of methyl 2-[(*E*)-(3-methoxybenzylidene)]-4-methoxycarbonyl-5-oxohex-anoate (**126b**), (1 mmol), with methanesulfonic acid (4 mmol), in dichloromethane (3 mL), at room temperature for 12 h provided the 3,5-dimethoxycarbonyl-9-methoxy-2-methyl-bicyclo[5.4.0]undeca-1(7),2,5,8,10-pentaene (**128b**) in 71% isolated yield (Eq. 49). Structure of this molecule was in full agreement with IR, ^{1}H NMR [for compound **128b** see Spectrum 15], ^{13}C NMR [for compound **128b** see Spectrum 16] mass spectral data and elemental analysis. We have also isolated 9-methoxy-5-methoxycarbonyl-2-methylbicyclo[5.4.0]undeca-1(7),2,5,8,10-pentaene-3-carboxylicacid (**128a**) in 16% yield which indicates the partial hydrolysis of methyl ester group into acid group (β to the keto group) under the reaction conditions.

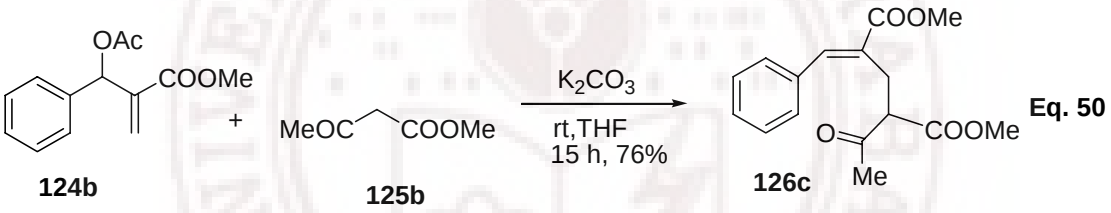


126b **128b** 71% **128a** 16%

Table VII. Crystal data and structure refinement for 128a

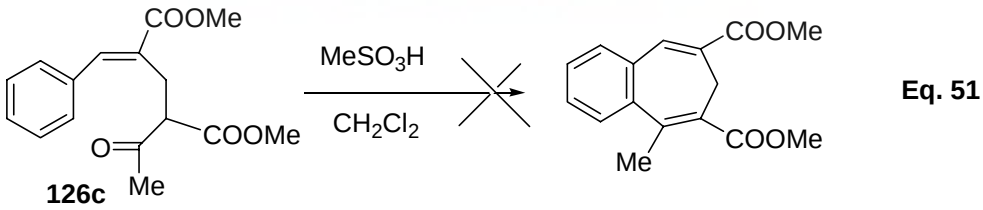
Identification code	: **128a**
Empirical formula	: $C_{16}H_{16}O_5$
Formula weight	: 288.0
Temperature	: 298 K
Wavelength	: 0.71073 Å
Crystal system	: Monoclinic
Space group	: P 2(1)/c
Unit cell dimensions	: a = 15.891(3) Å; α = 90 deg.
	: b = 6.7072(11) Å; β = 114.032(2) deg.
	: c = 14.160(2) Å; γ = 90 deg.
Volume	: 1378.4(4) $Å^3$
Z, Calculated density	: 4, 1.389 Mg/m^3
Absorption coefficient	: 0.103 mm^{-1}
F(000)	: 608
Crystal size	: 0.34 x 0.24 x 0.15 mm
Theta range for data collection	: 2.81 to 25.95 deg.
Limiting indices	: -19<=h<=19, -8<=k<=8, -17<=l<=17
Reflections collected / unique	: 13553 / 2678 [R(int) = 0.0329]
Completeness to theta = 25.95	: 99.4 %
Max. and min. transmission	: 0.9846 and 0.9657
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 2678 / 0 / 197
Goodness-of-fit on F^2	: 1.110
Final R indices [I>2sigma(I)]	: R1 = 0.0578, wR2 = 0.1284
R indices (all data)	: R1 = 0.0694, wR2 = 0.1347
Largest diff. peak and hole	: 0.232 and -0.167 $e.Å^{-3}$

In order to understand whether 3-methoxy group on the aromatic ring is necessary for cyclization, we have subjected methyl 3-acetoxy-2-methylene-3-phenylpropanoate (**124b**) for similar strategy. Thus the treatment of methyl 3-acetoxy-2-methylene-3-phenylp-ropanoate (**124b**) with methyl acetoacetate (**125b**), provided the methyl 2-[(*E*)-(benzylidene)]-4-methoxycarbonyl-5-oxohexanoate (**126c**) 76% isolated yield (Eq. 50). Structure of this molecule was in agreement with IR, ^{1}H NMR, ^{13}C NMR mass spectral data and elemental analysis.



124b **125b** **126c** **Eq. 50**

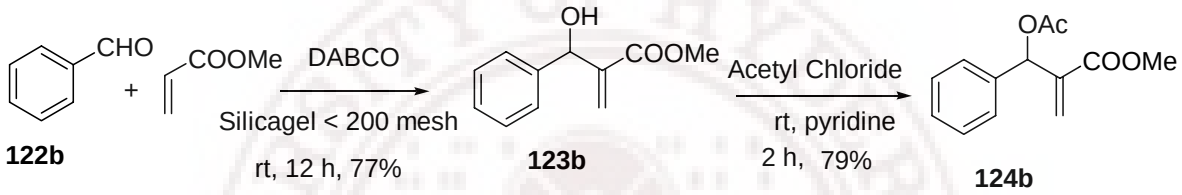
Reaction of methyl 2-[(*E*)-(benzylidene)]-4-methoxycarbonyl-5-oxohexanoate (**126c**), with methanesulfonic acid, did not provide the expected benzocycloheptadiene derivative (Eq. 51). This clearly indicates that 3-methoxy group in the aromatic ring is necessary for Friedel-Crafts reaction as this group makes aromatic ring carbon more nucleophilic to facilitate the Friedel-Crafts reaction.



126c **Eq. 51**

The required methyl 3-acetoxy-2-methylene-3-phenylpropanoate (**124b**) was prepared *via* the acetylation of methyl 3-hydroxy-2-methylene-3-phenylpropanoate (**123b**), which was obtained *via* the Baylis-Hillman coupling of benzaldehyde and methyl acrylate under the influence of DABCO (Scheme 62).

Scheme 62



With a view to understand the generality of this reaction we have prepared various Baylis-Hillman alcohols (**123c-l**), from representative alkoxybenzaldehydes (**122a, 122c-g**) and alkyl acrylates, which are subsequently converted into their corresponding acetates (**124c-l**) (Table 5 & 6) Scheme 63.

Scheme 63

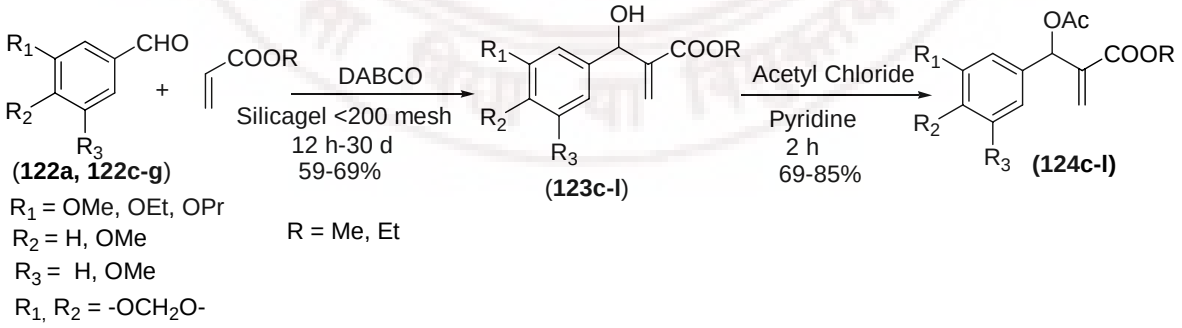
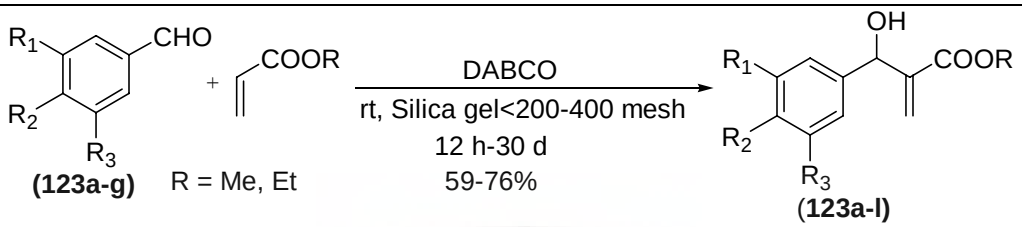


Table 5. Synthesis of Baylis-Hillman alcohols (123a-l)[$, a]



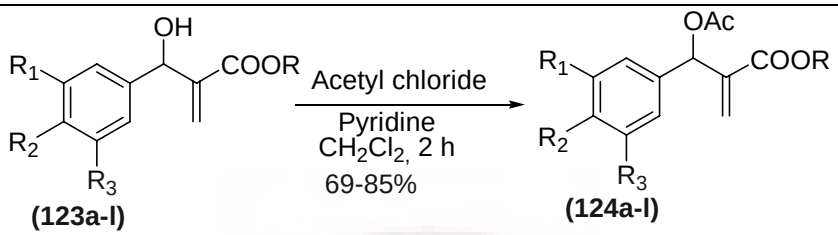
Aldehyde	R_1	R_2	R_3	R	Product [b]	Yield (%)[c]
122a	OMe	H	H	Me	**123a**	66
122b	H	H	H	Me	**123b**	76
122c	OEt	H	H	Me	**123c**	67
122d	OPr	H	H	Me	**123d**	66
122e	OMe	H	OMe	Me	**123e**	60
122f	OMe	OMe	OMe	Me	**123f**	64
122g	$-OCH_2O-$		H	Me	**123g**	59
122a	OMe	H	H	Et	**123h**	67
122c	OEt	H	H	Et	**123i**	66
122d	OPr	H	H	Et	**123j**	61
122e	OMe	H	OMe	Et	**123k**	65
122f	OMe	OMe	OMe	Et	**123l**	69

[a]All reactions were carried out on 50 mmol scale of aldehydes with 75 mmol of alkyl acrylates, under influence of DABCO (15 mol%) in the silica gel-solid phase medium (mesh <200-400) at room temperature

[b]All the compounds (**123a-l**) were obtained as colorless liquids and gave satisfactory IR, ^{1}H NMR, ^{13}C NMR spectral data. [c]Yields are based on aldehydes.

[$]For continuity and easy understandings we have numbered various aromatic aldehydes (alkoxyaryl and phenyl) and Baylis-Hillman alcohols (obtained from methyl acrylate and ethyl acrylate) as **122** and **123** respectively. We have also numbered B. H. alcohols derived from aldehydes **122a-g** and methyl acrylate as **123a-g** respectively. We also numbered the B. H. alcohols derived from **122a**, **122c**, **122d**, **122e**, **122f** and ethyl acrylate as **123h-l** respectively.

Table 6. **Synthesis of Baylis-Hillman acetates (124a-l)**[@, a]



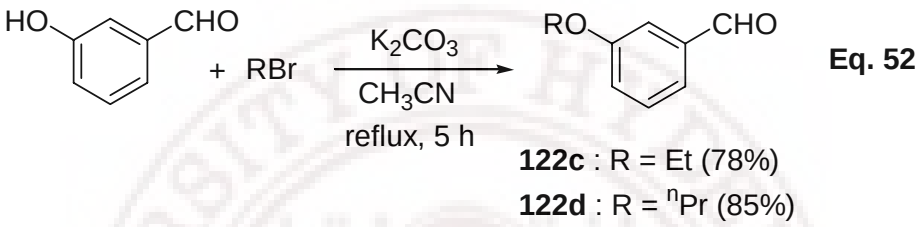
(123a-l) **(124a-l)**

B.H. Alcohol	R_1	R_2	R_3	R	Product [b]	Yield (%)[c]
123a	OMe	H	H	Me	**124a**	83
123b	H	H	H	Me	**124b**	79
123c	OEt	H	H	Me	**124c**	78
123d	OPr	H	H	Me	**124d**	69
123e	OMe	H	OMe	Me	**124e**	72
123f	OMe	OMe	OMe	Me	**124f**	82
123g	-OCH_2O-		H	Me	**124g**	72
123h	OMe	H	H	Et	**124h**	74
123i	OEt	H	H	Et	**124i**	78
123j	OPr	H	H	Et	**124j**	81
123k	OMe	H	OMe	Et	**124k**	81
123l	OMe	OMe	OMe	Et	**124l**	85

[a]All reactions were carried out on 20 mmol scale of Baylis-Hillman alcohols (**123a-l**) with acetyl chloride, in presence of pyridine at at room temperature for 2 h.
[b]All the compounds (**124a-l**) gave satisfactory IR, ^{1}H NMR, ^{13}C NMR spectral data, mass and elemental analyses.
[c] Yields are based on alcohols.

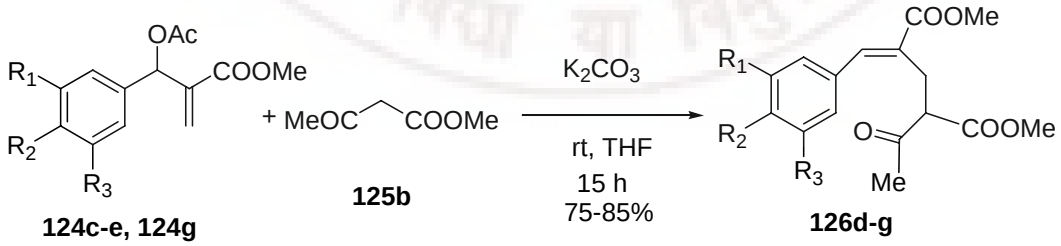
@For continuity and better understandings we have numbered Baylis-Hillman alcohols and Baylis-Hillman acetates as **123** and **124** respectively.

Required 3-ethoxybenzaldehyde (**122c**), and 3-propoxybenzaldehyde (**122d**) were prepared *via* the alkylation of 3-hydroxybenzaldehyde, with ethyl bromide and propyl bromide respectively according to the Eq. 52.



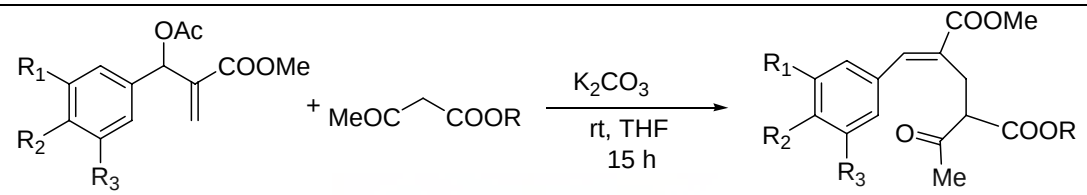
Eq. 52

These Baylis-Hillman acetates (**124c-e**, **124g**), were treated with methyl acetoacetate (**125b**), under the influence of K_2CO_3 at room temperature for 15 h to provide the corresponding trisubstituted alkenes (**126d-g**), in 75-85% isolated yields (Eq. 53, Table 7). Structures of these compounds is in agreement with IR, ^{1}H NMR, ^{13}C NMR, mass spectral data and elemental analysis.



Eq. 53

Table 7. Synthesis of trisubstituted alkenes (126b, 126d-h)[#,a]



124a, 124c-e, 124g **125b, 125c** **126b, 126d-h**

B.H. Acetate	R	Product [b]	Yield (%)[c]
124a	Me	**126b**	86
124c	Me	**126d**	85
124d	Me	**126e**	75
124e	Me	**126f**	82
124g	Me	**126g**	79
124a	Et	**126h**	75

[a] All reactions were carried out on 3 mmol scale of Baylis-Hillman acetates (**124a**, **124c-e**, **124g**) with 3.3 mmol of keto esters (**125b**) or (**125c**) in THF (3 mL), under influence of K_2CO_3 (3 mmol) and at room temperature for 15 h.

[b]All the compounds (**126b**, **126d-h**) were obtained as a colorless liquids and gave satisfactory IR, ^{1}H NMR, ^{13}C NMR mass spectral data and elemental analysis and all the compounds were obtained as a mixture of keto-enol forms.

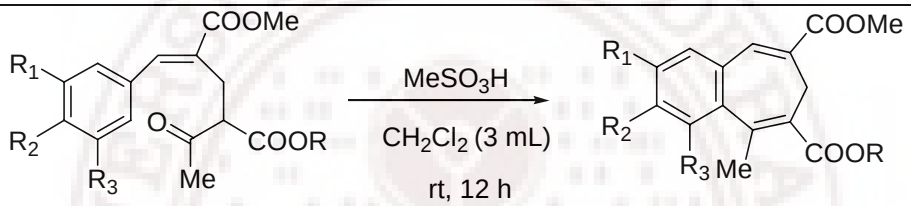
[c]Yields are based on B.H. acetates.

[#] For continuity and better understandings we have numbered trisubstituted alkene obtained from the reaction of **124a** with methyl acetoacetate (**125b**), as **126b**. Trisubstituted alkenes obtained *via* the reaction of **124c-e** with methyl acetoacetate (**125b**) as **126d-f** respectively and trisubstituted alkene obtained *via* the reaction of **124a** with ethyl acetoacetate (**125c**) as **126h**.

Subsequent treatment of these trisubstituted alkenes (**126d-g**) with methanesulfonic acid at room temperature provided the resulting benzocycloheptadiene derivatives (**128c-f**) in 61-

75% isolated yields (Table 8). Structures of these compounds are in complete agreement with IR, ^{1}H NMR [for compound **128f** see Spectrum 17], ^{13}C NMR [for compound **128f** see Spectrum 18], mass spectral data and elemental analyses. Structures of the molecules **128e**, **128f** were further confirmed by single crystal X-ray data analyses [Table VIII & Table IX]. For ORTEP diagrams see Fig.s X8 & X9.

Table 8. Synthesis of benzocycloheptadiene derivatives (128b-g)[a,®]



Trisubstituted alkene	R	Product	Yield (%)[b,c]	M.P ^{0}C
126b	Me	**128b**	71	76-78
126d	Me	**128c**	74	64-66
126e	Me	**128d**	75	-
126f	Me	**128e**	67[d]	102-104
126g	Me	**128f**	61[d]	138-140
126h	Et	**128g**	75	-

[a]All reactions were carried out on 1.0 mmol scale of trisubstitued alkenes (**126b**, **126d-h**) (1.0 mmol) with methanesulfonic acid (4 mmol) in CH_2Cl_2 at room temperature for 12 h. [b]All the compounds (**128b-g**) were fully characterized (IR, ^{1}H NMR, ^{13}C NMR), mass spectra data and elemental analyses. [c]Yields are based on trisubstituted alkenes. [d] Compounds **128e** & **128f** were further characterized by single crystal X-ray data see Fig X8 & X9.

®For clarity and better understandings we have numbered benzocycloheptadiene derivatives derived from **126b, 126d-h** as **128b-g** respectively.

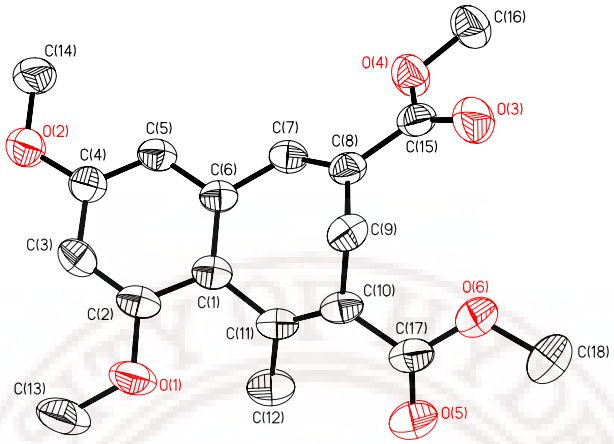


Fig. **X8** ORTEP diagram of compound **128e**
(Hydrogen atoms were omitted for clarity)

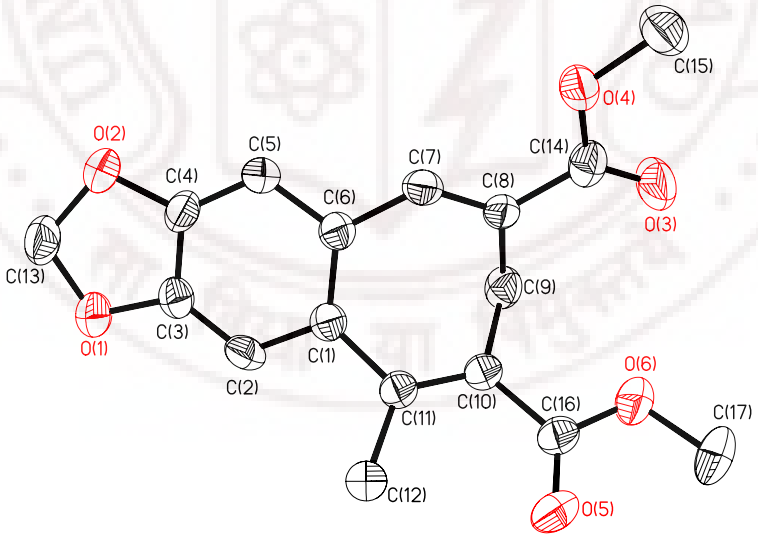


Fig. X9 ORTEP diagram of compound **128f**
(Hydrogen atoms were omitted for clarity)

Table VIII. Crystal data and structure refinement for 128e

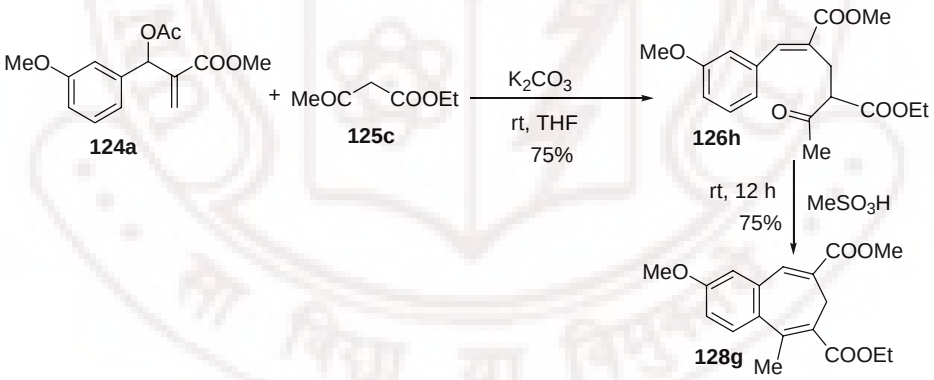
Identification code	: **128e**
Empirical formula	: $C_{18} H_{20} O_6$
Formula weight	: 332.34
Temperature	: 298 K
Wavelength	: 0.71073 Å
Crystal system	: Monoclinic
Space group	: P 2(1)/n
Unit cell dimensions	: a = 8.683(4) Å; α = 90 deg.
	: b = 16.353(7) Å; β = 104.583(7) deg.
	: c = 12.182(6) Å; γ = 90 deg.
Volume	: 1674.0(13) $Å^3$
Z, Calculated density	: 4, 1.319 Mg/m^3
Absorption coefficient	: 0.099 mm^{-1}
F(000)	: 704
Crystal size	: 0.26 x 0.23 x 0.17 mm
Theta range for data collection	: 2.13 to 26.22 deg.
Limiting indices	: -10<=h<=10, -20<=k<=20, -14<=l<=15
Reflections collected / unique	: 16076 / 3325 [R(int) = 0.0779]
Completeness to theta = 26.22	: 98.8 %
Max. and min. transmission	: 0.9834 and 0.9747
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 3325 / 0 / 222
Goodness-of-fit on F^2	: 0.944
Final R indices [I>2sigma(I)]	: R1 = 0.0618, wR2 = 0.1214
R indices (all data)	: R1 = 0.1280, wR2 = 0.1421
Largest diff. peak and hole	: 0.181 and -0.206 e. $Å^{-3}$

Table IX. Crystal data and structure refinement for 128f

Identification code	: **128f**
Empirical formula	: $C_{17}H_{16}O_6$
Formula weight	: 316.30
Temperature	: 298 K
Wavelength	: 0.71073 Å
Crystal system	: Triclinic
Space group	: P-1
Unit cell dimensions	: a = 5.735(3) Å; α = 78.772(9) deg.
	: b = 9.116(5) Å; β= 85.671(9) deg.
	: c = 15.048(9) Å; γ = 73.079(9) deg.
Volume	: 738.1(7) $Å^3$
Z, Calculated density	: 2, 1.423 Mg/m^3
Absorption coefficient	: 0.109 mm^{-1}
F(000)	: 332
Crystal size	: 0.42 x 0.34 x 0.05 mm
Theta range for data collection	: 2.37 to 25.20 deg.
Limiting indices	: -6<=h<=6, -10<=k<=10, -17<=l<=17
Reflections collected / unique	: 6230 / 2599 [R(int) = 0.1066]
Completeness to theta = 25.20	: 98.3 %
Max. and min. transmission	: 0.9934 and 0.9463
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 2599 / 0 / 219
Goodness-of-fit on F^2	: 1.090
Final R indices [I>2sigma(I)]	: R1 = 0.0693, wR2 = 0.1894
R indices (all data)	: R1 = 0.2498, wR2 = 0.2353
Largest diff. peak and hole	: 0.450 and -0.425 e. $Å^{-3}$

With a view to understand the generality of this reaction we have treated the methyl 3-acetoxy-3-(3-methoxyphenyl)-2-methylenepropanoate (**124a**) with ethyl acetoacetate (**125c)** in presence of K_2CO_3 at room temperature for 15 h, to provide the methyl 4-ethoxycarbonyl-2-[(*E*)-(3-methoxybenzylidene)]-5-oxohexanoate (**126h**) in 75% isolated yield (Scheme 64, Table 7). Subsequent treatment with methanesulfonic acid, provided the 3-ethoxycarbonyl-9-methoxy-5-methoxycarbonyl-2-methylbicyclo[5.4.0]undeca-1(7),2,5-8,10-pentaene (**128g**) in 75% isolated yield. Structure of this molecule is in agreement with IR, ^{1}H NMR [for compound **128g** see Spectrum 19], ^{13}C NMR [for compound **128g** see Spectrum 20], mass spectral data and elemental analysis.

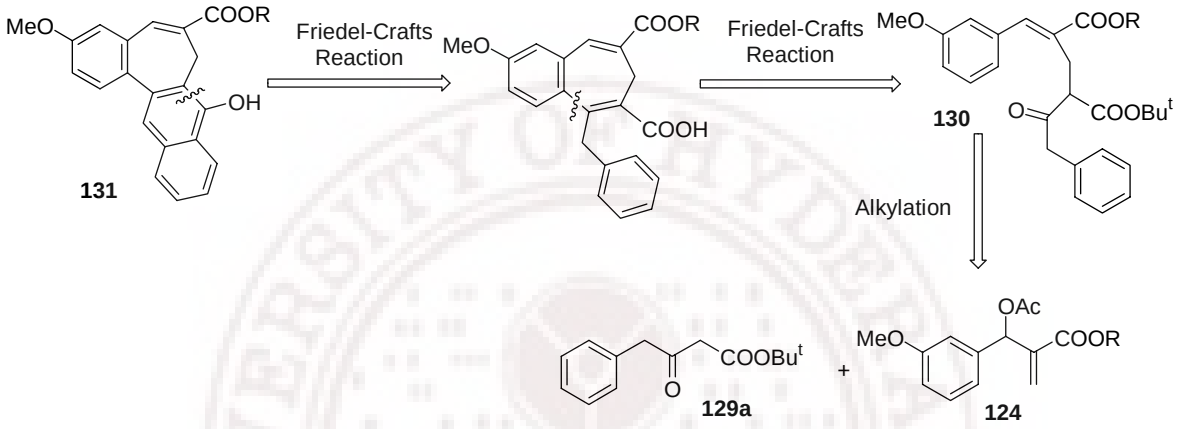
Scheme 64



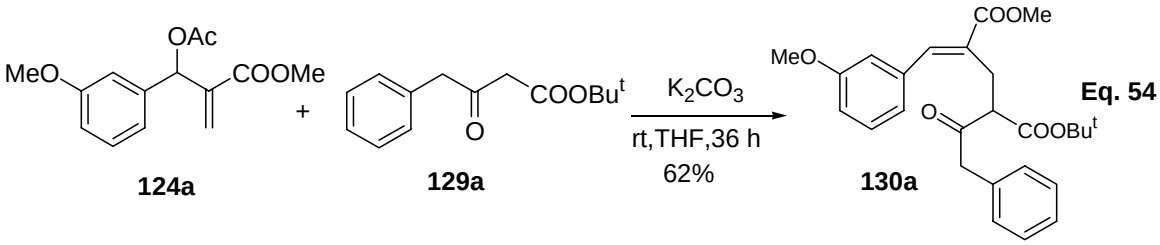
Encouraged by these results we have next directed our studies towards developing tetracyclic carbocyclic framework following the reaction strategy as shown in reterosynthetic strategy (Scheme 65). It occurred to us that alkylation of Baylis-Hillman acetate with *tert*-butyl 3-oxo-4-phenylbutanoate (**129a**) should provide the trisubstituted

alkene (**130a**) which would then undergo two intramolecular Friedel-Crafts reactions to provide tetracyclic carbocyclic framework (**131**) (Retro-synthetic strategy, Scheme 65).

Scheme 65 Retro-synthetic strategy

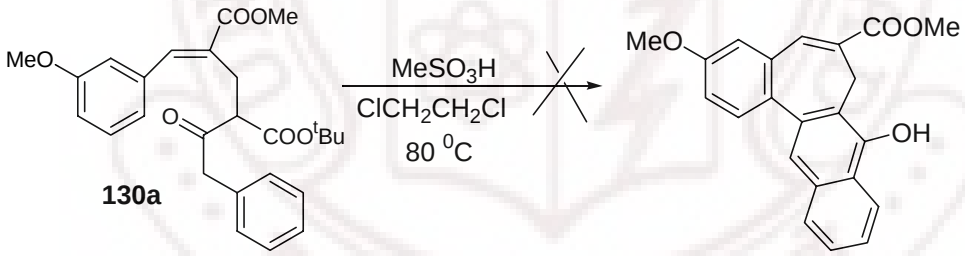


Accordingly, we have first selected *tert*-butyl 3-oxo-4-phenylbutanoate (**129a**) as an alkylating agent and methyl 3-acetoxy-3-(3-methoxyphenyl)-2-methylenepropanoate (**124a**) as a substrate for alkylation. Thus the treatment of methyl 3-acetoxy-3-(3-methoxyphenyl)-2-methylenepropanoate (**124a**) (3 mmol), with *tert*-butyl 3-oxo-4-phenylbutanoate (**129a**) (3.6 mmol) in presence of K_2CO_3 (3 mmol) at room temperature for 36 h provided methyl 2-[(*E*)-(3-methoxybenzylidene)]-4-*tert*-butoxycarbonyl-5-oxo-6-phenylhexanoate (**130a**) in 62% isolated yield (Eq. 54). Structure of this molecule was established by the IR, ^{1}H NMR, ^{13}C NMR, mass spectral data and elemental analysis.



124a **129a** **130a** **Eq. 54**

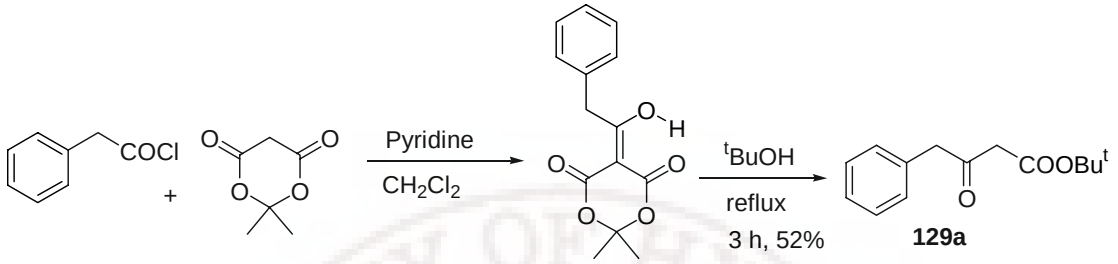
We have then treated the methyl 2-[(*E*)-(3-methoxybenzylidene)]-4-*tert*-butoxycarbonyl-5-oxo-6-phenylhexanoate (**130a**) (1 mmol), with methanesulfonic acid (5 mmol) at 80 ^{0}C. Unfortunately, the expected tetracyclic carbocyclic framework was not obtained. This may be due to the possible conversion of *tert*-butoxycarbonyl into carboxy group which might then undergo decarboxylation (Eq. 55).



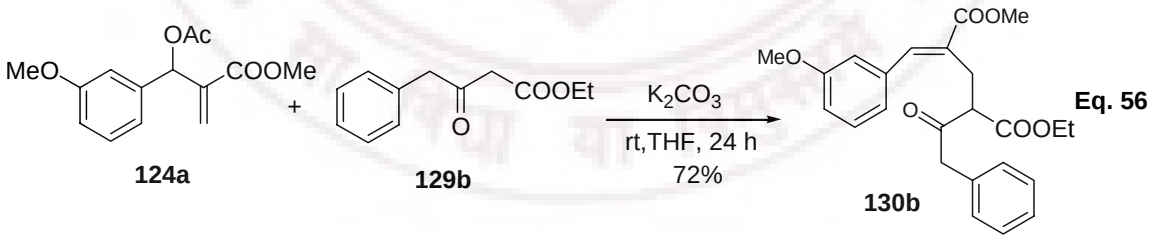
130a **Eq. 55**

Required *tert*-butyl 3-oxo-4-phenylbutanoate (**129a**) was prepared according to the literatutre procedure[223] from the Meldrum's acid. Thus the treatment of Meldrum's acid with phenylacetyl chloride following by the treatment with *tert*-butanol at reflux conditions provided *tert*-butyl 3-oxo-4-phenylbutanoate (**129a**) (Scheme 66).

Scheme 66



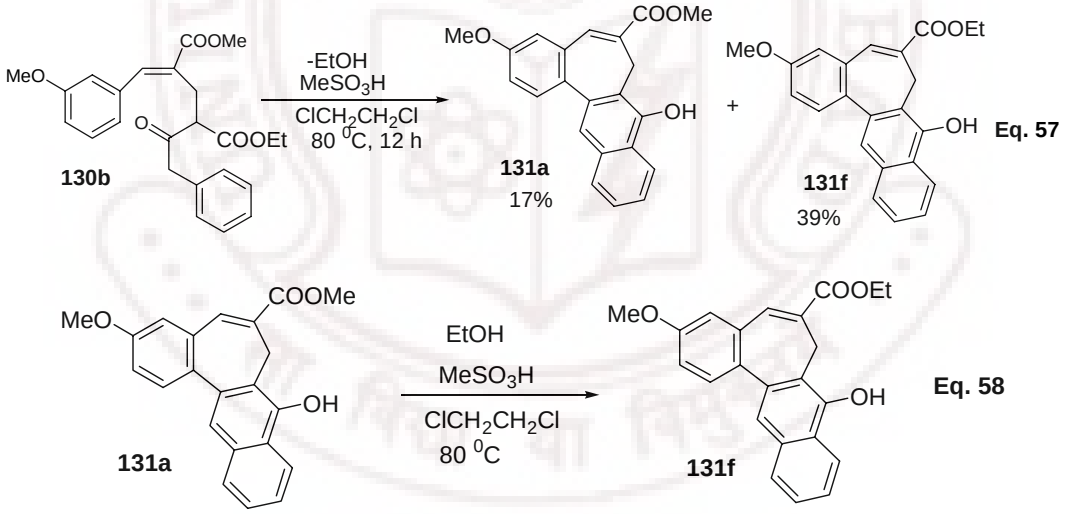
Then we have used ethyl 3-oxo-4-phenylbutanoate (**129b**), as an alkylating agent to avoid decarboxylation. Thus the treatment of methyl 3-acetoxy-3-(3-methoxyphenyl)-2-methylenepropanoate (**124a**), with ethyl 3-oxo-4-phenylbutanoate (**129b**), under the influence of K_2CO_3 at room temperature for 24 h (similar procedure described in Eq. 54) provided methyl 4-ethoxycarbonyl-2-[(*E*)-(3-methoxybenzylidene)]-5-oxo-6-phenylh-exanoate (**130b**), in 72% isolated yield (Eq. 56). Structure of this molecule is confirmed by IR, ^{1}H NMR, ^{13}C NMR, mass and elemental analysis.



Eq. 56

Treatment of methyl 4-ethoxycarbonyl-2-[(*E*)-(3-methoxybenzylidene)]-5-oxo-6-phenyl-hexanoate (**130b**) (1 mmol), with methanesulfonic acid (5 mmol) at 80 ^{0}C for 12 h provided the desired 10-hydroxy-17-methoxy-13-methoxycarbonyltetracyclo[13.4.-

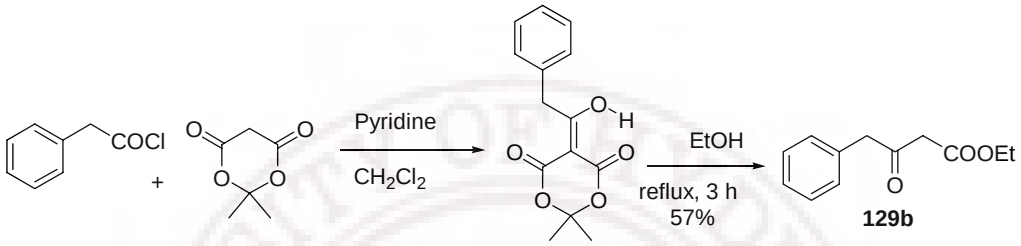
$0.0^{2,11}.0^{4,9}$]nonadeca-1(15),2(11),3,5,7,9,13,16,18-nonaene (**131a**) only in 17% isolated yield (Eq 57). We have also isolated 13-ethoxycarbonyl-10-hydroxy-17-methoxytetracyc-lo[13.4.0.$0^{2,11}.0^{4,9}$]nonadeca-1(15),2(11),3,5,7,9,13,16,18-nonaene (**131f**) in 39% isolated yield along with unseperable mixture (Eq. 57). Structures of these compounds are in agrement with IR, ^{1}H NMR, ^{13}C NMR, mass spectral data and elemental analysis. The formation of 13-ethoxycarbonyl-10-hydroxy-17-methoxytetracyc-lo[13.4.0.$0^{2,11}.0^{4,9}$]-nona-deca-1(15),2(11),3,5,7,9,13,16,18-nonaene in 39% yield clearly indicates that *trans* esterification is taking place in the reaction process as the ethanol is the leaving group (side product) in this reaction (**130b** to **131a**) (Eq. 58).



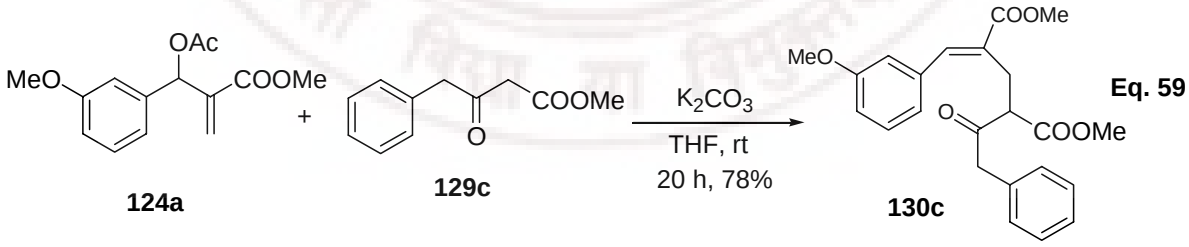
Required ethyl 3-oxo-4-phenylbutanoate (**129b**) was prepared according to the literature procedure from the Meldrum's acid. Thus the treatment of Meldrum's acid with

phenylacetyl chloride following by the treatment with ethanol at reflux conditions provided ethyl 3-oxo-4-phenylbutanoate (**129b**) (Scheme 67).[223]

Scheme 67



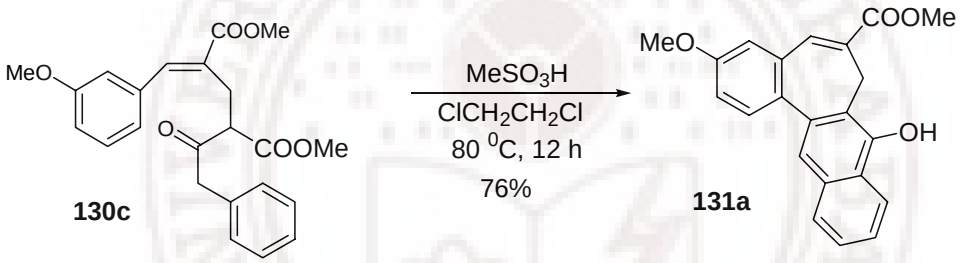
To overcome this *trans* esterification problem we have selected methyl 3-oxo-4-phenylbutanoate (**129c**), for alkylation. Thus methyl 3-acetoxy-3-(3-methoxyphenyl)-2-methylenepropanoate (**124a**) was treated with methyl 3-oxo-4-phenylbutanoate (**129c**), in presence of K_2CO_3 at room temperature for 20 h to provide methyl 2-[(*E*)-(3-methoxybenzylidene)]-4-methoxycarbonyl-5-oxo-6-phenylhexanoate (**130c**) in 78% isolated yields (Eq. 59). Structure of this molecule was in agreement with IR, ^{1}H NMR, ^{13}C NMR, mass spectral data and elemental analysis.



Eq. 59

Subsequent treatment with methanesulfonic acid (5 mmol) at 80 ^{0}C for 12 h provided the desired 10-hydroxy-17-methoxy-13-methoxycarbonyltetracyclo[13.4.0.0^{2,11}.0^{4,9}]nonade-

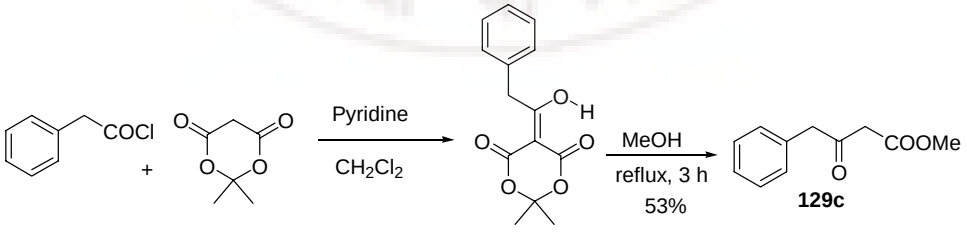
ca-1(15),2(11),3,5,7,9,13,16,18-nonaene (**131a**) in 76% isolated yield (Eq. 60). Structure of this molecule was established by IR, ^{1}H NMR [for compound **131a** see Spectrum 21], ^{13}C NMR [for compound **131a** see Spectrum 22, for hetero COSY see Spectrum 23], mass spectral data and elemental analysis. Thus the clean formation 10-hydroxy-17-methoxy-13-methoxycarbonyltetracyclo[13.4.0.0^{2,11}.0^{4,9}]nonadeca-1(15),2(11),3,5,7,9,13,16,18-nonaene (**131a**), indicated that transesterification was indeed the problem in this cyclization process in the earlier case (Eq. 57)



Eq. 60

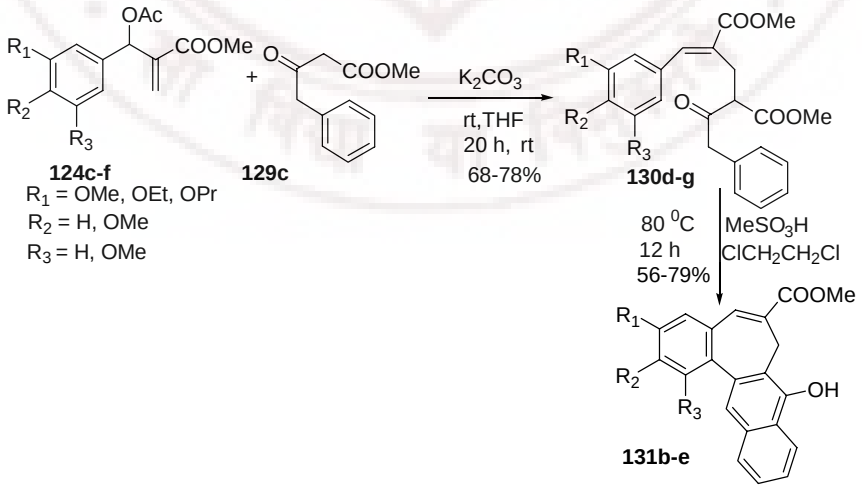
Methyl 3-oxo-4-phenylbutanoate (**129c**)[223] was prepared according the literature procedure from the Meldrum's acid *via* the treatment with phenylacetyl chloride followed by the reaction with methanol at reflux conditions (Scheme 68).

Scheme 68



With a view to understand the generality of this strategy (alkylation and two intramolecular Friedel-Crafts reaction) we have subjected the Baylis-Hillman acetates (**124c-f**) [obtained from corresponding Baylis-Hillman alcohols (**123c-f**) derived from various aromatic aldehydes and methyl acrylate] to the alkylation with methyl 3-oxo-4-phenylbutanoate (**129c**), which provided the trisubstituted alkenes (**130d-g**) in 68-78% isolated yields (Scheme 69, Table 9). Subsequent treatment with methanesulfonic acid at 80 ^{0}C furnished the desired tetracyclic carbocyclic derivatives (**131b-e**) in 56-79% isolated yields (Scheme 69, Table 10). Structures of these molecules were confirmed by IR, ^{1}H NMR [for compound **131e** see Spectrum 24], ^{13}C NMR [for compound **131e** see Spectrum 25], mass spectral data and elemental analysis. Structures of the compounds **131d** & **131e** were further confirmed by single crystal X-ray data [Table X and Table XI]. For ORTEP diagrams see Fig. X10 and Fig. X11.

Scheme 69



To further understand the generality of this reaction we have employed ethyl 3-oxo-4-phenylbutanoate (**129b**), for alkylation of the Baylis-Hillman acetates (**124h-l**), under similar reaction conditions which provided the trisubstituted alkenes (**130h-l**) in 67-78% isolated yields (Scheme 70, Table 9). Structures of these molecules (**130h-l**), were in full agreement with IR, ^{1}H NMR, ^{13}C NMR, mass spectral data and elemental analyses. Subsequent treatment with methanesulfonic acid furnished the desired tetracyclic carbocyclic derivatives (**131f-j**), in 59-81% isolated yields (Scheme 70, Table 10). Structures of these molecules were in agreement with IR, ^{1}H NMR [for compounds **131f**, **131h** see Spectrums 26, 28, respectively], ^{13}C NMR [for compounds **131f**, **131h** see Spectrums 27, 29 respectively], mass spectral data and elemental analyses.

Scheme 70

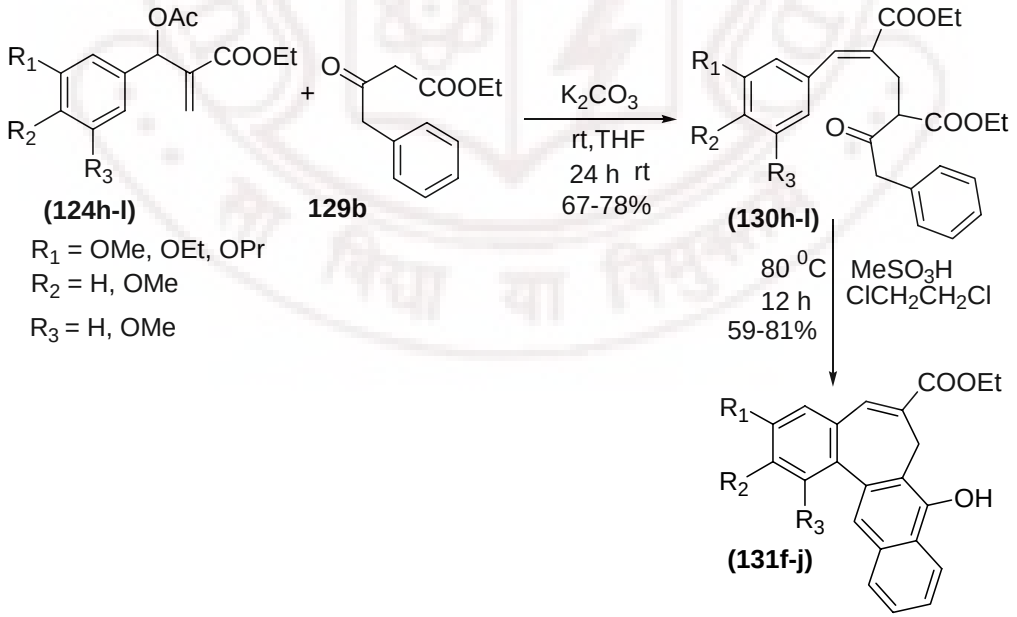
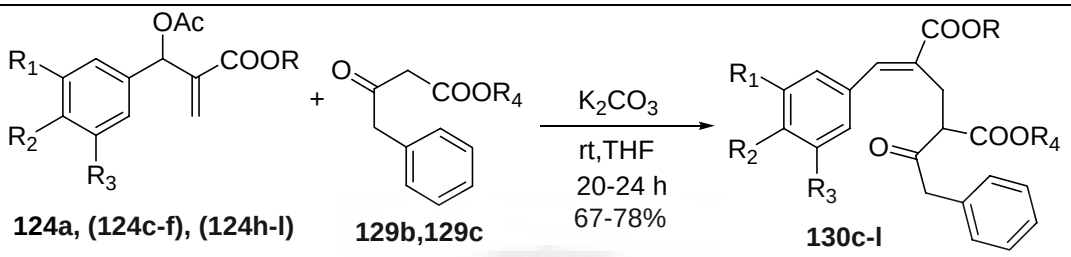


Table 9. Synthesis of trisubstituted alkenes (130c-l) [€,a]



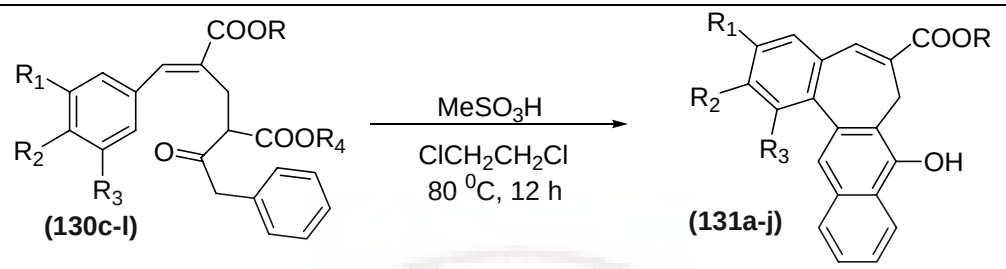
124a, (124c-f), (124h-l) **129b,129c** **130c-l**

B. H. Acetate	R	R_4	Time (h)	Product[a,b]	Yield (%)[c]
124a	Me	Me	20	**130c**	78
124c	Me	Me	20	**130d**	78
124d	Me	Me	20	**130e**	74
124e	Me	Me	20	**130f**	70
124f	Me	Me	20	**130g**	68
124h	Et	Et	24	**130h**	78
124i	Et	Et	24	**130i**	68
124j	Et	Et	24	**130j**	76
124k	Et	Et	24	**130k**	67
124l	Et	Et	24	**130l**	77

[a]All reactions were carried out on 3 mmol scale of Baylis-Hillman acetaes (**124a**, **124c-f**, **124h-l**) with methyl 3-oxo-4-phenylbutanoate (**129c**) (3.6 mmol) or ethyl 3-oxo-4-phenylbutanoate (**129b**) (3.6 mmol), under the influence of K_2CO_3 (3 mmol) at room temperature for 20-24 h.
[b]All compounds (**130c-l**) gave satisfactory IR, ^{1}H NMR, ^{13}C NMR mass spectral data and elemental analyses.
[c]Yields were based on Baylis-Hillman acetates.

[€]For clarity, continuty and better understanding we have numbered B. H. acetates, β-keto esters, and trisubstitued alkenes as **124**, **129** and **130** respectively. Trisubstituted alkene obtained from B. H acetate **124a** *via* the reaction with **129c** was numbered as **130c**. Trisubstituted alkenes obtained from the B. H. acetates (**124c-f**) via the reaction with **129c** were numbered as **130d-g** respectively. Trisubstituted alkenes obtained *via* the reaction of B. H. acetates (**124h-l**) with **129b** were numbered as **130h-l** respectively.

Table 10. Synthesis of tetracyclic carbocyclic derivatives (131a-j)[a,μ]



Trisubstituted Alkene	R	R_4	Product[b]	Yield (%)[c]	M.P ^{0}C
130c	Me	Me	**131a**	76	164-166
130d	Me	Me	**131b**	79	147-149
130e	Me	Me	**131c**	79	128-130
130f	Me	Me	**131d**	56[d]	218-220
130g	Me	Me	**131e**	73[d]	224-226
130h	Et	Et	**131f**	72	136-138
130i	Et	Et	**131g**	81	106-108
130j	Et	Et	**131h**	70	118-120
130k	Et	Et	**131i**	59	220-222
130l	Et	Et	**131j**	63	168 (dec.)

[a]All reactions were carried out on 1 mmol scale of trisubstituted alkenes (**130c-l**), with methanesulphonic acid (5 mmol) at reaction temperature at 80 ^{0}C, for 12 h. [b]All the compounds (**131a-j**) were obtained as solids and fully characterized (IR, ^{1}HNMR, ^{13}C NMR), mass spectral data and elemental analyses. [c]Yields were based on trisubstituted alkenes. [d] Structures of the molecules **131d** & **131e** were further confirmed by single crystal X-ray data see Fig.s X10 & X11.

[μ]For continuity and better understanding we have numbered tetracyclic carbocyclic derivatives as **131**. Tetracyclic carbocyclic derivatives obtained *via* the treatment of trisubstituted alkenes (**130c-l**) with methanesulfonic acid were numbered as **131a-j** respectively.

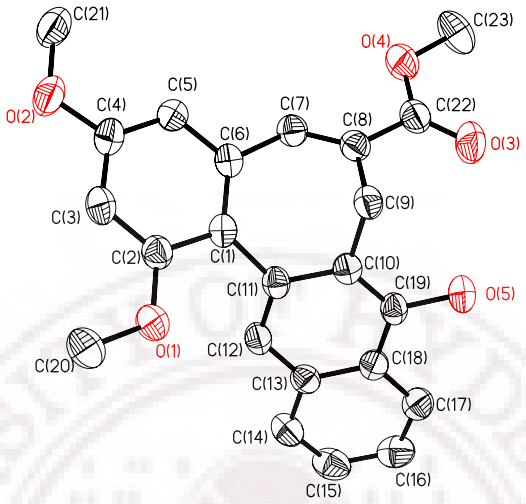


Fig. X10 ORTEP diagram of compound **131d**
(hydrogen atoms were omitted for clarity)

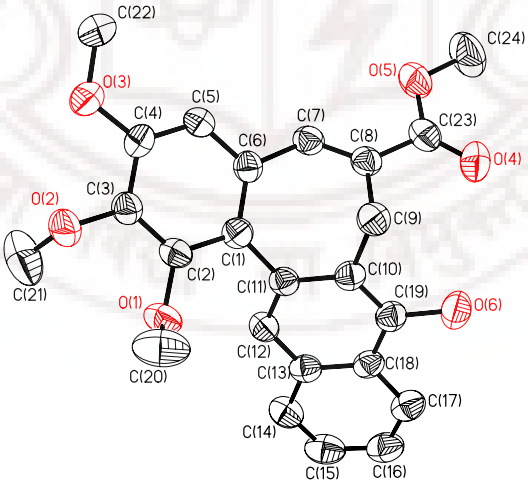


Fig. X11 ORTEP diagram of compound **131e**
(hydrogen atoms were omitted for clarity)

Table X. Crystal data and structure refinement for 131d

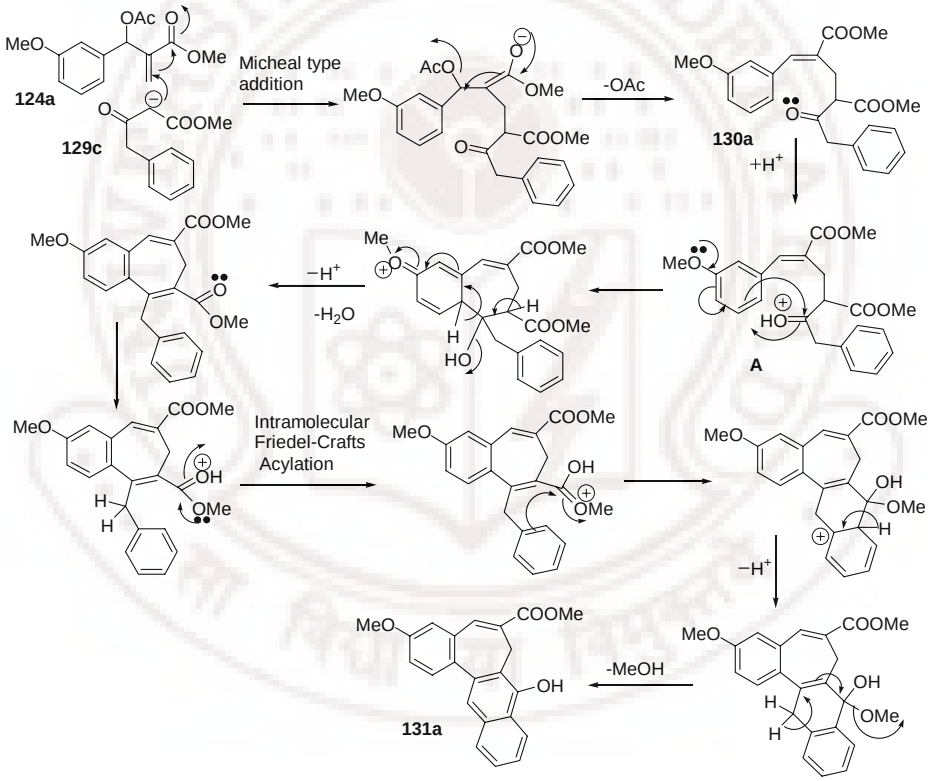
Identification code	: **131d**
Empirical formula	: $C_{23}\ H_{20}\ O_5$
Formula weight	: 376.39
Temperature	: 298 K
Wavelength	: 0.71073 Å
Crystal system	: Orthorombic
Space group	: Pca2(1)
Unit cell dimensions	: a = 21.5647(15) Å; α = 90 deg.
	: b = 8.8773(6) Å; β = 90 deg.
	: c = 9.6687(7) Å; γ = 90 deg.
Volume	: 1850.9(2) $Å^3$
Z, Calculated density	: 4, 1.351 Mg/m^3
Absorption coefficient	: 0.095 mm^{-1}
F(000)	: 792
Crystal size	: 0.34 x 0.24 x 0.13 mm
Theta range for data collection	: 1.89 to 25.95 deg.
Limiting indices	: -26<=h<=26, -10<=k<=10, -11<=l<=11
Reflections collected / unique	: 18261 / 3605 [R(int) = 0.0718]
Completeness to theta = 25.95	: 100.0 %
Max. and min. transmission	: 0.9878 and 0.9684
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 3605 / 1 / 257
Goodness-of-fit on F^2	: 0.987
Final R indices [I>2sigma(I)]	: R1 = 0.0447, wR2 = 0.1028
R indices (all data)	: R1 = 0.0526, wR2 = 0.1066
Largest diff. peak and hole	: 0.166 and -0.123 e. $Å^{-3}$

Table XI. **Crystal data and structure refinement for 131e**

Identification code	: **131e**
Empirical formula	: $C_{24}H_{22}O_6$
Formula weight	: 406.42
Temperature	: 298 K
Wavelength	: 0.71073 Å
Crystal system	: Monoclinic
Space group	: P 2(1)/c
Unit cell dimensions	: a = 7.868(3) Å; α = 90 deg.
	: b = 10.227(4) Å; β = 98.99 deg.
	: c = 25.163(10) Å; γ = 90 deg.
Volume	: 1999.9(14) $Å^3$
Z, Calculated density	: 4, 1.350 Mg/m^3
Absorption coefficient	: 0.097 mm^{-1}
F(000)	: 856
Crystal size	: 0.24 x 0.22 x 0.18 mm
Theta range for data collection	: 1.64 to 26.04 deg.
Limiting indices	: -9<=h<=9, -12<=k<=12, -30<=l<=30
Reflections collected / unique	: 20124 / 3928 [R(int) = 0.0841]
Completeness to theta = 26.04	: 99.4 %
Max. and min. transmission	: 0.9828 and 0.9771
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 3928 / 0 / 276
Goodness-of-fit on F^2	: 0.958
Final R indices [I>2sigma(I)]	: R1 = 0.0571, wR2 = 0.1105
R indices (all data)	: R1 = 0.1268, wR2 = 0.1298
Largest diff. peak and hole	: 0.154 and -0.143 e. $Å^{-3}$

Mechanism for the formation of tetracyclic carbocyclic system from the B.H. acetate is presented in Scheme 71 by taking reaction between methyl 3-acetoxy-3-(3-methoxyphenyl)-2-methylenepropanoate **124a** and methyl 3-oxo-4-phenylbutanoate **129c** as a model case. Michael type addition of **129c** to **124a** and followed by E2 elimination led to the formation of trisubstitued alkene derivative (**130a**). Subsequent treatment with methanesulfonic acid provided the tetracyclic system (**131a***) via* two intramolecular Friedel-Crafts reactions.

Scheme 71 Plausible Mechanism

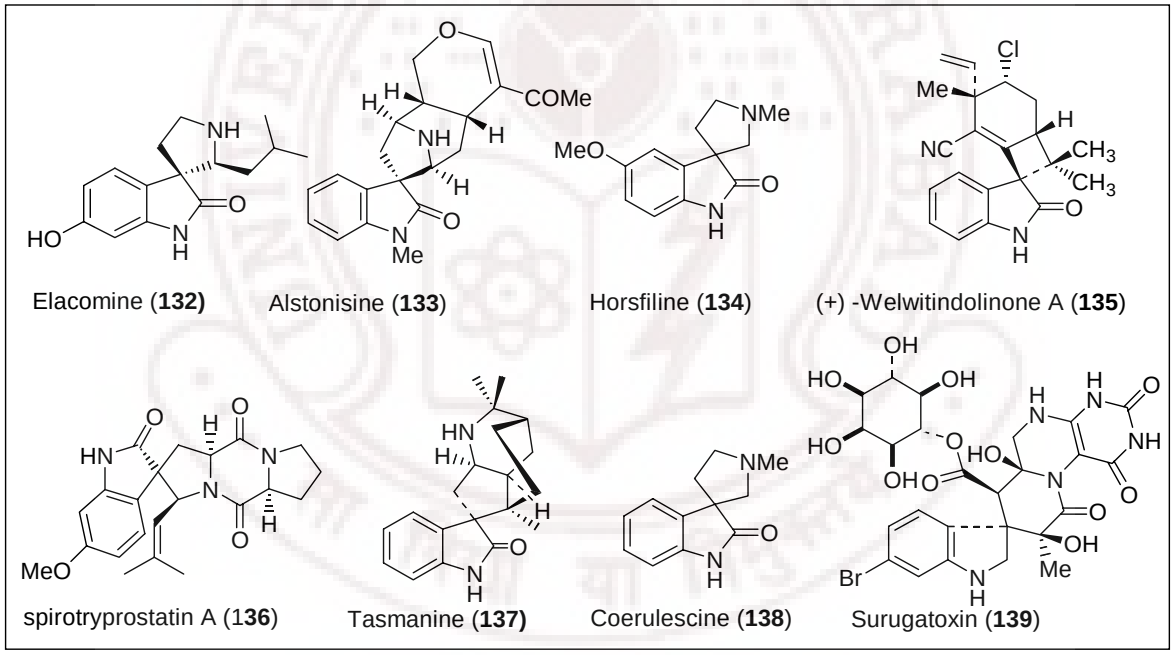


In conclusion, we have developed convenient, operationally simple synthesis of bicyclic and tetracyclic carbocyclic frameworks, contain 6,7 and 6,7,6,6 ring systems from the Baylis-Hillman acetates thus demonstrating the applications of Baylis-Hillman adducts in synthetic organic chemistry.

A simple and one pot protocol for synthesis of indene-spiro-oxindoles involving tandem Prins and Friedel-Crafts reactions

The spiro-oxindole framework represents an important structural organization present in a number of bioactive natural products such as elacomine (**132**),[224] alstonisine (**133**),[225] horsfiline (**134**),[226] welwitindolinone A (**135**),[227] spirotryprostatin A (**136**),[228] tasmanine (**137**),[229] coerulescine (**138**),[226] surugatoxin (**139**)[230] See Fig. 11.

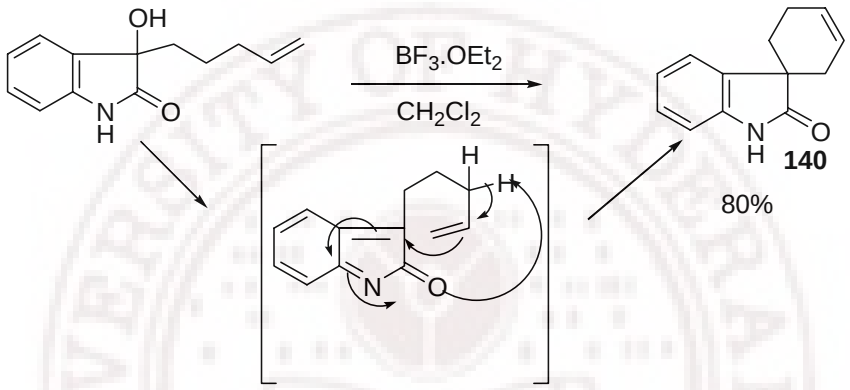
Fig. 11



Because of the importance of spiro-oxindole framework in medicinal chemistry there has been increasing the interset towards synthesis of spirooxindole derivatives. Some of the recent and relavent literature reports are describing here.

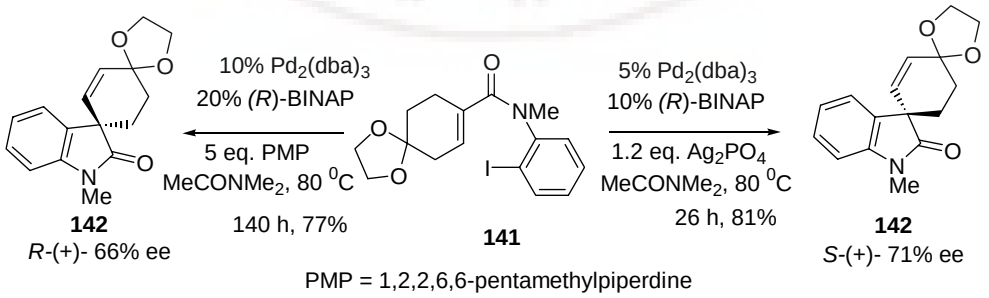
Padwa and co-workers[231] developed simple one-pot procedure for synthesis of spiro-oxindoles (**140**) *via* $BF_3.OEt_2$ catalyzed cyclization of 3-hydroxy-3-pent-4-enyl)-1,3-dihydroindole-2-one following the reaction sequence described in Scheme 72.

Scheme 72



Both enantiomers of spirooxindoles (**142**) were prepared by Overman and co-workers[232] from the acryloyl 2'-iodoanilide (**141**), involving the the palladium catalyzed cyclizations in the presence of single enantiomer of chiral diphoshine ligand *R*-(+)-BINAP by employing different reaction conditions. Representative examples are presented in Scheme 73.

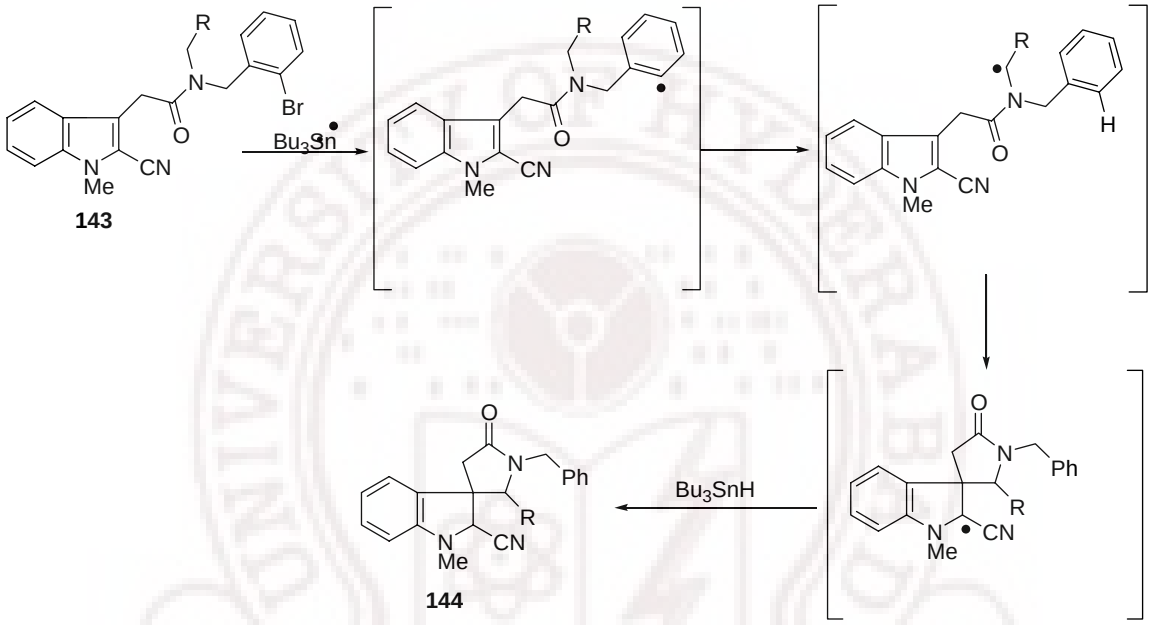
Scheme 73



PMP = 1,2,2,6,6-pentamethylpiperdine

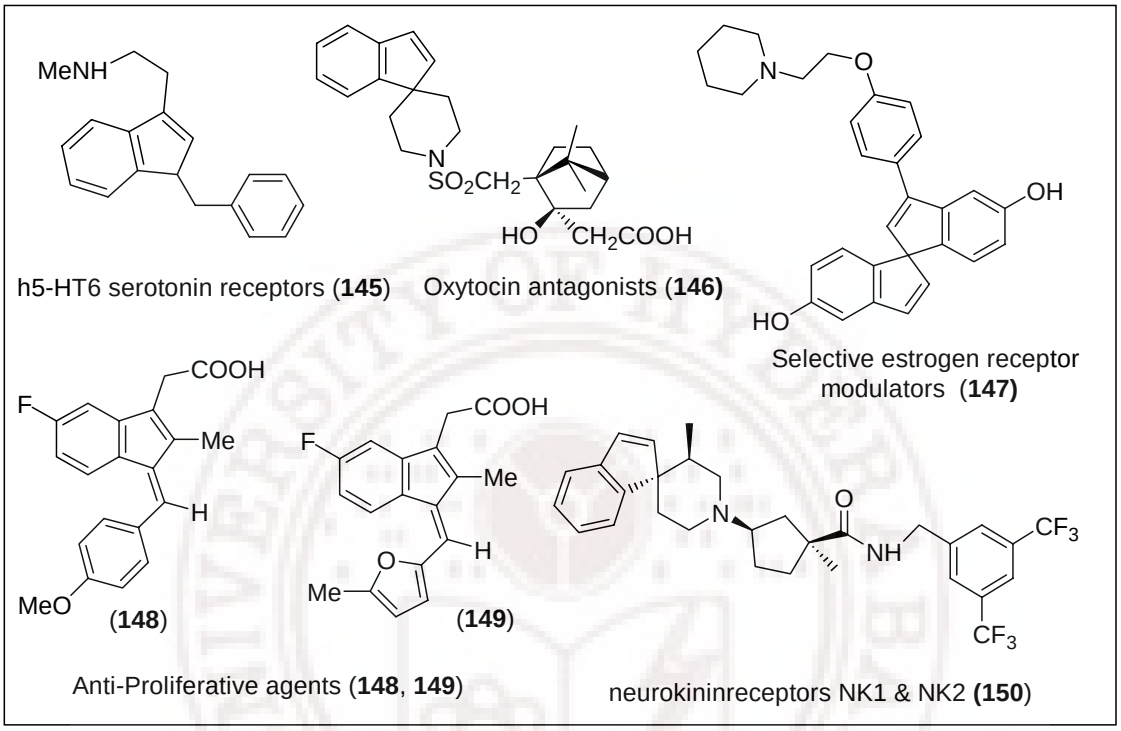
Jones and co-workers[225] reported an interesting methodology for synthesis of spiro-oxindoles derivatives (**144**), *via* tributylstannane mediated radical cyclization of amide (**143**) following the reaction sequence as described in the Scheme 74.

Scheme 74



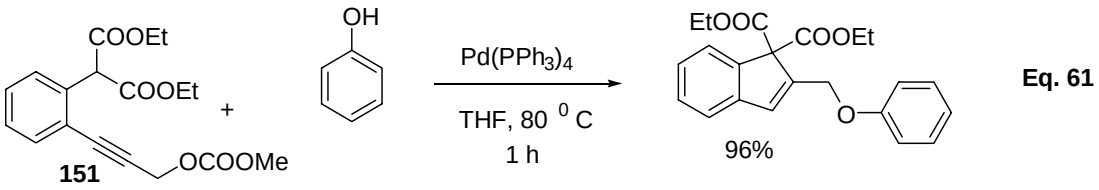
Indene and spiro-indene derivatives occupy a special place in organic and medicinal chemistry because these compounds are well known h5-HT6 serotonin receptors (**145**),[233] oxytocin antagonists (**146**),[234] estrogen receptor modulators (**147**),[235] anti-proliferative agents (**148**& **149**),[236] neurokininreceptors (**150**)[237]see Fig. 12.

Fig. 12



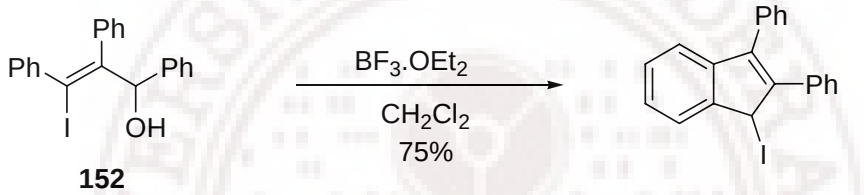
Due to the potential biological activity of these molecules, the development of simple methodologies for indene framework, has attracted the attention of organic chemists. Some of the recent and relevant reports are presented in this section.

Liang and co-workers[238] described a facile synthesis of indene derivatives *via* palladium catalyzed carboannulation of propargylic carbonates (**151**) with a variety of neucleophiles. One of the representative example is presented in Eq. 61.



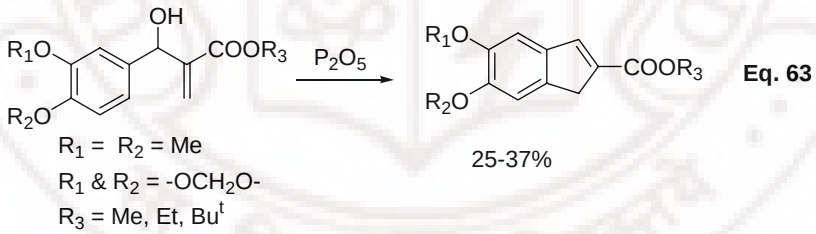
Eq. 61

Li and co-workers[239] conveniently prepared multisubstituted indene derivatives involving $BF_3.Et_2O$ catalyzed Friedel-Crafts reaction of iodinated allylic alcohols (**152**). One such example is presented in Eq. 62.



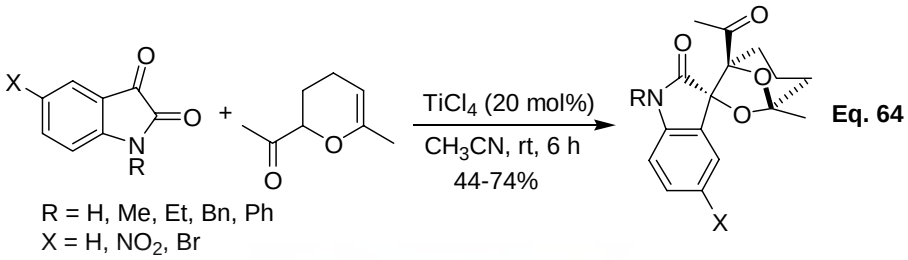
Eq. 62

Our research group[240] has developed the synthesis of indene derivatives involving P_2O_5 mediated Friedel-Crafts reaction of Baylis-Hillman alcohols as presented in Eq. 63.



Eq. 63

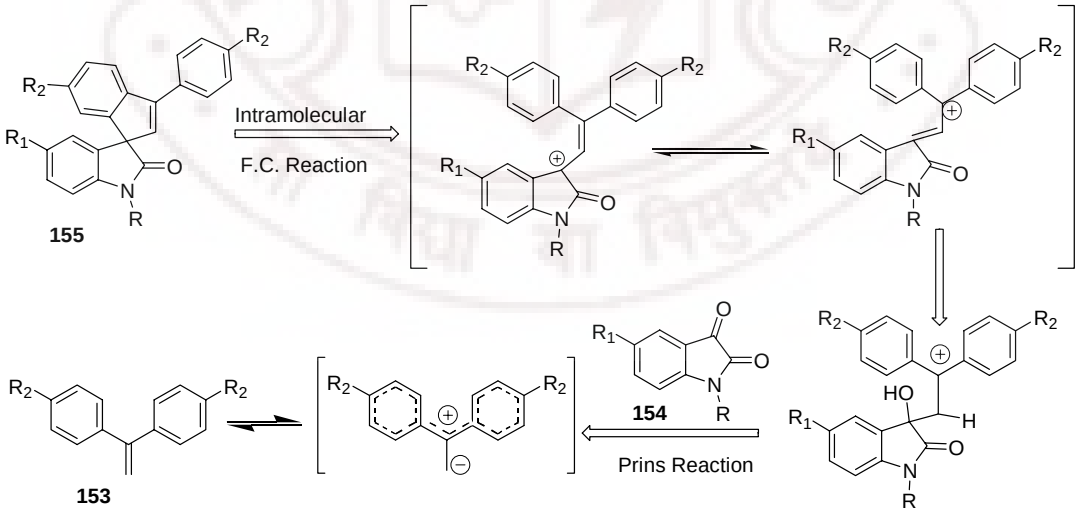
We have doveloped simple, atom economical, convinent, one-pot stereoselective methodology[241] for synthesis of spiro-oxindoles [{1-acetyl-5-methyl-6,8-dioxabic-yclo(3.2.1)octane}-7-spiro-3′-(indolin-2′-one)] *via* the $TiCl_4$ induced reaction between isatin derivatives and 2-acetyl-6-methyl-2,3-dihydro-4*H*-pyran as described in Eq. 64.



Eq. 64

It occurred to us that the molecules containing both the indene and oxindole frameworks connected by an interesting spiro-bridge would be of biological interest and also aesthetically appealing. In continuation of our interest in synthesis of hetrocyclic molecules we envisioned that the Prins reaction[242] of 1,1-diarylethylenes with isatin derivatives followed by intramolecular Friedel-Crafts reaction[243] would lead to the synthesis of 1*H*-indene-spiro-oxindoles (Retro-synthetic strategy, Scheme 75).

Scheme 75 Retro-synthetic strategy



Accordingly, we have selected 1,1-diphenylethylene (**153a**) and isatin (**154a**) as reaction partners for this one-pot multi step synthesis of indene-spiro-oxindole derivative. Thus we have first carried out the reaction between isatin (**154a**) (1 mmol), and 1,1-diphenylethylene (**153a)** (1 mmol), at room temperature under the influence of various acids (entries 1-6, Table 1). In this regard, the best results were obtained when a solution of isatin (**154a)** (1 mmol), 1,1-diphenylethylene (**153a)** (1 mmol), in CH_2Cl_2 (3 mL) was treated with $TiCl_4$ (1 mmol) (addition at 0 ^{0}C) at room temperature for 13 h, thus providing the desired (3-phenyl-1*H*-indene)-1-spiro-3′-(indolin-2′-one) (**155a**) in 90% isolated yield (Table 11, entry 5) after work up, followed by purification through silica gel column chromatography. The structure of this molecule was in agreement with IR, ^{1}H NMR [for compound **155a** see Spectrum 30], ^{13}C NMR [for compound **155a** see Spectrum 31], mass spectral data and elemental analysis. The structure of this molecule (**155a**) was further confirmed by single crystal X-ray data (see Fig. X12 & Table XII).

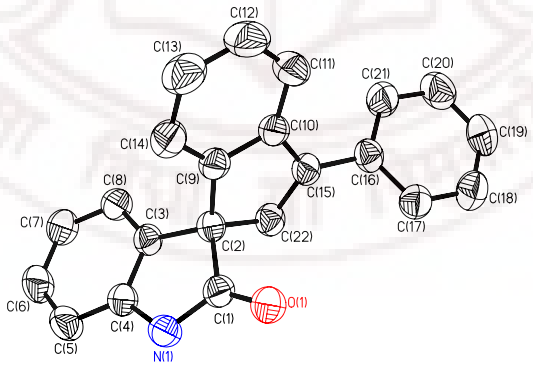
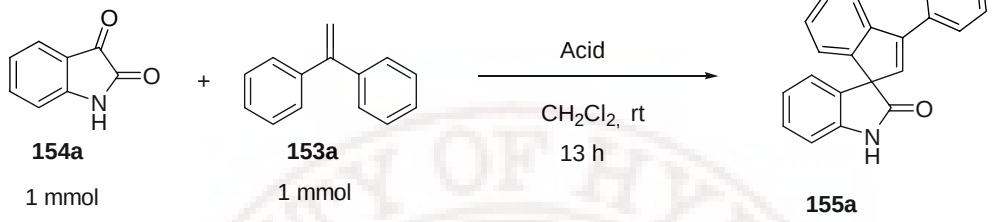


Fig. X12 ORTEP diagram of compound **155a**
(Hydrogen atoms were omitted for clarity)

Table XII. Crystal data and structure refinement for 155a

Identification code	: **155a**
Empirical formula	: $C_{22}H_{15}NO$
Formula weight	: 309.35
Temperature	: 298 K
Wavelength	: 0.71073 Å
Crystal system	: Monoclinic
space group	: P2(1)/c
Unit cell dimensions	: a = 12.2411(9) Å; α = 90 deg.
	: b = 8.0506(6) Å; β = 97.3520(10) deg.
	: c = 16.9934(12) Å; γ = 90 deg.
Volume	: 1660.9(2) $Å^3$
Z, Calculated density	: 4, 1.237 Mg/m^3
Absorption coefficient	: 0.076 mm^{-1}
F(000)	: 648
Crystal size	: 0.42 x 0.40 x 0.24 mm
Theta range for data collection	: 1.68 to 26.00 deg.
Limiting indices	: -15<=h<=14, -9<=k<=9, -20<=l<=20
Reflections collected / unique	: 16596 / 3254 [R(int) = 0.0229]
Completeness to theta = 26.00	: 99.8 %
Max. and min. transmission	: 0.9821 and 0.9689
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 3254 / 0 / 221
Goodness-of-fit on F^2	: 1.022
Final R indices [I>2sigma(I)]	: R1 = 0.0425, wR2 = 0.1104
R indices (all data)	: R1 = 0.0510, wR2 = 0.1170
Largest diff. peak and hole	: 0.198 and -0.202 e. $Å^{-3}$

Table 11 Standardization: **Synthesis of (3-Phenyl-1*H*-indene)-1-spiro-3′-(indolin-2′-one) (155a)**[®,a]



154a
1 mmol

153a
1 mmol

155a

Entry	Acid	Time (h)	Isolated Yield (%)[b,c]
1	Acid (1 mmol)	13	nil
2	*p*-TsOH (1 mmol)	13	nil
3	$MeSO_3H$ (1 mmol)	13	9
4	$SnCl_4$ (1 mmol)	13	Nil
5	**$TiCl_4$ (1 mmol)**	**13**	**90**
6	$TiCl_4$ (0.5 mmol)	13	14

[a] All reactions were carried out on 1 mmol scale of isatin (**154a**) with 1 mmol of diarylethylene (**153a**), under influence of 1 mmol of $TiCl_4$ (0.5 mL, 2 M solution in CH_2Cl_2) in CH_2Cl_2 (3 mL) at room temperature for 13 h at room temperature.

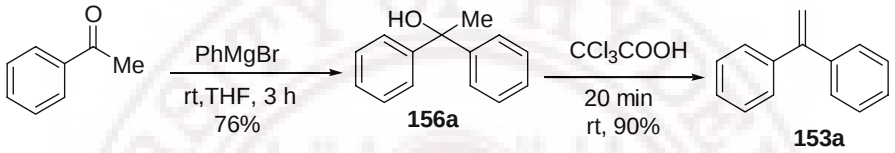
[b]Compound (3-phenyl-1*H*-indene)-1-spiro-3′-(indolin-2′-one)(**155a**) was fully characterized.

[c]Compound (3-phenyl-1*H*-indene)-1-spiro-3′-(indolin-2′-one) (**155a**) was further charecterized by single crystal X-ray data see Fig. X12.

[®]For continuity and better understandings we have numbered 1,1-diarylethylenes, isatin derivatives, Indene-spirooxindoles as **153**, **154**, **155** respectively. We have also numbered 1,1-diarylethanol derivatives as **156**.

The required 1,1-diphenylethylene (**153a**) was prepared in 90% isolated yield *via* the Grignard reaction of phenylmagnisium bromide with acetophenone followed by dehydration of the resulting 1,1-diphenylethanol (**156a**), with trichloacetic acid according to known procedure (Scheme 76).[244]

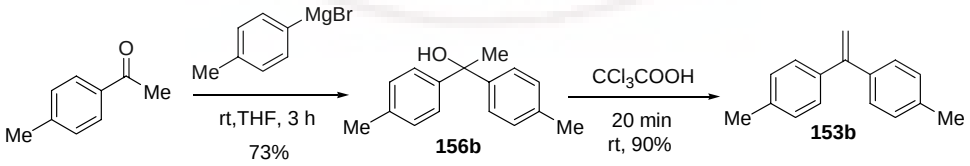
Scheme 76



With a view to understand the generality of this reaction we have selected 1,1-di(4-methylphenyl)ethylene (**153b**) and 1,1-di(4-methoxyphenyl)ethylene (**153c**) for reaction with various isatin derivatives.

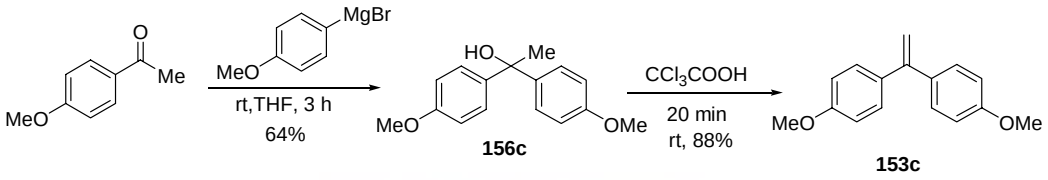
Reaction of 4-methylphenylmagnisumbromide with 4-methylacetophenone provided 2,2-di(4-methylpheny)ethanol (**156b**) which on subsequent treatment with trichloroacetic acid under neat reaction conditions furnished the 1,1-di(4-methylphenyl)ethylene (**153b**)[244] (Scheme 77).

Scheme 77

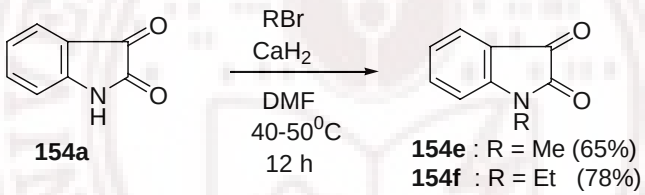


We have also prepared 1,1-di(4-methoxyphenyl)ethylene (**153c**)[244] from 4-methoxya-cetophenone following the reaction sequence as shown in Scheme 78.

Scheme 78



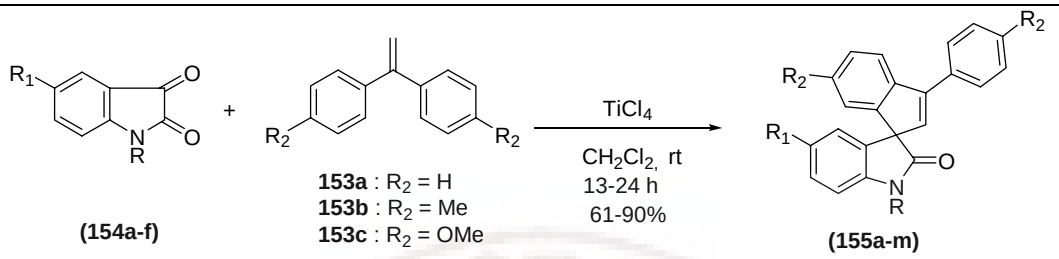
We have selected various isatin derivatives (**154a-f**) as reaction partners with 1,1-diarylethylenes (**153a-c**). The isatin derivatives **154a-d** are commercially available. We have prepared required *N*-methylisatin (**154e**) and *N*-ethylisatin (**154f**) according to the literature procedure (Eq. 65)[245]



Eq. 65

For understanding the generality of this Prins-Friedel-Crafts reaction, we have subjected various isatin derivatives (**154a-f**), to the reaction with 1,1-diarylethylenes (**153a-c**) under the influence of $TiCl_4$ to provide the resulting 1*H*-indene-spiro-oxindoles (**155b-m**) in moderate to excellent yields (Table 12). Structures of these molecules were in complete agreement with IR, ^{1}H NMR [for compounds **155h**, **155j** and **155l** see spectrums 32, 34 and 36 respectively], ^{13}C NMR [for compounds **155h**, **155j** and **155l** see spectrums 33, 35 and 37 respectively], mass spectral data and elemental analyses. The structures of the molecules **155c** and **155l** were further confirmed by single crystal X-ray data (For ORTEP diagrams see Fig.s X13 & X14 respectively). For Tables see Table XIII & Table XIV.

Table 12. Synthesis of 1*H*-indene-spiro-oxindole derivatives (155a-m)[a,b,¥]



Isatin	R	R_1	Olefin	Time (h)	Product	Yield (%)[c]	M.p ^{0}C
154a	H	H	**153a**	13	**155a**[d]	90	192-194
154a	H	H	**153b**	13	**155b**	82	182-184
154a	H	H	**153c**	13	**155c**[d]	69	204-206
154b	H	Cl	**153a**	18	**155d**	77	205-207
154b	H	Cl	**153b**	18	**155e**	80	130-132
154b	H	Cl	**153c**	18	**155f**	88	128-130
154c	H	Me	**153a**	13	**155g**	61	188-190
154c	H	Me	**153b**	13	**155h**	79	184-186
154c	H	Me	**153c**	13	**155i**	76	156-158
154d	H	Br	**153c**	18	**155j**	64	164-166
154e	Me	H	**153c**	18	**155k**	72	96-98
154f	Et	H	**153a**	24	**155l**[d]	63	122-124
154f	Et	H	**153c**	18	**155m**	71	96-98

[a] All reactions were carried out on 1 mmol scale of isatins (**154a-f**) with 1 mmol of olefins (**153a-c**), under influence of 1 mmol of $TiCl_4$ (0.5 mL, 2M solution in CH_2Cl_2) in CH_2Cl_2 (3 mL) at room temperature for 13-24 h at room temperature. [b]All the compounds (**155a-m**) were obtained as a solids and gave satisfactory IR, ^{1}HNMR, ^{13}C NMR mass spectral data and elemental analyses.[c]Yields were based on isatins.

[d] Structures of the compounds (**155a**, **155c**, **155l**) were further confirmed by single crystal X-ray data see Figs X12, X13, X14.

[¥] We have numbered various 1,1-diarylethylenes, isatin derivatives, and indene-spirooxindoles as **153**, **154**, **155** respectively.

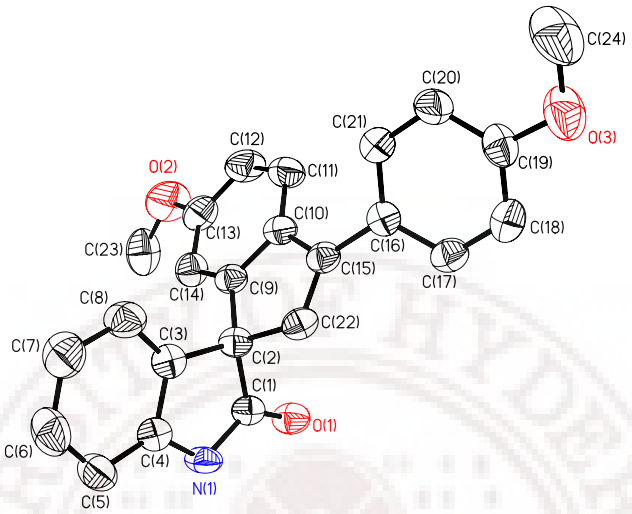


Fig. X13 ORTEP diagram of compound **155c**
(Hydrogen atoms were omitted for clarity)

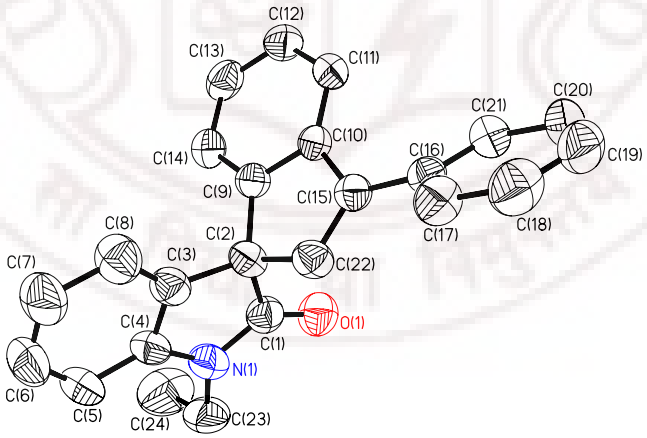


Fig. X14 ORTEP diagram of compound **155l**
(Hydrogen atoms were omitted for clarity)

Table XIII. Crystal data and structure refinement for 155c

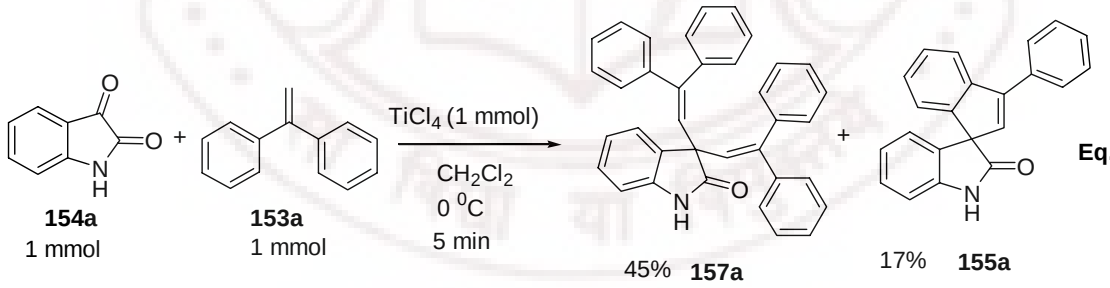
Identification code	: **155c**
Empirical formula	: $C_{24}\ H_{19}\ N\ O_3$
Formula weight	: 369.40
Temperature	: 298 K
Wavelength	: 0.71073 Å
Crystal system,	: Monoclnic
space group	: P21/c
Unit cell dimensions	: a = 23.3988(15) Å; α = 90 deg.
	: b = 9.0998(6) Å; β = 113.2430(10) deg.
	: c = 19.3653(13) Å; γ = 90 deg.
Volume	: 3788.7(4) $Å^3$
Z, Calculated density	: 8, 1.295 Mg/m^3
Absorption coefficient	: 0.086 mm^{-1}
F(000)	: 1552
Crystal size	: 0.29 x 0.12 x 0.08 mm
Theta range for data collection	: 1.89 to 26.06 deg.
Limiting indices	: -28<=h<=24, -11<=k<=7, -22<=l<=23
Reflections collected / unique	: 25510 / 7469 [R(int) = 0.0529]
Completeness to theta = 26.06	: 99.8 %
Max. and min. transmission	: 0.9898 and 0.9636
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 7467 / 0 / 509
Goodness-of-fit on F^2	: 1.021
Final R indices [I>2sigma(I)]	: R1 = 0.0661, wR2 = 0.1138
R indices (all data)	: R1 = 0.9980, wR2 = 0.1204
Largest diff. peak and hole	: 0.195 and -0.188 e. $Å^{-3}$

Table XIV. Crystal data and structure refinement for 155l

Identification code	: **155l**
Empirical formula	: C_{24} H_{19} N O
Formula weight	: 337.40
Temperature	: 298 K
Wavelength	: 0.71073 Å
Crystal system	: Monoclinic
Space group	: P 2(1)/n
Unit cell dimensions	: a = 12.038(2) Å; α = 90° deg.
	: b = 12.112(2) Å; β = 114.892 (3)° deg.
	: c = 14.089(2) Å; γ = 90° deg.
Volume	: 1863.5(5) $Å^3$
Z	: 4
Density (calculated)	: 1.203 Mg/m^3
Absorption coefficient	: 0.073 mm^{-1}
F(000)	: 712
Crystal size	: 0.31 x 0.25 x 0.20 mm^3
Theta range for data collection	: 1.87 to 26.06°
Index ranges	: -14<=h<=14, -12<=k<=14, -17<=l<=17
Reflections collected / unique	: 10110 / 3673 [R(int) = 0.0434]
Completeness to theta = 26.06°	: 99.7 %
Max. and min. transmission	: 0.9749 and 0.9615
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 3673 / 0 / 236
Goodness-of-fit on F^2	: 1.001
Final R indices [I>2sigma(I)]	: R1 = 0.0522, wR2 = 0.1277
R indices (all data)	: R1 = 0.0822, wR2 = 0.1397
Largest diff. peak and hole	: 0.277 and -0.183 e. $Å^{-3}$

To understand the mechanism

To understand the mechanistic pathway we have quenched the reaction in the case of isatin (**154a**) (1 mmol) with 1,1-diphenylethylene (**153a**) (1 mmol) in the presence of $TiCl_4$ (1 mmol) with water after 5 min stirring at 0 ^{0}C. Usual work up and purification through silica gel column chromatography (30% EtOAc in hexanes) provided the desired product, (3-phenyl-1*H*-indene)-1-spiro-3′-(indolin-2′-one) (**155a**), only in 17% isolated yield and the bis-adduct, 3,3-bis(2,2-diphenylvinyl)indolin-2-one (**157a**),[Œ] in 45% isolated yield (Eq. 66, Table 13) (along with recovered isatin, **154a**). Structure of the molecule was confirmed by IR, ^{1}H NMR [for compound **157a** see spectrum 38], ^{13}C NMR [for compound **157a** see spectrum 39], mass spectral data and elimental analysis. Finally the structure of this molecule (**157a**) was further established by single crystal X-ray data (Table XV & Fig. X15).



[Œ] For continuation and better understandings we have numbered bis adducts as **157**

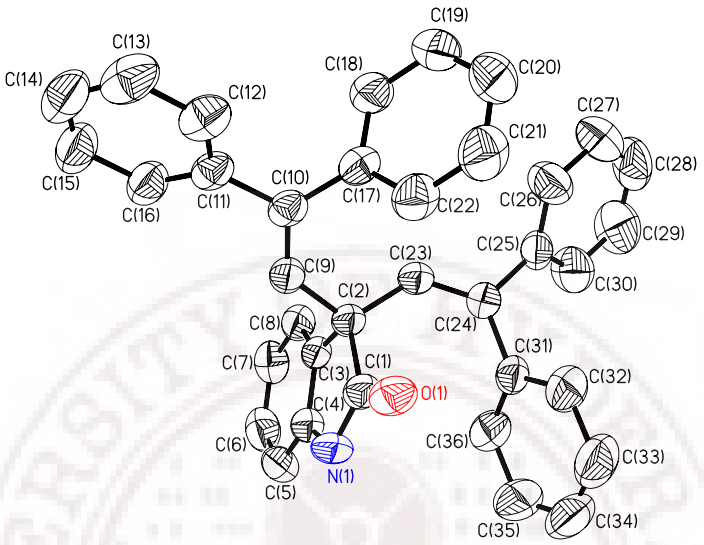
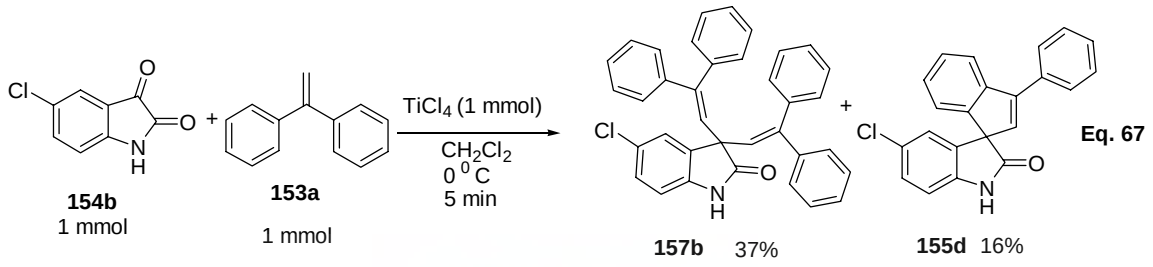


Fig. **X15** ORTEP diagram of compound **157a**
(hydrogen atoms were omitted for clarity)

With a view to understand the generality of this reaction we have treated 5-chloroisatin (**154b**) with 1,1-diphenylethylene (**1534a**) under the influence of $TiCl_4$ at 0 ^{0}C for 5 min (stirring) which provided 3,3-bis(2,2-diphenylvinyl)-5-chloroindolin-2-one(**157b**) and (3-Phenyl-1*H*-indene)-1-spiro-3′-(5′-chloroindolin-2′-one) (**155d**) in 37% and 16% isolated yields respectively (Eq. 67, Table 13). Structures of these molecules were in agreement with IR, ^{1}H NMR, ^{13}C NMR, mass spectral data and elemental analysis.



Similarly, we have treated *N*-ethylisatin (**154f**) with 1,1-diphenylethylene (**153a**) under influence of $TiCl_4$ at room temperature for 24 h which provided the resulting 3,3-bis(2,2-diphenylvinyl)-1-ethylindolin-2-one (**157c**) and 3-phenyl-1*H*-indene)-1-spiro-3′-(1′-ethyl-indolin-2′-one) (**155l**) in 23% and 63% isolated yields respectively (Eq. 68, Table 13). Structures of these molecules were in agreement with IR, ^{1}H NMR, ^{13}C NMR, mass spectral data and elemental analysis.

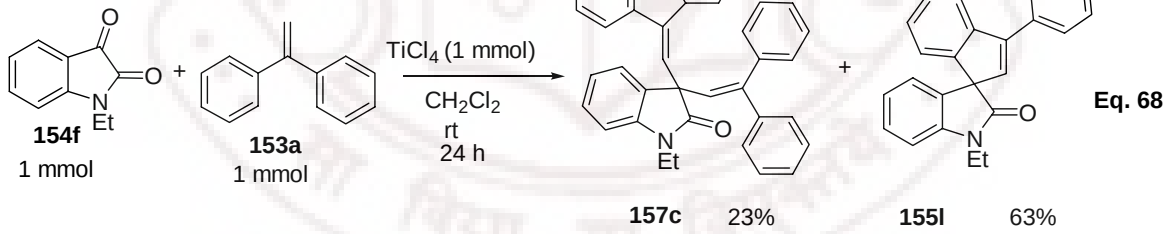
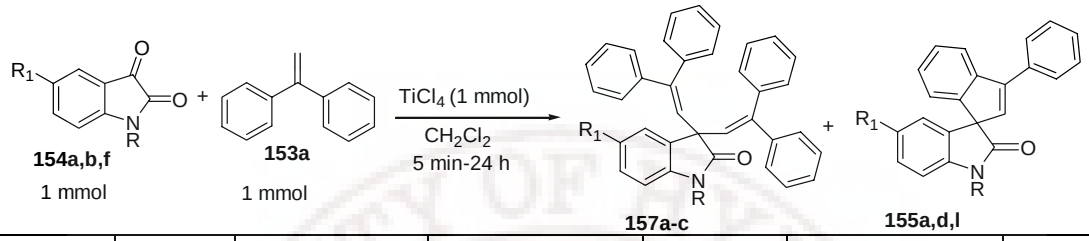


Table 13. Control reactions between isatins (154a,b, 154f) and 1,1-diphenylethylene (153a) [Ø,a,b,]



Isatin	Time	Temperature	Product (%)[c]	Yield (%)	Product (%)[d]	Yield (%)
154a	5 min	0 ^{0}C	**157a**[e]	45	**155a**	17
154b	5 min	0 ^{0}C	**157b**	37	**155d**	16
154f	24 h	rt	**157c**	23	**155l**	63

[a]All reactions were carried out on 1 mmol scale of isatins (**154a-b, 154f**) with 1 mmol of olefins (**153a**), under influence of 1 mmol of $TiCl_4$ (0.5 mL, 2M solution in CH_2Cl_2) in CH_2Cl_2 (3 mL) at 0 ^{0}C for 5 min (in case of **154a-b**) & at rt for 24 h (in case of **154f**).

[b]All the compounds (**157a-c**, **155a**, **155d**, **155l**) were obtained as a solids and gave satisfactory IR, ^{1}H NMR, ^{13}C NMR, mass spectral data and elemental analyses.

[c]Yields were based on 1,1-diphenylethylene (**153a**).

[d]Yields were based on isatin derivatives (**154a**, **154b**, **154f**).

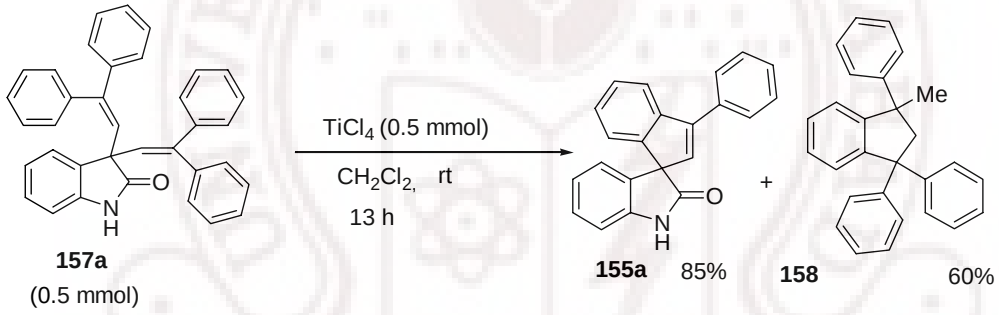
[e] Compound **157a** was further characterized by single crystal X-ray data (see Fig. X15).

[Ø]For continuity and better understandings we have numbered bis adducts obtained from **154a-b, f** as **157a-c** respectively

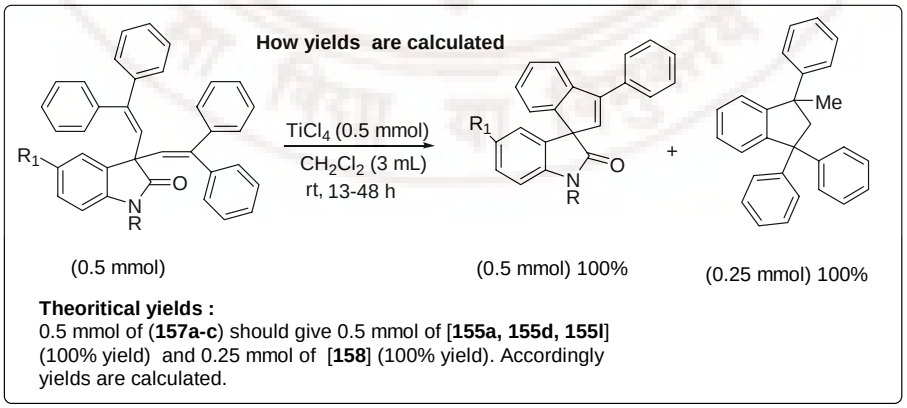
Table XV. Crystal data and structure refinement for 157a

Identification code	: **157a**
Empirical formula	: $C_{36}H_{27}NO$
Formula weight	: 489.59
Temperature	: 298 K
Wavelength	: 0.71073 Å
Crystal system	: Monoclinic
space group	: P2(1)/n
Unit cell dimensions	: a = 11.237(3) Å; α = 90 deg.
	: b = 17.494(4) Å; β = 94.841(5) deg.
	: c = 14.194(4) Å; γ = 90 deg.
Volume	: 2780.3(12) $Å^3$
Z, Calculated density	: 4, 1.169 Mg/m^3
Absorption coefficient	: 0.069 mm^{-1}
F(000)	: 1032
Crystal size	: 0.42 x 0.36 x 0.05 mm
Theta range for data collection	: 1.85 to 26.06 deg.
Limiting indices	: -13<=h<=13, -21<=k<=21, -17<=l<=17
Reflections collected / unique	: 31841 / 6898 [R(int) = 0.0565]
Completeness to theta = 26.06	: 99.4 %
Max. and min. transmission	: 0.9936 and 0.9477
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 6898 / 0 / 343
Goodness-of-fit on F^2	: 0.867
Final R indices [I>2sigma(I)]	: R1 = 0.0482, wR2 = 0.1060
R indices (all data)	: R1 = 0.0865, wR2 = 0.1261
Largest diff. peak and hole	: 0.166 and -0.140 e. $Å^{-3}$

From these reactions it looks that the bis-adduct might release *one equivalen*t of the alkene, there by providing the desired spiro-oxindoles. To examine this aspect we have treated the 3,3-bis(2,2-diphenylvinyl)indolin-2-one (**157a**) with $TiCl_4$ at room temperature (addition at 0 ^{0}C) for 13 h which provided the expected (3-phenyl-1*H*-indene)-1-spiro-3′-(indolin-2′-one) (**155a**) in 85% and 3-methyl-1,1,3-triphenylindane (**158**) in 60% isolated yields respectively (Eq. 69, Table 14). Structure of 3-methyl-1,1,3-triphenylindane (**158**) was in agreement with IR, ^{1}H NMR, ^{13}C NMR, mass spectral data, elemental analysis and also in agreement with literature data.[246]

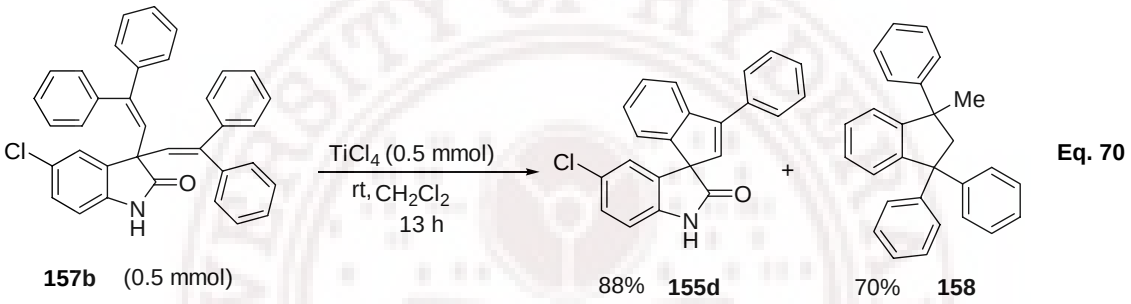


Eq. 69



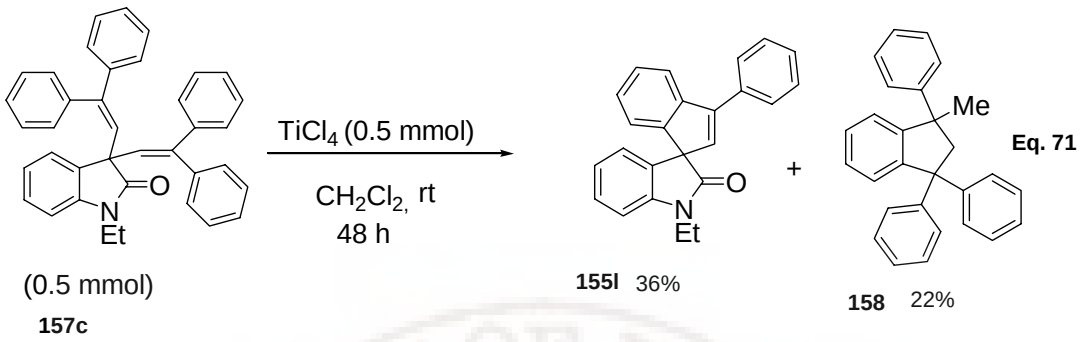
Theoritical yields :
0.5 mmol of (**157a-c**) should give 0.5 mmol of [**155a, 155d, 155l**] (100% yield) and 0.25 mmol of [**158**] (100% yield). Accordingly yields are calculated.

With a view to understand the generality of this reaction we have also treated 3,3-bis(2,2-diphenylvinyl)-5-chloroindolin-2-one (**157b**) with $TiCl_4$ at room temperature (addition at 0 ^{0}C) for 13 h to provide the (3-Phenyl-1*H*-indene)-1-spiro-3′-(5′-chloroindolin-2′-one) (**157d**) and 3-methyl-1,1,3-triphenylindane (**158**) in 88% and 70% isolated yields respectively (Eq. 70, Table 14).

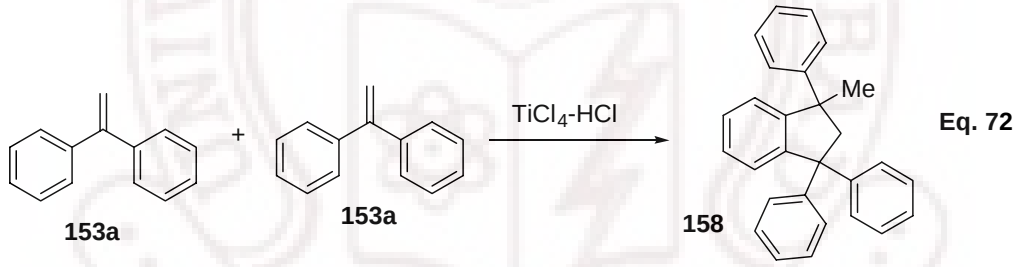


157b (0.5 mmol) 88% **155d** 70% **158** **Eq. 70**

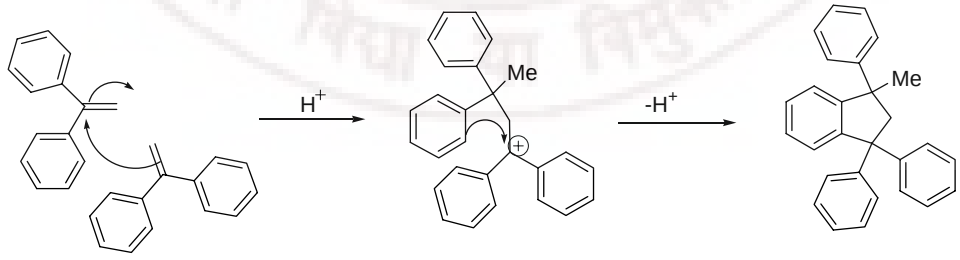
Similar treatment of 3,3-bis(2,2-diphenylvinyl)-1-ethylindolin-2-one (**157c**) with $TiCl_4$ at room temperature (addition at 0 ^{0}C) for 13 h provided the expected 3-Phenyl-1*H*-indene)-1-spiro-3′-(1′-ethylindolin-2′-one (**155l**) and 3-methyl-1,1,3-triphenylindane (**158**) in 36% and 22% isolated yields respectively (Eq. 71, Table 14). In this case we have also isolated unreacted starting material 3,3-bis(2,2-diphenylvinyl)-1-ethylindolin-2-one (**157c**) in 47% isolated yield (Eq. 71).



It is worth mentioning here that the reaction of 1,1-diarylethylene (**153a**) into 3-methyl-1,1,3-triphenylindane (**158**)[246] under the influence of $TiCl_4$-HCl and other acidic conditions is known in the literature Eq. 72. Mechanism of this dimerization is presented in Scheme 79.

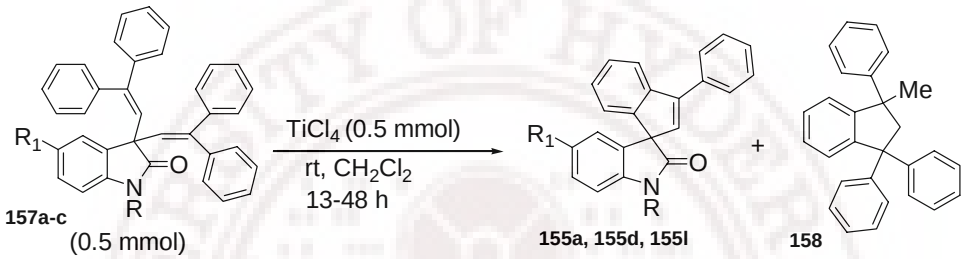


Scheme 79



To the best of our knowledge single crystal X-ray structure for this molecule (**158**) was not reported. We have therefore confirmed the structure of this molecule with single crystal X-ray data [Table XVI]. For ORTEP diagram see Fig. X16.

Table 14. Reactions with bis adducts (157a-c)[@,a,b]



157a-c (0.5 mmol) — **155a, 155d, 155l** — **158**

Bis-adduct	Time (h)	Product	Yield (%)[c]	Product[d]	Yield (%)[c]
157a	13	**155a**	85	**158**	60
157b	18	**155d**	88	**158**	70
157c	48	**155l**	36	**158**	22

[a]All reactions were carried out on 0.5 mmol scale of bisadducts (**157a-c**) with 0.5 mmol of $TiCl_4$ (0.5 mL, 2M solution in CH_2Cl_2) in CH_2Cl_2 (3 mL) at room temperature.

[b]All the compounds were obtained as a solids and gave satisfactory IR, ^{1}HNMR, ^{13}C NMR spectral data, mass analyses.

[C]Yields : 0.5 mmol of bisadducts should give 0.5 mmol of spiro-oxindoles (**155a**, **155d**, **155l**), and 0.25 mmol of 3-methyl-1,1,3-triphenylindane (**158**), accordingly yields were calculated.

[d] Structure of the compound **158** was further confirmed by single crystal X-ray data (see Fig. X16).

[@]For continuity and better understand we have numbered 3-methyl-1,1,3-triphenylindane as **158**

These results, to some extent, might suggest a plausible mechanism (Scheme 80) which involves the reaction between *one equivalent* of isatin and *one equivalent* of diarylethylene under the influence of $TiCl_4$ to provide the transient intermediate **T-A** which might then might then undergo intramolecular Friedel-Crafts reaction to generate the desired 1*H*-indene-spiro-oxindoles (path **X**). Alternatively the **T-A** might also react with diarylethylene to give first bis-adduct **B** which would then release *one equivalent* of diarylethylene to provide the desired 1*H*-indene-spiro-oxindole (path **Y**). Diarylethyene in turn would again react with isatin to furnish the expected product, 1*H*-indene-spiro-oxindole.

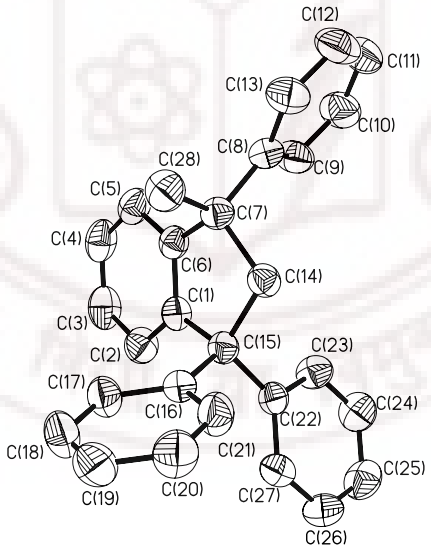
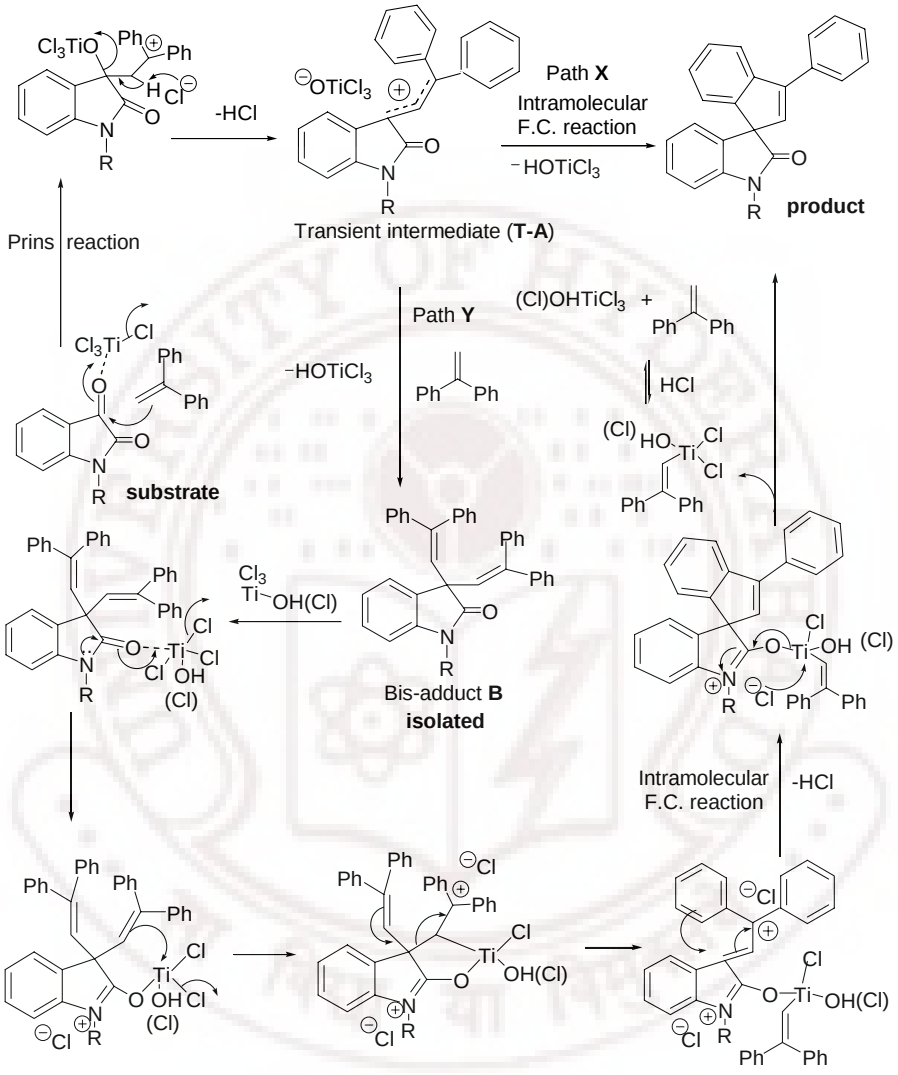


Fig. X16 ORTEP diagram of compound **158**
(Hydrogen atoms were omitted for clarity)

Table XVI. Crystal data and structure refinement for 158

Identification code	: **158**
Empirical formula	: C_{28} H_{24}
Formula weight	: 360.47
Temperature	: 298 K
Wavelength	: 0.71073 Å
Crystal system	: Monoclinic
space group	: P21/n
Unit cell dimensions	: a = 11.0005(13) Å; α = 90 deg.
	: b = 17.408(2) Å; β = 111.791(2) deg.
	: c = 11.3602(14) Å; γ = 90 deg.
Volume	: 2020.0(4) $Å^3$
Z, Calculated density	: 4, 1.185 Mg/m^3
Absorption coefficient	: 0.067 mm^{-1}
F(000)	: 768
Crystal size	: 0.38 x 0.32 x 0.28 mm
Theta range for data collection	: 2.20 to 25.91 deg.
Limiting indices	: -13<=h<=13, -21<=k<=21, -13<=l<=13
Reflections collected / unique	: 20400 / 3926 [R(int) = 0.0333]
Completeness to theta = 25.91	: 99.8 %
Max. and min. transmission	: 0.9816 and 0.9751
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 3926 / 0 / 254
Goodness-of-fit on F^2	: 1.038
Final R indices [I>2sigma(I)]	: R1 = 0.0499, wR2 = 0.1095
R indices (all data)	: R1 = 0.0659, wR2 = 0.1176
Largest diff. peak and hole	: 0.195 and -0.193 $e.Å^{-3}$

Scheme 80 Plausible mechanism



In conclusion, we have developed a simple and one pot $TiCl_4$ mediated synthesis of 1*H*-indene-spiro-oxindoles involving tandem Prins and Friedel-Crafts (PFC) reactions, using diarylethylenes and isatins as reaction partners.

Conclusions

We have made considerable progress in our objectives on the synthesis of representative heterocycles & carbocyclics using Baylis-Hillman addducts and synthesis of indene-spiro-oxindoles involving the tandem Prins-Friedel-Crafts reactions as mentioned in the begning of this chapter. We have transformed 3-hydroxy-2-methylene-3-(2-nitroaryl)propanenitrile (**93a-f**) [derived from various 2-nitroarylaldehydes (**92a-f**) and acrylonitrile] into benzo[*b*][1,8]naphthyridine derivatives (**95a-l**) via the Johnson-Claisen rearrengement followed by reductive cyclization using Fe/AcOH. We have developed a convenient, one-pot synthesis of quinoline derivatives (**109a-n**), from the Baylis-Hillman acetates 4-acetoxy-3-methylene-4-(2-nitroaryl)butan-2-one (**106a-e**) [prepared from the Baylis-Hillman alcohols, 4-hydroxy-3-methylene-4-(2-nitroaryl)butane-2-ones (**105a-e**)] *via* the reaction with and β-keto esters (**107a-c**) followed by reductive cyclization using Fe/ AcOH. We have developed a simple protocl for synthesis of benzocycloheptadiene derivatives (**128a-g**), *via* the alkylation of the Baylis-Hillman acetates (**124a**, **124c-e, 124g**) with β-keto esters (**125a-c**) followed by intramolecular Friedel-Crafts reaction using methanesulfonic acid. We have developed a simple procedure for synthesis of tetracyclic carbocyclic derivatives (**131a-j**) from the Baylis-Hillman acetates (**124a, 124c-f, 124h-l**) *via* the treatment with β-keto esters (**129b-c**) followed by two intramolecular Friedel-Crafts reactions.

We have also sucessfully developed simple, one-pot synthesis of indene-spiro-oxindoles derivatives (**155a-m**), *via* tandem construction of two carbon-carbon bonds involving $TiCl_4$ catalyzed Prins and intramolecular Friedel-Crafts reactions between isatin derivatves (**154a-f**) and 1,1-diarylethylenes (**153a-c**).

Our studies clearly demonstrate the potential of Baylis-Hillman adducts as valuable synthons for synthesis of various heterocycles and carbocycles. Our studies also demonstrate the applications of tandem Prins and Friedel-Crafts reactions in the synthesis of indene-spiro-oxindoles.

EXPERIMENTAL

Melting Points: All melting points were recorded on a Superfit (India) capillary melting point apparatus and are uncorrected.

Boiling Points: Boiling points refer to the temperature measured using short path distillation units and are uncorrected.

Infrared Spectra: Infrared spectra were recorded on a JASCO FT / IR-5300 spectrophotometer. All the spectra were calibrated against polystyrene absorption at 1601 cm^{-1}. Solid samples were recorded as KBr wafers and liquid samples as thin film between NaCl plates or solution spectra in CH_2Cl_2.

Nuclear Magnetic Resonance Spectra: Proton magnetic resonance spectra and carbon-13 magnetic resonance spectra were recorded on a BRUKER-AC-200 and BRUKER-AVANCE-400 spectrometers. ^1H NMR (400 MHz) spectra for all the samples were measured in chloroform-*d*, unless otherwise mentioned (δ = 2.50 ppm for ^1H NMR in the case of DMSO-d_6), with TMS (δ = 0 ppm) as an internal standard. ^{13}C NMR (50 MHz / 100 MHz) spectra for all the samples were measured in chloroform-*d*, unless otherwise mentioned (in the case of DMSO-d_6, δ = 39.70 ppm its middle peak of the septet), with its middle peak of the triplet (δ = 77.10 ppm) as an internal standard. Spectral assignments are as follows: (1) chemical shifts on the δ scale, (2) standard abbreviation for multiplicity,

that is, s = singlet, d = doublet, t = triplet, q = quartet, sept = septet, m = multiplet, dd = doublet of doublet, td = triplet of doublet, dt = doublet of triplet, br = broad, d of ABq = doublet of AB quartet, t of ABq = triplet of AB quartet. (3) number of hydrogens integrated for the signal, (4) coupling constant *J* in Hertz.

Mass Spectral Analysis: Shimadzu LCMS 2010A mass spectrometer.

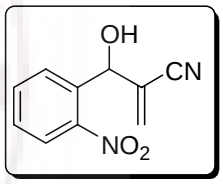
Elemental Analysis: Elemental analyses were performed on a Thermo Finnigan Flash EA 1112-CHN analyzer.

X-ray Crystallography: The X-ray diffraction measurements were carried out at 293 Kor 100 K on a Bruker SMART APEX CCD area detector system equipped with a graphite monochromator and a Mo-K_α fine-focus sealed tube (λ = 0.71073 A^o) operated at 1500 W power (50 kV, 30 mA). The detector was placed at a distance of 4.995 cm from the crystal. The frames were integrated with the Bruker SAINT Software package using a narrow-frame algorithm. Data were corrected for absorption effects using the multi-scan technique (SADABS). The structure was solved and refined using the Bruker SHELXTL (Version 6.1) Software package.

General: All the solvents were dried and distilled using suitable drying agents before use. Moisture sensitive reactions were carried out using standard syringe-septum techniques under nitrogen atmosphere. All reactions were monitored using Thin Layer Chromatography (TLC).

3-Hydroxy-2-methylene-3-(2-nitrophenyl)propanenitrile (93a)

A solution of 2-nitrobenzaldehyde (**92a**) (50 mmol, 7.55 g), acrylonitrile (75 mmol, 3.97 g) and DABCO (15 mol %, 0.84 g) in THF (50 mL) was kept at room temperature for 8 h. Then the reaction mixture was diluted with diethyl ether (50 mL) and washed successively with 2N HCl, aqueous $NaHCO_3$ solution and water. Organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and the crude product thus obtained, was purified by column chromatography, to provide the desired product as a brown solid in 79 % (8.10 g).



Reaction time : 8 h

Mp : 58-60 ^{0}C

IR (KBr) : ν 3526, 2229, 1610 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.04 (br s, 1H), 6.01 (s, 1H), 6.15 (s, 1H), 6.18 (s, 1H), 7.52-7.60 (m, 1H), 7.71-7.77 (m, 1H), 7.85 (d, 1H, *J* = 8.0 Hz), 8.05 (d, 1H, *J* = 8.2 Hz)

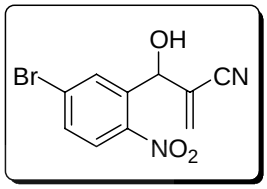
^{13}C NMR (50 MHz) : δ 68.90, 116.66, 124.49, 124.91, 129.01, 129.61, 132.16, 134.08, 134.46, 147.80

3-(5-Bromo-2-nitrophenyl)-3-hydroxy-2-methylenepropanenitrile (93b)

This was obtained as a yellow solid *via* the Baylis-Hillman coupling of 5-bromo-2-nitrobenzaldehyde (**92b**) with acrylonitrile under the catalytical influence of DABCO following the similar procedure described for the molecule **93a**.

Reaction time : 8 h

Mp : 88-90 ^{0}C



Yield : 74%

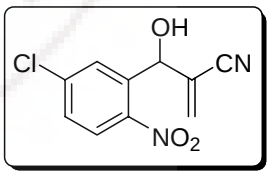
IR (KBr) : ν 3447, 2235, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.15 (br s, 1H), 6.06 (s, 1H), 6.15 (s, 2H), 7.68 (dd, 1H, *J* = 2.0 Hz & 8.8 Hz), 7.94 (d, 1H, *J* = 8.8 Hz), 8.02 (d, 1H, *J* = 2.0 Hz)

^{13}C NMR (50 MHz) : δ 68.56, 116.46, 123.98, 126.60, 129.54, 132.21, 132.74, 132.89, 136.50, 146.35

3-(5-Chloro-2-nitrophenyl)-3-hydroxy-2-methylenepropanenitrile (93c)

This allyl alcohol was prepared as a colorless solid *via* the DABCO catalyzed Baylis-Hillman coupling of 5-chloro-2-nitrobenzaldehyde (**92c**) with acrylonitrile following the similar procedure described for the molecule **93a**.



Reaction time : 8 h

Yield : 65%

Mp : 58-60 ^{0}C

IR (KBr) : ν 3470, 2231, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.16 (br s, 1H), 6.08 (s, 1H), 6.15 (d, 1H, *J* = 1.2 Hz), 6.16 (d, 1H, *J* = 1.2 Hz), 7.51 (dd, 1H, *J* = 2.2 Hz & 8.8 Hz), 7.86 (d, 1H, *J* = 2.2 Hz), 8.03 (d, 1H, *J* = 8.8 Hz)

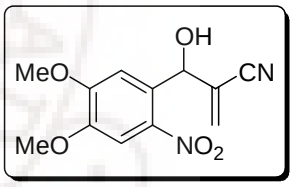
^{13}C NMR (50 MHz) : δ 68.68, 116.46, 124.03, 126.68, 129.25, 129.83, 132.67, 136.65, 141.09, 145.86

3-(4,5-Dimethoxy-2-nitrophenyl)-3-hydroxy-2-methylenepropanenitrile (93d)

DABCO catalyzed coupling of 4,5-dimethoxy-2-nitrobenzaldehyde (**92d**) with acrylonitrile, following the similar procedure described for molecule **93a** provided the title compound as pale yellow viscouss liquid.

Reaction time : 24 h

Yield : 62%



IR (neat) : ν 3499, 2227, 1614 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.26 (br s, 1H), 3.95 (s, 3H), 4.00 (s, 3H), 6.05 (s, 1H), 6.06 (s, 1H), 6.13 (s, 1H), 7.34 (s, 1H), 7.62 (s, 1H)

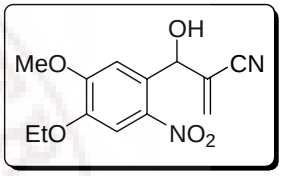
^{13}C NMR (50 MHz) : δ 56.40, 56.55, 68.92, 108.10, 110.01, 116.85, 124.71, 129.78, 131.80, 139.87, 148.70, 153.89

3-(4-Ethoxy-5-methoxy-2-nitrophenyl)-3-hydroxy-2-methylenepropanenitrile (93e)

This compound was prepared *via* the DABCO catalyzed Baylis-Hillman coupling of 4-ethoxy-5-methoxy-2-nitrobenzaldehyde (**92e**) with acrylonitrile following the similar procedure described for the molecule **93a**.

Reaction time : 24 h

Yield : 64%



Mp : 98-100 ^{0}C

IR (KBr) : ν 3450, 2229, 1605 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.50 (t, 3H, *J* = 7.0 Hz), 3.26 (br s, 1H), 4.00 (s, 3H), 4.17 (q, 2H, *J* = 7.0 Hz), 6.08 (s, 1H), 6.12 (s, 2H), 7.30 (s, 1H), 7.63 (s, 1H)

^{13}C NMR (50 MHz) : δ 14.44, 56.55, 65.09, 68.99, 109.02, 110.11, 116.88, 124.71, 129.54, 131.80, 139.82, 148.05, 154.11

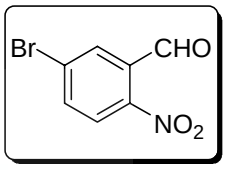
5-Bromo-2-nitrobenzaldehyde (92b)

This was prepared according to the literature procedure with slight modification[191]

To a stirred mixture 3-bromobenzaldehyde (50 mmol, 9.25 g) and KNO_3 (50 mmol, 5.05 g), at 0 ^{0}C was added conc. H_2SO_4 (92.7 mmol, 9.09 g) drop wise. After stirring for 30 min at room temperature, reaction mixture was poured in ice-cold water. The solid obtained

after filtration was crystallized from methanol, to provide 5-bromo-2-nitrobenzaldehyde as colorless needles in 60% (6.89 g) isolated yield.

Reaction time : 30 min



Mp : 76-77 ^{0}C

IR (KBr) : ν 2931, 1697 cm^{-1}

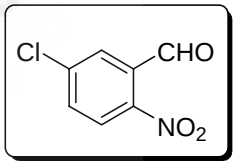
^{1}H NMR (400 MHz) : δ 7.88 (dd, 1H, *J* = 2.0 Hz & 6.4 Hz), 8.02 (d, 1H, *J* = 6.4 Hz), 8.06 (d, 1H, *J* = 2.0 Hz), 10.41 (s, 1H)

^{13}C NMR (50 MHz) : δ 126.12, 129.44, 132.55, 136.50, 148.07, 186.71

5-Chloro-2-nitrobenzaldehyde (92c)

This aldehyde was prepared as a solid *via* the nitration of 3-chlorobenzaldehyde with KNO_3 in presence of conc. H_2SO_4 following the similar procedure described for the molecule **92b**.

Reaction time : 30 min



Yield : 67%

Mp : 76-78 ^{0}C

IR (KBr) : ν 2935, 1699 cm^{-1}

^{1}H NMR (400 MHz) : δ 7.71 (dd, 1H, *J* = 2.0 Hz & 8.4 Hz), 7.90 (d, 1H, *J* = 2.0 Hz), 8.12 (d, 1H, *J* = 8.4 Hz), 10.42 (s, 1H)

^{13}C NMR (50 MHz) : δ 126.22, 129.66, 132.81, 133.47, 141.26, 147.56, 186.86

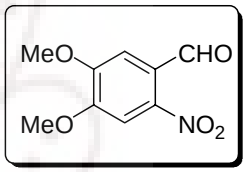
4,5-Dimethoxy-2-nitrobenzaldehyde (92d)

This was prepared according to the literature procedurewith slight modification[192]

Conc. HNO_3 (25 mL) was added slowly to 3,4-dimethoxybenzaldehyde (25 mmol, 4.15 g), with stirring at room temperature. After the addition is complete the reaction mixture was heated at 40 ^{0}C for 30 min. Reaction mixture was cooled to room temperature and then poured into ice-cold water. The solid, thus separated, was removed by filtration and treated with sodium metabisulphite solution and filtered to remove insoluble impurities. The filtrate was treated with aq. KOH solution to generate the aldehyde as yellow solid, which was recrystallized from methanol at 0 ^{0}C to provide the title compound as a yellow crystalline solid in 52% (2.76 g) isolated yield.

Reaction time : 30 min

Mp : 126-128 ^{0}C (lit 128 ^{0}C)[192]



IR (KBr) : ν 2989, 1685 cm^{-1}

^{1}H NMR (400 MHz) : δ 4.03 (s, 3H), 4.04 (s, 3H), 7.42 (s, 1H), 7.62 (s, 1H), 10.45 (s, 1H)

^{13}C NMR (50 MHz) : δ 56.74, 107.27, 109.84, 125.61, 143.92, 152.49, 153.31, 187.61

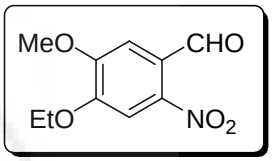
4-Ethoxy-5-methoxy-2-nitrobenzaldehyde (92e)

This was obtained as a yellow solid *via* the nitration of 4-ethoxy-3-methoxybenzaldehyde using the conc. HNO_3, at room temperature following similar procedure described for the molecule **92d**.

Reaction time : 30 min

Yield : 27%

Mp : 124-126 ^{0}C



IR (KBr) : ν 2989, 1689 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.54 (t, 3H, *J* = 7.2 Hz), 4.01 (s, 3H), 4.25 (q, 2H, *J* = 7.2 Hz), 7.41 (s, 1H), 7.59 (s, 1H), 10.44 (s, 1H)

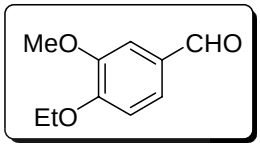
^{13}C NMR (50 MHz) : δ 14.41, 56.72, 65.60, 108.00, 109.92, 125.34, 143.95, 151.93, 153.46, 187.68

4-Ethoxy-3-methoxybenzaldehyde

To a stirred mixture of vanillin (30 mmol, 4.56 g) and anhydrous K_2CO_3 (90 mmol, 12.43 g) in acetonitrile (50 mL) was added bromoethane (60 mmol, 6.53 g) at room temperature. Reaction mixture was heated under reflux for 5 h and was cooled to room temperature. Solvent was removed and the residue was diluted with water (15 mL), extracted with diethyl ether (3X25 mL). Combined organic layer was dried over anhydrous Na_2SO_4. Solvent was removed and the crude product thus obtained was purified by column chromatography (10% EtOAc in hexanes) to provide the title compound.

Reaction time : 5 h

Yield : 80% (4.36 g)



Mp : 55-57 ^{0}C

IR (KBr) : ν 2999, 1682 cm^{-1}

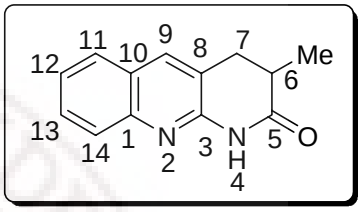
^{1}H NMR (400 MHz) : δ 1.51 (t, 3H, *J* = 7.0 Hz), 3.94 (s, 3H), 4.19 (q, 2H, *J* = 7.0 Hz), 6.97 (d, 1H, *J* = 8.0 Hz), 7.38-7.47 (m, 2H), 9.85 (s, 1H)

^{13}C NMR (50 MHz) : δ 14.49, 55.92, 64.53, 109.28, 111.32, 126.58, 129.90, 149.75, 153.89, 190.69

2,4-Diaza-6-methyltricylo[8.4.0.0^{3,8}]tetradeca-1(10), 2,8,11,13-pentaene-5-one (95a)

To a stirred solution of 3-hydroxy-2-methylene-3-(2-nitrophenyl)propanenitrile (**93a**) (1 mmol, 0.204 g) in triethyl orthopropionate (1.25 mL) was added catalytic amount of propanoic acid (4 drops), and the reaction mixture was heated at 145 ^{0}C for 70 h. Reaction mixture was then allowed to come to room temperature. Excess triethyl orthopropionate was removed under reduced pressure. The residue, thus obtained was diluted with AcOH (5 mL) and electrolytic Fe powder (6 mmol, 0.336 g), was added at room temperature, Then the reaction mixture was heated at 110 ^{0}C for 1 h and cooled to room temperature. AcOH was removed under reduced pressure and reaction mixture was diluted with EtOAc (15 mL). The resulting mixture was filtered to remove any iron impurities. Iron residue was washed twice with EtOAc (15 mL). Filtrate and washings were combined and dried

over anhydrous Na_2SO_4. Solvent was evaporated and the residue thus obtained was purified by column chromatography (40% EtOAc in hexanes) to provide the desired product as colorless solid in 69% (0.147 g) isolated yield.



Reaction time : 71 h (70 h +1 h)

Mp : 212-214 ^{0}C

IR (KBr) : ν 3350-3150 (multiple bands), 1693, 1678, 1626 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.35 (d, 3H, *J* = 6.8 Hz), 2.71-2.97 (m, 2H), 3.18 (dd, 1H, *J* = 5.2 Hz & 15.6 Hz), 7.38-7.48 (m, 1H), 7.60-7.68 (m, 1H), 7.71 (d, 1H, *J* = 8.0 Hz), 7.88-7.95 (m, 2H), 8.55 (s, 1H, D_2O exchangeable)

^{13}C NMR (100 MHz) : δ 15.53, 32.73, 35.26, 119.63, 125.08, 125.91, 127.11, 127.49, 129.65, 135.40, 146.20, 150.64, 174.60

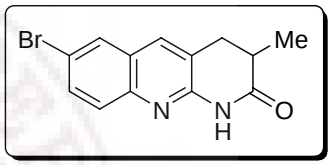
LCMS (m/z) : 213 $(M+H)^+$

Anal calc'd for $C_{13}H_{12}N_2O$: C, 73.56; H, 5.70; N, 13.20

Found : C, 73.71; H, 5.69; N, 13.28

12-Bromo-2,4-diaza-6-methyltricyclo[8.4.0.0^{3,8}]tetradeca-1(10),2,8,11,13-pentaene-5-one (95b)

This compound was obtained as a colorless solid *via* the Johnson-Claisen rearrangement of 3-(5-bromo-2-nitrophenyl)-3-hydroxy-2-methylenepropanenitrile (**93b**), with triethyl orthopropionate (1.25 mL) in presence of propanoic acid followed by treatment with Fe/AcOH, following the similar procedure described for the compound **95a**.



Reaction time : 71 h (70 h +1 h)

Yield : 56%

Mp : 215-217 ^{0}C

IR (KBr) : ν 3350-3160 (multiple bands), 1691, 1624 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.35 (d, 3H, *J* = 6.8 Hz), 2.72-2.96 (m, 2H), 3.18 (dd, 1H, *J* = 5.6 Hz & 15.6 Hz), 7.69 (d, 1H, *J* = 9.2 Hz), 7.78 (d, 1H, *J* = 9.2 Hz), 7.81 (s, 1H), 7.86 (s, 1H), 8.61 (s, 1H, D_2O exchangeable)

^{13}C NMR (100 MHz, [90% $CDCl_3$ + 10% DMSO-d_6]): δ 15.28, 32.46, 34.88, 118.17, 120.66, 126.81, 128.94, 128.99, 132.62, 134.12, 144.58, 150.90, 174.46

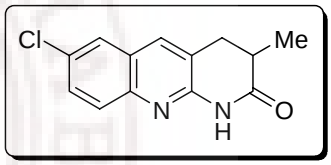
LCMS (m/z) : 291 $(M+H)^+$, 293 $(M+2+H)^+$

Anal calc'd for $C_{13}H_{11}BrN_2O$: C, 53.63; H, 3.81; N, 9.62

Found : C, 53.67; H, 3.71; N, 9.58

12-Chloro-2,4-diaza-6-methyltricyclo[8.4.0.0^{3,8}]tetradeca-1(10),2,8,11,13-pentaene-5-one (95c)

This molecule was prepared *via* the treatment of 3-(5-chloro-2-nitrophenyl)-3-hydroxy-2-methylenepropanenitrile (**93c**with triethyl orthopropionate (1.25 mL) under the catalytical influence of propanoic acid (cat.) followed by reductive cyclization using Fe/AcOH, following the similar procedure described for the molecule **95a**.



Reaction time : 71 h (70 h +1 h)

Yield : 63%

Mp : 210-212 ^{0}C (dec.)

IR (KBr) : ν 3350-3150 (multiple bands), 1709, 1685, 1626 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.35 (d, 3H, *J* = 6.8 Hz), 2.72-2.95 (m, 2H), 3.18 (dd, 1H, *J* = 5.2 Hz & 15.6 Hz), 7.57 (dd, 1H, *J* = 2.4 Hz & 8.8 Hz), 7.69 (d, 1H, *J* = 2.4 Hz), 7.82 (s, 1H,), 7.89 (d, 1H, *J* = 8.8 Hz), 8.91 (br s, 1H, D_2O exchangeable)

^{13}C NMR (100 MHz) : δ 15.51, 32.72, 35.17, 120.78, 125.88, 126.53, 129.01, 130.45, 130.63, 134.45, 144.45, 144.59, 150.81, 174.37

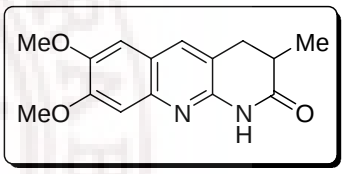
LCMS (m/z) : 247 $(M+H)^{+}$, 249 $(M+H+2)^{+}$

Anal calc'd for $C_{13}H_{11}ClN_2O$: C, 63.29; H, 4.49: N, 11.36

Found : C, 63.31; H, 4.44; N, 11.41

2,4-Diaza-12,13-dimethoxy-6-methyltricyclo[8.4.0.0^{3,8}]tetradeca-1(10),2,8,11,13-pentaen-e-5-one (95d)

This molecule was obtained as a colorless solid *via* the treatment of 3-(4,5-dimethxy-2-nitrophenyl)-3-hydroxy-2-methylenepropanenitrile (**93d**) with triethyl orthopropionate (1.25 mL) in presence of propanoic acid (cat.) followed by reductive cyclization using Fe/AcOH following the similar procedure described for molecule **95a**.



Reaction time : 71 h (70 h +1 h)

Yield : 60%

Mp : 236-238 ^{0}C (dec.)

IR (KBr) : ν 3300-3000 (multiple bands), 1682, 1626 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.33 (d, 3H, *J* = 6.8 Hz), 2.70-2.90 (m, 2H), 3.13 (dd, 1H, *J* = 5.2 Hz & 15.2 Hz), 3.98 (s, 3H), 4.02 (s, 3H), 6.98 (s, 1H), 7.38 (s, 1H), 7.76 (s, 1H), 8.93 (br s, 1H, D_2O exchangeable)

^{13}C NMR (100 MHz) : δ 15.58, 32.66, 35.41, 56.07, 56.30, 105.24, 106.99, 117.01, 120.91, 134.00, 142.91, 148.71, 149.07, 152.56, 174.45

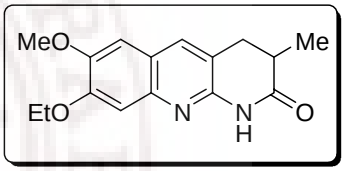
LCMS (m/z) : 273 $(M+H)^{+}$

Anal calc'd for $C_{15}H_{16}N_2O_3$: C, 66.16; H, 5.92; N, 10.29

Found : C, 66.26; H, 5.86; N,10.43

2,4-Diaza-13-ethoxy-12-methoxy-6-methyltricyclo[8.4.0.0^{3,8}]tetradeca-1(10),2,8,11,-13-pentaene-5-one (95e)

This compound was obtained as a colorless solid *via* the Johnson-Claisen rearrangement of 3-(4-ethoxy-5-methoxy-2-nitrophenyl)-3-hydroxy-2-methylenepropanenitrile (**93e**) with triethyl orthopropionate (1.25 mL) in presence of propanoic acid (cat.) and subsequent treatment with Fe/AcOH, following the similar procedure described for the molecule **95a**.

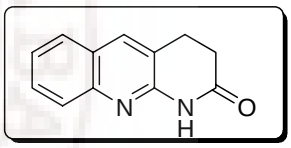


Reaction time	: 71 h (70 h +1 h)
Yield	: 56%
Mp	: 227-228 (dec.)
IR (KBr)	: ν 3250-3050 (multiple bands), 1688, 1626 cm^{-1}
^{1}H NMR (400 MHz)	: δ 1.33 (t, 3H, *J* = 6.0 Hz), 1.53 (t, 3H, *J* = 7.2 Hz), 2.68-2.92 (m, 2H), 3.12 (dd, 1H, *J* = 4.4 & Hz 15.2 Hz), 3.97 (s, 3H), 4.24 (q, 2H, *J* = 7.2 Hz), 6.97 (s, 1H), 7.33 (s, 1H), 7.75 (s, 1H), 8.92 (s, 1H, D_2O exchangeable)
^{13}C NMR (100 MHz)	: δ 14.62, 15.56, 32.62, 35.38, 56.09, 64.52, 105.32, 107.54, 116.87, 120.77, 133.96, 142.86, 148.86, 148.92, 151.86, 174.49
LCMS (m/z)	: 287 $(M+H)^+$
Anal calc'd for $C_{16}H_{18}N_2O_3$	: C, 67.12; H, 6.34; N, 9.78

Found : C, 67.26; H, 6.36; N, 9.70

2,4-Diazatricyclo[8.4.0.0^{3,8}]tetradeca-1(10), 2,8,11,13-pentaene-5-one (95f)

The Johnson-Claisen rearrangement of 3-hydroxy-3-(2-nitrophenyl)-2-methylenepropanenitrile (**93a**) with triethyl orthoacetate (2.0 mL) under the catalytical influence of propanoic acid and subsequent reductive cyclization using Fe/AcOH following the similar procedure described for molecule **95a** provided the title compound as a colorless solid.



Reaction time : 71 h (70 h +1 h)

Yield : 55%

Mp : 210-211 ^{0}C (dec.)

IR (KBr) : ν 3350-3100 (multiple bands), 1695, 1682, 1626 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.76 (t, 2H, *J* = 7.2 Hz), 3.14 (t, 2H, *J* = 7.2 Hz), 7.40-7.47 (m, 1H), 7.61-7.68 (m, 1H), 7.72 (d, 1H, *J* = 8.0 Hz), 7.86 (d, 1H, *J* = 8.4 Hz), 7.92 (s, 1H), 8.28 (s, 1H, D_2O exchangeable)

^{13}C NMR (100 MHz) : δ 24.70, 30.80, 119.57, 125.22, 125.97, 127.19, 127.53, 129.73, 135.26, 146.21, 150.54, 171.83

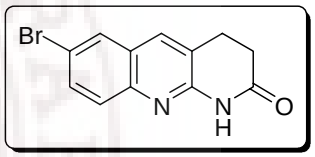
LCMS (m/z) : 199 $(M+H)^{+}$

Anal calc'd for $C_{12}H_{10}N_2O$: C, 72.71; H, 5.08; N, 14.13

Found : C, 72.59; H, 5.12; N, 14.23

12-Bromo-2,4-diazatricyclo[8.4.0.0^{3,8}]tetradeca-1(10),2,8,11,13-pentaene-5-one (95g)

This compound was obtained *via* the treatment of 3-(5-bromo-2-nitrophenyl)-3-hydroxy-2-methylenepropanenitrile (**93b**) with triethyl orthoacetate (2.0 mL) in presence of propanoic acid (cat.) followed by subsequent treatment with Fe/AcOH, following the similar procedure described for **95a**.



Reaction time : 71 h (70 h +1 h)

Yield : 45%

Mp : 248-249 ^{0}C (dec.)

IR (KBr) : ν 32500-3000 (multiple bands), 1685, 1626 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.77 (t, 2H, *J* = 7.0 Hz), 3.14 (t, 2H, *J* = 7.0 Hz), 7.69 (dd, 1H, *J* = 2.0 Hz & 9.2 Hz), 7.78 (d, 1H, *J* = 8.8 Hz), 7.82 (s, 1H,), 7.86 (d, 1H, *J* = 2.0 Hz), 8.65 (br s, 1H, D_2O exchangeable)

^{13}C NMR (100 MHz) : δ 24.69, 30.61, 118.66, 120.66, 127.10, 129.18, 129.23, 133.07, 134.22, 144.81, 150.82, 171.63

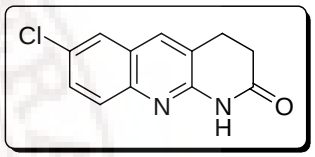
LCMS (m/z) : 275 $(M-H)^{+}$, 277 $(M-H+2)^{+}$

Anal calc'd for $C_{12}H_9BrN_2O$: C, 52.01, H, 3.27; N, 10.11

Found : C, 52.20; H, 3.29; N, 10.04

12-Chloro-2,4-diazatricyclo[8.4.0.0^{3,8}]tetradeca-1(10),2,8,11,13-pentaene-5-one (95h)

The Johnson-Claisen rearrangement of 3-(5-chloro-2-nitrophenyl)-3-hydroxy-2-methylenepropanenitrile (**93c**) with triethyl orthoacetate (2.0 mL) in presence of propanoic acid (cat.) and subsequent reductive cyclization with Fe/AcOH, following the similar procedure described for molecule **95a** afforded the title compound as a colorless solid.



Reaction time : 71 h (70 h +1 h)

Yield : 58%

Mp : 246-248 ^{0}C

IR (KBr) : ν 3300-3000 (multiple bands), 1700, 1687, 1626 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.77 (t, 2H, *J* = 7.2 Hz), 3.14 (t, 2H, *J* = 7.2 Hz), 7.57 (d, 1H, *J* = 8.8 Hz), 7.68 (s, 1H), 7.83 (s, 1H), 7.92 (d, 1H, *J* = 8.8 Hz), 9.12 (s, 1H, D_2O exchangeable)

^{13}C NMR (100 MHz) : δ 24.72, 30.64, 120.68, 125.94, 126.59, 129.09, 130.53, 134.31, 144.63, 150.70, 171.52

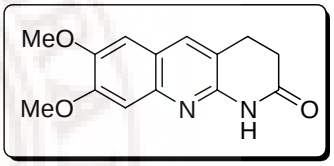
LCMS (m/z) : 233 $(M+H)^+$, 235 $(M+H+2)^+$

Anal calc'd for $C_{12}H_9ClN_2O$: C, 61.95, H, 3.90; N, 12.04

Found : C, 61.78; H, 3.95; N, 12.00

2,4-Diaza-12,13-dimethoxytricyclo[8.4.0.0^{3,8}]tetradeca-1(10),2,8,11,13-pentaene-5-one (95i)

This molecule was obtained as a colorless solid *via* the Johnson-Claisen rearrangement of 3-(4,5-dimethoxy-2-nitrophenyl)-3-hydroxy-2-methylenepropanenitrile (**93d**) with triethyl orthoacetate (2.0 mL) in presence of propanoic acid (cat.) followed by reductive cyclization using Fe/AcOH following the similar procedure described for molecule **95a**.



Reaction time : 71 h (70 h +1 h)

Yield : 48%

Mp : 234-236 ^{0}C (dec.)

IR (KBr) : ν 3250-3000 (multiple bands), 1685, 1626 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.74 (t, 2H, *J* = 6.8 Hz), 3.09 (t, 2H, *J* = 6.8 Hz), 3.99 (s, 3H), 4.01 (s, 3H), 6.98 (s, 1H), 7.32 (s, 1H), 7.77 (s, 1H), 8.74 (s, 1H, D_2O exchangeable)

^{13}C NMR (100 MHz) : δ 24.60, 31.01, 56.09, 56.28, 105.31, 107.00, 117.00, 120.98, 133.83, 142.93, 148.85, 149.04, 152.68, 171.65

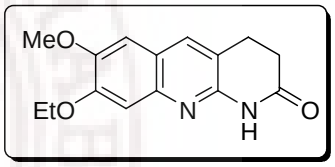
LCMS (m/z) : 259 $(M+H)^{+}$

Anal calc'd for $C_{14}H_{14}N_2O_3$: C, 65.11; H, 5.46; N, 10.85

Found : C, 65.00; H, 5.43; N, 10.83

2,4-Diaza-13-ethoxy-12-methoxytricyclo[8.4.0.0^{3,8}]tetradeca-1(10),2,8,11,13-pentaene-5-one (95j)

This compound was prepared as a colorless solid *via* the Johnson-Claisen rearrangement of 3-(4-ethoxy-5-methoxy-2-nitrophenyl)-3-hydroxy-2-methylenepropanenitrile (**93e**) with triethyl orthoacetate (2.0 mL) in presence of propanoic acid (cat.) followed by reaction with Fe/AcOH following the similar procedure described for molecule **95a**.



Reaction time : 71 h (70 h +1 h)

Yield : 49%

Mp : 247-248 ^{0}C (dec.)

IR (KBr) : ν 3250-3050 (multiple bands), 1687 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.46 (t, 3H, *J* = 6.8 Hz), 2.66 (t, 2H, *J* = 7.2 Hz), 3.01 (t, 2H, *J* = 7.2 Hz), 3.90 (s, 3H), 4.17 (q, 2H, *J* = 6.8 Hz), 6.89 (s, 1H), 7.27 (s, 1H), 7.68 (s, 1H), 8.99 (br s, 1H, D_2O exchangeable)

^{1}H NMR (100 MHz) : δ 14.63, 24.58, 30.99, 56.11, 64.54, 105.35, 107.57, 116.85, 120.84, 133.80, 142.88, 148.90, 148.99, 151.95, 171.71.

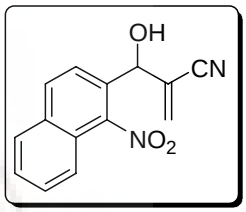
LCMS (m/z) : 273 $(M+H)^{+}$

Anal calc'd for $C_{15}H_{16}N_2O_3$: C, 66.16; H, 5.92; N, 10.29

Found : C, 66.0.3; H, 5.96; N, 10.15

3-Hydroxy-2-methylene-3-(1-nitronaphth-2-yl)propanenitrile (93f)

This compound was obtained as a brown solid *via* the reaction of 1-nitro-2-naphthaldehyde (**92f**) with acrylonitrile under the catalytical influence of DABCO following the similar procedure described for the molecule **93a**.



Reaction time : 20 h

Yield : 66%

Mp : 94-96 ^{0}C

IR (KBr) : ν 3435, 2239, 1614 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.21 (br s, 1H), 5.57 (s, 1H), 6.11 (s, 1H), 6.12 (s, 1H), 7.58-7.68 (m, 2H), 7.70 (d, 1H, *J* = 8.0 Hz), 7.75 (d, 1H, *J* = 8.0 Hz), 7.90 (d, 1H, *J* = 8.0 Hz), 8.02 (d, 1H, *J* = 8.0 Hz)

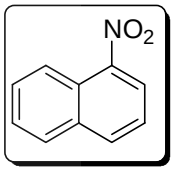
^{13}C NMR (100 MHz) : δ 69.35, 116.34, 122.00, 123.37, 123.99, 124.19, 128.23, 128.58, 129.23, 131.97, 132.29, 133.87, 146.82

1-Nitronaphthalene

This was prepared according to the literature procedure with slight modification[193a]

To a stirred mixture of 40 mL of conc. HNO_3 and 40 mL of conc. H_2SO_4 at room temperature, finely powdered naphthalene (390 mmol, 50 g) was added in small quantities maintaing the temperature at 45-50 ^{0}C. After the addition was completed the reaction mixture was heated on a water bath at 55-60 ^{0}C for 30 min (until the smell of naphthalene

disapperead). Reaction mixture was poured in ice cold water (200 mL) and extracted with diethyl ether (3X200 mL), Combined organic layer was dried over anhydrous Na_2SO_4. Crude product was obtained after solvent evaporation was purified by column chromatography (2% EtOAc in hexanes).



Yield : 71% (48.31 g)

Mp : 58-60 ^{0}C

IR (KBr) : ν 1520, 1338 cm^{-1}

^{1}H NMR (400 MHz) : δ 7.49-7.56 (m, 1H), 7.58-7.65 (m, 1H), 7.67-7.76 (m, 1H), 7.94 (d, 1H, *J* = 8.0 Hz), 8.10 (d, 1H, *J* = 8.4 Hz), 8.21 (d, 1H, *J* = 7.2 Hz), 8.55 (d, 1H, *J* = 8.8 Hz)

^{13}C NMR (50 MHz) : δ 123.07, 123.97, 124.11, 125.09, 127.33, 128.60, 129.42, 134.32, 134.65, 146.56

2-Dichloromethyl-1-nitronaphthalene

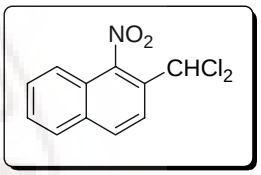
This was prepared according to the literature procedure with slight modification[193b]

To a precooled stirred solution of potassium *tert*-butoxide (120 mmol, 13.46 g), in a mixture of dry THF (50 mL) and dry DMF (40 mL), at -73 ^{0}C under nitrogen atmosphere, a solution of nitronaphthalene (30 mmol, 5.19 g), in a mixture of chloroform (33 mmol, 3.93 g) and DMF (2 mL) was added dropwise, keeping the temperature below -68 ^{0}C. Reaction mixture was then stirred at this temperature for 10 min and acetic acid (15 mL)

was added. Then reaction mixture was allowed to come to room temperature and then poured into water (150 mL) and extracted with dichloromethane (3X50 mL). Combined organic layer was washed with water (3X100 mL) and dried over anhydrous Na_2SO_4. Crude product was obtained after solvent evaporation was purified by column chromatography (5% EtOAc in hexanes).

Reaction time : 10 min

Yield : 77% (5.87 g)



Mp : 78-80 ^{0}C

IR (KBr) : ν 3736, 1539 cm^{-1}

^{1}H NMR (400 MHz) : δ 6.93 (s, 1H), 7.61-7.71 (m, 2H), 7.75-7.82 (m, 1H), 7.87-7.95 (m, 1H), 8.02 (d, 1H, *J* = 8.8 Hz), 8.08 (d, 1H, *J* = 8.8 Hz)

^{13}C NMR (50 MHz) : δ 65.80, 122.66, 123.42, 123.62, 128.26, 128.92, 129.24, 129.60, 132.31, 134.20, 144.03

1-Nitronaphalene-2-carboxaldehyde (92f)

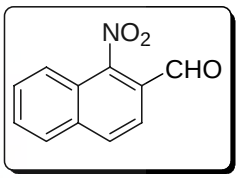
This was prepared according to the literature procedure with slight modification[193b]

A mixture of 2-dichloromethyl-1-nitronaphthalene (10.5 mmol, 2.68 g), zinc chloride (6 g) in 85% formic acid (48 mL) was refluxed under nitrogen atmosphere for 4 h with stirring. After cooling to room temperature, the reaction mixture was poured into water (150 mL)

and extracted with dichloromethane (3X50 mL). Combined organic layer were dried over anhydrous Na_2SO_4. Crude product was obtained after solvent evaporation was purified by column chromatography (2% EtOAc in hexanes).

Reaction time : 4 h

Yield : 79% (1.6 g)



Mp : 83-85 ^{0}C

IR (KBr) : ν 1711 cm^{-1}

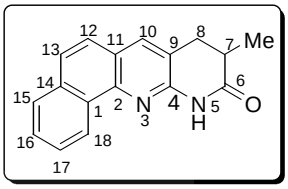
^{1}H NMR (400 MHz) : δ 7.68-7.79 (m, 2H), 7.91 (d, 1H, *J* = 8.0 Hz), 7.95-8.02 (m, 2H), 8.09 (d, 1H, *J* = 8.4 Hz), 10.16 (s, 1H)

^{13}C NMR (50 MHz) : δ 122.93, 123.06, 123.85, 124.11, 128.49, 129.76, 130.34, 131.58, 136.74, 186.88

3,5-Diaza-7-methyltetracyclo[12.4.0.0^{2,11}.0^{4,9}]octadeca-1(14),2(11),3,9,12,15,17-heptaene-6-one (95k)

This compound was obtained as a colorless solid *via* the Johnson-Claisen rearrangement of 3-hydroxy-2-methylene-3-(1-nitronaphth-2-yl)propanenitrile (**93f**) with triethyl orthopropionate (1.25 mL) in presence of propanoic acid (cat.) and subsequent treatment with Fe/AcOH, following the similar procedure described for the compound **95a**.

Reaction time : 71 h (70 h +1 h)



Yield : 59%

Mp : 185-187 ^{0}C

IR (KBr) : ν 3250-3150 (multiple bands), 1697 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.37 (d, 3H, *J* = 8.0 Hz), 2.73-2.86 (m, 1H), 2.87-2.98 (m, 1H), 3.20 (dd, 1H, *J* = 4.0 Hz & 16.0 Hz), 7.58-7.75 (m, 4H), 7.84-7.92 (m, 1H), 7.93 (s, 1H,), 8.13 (s, 1H, D_2O exchangeable), 9.04-9.10 (m, 1H)

^{13}C NMR (100 MHz) : δ 15.51, 32.43, 35.21, 118.77, 123.31, 124.19, 124.72, 125.96, 126.72, 127.79, 128.00, 130.56, 133.75, 135.35, 144.26, 149.25, 174.17

LCMS (m/z) : 263 $(M+H)^+$

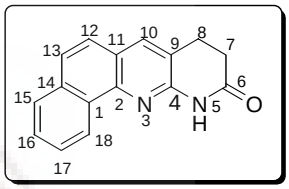
Anal calc'd for $C_{17}H_{14}N_2O$: C, 77.84; H, 5.38; N, 10.68

Found : C, 77.88; H, 5.37; N, 10.88

3,5-Diazatetracyclo[12.4.0.0^{2,11}.0^{4,9}]octadeca-1(14),2(11),3,9,12,15,17-heptaene-6-one (95l)

This compound was obtained as a colorless solid *via* the Johnson-Claisen rearrangement of 3-hydroxy-2-methylene-3-(1-nitronaphth-2-yl)propanenitrile (**93f**) with triethyl

orthoacetate (2.0 mL) in presence of propanoic acid (cat.) followed by subsequent reductive cyclization with Fe/AcOH, following the similar procedure described for the compound (**95a**).



Reaction time : 71 h (70 h +1 h)

Yield : 51%

Mp : 197-198 ^{0}C (dec.)

IR (KBr) : ν 3250-3100 (multiple bands), 1676, 1642 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.79 (t, 2H, *J* = 7.2 Hz), 3.17 (t, 2H, *J* = 7.2 Hz), 7.58-7.78 (m, 4H), 7.88 (d, 1H, *J* = 6.8 Hz), 7.94 (s, 1H), 8.17 (s, 1H, D_2O exchangeable), 9.08 (d, 1H, *J* = 8.0 Hz)

^{13}C NMR (100 MHz) : δ 24.37, 30.71, 118.70, 123.35, 124.23, 124.71, 126.07, 126.73, 127.78, 128.02, 130.55, 133.76, 135.23, 144.25, 149.26, 171.51

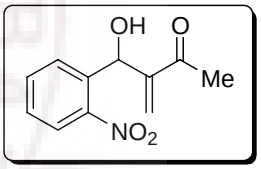
LCMS (m/z) : 249 $(M+H)^{+}$

Anal calc'd for $C_{16}H_{12}N_2O$: C, 77.40; H, 4.87; N, 11.28

Found : C, 77.30; H, 4.85; N, 11.36

4-Hydroxy-3-methylene-4-(2-nitrophenyl)butane-2-one (105a)

To a solution of 2-nitrobenzaldehyde (20 mmol, 3.02 g) and methyl vinyl ketone (20 mmol, 1.40 g) in THF (20 mL) was added DABCO (15 mol%, 0.336 g) and the reaction mixture was kept at room temperature for 12 h. The reaction mixture was diluted with diethyl ether (75 mL) and treated with 2N HCl. Organic layer was separated and washed successively with aqueous $NaHCO_3$ solution, water and then dreid over Na_2SO_4. Solvent was evaporated and the residue thus obtained was purified by column chromatography (20% EtOAc in hexanes) to provide the desired product as a pale yellow solid in 70% (3.12 g) isolated yield.



Reaction time : 12 h

Mp : 80-82 ^{0}C

IR (KBr) : ν 3362, 1666, 1626 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.36 (s, 3H), 3.64 (d, 1H, *J* = 4.0 Hz), 5.80 (s, 1H), 6.17 (s, 1H), 6.21 (d, 1H, *J* = 4.0 Hz), 7.40-7.50 (m, 1H), 7.61-7.70 (m, 1H), 7.77 (d, 1H, *J* = 8.0 Hz), 7.95 (d, 1H, *J* = 8.0 Hz)

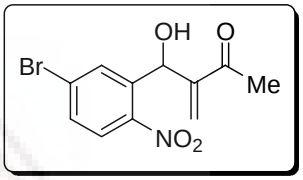
^{13}C NMR (100 MHz) : δ 26.04, 67.35, 124.66, 126.56, 128.54, 128.88, 133.51, 136.55, 148.04, 148.97, 199.84

4-(5-Bromo-2-nitrophenyl)-4-hydroxy-3-methylenebutan-2-one (105b)

This molecule was prepared *via* Baylis-Hillman coupling of 5-bromo-2-nitrobenzaldehyde (**92b**) and methyl vinyl ketone under the catalytical influence of DABCO following the similar procedure described for the molecule **105a**.

Reaction time : 12 h

Yield : 69%



M.p : 80-82 ^{0}C

IR (KBr) : ν 3578, 1674, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.38 (s, 3H), 3.55 (br s, 1H), 5.78 (s, 1H), 6.17 (s, 1H), 6.23 (s, 1H), 7.58 (dd, 1H, *J* = 2.0 Hz & 8.4 Hz), 7.86 (d, 1H, *J* = 8.4 Hz), 7.95 (d, 1H, *J* = 2.0 Hz)

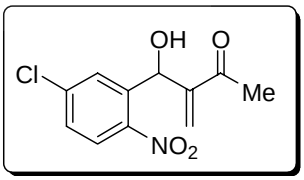
^{13}C NMR (100 MHz) : δ 26.00, 67.16, 126.28, 126.68, 128.86, 131.77, 132.16, 138.70, 146.68, 148.66, 199.77

4-(5-Chloro-2-nitrophenyl)-4-hydroxy-3-methylenebutan-2-one (105c)

This molecule was obtained as a yellow solid *via* the Baylis-Hillman coupling between 5-chloro-2-nitrobenzaldehyde (**92c**) and methyl vinyl ketone using DABCO as a catalyst following a similar procedure described for the molecule **105a**.

Reaction time : 12 h

Yield : 73%



Mp : 70-72 ^{0}C

IR (KBr) : ν 3358, 1666, 1625 cm^{-1}

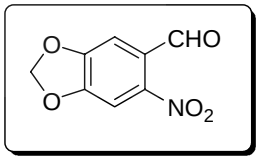
^{1}H NMR (400 MHz) : δ 2.39 (s, 3H), 3.51 (br s, 1H), 5.78 (s, 1H), 6.18 (s, 1H), 6.24 (s, 1H), 7.43 (dd, 1H, *J* = 2.0 Hz & 8.0 Hz), 7.80 (d, 1H, *J* = 2.0 Hz), 7.96 (d, 1H, *J* = 8.0 Hz)

^{13}C NMR (100 MHz) : δ 26.03, 67.28, 126.34, 126.69, 128.74, 129.20, 138.78, 140.42, 146.14, 148.63, 199.83.

6-Nitropiperonal (92g)

This molecule was prepared following the literature procedure[208]

Fuming HNO_3 (150 mmol, 9.45 g) was added to a stirred solution of piperonal (20 mmol, 3.0 g) at -30 ^{0}C in 1,2-dichloroethane (15 mL). The reaction mixture was stirred at -15 ^{0}C untill the piperonal disappearance (monitered by TLC). The reaction mixture was poured into ice-cold water (100 mL) extracted with ethyl acetate (3X75 mL). Combined organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and the crude thus obtained was purified by column chromatography (30% EtOAc in hexanes) to provide the title compound as a colorless solid.



Reaction time : 8 h

Yield : 83% (3.23 g)

Mp : 95-97 ^{0}C (93-94 ^{0}C)[208]

IR (KBr) : ν 2926, 1682 cm^{-1}

^{1}H NMR (400 MHz) : δ 6.23 (s, 2H), 7.34 (s, 1H), 7.53 (s, 1H), 10.30 (s, 1H)

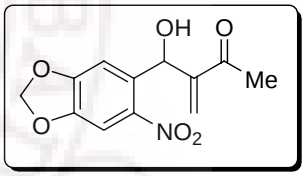
^{13}C NMR (100 MHz) : δ 103.96, 105.22, 107.66, 128.32, 146.21, 151.61, 152.32, 186.93

4-Hydrxy-3-methylene -4-(4,5-methylenedioxy-2-nitrophenyl)butan-2-one (105d)

This molecule was obtained as a light yellow solid *via* Baylis-Hillman coupling of 6-nitropiperonal (**92g**) with methyl vinyl ketone under the catalytical influence of DABCO following the similar procedure described for the molecule **105a**.

Reaction time : 48 h

Yield : 64%



Mp : 95-97 ^{0}C

IR (KBr) : ν 3481, 1668, 1608 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.38 (s, 3H), 3.69 (br s, 1H), 5.76 (s, 1H), 6.08-6.16 (m 3H), 6.19 (s, 1H), 7.20 (s, 1H), 7.51 (s, 1H)

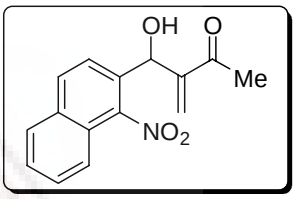
^{13}C NMR (100 MHz) : δ 26.01, 67.33, 103.11, 105.52, 107.74, 126.10, 134.32, 141.80, 147.25, 149.18, 152.23, 199.92

4-Hydroxy-3-methylene-4-(1-nitronaphth-2-yl)butan-2-one (**105e)**

This molecule was prepared *via* the reaction between 1-nitronaphalene-2-carboxaldehyde (**92f**) and methyl vinyl ketone under the catalytic influence of DABCO following the similar procedure described for the molecule **105a**.

Reaction time : 24 h

Yield : 62%



Mp : 127-129 ^{0}C

IR (KBr) : ν 3414, 1674, 1625 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.31 (s, 3H), 3.68 (d, 1H, *J* = 1.2 Hz), 5.86 (s, 1H), 6.00 (s, 1H), 6.25 (s, 1H), 7.52-7.64 (m, 3H), 7.73 (d, 1H, *J* = 8.0 Hz), 7.85 (d, 1H, *J* = 8.4 Hz), 7.93 (d, 1H, *J* = 8.8 Hz)

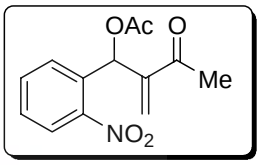
^{13}C NMR (100 MHz) : δ 26.15, 68.39, 121.86, 124.15, 124.34, 127.55, 127.96, 128.02, 128.74, 130.10, 131.10, 133.31, 146.55, 147.73, 199.84

4-Acetoxy-3-methylene-4-(2-nitrophenyl)butan-2-one (106a)

To a stirred solution of 4-hydroxy-3-methylene-4-(2-nitrophenyl)butane-2-one (**105a**) (10 mmol, 2.21 g) in dichloromethane (20 mL) was added pyridine (20 mmol, 1.57 g) and acetyl chloride (20 mmol, 1.58 g) at 0 ^{0}C. Reaction mixture was stirred at the room temperature for 20 min and diluted with diethyl ether (25 mL) and washed with 2N HCl (10 mL). Organic layer was separated and washed successively with saturated $NaHCO_3$

solution, water and dried over anhydrous Na_2SO_4. Solvent was removed and the crude thus obtained was purified by column chromatography (20% EtOAc in hexanes).

Reaction time : 20 min



Yield : 75% (1.98 g)

Mp : 62-64 ^{0}C

IR (KBr) : ν 1745, 1672, 1603 cm^{-1}

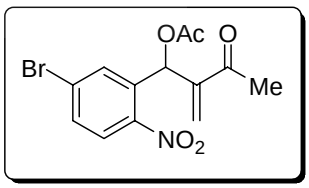
^{1}H NMR (400 MHz) : δ 2.10 (s, 3H), 2.36 (s, 3H), 5.71 (s, 1H), 6.23 (s, 1H), 7.29 (s, 1H), 7.45-7.51 (m, 1H), 7.53 (d, 1H, *J* = 8.0 Hz), 7.60-7.67 (m, 1H), 8.01 (d, 1H, *J* = 8.0 Hz)

^{13}C NMR (100 MHz) : δ 20.80, 25.97, 68.41, 125.14, 127.39, 128.64, 129.07, 133.35, 133.75, 146.54, 148.00, 169.17, 196.83

4-Acetoxy-4-(5-bromo-2-nitrophenyl)-3-methylenebutan-2-one (106b)

Treatment of 4-(5-bromo-2-nitrophenyl)-4-hydroxy-3-methylenebutan-2-one (**105b**) with acetyl chloride in the presence of pyridine following the similar procedure described for the molecule **106a** provided the title compound as a colorles solid.

Reaction time : 20 min



Yield : 77%

Mp : 115-117 ^{0}C

IR (KBr) : ν 1747, 1682, 1602 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.14 (s, 3H), 2.38 (s, 3H), 5.78 (s, 1H), 6.27 (s, 1H), 7.28 (s, 1H), 7.61 (dd, 1H, *J* = 2.0 Hz & 8.8 Hz), 7.64 (d, 1H, *J* = 2.0 Hz), 7.91 (d, 1H, *J* = 8.8 Hz)

^{13}C NMR (100 MHz) : δ 20.84, 25.95, 67.99, 126.72, 127.59, 128.43, 131.79, 132.26, 135.92, 146.10, 146.79, 169.07, 196.68

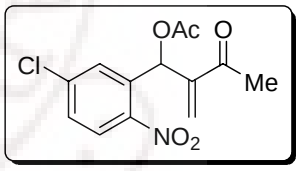
4-Acetoxy-4-(5-chloro-2-nitrophenyl)-3-methylenebutan-2-one (106c)

This was obtained as a colorless solid *via* the acetylation of 4-(5-chloro-2-nitrophenyl)-4-hydroxy-3-methylenebutan-2-one (**105c**) with acetyl chloride in presence of pyridine similar procedure described for the molecule **105a.**

Reaction time : 20 min

Yield : 87%

Mp : 84-86 ^{0}C



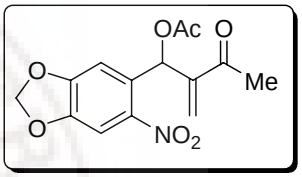
IR (KBr) : ν 1747, 1682, 1620 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.14 (s, 3H), 2.38 (s, 3H), 5.78 (s, 1H), 6.27 (s, 1H), 7.29 (s, 1H), 7.45 (d, 1H, *J* = 8.4 Hz), 7.49 (s, 1H), 8.00 (d, 1H, *J* = 8.4 Hz)

^{13}C NMR (100 MHz) : δ 20.83, 25.94, 68.01, 126.76, 127.63, 128.78, 129.19, 136.01, 140.04, 146.06, 146.19, 169.09, 196.68

4-Acetoxy-3-methylene-4-(4,5-methylenedioxy-2-nitrophenyl)butan-2-one (106d)

Treatment of 4-hydroxy-3-methylene-4-(4,5-methylenedioxy-2-nitrophenyl)butan-2-one **(105d)** with acetyl chloride in the presence of pyridine following the similar procedure described for the molecule **106a** provided the desired compound as a colorles solid.



Reaction time : 20 min

Yield : 84%

Mp : 118-120 ^{0}C

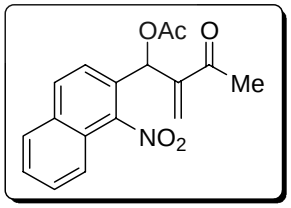
IR (KBr) : ν 1747, 1672, 1616 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.12 (s 3H), 2.38 (s, 2H), 5.71 (s, 1H), 6.11-6.19 (m, 2H), 6.23 (s, 1H), 6.95 (s, 1H), 7.29 (s, 1H), 7.57 (s, 1H)

^{13}C NMR (100 MHz) : δ 20.86, 25.98, 68.57, 103.31, 106.01, 107.24, 127.24 131.13, 141.97, 146.57, 147.69, 152.27, 169.20, 196.80

4-Acetoxy-3-methylene-4-(1-nitronaphth-2-yl)butan-2-one (**106e**)

Treatment of 4-hydroxy-3-methylene-4-(1-nitronaphth-2-yl)butane-2-one (**105e**) with acetyl chloride in the presence of pyridine following the similar procedure described for the molecule **106a** provided the title product as a black solid.



Reaction time : 20 min

Yield : 82%

Mp : 127-129 ^{0}C

IR (KBr) : ν 1745, 1672, 1605 cm^{-1}

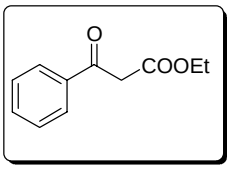
^{1}H NMR (400 MHz) : δ 2.11 (s, 3H), 2.34 (s, 3H), 6.01 (s, 1H), 6.33 (s, 1H), 6.98 (s, 1H), 7.48-7.65 (m, 3H), 7.71 (d, 1H, *J* = 8.0 Hz), 7.86 (d, 1H, *J* = 7.6 Hz), 7.94 (d, 1H, *J* = 8.4 Hz)

^{13}C NMR (100 MHz) : δ 20.65, 26.02, 69.09, 121.87, 124.52, 124.80, 127.04, 127.82, 127.95, 128.04, 128.82, 130.75, 133.47, 145.53, 146.74, 169.04, 196.99

Ethyl 3-oxo-3-phenylpropionate (107a)

This compound was prepared according to the literature with slight modifications[205]

To a stirred mixture of oil free sodium hydride (125 mmol, 3.00 g) and diethyl carbonate (150 mmol, 17.71 g) in toluene (75 mL) was heated at 80 ^{0}C for 0.5 h. Then a solution of acetophenone (50 mmol, 6.0 g) and diethyl carbonate (100 mmol, 11.82 g) in toluene (75 mL) was added drop by drop at the same temperature for 1.5 h and stirring was continued for another 0.5 h. Then reaction mixture was cooled to room temperature and acetic acid (5 mL) was added carefully. Then it was diluted with water (15 mL) and extracted with ether (3X150 mL). Combined organic layer was dried over anhydrous Na_2SO_4. Crude product was obtained after solvent evaporation was purified by column-chromatography (10% EtOAc in hexanes) to provide the ethyl 3-oxo-3-phenylpropionate as a colorless liquid in 70% (6.82 g) isolated yield.



IR (neat) : ν 1745, 1672, 1605 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.25 & 1.34 (2t, 3H, *J* = 7.12 Hz), 3.99 (s, 2H), 4.17-4.30 (m, 2H) (2q, 2H, *J* = 7.12 Hz), 7.38-7.65 (m, 3H), 7.78 & 7.95 (2d, 2H, *J* = 7.6 Hz)

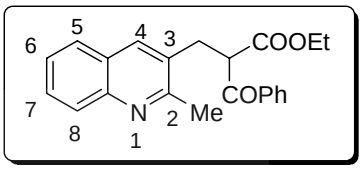
^{13}C NMR (100 MHz) : δ 14.06, 14.29, 45.98, 60.32, 61.44, 87.38, 126.03, 128.49, 128. 53, 128.53, 128.77, 131.23, 133.44, 133.72, 136.03, 167.51, 171.43, 173.20, 192.54

The underlined chemical shift values with low intensity in ^{1}HNMR and ^{13}C NMR spectra indicate the presence of minor enolic isomer in the compound.

3-(2-Ethoxycarbonyl-3-oxo-3-phenylpropyl)-2-methylquinoline (109a)

To a stirred solution of 4-acetoxy-3-methylene-4-(2-nitrophenyl)butan-2-one (**106a**) (1 mmol, 0.263 g) and ethyl 3-oxo-3-phenylpropionate (**107a**) (1 mmol, 0.193 g) in THF (1 mL) was added K_2CO_3 (1 mmol, 0.138 g). After stirring at room temperature for 20 h THF was removed under reduced pressure. The residue was diluted with AcOH (5 mL), and Fe powder (6 mmol, 0.336g) was added. Then the reaction mixture was heated at 110^0C for 2 h. Reaction mixture was cooled to room temperature and AcOH was removed under reduced pressure. The residue was dissolved in EtOAc (15 mL), and filtered to remove any Fe impurities. The iron residue was washed with EtOAc (15 mL). Filtrate and washings were combined and dried over anhydrous Na_2SO_4. Solvent was evaporated and

the crude thus obtained was purified by column chromatography (30% EtOAc in hexanes) to provide the desired product in 75% (0.260 g) isolated yield.



Reaction time : 22 h (20 h +2 h)

Mp : 55-57 ^{0}C

IR (KBr) : ν 1732, 1693 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.08 (t, 3H, *J* = 7.2 Hz); 2.79 (s, 3H), 3.52 (d, 2H, *J* = 7.2 Hz), 4.02-4.18 (m, 2H), 4.74 (t, 1H, *J* = 7.2 Hz), 7.44-7.50 (m, 3H), 7.52-7.66 (m, 2H), 7.68 (d, 1H, *J* = 8.0 Hz), 7.90 (s, 1H); 7.95-8.04 (m, 3H)

^{13}C NMR (100 MHz) : δ 13.91, 23.43, 31.52, 53.98, 61.79, 125.91, 127.01, 127.12, 128.24, 128.61, 128.81, 129.08, 130.24, 133.78, 135.98, 136.05, 146.70, 158.15, 169.01, 193.91

LCMS (m/z) : 348 $(M+H)^+$

Anal calc′d for $C_{22}H_{21}NO_3$: C, 76.06; H, 6.09; N, 4.03

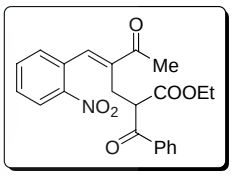
Found : C, 76.12; H, 6.05; N, 4.10

Ethyl 2-benzoyl-4-(2-nitrophenyl)methyledene-5-oxo-hexanoate (108a)

To a stirred solution of 4-acetoxy-3-methylene-4-(2-nitrophenyl)butan-2-one (**106a**) (1 mmol, 0.263 g) and ethyl 3-oxo-3-phenylpropionate (**107a**) (1 mmol, 0.193 g) in THF (1 mL) was added K_2CO_3 at room temperature and stirring was continued for 20 h. Then the

reaction mixture was diluted with water (2 mL) and extracted with diethyl ether (3X10 mL). Combined organic layer was dried over Na_2SO_4. Solvent was evaporated and thus obtained crude product was crystallized from (30% EtOAc in hexanes to provide title compound in 74% (0.294 g) isolated yield.

Reaction time : 20 h



M. P : 163-164 ^{0}C

IR (KBr) : ν 1745, 1682, 1666, 1597 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.06 (t, 3H, *J* = 7.20 Hz), 2.48 (s, 3H), 2.88 & 2.98 (d of ABq, 2H, *J* = 15.6 Hz & 6.4 Hz [8.4 Hz]), 3.89-4.06 (m, 2H), 4.70-4.76 (m, 1H), 7.37 (d, 1H, *J* = 8.0 Hz), 7.40-7.48 (m, 2H), 7.52-7.61 (m, 2H), 7.65-7.74 (m, 1H), 7.92-8.00 (m, 3H), 8.27 (d, 1H, *J* = 8.4 Hz)

^{13}C NMR (100 MHz) : δ 13.89, 26.10, 26.20, 51.97, 61.28, 125.13, 128.67, 128.80, 129.53, 130.83, 131.71, 133.62, 133.96, 135.76, 138.01, 141.28, 147.04, 169.13, 194.91, 200.07

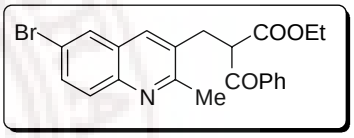
LCMS (m/z) : 396 $(M+H)^+$

Anal calc′d for $C_{22}H_{21}NO_6$: C, 66.83; H, 5.35; N, 3.54

Found : C, 66.72; H, 5.33; N, 3.61

6-Bromo-3-(2-ethoxycarbonyl-3-oxo-3-phenylpropyl)-2-methylquinoline (109b)

This compound was obtained as a viscous liquid *via* the treatment of 4-acetoxy-4-(5-bromo-2-nitrophenyl)-3-methylenebutan-2-one (**106b**) with ethyl 3-oxo-3-phenylpropionate (**107a**) and subsequent treatment of the resulting product with Fe/AcOH following the one-pot procedure described for the molecule **109a**.



Reaction time : 22 h (20 h + 2 h)

Yield : 72%

IR (neat) : ν 1732, 1687 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.09 (t, 3H, *J* = 8.0 Hz), 2.77 (s, 3H), 3.51 (dd, 2H, *J* = 2.8 Hz & 7.2 Hz), 4.04-4.18 (m, 2H), 4.72 (t, 1H, *J* = 7.2 Hz), 7.42-7.50 (m, 2H), 7.54-7.61 (m, 1H), 7.65-7.72 (m, 1H), 7.77-7.86 (m, 3H), 7.97 (d, 2H, *J* = 7.2 Hz)

^{13}C NMR (100 MHz) : δ 13.96, 23.49, 31.46, 53.85, 61.91, 119.65, 128.18, 128.66, 128.89, 129.15, 130.10, 131.38, 132.50, 133.90, 134.88, 136.00, 145.28, 158.80, 168.92, 193.72

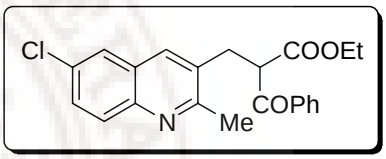
LCMS (m/z) : 426 $(M+H)^{+}$, 428 $(M+H+2)^{+}$

Anal calc′d for $C_{22}H_{20}BrNO_3$: C, 61.98; H, 4.73; N, 3.29

Found : C, 61.93; H, 4.76, N, 3.32

6-Chloro-3-(2-ethoxycarbonyl-3-oxo-3-phenylpropyl)-2-methylquinoline (109c)

This molecule was prepared by the Michael reaction of 4-acetoxy-4-(5-chloro-2-nitrophenyl)-3-methylenebutan-2-one (**106c**) with ethyl 3-oxo-3-phenylpropionate (**107a**) and subsequent treatment of *in situ* generated trisubstitued alkene with Fe/AcOH following the similar procedure described for the molecule **109a**.



Reaction time : 22 h (20 h +2 h)

Yield : 71%

IR (neat) : ν 1716, 1682 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.09 (t, 3H, *J* = 7.2 Hz), 2.77 (s, 3H), 3.51 (dd, 2H, *J* = 2.0 Hz & 7.6 Hz), 4.01-4.19 (m, 2H), 4.72 (t, 1H, *J* = 7.2 Hz), 7.42-7.48 (m, 2H), 7.52-7.62 (m, 2H), 7.65 (d, 1H, *J* = 2.0 Hz), 7.81 (s, 1H), 7.89 (d, 1H, *J* = 8.8 Hz), 7.97 (d, 2H, *J* = 8.0 Hz)

^{13}C NMR (100 MHz) : δ 13.98, 23.48, 31.50, 53.89, 61.93, 125.82, 127.66, 128.68, 128.91, 130.00, 131.41, 131.58, 133.91, 134.91, 135.01, 136.04, 145.13, 158.65, 168.95, 193.76

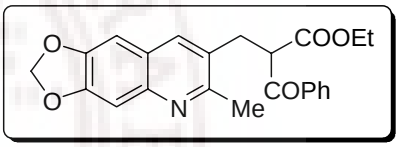
LCMS (m/z) : 382 $(M+H)^{+}$, 384 $(M+H+2)^{+}$

Anal calc′d for $C_{22}H_{20}ClNO_3$: C, 69.20; H, 5.28; N, 3.67

Found : C, 69 28; H, 5.25, N, 3.71

3-(2-Ethoxycarbonyl-3-oxo-3-phenylpropyl)-6,7-methylenedioxy-2-methylquinoline (109d)

This was obtained as solid *via* the treatment of 4-acetoxy-3-methylene-4-(4,5-methylenedioxy-2-nitrophenyl)butan-2-one **(106d** with ethyl 3-oxo-3-phenylpropionate (**107a**) followed by treatment of the resulting trisubstitued alkene with Fe/AcOH following the similar procedure described for the molecule **109a**.



Reaction time : 22 h (20 h +2 h)

Yield : 79%

Mp : 119-121 ^{0}C

IR (KBr) : ν 1716, 1682 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.08 (t, 3H, *J* = 6.8 Hz), 2.70 (s, 3H), 3.45 (d, 2H, *J* = 7.6 Hz), 4.04-4.16 (m, 2H), 4.69 (t, 1H, *J* = 7.6 Hz), 6.04 (s, 2H), 6.91(s, 1H), 7.25 (s, 1H), 7.41-7.52 (m, 2H), 7.53-7.62 (m, 1H), 7.71 (s, 1H), 7.95 (d, 2H, *J* = 7.6 Hz)

^{13}C NMR (100 MHz) : δ 13.99, 23.02, 31.53, 54.19, 61.79, 101.57, 102.34, 105.06, 123.77, 128.30, 128.66, 128.85, 133.78, 135.40, 136.20, 144.91, 147.35, 150.41, 155.58, 169.13, 194.14

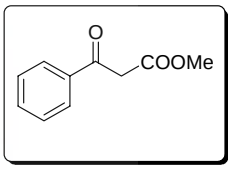
LCMS (m/z) : 392 $(M+H)^+$

Anal calc′d for $C_{23}H_{21}NO_5$: C, 70.58; H, 5.41; N, 3.58

Found : C, 70.49; H, 5.45; N, 3.65

Methyl 3-oxo-3-phenylpropionate (107b)

This compound was obtained as a colorless liquid *via* the treatment of acetophenone with dimethyl carbonate in presence of sodium hydride following the similar procedure described for compound **107a**.



Yield : 65%

IR (Neat) : ν 1745, 1685 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.77 & 3.80 (2s, 3H), 4.01 (s, 2H), 7.38-7.52 (m, 2H), 7.56-7.64 (m, 1H), 7.78 & 7.94 (d, 2H, *J* = 8.0 Hz), 12.50 (s, enolic)

^{13}C NMR (100 MHz) : δ 45.69, 51.42, 52.47, 87.06, 126.09, 128.53, 128.56, 128.82, 131.32, 133.36, 133.81, 135.97, 167.96, 171.53, 173.53, 192.39 (mixture of keto enol forms)

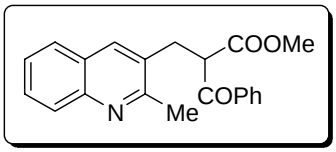
The underlined chemical shift values with low intensity in ^{1}H NMR spectrum indicate the presence of its minor enolic isomer in the compound.

3-(2-Methoxycarbonyl-3-oxo-3-phenylpropyl)-2-methylquinoline (109e)

This compound was obtained as a brown solid *via* the treatment of 4-acetoxy-3-methylene-4-(2-nitrophenyl)butan-2-one (**106a**) with methyl 3-oxo-3-phenylpropionate (**107b**) and subsequent treatment of the resulting product with Fe/AcOH following the similar one-pot procedure described for the molecule **109a**.

Reaction time : 22 h (20 h +2 h)

Yield : 77%



Mp : 98-100 ^{0}C

IR (KBr) : ν 1739, 1685 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.77 (s, 3H), 3.51 (d, 2H, *J* = 7.2 Hz), 3.63 (s, 3H), 4.77 (t, 1H, *J* = 7.2 Hz), 7.38-7.50 (m, 3H), 7.52-7.64 (m, 2H), 7.66 (d, 1H, *J* = 8.0 Hz), 7.87 (s, 1H), 7.94-8.02 (m, 3H)

^{13}C NMR (100 MHz) : δ 23.35, 31.64, 52.81, 53.69, 125.96, 127.04, 127.17, 128.20, 128.64, 128.90, 129.16, 130.18, 133.88, 135.99, 136.04, 146.69, 158.12, 169.50, 193.88

LCMS (m/z) : 334 $(M+H)^+$

Anal calc′d for $C_{21}H_{19}NO_3$: C, 75.66; H, 5.74; N, 4.20

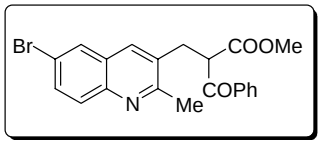
Found : C, 75.71; H, 5.70; N, 4.25

6-Bromo-3-(2-methoxycarbonyl-3-oxo-3-phenylpropyl)-2-methylquinoline (109f)

This compound was obtained as a brown viscous liquid *via* the treatment of 4-acetoxy-4-(5-bromo-2-nitrophenyl)-3-methylenebutan-2-one (**106b**) with methyl 3-oxo-3-phenyl-propionate (**107b**) and subsequent treatment of the resulting product with Fe/AcOH following the similar one-pot procedure described for the molecule **109a**.

Reaction time : 22 h (20 h +2 h)

Yield : 72%



IR (neat) : ν 1739, 1685 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.77 (s, 3H), 3.49-3.58 (m, 2H), 3.65 (s, 3H), 4.75 (t, 1H, *J* = 7.2 Hz), 7.43-7.52 (m, 2H), 7.55-7.64 (m, 1H), 7.66-7.74 (m, 1H), 7.78-7.90 (m, 3H), 7.96 (d, 2H, *J* = 8.0 Hz)

^{13}C NMR (100 MHz) : δ 23.43, 31.54, 52.88, 53.50, 119.64, 128.14, 128.64, 128.94, 129.15, 130.04, 131.25, 132.51, 133.97, 134.84, 135.88, 145.24, 158.72, 169.37, 193.63

LCMS (m/z) : 411 $(M+H)^+$, 413 $(M+H+2)^+$

Anal calc′d for $C_{21}H_{18}BrNO_3$: C, 61.18; H, 4.40; N, 3.40

Found : C, 61.12; H, 4.45; N, 3.48

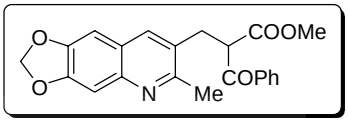
3-(2-Methoxycarbonyl-3-oxo-3-phenylpropyl)-6,7-methylenedioxy-2-methylquinoli-ne (109g)

This compound was obtained as a brown solid *via* the treatment of 4-acetoxy-3-methylene-4-(4,5-methylenedioxy-2-nitrophenyl)butan-2-one **(106d** with methyl 3-oxo-3-phenyl-propionate (**107b**) followed by reaction of the resulting product with Fe/AcOH following the one-pot procedure described for the molecule **109a**.

Reaction time : 22 h (20 h +2 h)

Yield : 69%

Mp : 136-138 ^{0}C



IR (KBr) : ν 1739, 1685 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.70 (s, 3H), 3.45 (d, 2H, *J* = 8.0 Hz), 3.64 (s, 3H), 4.72 (t, 1H, *J* = 8.0 Hz), 6.04 (s, 2H), 6.92 (s, 1H), 7.26 (s, 1H) 7.40-7.48 (m, 2H), 7.53-7.60 (m, 1H), 7.70 (s, 1H), 7.92-7.98 (m, 2H)

^{13}C NMR (100 MHz) : δ 22.89, 31.60, 52.79, 53.84, 101.57, 102.35, 104.94, 123.77, 128.19, 128.65, 128.90, 133.86, 135.42, 136.08, 144.84, 147.36, 150.45, 155.48, 169.59, 194.07

LCMS (m/z) : 378 $(M+H)^+$

Anal calc′d for $C_{22}H_{19}NO_5$: C, 70.02; H, 5.07; N, 3.71

Found : C, 70.11; H, 5.03; N, 3.76

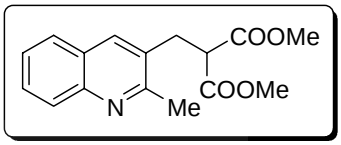
3-(2,2-Dimethoxycarbonylethyl)-2-methylquinoline (109h)

This compound was obtained as a brown solid *via* the treatment of 4-acetoxy-3-methylene-4-(2-nitrophenyl)butan-2-one (**106a**) with dimethyl malonate (**107c**) followed by subsequent treatment of the resulting product with Fe/AcOH according to the smilar one-pot procedure described for the molecule **109a**.

Reaction time : 26 h (24 h +2 h)

Yield : 69%

Mp : 98-100 ^{0}C



IR (KBr) : ν 1749, 1732 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.76 (s, 3H), 3.41 (d, 2H, *J* = 7.6 Hz), 3.71 (s, 6H), 3.80 (t, 1H, *J* = 7.6 Hz), 7.43-7.50 (m, 1H), 7.61-7.68 (m, 1H), 7.72 (d, 1H, *J* = 8.0 Hz), 7.88 (s, 1H), 7.98 (d, 1H, *J* = 8.4 Hz)

^{13}C NMR (100 MHz) : δ 23.29, 31.76, 51.65, 52.83, 126.02, 127.08, 127.22, 128.39, 129.24, 129.71, 135.84, 146.90, 158.15, 169.01

LCMS (m/z) : 288 $(M+H)^+$

Anal calc′d for $C_{16}H_{17}NO_4$: C, 66.89; H, 5.96; N, 4.88

Found : C, 66.92; H, 5.93; N, 4.85

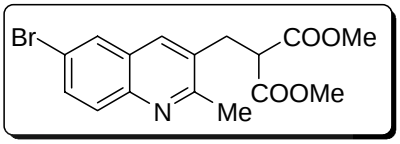
6-Bromo-3-(2,2-dimethoxycarbonylethyl)-2-methylquinoline (109i)

Treatment of 4-acetoxy-4-(5-bromo-2-nitrophenyl)-3-methylenebutan-2-one (**106b**) with dimethyl malonate (**107c**) in presence of K_2CO_3 followed by reductive cyclization with Fe/AcOH provided the title compound as a colorless solid following the similar procedure described for the molecule **109a**.

Reaction time : 26 h (24 h +2 h)

Yield : 60%

Mp : 117-119 ^{0}C



IR (KBr) : ν 1751, 1724 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.74 (s, 3H), 3.42 (d, 2H, *J* = 7.6 Hz), 3.73 (s, 6H), 3.80 (t, 1H, *J* = 7.6 Hz), 7.72 (dd, 1H, *J* = 2.0 Hz & 8.8 Hz), 7.80 (s, 1H), 7.80 (d, 1H, *J* = 8.8 Hz), 7.90 (d, 1H, *J* = 2.0 Hz)

^{13}C NMR (100 MHz) : δ 23.29, 31.63, 51.44, 52.85, 119.70, 128.16, 129.18, 130.17, 130.76, 132.59, 134.64, 145.40, 158.70, 168.83

LCMS (m/z) : 366 $(M+H)^+$, 368 $(M+2+H)^+$

Anal calc′d for $C_{16}H_{16}BrNO_4$: C, 52.48; H, 4.40; N, 3.82

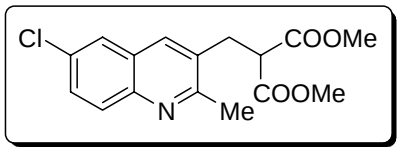
Found : C, 52.51; H, 4.37; N, 3.86

6-Chloro-3-(2,2-dimethoxycarbonylethyl)-2-methylquinoline (109j)

This was obtained as a colorless solid *via* the Michael addition of 4-acetoxy-4-(5-chloro-2-nitrophenyl)-3-methylenebutan-2-one (**106c**) with dimethyl malonate (**107c**) in presence of K_2CO_3 and subsequent reductive cyclization with Fe/AcOH following the similar procedure described for the molecule **109a**.

Reaction time : 26 h (24 h +2 h)

Yield : 54%



Mp : 128-130 ^{0}C

IR (KBr) : ν 1753, 1722 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.75 (s, 3H), 3.40 (d, 2H, *J* = 7.6 Hz), 3.72 (s, 6H), 3.78 (t, 1H, *J* = 7.6 Hz), 7.57 (dd, 1H, *J* = 2.0 & 8.8 Hz Hz), 7.70 (d, 1H, *J* = 2.0 Hz), 7.80 (s, 1H), 7.91 (d, 1H, *J* = 8.8 Hz)

^{13}C NMR (100 MHz) : δ 23.30, 31.69, 51.49, 52.91, 125.88, 127.68, 130.08, 130.13, 130.82, 131.68, 134.82, 145.26, 158.58, 168.90

LCMS (m/z) : 322 $(M+H)^+$, 324 $(M+H+2)^+$

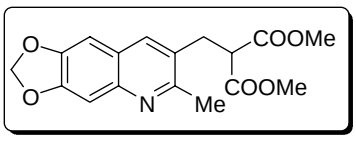
Anal calc′d for $C_{16}H_{16}ClNO_4$: C, 59.73; H, 5.01; N, 4.35

Found : C, 59.78; H, 5.06; N, 4.42

3-(2,2-Dimethoxycarbonylethyl)-6,7-methylenedioxy-2-methylquinoline (109k)

This compound was obtained as a colorless solid *via* the treatment of 4-acetoxy-3-methylene-4-(4,5-methylenedioxy-2-nitrophenyl)butan-2-one (**106d**) with dimethyl malonate (**107c**) in presence of K_2CO_3 followed by the reaction of the resulting product with Fe/AcOH following the one-pot procedure described for the molecule **109a**.

Reaction time : 26 h (24 h +2 h)



Yield : 61%

Mp : 88-90 ^{0}C

IR (KBr) : ν 1732, 1722 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.68 (s, 3H), 3.34 (d, 2H, *J* = 7.6 Hz), 3.70 (s, 6H), 3.75 (t, 1H, *J* = 7.6 Hz), 6.06 (s, 2H), 6.96 (s, 1H), 7.28 (s, 1H), 7.69 (s, 1H)

^{13}C NMR (100 MHz) : δ 22.73, 31.63, 51.76, 52.74, 101.58, 102.33, 105.03, 123.75, 127.69, 135.14, 144.97, 147.39, 150.48, 155.49, 169.04

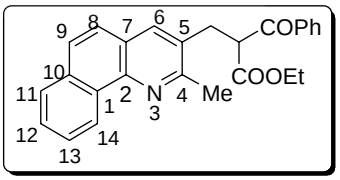
LCMS (m/z) : 332 $(M+H)^+$

Anal calc′d for $C_{17}H_{17}NO_6$: C, 61.63; H, 5.17; N, 4.23

Found : C, 61.55; H, 5.19; N, 4.26

3-Aza-5-(2-ethoxycarbonyl-3-oxo-3-phenylpropyl)-4-methyltricyclo(8.4.0.0^{2,7})tetra-deca-1(10),2(7),3,5,8,11,13-heptaene (109l)

This compound was prepared *via* Michael reaction of 4-acetoxy-3-methylene-4-(1-nitronaphth-2-yl)butan-2-one (**106e**) with ethyl 3-oxo-3-phenylpropionate (**107a**),in presence of K_2CO_3 followed by subsequent reaction with Fe/AcOH, using the similar procedure described for the molecule **109a**.



Reaction time : 22 h (20 h +2 h)

Yield : 65%

Mp : 83-85 ^{0}C

IR (KBr) : ν 1734, 1684 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.06 (t, 3H, *J* = 8.0 Hz), 2.86 (s, 3H), 3.54 (d, 2H, *J* = 7.2 Hz), 4.01-4.20 (m, 2H), 4.75 (t, 1H, *J* = 7.2 Hz), 7.37-7.49 (m, 2H), 7.50-7.58 (m, 2H), 7.59-7.78 (m, 3H), 7.83 (d, 1H, *J* = 7.6 Hz), 7.88 (s, 1H), 7.97 (d, 2H, *J* = 8.0 Hz), 9.26 (d, 1H, *J* = 7.6 Hz)

^{13}C NMR (100 MHz) : δ 13.96, 23.55, 31.61, 54.16, 61.79, 124.25, 124.77, 124.97, 126.81, 126.94, 127.74, 127.79, 128.65, 128.83, 130.57, 131.16, 133.53, 133.76, 136.11, 136.16, 144.65, 156.61, 169.12, 194.11

LCMS (m/z) : 398 $(M+H)^+$

Anal calc′d for $C_{26}H_{23}NO_3$: C, 78.57; H, 5.83; N, 3.52

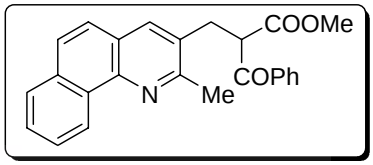
Found : C, 78.52; H, 5.86; N, 3.61

3-Aza-5-(2-methoxycarbonyl-3-oxo-3-phenylpropyl)-4-methyltricyclo(8.4.0.0^{2,7})tetradeca-1(10),2(7),3,5,8,11,13-heptaene (109m)

This compound was obtained as a brown solid *via* the treatment of 4-acetoxy-3-methylene-4-(1-nitronaphth-2-yl)butan-2-one (**106e**) with methyl-3-oxo-3-phenylpro-pionate (**107b**) in presence of K_2CO_3 and subsequent treatment of the resulting product with Fe/AcOH following the one-pot procedure described for the molecule **109a**.

Reaction time : 22 h (20 h +2 h)

Yield : 63%



Mp : 90-92 ^{0}C

IR (KBr) : ν 1739, 1682 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.88 (s, 3H), 3.56 (d, 2H, *J* = 7.2 Hz), 3.64 (s, 3H), 4.81 (t, 1H, *J* = 7.2 Hz), 7.38-7.46 (m, 2H), 7.50-7.57 (m, 2H), 7.58-7.74 (m, 3H), 7.85 (d, 1H, *J* = 7.6 Hz), 7.89 (s, 1H), 7.97 (d, 2H, *J* = 7.6 Hz), 9.28 (d, 1H, *J* = 8.0 Hz)

^{13}C NMR (100 MHz) : δ 23.51, 31.70, 52.76, 53.83, 124.23, 124.76, 124.96, 126.81, 126.94, 127.73, 127.80, 128.64, 128.88, 130.44, 131.12, 133.52, 133.83, 136.07, 144.66, 156.54, 169.58, 194.04

LCMS (m/z) : 384 $(M+H)^{+}$

Anal calc′d for $C_{25}H_{21}NO_3$: C, 78.31; H, 5.52; N, 3.65

Found : C, 78.42.H, 5.49; N, 3.71

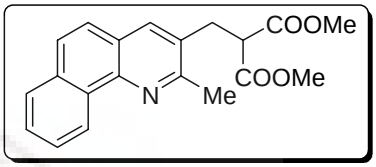
3-Aza-5-(2,2-dimethoxycarbonylethyl)-4-methyltricyclo(8.4.0.0^{2,7})tetradeca-1(10),2(7),3,5,8,11,13-heptaene (109n)

This was obtained as a colorless solid *via* the Michael reaction of 4-acetoxy-3-methylene-4-(1-nitronaphth-2-yl)butan-2-one (**106e**) with dimethyl malonate (**107c**) in presence of

K_2CO_3 and subsequent treatment with Fe/AcOH following the similar procedure described for molecule **109a**.

Reaction time : 26 h (24 h +2 h)

Yield : 58%



Mp : 90-92 ^{0}C

IR (KBr) : ν 1740 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.86 (s, 3H), 3.46 (d, 2H, *J* = 7.6 Hz), 3.71 (s, 6H), 3.83 (t, 1H, *J* = 7.6 Hz), 7.55-7.76 (m, 4H), 7.87 (d, 1H, *J* = 8.0 Hz), 7.90 (s, 1H), 9.29 (d, 1H, *J* = 8.0 Hz)

^{13}C NMR (100 MHz) : δ 23.31, 31.75, 51.73, 52.75, 124.26, 124.77, 124.93, 126.85, 127.01, 127.74, 127.85, 129.93, 131.12, 133.56, 135.91, 144.66, 156.55, 169.06

LCMS (m/z) : 338 $(M+H)^+$

Anal calc′d for $C_{20}H_{19}NO_4$: C, 71.20; H, 5.68; N, 4.15

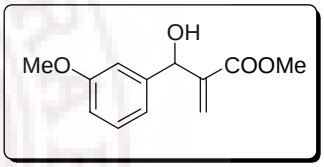
Found : C, 71.25; H, 5.64; N, 4.19

Methyl 3-hydroxy-3-(3-methoxyphenyl)-2-methylenepropanoate (123a)

This compound was prepared according to the procedure developed in our laboratory[222]

To a clear solution of 3-methoxybenzaldeyhde (**122a**) (50 mmol, 6.80 g) and methyl acrylate (75 mmol, 6.45 g) was added DABCO (7.5 mmol, 0.841 g) at room temperature.

Then 10 g of silicagel (>200 mesh) was added and throughly mixed. The resulting solid reaction mixture was kept at room temperature for 10 days. The reaction mixture was washed with ethyl acetate (3X30 mL). Combined organic layer was washed successively, with 2N HCl (15 mL), saturated $NaHCO_3$ solution (15 mL), water (15 mL) and then dried over anhydrous Na_2SO_4. Solvent was evaporated and the crude thus obtained was purified by column chromatography to provide the desired product as a colorless liquid in 66% (7.31 g) isolated yield.



Reaction time : 10 d

Yield : 66%

IR (neat) : ν 3479, 1722, 1624 cm^{-1}

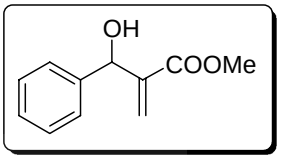
^1H NMR (400 MHz) : δ 3.12 (br s, 1H), 3.72 (s, 3H), 3.79 (s, 3H), 5.53 (s, 1H), 5.83 (s, 1H), 6.33(s, 1H), 6.82 (d, 1H, *J* = 8.4 Hz), 6.94 (br s, 2H), 7.23-7.28 (m, 1H)

^{13}C NMR (100 MHz) : δ 52.05, 55.29, 73.27, 112.15, 113.43, 118.95, 126.37, 129.52, 141.86, 142.99, 159.78, 166.87

Methyl 3-hydroxy-2-methylene-3-phenylpropanoate (123b)

This was prepared as a colorless liquid *via* the coupling of benzaldehyde (**122b**) with methyl acrylate under the catalytical influence of DABCO at room temperature following the similar procedure described for molecule **123a**.

Reaction time : 12 h



Yield : 77%

IR (neat) : ν 3447, 1720, 1630 cm^{-1}

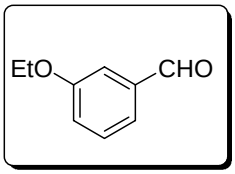
^{1}H NMR (400 MHz) : δ 2.99 (br s, 1H), 3.68 (s, 3H), 5.53 (s, 1H), 5.83 (s, 1H), 6.31 (s, 1H), 7.22-7.39 (m, 5H)

^{13}C NMR (100 MHz) : δ 51.94, 73.13, 126.02, 126.64, 127.82, 128.43, 141.34, 142.06, 166.78

3-Ethoxybenzaldehyde (122c)

To a stirred suspension of 3-hydroxybenzaldehyde (150 mmol, 18.31 g) and anhydrous K_2CO_3 (150 mmol, 20.73 g) in acetonitrile (200 mL) was added bromoethane (150 mmol, 16.64 g). Then reaction mixture was heated under reflux for 5 h. Reaction mixture was cooled to room temperature and acetonitrile was removed under reduced pressure. The residue was diluted with water (150 mL) and extracted with diethyl ether (3X200 mL). Combined organic layer was dried over anhydrous Na_2SO_4. Crude product obtained after solvent evaporation was purified by column chromatography (10% EtOAc in hexanes) to provide the desired product as a color less liquid.

Reaction time : 5 h



Yield : 78% (17.54 g)

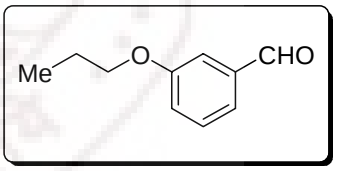
IR (neat) : ν 2729, 1699, 1599 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.43 (t, 3H, *J* = 6.8 Hz), 4.08 (q, 2H, *J* = 6.8 Hz), 7.13-7.22 (m, 1H), 7.37 (d, 1H, *J* = 1.80 Hz), 7.39-7.49 (m, 2H), 9.96 (s, 1H)

^{13}C NMR (100 MHz) : δ 14.72, 63.80, 112.83, 121.97, 123.35, 130.05, 137.82, 159.56, 192.25

3-Propoxybenzaldehyde (122d)

This was obtained as a colorless liquid *via* the treatment of 3-hydroxybenzaldehyde with 1-bromopropane in presence of K_2CO_3 in acetonitrile solvent following similar procedure described for the molecule **122c**.



Reaction time : 5 h

Yield : 85%

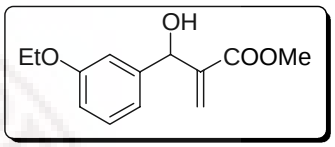
IR (neat) : ν 2727, 1699, 1599 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.05 (t, 3H, *J* = 7.2 Hz), 1.78-1.95 (m, 2H), 3.98 (t, 2H, *J* = 7.2 Hz), 7.14-7.22 (m, 1H), 7.38 (br s, 1H), 7.42-7.48 (m, 2H), 9.97 (s, 1H)

^{13}C NMR (100 MHz) : δ 10.49, 22.49, 69.80, 112.87, 121.95, 123.27, 130.01, 137.81, 159.74, 192.21

Methyl 3-(3-ethoxyphenyl)-3-hydroxy-2-methylenepropanoate (123c)

This compound was obtained as a color less liquid by the Baylis–Hillman coupling of 3-ethoxybenzaldehyde (**122c**) and methyl acrylate in presence of DABCO as a catalyst, following similar procedure described for the molecule **123a**.



Reaction time : 10 d

Yield : 67%

IR (neat) : ν 3481, 1718, 1620 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.40 (t, 3H, *J* = 7.0 Hz), 2.98 (d, 1H, *J* = 4.4 Hz), 3.73 (s, 3H), 4.03 (q, 2H, *J* = 7.0 Hz), 5.52 (d, 1H, *J* = 4.4 Hz), 5.82 (s, 1H), 6.33 (s, 1H), 6.81 (dd, 1H, *J* = 1.6 Hz & 8.4 Hz), 6.91-6.97 (m, 2H), 7.23 (d, 1H, *J* = 8.4 Hz)

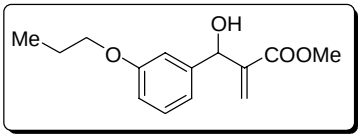
^{13}C NMR (100 MHz) : δ 14.88, 52.02, 63.46, 73.27, 112.77, 113.94, 118.83, 126.30, 129.50, 141.90, 142.96, 159.15, 166.86

Methyl 3-hydroxy-2-methylene-3-(3-propoxyphenyl)propanoate (123d)

Baylis–Hillman coupling of 3-propoxybenzaldehyde (**122d**) with methyl acrylate in presence of DABCO as a catalyst following the similar procedure described for the molecule **123a**, provided the title compound as a colorless liquid.

Reaction time : 10 d

Yield : 66%



IR (neat) : ν 3476, 1714, 1624 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.03 (t, 3H, *J* = 7.2 Hz), 1.75-1.85 (m, 2H), 2.98 (br s, 1H), 3.73 (s, 3H), 3.91 (t. 3H, *J* = 6.8 Hz), 5.52 (s, 1H), 5.83 (s, 1H), 6.33 (s, 1H), 6.78-6.84 (m, 1H), 6.91-6.98 (m, 2H), 7.23 (d, 1H, *J* = 8.4 Hz)

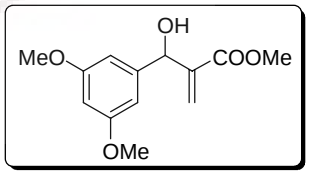
^{13}C NMR (100 MHz) : δ 10.60, 22.67, 52.03, 69.55. 73.31, 112.78, 113.99, 118.78, 126.33, 129.48, 141.90, 142.93, 159.38, 166.88

Methyl 3-(3,5-dimethoxyphenyl)-3-hydroxy-2-methylenepropanoate (123e)

This compound was prepared as a colorless liquid *via* DABCO catalyzed Baylis–Hillman coupling of 3,5-dimethoxybenzaldehyde (**122e**) with methyl acrylate following a similar procedure described for the molecule **123a**.

Reaction time : 10 d

Yield : 60%



IR (neat) : ν 3479, 1720, 1620 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.11 (d, 1H, *J* = 5.2 Hz), 3.73 (s, 3H), 3.77 (s, 6H), 5.48 (d, 1H, *J* = 5.2 Hz), 5.82 (s, 1H), 6.33 (s, 1H), 6.36-6.40 (m, 1H), 6.53 (d, 2H, *J* = 2.2 Hz)

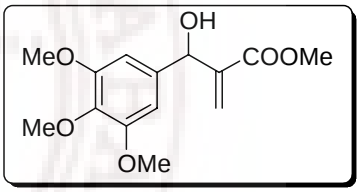
^{13}C NMR (100 MHz) : δ 52.07, 55.41, 73.38, 99.87, 104.60, 126.52, 141.69, 143.84, 160.93, 166.89

Methyl 3-hydroxy-2-methylene-3-(3,4,5-trimethoxyphenyl)propanoate (123f)

This molecule was obtained as a colorless viscous liquid *via* the Baylis–Hillman coupling reaction of 3,4,5-trimethoxybenzaldehyde (**122f**) with methyl acrylate in the presence of DABCO (cat.) in silica gel solid phase medium, following a similar procedure described for the molecule **123a**.

Reaction time : 10 d

Yield : 64%



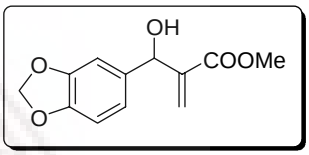
IR (neat) : ν 3485, 1726, 1621 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.10 (d, 1H, *J* = 4.8 Hz), 3.75 (s, 3H), 3.83 (s, 3H), 3.85 (s, 6H), 5.51 (d, 1H, *J* = 4.8 Hz), 5.83 (s, 1H), 6.34 (s, 1H), 6.60 (s, 2H)

^{13}C NMR (100 MHz) : δ 52.13, 56.16, 60.88, 73.34, 103.64, 126.33, 136.90, 137.53, 141.89, 153.30, 166.97

Methyl 3-hydroxy-2-methylene-3-(3,4-methylenedioxyphenyl)propanoate (**123g**)

This molecule was obtained as a colorless viscous liquid *via* the Baylis–Hillman coupling of piperonal (**122g**) with methyl acrylate catalyzed by DABCO in silica gel solid phase medium, following a similar procedure described for the molecule **123a**.



Reaction time : 30 d

Yield : 59%

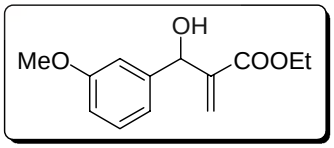
IR (neat) : ν 3429, 1714, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.95 (d, 1H, *J* = 4.8 Hz), 3.72 (s, 3H), 5.47 (d, 1H, *J* = 4.8 Hz), 5.85 (s, 1H), 5.94 (s, 2H), 6.32 (s, 1H), 6.76 (d, 1H, *J* = 8.0 Hz), 6.83 (d, 1H, *J* = 8.0 Hz), 6.86 (s, 1H)

^{13}C NMR (100 MHz) : δ 52.00, 72.93, 101.11, 107.25, 108.16, 120.24, 125.82, 135.38, 142.03, 147.23, 147.78, 166.77

Ethyl 3-hydroxy-3-(3-methoxyphenyl)-2-methylenepropanoate (123h)

This was obtained *via* the DABCO catalyzed coupling of 3-methoxybenzaldehyde (**122a**) with ethyl acrylate, following a similar procedure described for the molecule **123a** as a colorless liquid.



Reaction time : 10 d

Yield : 67%

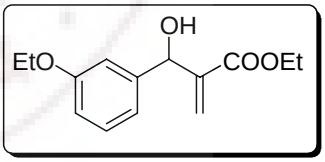
IR (neat) : ν 3503, 1714, 1620 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.25 (t, 3H, *J* = 7.2 Hz), 3.14 (d, 1H, *J* = 4.8 Hz), 3.80 (s, 3H), 4.80 (q, 2H, *J* = 7.2 Hz), 5.53 (d, 1H, *J* = 4.8 Hz), 5.80 (s, 1H), 6.33 (s, 1H), 6.82 (dd, 1H, *J* = 2.0 Hz & 8.4 Hz), 6.91-7.00 (m, 2H), 7.21-7.28 (m, 1H)

^{13}C NMR (100 MHz) : δ 14.12, 55.29, 61.04, 73.34, 112.12, 113.41, 118.96, 126.13, 129.48, 142.09, 143.07, 159.77, 166.45

Ethyl 3-(3-ethoxyphenyl)-3-hydroxy- 2-methylenepropanoate (123i)

This was obtained as a colorless liquid *via* DABCO catalyzed coupling of 3-ethoxybenzaldehyde (**122c**) with ethyl acrylate following the similar procedure described for the molecule **123a**.



Reaction time : 10 d

Yield : 66%

IR (neat) : ν 3456, 1714, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.25 (t, 3H, *J* = 7.2 Hz), 1.40 (t, 3H, *J* = 6.8 Hz), 3.06 (d, 1H, *J* = 5.6 Hz), 4.02 (q, 2H, *J* = 6.8 Hz), 4.18 (q, 2H, *J* = 7.2 Hz), 5.52 (d, 1H, *J* = 5.6 Hz), 5.80 (s, 1H), 6.33 (s, 1H),

6.81 (d, 1H, *J* = 8.0 Hz), 6.93 (s, 2H), 7.23 (d, 1H, *J* = 8.0 Hz)

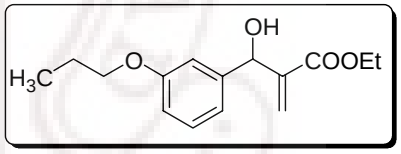
^{13}C NMR (100 MHz) : δ 14.08, 14.85, 60.96, 63.41, 73.24, 112.72, 113.88, 118.84, 125.95, 129.41, 142.15, 143.05, 159.09, 166.39

Ethyl 3-hydroxy-2-methylene-3-(3-propoxyphenyl)propanoate (123j)

This compound was obtained as a liquid *via* the treatment of 3-propoxybenzaldehyde (**122d**) with ethyl acrylate under the catalytical influence of DABCO in silica gel solid phase medium, following a similar procedure described for the molecule **123a**.

Reaction time : 10 d

Yield : 61%



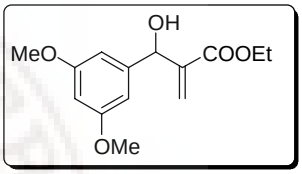
IR (neat) : ν 3456, 1714, 1620 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.02 (t, 3H, *J* = 7.2 Hz), 1.25 (t, 3H, *J* = 7.2 Hz), 1.72-1.85 (m, 2H), 3.08 (br s, 1H), 3.91 (t, 2H, *J* = 7.2 Hz), 4.18 (q, 2H, *J* = 7.2 Hz), 5.52 (s, 1H), 5.80 (s, 1H), 6.33 (s, 1H), 6.81 (d, 1H, *J* = 8.0 Hz), 6.89-6.98 (m, 2H), 7.23 (d, 1H, *J* = 8.0 Hz)

^{13}C NMR (100 MHz) : δ 10.57, 14.09, 22.64, 60.98, 69.50, 73.26, 112.75, 113.93, 118.79, 125.98, 129.40, 142.15, 143.01, 159.31, 166.42

Ethyl 3-(3,5-dimethoxyphenyl)-3-hydroxy-2-methylenepropanoate (123k)

This Baylis-Hillman alcohol was obtained as colorless viscous liquid *via* the treatment of of 3,5-dimethoxybenzaldehyde (**122e**) with ethyl acrylateunder the catalytical influence of DABCO following similar procedure described for molecule **123a**.



Reaction time : 10 d

Yield : 65%

IR (neat) : ν 3487, 1714, 1620 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.26 (t, 3H, *J* = 7.2 Hz), 3.11 (d, 1H, *J* = 6.0 Hz), 3.78 (s, 6H), 4.19 (q, 2H, *J* = 7.2 Hz), 5.48 (d, 1H, *J* = 6.0 Hz), 5.80 (s, 1H), 6.33 (s, 1H), 6.35-6.40 (m, 1H), 6.54 (d, 2H, *J* = 2.0 Hz)

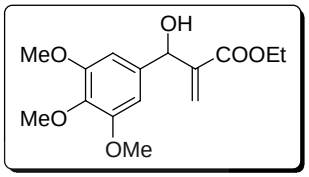
^{13}C NMR (100 MHz) : δ 14.12, 55.37, 61.03, 73.37, 99.82, 104.58, 126.20, 141.94, 143.93, 160.87, 166.44

Ethyl 3-hydroxy-2-methylene-3-(3,4,5-trimethoxyphenyl)propanoate (123l)

This compound was prepared as a solid *via* DABCO catalyzed Baylis-Hillman coupling of 3,4,5-trimethoxybenzaldehyde (**122f**) with ethyl acrylate, following a similar procedure described for the molecule **123a**.

Reaction time : 10 d

Yield : 69%



Mp : 86-88 ^{0}C

IR (KBr) : ν 3479, 1716, 1635 cm^{-1}

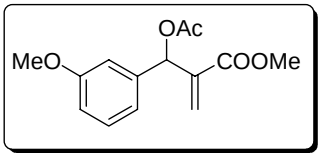
^{1}H NMR (400 MHz) : δ 1.27 (t, 3H, *J* = 7.2 Hz), 3.12 (br s, 1H), 3.83 (s, 3H), 3.84 (s, 6H), 4.20 (q, 2H, *J* = 7.2 Hz), 5.49 (s, 1H), 5.80 (s, 1H), 6.33 (s, 1H), 6.60 (s, 2H)

^{13}C NMR (100 MHz) : δ 14.07, 56.04, 60.76, 60.92, 73.14, 103.61, 125.76, 137.06, 137.37, 142.19, 153.15, 166.41

Methyl 3-acetoxy-3-(3-methoxyphenyl)-2-methylenepropanoate (124a)

To a stirred solution of methyl 3-hydroxy-3-(3-methoxyphenyl)-2-methylenepropanoate (**123a**) (20 mmol, 4.44 g) in dichloromethane (20 mL) was added pyridine (40 mmol, 3.14 g) followed by acetyl chloride (40 mmol, 3.16 g) at 0 ^{0}C and stirring continued at room temperature for 2 h. Reaction mixture was diluted with diethyl ether (50 mL) and 2N HCl (15 mL). Organic layer was separated and was washed successively with saturated aq. $NaHCO_3$ solution, water and dried over anhydrous Na_2SO_4. Crude product thus obtained after solvent evaporation, was purified by column chromatography (10% EtOAc in hexanes).

Reaction time : 2 h



Yield : 83% (4.38 g)

IR (neat) : ν 1745, 1718, 1633 cm^{-1}

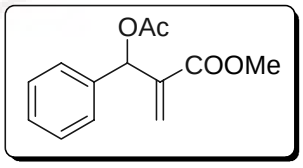
^{1}H NMR (400 MHz) : δ 2.121(s, 3H), 3.72 (s, 3H), 3.80 (s, 3H), 5.85 (s, 1H), 6.40 (s, 1H), 6.66 (s, 1H), 6.78-6.90 (m, 1H), 6.96 (d, 1H, *J* = 7.6 Hz), 7.25 (d, 1H, *J* = 8.8 Hz)

^{13}C NMR (100 MHz) : δ 21.17, 52.10, 55.31, 73.00, 113.44, 113.81, 120.03, 126.10, 129.59, 139.39, 139.64, 159.69, 165.51, 169.51

Methyl 3-acetoxy-2-methylene-3-phenylpropanoate (124b)

This was prepared as a colorless liquid *via* the treatment of methyl 3-hydroxy-2-methylene-3-phenylpropanoate (**123b)** with acetyl chloride in presence of pyridine following the similar procedure described for molecule **124a**.

Reaction time : 2 h



Yield : 79%

IR (neat) : ν 1743, 1726, 1633 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.10 (s, 3H), 3.70 (s, 3H), 5.85 (s, 1H), 6.39 (s, 1H), 6.81 (s, 1H), 7.25-7.42 (m, 5H)

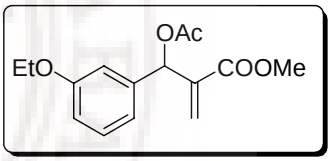
^{13}C NMR (100 MHz) : δ 21.16, 52.06, 73.21, 125.87, 127.74, 128.46, 128.54, 137.88, 139.77, 165.52, 169.50

Methyl 3-acetoxy-3-(3-ethoxyphenyl)-2-methylenepropanoate (124c)

This was prepared *via* the acetylation of Baylis-Hillman alcohol methyl 3-(3-ethoxyphenyl)-3-hydroxy-2-methylenepropanoate (**123c**)**,** with acetyl chloride in the presence of pyridine following the similar procedure described for molecule **124a**.

Reaction time : 2 h

Yield : 78%



IR (neat) : ν 1745, 1720, 1633 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.40 (t, 3H, *J* = 7.2 Hz), 2.10 (s, 3H), 3.71 (s, 3H), 4.02 (q, 2H, *J* = 7.2 Hz), 5.84 (s, 1H), 6.38 (s, 1H), 6.65 (s, 1H), 6.82 (dd, 1H, *J* = 2.0 Hz & 8.0 Hz), 6.88-6.92 (m, 1H), 6.94 (d, 1H, *J* = 7.6 Hz), 7.23 (d, 1H, *J* = 8.0 Hz)

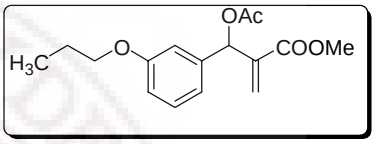
^{13}C NMR (100 MHz) : δ 14.83, 21.12, 52.04, 63.46, 73.00, 113.99, 114.27, 119.88, 126.01, 129.52, 139.33, 139.67, 159.05, 165.49, 169.46

Methyl 3-acetoxy-2-methylene-3-(3-propoxyphenyl)propanoate (124d)

This was prepared as a colorless liquid *via* the treatment of methyl 3-hydroxy-2-methylene-3-(3-propoxyphenyl)propanoate (**123d)** with acetyl chloride in presence of pyridine following the similar procedure described for molecule **124a**.

Reaction time : 2 h

Yield : 69%



IR (neat) : ν 1747, 1728, 1633 cm^{-1}

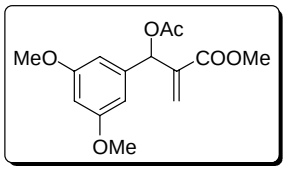
^{1}H NMR (400 MHz) : δ 1.03 (t, 3H, *J* = 7.6 Hz), 1.75-1.85 (m, 2H), 2.10 (s, 3H), 3.71 (s, 3H), 3.90 (t, 2H, *J* = 6.4 Hz), 5.84 (s, 1H), 6.39 (s, 1H), 6.65 (s, 1H), 6.83 (dd, 1H, *J* = 2.0 Hz & 8.0 Hz), 6.88-6.92 (m, 1H), 6.94 (d, 1H, *J* = 7.6 Hz), 7.22 (d, 1H, *J* = 8.0 Hz)

^{13}C NMR (100 MHz) : δ 10.58, 21.14, 22.64, 52.05, 69.53, 73.04, 114.00, 114.34, 119.84, 126.02, 129.51, 139.30, 139.68, 159.26, 165.52, 169.49

Methyl 3-acetoxy-3-(3,5-dimethoxyphenyl)-2-methylene propanoate (124e)

Treatment of methyl 3-(3,5-dimethoxyphenyl)-3-hydroxy-2-methylenepropanoate (**123e**) with acetyl chloride in the presence of pyridine following the similar procedure described for the molecule **124a** provided the title compound as a colorless viscous liquid.

Reaction time : 2 h



Yield : 72%

IR (neat) : ν 1747, 1714, 1630 cm^{-1}

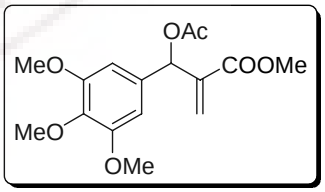
^{1}H NMR (400 MHz) : δ 2.10 (s, 3H), 3.72 (s, 3H), 3.77 (s, 6H), 5.83 (s, 1H), 6.38 (s, 2H), 6.51 (d, 2H, *J* = 2.0 Hz), 6.61 (s, 1H)

^{13}C NMR (100 MHz) : δ 21.15, 52.10, 55.42, 72.95, 100.27, 105.77, 126.31, 139.55, 140.15, 160.87, 165.53, 169.48

Methyl 3-acetoxy-2-methylene-3-(3,4,5-trimethoxyphenyl)propanoate (124f)

This was prepared as a colorless viscous liquid *via* the acetylation of methyl 3-hydroxy 3-(3,4,5-trimethoxyphenyl)-2-methylenepropanoate (**123f)** with acetyl chloride in the presence of pyridine following a similar procedure described for molecule **124a**.

Reaction time : 2 h



Yield : 82%

Mp : 63-65 ^{0}C

IR (KBr) : ν 1751, 1728, 1633 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.12 (s, 3H), 3.73 (s, 3H), 3.83 (s, 3H), 3.85 (s, 6H), 5.86 (s, 1H), 6.39 (s, 1H), 6.59 (s, 2H), 6.62 (s, 1H)

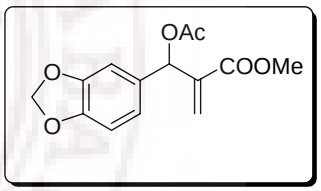
^{13}C NMR (100 MHz) : δ 21.19, 52.12, 56.20, 60.83, 73.21, 104.97, 125.76, 133.22, 138.15, 139.62, 153.29, 165.51, 169.49

Methyl 3-acetoxy-2-methylene-3-(3,4-methylenedioxyphenyl)propanoate (124g)

This compound was prepared as a colorless liquid *via* the treatment of methyl 3-hydroxy-2-methylene-3-(3,4-methylenedioxyphenyl)propanoate (**123g**) with acetyl chloride in presence of pyridine according to the similar procedure described for compound **124a**.

Reaction time : 2 h

Yield : 72%



IR (neat) : ν 1734, 1633 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.09 (s, 3H), 3.71 (s, 3H), 5.86 (s, 1H), 5.94 (s, 2H), 6.37 (s, 1H), 6.59 (s, 1H), 6.76 (d, 1H, *J* = 8.0 Hz), 6.80-6.92 (m, 2H)

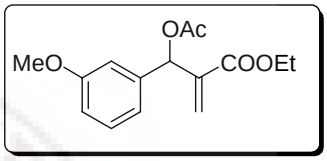
^{13}C NMR (100 MHz) : δ 21.13, 52.04, 72.95, 101.23, 108.18, 108.21, 121.75, 125.36, 131.57, 139.64, 147.72, 147.74, 165.42, 169.41

Ethyl 3-acetoxy-3-(3-methoxyphenyl)-2-methylenepropanoate (124h)

This compound was prepared as a colorless liquid *via* the treatment of ethyl 3-hydroxy-3-(3-methoxyphenyl)-2-methylenepropanoate (**123h**) with acetyl chloride, in the presence of pyridine, following a similar procedure described for the molecule **124a**.

Reaction time : 2 h

Yield : 74%



IR (neat) : ν 1747, 1722, 1620 cm^{-1}

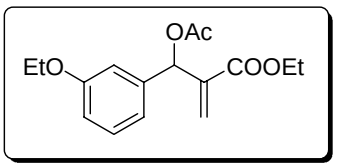
^{1}H NMR (400 MHz) : δ 1.23 (t, 3H, *J* = 7.08 Hz), 2.10 (s, 3H), 3.79 (s, 3H), 4.16 (q, 2H, *J* = 7.08 Hz), 5.81 (s, 1H), 6.39 (s, 1H), 6.66 (s, 1H), 6.81-6.88 (m, 1H), 6.91 (s, 1H), 6.96 (d, 1H, *J* = 7.6 Hz), 7.21-7.32 (m, 1H)

^{13}C NMR (100 MHz) : δ 14.08, 21.15, 55.27, 61.03, 73.03, 113.42, 113.78, 120.06, 125.82, 129.52, 139.44, 139.87, 159.63, 165.03, 169.49

Ethyl 3-acetoxy-3-(3-ethoxyphenyl)-2-methylene propanoate (124i)

Treatment of ethyl 3-(3-ethoxyphenyl)-3-hydroxy-2-methylenepropanoate (**123i**) with acetyl chloride in the presence of pyridine following the similar procedure described for the molecule **124a** provided the title compound as a colorless viscous liquid.

Reaction time : 2 h



Yield : 78%

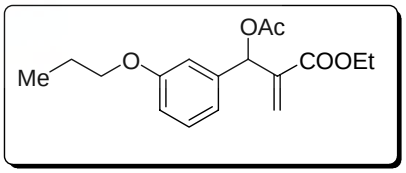
IR (neat) : ν 1747, 1722, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.22 (t, 3H, *J* = 7.2 Hz), 1.40 (t, 3H, *J* = 6.8 Hz), 2.10 (s, 3H), 4.01 (q, 2H, *J* = 6.8 Hz), 4.16 (q, 2H, *J* = 7.2 Hz), 5.81 (s, 1H), 6.38 (s, 1H), 6.65 (s, 1H), 6.82 (d, 1H, *J* = 8.2 Hz), 6.90 (s, 1H), 6.94 (d, 1H, *J* = 7.6 Hz), 7.22 (d, 1H, *J* = 7.6 Hz)

^{13}C NMR (100 MHz) : δ 14.07, 14.83, 21.12, 60.98, 63.44, 73.05, 113.99, 114.26, 119.95, 125.74, 129.47, 139.40, 139.93, 159.02, 165.03, 169.44

Ethyl 3-acetoxy-2-methylene-3-(3-propoxyphenyl)propanoate (124j)

This compound was obtained as a colorless liquid *via* the treatment of ethyl 3-hydroxy-2-methylene-3-(3-propoxyphenyl)propanoate (**123j**) with acetyl chloride, in the presence of Pyridine, following a similar procedure described for the molecule **124a**.



Reaction time : 2 h

Yield : 81%

IR (neat) : ν 1747, 1726, 1633 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.03 (t, 3H, *J* = 7.2 Hz), 1.23 (t, 3H, *J* = 7.2 Hz), 1.75-1.88 (m, 2H), 2.10 (s, 3H), 3.90 (t, 2H, *J* = 6.4 Hz), 4.16 (q, 2H, *J* = 7.2 Hz), 5.81 (s, 1H), 6.38 (s, 1H), 6.65 (s, 1H), 6.82 (d, 1H, *J* = 8.0 Hz), 6.90 (s, 1H), 6.94 (d, 1H, *J* = 7.2 Hz), 7.22 (d, 1H, *J* = 8.0 Hz)

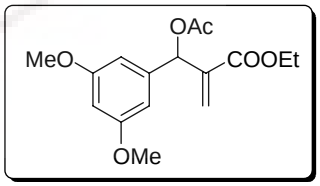
^{13}C NMR (100 MHz) : δ 10.56, 14.06, 21.12, 22.62, 60.99, 69.50, 73.08, 114.00, 114.31, 119.88, 125.74, 129.44, 139.36, 139.92, 159.22, 165.04, 169.47

Ethyl 3-acetoxy-3-(3,5-dimethoxyphenyl)-2-methylenepropanoate (124k)

Treatment of ethyl 3-(3,5-dimethoxyphenyl)-3-hydroxy-2-methylenepropanoate (**123k**) with acetyl chloride in the presence of pyridine following the similar procedure described for the molecule **124a** provided the title compound as a colorless viscous liquid.

Reaction time : 2 h

Yield : 81%



IR (neat) : ν 1745, 1718, 1620 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.24 (t, 3H, *J* = 7.2 Hz), 2.11 (s, 3H), 3.77 (s, 6H), 4.17 (q, 2H, *J* = 7.2 Hz), 5.80 (s, 1H), 6.39 (s, 2H), 6.52 (s, 2H), 6.62 (s, 1H)

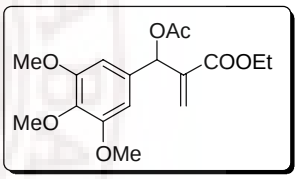
^{13}C NMR (100 MHz) : δ 14.11, 21.13, 55.38, 61.03, 72.98, 100.24, 105.76, 126.04, 139.79, 140.21, 160.82, 165.05, 169.45

Ethyl 3-acetoxy-2-methylene-3-(3,4,5-trimethoxyphenyl)propanoate (124l)

This was prepared *via* the acetylation of ethyl 3-hydroxy-2-methylene-3-(3,4,5-trimethoxyphenyl)propanoate (**123l)** with acetyl chloride in the presence of pyridine following a similar procedure described for molecule **124a** provided as a colorless viscous liquid.

Reaction time : 2 h

Yield : 85%



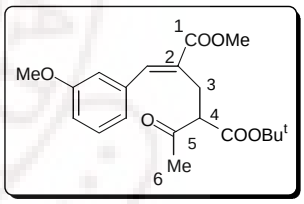
IR (neat) : ν 1745, 1718, 1637 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.24 (t, 3H, *J* = 7.2 Hz), 2.12 (s, 3H), 3.83 (s, 3H), 3.85 (s, 6H), 4.12-4.24 (m, 2H), 5.83 (s, 1H), 6.39 (s, 1H), 6.59 (s, 2H), 6.63 (s, 1H)

^{13}C NMR (100 MHz) : δ 14.15, 21.22, 56.19 60.86, 61.08, 73.28, 104.97, 125.54, 133.34, 138.08, 139.88, 153.27, 165.08, 169.52

Methyl 2-[(*E*)-(3-methoxybenzylidene)]-4-*tert*-butoxycarbonyl-5-oxohexanoate (126a)

To a stirred solution of methyl 3-acetoxy-3-(3-methoxyphenyl)-2-methylenepropanoate (3 mmol, 0.792 g) (**124a**) and *tert*-butyl acetoacetate (**125a**) (3.3 mmol, 0.521 g) in THF (3 mL) was added K_2CO_3 (3 mmol, 0.414 g) at room temperature and reaction mixture was stirred at the same temperature for 36 h. Reaction mixture was diluted with water (3 mL) and extracted with diethyl ether (3X30 mL). Combined organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and crude product obtained was purified by column chromatography (10% EtOAc in hexanes) to provide the title compound as a colorless liquid.



Reaction time : 36 h

Yield : 63% (0.758 g)

IR (neat) : ν 1745, 1712, 1631 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.37 (s, 9H), 2.14 (s, 3H), 3.00 & 3.22 (d of ABq, 2H, *J* = 14.6 Hz & 7.2 Hz [8.4 Hz]), 3.70-3.90 (m, 7H), 6.83-6.90 (m, 1H), 6.93-7.00 (m, 2H), 7.20-7.33 (m, 1H), 7.72 (s, 1H) in addition to the above peaks, low intensity (5-7%) peaks at δ 1.45 (s), 2.27 (s), 3.64 (s), 6.70-6.82 (m), 7.18-7.22 (m)

The underlined chemical shift values with low intensity in ^{1}H NMR spectrum indicate the presence of its minor enolic isomer in the compound.

^{13}C NMR (100 MHz) (Major isomer) : δ 25.53, 27.73, 28.68, 52.04, 55.29, 58.91, 82.09, 114.25 114.78, 121.74, 129.42, 129.56, 136.22, 141.37, 159.62, 168.12, 168.61, 202.47

LCMS (m/z) : 363 $(M+H)^+$

Anal calc′d for $C_{20}H_{26}O_6$: C, 66.28; H, 7.23

Found : C, 66.35; H, 7.18

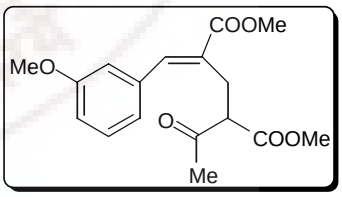
Methyl 2-[(*E*)-(3-methoxybenzylidene)]-4-methoxycarbonyl-5-oxohexanoate (126b)

This was obtained as a colorless liquid *via* the alkylation of methyl 3-acetoxy-3-(3-methoxyphenyl)-2-methylenepropanoate (**124a**) with methyl acetoacetate (**125b**) in presence of K_2CO_3 at room temperature following a similar procedure described for molecule **126a**.

Reaction time : 15 h

Yield : 86%

IR (neat) : ν 1743, 1714, 1629 cm^{-1}



^{1}H NMR (400 MHz) : δ 2.15 & 2.28 (2s, 3H), 3.08 & 3.20 (d of ABq, 2H, *J* = 14.6 Hz & 6.4 Hz [8.4 Hz]), 3.50-3.9 (m, 10H)*, 6.70-7.00 (m, 3H), 7.29-7.35 (m, 1H), 7.74 (s, 1H)

* This multiplet contains δ 3.55 (s), 3.59 (s), 3.65 (s), 3.72-3.91 (m)

The underlined chemical shift values with low intensity in ^1H NMR spectrum indicate the presence of its minor enolic isomer in the compound

^{13}C NMR (100 MHz) (Major keto form) : δ 25.67, 28.86, 52.14, 52.34, 55.31, 58.07, 114.26, 114.62, 121.51, 129.20, 129.64, 136.24, 141.80, 159.67, 168.03, 169.76, 202.08

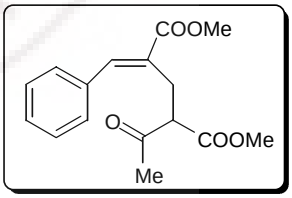
LCMS (m/z) : 321 $(M+H)^+$

Anal calc′d for $C_{17}H_{20}O_6$: C, 63.74; H, 6.29

Found : C, 63.68; H, 6.33

Methyl 2-[(*E*)-(benzylidene)]-4-methoxycarbonyl-5-oxohexanoate (126c)

This was obtained as a colorless liquid *via* the reaction of methyl acetoacetate (**125b**) with methyl 3-acetoxy-2-methylene-3-phenylpropanoate (**124b**) in presence of K_2CO_3 at room temperature following a similar procedure described for molecule **126a**.



Reaction time : 15 h

Yield : 76%

IR (neat) : ν 1743, 1716, 1631 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.13 & 2.28 (2s, 3H), 3.08$ & 3.20 (d of ABq, 2H, *J* = 14.6 Hz & 6.8 Hz [8.4 Hz]), 3.53-3.87 (m, 7H)* , 7.16-7.43 (m, 5H), 7.77 (s, 1H)

$ The first part of the (d of ABq), further splits into doublet (*J* = 0.8 Hz) due to allylic coupling

*This multiplet contains 3.56 (s), 3.63 (s), 3.73 (s), 3.81 (s), 3.82-3.86 (m)

The underlined chemical shift values with low intensity in ^{1}H NMR spectrum indicate the presence of minor enol form of the compound

^{13}C NMR (100 MHz) (Major isomer) : δ 25.50, 28.76, 52.11, 52.28, 58.12, 128.59, 128.71, 129.01, 129.06, 134.95, 141.89, 168.01, 169.69, 202.01

LCMS (m/z) : 291 $(M+H)^+$

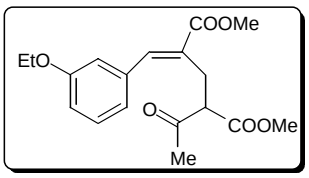
Anal calc′d for $C_{16}H_{18}O_5$: C, 66.19; H, 6.25

Found : C, 66.27; H, 6.21

Methyl 2-[(*E*)-(3-ethoxybenzylidene)]-4-methoxycarbonyl-5-oxohexanoate (126d)

This was obtained as a colorless liquid *via* the treatment of methyl acetoacetate (**125b**) with methyl 3-acetoxy-3-(3-ethoxyphenyl)-2-methylenepropanoate (**124c**) in presence of K_2CO_3 following the similar procedure described for the molecule **126a**.

Reaction time : 15 h



Yield : 85%

IR (neat) : ν 1739, 1722, 1624 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.38-1.46 (m, 3H), 2.14 & 2.28 (2s, 3H), 3.07[$] & 3.20 (d of ABq, 2H, *J* = 14.6 Hz & 6.4 Hz [8.4 Hz]), 3.50-4.10 (m, 9H)*, 6.70-6.96 (m, 3H), 7.15-7.35 (m, 1H), 7.74 (s, 1H)

[$]The first part of (d of ABq) further splits into doublet (*J* = 0.8 Hz), due to allylic coupling.

*This multiplet contains 3.59 (s), 3.64 (s), 3.73 (s), 3.81 (s), 3.82-3.87 (m), 4.04 (q, *J* = 6.96 Hz)

^{13}C NMR (100 MHz) (Major isomer) : δ 14.87, 25.73, 28.91, 52.22, 52.40, 58.20, 63.59, 114.87, 115.28, 121.43, 129.17, 129.69, 136.28, 142.00, 159.10, 168.13, 169.82, 202.16

The underlined chemical shift values with low intensity in ^{1}H NMR spectrum indicate the presence of its minor enolic isomer in the compound

LCMS (m/z) : 335 $(M+H)^{+}$

Anal calc′d for $C_{18}H_{22}O_6$: C, 64.66; H, 6.63

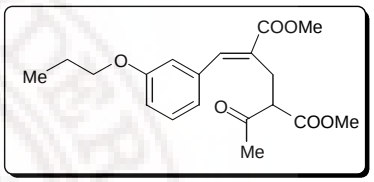
Found : C, 64.72; H, 6.59

Methyl 4-methoxycarbonyl-2-[(*E*)-(3-propoxybenzylidene)]-5-oxohexanoate (126e)

Treatment of methyl 3-acetoxy-2-methylene-3-(3-propoxyphenyl)propanoate (**124d**) with methyl acetoacetate (**125b**) in presence of K_2CO_3 following the similar procedure described for the molecule **126a** provided methyl 4-methoxycarbonyl-2-[(*E*)-(3-propoxybenzylidene)]-5-oxohexanoate (**126e**) as a colorless liquid.

Reaction time : 15 h

Yield : 75%



IR (neat) : ν 1739, 1718, 1631 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.03 (t, 3H, *J* = 7.2 Hz), 1.76-1.87 (m, 2H), 2.14 & 2.28 (2s, 3H), 3.08 & 3.20 (d of ABq, 2H, *J* = 14.2 Hz & 6.8 Hz [8.4 Hz]), 3.50-3.96 (m, 9H)*, 6.72-6.95 (m, 3H), 7.16-7.32 (m, 1H), 7.74 (s, 1H)

This multiplet contains δ 3.59 (s), 3.64 (s), 3.73 (s), 3.81 (s), 3.82-3.96 (m)

The underlined chemical shift values with low intensity in ^{1}H NMR spectrum indicate the presence of its minor enolic isomer (7-10%) in the compound

^{13}C NMR (100 MHz) (Major isomer) : δ 10.49, 22.55, 25.66, 28.82, 52.13, 52.32, 58.14, 69.57, 114.85, 115.22, 121.29, 129.10, 129.61, 136.19, 141.90, 159.22, 168.05, 169.74, 202.06

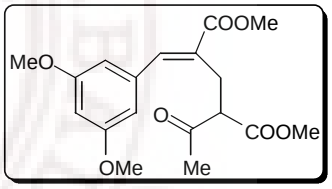
LCMS (m/z) : 349 $(M+H)^+$

Anal calc′d for $C_{19}H_{24}O_6$: C, 65.50; H 6.94

Found : C, 65.41; H, 6.98

Methyl 2-[(*E*)-(3,5-dimethoxybenzylidene)]-4-methoxycarbonyl-5-oxohexanoate (126f)

This product was obtained as a colorless liquid, *via* the treatment of methyl 3-acetoxy-3-(3,5-dimethoxyphenyl)-2-methylene propanoate (**124e**) with methyl acetoacetate (**125b**) in presence of K_2CO_3 in THF at room temperature following the similar procedure described for the molecule **126a**.



Reaction time : 15 h

Yield : 82%

IR (neat) : ν 1745, 1720, 1624 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.16 & 2.28 (2s, 3H), 3.07$^{\$}$ & 3.19 (d of ABq, 2H, *J* = 14.2 Hz & 6.4 Hz [8.4 Hz]), 3.58-3.92 (m, 13H)*, 6.30-6.56 (m, 3H), 7.70 (s, 1H)

$^{\$}$The first part of the (d of ABq), further splits into doublet (*J* = 0.8 Hz), due to allylic coupling

*This multiplet contains δ 3.62 (s), 3.66 (s), 3.72-3.78 (m), 3.79 (s), 3.81 (s), 3.82-3.92 (m)

The underlined chemical shift values with low intensity in ^{1}H NMR spectrum indicate the presence minor enolic isomer (6-7%) of the compound

^{13}C NMR (100 MHz) (Major isomer) : δ 25.85, 28.98, 52.20, 52.41, 55.49, 58.07, 101.13, 106.99, 129.40, 136.76, 141.95, 160.89, 168.06, 169. 84, 202.17

LCMS (m/z) : 351 $(M+H)^+$

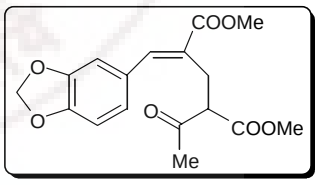
Anal calc′d for $C_{18}H_{22}O_7$: C, 61.71; H, 6.33

Found : C, 61.65; H, 6.38

Methyl 4-methoxycarbonyl-2-[(*E*)-(3,4-methylenedioxybenzylidene)]-5-oxohexano-ate (126g)

Reaction of methyl acetoacetate (**125b**) with methyl 3-acetoxy-2-methylene-3-(3,4-methylenedioxyphenyl)propanoate (**124g**) in the influence of K_2CO_3 at room temperature following the similar procedure described for molecule **126a**.

Reaction time : 15 h



Yield : 79%

IR (neat) : ν 1739, 1720, 1622 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.18 (s, 3H), 3.08 & 3.19 (d of ABq, 2H, *J* = 14.2 Hz & 6.4 Hz [8.0 Hz]), 3.58-3.92 (m, 7H), 5.99 (s, 2H), 6.82 (d, 1H, *J* = 8.0 Hz), 6.89 (dd, 1H, *J* = 8.0 Hz & 1.2 Hz), 6.93 (d, 1H, *J* = 1.2 Hz), 7.67 (s, 1H) in addition to the above peaks

at δ 2.27 (s), 5.95 (s), 6.64-6.75 (m) are due to minor enol isomer also observed

The underlined chemical shift values with low intensity in ^{1}H NMR spectrum indicate the presence of its minor enolic isomer (6-7%) in the compound

^{13}C NMR (100 MHz) isomer) : δ 25.63, 28.98, 52.10, 52.38, 58.06, 101.43, 108.52, (Major 109.18, 124.28, 127.41, 128.84, 141.60, 147.96, 148.18, 168.22, 169.80, 202.19

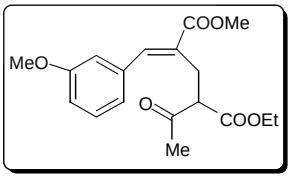
LCMS (m/z) : 333 $(M-H)^+$

Anal calc′d for $C_{17}H_{18}O_7$: C, 61.07; H, 5.43

Found : C, 61.18; H, 5.48

Methyl 4-ethoxycarbonyl-2-[(*E*)-(3-methoxybenzylidene)]-5-oxohexanoate (126h)

This was obtained as a colorless liquid *via* the alkylation of methyl 3-acetoxy-3-(3-methoxyphenyl)-2-methylenepropanoate (**124a**) with ethyl acetoacetate (**125c**) in presence of K_2CO_3 at room temperature following the similar procedure described for molecule **126a**.



Reaction time : 15 h

Yield : 75%

IR (neat) : ν 1739, 1712, 1631 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.17 (t, 3H, *J* = 7.2 Hz), 2.17 (s, 3H), 3.08$ & 3.23 (d of AB q, 2H, *J* = 14.6 Hz & 6.8 Hz [8.0 Hz]), 3.70-4.20 (m, 9H), 6.85-6.95 (m, 3H), 7.28-7.34 (m, 1H), 7.75 (s, 1H) in addition to the above peaks 1.29 (t, *J* = 7.2 Hz), 2.28 (s), 6.70-6.81 (m), 7.15-7.24 (m)

The underlined chemical shift values with low intensity in ^{1}H NMR spectrum indicate the presence of its minor enolic isomer (4-5%) in the compound

^{13}C NMR (100 MHz) (Major isomer) : δ 13.87, 25.59, 28.78, 52.10, 55.27, 58.13, 61.43, 114.23, 114.60, 121.55, 129.22, 129.60, 136.20, 141.66, 159.62, 168.02, 169.32, 202.16

LCMS (m/z) : 335 $(M+H)^{+}$

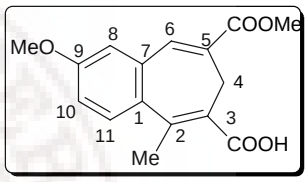
Anal calc′d for $C_{18}H_{22}O_6$: C, 64.66; H, 6.63

Found : C, 64.74; H, 6.58

9-Methoxy-5-methoxycarbonyl-2-methylbicyclo[5.4.0]undeca-1(7),2,5,8,10-penta-ene-3-carboxylicacid (128a)

To a stirred solution of methyl 2-[(*E*)-(3-methoxybenzylidene)]-4-*tert*-butoxycarbonyl-5-oxohexanoate (**126a**) (1 mmol, 0.362 g) in dichloromethane (3 mL) was added methanesulfonic acid (4 mmol, 0.384 g) at room temperature and stirring continued at room temperature for 12 h. Reaction mixture was diluted with water (3 mL), and extracted

with ethyl acetate (3X15 mL). Combined organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and the crude product thus obtained was purified by column chromatography in 80% EtOAc in hexanes to provide the title compound in 61% (0.176 g) isolated yield.



Reaction time : 12 h

Yield : 61%

Mp : 178-180 ^{0}C

IR (KBr) : ν 3200-3000, 1705, 1658 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.45 (s, 3H), 2.94 (s, 2H), 3.87 (s, 6H), 6.91 (d, 1H, *J* = 2.4 Hz), 7.00 (dd, 1H, *J* = 2.4 Hz & 8.8 Hz), 7.60 (s, 1H), 7.62 (d, 1H, *J* = 8.8 Hz)

^{13}C NMR (100 MHz) : δ 21.77, 26.73, 52.50, 55.48, 113.23, 115.55, 126.75, 130.71, 133.89, 135.32, 136.50, 136.92, 145.55, 158.42, 167.08, 171.47

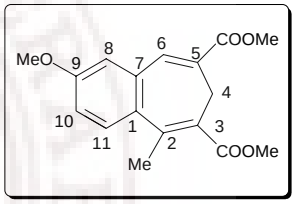
LCMS (m/z) : 287 $(M-H)^+$

Anal calc′d for $C_{16}H_{16}O_5$: C, 66.66; H, 5.59

Found : C, 66.75; H, 5.56

3,5-Dimethoxycarbonyl-9-methoxy-2-methylbicyclo[5.4.0]undeca-1(7),2,5,8,10-pentaene (128b)

This was obtained as a colorless solid *via* the treatment of methyl 2-[(*E*)-(3-methoxybenzylidene)]-4-methoxycarbonyl-5-oxohexanoate (**126b**), with methanesulfon-ic acid at room temperature following the similar procedure described for compound **128a**.



Reaction time : 12 h

Yield : 71%

Mp : 76-78 ^{0}C

IR (KBr) : ν 1707, 1635, 1608 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.37 (s, 3H), 2.92 (s, 2H), 3.81 (s, 3H), 3.84 (s, 3H), 3.86 (s, 3H), 6.89 (d, 1H, *J* = 2.4 Hz), 6.98 (dd, 1H, *J* = 2.4 Hz & 8.8 Hz), 7.57-7.65 (m, 2H)

^{13}C NMR (100 MHz) : δ 21.11, 26.60, 51.72, 52.08, 55.31, 113.24, 115.30, 127.30, 130.39, 134.02, 134.93, 136.46, 136.97, 142.43, 158.13, 166.11, 168.10

LCMS (m/z) : 303 $(M+H)^{+}$

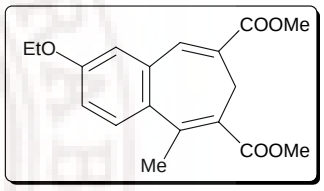
Anal calc′d for $C_{17}H_{18}O_5$: C, 67.54; H, 6.00

Found : C, 67.62; H, 5.96

In addition to the ester compound **128b,** we have also isolated **128a**, in 16% yield

3,5-Dimethoxycarbonyl-9-ethoxy-2-methylbicyclo[5.4.0]undeca-1(7),2,5,8,10-penta-ene (128c)

This was obtained as a colorless solid *via* the treatment of methyl 2-[(*E*)-(3-ethoxybenzylidene)]-4-methoxycarbonyl-5-oxo-hexanoate (**126d**) with methanesulfonic acid following the similar procedure described for molecule **128a**.



Reaction time : 12 h

Yield : 74%

Mp : 64-66 ^{0}C

IR (KBr) : ν 1714, 1705, 1602 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.44 (t, 3H, *J* = 7.2 Hz), 2.37 (s, 3H), 2.92 (s, 2H), 3.81 (s, 3H), 3.84 (s, 3H), 4.08 (q, 2H, *J* = 7.2 Hz), 6.87 (d, 1H, *J* = 2.8 Hz), 6.97 (dd, 1H, *J* = 2.8 Hz & 8.8 Hz), 7.55-7.63 (m, 2H), 7.58 (s, 1H)*, 7.59 (d, 1H, *J* = 8.8 Hz)*

* (The doublet and singlet overlap some extent)

^{13}C NMR (100 MHz) : δ 14.76, 21.13, 26.62, 51.73, 52.09, 63.60, 113.84, 115.74, 127.22, 130.39, 133.94, 134.81, 136.47, 137.05, 142.53, 157.55, 166.16, 168.14

LCMS (m/z) : 315 $(M-H)^{+}$

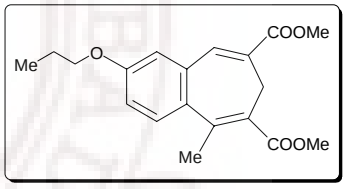
Anal calc′d for $C_{18}H_{20}O_5$: C, 68.34; H, 6.37

Found : C, 68.45; H, 6.33

In addition to this we have also isolated corresponding acid in 10% in impure form.

3,5-Dimethoxycarbonyl-2-methyl-9-propoxybicyclo[5.4.0]undeca-1(7),2,5,8,10-pentaene (128d)

This compound was obtained as a colorless liquid *via* the reaction of methyl 4-methoxycarbonyl-2-[(*E*)-(3-propoxybenzylidene)]-5-oxohexanoate (**126e**) with methanesulfonic acid following similar procedure described for the molecule **128a**.



Reaction time : 12 h

Yield : 75%

IR (neat) : ν 1714, 1705, 1633 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.05 (t, 3H, *J* = 7.6 Hz), 1.78-1.88 (m, 2H), 2.37 (s, 3H), 2.92 (s, 2H), 3.81 (s, 3H), 3.84 (s, 3H), 3.97 (t, 2H, *J* = 6.4 Hz), 6.88 (d, 1H, *J* = 2.4 Hz), 6.97 (dd, 1H, *J* = 2.4 Hz & 8.8 Hz), 7.56-7.64 (m, 2H)

^{13}C NMR (100 MHz) : δ 10.50, 21.15, 22.51, 26.62, 51.74, 52.10, 69.62, 113.84, 115.77, 127.18, 130.38, 133.92, 134.77, 136.46, 137.08, 142.57, 157.74, 166.16, 168.15

LCMS (m/z) : 331 $(M+H)^{+}$

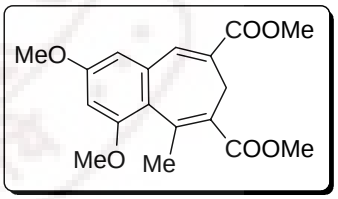
Anal calc′d for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71

Found : C, 69.15; H, 6.68

In addition to this we have also isolated corresponding acid in 10% impure form

9,11-Dimethoxy-3,5-dimethoxycarbonyl-2-methylbicyclo[5.4.0]undeca-1(7),2,5,8,10-pentaene (128e)

Treatment of methyl 2-[(*E*)-(3,5-dimethoxybenzylidene)]-4-methoxycarbonyl-5-oxo-hexanoate (**126f**) with methanesulfonic acid, following the similar procedure described for the molecule **128a**, provided the title compound 9,11-dimethoxy-3,5-dimethoxycarbonyl-2-methylbicyclo[5.4.0]undeca-1(7),2,5,8,10-pentaene **(128e)** as a colorless solid.



Reaction time : 12 h

Yield : 67%

Mp : 102-104 ^{0}C

IR (KBr) : ν 1716, 1699, 1628 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.00* (d, 1H, *J* = 13.2 Hz), 2.24 (s, 3H), 3.78 (s, 3H), 3.82-3.90 (m, 10 H), 6.50 (s, 1H), 6.52 (s, 1H), 7.57 (s, 1H)

*Another doublet of CH_2 protons merges with singlets of methoxy protons and these appears as multiplet

^{13}C NMR (100 MHz) : δ 21.54, 27.00, 51.55, 52.08, 55.39, 55.65, 99.59, 104.13, 125.93, 128.66, 136.06, 136.58, 136.90, 142.64, 158.99, 158.29, 166.21, 167.61

LCMS (m/z) : 333 $(M+H)^+$

Anal calc′d for $C_{18}H_{20}O_6$: C, 65.05; H, 6.07

Found : C, 65.12; H, 6.11

In addition to this we have also isolated corresponding acid in 10% impure form

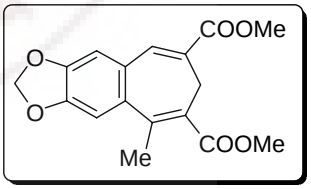
3,5-Dimethoxycarbonyl-2-methyl-9,10-methylenedioxybicyclo[5.4.0]undeca-1(7),2,-5,8,10-pentaene (128f)

This compound was obtained as a colorless solid *via* reaction of methyl 4-methoxycarbonyl-2-[(*E*)-(3,4-methylenedimethoxybenzylidene)]-5-oxohexanoate (**126g**) with methanesulofonic acid similar procedure described for compound **128a**.

Reaction time : 12 h

Yield : 61%

Mp : 138-140 ^{0}C



IR (KBr) : ν 1697, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.33 (s, 3H), 2.88 (s, 2H), 3.80 (s, 3H), 3.83 (s, 3H), 6.04 (s, 2H), 6.83 (s, 1H), 7.08 (s, 1H), 7.51 (s, 1H)

^{13}C NMR (100 MHz) : δ 21.19, 26.72, 51.77, 52.01, 101.68, 108.11, 108.72, 127.17, 130.13, 131.63, 136.60, 137.39, 141.37, 146.85, 147.61, 166.07, 168.03

LCMS (m/z) : 315 $(M-H)^+$

Anal calc′d for $C_{17}H_{16}O_6$: C, 64.55; H, 5.10

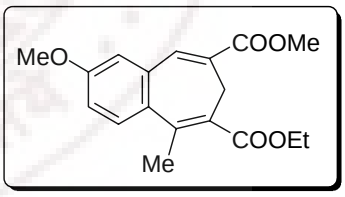
Found C, 64.48; H, 5.13

In addition to this we have also isolated corresponding acid in 10% impure form

3-Ethoxycarbonyl-9-methoxy-5-methoxycarbonyl-2-methylbicyclo[5.4.0]undeca-1(7),-2,5,8,10-pentaene (128g)

This compound was obtained as a colorless liquid *via* the reaction with methyl 4-ethoxycarbonyl-2-[(*E*)-(3-methoxybenzylidene)]-5-oxohexanoate (**126h**) and $MeSO_3H$ following the similar procedure described for molecule **128a**.

Reaction time : 12 h



Yield : 75%

IR (neat) : ν 1712, 1604 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.35 (t, 3H, *J* = 7.2 Hz), 2.36 (s, 3H), 2.92 (s, 2H), 3.84 (s, 3H), 3.86 (s, 3H), 4.26 (q, 2H, *J* = 7.2 Hz), 6.89 (d, 1H, *J* = 2.8 Hz), 6.98 (dd, 1H, *J* = 2.8 Hz & 8.8 Hz), 7.59 (d, 1H, *J* = 8.8 Hz), 7.60 (s, 1H)

^{13}C NMR (100 MHz) : δ 14.22, 20.98, 26.70, 52.06, 55.33, 60.56, 113.24, 115.30, 127.64, 130.38, 134.10, 135.00, 136.45, 136.96, 141.86, 158.09, 166.13, 167.76

LCMS (m/z) : 315 $(M-H)^+$

Anal calc′d for $C_{18}H_{20}O_5$: C, 68.34; H, 6.37

Found : C, 68.27; H, 6.40

In addition to this we have also isolated **128a** in10% pure form.

Preparation of phenyl acetyl Meldrum's acid

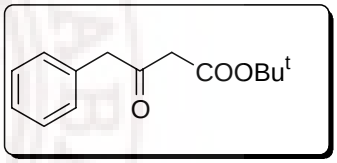
This compound was prepared according to the literature procedure with slight modification[223]

To a stirred solution of Meldrum's acid (100 mmol, 14.40 g) in dry dichloromethane (100 mL), pyridine (200 mmol, 15.82 g) was added at room temperature over a time period of 10 min. The reaction mixture was cooled to 0 ^{0}C and freshly distilled phenylacetyl chloride (110 mmol, 17.00 g) was added drop wise at 0 ^{0}C. After stirring for 1h at 0 ^{0}C and then at room temperature for 1 h the reaction mixture was diluted with dichlo-romethane (50 mL) and washed successively with 2N HCl (2X30 mL), brine solution (100 mL), and water (100 mL). Organic layer was dried over Na_2SO_4. Crude product was obtained, after solvent evaporation was used for the next step with out purification.

tert-Butyl 3-oxo-4-phenylbutanoate (129a)

This was prepared according to the literature procedure with slight modification[223]

The crude phenylacetyl Meldrum's acid (50 mmol, 13.10 g) prepared as above was dissolved in *tert*-BuOH (300 mmol, 22.23 g) at room temperature and reaction mixture was heated under reflux (at 85 ^{0}C) for 3 h. Reaction mixture was allowed to come to room temperature. *tert*-BuOH was removed under reduced pressure. The crude thus obtained, was further purified by column chromatography (10% EtOAc in hexanes) to provide the title compound as a colorless liquid in 52% (6.12 g) isolated yield.



Reaction time : 3 h

Yield : 52%

IR (neat) : ν 3435, 1738, 1718 cm^{-1}

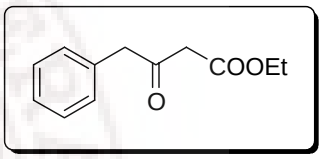
^{1}H NMR (400 MHz) : δ 1.44 (s, 9H), 3.37 (s, 2H), 3.81 (s, 2H), 7.12-7.35 (m, 5H), in addition of these major peaks some of the minor singlets at δ 1.43 (s), 3.38 (s), 3.39 (s), 4.91 (s), 12.3 (s) indicates the presence of enol form (4-6%) of the compound

The underlined chemical shift values with low intensity in ^{1}H NMR spectrum indicate the presence of its minor enolic isomer in the compound

^{13}C NMR (100 MHz) (Major keto form) : δ 27.98, 49.61, 49.96, 82.06, 127.29, 128.82, 129.61, 133.42, 166.35, 200.92

Ethyl 3-oxo-4-phenylbutanoate (129b)

Thus crude phenylacetyl Meldrums acid (50 mmol, 13.10 g), was dissolved in EtOH (300 mmol, 13.82 g), at room temperature and reaction mixture was heated at 85 ^{0}C for 3 h. Reaction mixture was allowed to come to room temperature. EtOH was removed under reduced pressure and purified by column-chromatography (10% EtOAc in hexanes) to provide the title compound as a pale yellow liquid in 57% (5.86 g) isolated yield.[223]



Reaction time : 3 h

Yield : 57%

IR (neat) : ν 3437, 1741, 1718 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.25 (t, 3H, *J* = 7.2 Hz), 3.44 (s, 2H), 3.82 (s, 2H), 4.16 (q, 2H, *J* = 7.16 Hz), 7.17-7.43 (m, 5H) in addition peaks at δ 3.50 (s, 2H), 3.69 (s, 2H), 4.91 (s, 1H), 12.13 (s) indicates the minor enol form (30%) in the compound

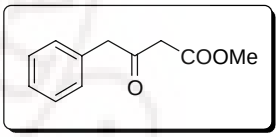
The underlined chemical shift values with low intensity in ^{1}H NMR spectrum indicate the presence of its minor enolic isomer in the compound

^{13}C NMR (100 MHz) : δ 14.13, 14.27, 41.48, 48.35, 50.10, 51.09, 60.13, 61.47, 90.27, 127.12, 127.16, 127.42, 128.67, 128.82, 128.91, 129.34, 129.45, 129.63, 133.29, 134.32, 135.65, 167.15, 177.10, 200.52 mixture of keto enol forms present in the

compound) [More carbons are observed, may be due to possibility of formation of *Cis*/*Trans* enol isomers]

Methyl 3-oxo-4-phenylbutanoate (129c)

Thus crude phenylacetyl Meldrum's acid (50 mmol, 13.10 g) was dissolved in MeOH (300 mmol, 9.61 g) at room temperature and reaction mixture was heated at 85 ^{0}C for 3 h. Reaction mixture was allowed to come to room temperature. Then MeOH was removed under reduced pressure. Residue thus obtained was purified by column-chromatography (10% EtOAc in hexanes) to provide the title compound in 53% (5.12 g) isolated yield.[223]



Reaction time : 3 h

Yield : 53%

IR (neat) : ν 3032, 1739, 1714 cm^{-1}

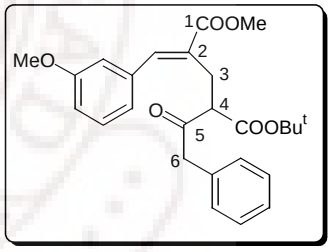
^{1}H NMR (400 MHz) : δ 3.45 (s, 2H), 3.70 (s, 3H), 3.82 (s, 2H), 7.15-7.38 (m, 5H), in addition to the above peaks we have also observed peaks at 3.50 (s), 4.93 (s, 2H), 12.03 (s)

The underlined chemical shift values with low intensity in ^{1}H NMR and ^{13}C NMR spectra indicate the presence of its minor enol form (4-5%) in the compound

^{13}C NMR (100 MHz) : δ 41.12, 48.04, 50.12, 52.41, 127.00 127.46, 128.67, 128.94, 129.31, 129.61, 133.21, 167.59, 200.42

Methyl 2-[(*E*)-(3-methoxybenzylidene)]-4-*tert*-butoxycarbonyl-5-oxo-6-phenylhexanoate (**130a**)

To a stirred solution of methyl 3-acetoxy-3-(3-methoxyphenyl)-2-methylenepropanoate (**124a**) (3 mmol, 0.792 g) and of *tert*-butyl 3-oxo-4-phenylbutanoate (**129a**) (3.6 mmol, 0.842 g) in THF (3 mL) was added K_2CO_3 (3 mmol, 0.414 g) at room temperature and reaction mixture was stirred at the same temperature for 36 h. Reaction mixture was diluted with water (3 mL) and extracted with diethyl ether (3X30 mL). Combined organic layer was dried over anhydrous Na_2SO_4. Crude product, obtained after solvent evaporation was purified by column chromatography (15% EtOAc in hexanes) to provide the title compound as a colorless liquid.



Reaction time : 36 h

Yield : 62% (0.815 g)

IR (neat) : ν 1732, 1720, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.36 (s, 9H), 3.03 & 3.21 (d of ABq, 2H, *J* = 14.8 Hz & 7.2 Hz [8.0 Hz]), 3.75 (s, 5H), 3.80 (s, 3H), 3.96 (t, 1H, *J* = 7.6 Hz), 6.83-6.90 (m, 1H), 6.91-6.99 (m, 2H), 7.13 (d, 2H, *J* = 6.8 Hz), 7.21-7.34 (m, 4H), 7.67 (s, 1H)

^{13}C NMR (100 MHz) : δ 25.75, 27.87, 49.12, 52.07, 55.39, 57.11, 82.31, 114.32, 114.93, 121.83, 127.12, 128.65, 129.37, 129.62,

129.72, 133.41, 136.29, 141.52, 159.69, 168.18, 168.39, 202.16

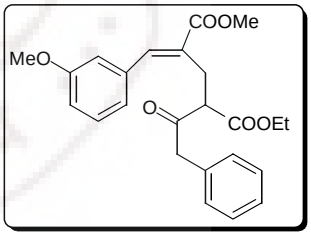
LCMS (m/z) : 437 $(M-H)^+$

Anal calc′d for $C_{26}H_{30}O_6$: C, 71.21; H, 6.90

Found : C, 71.25; H, 6.87.

Methyl 4-ethoxycarbonyl-2-[(*E*)-(3-methoxybenzylidene)]-5-oxo-6-phenylhexanoate (130b)

This was obtained as a colorless liquid *via* the treatment of ethyl 3-oxo-4-phenylbutanoate (**129b**) with methyl 3-acetoxy-3-(3-methoxyphenyl)-2-methylen-epropanoate (**124a**) in presence of K_2CO_3 at room temperature following a similar procedure described for molecule **130a**.



Reaction time : 24 h

Yield : 72%

IR (neat) : ν 1741, 1716, 1638 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.12 & 1.23 (2t, 3H, *J* = 7.2 Hz), 3.09 & 3.19 (d of ABq, 2H, *J* = 14.6 Hz & 6.8 Hz [8.0 Hz]), 3.55-4.20 (m, 11H)*, 6.65-6.94 (m, 3H), 7.08-7.36 (m, 6H), 7.69 (s, 1H)

* This multiplet contains δ 3.59 (s), 3.75 (s), 3.80 (s), 3.85-4.20 (m)

^{13}C NMR (100 MHz) (Major keto form) : δ 13.94, 25.77, 49.14, 52.12, 55.37, 56.44, 61.57, 114.30, 114.77, 121.65, 127.19, 128.66, 129.17, 129.66, 129.70, 133.25, 136.27, 141.79, 159.69, 168.08, 169.15, 201.84

The underlined chemical shift values with low intensity in ^{1}H NMR spectrum indicate the presence of its minor enolic isomer in the compound

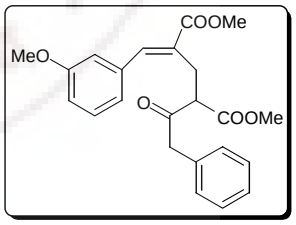
LCMS (m/z) : 411 $(M+H)^+$

Anal calc′d for $C_{24}H_{26}O_6$: C, 70.23; H, 6.38

Found : C, 70.29; H, 6.33

Methyl 2-[(*E*)-(3-methoxybenzylidene)]-4-methoxycarbonyl-5-oxo-6-phenylhexanoate (130c)

This was obtained as a colorless liquid *via* the reaction of methyl 3-acetoxy-3-(3-methoxyphenyl)-2-methylenepropanoate (**124a**) with methyl 3-oxo-4-phenylbutanoate (**129c**) in presence of K_2CO_3 at room temperature, following the similar procedure described for molecule **130a**.



Reaction time : 20 h

Yield : 78%

IR (neat) : ν 1743, 1714, 1637 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.09 & 3.18 (d of ABq, 2H, *J* = 14.4 Hz & 6.8 Hz [8.0 Hz]), 3.53-4.07 (m, 12H)*, 6.65-6.93 (m, 3H), 7.08-7.34 (m, 6H), 7.69 (s, 1H)

* This multplet contains δ 3.54 (s), 3.59 (s), 3.68 (s), 3.74 (s), 3.75 (s), 3.77 (s), 3.79 (s), 3.85-3.92 (m), 3.98-4.07 (m)

The underlined chemical shift values with low intensity in ^{1}H NMR spectrum indicates the presence of its minor enol form in the compound

^{13}C NMR (100 MHz) (Major keto form) : δ 25.77, 49.13, 52.11, 52.36, 55.32, 56.30, 114.24, 114.70, 121.54, 127.18, 128.64, 129.05, 129.65, 133.14, 136.23, 141.87, 159.66, 168.00, 169.51, 201.70

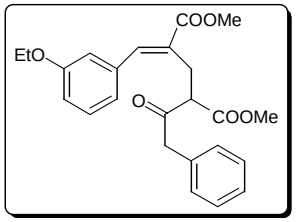
LCMS (m/z) : 395 $(M-H)^{+}$

Anal calc′d for $C_{23}H_{24}O_6$: C, 69.68; H, 6.10

Found : C, 69.74; H, 6.07

Methyl 2-[(*E*)-(3-ethoxybenzylidene)]-4-methoxycarbonyl-5-oxo-6-phenylhexanoate (130d)

This was obtained as a colorless liquid *via* the alkylation of methyl 3-acetoxy-3-(3-ethoxyphenyl)-2-methylenepropanoate (**124c**) with methyl 3-oxo-4-phenylbutanoate (**129c**) in the presence of K_2CO_3 following the similar procedure described for the molecule **130a**.



Reaction time : 20 h

Yield : 78%

IR (neat) : ν 1770, 1720, 1604 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.40 (t, 3H, *J* = 6.8 Hz), 3.09 & 3.18 (d of ABq, 2H, *J* = 14.4 Hz & 6.8 Hz [8.0 Hz]), 3.51-4.08 (m, 11H)*, 6.66-6.93 (m, 3H), 7.08-7.35 (m, 6H), 7.69 (s, 1H)

* This multiplet contains δ 3.54 (s), 3.59 (s), 3.68 (s), 3.74 (s), 3.81-3.92 (m), 3.96-4.08 (m)

The underlined chemical shift values with low intensity in ^{1}H NMR spectrum indicates the presence of its minor enolic isomer in the compound.

^{13}C NMR (100 MHz) (Major keto form) : δ 14.86, 25.76, 49.11, 52.13, 52.38, 56.39, 63.55, 114.81 115.29, 121.42, 127.21, 128.67, 128.99, 129.65, 129.68, 133.18, 136.23, 142.00, 159.05, 168.05, 169.54, 201.73

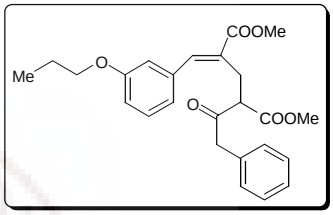
LCMS (m/z) : 411 $(M+H)^+$

Anal calc′d for $C_{24}H_{26}O_6$: C, 70.23; H, 6.38

Found : C, 70.15; H, 6.41

Methyl 4-methoxycarbonyl-5-oxo-6-phenyl-2-[(*E*)-(3-propoxybenzylidene)]hexano-ate (130e)

Alkylaion of methyl 3-acetoxy-2-methylene-3-(3-propoxyphenyl)propanoate (**124d**) with methyl 3-oxo-4-phenylbutanoate (**129c**) in presence of K_2CO_3 following the similar procedure described for the molecule **130a** provided the title compound as a colorless liquid.



Reaction time : 20 h

Yield : 74%

IR (neat) : ν 1743, 1720, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.03 (t, 3H, *J* = 7.2 Hz), 1.73-1.84 (m, 2H), 3.09 & 3.18 (d of ABq, 2H, *J* = 14.4 Hz & 6.8 Hz [8.0 Hz]), 3.50-4.05 (m, 11H)*, 6.60-6.93 (m, 3H), 7.06-7.35 (m, 6H), 7.69 (s, 1H).

* It contains δ 3.54 (s), 3.59 (s), 3.68 (s), 3.74 (s), 3.85-3.94 (m), 3.95-4.06 (m)

The underlined chemical shift values with low intensity in ^{1}H NMR spectrum indicates the presence of its minor enolic isomer in the compound.

^{13}C NMR (100 MHz) (Major keto form) : δ 10.56, 22.62, 25.78, 49.10, 52.14, 52.39, 56.44, 69.62, 114.91, 115.32, 121.34, 127.21, 128.67, 129.65, 129.70, 133.21, 136.23, 142.02, 159.26, 168.07, 169.55, 201.71

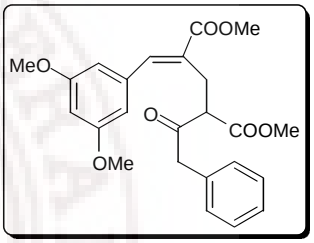
LCMS (m/z) : 425 $(M+H)^+$

Anal calc′d for $C_{25}H_{28}O_6$: C, 70.74; H, 6.65

Found : C, 70.65; H, 6.69

Methyl 2-[(*E*)-(3,5-dimethoxybenzylidene)]-4-methoxycarbonyl-5-oxo-6-phenylhexanoate (130f)

This product was obtained as a colorless liquid *via* the treatment of methyl 3-acetoxy-3-(3,5-dimethoxyphenyl)-2-methylenepropanoate (**124e**) with methyl 3-oxo-4-phenylbutanoate (**129c**) in presence of K_2CO_3 at room temperature following the similar procedure described for the molecule **130a**.



Reaction time : 20 h

Yield : 70%

IR (neat) : ν 1739, 1726, 1629 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.09 & 3.17 (d of ABq, 2H, *J* = 14.4 Hz & 6.8 Hz [8.0 Hz]), 3.55-4.06 (m, 15H)*, 6.30-6.55 (m, 3H), 7.05-7.39 (m, 5H), 7.65 (s, 1H)

* It contains δ 3.57 (s), 3.61 (s), 3.69 (s), 3.74 (s), 3.75 (s), 3.77 (s), 4.02 (t, *J* = 7.6 Hz)

The underlined chemical shift values with low intensity in ^{1}H NMR spectrum indicates the presence of its minor enolic isomer in the compound.

^{13}C NMR (100 MHz) (Major keto form) : δ 25.94, 49.21, 52.16, 52.43, 55.50, 56.29, 101.20, 106.99 127.22, 128.67, 129.24, 129.70, 133.17, 136.75, 142.02, 160.86, 168.01, 169.60, 201.81

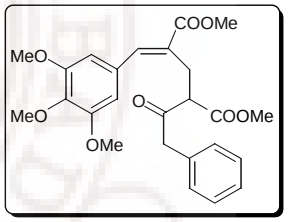
LCMS (m/z) : 427 $(M+H)^+$

Anal calc′d for $C_{24}H_{26}O_7$: C, 67.59; H, 6.15

Found : C, 67.62 H, 6.18

Methyl 4-methoxycarbonyl-5-oxo-6-phenyl-2-[(*E*)-(3,4,5-trimethoxybenzylidene)]-hexanoate (130g)

This was obtained as a colorless viscous liquid *via* the reaction of methyl 3-oxo-4-phenylbutanoate (**129c**) with methyl 3-acetoxy-2-methylene-3-(3,4,5-trimethoxyphenyl)propanoate (**124f**) in presence of K_2CO_3 at room temperature following a similar procedure described for molecule **130a**.



Reaction time : 20 h

Yield : 68%

IR (neat) : ν 1743, 1724, 1626 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.14 & 3.21 (d of ABq, 2H, *J* = 14.8 Hz & 7.2 Hz [8.0 Hz]), 3.60 (s, 3H), 3.75 (s, 3H), 3.79 (s, 2H), 3.84 (s, 6H), 3.87 (s, 3H), 4.11 (s, 1H, *J* = 7.2 Hz), 6.67 (s, 2H), 713 (d, 2H, *J* = 7.20 Hz), 7.21-7.35 (m, 3H), 7.65 (s, 1H)

^{13}C NMR (100 MHz) : δ 26.03, 49.50, 52.14, 52.46, 55.94, 56.25, 60.94, 106.71, 127.26, 127.83, 128.68, 129.66, 130.17, 133.03, 138.67, 141.96, 153.21, 168.16, 169.69, 202.08

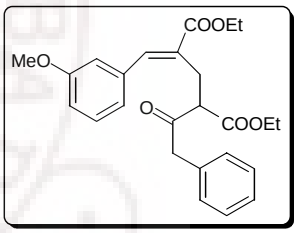
LCMS (m/z) : 455 $(M-H)^+$

Anal calc′d for $C_{25}H_{28}O_8$: C, 65.78; H, 6.18

Found : C, 65.83; H, 6.15

Ethyl 4-ethoxycarbonyl-2-[(*E*)-(3-methoxybenzylidene)]-5-oxo-6-phenylhexanoate (130h)

This was obtained as a colorless liquid *via* the reaction of ethyl 3-oxo-4-phenylbutanoate (**129b**) with ethyl 3-acetyl-3-(3-methoxyphenyl)-2-methylenepropanoate (**124h**) in presence K_2CO_3 at room temperature following a similar procedure described for molecule **130a**.



Reaction time : 24 h

Yield : 78%

IR (neat) : ν 1736, 1720, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.07 & 1.12 (2t, 3H, *J* = 7.2 Hz), 1.20-1.23 (m) & 1.30 (t, 3H, *J* = 7.2 Hz), 3.08$ & 3.20 (d of ABq, 2H, *J* = 14.4 Hz, 6.8 Hz [8.0 Hz]), 3.73-4.26 (m, 10H)*, 6.63-6.98 (m, 3H), 7.09-7.34 (m, 6H), 7.69 (s, 1H)

$ First part of (d of ABq) splits further into doublet (*J* = 0.8 Hz) due to allylic coupling.

* This multiplet contains δ 2.09 (s), 3.77 (s), 3.80 (s), 3.85-4.16 (m), 4.26 (q, *J* = 4.26 Hz)

^{13}C NMR (100 MHz) (Major keto form) : δ 13.94, 14.28, 25.77, 49.11, 55.36, 56.46, 61.06, 61.53, 114.25, 114.72, 121.64, 127.17, 128.65, 129.46, 129.63, 129.69, 133.29, 136.36, 141.50, 159.68, 167.60, 169.20, 201.87

The underlined chemical shift values with low intensity in ^{1}H NMR spectrum indicate the presence of its minor enol form in the compound.

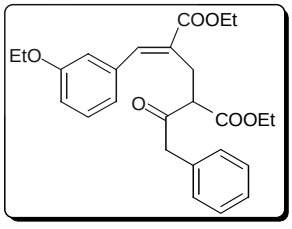
LCMS (m/z) : 425 $(M+H)^+$

Anal calc′d for $C_{25}H_{28}O_6$: C, 70.74; H, 6.65

Found : C, 70.81; H, 6.62

Ethyl 2-[(*E*)-(3-ethoxybenzylidene)]-4-ethoxycarbonyl-5-oxo-6-phenylhexanoate (130i)

This was obtained as a colorless liquid *via* the reaction of ethyl 3-oxo-4-phenylbutanoate (**129b**) with ethyl 3-acetoxy-3-(3-ethoxyphenyl)-2-methylenepropanoate (**124i**) in presence of K_2CO_3 at room temperature following the similar procedure described for molecule **130a**.



Reaction time : 24 h

Yield : 68%

IR (neat) : ν 1739, 1721, 1631 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.07 & 1.22 (2t, 3H, *J* = 7.2 Hz), 1.23 & 1.29 (2t, 3H, *J* = 7.2 Hz), 1.36-1.45 (m, 3H), 3.08 & 3.20 (d of ABq, 2H, *J* = 14.4 Hz & 6.8 Hz [8.0 Hz]), 3.73-4.26 (m, 9H)*, 6.64-6.94 (m, 3H), 7.07-7.35 (m, 6H), 7.69 (s, 1H)

* This multiplet contains δ 3.74 (s), 3.85-4.17 (m), 4.21 (q, *J* = 7.12 Hz)

^{13}C NMR (100 MHz) (Major keto form) : δ 13.87, 14.21, 14.79, 25.68, 48.99, 56.45, 60.96, 61.44, 63.46, 114.72, 115.22, 121.43, 127.09, 128.56, 129.31, 129.55, 129.62, 133.25, 136.25, 141.50, 158.98, 167.52, 169.11, 201.76

LCMS (m/z) : 439 $(M+H)^+$

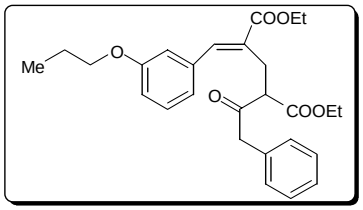
Anal calc′d for $C_{26}H_{30}O_6$: C, 71.21; H, 6.90

Found : C, 71.18; H, 6.95

Ethyl 4-ethoxycarbonyl-5-oxo-6-phenyl-2-[(*E*)-(3-propoxybenzylidene)]hexanoate (130j)

Alkylation of ethyl 3-acetoxy-2-methylene-3-(3-propoxyphenyl)propanoate (**124j**) with ethyl 3-oxo-4-phenylbutanoate (**129b**) at room temperature in presence of K_2CO_3 following the similar procedure described for the molecule **130a** provided **130j** as a colorless liquid.

Reaction time : 24 h



Yield : 76%

IR (neat) : ν 1743, 1719, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 0.98-1.08 (m, 3H), 1.09-1.16 (m, 3H), 1.21-1.35 (m, 3H), 1.73-1.88 (m, 2H), 3.08 & 3.20 (d of ABq, 2H, *J* = 14.4 Hz & 6.8 Hz [8.0 Hz]), 3.74 (s, 2H), 3.80-4.28 (m, 7H), 6.65-6.94 (m, 3H), 7.08-7.35 (m, 6H), 7.69 (s, 1H)

^{1}HNMR spectrum indicates the presence of its minor enolic isomer in the compound.

^{13}C NMR (100 MHz) : δ 10.56, 13.94, 14.28, 22.61, 25.75, 49.03, 56.58, 61.04,

(Major keto form) 61.51, 69.61, 114.91, 115.30, 121.40, 127.15, 128.63, 129.40, 129.61, 129.69, 133.33, 136.32, 141.60, 159.26, 167.62, 169.19, 201.82

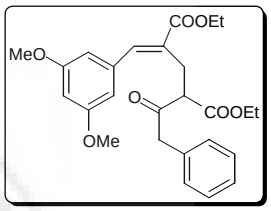
LCMS (m/z) : 451 $(M-H)^+$

Anal calc′d for $C_{27}H_{32}O_6$: C, 71.66; H, 7.13

Found : C, 71.54; H, 7.16

Ethyl 2-[(*E*)-(3,5-dimethoybenzylidene)]-4-ethoxycarbonyl-5-oxo-6-phenylhexanoate (130k)

This product was obtained as a colorless viscous liquid, *via* the treatment of ethyl 3-acetoxy-3-(3,5-dimethoxyphenyl)-2-methylenepropanoate (**124k**) with ethyl 3-oxo-4-phenylbutanoate (**129b**) in presence of K_2CO_3 in THF at room temperature following the similar procedure described for the molecule **130a**.



Reaction time : 24 h

Yield : 67%

IR (neat) : ν 1747, 1712, 1631 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.07-1.20 (m, 3H, *J* = 7.12 Hz), 1.21-1.37 (m, 3H), 3.08 & 3.20 (d of ABq, 2H, *J* = 14.8 Hz & 7.2 Hz [7.6 Hz]), 3.73-4.30 (m, 13H)*, 6.35-6.60 (m, 3H), 7.08-7.33 (m, 5H), 7.65 (s, 1H)

***** This multiplet contains δ 3.76 (s), 3.77 (s), <u>3.79</u> (s), 3.94-4.13 (m), 4.21 (q, *J* = 7.2 Hz)

The underlined chemical shift value with low intensity in ^{1}HNMR spectrum indicates the presence of its minor enolic isomer in the compound.

^{13}C NMR (100 MHz) (Major keto form) : δ 13.96, 14.29, 25.92, 49.17, 55.51, 56.41, 61.08, 61.55, 101.22, 107.02, 127.18, 128.65, 129.64, 129.70, 133.30, 136.85, 141.62, 160.86, 167.58, 169.26, 201.93

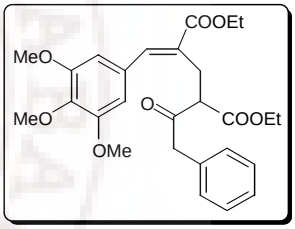
LCMS (m/z) : 455 $(M+H)^+$

Anal calc′d for $C_{26}H_{30}O_7$: C, 68.71; H, 6.65

Found : C, 68.79; H, 6.61

Ethyl 4-ethoxycarbonyl-5-oxo-6-pheny-2-[(*E*)-(3,4,5-trimethoxybenzylidene)]hexanoate (130l)

This was obtained as a colorless viscouss liquid *via* the reaction of ethyl 3-oxo-4-phenylbutanoate (**129b**) and ethyl 3-acetoxy-2-methylene-3-(3,4,5-trimethoxyphenyl)propanoate (**124l**) in presence of K_2CO_3 at room temperature following the similar procedure described for molecule **130a**.



Reaction time : 24 h

Yield : 77%

IR (neat) : ν 1738, 1714, 1624 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.15 (t, 3H, *J* = 7.2 Hz), 1.31 (t, 3H, *J* = 7.2 Hz), 3.10 & 3.24 (d of ABq, 2H, *J* = 14.4 Hz & 7.2 Hz [8.0 Hz]), 3.75-4.26 (m, 16H)*, 6.68 (s, 2H), 7.13 (d, 2H, *J* = 7.2 Hz), 7.22-7.34 (m, 3H), 7.64 (s, 1H)

* This multiplet contains δ 3.79 (s), <u>3.81</u> (s), 3.85 (s), 3.87 (s), 3.95-4.15 (m, H), 4.22 (q, 2H, *J* = 7.2 Hz)

The underlined chemical shift value with low intensity in ^{1}H NMR spectrum indicates the presence of its minor enolic isomer in the compound

^{13}C NMR (100 MHz) (Major keto form) : δ 13.97, 14.27, 25.96, 49.45, 55.98, 56.23, 60.90, 61.02, 61.54, 106.65, 127.19, 128.22, 128.64, 130.26, 133.13, 138.51, 141.55, 153.16, 167.68, 169.32, 202.17

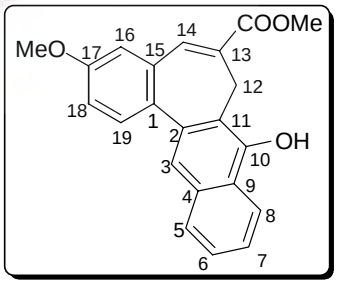
LCMS (m/z) : 485 $(M+H)^+$

Anal calc′d for $C_{27}H_{32}O_8$: C, 66.93; H, 6.66

Found : C, 66.85; H, 6.71

10-Hydroxy-17-methoxy-13-methoxycarbonyltetracyclo[13.4.0.0^{2,11}.0^{4,9}]nonadeca-1(15),2(11),3,5,7,9,13,16,18-nonaene (**131a**)

To a stirred solution of methyl 2-[(*E*)-(3-methoxybenzylidene)]-4-methoxycarbonyl-5-oxo-6-phenylhexanoate (**130c**) (1 mmol, 0.396 g) in dichloroethane (3 mL) was added methanesulfonic acid (5 mmol, 0.480 g) at room temperature and then reaction mixture was heated at 80 ^{0}C for 12 h. Then reaction mixture was cooled to room temperature and diluted with water (3 mL) and extracted with ethyl acetate (3X30 mL). Combined organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and the crude thus obtained was purified by column chromatography to provide the desired product as in 76% (0.265 g) isolated yield (15% EtOAc in hexanes).



Reaction time : 12 h

Mp : 164-166 ^{0}C

IR (KBr) : ν 3483, 1682, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.82 (d, 1H, *J* = 13.6 Hz), 3.86 (s, 3H), 3.90 (s, 3H), 4.19 (d, 1H, *J* = 13.6 Hz), 6.96 (d, 1H, *J* = 2.8 Hz), 7.05-7.13 (m, 2H), 7.40-7.51 (m, 3H), 7.54 (s, 1H), 7.76-7.83 (m, 1H), 7.89 (d, 1H, *J* = 8.8 Hz), 8.26-8.33 (m, 1H)

^{13}C NMR (100 MHz) : δ 25.65, 52.77, 55.51, 114.26, 115.52, 120.71, 122.19, 123.04, 124.62, 125.23, 125.98, 127.68, 131.29, 132.87, 133.28, 133.95, 135.31, 136.39, 137.30, 146.60, 158.69, 168.81

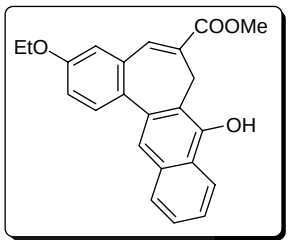
LCMS (m/z) : 347 $(M+H)^{+}$

Anal calc′d for $C_{22}H_{18}O_4$: C, 76.29; H, 5.24

Found : C, 76.21; H, 5.27

17-Ethoxy-10-hydroxy-13-methoxycarbonyltetracyclo[13.4.0.0^{2,11}.0^{4,9}]nonadeca-1(15)-2(11),3,5,7,9,13,16,18-nonaene (131b)

This molecule was prepared *via* the treatment of methyl 2-[(*E*)-(3-ethoxybenzylidene)]- 4-methoxycarbonyl-5-oxo-6-phenylhexanoate (**130d**) with methanesulfonic acid following the similar procedure described for the molecule **131a**.



Reaction time : 12 h

Yield : 79%

Mp : 147-149 ^{0}C

IR (KBr) : ν 3346, 1660, 1624 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.47 (t, 3H, *J* = 7.2 Hz), 2.82 (d, 1H, *J* = 13.2 Hz), 3.86 (s, 3H), 4.13 (q, 2H, *J* = 7.2 Hz)*, 4.19 (d, 1H, *J* = 13.2 Hz)*, 6.95 (d, 1H, *J* = 2.8 Hz), 7.05-7.14 (m, 2H), 7.41-7.51 (m, 3H), 7.54 (s, 1H), 7.76-7.82 (m, 1H), 7.88 (d, 1H, *J* = 8.4 Hz) 8.26-8.33 (m, 1H)

* These two peaks partially merges

^{13}C NMR (100 MHz) : δ 14.92, 25.68, 52.77, 63.76, 114.86, 116.03, 120.68, 122.20, 123.05, 124.62, 125.21, 125.97, 127.68, 131.27, 132.89, 133.19, 133.82, 135.30, 136.47, 137.36, 146.59, 158.09, 168.84

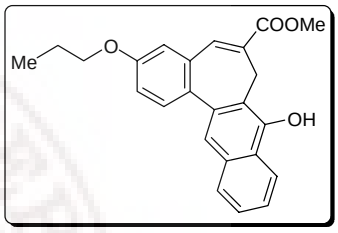
LCMS (m/z) : 361 $(M+H)^+$

Anal calc′d for $C_{23}H_{20}O_4$: C, 76.65; H, 5.59

Found : C, 76.55; H, 5.62

10-Hydroxy-13-methoxycarbonyl-17-propoxytetracyclo[13.4.0.0^{2,11}.0^{4,9}]nonadeca-1(15),2(11),3,5,7,9,13,16,18-nonaene (131c)

This product was obtained as a yellow solid *via* the reaction of methyl 4-methoxycarbonyl-5-oxo-6-phenyl-2-[(*E*)-(3-propoxybenzylidene)]hexanoate (**130e**) with methanesulfonic acid following the similar procedure described for the molecule **131a**.



Reaction time : 12 h

Yield : 79%

Mp : 128-130 ^{0}C

IR (KBr) : ν 3396, 1680, 1626 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.07 (t, 3H, *J* = 7.2 Hz), 1.80-1.92 (m, 2H), 2.82 (d, 1H, *J* = 13.6 Hz), 3.86 (s, 3H), 4.01 (t, 2H, *J* = 6.8 Hz), 4.19 (d, 1H, *J* = 13.6 Hz), 6.95 (d, 1H, *J* = 2.8 Hz), 7.05-7.12 (m, 2H), 7.41-7.49 (m, 3H), 7.53 (s, 1H), 7.76-7.82 (m, 1H), 7.88 (d, 1H, *J* = 8.8 Hz), 8.26-8.35 (m, 1H)

^{13}C NMR (100 MHz) : δ 10.60, 22.65, 25.66, 52.74, 69.79, 114.88, 116.04, 120.66, 122.20, 123.05, 124.61, 125.18, 125.95, 127.68, 131.24, 132.88, 133.15, 133.75, 135.28, 136.49, 137.38, 146.59, 158.28, 168.82

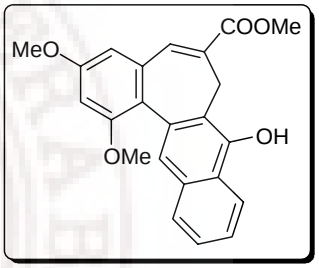
LCMS (m/z) : 375 $(M+H)^{+}$

Anal calc′d for $C_{24}H_{22}O_4$: C, 76.99; H, 5.92

Found : C, 77.12; H, 5.89

17,19-Dimethoxy-10-hydroxy-13-methoxycarbonyltetracyclo[13.4.0.0^{2,11}.0^{4,9}]nona-deca-1(15),2(11),3,5,7,9,13,16,18-nonaene (131d)

This compound was obtained as a colorless solid *via* the treatment of methyl 2-[(*E*)-(3,5-dimethoxybenzylidene)]-4-methoxycarbonyl-5-oxo-6-phenylhexanoate (**130f**) with methanesulfonic acid following the similar procedure described for **131a**.



Reaction time : 12 h

Yield : 56%

Mp : 218-220 ^{0}C

IR (KBr) : ν 3400, 1670, 1628 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.84 (d, 1H, *J* = 13.2 Hz), 3.84 (s, 3H), 3.86 (s, 3H), 3.88 (s, 3H), 4.16 (d, 1H, *J* = 13.2 Hz), 6.57 (s, 1H) 6.68 (s, 1H), 7.04 (s, 1H, D_2O exchangeable), 7.34-7.48 (m, 3H), 7.70-7.83 (m, 2H), 8.27 (d, 1H, *J* = 7.6 Hz)

^{13}C NMR (100 MHz) : δ 25.74, 52.80, 55.55, 56.22, 100.35, 105.26, 122.11, 123.38, 123.50, 124.58, 124.87, 125.15, 125.64, 127.82, 131.63, 132.05, 134.53, 136.35, 136.80, 146.28, 158.69, 158.96, 168.92

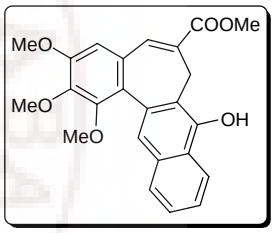
LCMS (m/z) : 377 $(M+H)^+$

Anal calc′d for $C_{23}H_{20}O_5$: C, 73.39; H, 5.36

Found : C, 73.45; H, 5.39

10-Hydroxy-13-methoxycarbonyl-17,18,19-trimethoxytetracyclo[13.4.0.0^{2,11}.0^{4,9}]nonadeca-1(15),2(11),3,5,7,9,13,16,18-nonaene (131e)

This compound was obtained as a colorless solid *via* the reaction of methyl 4-methoxycarbonyl-5-oxo-6-phenyl-2-[(*E*)-(3,4,5-trimethoxybenzylidene)]hexanoate (**130g**) with methanesulfonic acid following the similar procedure described for molecule **131a**.



Reaction time : 12 h

Yield : 73%

Mp : 224-226 ^{0}C

IR (KBr) : ν 3433, 1680, 1607 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.80 (dd, 1H, *J* = 1.2 Hz & 13.2 Hz), 3.62 (s, 3H), 3.85 (s, 3H), 3.94 (s, 3H), 4.04 (s, 3H), 4.21 (dd, 1H, *J* = 1.2 Hz &13.2 Hz), 6.75 (s, 1H), 7.05 (s, 1H), 7.38 (s, 1H), 7.39-7.49 (m, 2H), 7.77 (dd, 1H, *J* = 2.0 Hz & 7.6 Hz), 7.79 (s, 1H), 8.26-8.32 (m, 1H)

^{13}C NMR (100 MHz) : δ 25.81, 52.77, 56.09, 61.31, 61.46, 108.48, 122.09, 123.00, 124.11, 124.74, 125.31, 125.74, 127.94, 128.23, 130.98,

131.78, 132.36, 133.34, 136.19, 143.02, 146.27, 152.21, 152.73, 168.90

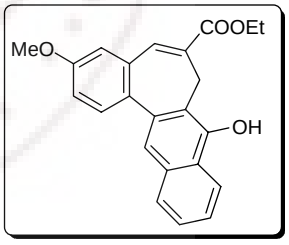
LCMS (m/z) : 407 $(M-H)^+$

Anal calc′d for $C_{24}H_{22}O_6$: C, 70.92; H, 5.46

Found : C, 70.98; H, 5.41

13-Ethoxycarbonyl-10-hydroxy-17-methoxytetracyclo[13.4.0.0^{2,11}.0^{4,9}]nonadeca-1(15)-2(11),3,5,7,9,13,16,18-nonaene (131f)

This was obtained as a light yellow solid *via* the treatment of ethyl 4-ethoxycarbonyl-2-[(*E*)-(3-methoxybenzylidene)]-5-oxo-6-phenylhexanoate (**130h**) with methanesulfonic acid following the similar procedure described for the molecule **131a**.



Reaction time : 12 h

Yield : 72%

Mp : 136-138 ^{0}C

IR (KBr) : ν 3485, 1697, 1606 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.37 (t, 3H, *J* = 7.2 Hz), 2.82 (d, 1H, *J* = 13.6 Hz), 3.90 (s, 3H), 4.20 (d, 1H, *J* = 13.6 Hz), 4.23-4.38 (m, 2H, Hz), 6.97 (d, 1H, *J* = 2.8 Hz), 7.09 (dd, 1H, *J* = 2.8 Hz & 8.8 Hz), 7.13 (s, 1H, D_2O exchangeable), 7.42-7.49 (m, 3H), 7.54 (s,

1H), 7.76 -7.82 (m, 1H), 7.90 (d, 1H, *J* = 8.8 Hz), 8.26-8.33 (m, 1H)

^{13}C NMR (100 MHz) : δ 14.32, 25.70, 55.53, 61.91, 114.21, 115.55, 120.66, 122.24, 123.14, 124.66, 125.21, 125.97, 127.68, 131.28, 132.88, 133.70, 133.96, 135.40, 136.05, 137.34, 146.65, 158.71, 168.39

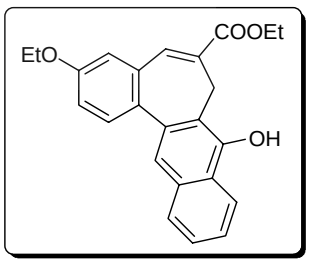
LCMS (m/z) : 359 $(M-H)^+$

Anal calc′d for $C_{23}H_{20}O_4$: C, 76.65; H, 5.59

Found : C, 76.72; H, 5.53

17-Ethoxy-13-ethoxycarbonyl-10-hydroxytetracyclo[13.4.0.0^{2,11}.0^{4,9}]nonadeca-(15),-2(11),3,5,7,9,13,16,18-nonaene (131g)

Treatment of ethyl 2-[(*E*)-(3-ethoxybenzylidene)]-4-ethoxycarbonyl-5-oxo-6-phenyl hexanoate (**130i**) with methanesulfonic acid, following the similar procedure described for the molecule **131a**, provided the title compound **131g** as a pale yellow solid.



Reaction time : 12 h

Yield : 81%

Mp : 106-108 ^{0}C

IR (KBr) : ν 3402, 1678, 1631 cm^{-1}

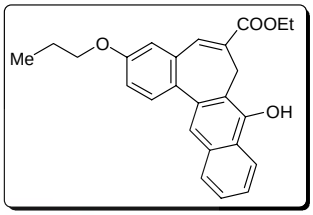
^{1}H NMR (400 MHz)	: δ 1.36 (t, 3H, *J* = 7.2 Hz), 1.47 (t, 3H, *J* = 7.2 Hz,), 2.80 (d, 1H, *J* = 13.6 Hz), 4.12 (q, 2H, *J* = 7.2 Hz), 4.18 (d, 1H, *J* = 13.6 Hz), 4.25-4.39 (m, 2H), 6.95 (d, 1H, *J* = 2.4 Hz), 7.07 (dd, 1H, *J* = 2.8 Hz & 8.4 Hz,), 7.15 (s, 1H, D_2O exchangable), 7.40-7.49 (m, 3H), 7.53 (s, 1H), 7.76-7.83 (m, 1H), 7.88 (d, 1H, *J* = 8.4 Hz), 8.26-8.33 (m, 1H)
^{13}C NMR (100 MHz)	: δ 14.28, 14.88, 25.64, 61.85, 63.70, 114.74, 116.00, 120.58, 122.19, 123.10, 124,60, 125.13, 125.90, 127.65, 131.20, 132.84, 133.50, 133.73, 135.31, 136.12, 137.37, 146.60, 158.04, 168.35
LCMS (m/z)	: 375 $(M+H)^+$
Anal calc′d for $C_{24}H_{22}O_4$	: C, 76.99; H, 5.92
Found	: C, 76.91; H, 5.96

13-Ethoxycarbonyl-10-hydroxy-17-propoxytetracyclo[13.4.0.0^{2,11}.0^{4,9}]nonadeca-1(15),2(11),3,5,7,9,13,16,18-nonaene (131h)

This product was obtained as a yellow solid *via* the Friedel-Crafts reactions of ethyl 4-ethoxycarbonyl-5-oxo-6-phenyl-2-[(*E*)-(3-propoxybenzylidene)]hexanoate (**130j**) with methanesulfonic acid following the similar procedure described for the molecule **131a**.

Reaction time : 12 h

Yield : 70 %



Mp : 118-120 ^{0}C

IR (KBr) : ν 3398, 1678, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.07 (t, 3H, *J* = 7.2 Hz), 1.36 (t, 3H, *J* = 7.2 Hz), 1.81-1.92 (m, 2H), 2.81 (d, 1H, *J* = 13.6 Hz), 4.01 (t, 2H, *J* = 6.4 Hz), 4.18 (d, 1H, *J* = 13.6 Hz), 4.25-4.41 (m, 2H), 6.96 (d, 1H, *J* = 2.8 Hz), 7.07 (dd, 1H, *J* = 8.8 Hz & 2.8 Hz), 7.14 (s, 1H, D_2O exchangeable), 7.41-7.50 (m, 3H), 7.54 (s, 1H), 7.76-7.83 (m, 1H), 7.88 (d, 1H, *J* = 8.8 Hz), 8.26-8.34 (m, 1H)

^{13}C NMR (100 MHz) : δ 10.60, 14.29, 22.65, 25.67, 61.86, 69.77, 114.79, 116.05, 120.59, 122.21, 123.11, 124.62, 125.14, 125.91, 127.66, 131.20, 132.87, 133.52, 133.72, 135.33, 136.14, 137.40, 146.62, 158.26, 168.38

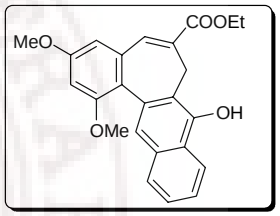
LCMS (m/z) : 389 $(M+H)^{+}$

Anal calc′d for $C_{25}H_{24}O_4$: C, 77.30; H, 6.23

Found : C, 77.25; H, 6.26

17,19-Dimethoxy-13-ethoxycarbonyl-10-hydroxytetraracyclo[13.4.0.0^{2,11}.0^{4,9}]nonad-eca-1(15),2(11),3,5,7,9,13,16,18-nonaene (131i)

This compound was obtained as a colorless solid *via* the reaction of ethyl 2-[(*E*)-(3,5-dimethoxybenzylidene)]-4-ethoxycarbonyl-5-oxo-6-phenylhexanoate (**130k**) with methanesulfonic acid following the similar procedure described for the molecule **131a**.



Reaction time : 12 h

Yield : 59%

Mp : 220-222 ^{0}C

IR (KBr) : ν 3381, 1668, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.35 (t, 3H, *J* = 7.2 Hz), 2.83 (d, 1H, *J* = 13.6 Hz), 3.87 (s, 3H), 3.89 (s, 3H), 4.15 (d, 1H, *J* = 13.6 Hz), 4.22-4.38 (m, 2H), 6.58 (d, 1H, *J* = 2.4 Hz), 6.68 (d, 1H, *J* = 2.4 Hz), 7.11 (s, 1H, D_2O exchangeable), 7.35-7.47 (m, 3H), 7.71-7.78 (m, 2H), 8.27 (d, 1H, *J* = 7.6 Hz)

^{13}C NMR (100 MHz) : δ 14.31, 25.77, 55.55, 56.23, 61.93, 100.39, 105.30, 122.16, 123.33, 123.54, 124.63, 124.97, 125.11, 125.61, 127.82, 131.70, 132.06, 134.93,136.01, 136.90, 146.34, 158.72, 158.98, 168.47

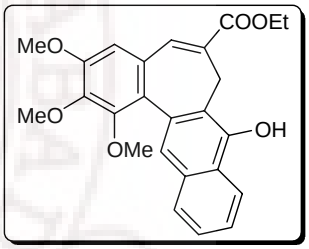
LCMS (m/z) : 391 $(M+H)^+$

Anal calc′d for $C_{24}H_{22}O_5$: C, 73.83; H, 5.68

Found : C, 73.88; H, 5.63

13-Ethoxycarbonyl-10-hydroxy-17,18,19-trimethoxytetracyclo[13.4.0.0^{2,11}.0^{4,9}]-nona-deca-1(15),2(11),3,5,7,9,13,16,18-nonaene (131j)

Treatment of ethyl 4-ethoxycarbonyl-5-oxo-6-phenyl-2-[(*E*)-(3,4,5-trimethoxybenzylid-ene)]hexanoate (**130l**) with methanesulfonic acid, following similar procedure described for molecule **131a**, provided the desired tetracyclic carbocyclic derivative **131j** as a colorless solid.



Reaction time : 12 h

Yield : 63%

Mp : 168 ^{0}C (dec.)

IR (KBr) : ν 3420, 1670, 1622 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.35 (t, 3H, *J* = 7.2 Hz), 2.79 (d, 1H, *J* = 13.6 Hz), 3.62 (s, 3H), 3.94 (s, 3H), 4.04 (s, 3H), 4.20 (d, 1H, *J* = 13.6 Hz), 4.25-4.40 (m, 2H), 6.76 (s, 1H), 7.13 (s, 1H), 7.37 (s, 1H), 7.39-7.50 (m, 2H), 7.76 (d, 1H, *J* = 8.0 Hz), 7.79 (s, 1H), 8.29 (d, 1H, *J* = 8.0 Hz)

^{13}C NMR (100 MHz) : δ 14.28, 25.81, 56.07, 61.28, 61.43, 61.88, 108.48, 122.10, 122.92, 124.19, 124.76, 125.25, 125.69, 127.91, 128.19,

131.04, 131.81, 132.34, 133.72, 135.82, 142.94, 146.30, 152.18, 152.70, 168.45

LCMS (m/z) : 421 $(M+H)^+$

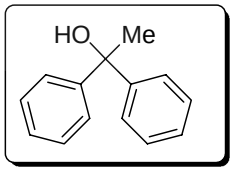
Anal calc′d for $C_{25}H_{24}O_6$: C, 71.41; H, 5.75

Found : C, 71.36; H, 5.78

1,1-Diphenylethanol (156a)

To stirred solution of acetophenone (50 mmol, 6.0 g) in anhydrous THF (20 mL) was added phenylmagnisum bromide [prepared from Mg turnings (70 mmol, 1.70 g) and bromobenzene (65 mmol, 10.14 g)] at 0 ^{0}C. After stirring for 3 h at room temperature, reaction mixture was quenched with satured NH_4Cl solution and extracted with diethyl ether (3X75 mL). Combined organic layer was dried over anhydrous Na_2SO_4. Crude product thus obtained, was purified by column chromatography to provide the desired 1,1-diphenylethanol (**156a**) as a colorless solid in 76% (7.56 g) isolated yield.

Yield : 76%



Mp : 74-76 ^{0}C

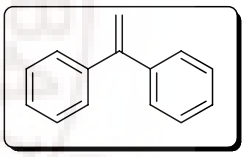
IR (KBr) : ν 3435 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.95 (s, 3H), 2.19 (s, 1H), 7.21-7.24 (m, 2H), 7.28-7.35 (m, 4H), 7.41 (d, 4H, *J* = 8.0 Hz)

^{13}C NMR (50 MHz) : δ 30.76, 76.17, 125.88, 126.90, 128.13, 148.00

1, 1-Diphenylethylene (153a) [244]

A mixture of powdered 1,1-diphenylethanol (**156a**) (27 mmol, 5.35 g), trichloroacetic acid (27 mmol, 4.41 g) was stirred at room temperature for 20 min. Reaction mixture was diluted with water (10 mL) and extracted with diethyl ether (3X30 mL). Combined organic layer was dried over anhydrous Na_2SO_4. Crude product was obtained, after solvent evaporation was purified by column chromatography (5% EtOAc in hexanes) provide the desired product 1,1-diphenylethylene (**153a**) as a colorless liquid in 90% (4.39 g).[244]



IR (neat) : ν 1610 cm^{-1}

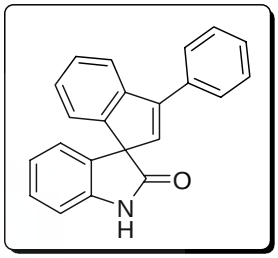
^{1}H NMR (400 MHz) : δ 5.45 (s, 2H), 7.32 (s, 10H)

^{13}C NMR (50 MHz) : δ 114.33, 127.77, 128.23, 128.33, 141.57, 150.16

General procedure for the synthesis of (3-phenyl-1*H*-indene)-1-spiro-3′-(indolin-2′-one) (155a)

To a stirred solution of isatin (**154a**) (1 mmol, 0.147 g), 1,1-diphenylethylene (**153a**) (1 mmol, 0.180 g) in dichloromethane (3 mL), $TiCl_4$ (1 mmol, 0.5 mL, 2M solution in dichloromethane) was added at 0 ^{0}C. Reaction mixture was stirred at room temperature for 13 h and diluted with water (10 mL) and extracted with ether (3x15 mL). Combined

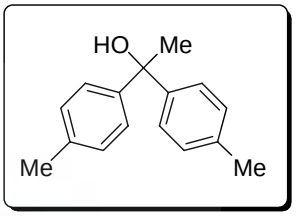
organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and the residue thus obtained was purified by column chromatography (30% EtOAc in hexanes) to provide the title compound as a colorless solid.



Yield	: 90% (0.279 g)
Reaction time	: 13 h
M.p	: 192-194 ^{0}C
IR (KBr)	: ν 3250-2800 (multiple bands), 1701, 1610 cm^{-1}
^{1}H NMR (400 MHz)	: δ 6.33 (s, 1H), 6.77 (d, 1H, *J* = 7.6 Hz), 6.88-6.98 (m, 2H), 7.05 (d, 1H, *J* = 7.6 Hz), 7.15-7.22 (m, 2H), 7.33-7.50 (m, 4H), 7.63 (d, 1H, *J* = 7.6 Hz), 7.65-7.72 (m, 2H), 9.51 (s, 1H, D_2O exchangeable)
^{13}C NMR (50 MHz)	: δ 65.31, 110.74, 121.29, 122.67, 122.89, 123.64, 126.65, 127.77, 127.91, 128.33, 128.64, 128.76, 131.84, 134.68, 142.47, 144.00, 146.37, 148.51, 178.32
LCMS (m/z)	: 310 $(M+H)^+$
Anal calc′d for $C_{22}H_{15}NO$	: C, 85.41; H, 4.89; N, 4.53
Found	: C, 85.57; H, 4.88; N, 4.50

1,1-Di(4-methylphenyl)ethanol (156b)

This was prepared as a colorless liquid by the treatment of 4-methylacetophenone with 4-methylphenylmagnesium bromide in dry THF solvent following the similar procedure described for the molecule **156a**.



Yield : 73%

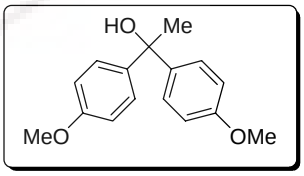
IR (neat) : ν 3562 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.90 (s, 3H), 2.15 (br s, 1H), 2.31 (s, 6H), 7. 10 (d, 4H, *J* = 8.0 Hz), 7. 27 (d, 4H, *J* = 8.0 Hz)

^{13}C NMR (50 MHz) : δ 20.99, 30.89, 75.95, 125.78, 128.79, 136.40, 145.38

1,1-Di(4-methoxyphenyl)ethanol (156c)

This was prepared as pale yellow liquid by the treatment of 4-methoxyacetophenone with 4-methoxyphenylmagnesium bromide in dry THF solvent following the similar procedure described for the molecule **156a**.



Yield : 64%

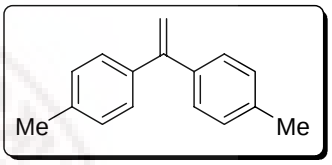
IR (neat) : ν 3485 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.89 (s, 3H), 2.16 (s, 1H), 3.78 (s, 6H), 6.83 (d, 4H, *J* = 7.2 Hz), 7.30 (d, 4H, *J* = 7.2 Hz)

^{13}C NMR (50 MHz) : δ 31.18, 55.29, 75.71, 113.46, 127.14, 140.70, 158.48

1,1-Di(4-methylphenyl)ethylene (153b)

Treatment of 1,1-di(4-methylpheny)ethanol (**156b**), with trichloroacetic acid under neat conditions following the similar procedure described for the molecule **153a** provided 1,1-di(4-methylphenyl)ethylene (**153b**) as a colorless solid.[244]



Yield : 90%

MP : 58-60 ^{0}C

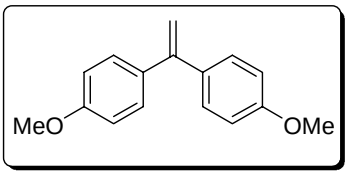
IR (KBr) : ν 1604 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.36 (s, 6H), 5.37 (s, 2H), 7.13 (d, 4H, *J* = 7.6 Hz), 7.23 (d, 4H, *J* = 7.6 Hz)

^{13}C NMR (50 MHz) : δ 21.23, 113.02, 128.25, 128.88, 137.47, 138.90, 149.87

1, 1-Di(4-methoxyphenyl)ethylene (153c)

This was obtained as a color less solid *via* the treatment 1,1-di(4-methoxyphenyl)ethanol (**156c**) with trichloroacetic acid following the similar procedure[244] described for the molecule **153a**



Yield : 88%

MP : 136-138 ^{0}C

IR (KBr) : ν 1604 cm^{-1}

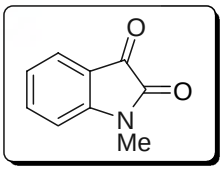
^{1}H NMR (400 MHz) : δ 3.81 (s, 6H), 5.28 (s, 2H) 6.82-6.88 (m, 4H), 7.26-7.29 (m, 4H)

^{13}C NMR (50 MHz) : δ 55.29, 111.69, 113.55, 129.47, 134.37, 149.04, 159.35

_N_-Methylisatin (154e)

This molecule was prepared following the known procedure[245]

A stirred suspension of isatin **154a** (20 mmol, 2.94 g) and powdered CaH_2 (66.6 mmol, 2.79 g) in DMF (36 mL) was heated at 40-50 ^{0}C for 20 min. Methyl iodide (50 mmol, 7.9 g) was added at the same temperature and stirring was continued at room temperature for 12 h. Then the reaction mixture was poured into ice-cold HCl (0.2 M) solution and 10% aqueous NaCl solution (50 mL) was added. Reaction mixture was extracted with ethyl acetate (3X25 mL). Combined organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and the crude product thus obtained, was purified by column chromatography (20% EtOAc in hexanes) to provide the title compound in 65% (2.08 g) yield as brick red solid.



Mp : 129-131 °C (lit. 129-130 °C)[245]

IR (KBr) : ν 1747, 1728, 1606 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.25 (s, 3H), 6.90 (d, 1H, *J* = 8.0 Hz), 7.10-7.16 (m, 1H), 7.57-7.65 (m, 2H).

^{13}C NMR (50 MHz) : δ 26.11, 109.96, 117.34, 123.72, 125.00, 138.42, 151.39, 158.14, 183.24

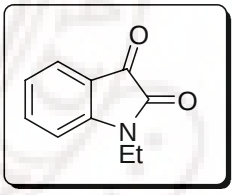
_N_-Ethylisatin (154f)

Treatment of isatin (**154a**) with ethyl bromide in presence of CaH_2 following the similar procedure described for the molecule **154e** provided the title compound **154f** as an orange solid.[245]

Reaction time : 12 h

Yield : 78%

Mp : 86-88 °C



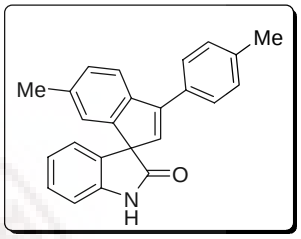
IR (KBr) : ν 1736, 1610 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.30 (t, 3H, *J* = 7.2 Hz), 3.77 (q, 2H, *J* = 7.2 Hz), 6.87-6.97 (m, 1H), 7.06-7.12 (m, 1H), 7.54-7.62 (m, 2H)

^{13}C NMR (50 MHz) : δ 12.43, 34.89, 110.04, 117.56, 123.55, 125.27, 138.34, 150.62, 157.80, 183.61

[6-Methyl-3-(4-methylphenyl)-1*H*-indene]-1-spiro-3′-(indolin-2′-one) (155b)

This was prepared *via* tandem Prins and Friedel-Crafts reactions of 1,1-di(4-methylphenyl)ethylene (**153b**) with isatin (**154a**) in presence of $TiCl_4$ following the similar procedure described for the molecule **155a** as a colorless solid.



Reaction time : 13 h

Yield : 82%

Mp : 182-184 ^{0}C

IR (KBr) : ν 3300-2800 (multiple bands), 1714, 1614 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.29 (s, 3H), 2.41 (s, 3H), 6.23 (s, 1H), 6.81 (d, 1H, *J* = 7.6 Hz), 6.86 (s, 1H), 6.92-6.98 (m, 1H), 7.00 (d, 1H, *J* = 7.6 Hz), 7.15 (d, 1H, *J* = 8.0 Hz), 7.22-7.29 (m, 3H), 7.49 (d, 1H, *J* = 8.0 Hz), 7.58 (d, 2H, *J* = 8.8 Hz), 7.87 (s, 1H, D_2O exchangeable)

^{13}C NMR (50 MHz) : δ 21.42, 64.89, 110.35, 121.19, 122.92, 123.69, 124.06, 127.77, 128.64, 128.79, 129.39, 130.19, 132.11, 136.65, 138.22, 141.57, 142.15, 146.66, 148.53, 178.25

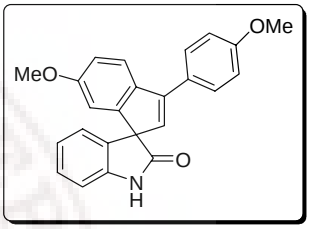
LCMS (m/z) : 338 $(M+H)^+$

Anal calc′d for $C_{24}H_{19}NO$: C, 85.43; H, 5.68; N, 4.15

Found : C, 85.28; H, 5.65; N, 4.16

[6-Methoxy-3-(4-methoxyphenyl)-1*H*-indene]-1-spiro-3′-(indolin-2′-one) (155c)

This was obtained as a colorless solid *via* the reaction between isatin (**154a**) and 1,1-di (4-methoxyphenyl)ethylene (**153c**) under the influence of $TiCl_4$ following the similar procedure described for the molecule **155a**.



Reaction time : 13 h

Yield : 69%

Mp : 204-206 ^{0}C

IR (KBr) : ν 3300-2800 (multiple bands), 1714, 1610 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.73 (s, 3H), 3.86 (s, 3H), 6.15 (s, 1H), 6.61(d, 1H, *J* = 2.4 Hz), 6.80 (d, 1H, *J* = 7.6 Hz), 6.89 (dd, 1H, *J* = 8.4 Hz & 2.4 Hz), 6.91-7.04 (m, 4H), 7.19-7.24 (m, 1H), 7.52 (d, 1H, *J* = 8.4 Hz), 7.63 (d, 2H, *J* = 8.8 Hz), 9.02 (s, 1H, D_2O exchangeable)

^{13}C NMR (50 MHz) : δ 55.38, 55.58, 64.94, 109.33, 110.59, 113.38, 114.06, 121.87, 122.82, 123.91, 127.48, 128.45, 128.59, 128.93, 129.42, 137.01, 142.25, 147.63, 148.10, 159.04, 159.72, 178.66

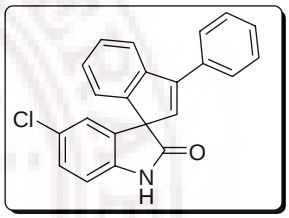
LCMS (m/z) : 370 $(M+H)^+$

Anal calc′d for $C_{24}H_{19}NO_3$: C, 78.03; H, 5.18; N, 3.79

Found : C, 78.30; H, 5.16; N, 3.77

(3-Phenyl-1*H*-indene)-1-spiro-3′-(5′-chloroindolin-2′-one) (155d)

This molecule was prepared as a colorless solid *via* the Prins and intramolecular Friedel-Crafts reaction of 5-chloroisatin (**154b**) with 1,1-diphenylethylene (**153a**) under the influence of $TiCl_4$ following the similar procedure described for the molecule **155a**.



Reaction time : 18 h

Yield : 77%

Mp : 205-207 ^{0}C

IR (KBr) : ν 3250-2800 (multiple bands), 1716, 1614 cm^{-1}

^{1}H NMR (400 MHz) : δ 6.30 (s, 1H), 6.77 (s, 1H), 6.91 (d, 1H, *J* = 8.4 Hz), 7.05 (d, 1H, *J* = 7.6 Hz), 7.18-7.25 (m, 2H), 7.35-7.55 (m, 4H), 7.63 (d, 1H, *J* = 7.6 Hz), 7.69 (d, 2H, *J* = 7.6 Hz), 8.87 (s, 1H, D_2O exchangeable)

^{13}C NMR (50 MHz) : δ 65.23, 111.71, 121.63, 122.94, 124.15, 126.94, 127.84, 128.23, 128.37, 128.71, 128.81, 130.70, 130.92, 134.44, 140.89, 144.00, 145.67, 149.26, 178.13

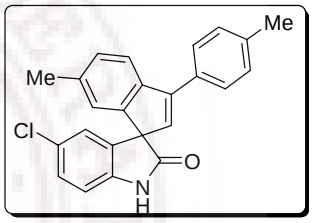
LCMS (m/z) : 344 $(M+H)^+$, 346 $(M+H+2)^+$

Anal calc′d for $C_{22}H_{14}ClNO$: C, 76.86; H, 4.10; N, 4.07

Found : C, 76.74; H, 4.12; N, 4.02

[6-Methyl-3-(4-methylphenyl)-1*H*-indene]-1-spiro-3′-(5′-chloroindolin-2′-one) (155e)

This compound was obtained as a colorless solid *via* the treatment of 5-chloroisatin (**154b**) with 1,1-di(4-methylphenyl)ethylene (**153b**) under the influence of $TiCl_4$ following the similar procedure described for the molecule **155a**.



Reaction time : 18 h

Yield : 80%

Mp : 130-132 ^{0}C

IR (KBr) : ν 3300-2800 (multiple bands), 1714, 1610 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.31 (s, 3H), 2.42 (s, 3H), 6.19 (s, 1H), 6.78 (d, 1H, *J* = 2.0 Hz), 6.85 (s, 1H), 6.93 (d, 1H, *J* = 8.4 Hz), 7.17 (d, 1H, *J* = 8.0 Hz), 7.22 (dd, 1H, *J* = 8.4 Hz & 2.4 Hz), 7.27 (d, 2H, *J* = 8.0 Hz), 7.50 (d, 1H, *J* = 8.0 Hz), 7.58 (d, 2H, *J* = 8.0 Hz), 8.24 (s, 1H, D_2O exchangeable)

^{13}C NMR (50 MHz) : δ 21.40, 64.97, 111.64, 121.34, 123.69, 124.18, 127.67, 128.13, 128.57, 129.03, 129.44, 131.19, 131.75, 136.86, 138.42, 140.87, 141.43, 145.94, 148.99, 178.49

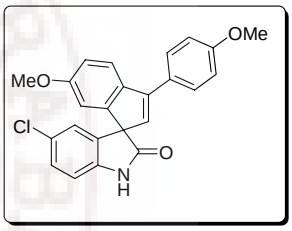
LCMS (m/z) : 370 $(M-H)^+$, 372 $(M-H+2)^+$

Anal calc′d for $C_{24}H_{18}ClNO$: C, 77.52; H, 4.88; N, 3.77

Found : C, 77.63; H, 4.89; N, 3.73

[6-Methoxy-3-(4-methoxyphenyl)-1*H*-indene]-1-spiro-3′-(5′-chloroindolin-2′-one) (155f)

This compound was prepared *via* the tandem Prins and Friedel-Crafts reactions of 5-chloroisatin (**154b**) with 1,1-di(4-methoxyphenyl)ethylene (**153c**) using $TiCl_4$ following the similar procedure described for the molecule **155a**.



Reaction time : 18 h

Yield : 88%

Mp : 128-130 ^{0}C

IR (KBr) : ν 3300-2800 (multiple bands), 1714, 1610 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.75 (s, 3H), 3.87 (s, 3H), 6.11 (s, 1H), 6.60 (d, 1H, *J* = 2.4 Hz), 6.79 (s, 1H), 6.86-6.95 (m, 2H), 6.99 (d, 2H, *J* = 8.4 Hz), 7.22 (dd, 1H, *J* = 8.4 Hz & 2.4 Hz), 7.51 (d, 1H, *J* = 8.4 Hz), 7.62 (d, 2H, *J* = 8.4 Hz), 8.20 (s, 1H, D_2O exchangeable)

^{13}C NMR (50 MHz) : δ 55.46, 55.68, 64.85, 109.55, 111.49, 113.51, 114.18, 122.19, 124.37, 127.23, 127.55, 128.30, 128.64, 129.01,

131.36, 136.94, 140.65, 147.47, 148.34, 159.23, 159.93, 178.17

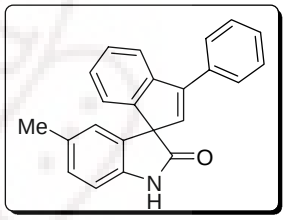
LCMS (m/z) : 404 $(M+H)^+$; 406 $(M+H+2)^+$

Anal calc′d for $C_{24}H_{18}ClNO_3$: C, 71.38; H, 4.49; N, 3.47

Found : C, 71.60; H, 4.49; N, 3.49

(3-Phenyl-1*H*-indene)-1-spiro-3′-(5′-methylindolin-2′-one) (155g)

This compound was prepared as a colorless solid *via* the reaction of 1,1-diphenylethylene (**153a**) with 5-methylisatin (**154c**) under the influence of $TiCl_4$ following the similar procedure described for molecule **155a**.



Reaction time : 13 h

Yield : 61%

Mp : 188-190 ^{0}C

IR (KBr) : ν 3250-2800 (multiple bands), 1707, 1622 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.20 (s, 3H), 6.34 (s, 1H), 6.61 (s, 1H), 6.89 (d, 1H, *J* = 8.0 Hz), 7.03 (d, 1H, *J* = 7.6 Hz), 7.08 (d, 1H, *J* = 7.2 Hz), 7.18-7.25 (m, 1H), 7.35-7.51 (m, 4H), 7.64 (d, 1H, *J* = 7.6 Hz), 7.71 (d, 2H, *J* = 7.2 Hz), 8.73 (s, 1H, D_2O exchangeable)

^{13}C NMR (50 MHz) : δ 20.96, 65.33, 110.40, 121.36, 122.97, 124.40, 126.68, 127.87, 127.99, 128.37, 128.69, 128.84, 129.03, 132.01, 132.35, 134.75, 139.90, 144.02, 146.52, 148.48, 178.39

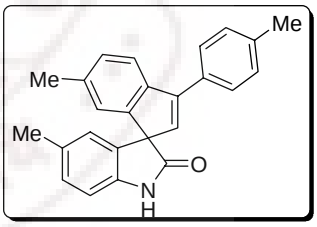
LCMS (m/z) : 346 $(M+Na)^+$

Anal calc′d for $C_{23}H_{17}NO$: C, 85.42; H, 5.30; N, 4.33

Found : C, 85.22; H, 5.31; N, 4.35

[6-Methyl-3-(4-methylphenyl)-1*H*-indene]-1-spiro-3′-(5′-methylindolin-2′-one) (155h)

This compound was prepared *via* the tandem Prins and Friedel-Crafts reactions between 5-methylisatin (**154c**) and 1,1-di(4-methylyphenyl)ethylene (**153b**) under the influence of $TiCl_4$, following the procedure described for the molecule **155a**.



Reaction time : 13 h

Yield : 79%

Mp : 184-186 ^{0}C

IR (KBr) : ν 3250-2800 (multiple bands), 1707, 1622 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.21 (s, 3H), 2.30 (s, 3H), 2.41 (s, 3H), 6.22 (s, 1H), 6.62 (s, 1H), 6.86-6.93 (m, 2H), 7.05 (d, 1H, *J* = 8.0 Hz), 7.16 (d, 1H, *J* = 7.6 Hz), 7.27 (d, 2H, *J* = 8.0 Hz), 7.50 (d, 1H, *J* =

7.6 Hz), 7.59 (d, 2H, *J* = 8.0 Hz), 7.85 (s, 1H, D_2O exchangeable)

^{13}C NMR (50 MHz) : δ 20.92, 21.35, 65.11, 110.38, 121.05, 123.69, 124.35, 127.67, 128.64, 128.88, 129.30, 130.46, 132.06, 132.18, 136.50, 138.05, 139.95, 141.47, 146.79, 148.17, 178.88

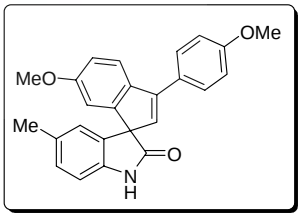
LCMS (m/z) : 352 $(M+H)^+$

Anal calc′d for $C_{25}H_{21}NO$: C, 85.44; H, 6.02; N, 3.99

Found : C, 85.27; H, 6.03; N, 4.04

[6-Methoxy-3-(4-methoxyphenyl)-1*H*-indene]-1-spiro-3′-(5′-methylindolin-2′-one) (155i)

This was obtained as a colorless solid, *via* the reaction between 5-methylisatin (**154c**) and 1,1-di(4-methoxyphenyl)ethylene (**153c**) under the influence of $TiCl_4$ following the similar procedure described for the molecule **155a**.



Reaction time : 13 h

Yield : 76%

Mp : 156-158 ^{0}C

IR (KBr) : ν 3250-2800 (multiple bands), 1707, 1610 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.21 (s, 3H), 3.74 (s, 3H), 3.87 (s, 3H), 6.15 (s, 1H), 6.62 (s, 2H), 6.86-6.92 (m, 2H), 6.99 (d, 2H, *J* = 8.8 Hz), 7.03 (d, 1H, *J* = 8.0 Hz), 7.52 (d, 1H, *J* = 8.4 Hz), 7.64 (d, 2H, *J* = 8.8 Hz), 8.53 (s, 1H, D_2O exchangeable)

^{13}C NMR (50 MHz) : δ 20.96, 55.38, 55.58, 65.09, 109.41, 110.33, 113.34, 114.09, 121.85, 124.49, 127.57, 128.74, 128.96, 129.44, 132.35, 137.03, 139.82, 147.49, 148.31, 159.04, 159.72, 178.68

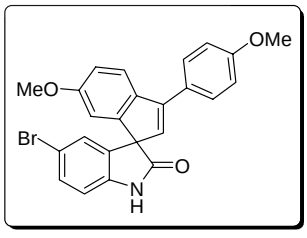
LCMS (m/z) : 382 $(M-H)^+$

Anal calc′d for $C_{25}H_{21}NO_3$: C, 78.31; H, 5.52; N, 3.65

Found : C, 78.09; H, 5.49; N, 3.61

[6-Methoxy-3-(4-methoxyphenyl)-1*H*-indene]-1-spiro-3′-(5′-bromoindolin-2′-one) (155j)

This molecule was prepared as a colorless solid *via* the reaction of 5-bromoisatin (**154d**) with 1,1-di(4-methoxyphenylethylene) (**153c**) under the influence of $TiCl_4$ following the similar procedure described for the molecule **155a**.



Reaction time : 18 h

Yield : 64%

Mp : 164-166 ^{0}C

IR (KBr) : ν 3250-2800 (multiple bands), 1712, 1610 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.75 (s, 3H), 3.87 (s, 3H), 6.10 (s, 1H), 6.60 (d, 1H, *J* = 2.4 Hz), 6.83 (d, 1H, *J* = 8.4 Hz), 6.89-6.95 (m, 2H), 7.00 (d, 2H, *J* = 8.8 Hz), 7.31 (dd, 1H, *J* = 8.4 Hz & 2.0 Hz), 7.53 (d, 1H, *J* = 8.4 Hz), 7.63 (d, 2H, *J* = 8.4 Hz), 9.33 (s, 1H, D_2O exchangeable)

^{13}C NMR (50 MHz) : δ 55.38, 55.60, 64.85, 109.58, 112.17, 113.41, 114.18, 115.40, 122.09, 126.90, 127.16, 127.55, 128.93, 131.46, 131.60, 136.89, 141.30, 147.42, 148.19, 159.18, 159.91, 178.27

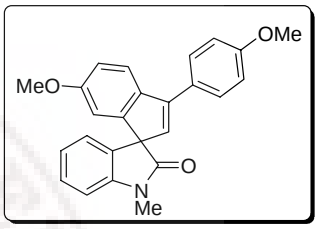
LCMS (m/z) : 446 $(M-H)^+$, 448 $(M+2-H)^+$

Anal calc′d for $C_{24}H_{18}BrNO_3$: C, 64.30; H, 4.05; N, 3.12.

Found : C, 64.14; H, 4.09; N, 3.18

[6-Methoxy-3-(4-methoxyphenyl)-1*H*-indene]-1-spiro-3′–(1′-methylindolin-2′-one) (155k)

This was obtained as a colorless solid, *via* the treatment of *N*-methylisatin (**154e**) with 1,1-di(4-methoxyphenyl)ethylene (**153c**) under the influence of $TiCl_4$ following the similar procedure described for the molecule **155a**.



Reaction time : 18 h

Yield : 72%

Mp : 96-98 ^{0}C

IR (KBr) : ν 1714, 1608 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.35 (s, 3H), 3.72 (s, 3H), 3.86 (s, 3H), 6.09 (s, 1H), 6.51 (d, 1H, *J* = 2.4 Hz), 6.81-6.89 (m, 2H), 6.95-7.02 (m, 4H), 7.30-7.37 (m, 1H), 7.50 (d, 1H, *J* = 8.4 Hz), 7.60-7.64 (m, 2H)

^{13}C NMR (50 MHz) : δ 26.98, 55.36, 55.58, 64.36, 108.39, 109.48, 113.07, 114.06, 121.83, 122.97, 123.72, 127.60, 128.64, 128.71, 128.96, 137.18, 144.87, 147.51, 148.29, 159.01, 159.72, 175.29

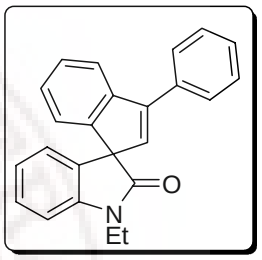
LCMS (m/z) : 384 $(M+H)^+$

Anal calc′d for $C_{25}H_{21}NO_3$: C, 78.31; H, 5.52; N, 3.65

Found : C, 78.53; H, 5.50; N, 3.69

(3-Phenyl-1*H*-indene)-1-spiro-3′-(1′-ethylindolin-2′-one) (155l)

This compound was obtained *via* the treatment of *N*-ethylisatin (**154f**) with 1,1-diphenylethylene (**153a**) under the influence of $TiCl_4$ following similar procedure described for the molecule **155a** as a colorless solid.



Reaction time : 24 h

Yield : 63%

Mp : 122-124 ^{0}C

IR (KBr) : ν 1716, 1610 cm^{-1}

H NMR (400 MHz) : δ 1.37 (t, 3H, *J* = 7.2 Hz), 3.84-4.00 (m, 2H), 6.29 (s, 1H), 6.80-6.88 (m, 1H), 6.92-7.04 (m, 3H), 7.16-7.20 (m, 1H), 7.28-7.50 (m, 5H), 7.61 (d, 1H, *J* = 7.6 Hz), 7.65-7.75 (m, 2H)

^{13}C NMR (50 MHz) : δ 12.72, 35.23, 64.51, 108.48, 121.17, 122.43, 122.58, 123.67, 126.43, 127.70, 128.18, 128.52, 131.89, 134.71, 143.90, 146.66, 148.39, 174.22

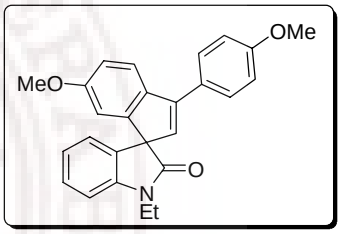
LCMS (m/z) : 338 $(M+H)^+$

Anal calc′d for $C_{24}H_{19}NO$: C, 85.43; H, 5.68; N, 4.15

Found : C, 85.20; H, 5.65; N, 4.13

[6-Methoxy-3-(4-methoxyphenyl)-1*H*-indene]-1-spiro-3′–(1′-ethylindolin-2′-one) (155m)

This molecule was prepared as a colorless solid *via* the tandem Prins and intramolecular Friedel-Crafts reactions between *N*-ethylisatin (**154f**) and 1,1-di(4-methoxyphenylethylene) (**153c**) under the influence of $TiCl_4$ following the similar procedure described for the molecule **155a**.



Reaction time : 18 h

Yield : 71%

Mp : 96-98 ^{0}C

IR (KBr) : ν 1714, 1608 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.37 (t, 3H, *J* = 7.2 Hz), 3.72 (s, 3H), 3.84-4.04 (m, 5H), 6.10 (s, 1H), 6.49 (s, 1H), 6.82-6.89 (m, 2H), 6.92-7.04 (m, 4H), 7.28-7.35 (m, 1H), 7.50 (d, 1H, *J* = 8.0 Hz), 7.62 (d, 2H, *J* = 8.8 Hz)

^{13}C NMR (50 MHz) : δ 12.57, 35.03, 54.97, 55.17, 64.09, 108.34, 109.24, 112.51, 113.84, 121.51, 122.43, 123.52, 127.28, 128.37, 128.47, 128.62, 128.88, 136.79, 143.66, 147.20, 148.34, 158.74, 159.50, 174.39

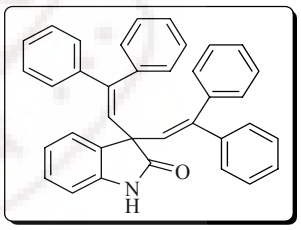
LCMS (m/z) : 398 $(M+H)^+$

Anal calc′d for $C_{26}H_{23}NO_3$: C, 78.57; H, 5.83; N, 3.52

Found : C, 78.82; H, 5.80; N, 3.60

3,3-Bis (2,2-diphenylvinyl)indolin-2-one (157a)

Reaction of isatin (**154a**) (1 mmol, 0.147 g**)** with 1,1-diphenylethylene (**153a**) (1 mmol, 0.180 g) in the presence of $TiCl_4$ (1 mmol, 0.5 mL, 2M solution in dichloromethane) at 0 ^{0}C for 5 minutes provided (3-phenyl-1*H*-indene)-1-spiro-3′-(indolin-2′-one) (**155a**) in 17% (0.053 g) (based on isatin **154a**) isolated yield and 3,3-bis(2,2-diphenylvinyl)-indolin-2-one (**157a**) in 45% (0.110 g) (based on alkene **153a**) isolated yields. We have also recovered isatin (**154a**) in 31% (0.045 g) and alkene (**153a**) in 17% (0.030 g) isolated yields.



Reaction time : 5 min

Yield : 45%

Mp : 218-220 ^{0}C

IR (KBr) : ν 3350-2950 (multiple bands), 1716, 1614 cm^{-1}

^{1}H NMR (400 MHz) : δ 6.30-6.36 (m, 3H), 6.61 (s, 1H, D_2O exchangeable), 6.84-7.24 (m, 23H)

^{13}C NMR (50 MHz) : δ 56.28, 109.72, 122.48, 124.76, 127.21, 127.33, 127.60, 127.96, 129.54, 130.07, 136.53, 138.32, 140.19, 142.86, 144.46, 178.66

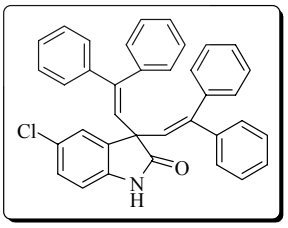
LCMS (m/z) : 490 $(M+H)^+$

Anal calc′d for $C_{36}H_{27}NO$: C, 88.31; H, 5.56; N, 2.86

Found : C, 88.11; H, 5.59; N, 2.89

3,3-Bis(2,2-diphenylvinyl)-5-chloroindolin-2-one (157b)

Reaction of 5-chloroisatin (**154b**) (1 mmol, 0.181 g) with 1,1-diphenylethylene (**153a**) (1 mmol, 0.180 g) in the presence of $TiCl_4$ (1 mmol, 0.5 mL, 2M solution in dichloromethane) at 0 ^{0}C for five minutes provided (3-phenyl-1*H*-indene)-1-spiro-3′-(5′-chloroindolin-2′-one) (**155d**) in 16% (0.055 g) isolated yield (based on **154b**) and 3,3-bis(2,2-diphenylvinyl)-5-chloroindolin-2-one (**157b**) in 37% (0.098 g) (based on alkene **153a**) isolated yield. We also recovered 5-chloroisatin (**154b**) in 25% (0.045 g) and alkene (**153a**) in about 6% (0.010 g) isolated yields.



Reaction time : 5 min

Yield : 37%

Mp : 168-170 ^{0}C

IR (KBr) : ν 3300-2800 (multiple bands), 1711, 1614 cm^{-1}

^{1}H NMR (400 MHz) : δ 6.22 (d, 1H, *J* = 8.4 Hz), 6.36 (s, 2H), 6.85-6.90 (m, 5H), 6.91-6.96 (m, 1H), 7.00-7.06 (m, 5H), 7.07-7.18 (m, 6H), 7.19-7.24 (m, 6H)

^{13}C NMR (50 MHz) : δ 56.57, 110.72, 125.56, 127.26, 127.38, 127.62, 128.06, 128.62, 129.73, 136.69, 138.00, 138.93, 142.40, 144.92, 179.36.

LCMS (m/z) : 524 $(M+H)^+$, 526 $(M+2+H)^+$

Anal calc′d for $C_{36}H_{26}ClNO$: C, 82.51; H, 5.00; N, 2.67

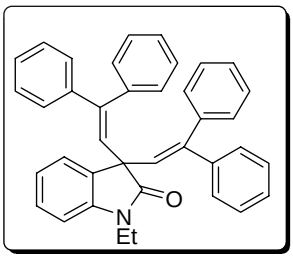
Found : C, 82.79; H, 5.03; N, 2.64

3,3-Bis(2,2-diphenylvinyl)-1-ethylindolin-2-one (157c)

Reaction of *N*-ethylisatin (**154f**) (1 mmol, 0.175 g) with 1,1-diphenylethylene (**153a**) (1 mmol, 0.180g) in the presence of $TiCl_4$ (1 mmol, 0.5 mL, 2M solution in dichloromethane) at room temperature for 24 h provided 3,3-bis(2,2-diphenylvinyl)-1-ethylindolin-2-one (**157c)** in 23% (0.060g) (based on olefin (**153a**), and 3-phenyl-1*H*-indene)-1-spiro-3′-(1′-ethylindolin-2′-one (**155l**) in 63% (0.212 g) isolated yields (based on *N*-ethylisatin) (**154f**).

Reaction time : 24 h

Yield : 23%



Mp : 80-82 ^{0}C

IR (KBr) : ν 1712, 1606 cm^{-1}

^{1}H NMR (400 MHz) : δ 0.91 (t, 3H, *J* = 7.2 Hz), 2.99 (q, 2H, *J* = 7.2 Hz), 6.19 (s, 2H), 6.41 (d, 1H, *J* = 7.6 Hz), 6.82-7.02 (m, 9H), 7.08-7.23 (m, 14H)

^{13}C NMR (50 MHz) : δ 12.62, 34.96, 55.92, 108.14, 122.41, 124.57, 127.21, 127.28, 127.43, 127.67, 127.89, 129.49, 130.10, 136.57, 138.49, 141.98, 143.27, 144.04, 175.53

LCMS (m/z) : 518 $(M+H)^+$

Anal calc′d for $C_{38}H_{31}NO$: C, 88.17; H, 6.04; N, 2.71

Found : C, 88.03; H, 6.06; N, 2.76

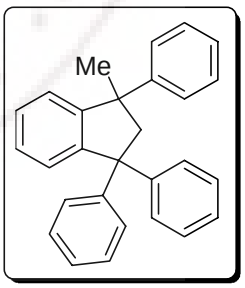
We have also carried out the following experiments with a view to prove the mechanistic path-way (**Y**)

Reaction of 3,3-bis(2,2-diphenylvinyl)indolin-2-one (0.5 mmol, 0.244 g) (**157a**) with $TiCl_4$ (0.5 mmol, 0.25 mL of 2M solution in CH_2Cl_2) in dichloromethane for 13 h at room temperature provided (3-phenyl-1*H*-indene)-1-spiro-3′-(indolin-2′-one) **(155a)** in 85% (0.132 g) isolated yield and 3-methyl-1,1,3-triphenylindane (**158**)[246] in 60% (0.054 g) isolated yield.

Similar reaction of 3,3-bis(2,2-diphenylvinyl)-5-chloroindolin-2-one (0. 5 mmol, 0.258 g) (**157b**) with $TiCl_4$ in dichloromethane for 18 h at room temperature provided (3-phenyl-1*H*-indene)-1-spiro-3′-(5-chloroindolin-2′-one) (**155d**) in 88% (0.152g) isolated yield and 3-methyl-1,1,3-triphenylindane (**158**) in 70% (0.063 g) isolated yield.

Similar reaction of 3,3-bis(2,2-diphenylvinyl)-1-ethylindolin-2-one (**157c**), (0.5 mmol, 0.258 g) with $TiCl_4$ (0.5 mmol, 0.25 mL in 2M solution of dichloromethane) in dichloromethane for 48 h at room temperature provided [3-phenyl-1*H*-indene]-1-spiro-3′-(1′-ethylindolin-2′-one) (**155l**) and 3-methyl-1,1,3-triphenylindane (**158**) in 36% (0.061g) and 22% (0.020 g) isolated yields respectively. We have also recovered the starting material **157c** in 47% (0.122 g) isolated yield.

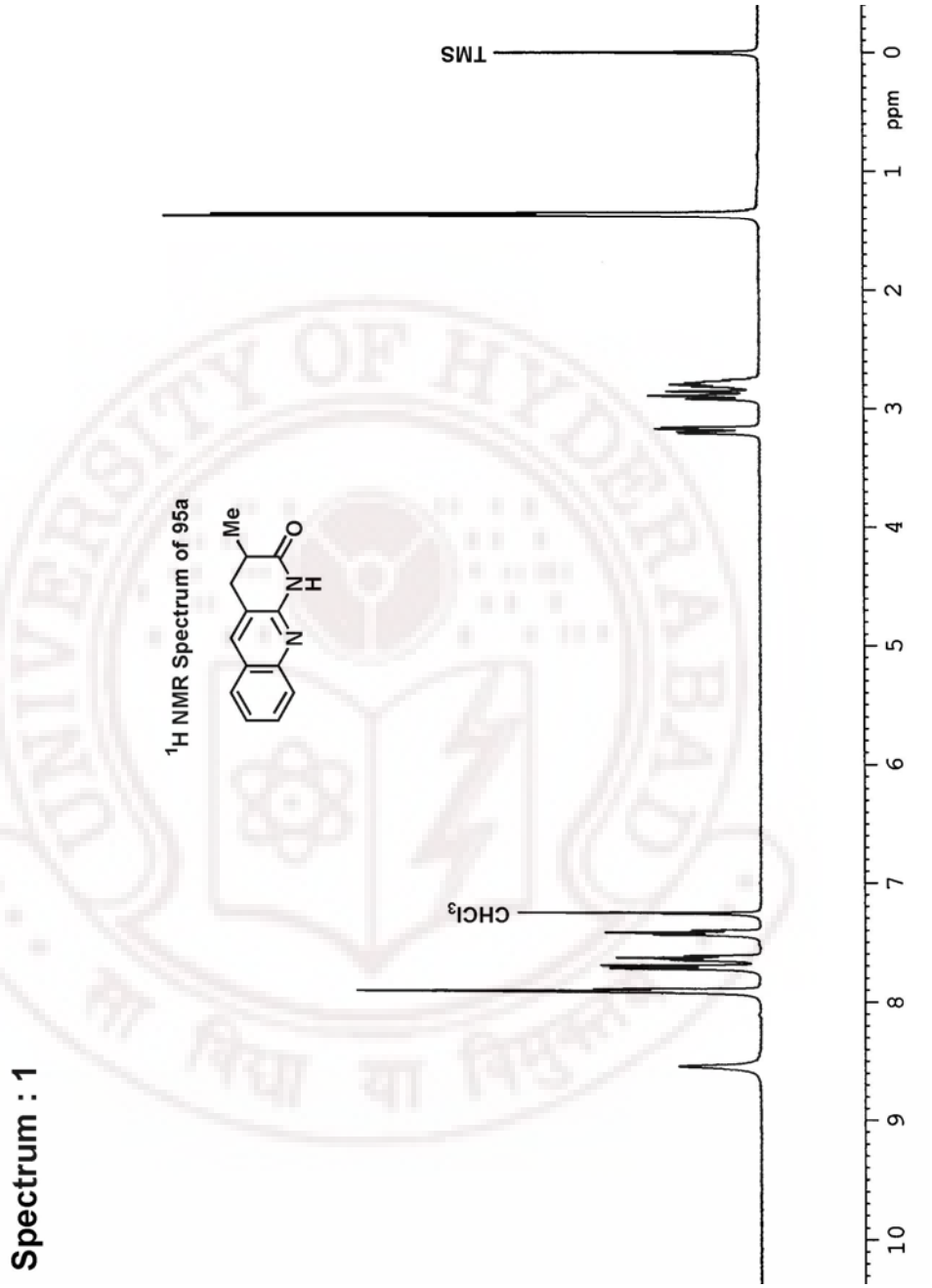
3-Methyl-1,1,3-triphenylindane (158)[246]

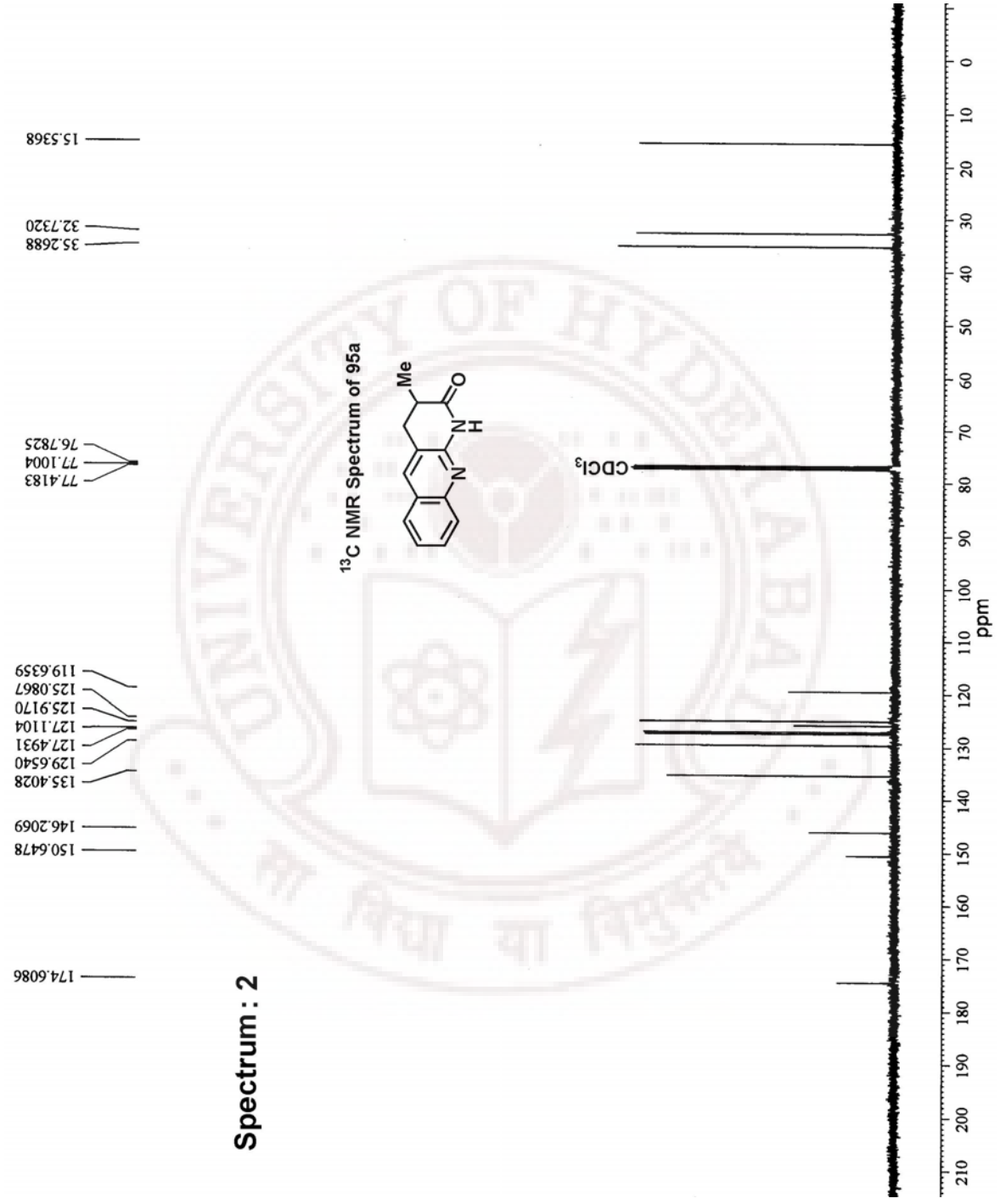


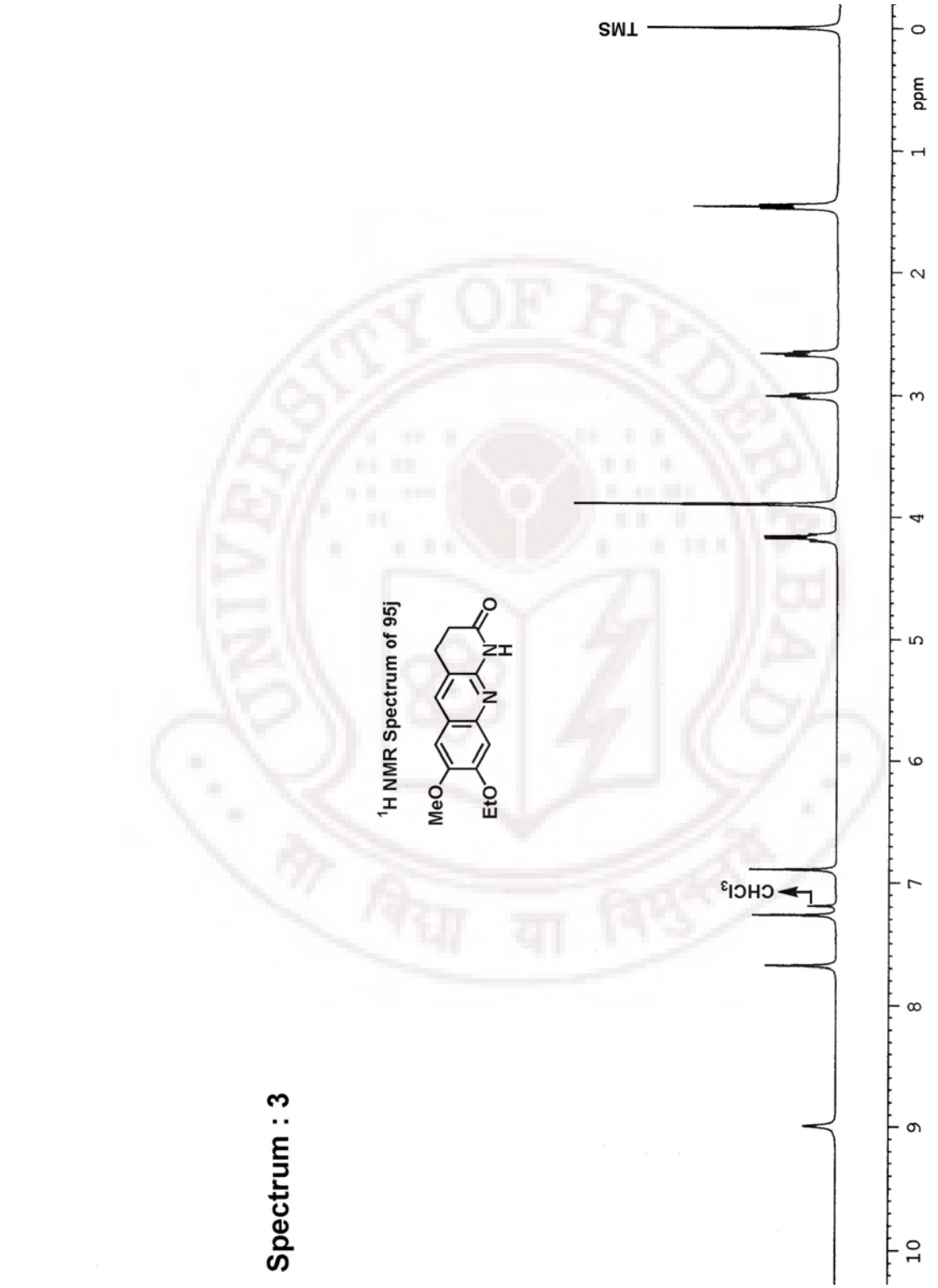
Mp : 138-140 ^{0}C (lit. 143-144 ^{0}C) [246]

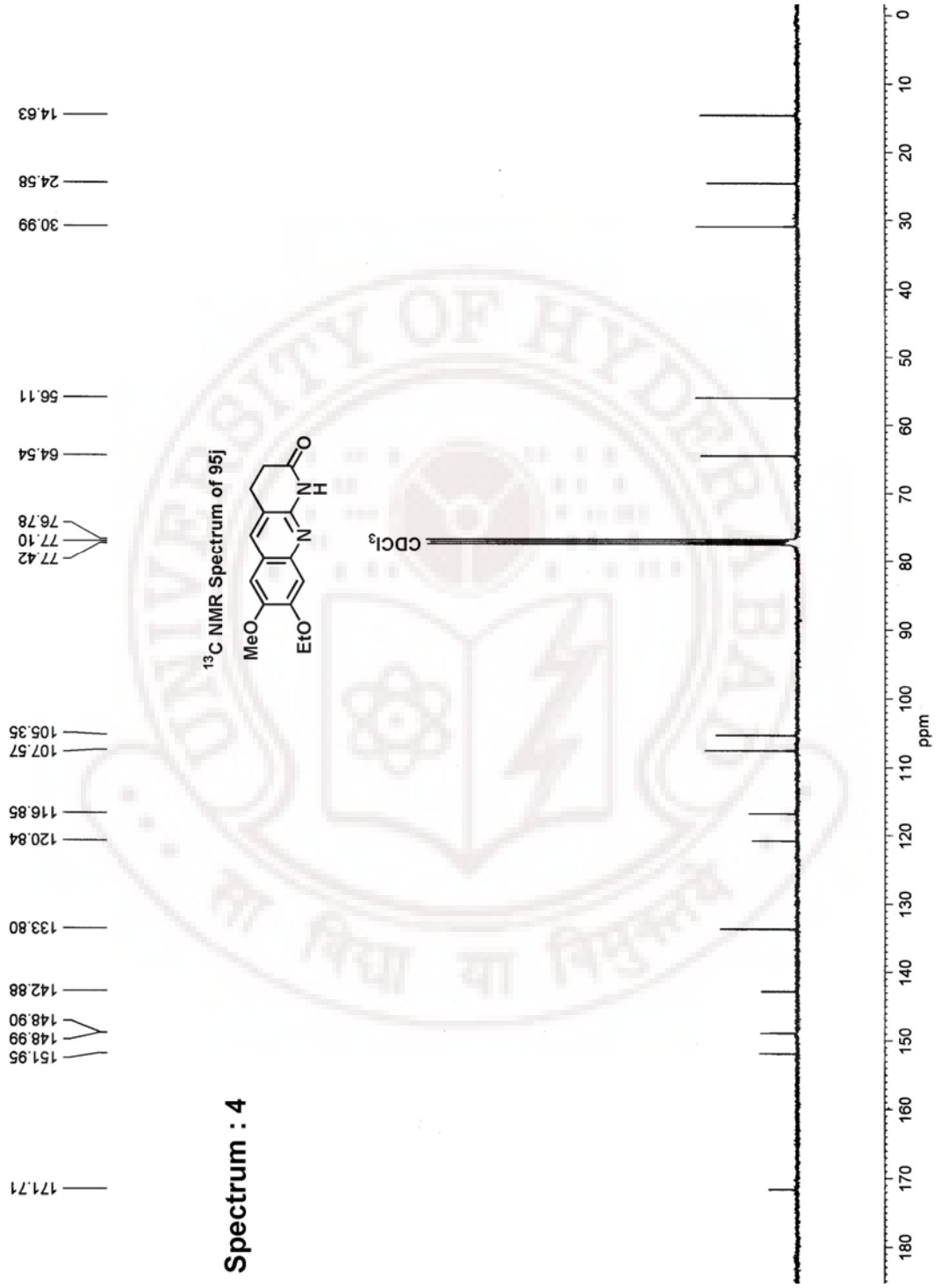
IR (KBr) : ν 2968, 1595 cm^{-1}

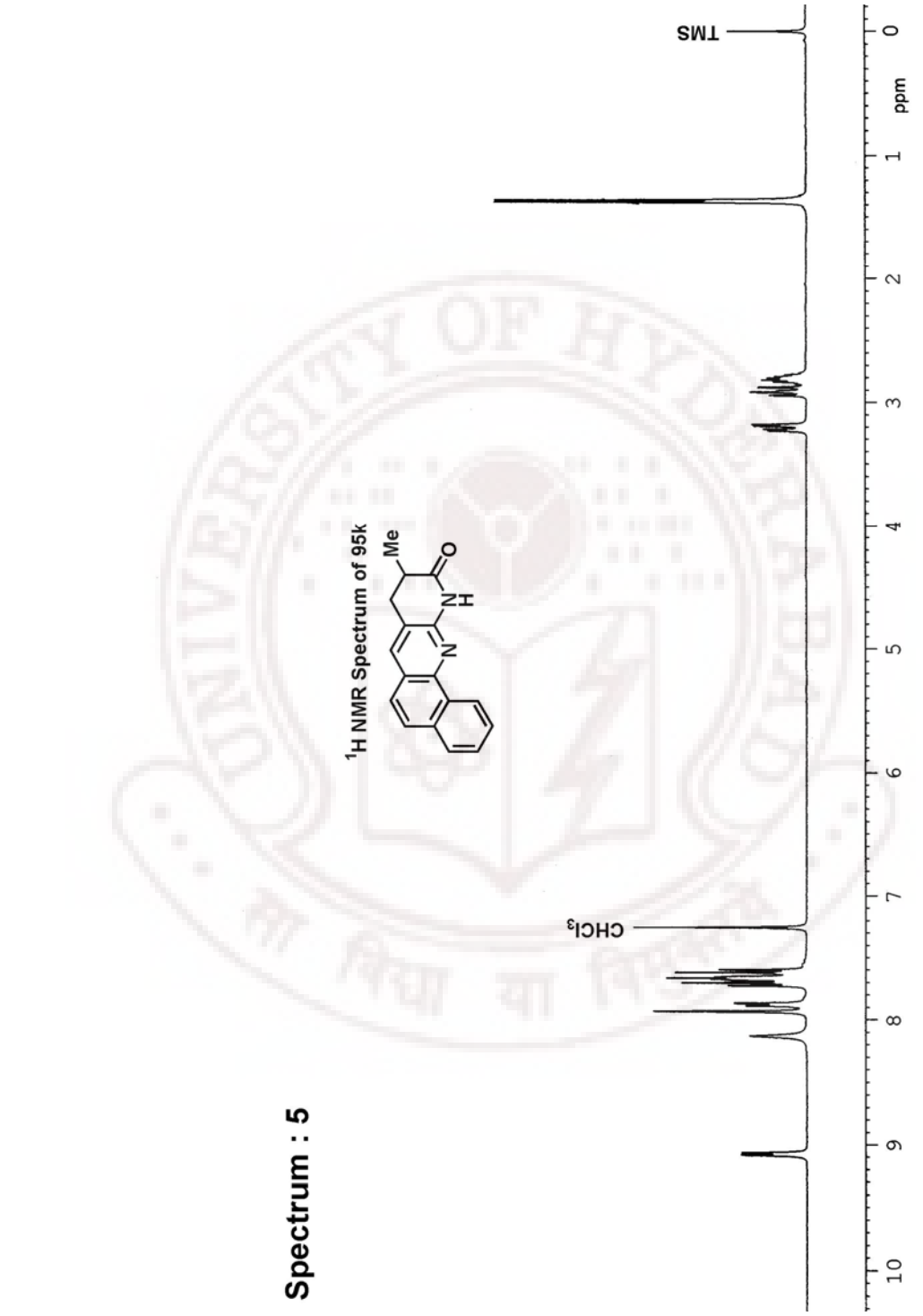
^{1}H NMR (400 MHz)	: δ 1.54 (s, 3H), 3.09 & 3.39 (ABq, 2H, *J* = 13.5 Hz), 6.98-7.34 (m, 19H)
^{13}C NMR (50 MHz)	: δ 28.99, 51.29, 61.06, 61.45, 125.12, 125.68, 126.07, 126.97, 127.53, 127.67, 127.96, 128.04, 128.76, 128.86, 147.59, 148.68, 148.97, 149.43, 150.62
LCMS (m/z)	: 361 $(M+H)^{+}$
Anal calc′d for $C_{28}H_{24}$	: C, 93.29; H, 6.71
Found	: C, 93.42; H, 6.74

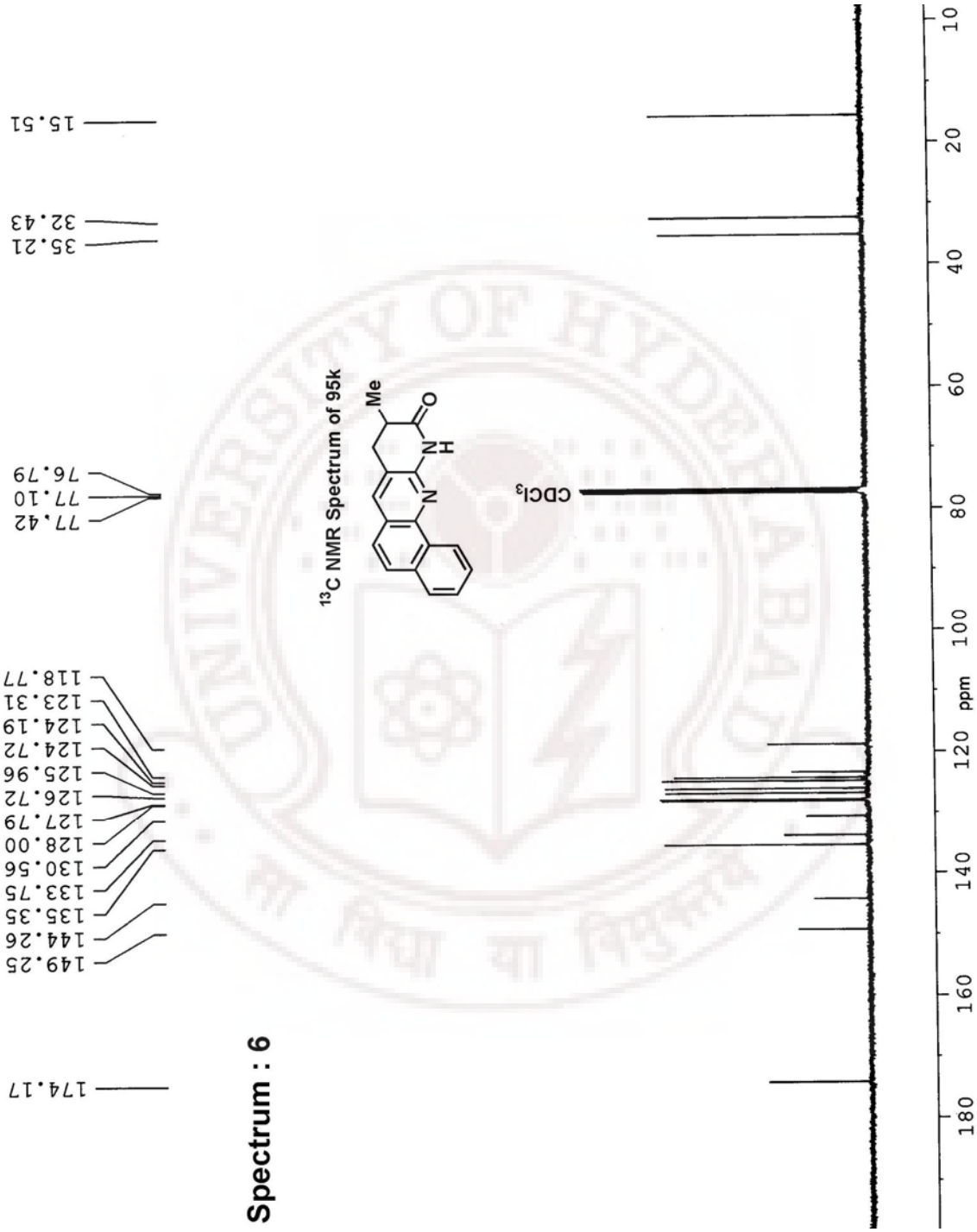

Spectrum : 1
^{1}H NMR Spectrum of 95a
Me
O
N
H
N
TMS
CHCl$_3$
10
9
8
7
6
5
4
3
2
1
ppm
0


Spectrum : 2
^{13}C NMR Spectrum of 95a
Me
O
NH
N
CDCl$_3$
174.6086
150.6478
146.2069
135.4028
129.6540
127.4931
127.1104
125.9170
125.0867
119.6359
77.4183
77.1004
76.7825
35.2688
32.7320
15.5368
ppm
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210


Spectrum : 3
^{1}H NMR Spectrum of 95j
MeO
EtO
N
H
O
CHCl$_3$
TMS
ppm
0
1
2
3
4
5
6
7
8
9
10


Spectrum : 4
^{13}C NMR Spectrum of 95j
MeO
EtO
CDCl$_3$
14.63
24.58
30.99
56.11
64.54
76.78
77.10
77.42
105.35
107.57
116.85
120.84
133.80
142.88
148.90
148.99
151.95
171.71
ppm


Spectrum : 5
^{1}H NMR Spectrum of 95k
Me
O
H
N
N
CHCl$_3$
TMS
ppm
0
1
2
3
4
5
6
7
8
9
10


Spectrum : 6
^{13}C NMR Spectrum of 95k
Me
O
NH
N
CDCl$_3$
174.17
149.25
144.26
135.35
133.75
130.56
128.00
127.79
126.72
125.96
124.72
124.19
123.31
118.77
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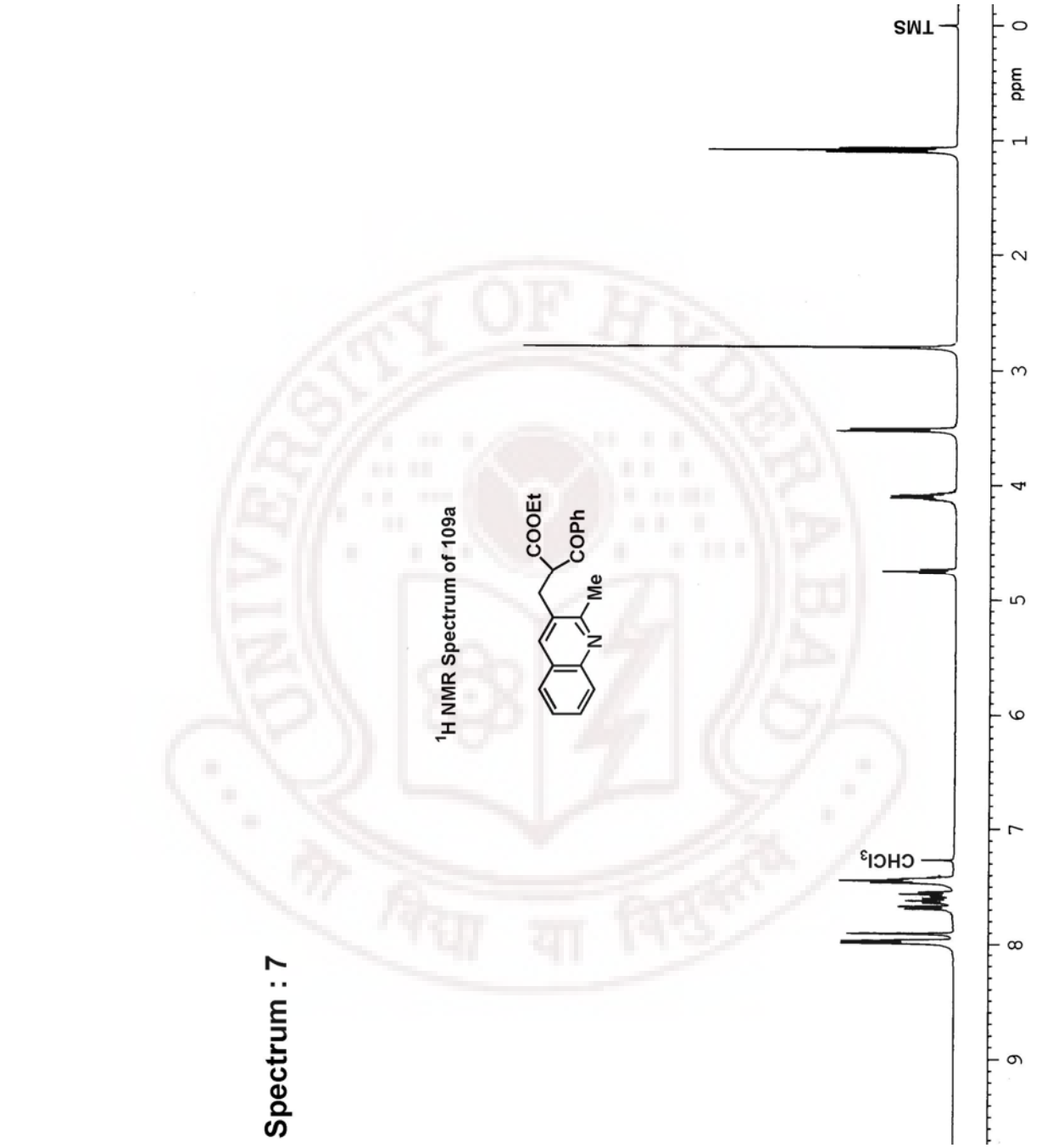
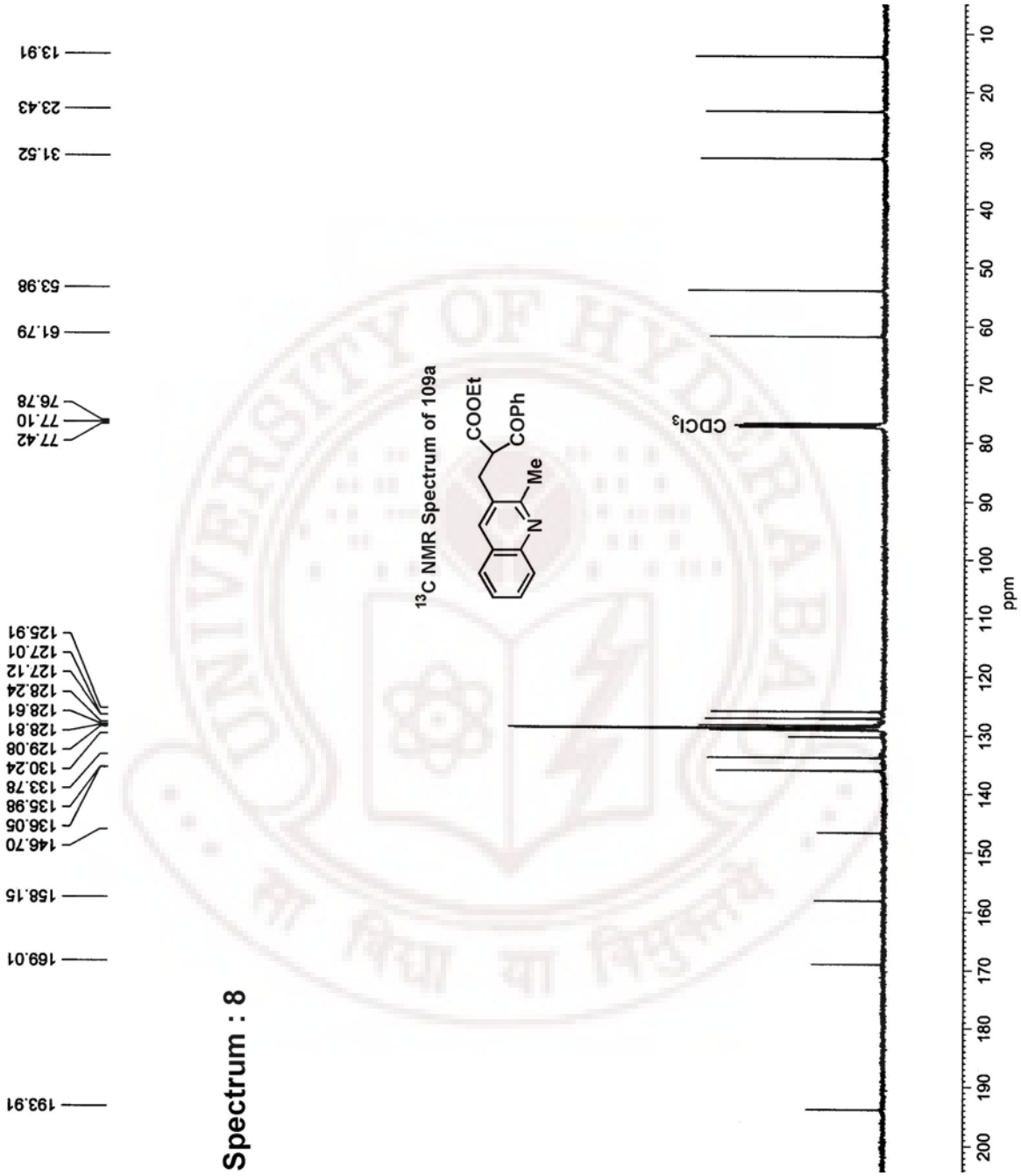
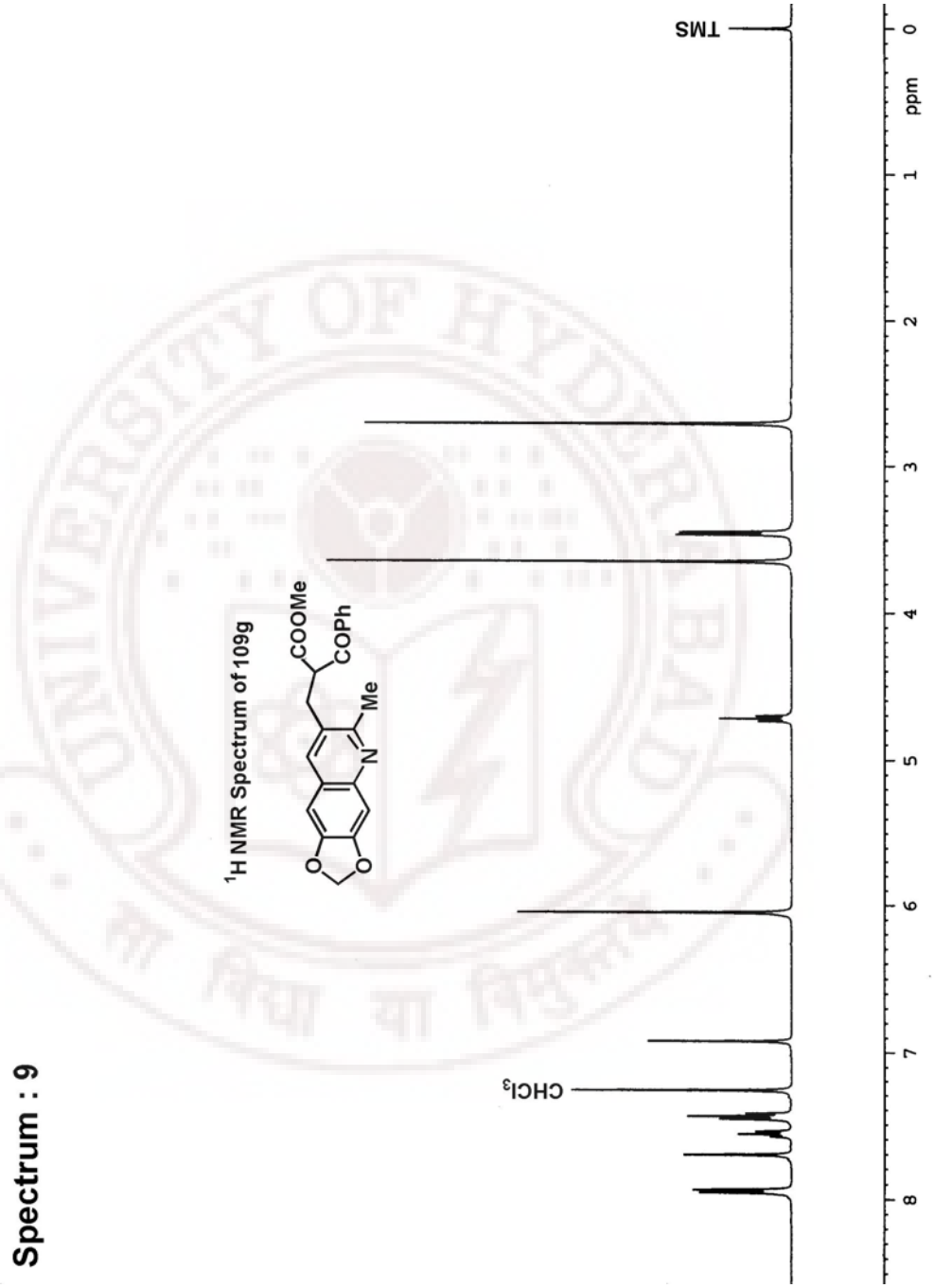
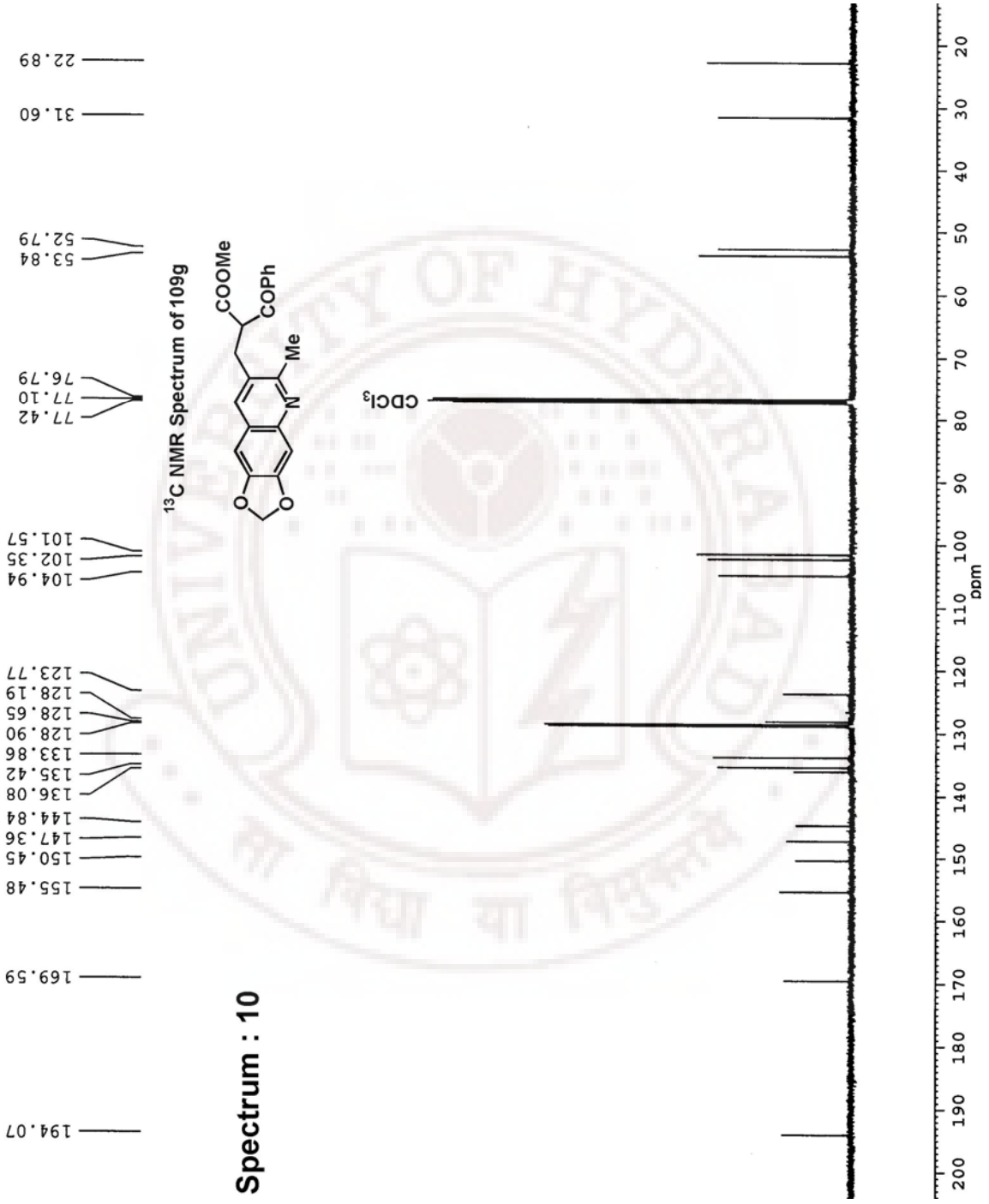
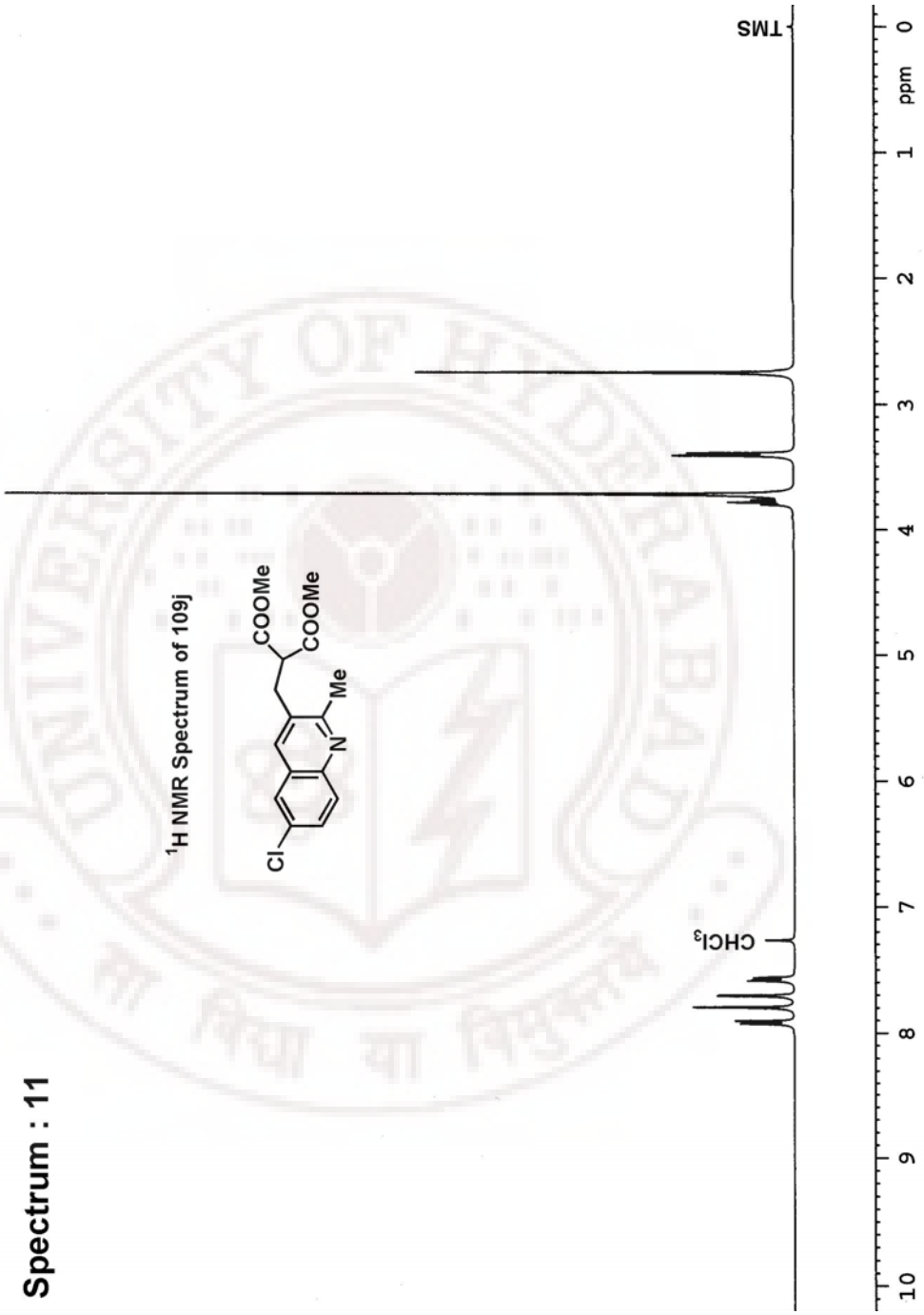
10
20
40
60
80
100
120
140
160
180

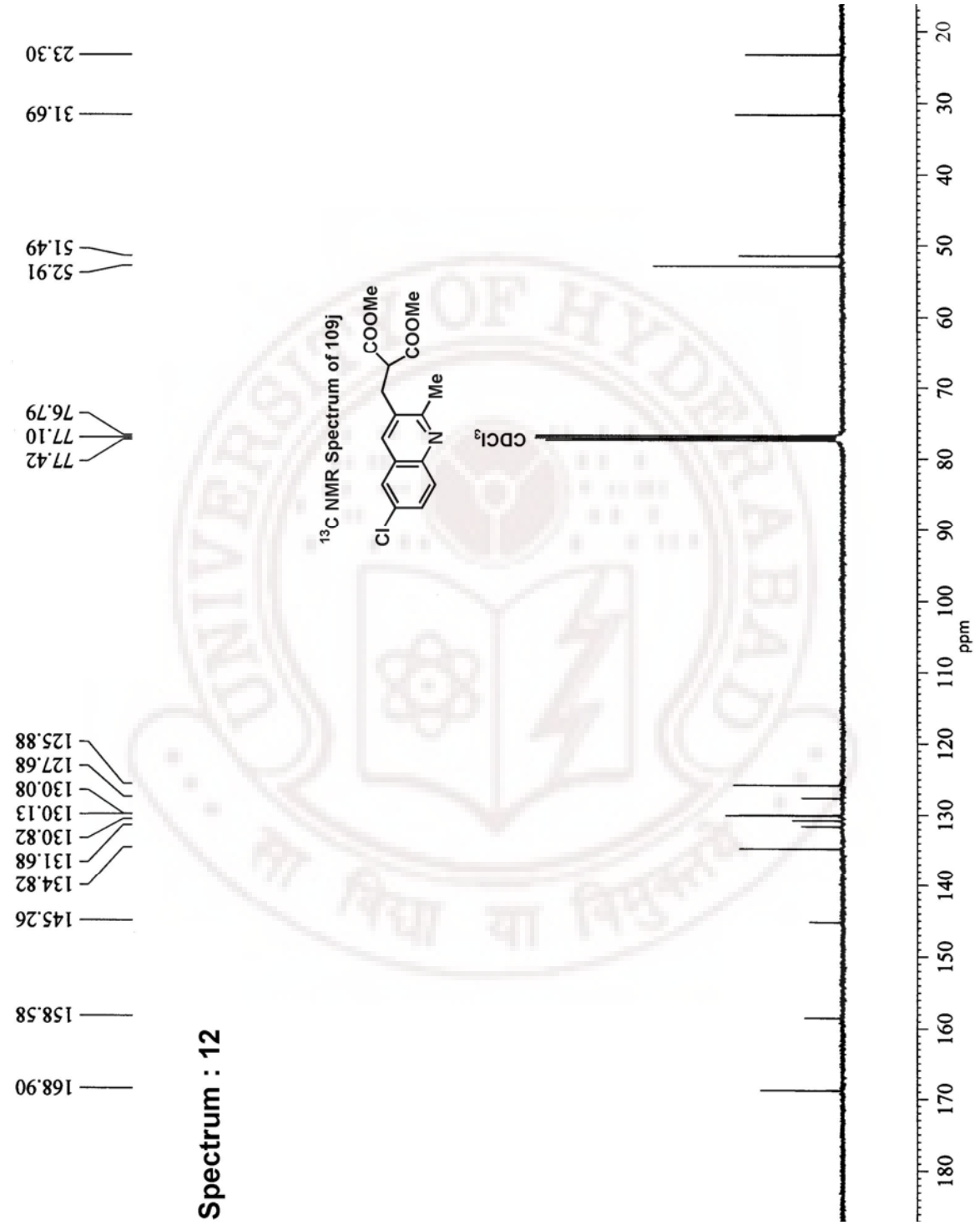

Spectrum : 7
^{1}H NMR Spectrum of 109a
COOEt
COPh
Me
N
CHCl$_3$
TMS
ppm
0
1
2
3
4
5
6
7
8
9

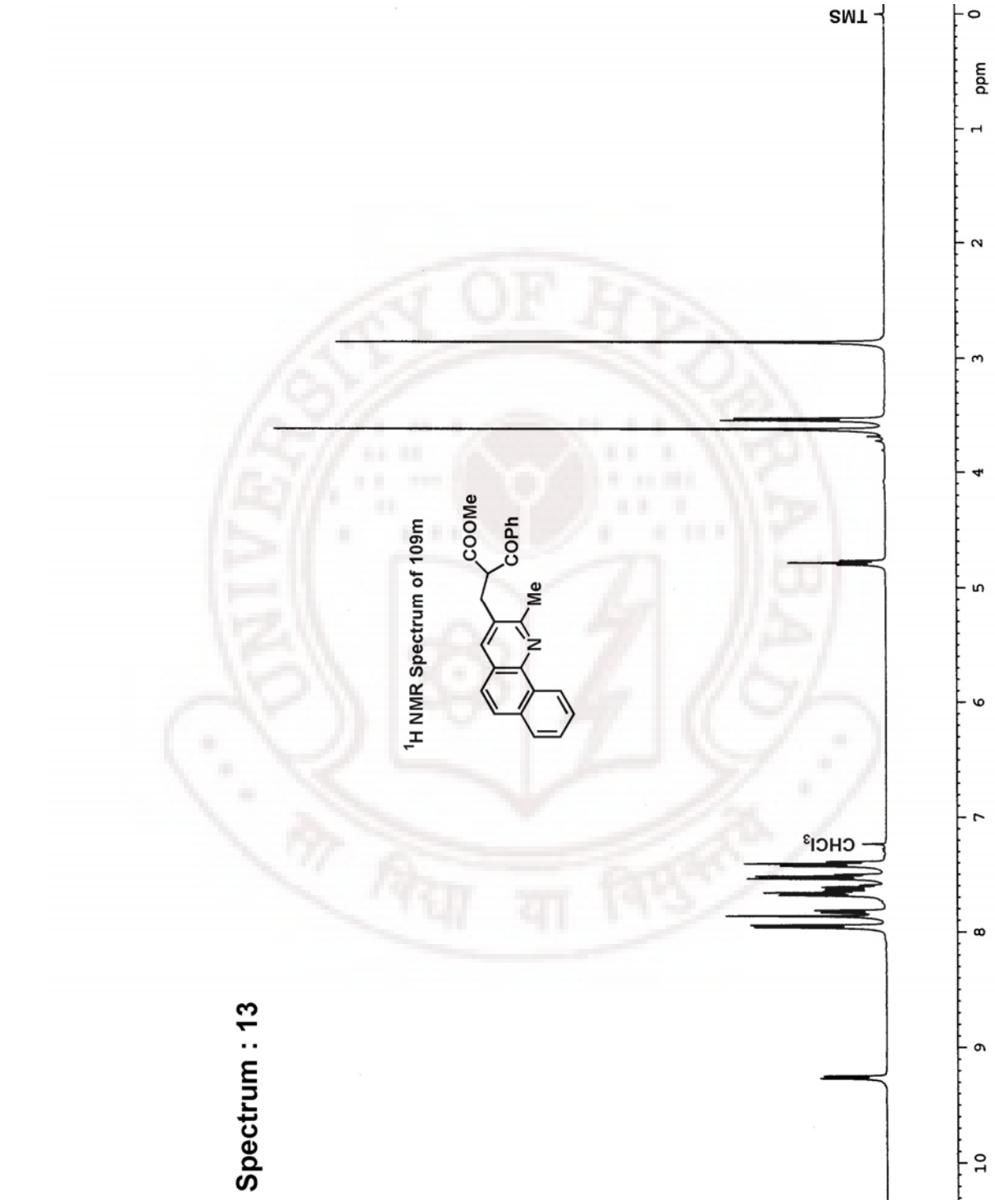

Spectrum : 8
^{13}C NMR Spectrum of 109a
COOEt
COPh
Me
N
CDCl$_3$
ppm
13.91
23.43
31.52
53.98
61.79
76.78
77.10
77.42
125.91
127.01
127.12
128.24
128.61
128.81
129.08
130.24
133.78
135.98
136.05
146.70
158.15
169.01
193.91

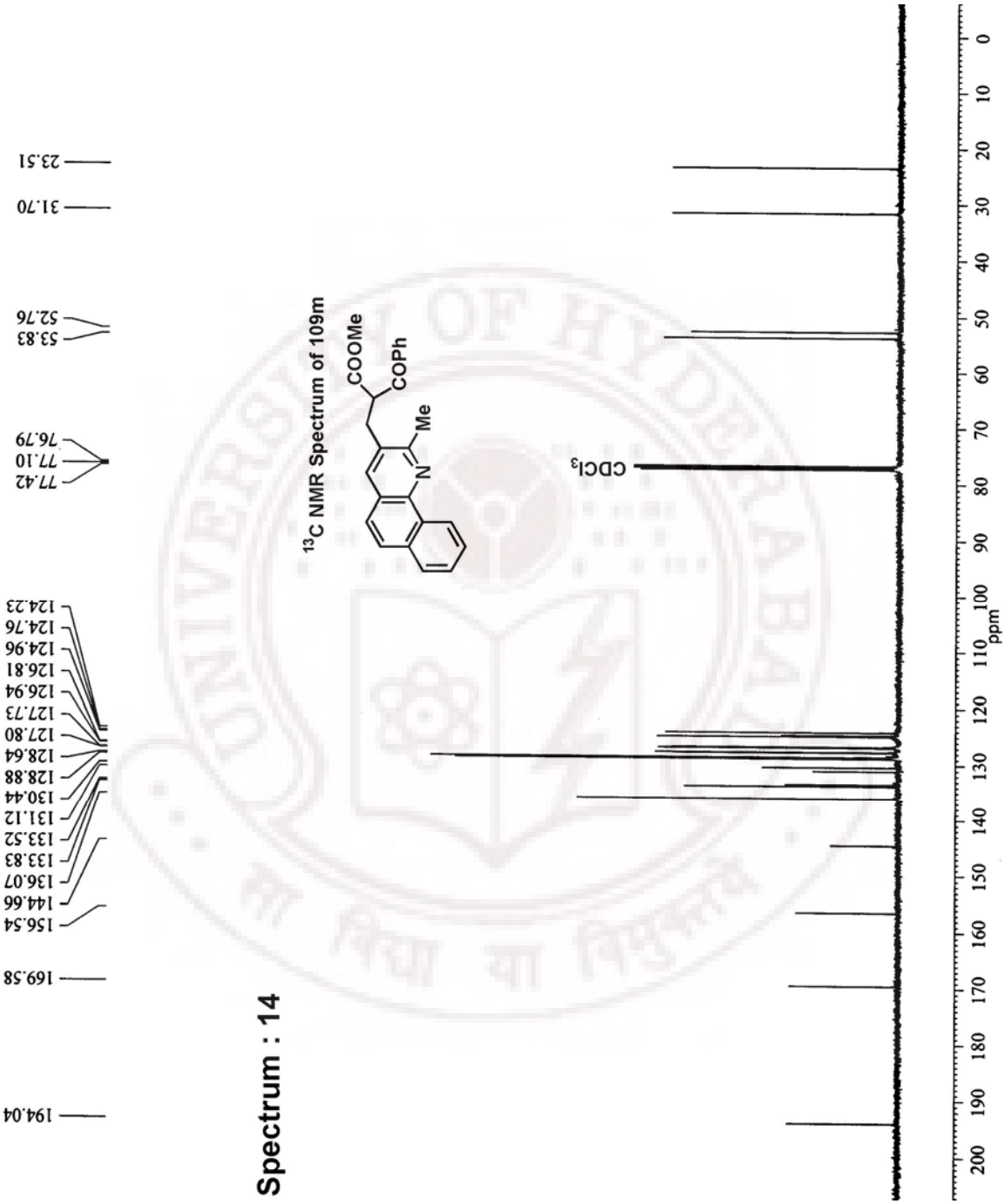

Spectrum : 9
^{1}H NMR Spectrum of 109g
COOMe
COPh
Me
N
O
O
CHCl$_3$
TMS
8
7
6
5
4
3
2
1
ppm
0

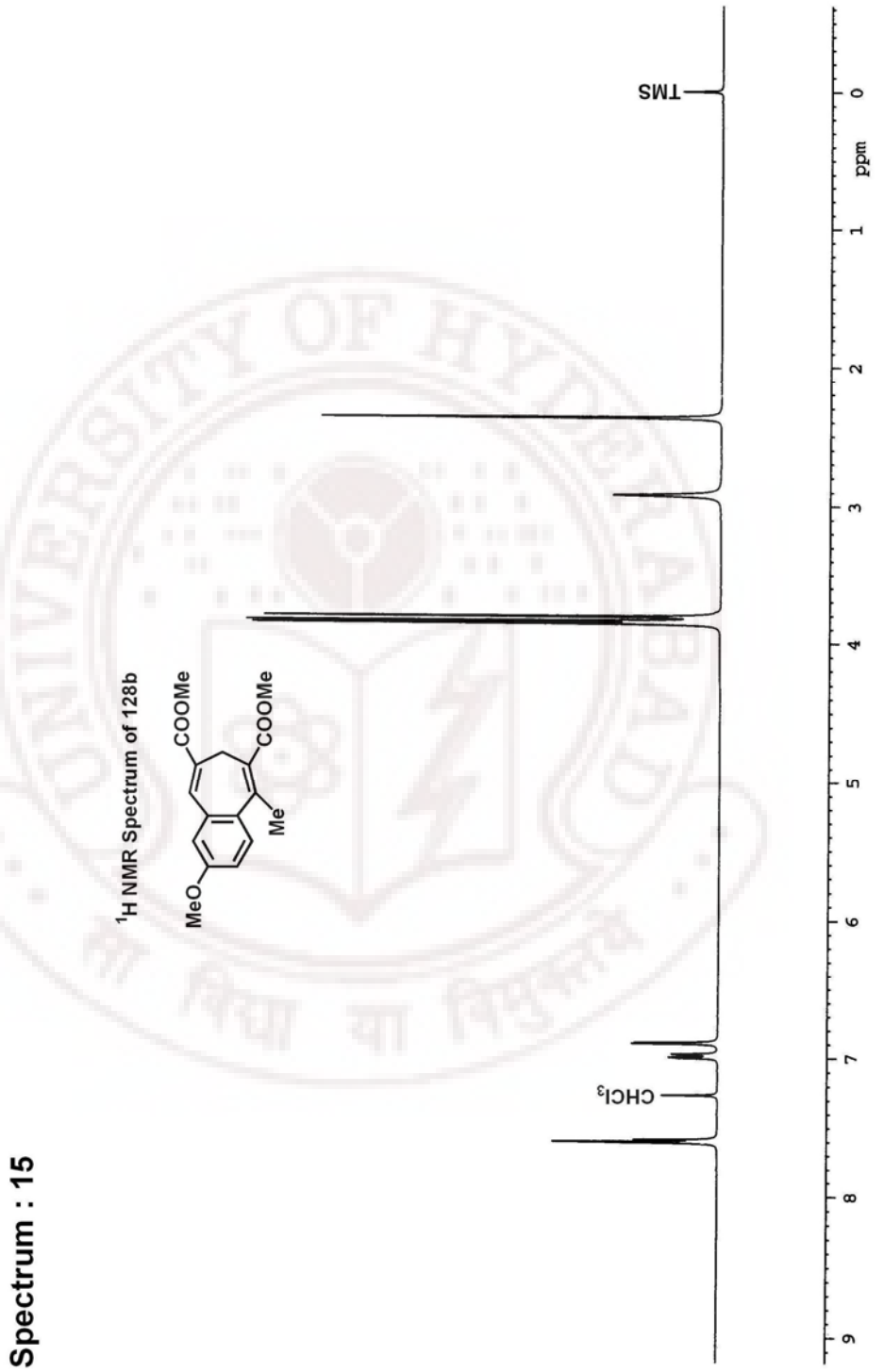

Spectrum : 10
^{13}C NMR Spectrum of 109g
COOMe
COPh
Me
N
O
O
CDCl$_3$
22.89
31.60
52.79
53.84
76.79
77.10
77.42
101.57
102.35
104.94
123.77
128.19
128.65
128.90
133.86
135.42
136.08
144.84
147.36
150.45
155.48
169.59
194.07
ppm

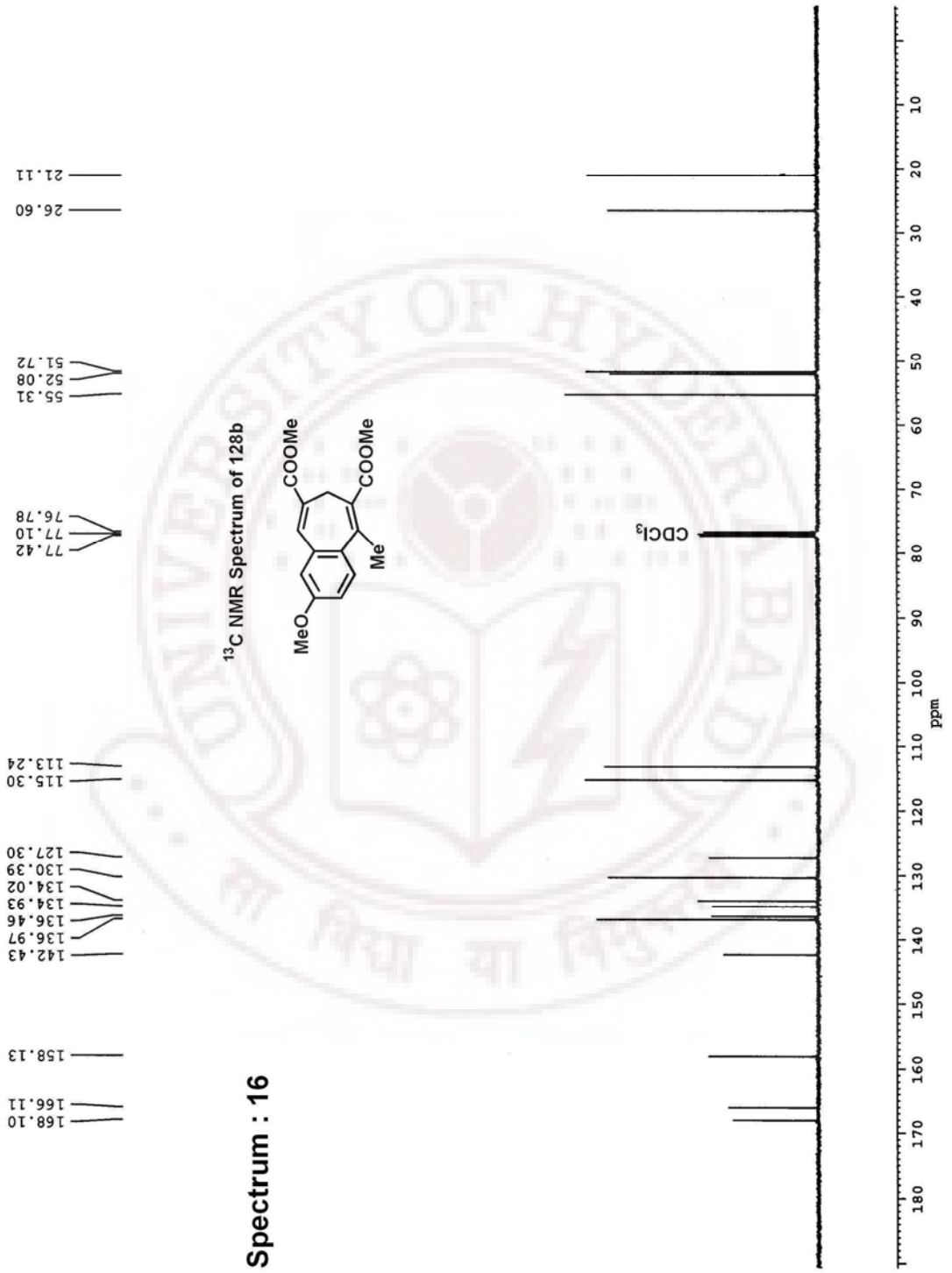

Spectrum : 11
^{1}H NMR Spectrum of 109j
COOMe
COOMe
Me
N
Cl
CHCl$_3$
TMS
ppm
0
1
2
3
4
5
6
7
8
9
10

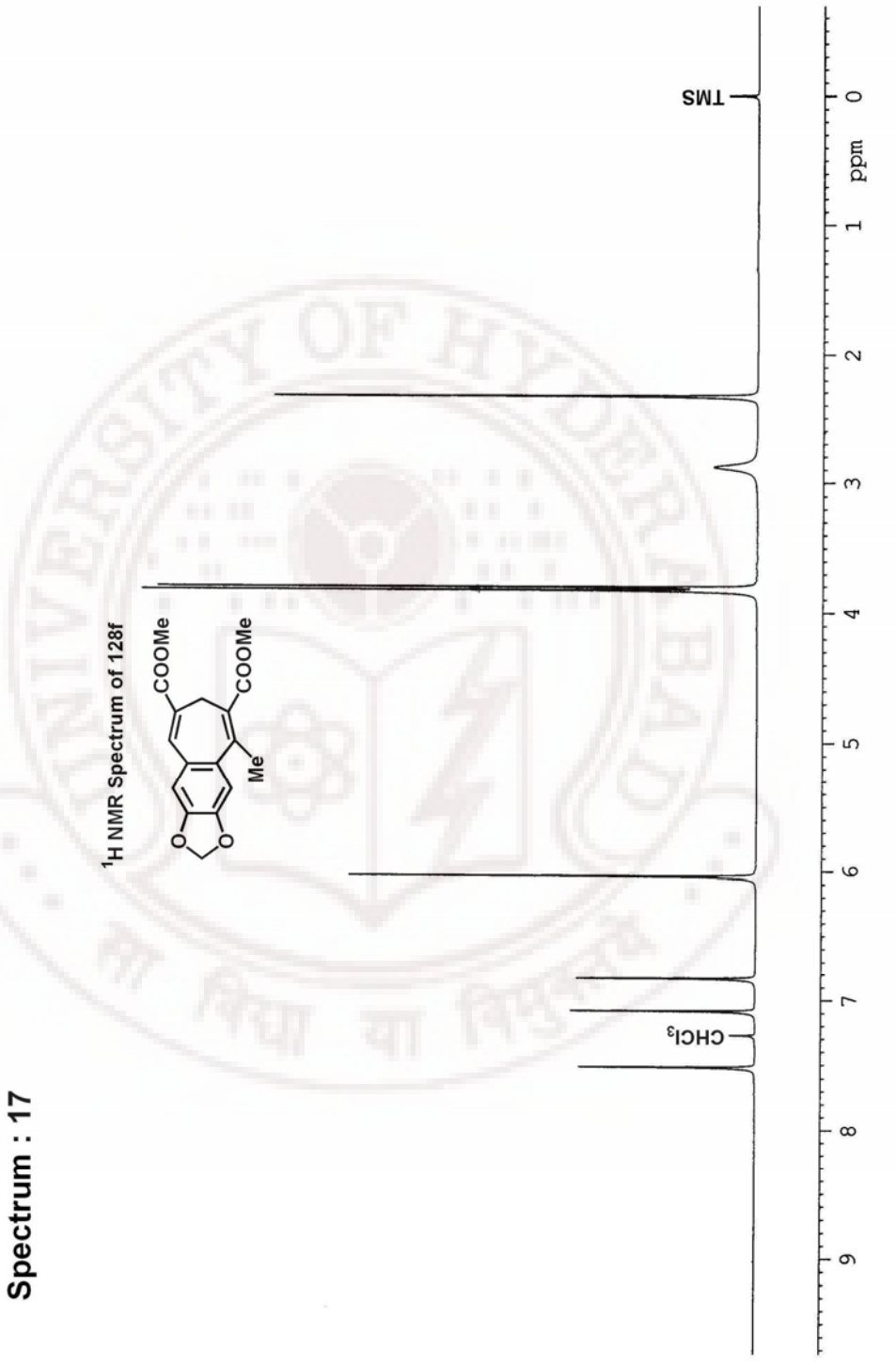

Spectrum : 12
^{13}C NMR Spectrum of 109j
COOMe
COOMe
Me
N
Cl
CDCl3
168.90
158.58
145.26
134.82
131.68
130.82
130.13
130.08
127.68
125.88
77.42
77.10
76.79
52.91
51.49
31.69
23.30
ppm

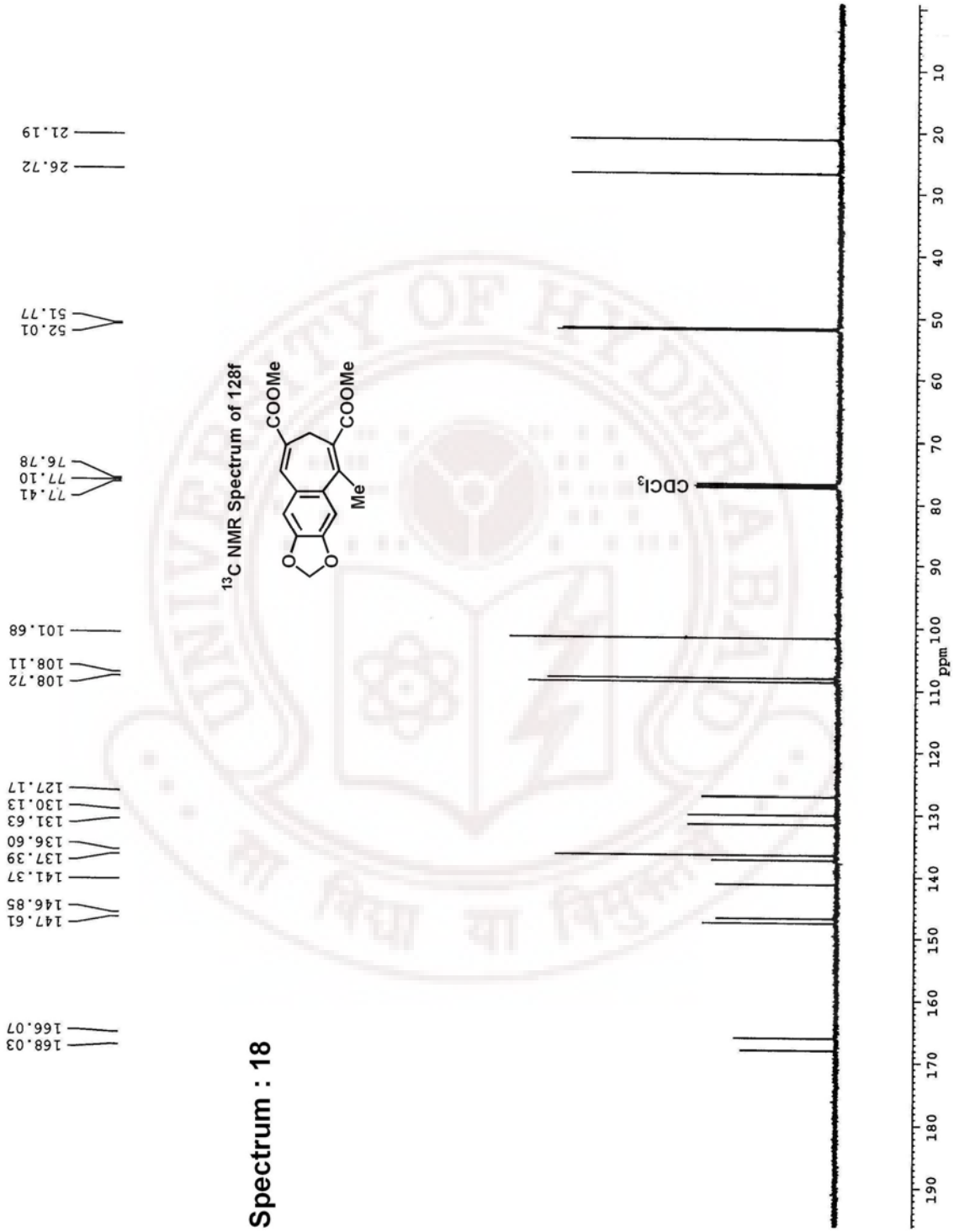

Spectrum : 13
^{1}H NMR Spectrum of 109m
COOMe
COPh
Me
N
CHCl$_3$
TMS
ppm
0
1
2
3
4
5
6
7
8
9
10

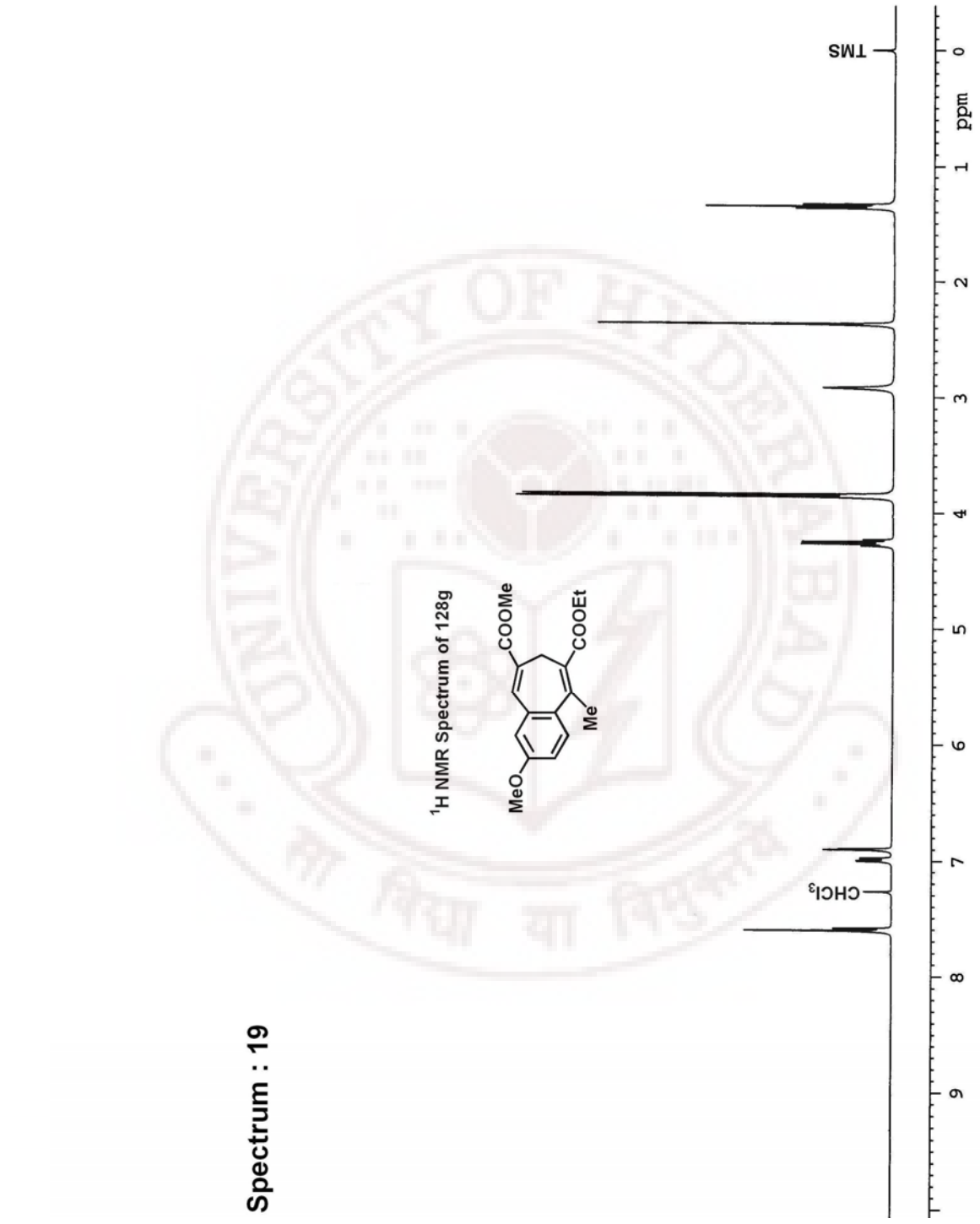

Spectrum : 14
^{13}C NMR Spectrum of 109m
COOMe
COPh
Me
N
CDCl$_3$
194.04
169.58
156.54
144.66
136.07
133.83
133.52
131.12
130.44
128.88
128.64
127.80
127.73
126.94
126.81
124.96
124.76
124.23
77.42
77.10
76.79
53.83
52.76
31.70
23.51
ppm

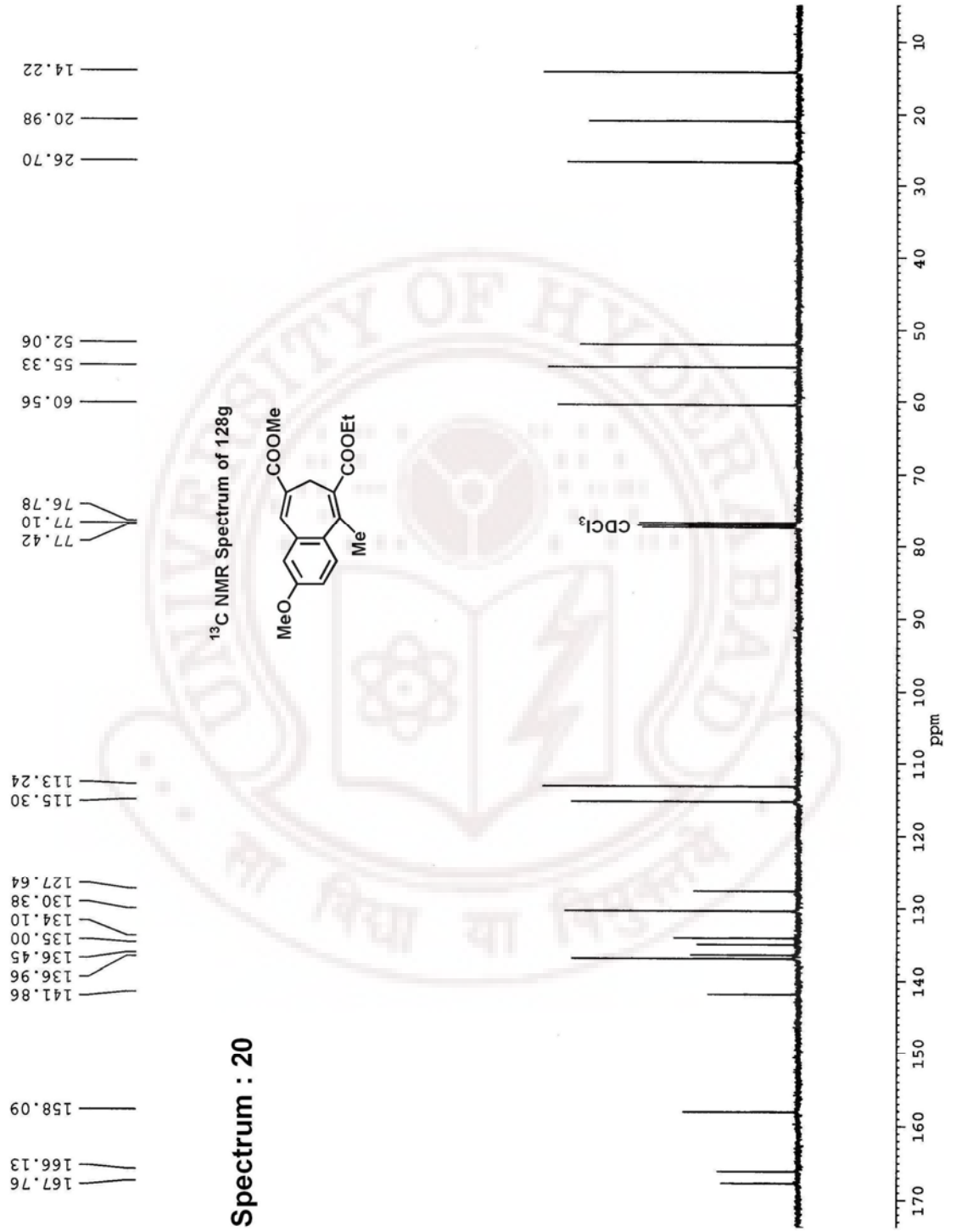

Spectrum : 15
^{1}H NMR Spectrum of 128b
COOMe
COOMe
Me
MeO
CHCl$_3$
TMS
ppm
0
1
2
3
4
5
6
7
8
9

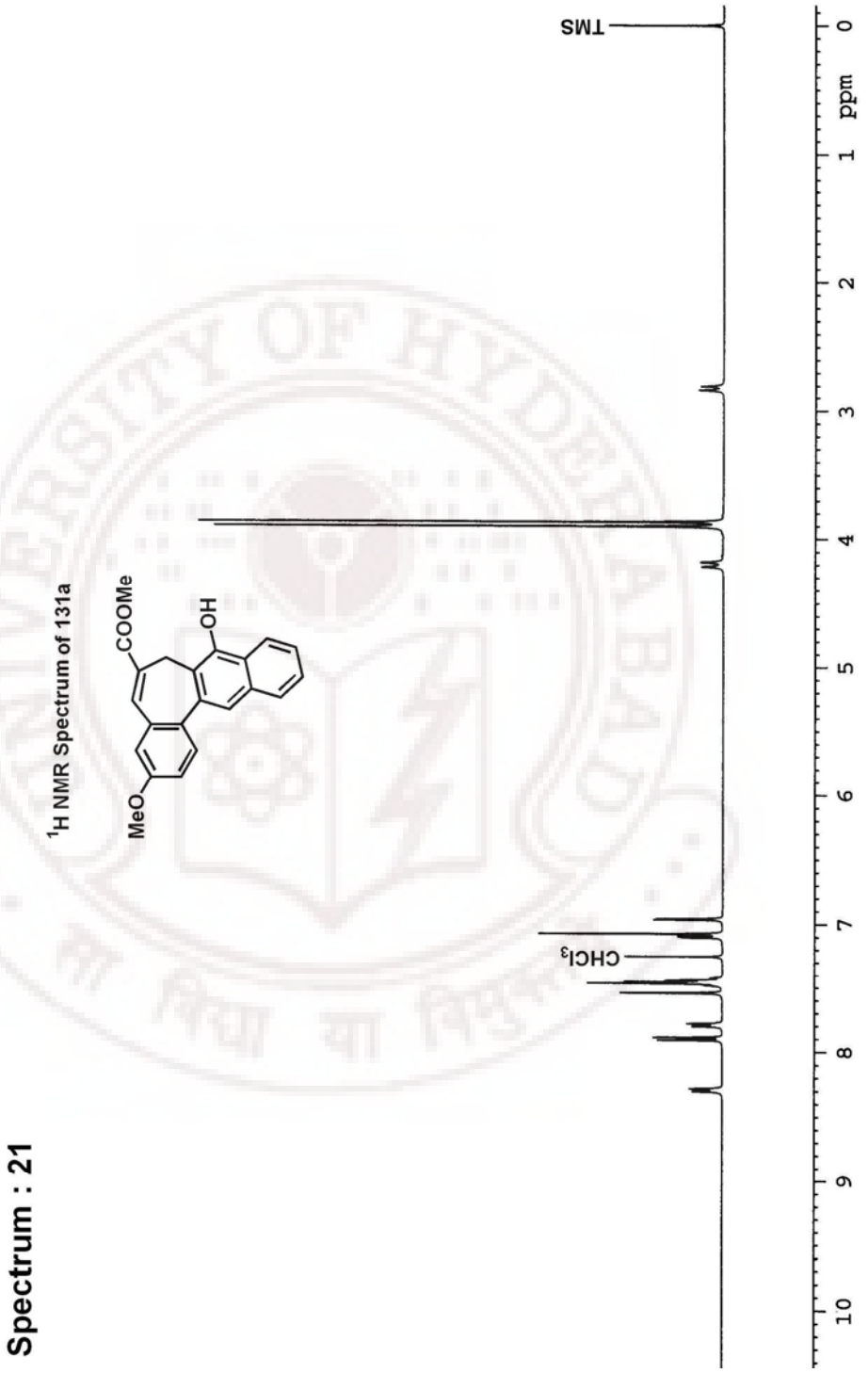

Spectrum : 16
^{13}C NMR Spectrum of 128b
COOMe
COOMe
Me
MeO
CDCl$_3$
168.10
166.11
158.13
142.43
136.97
136.46
134.93
134.02
130.39
127.30
115.30
113.24
77.42
77.10
76.78
55.31
52.08
51.72
26.60
21.11
ppm

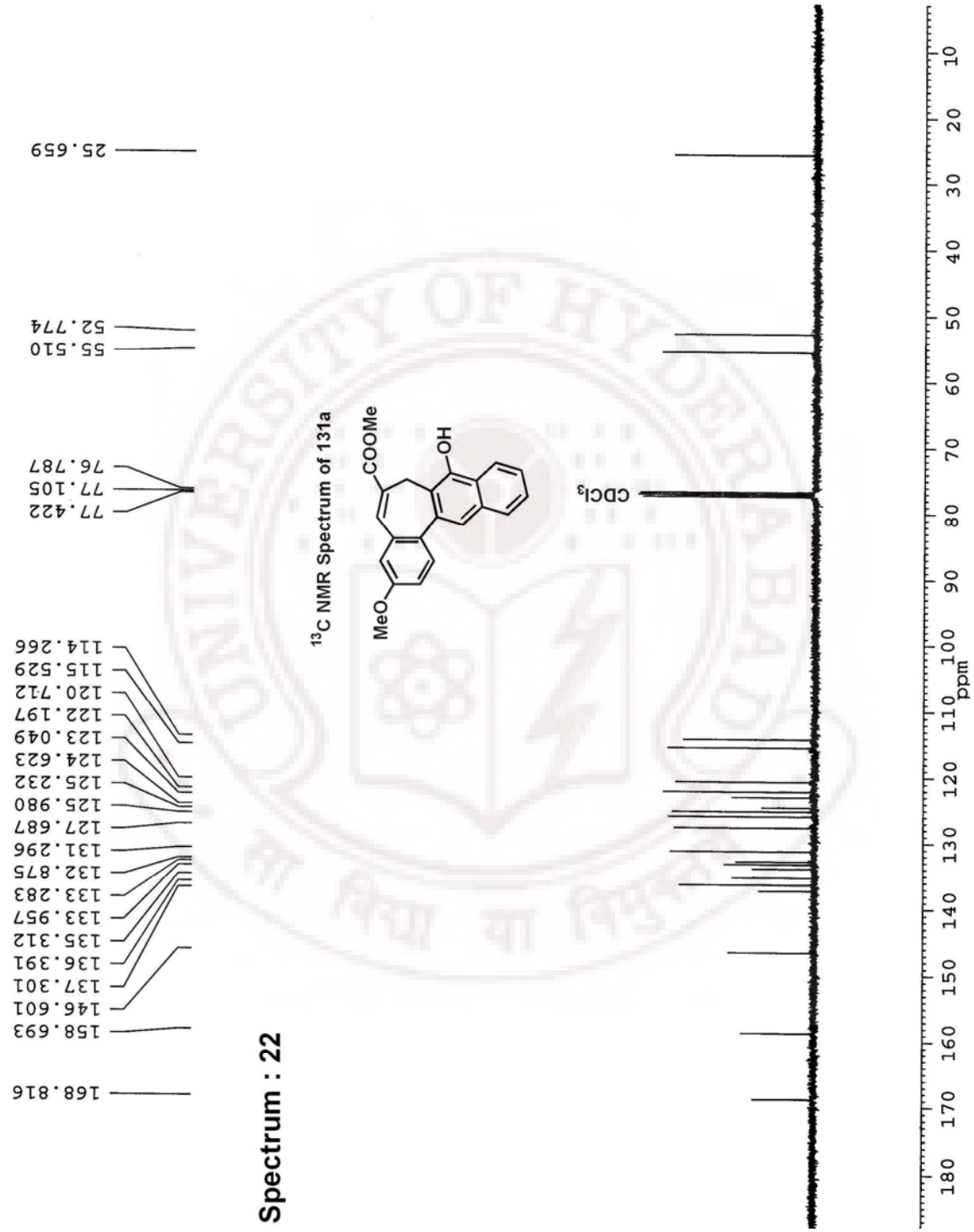

Spectrum : 17
^{1}H NMR Spectrum of 128f
COOMe
COOMe
Me
CHCl$_3$
TMS
9
8
7
6
5
4
3
2
1
ppm
0

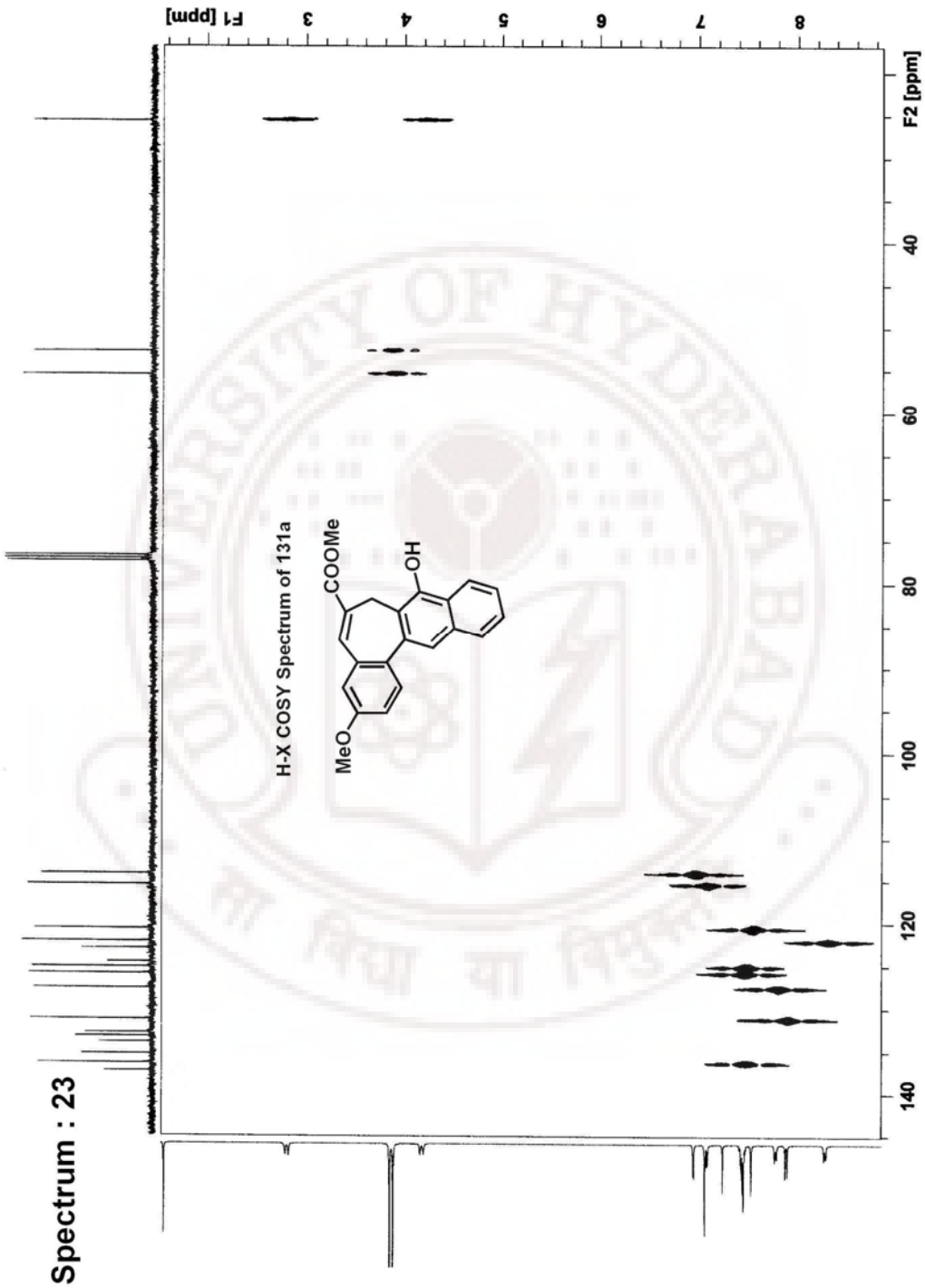

Spectrum : 18
^{13}C NMR Spectrum of 128f
COOMe
COOMe
Me
O
O
O
CDCl3
21.19
26.72
51.77
52.01
76.78
77.10
77.41
101.68
108.72
108.11
127.17
130.13
131.63
136.60
137.39
141.37
146.85
147.61
166.07
168.03
ppm

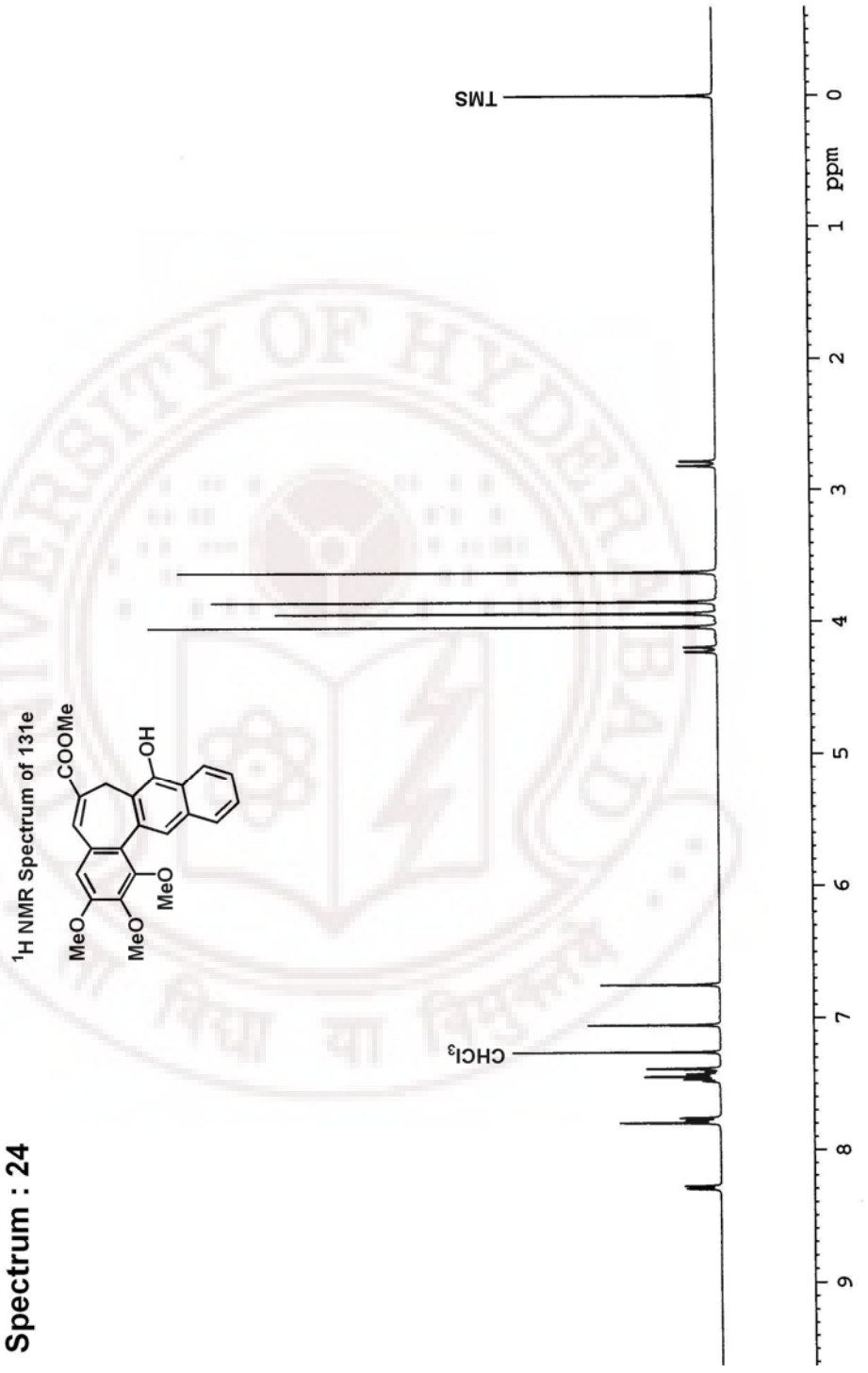

Spectrum : 19
^{1}H NMR Spectrum of 128g
COOMe
COOEt
Me
MeO
CHCl$_3$
TMS
ppm
0
1
2
3
4
5
6
7
8
9

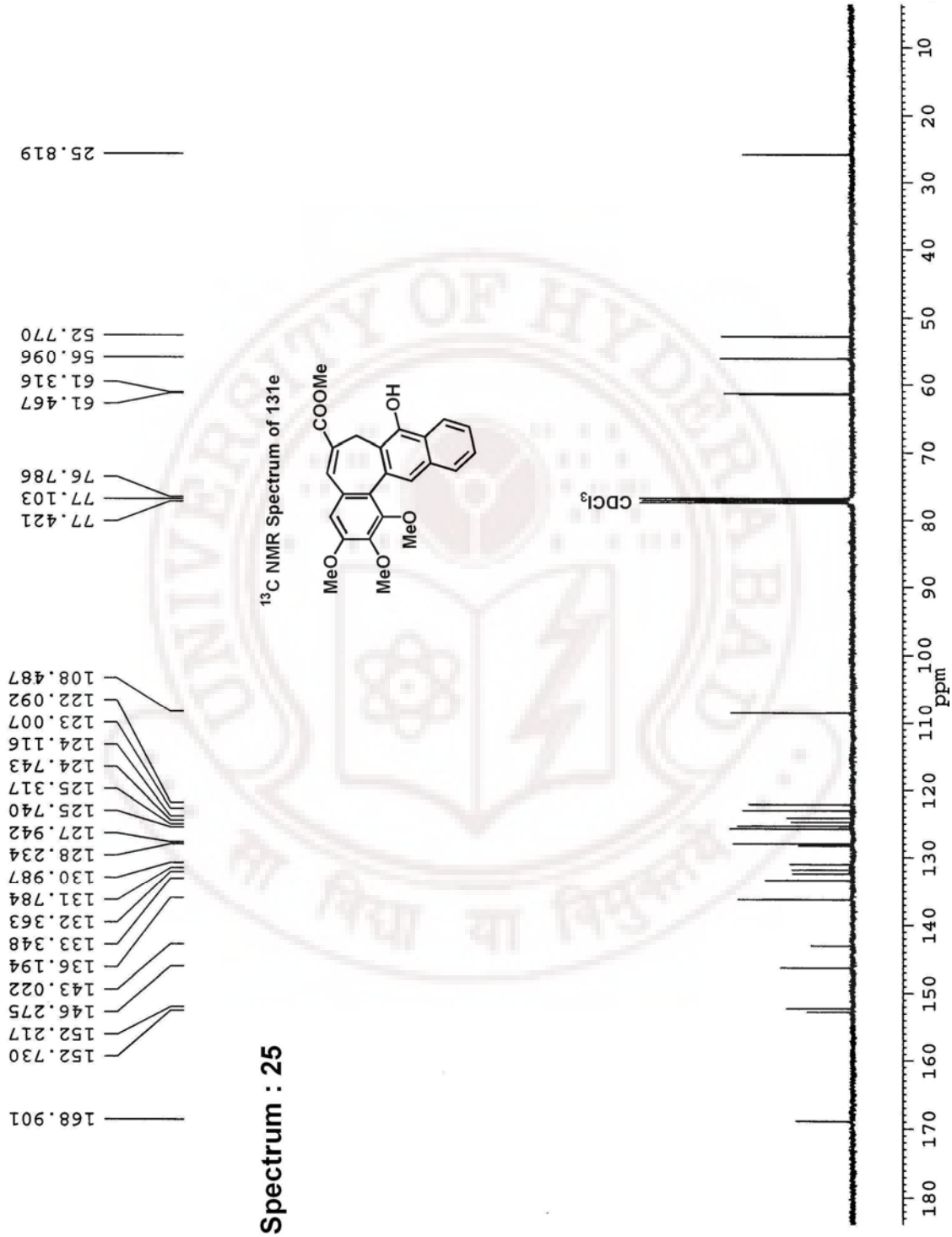

Spectrum : 20
^{13}C NMR Spectrum of 128g
COOMe
COOEt
Me
MeO
CDCl3
14.22
20.98
26.70
52.06
55.33
60.56
76.78
77.10
77.42
113.24
115.30
127.64
130.38
134.10
135.00
136.45
136.96
141.86
158.09
166.13
167.76
ppm

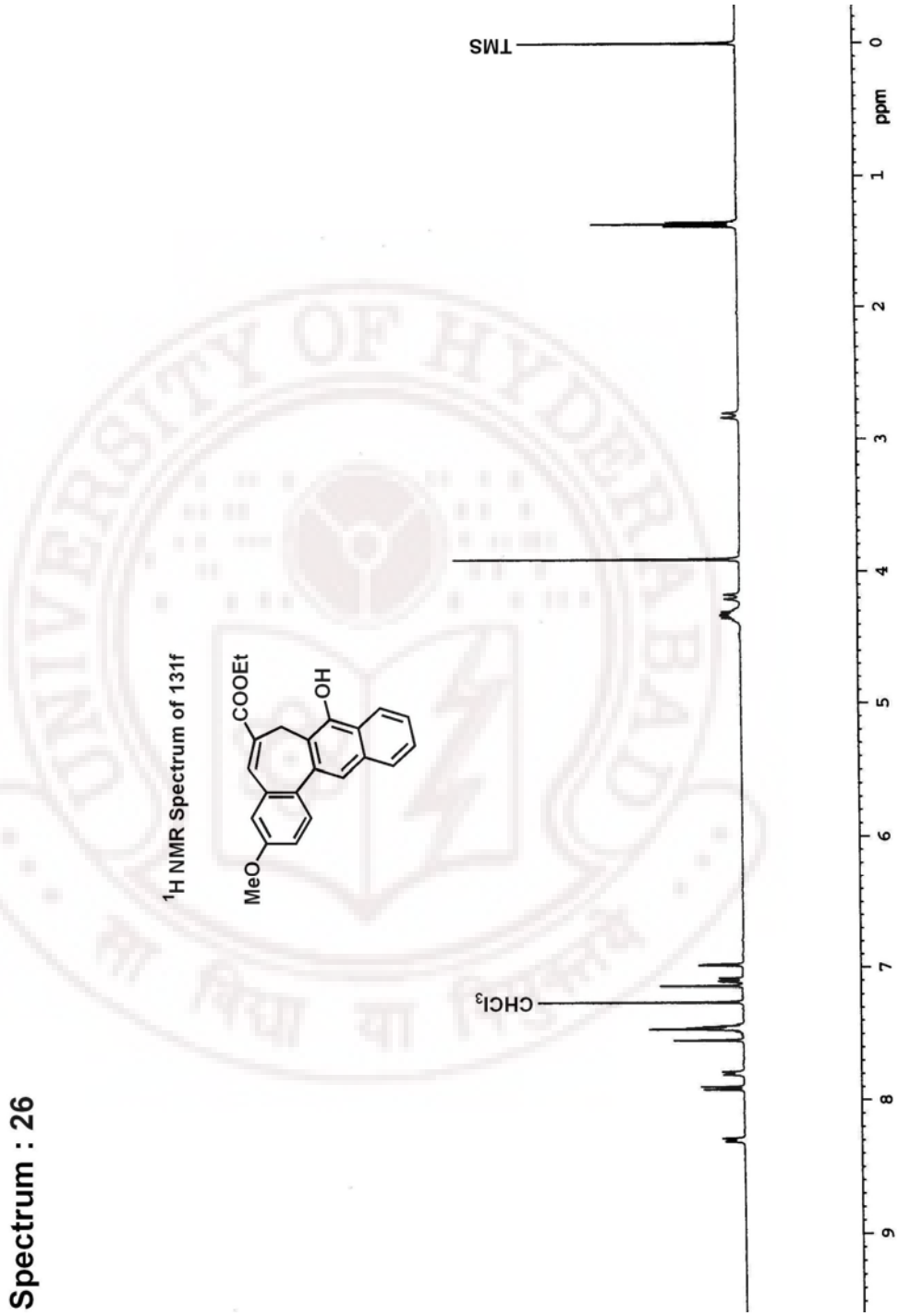

Spectrum : 21
^{1}H NMR Spectrum of 131a
COOMe
OH
MeO
CHCl$_3$
TMS
10
9
8
7
6
5
4
3
2
1
ppm
0

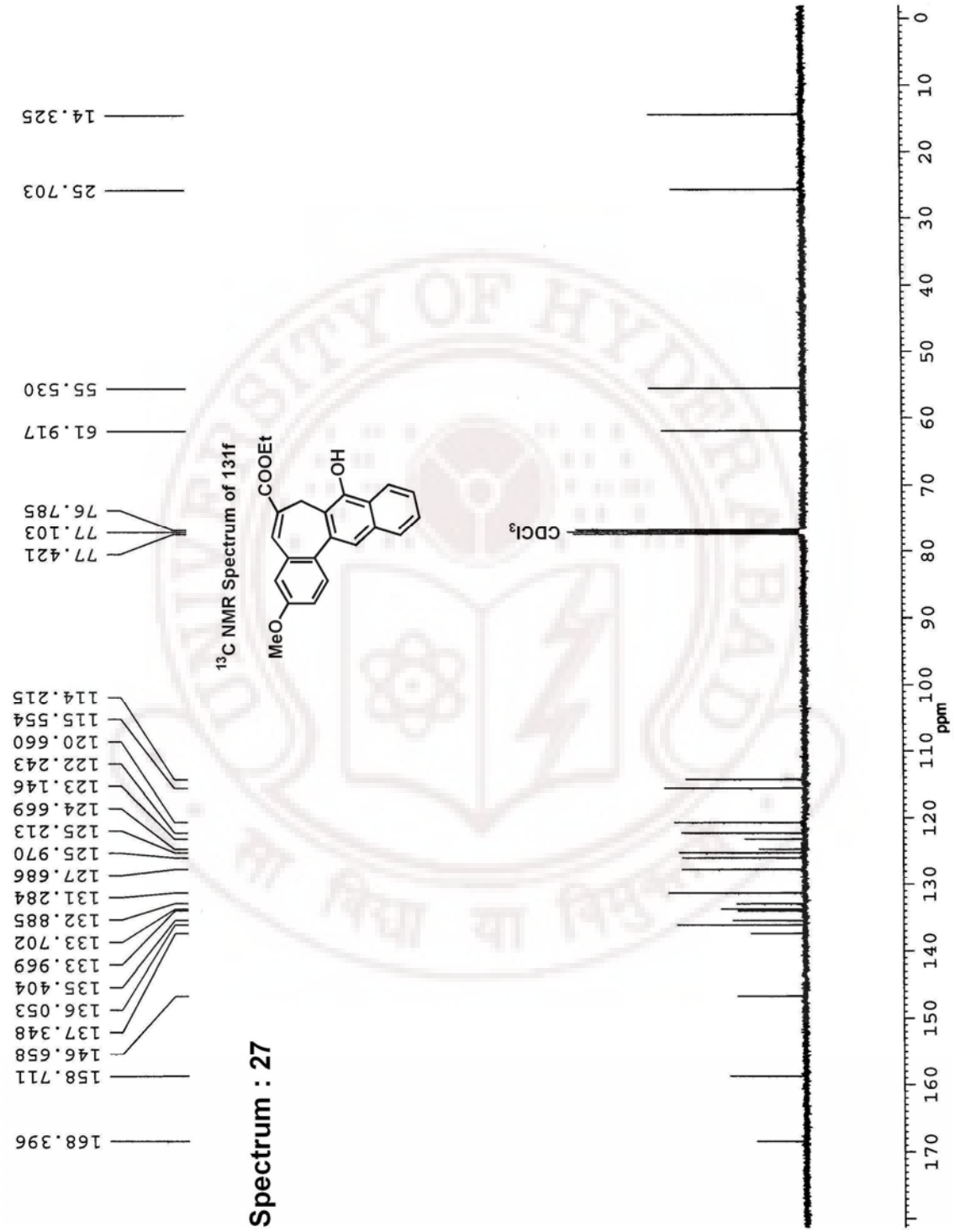

Spectrum : 22
^{13}C NMR Spectrum of 131a
COOMe
OH
MeO
CDCl$_3$
168.816
158.693
146.601
137.301
136.391
135.312
133.957
133.283
132.875
131.296
127.687
125.980
125.232
124.623
123.049
122.197
120.712
115.529
114.266
77.422
77.105
76.787
55.510
52.774
25.659
ppm

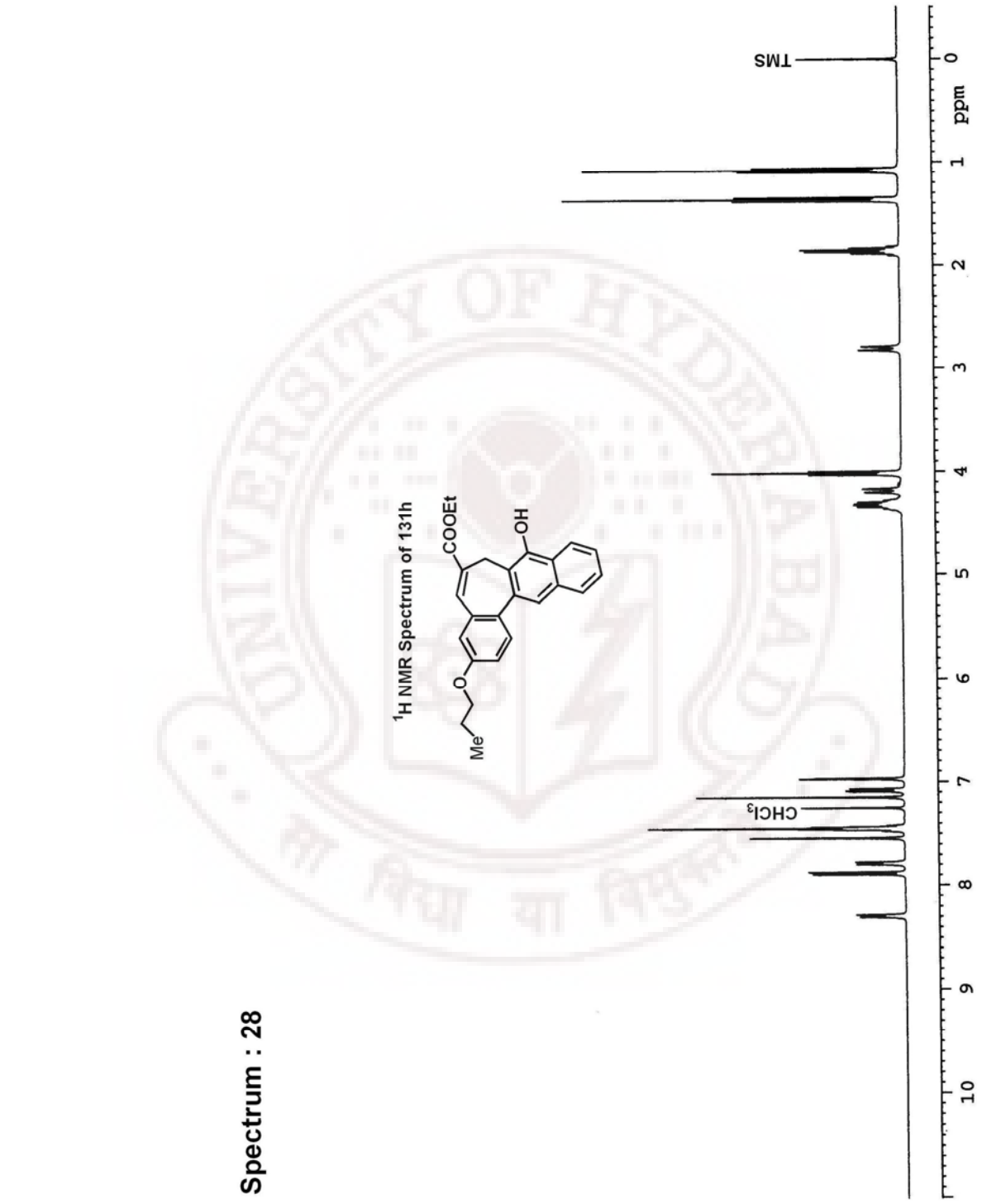

Spectrum : 23
H-X COSY Spectrum of 131a
COOMe
OH
MeO
F1 [ppm]
F2 [ppm]

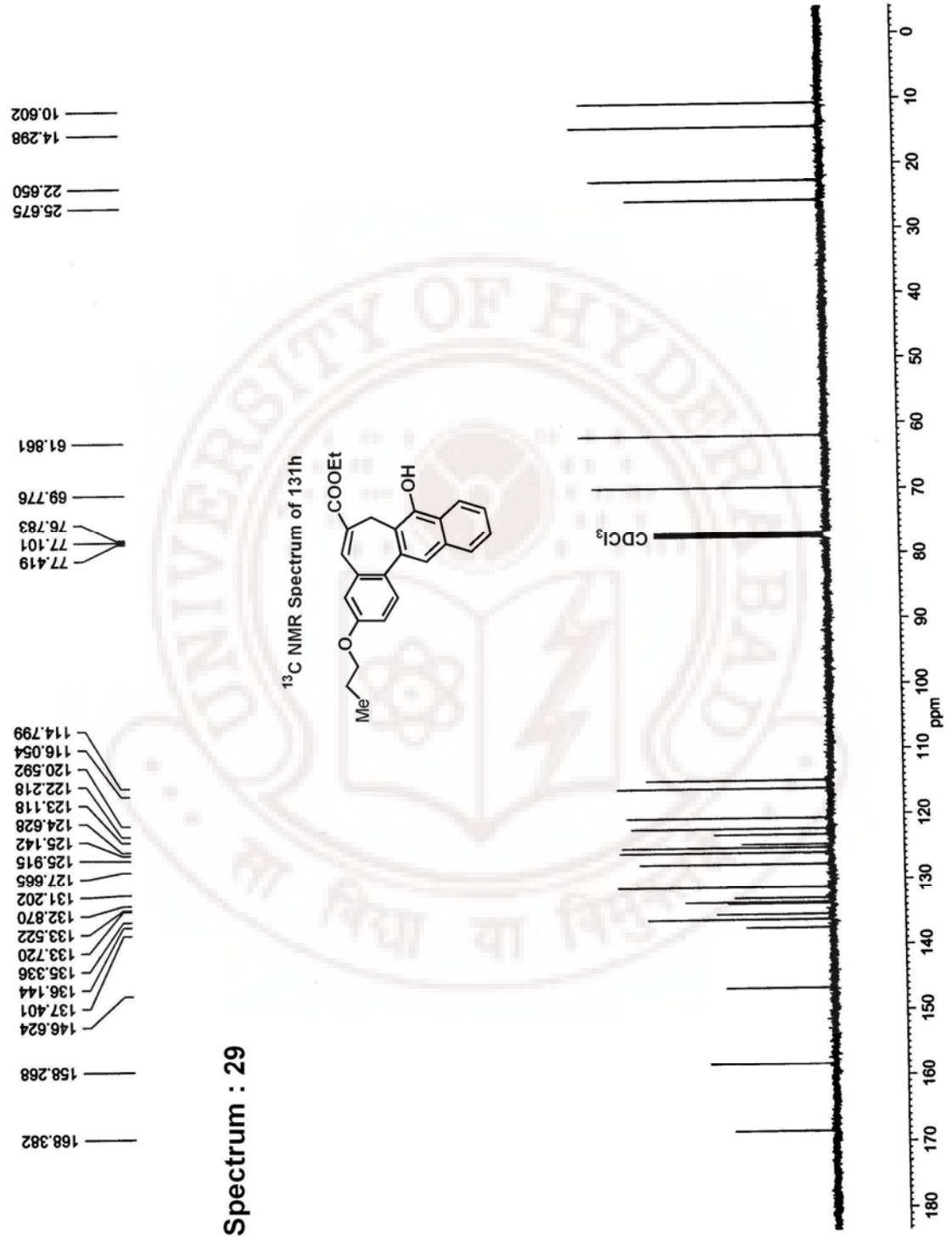

Spectrum : 24
^{1}H NMR Spectrum of 131e
COOMe
OH
MeO
MeO
MeO
CHCl$_3$
TMS
9
8
7
6
5
4
3
2
1
ppm
0

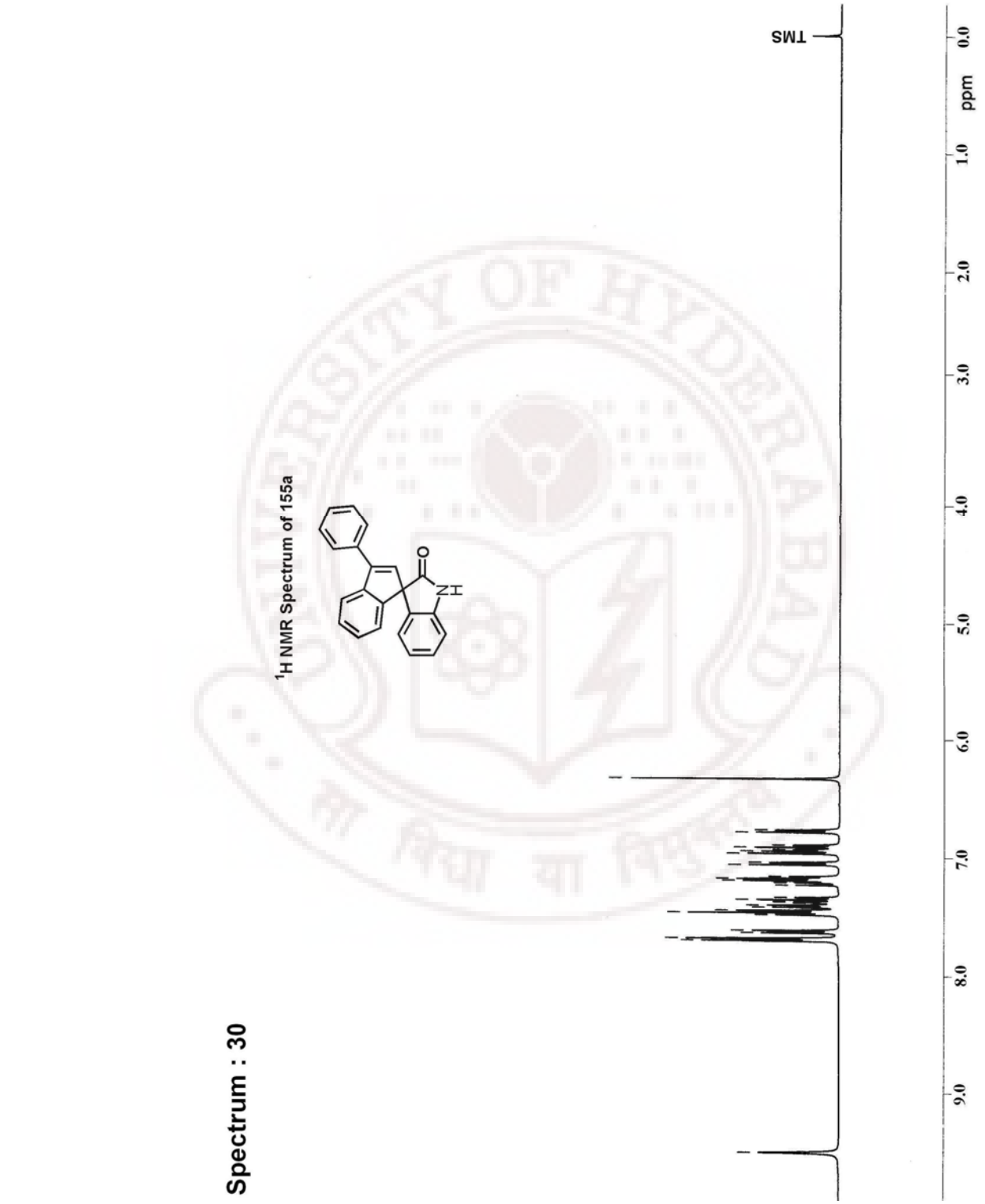

Spectrum : 25
^{13}C NMR Spectrum of 131e
COOMe
OH
MeO
MeO
MeO
CDCl$_3$
168.901
152.730
152.217
146.275
143.022
136.194
133.348
132.363
131.784
130.987
128.234
127.942
125.740
125.317
124.743
124.116
123.007
122.092
108.487
77.421
77.103
76.786
61.467
61.316
56.096
52.770
25.819
ppm

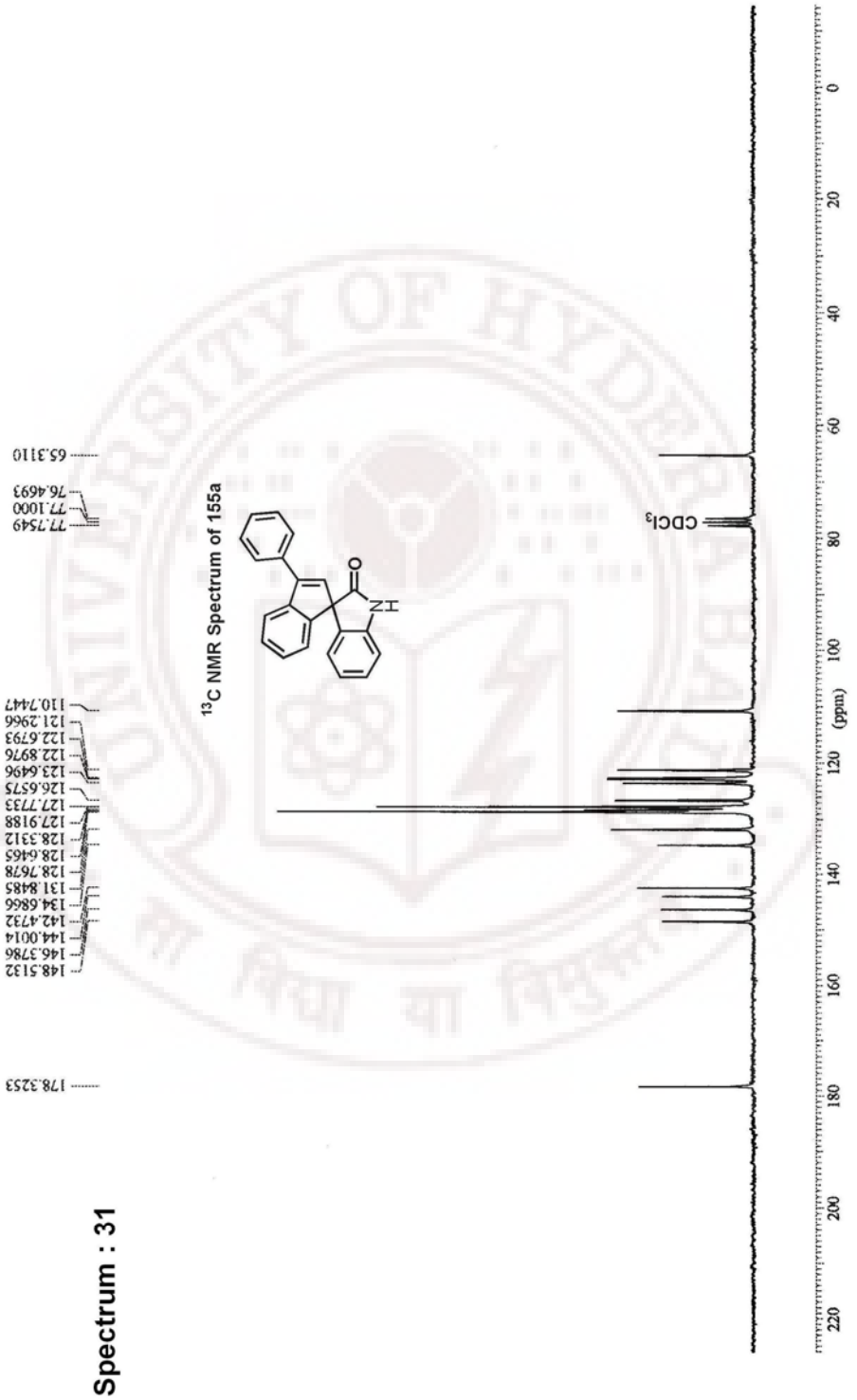

Spectrum : 26
^{1}H NMR Spectrum of 131f
COOEt
OH
MeO
CHCl$_3$
TMS
ppm

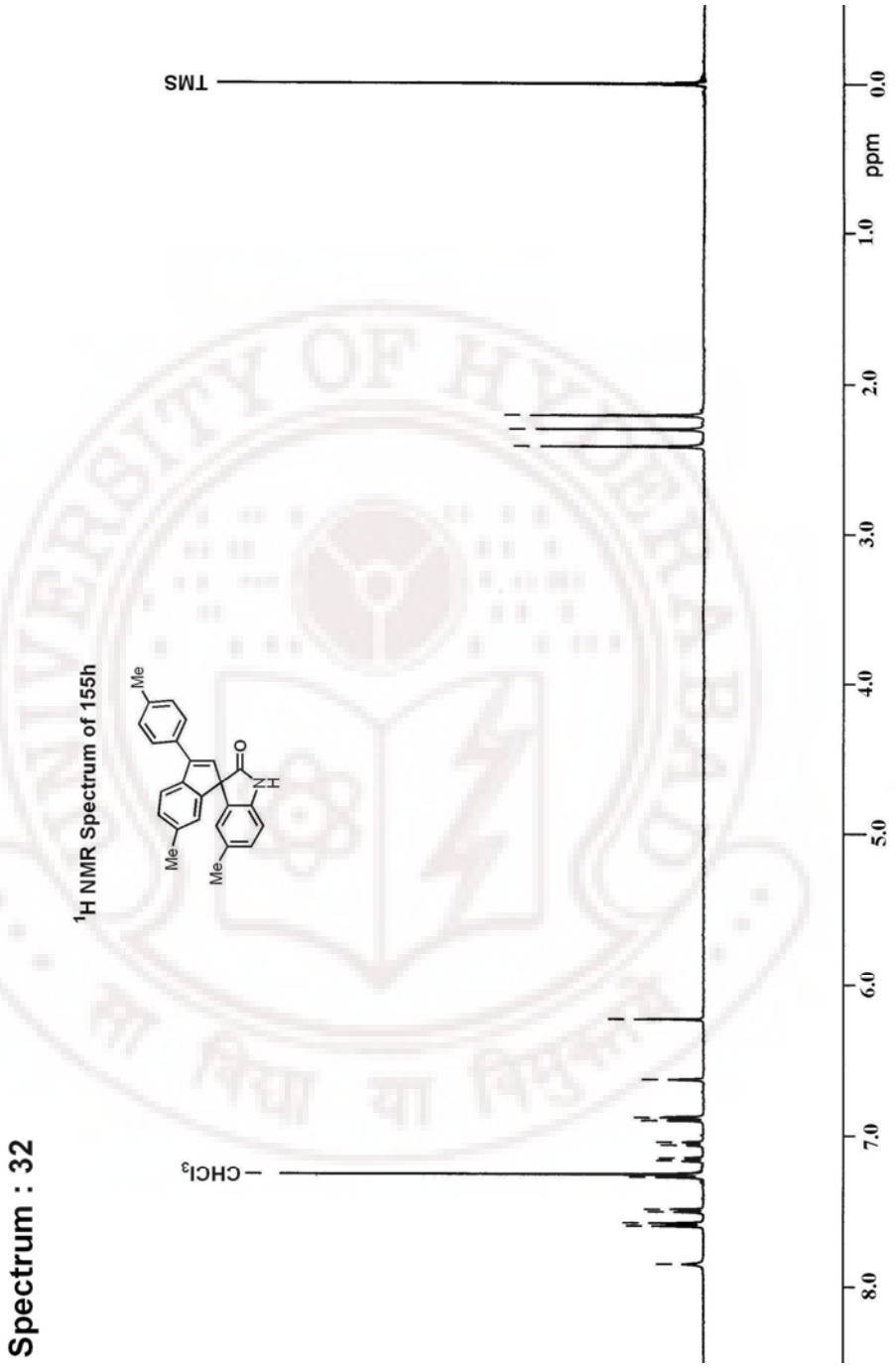

Spectrum : 27
^{13}C NMR Spectrum of 131f
COOEt
OH
MeO
CDCl$_3$
ppm
14.325
25.703
55.530
61.917
76.785
77.103
77.421
114.215
115.554
120.660
122.243
123.146
124.669
125.213
125.970
127.686
131.284
132.885
133.702
133.969
135.404
136.053
137.348
146.658
158.711
168.396

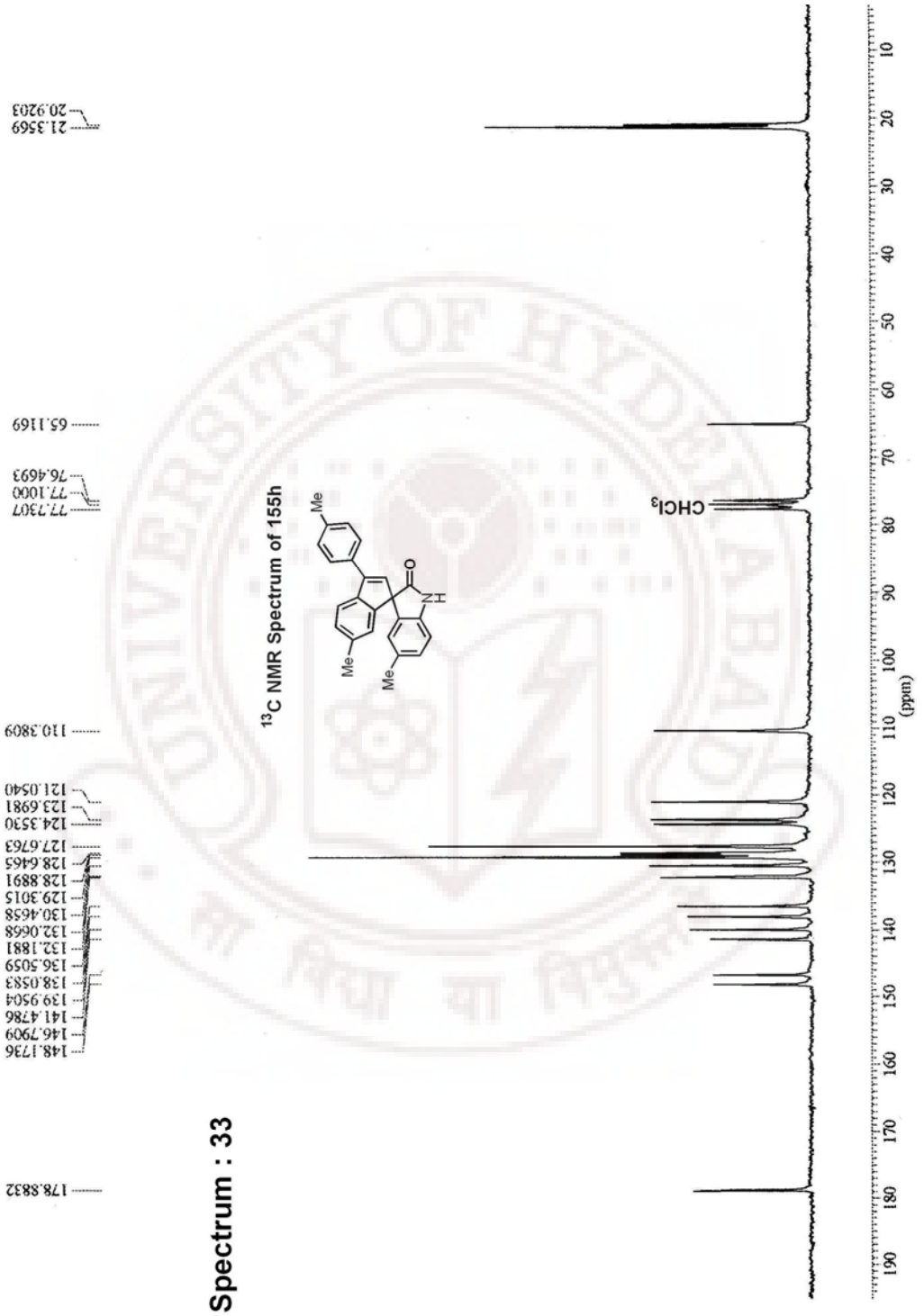

Spectrum : 28
^{1}H NMR Spectrum of 131h
COOEt
OH
O
Me
CHCl$_3$
TMS
ppm
0
1
2
3
4
5
6
7
8
9
10

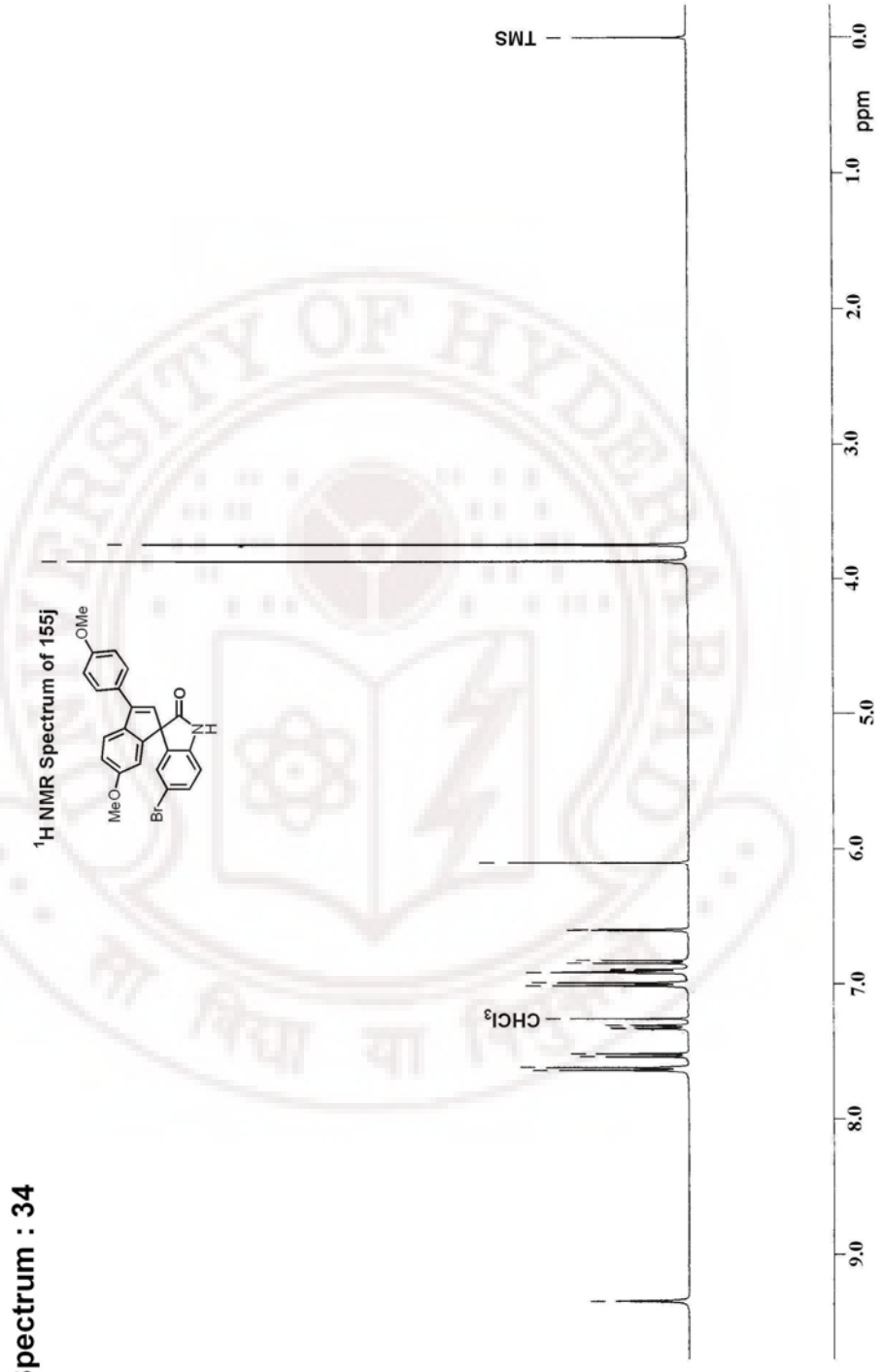

Spectrum : 29
^{13}C NMR Spectrum of 131h
COOEt
OH
O
Me
CDCl$_3$
ppm
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
10.602
14.298
22.650
25.675
61.861
69.776
76.783
77.101
77.419
114.799
116.054
120.592
122.218
123.118
124.628
125.142
125.915
127.665
131.202
132.870
133.522
133.720
135.336
136.144
137.401
146.624
158.268
168.382

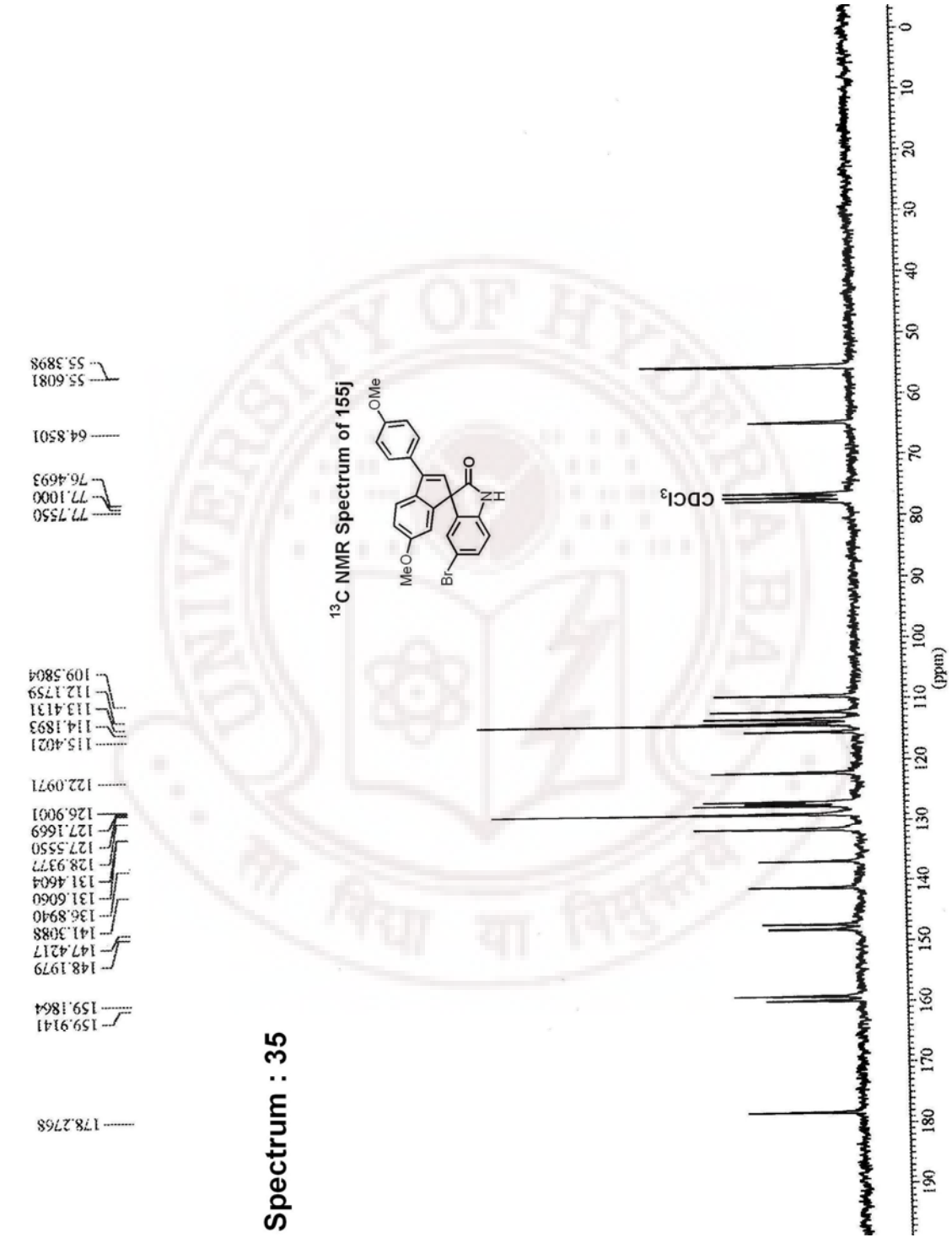

Spectrum : 30
^{1}H NMR Spectrum of 155a
O
N
H
TMS
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm

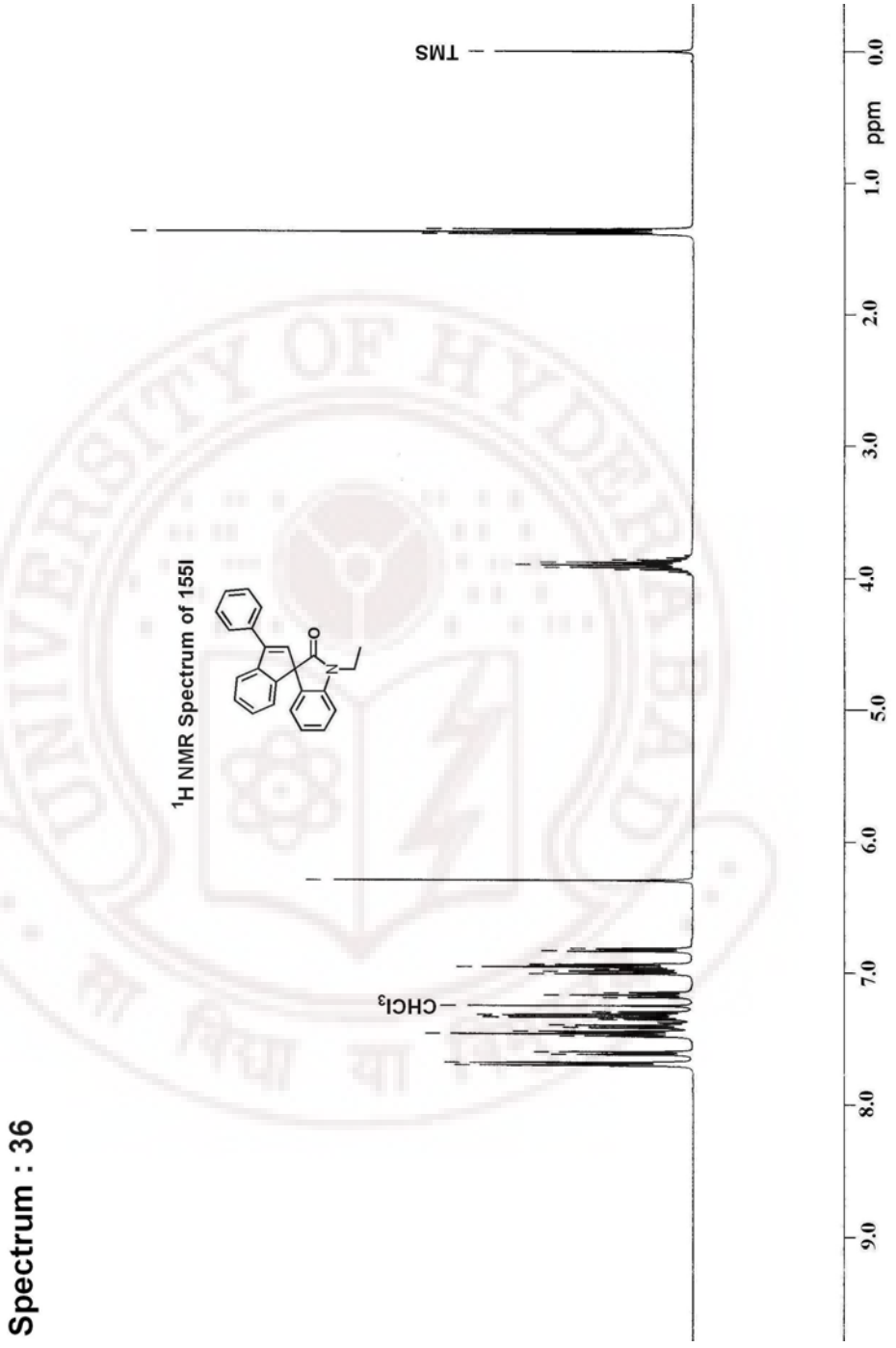

Spectrum : 31
178.3253
148.5132
146.3786
144.0014
142.4732
134.6866
131.8485
128.7678
128.6465
128.3312
127.9188
127.7733
126.6575
123.6496
122.8976
122.6793
121.2966
110.7447
77.7549
77.1000
76.4693
65.3110
^{13}C NMR Spectrum of 155a
CDCl$_3$
220
200
180
160
140
120
100
80
60
40
20
0
(ppm)

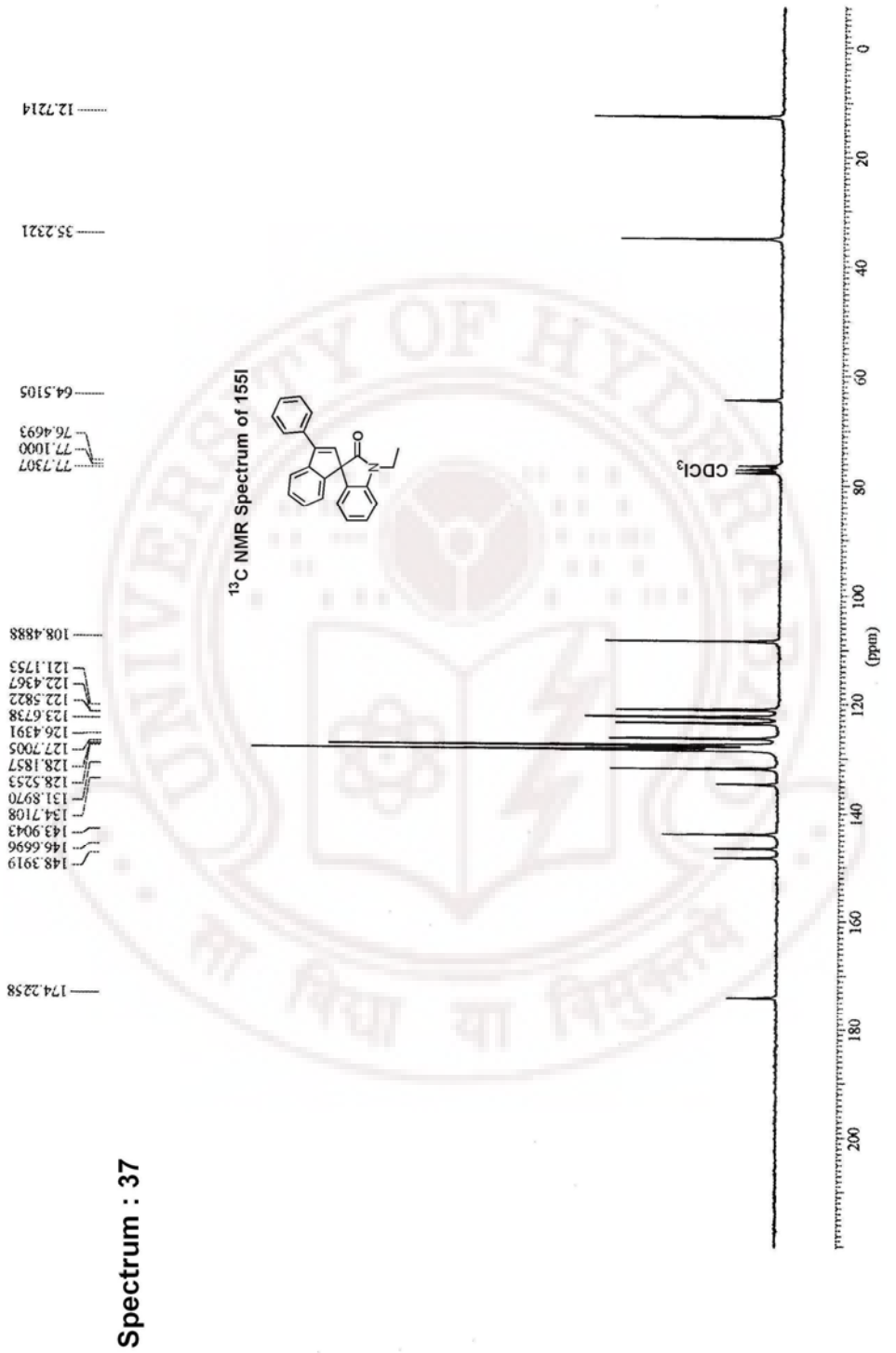

Spectrum : 32
^{1}H NMR Spectrum of 155h
Me
Me
Me
O
N
H
CHCl$_3$
TMS
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm

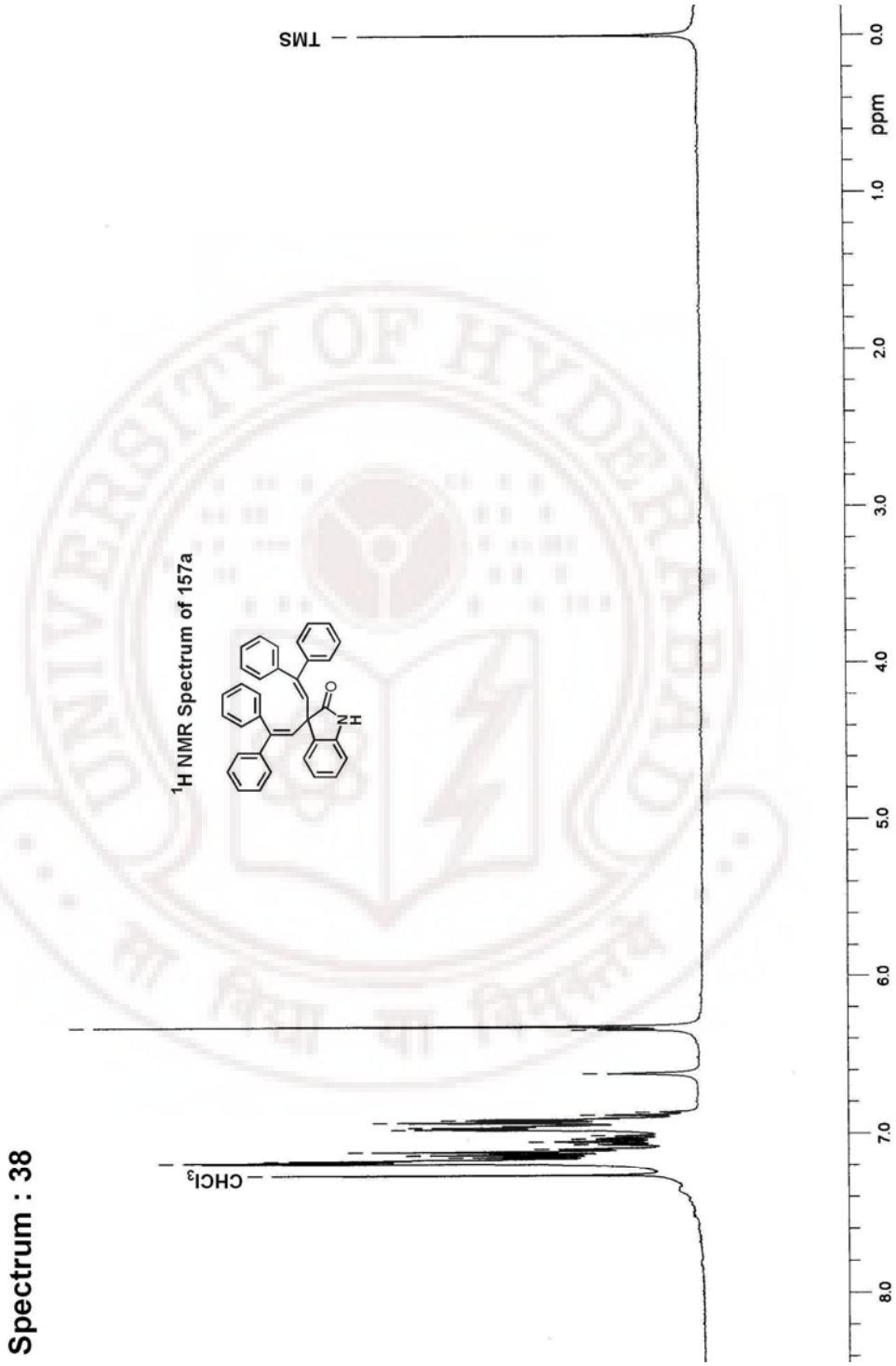

Spectrum : 33
^{13}C NMR Spectrum of 155h
Me
Me
Me
O
NH
CHCl3
(ppm)
178.8832
148.1736
146.7909
141.4786
139.9504
138.0583
136.5059
132.1881
132.0668
130.4658
129.3015
128.8891
128.6465
127.6763
124.3530
123.6981
121.0540
110.3809
77.7307
77.1000
76.4693
65.1169
21.3569
20.9203

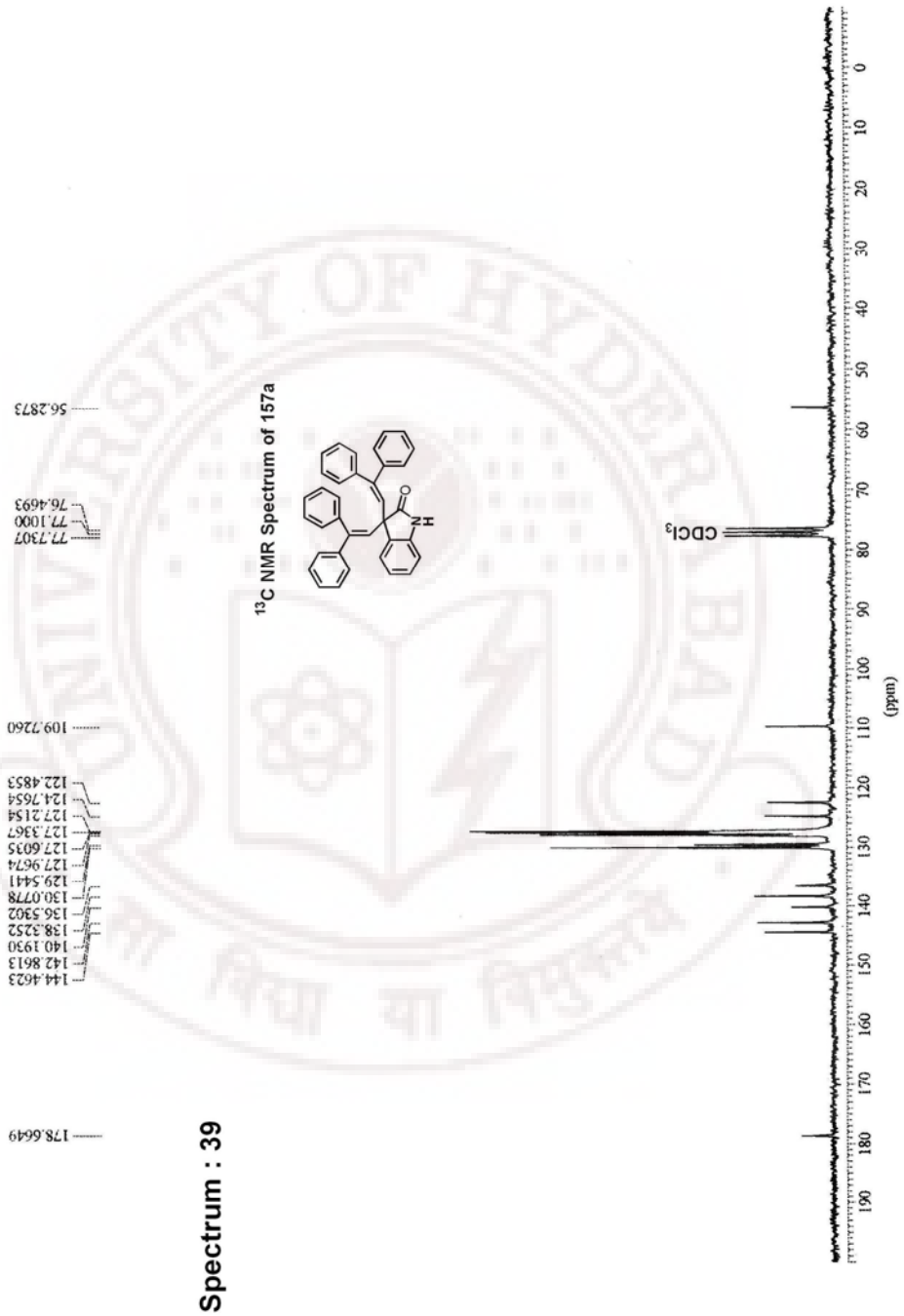

Spectrum : 34
^{1}H NMR Spectrum of 155j
OMe
MeO
Br
O
N
H
TMS
CHCl$_3$
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm


Spectrum : 35
^{13}C NMR Spectrum of 155j
OMe
MeO
Br
NH
O
CDCl3
(ppm)
178.2768
159.9141
159.1864
148.1979
147.4217
141.3088
136.8940
131.6060
131.4604
128.9377
127.5550
127.1669
126.9001
122.0971
115.4021
114.1893
113.4131
112.1759
109.5804
77.7550
77.1000
76.4693
64.8501
55.6081
55.3898


Spectrum : 36
^{1}H NMR Spectrum of 155l
TMS
CHCl$_3$
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm


Spectrum : 37
^{13}C NMR Spectrum of 155l
CDCl$_3$
(ppm)
0
20
40
60
80
100
120
140
160
180
200
12.7214
35.2321
64.5105
76.4693
77.1000
77.7307
108.4888
121.1753
122.4367
122.5822
123.6738
126.4391
127.7005
128.1857
128.5253
131.8970
134.7108
143.9043
146.6696
148.3919
174.2258


Spectrum : 38
^{1}H NMR Spectrum of 157a
TMS
CHCl$_3$
ppm
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0


Spectrum : 39
^{13}C NMR Spectrum of 157a
CDCl$_3$
(ppm)
178.6649
144.4623
142.8613
140.1930
138.3252
136.5302
130.0778
129.5441
127.9674
127.6035
127.3367
127.2154
124.7654
122.4853
109.7260
77.7307
77.1000
76.4693
56.2873

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(1) Smith, M. B.; March, J. *March's Advanced Organic Chemistry*; 6th edition.

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LIST OF PUBLICATIONS

1. A simple and one pot protocol for synthesis of indene-spiro-oxindoles involving tandem Prins and Friedel-Crafts reactions.
   D. Basavaiah, **K. Ramesh Reddy** *Org. Lett.* **2007**, *9*, 57-60.

2. An expedient, facile and simple one-pot synthesis of 2-methylenealkanoates and 2-methylenealkanenitriles from the Baylis-Hillman bromides in aqueous media.
   D. Basavaiah, **K. Ramesh Reddy**, N. Kumaragurubaran, *Nature Protocols*. **2007**, *2*, 2665-2676.

3. Simple and one-pot synthesis of tri and tetracyclic frameworks containing [1,8]naphthyridin-2-one moiety from the Baylis-Hillman adducts.
   D. Basavaiah, **K. Ramesh Reddy** *communicated*.

4. Development of a simple synthesis of bicyclic and tetracyclic carbocyclic framework having 6,7 and 6,7,6,6 fused ring systems from the Baylis-Hillman acetates
   D. Basavaiah, **K. Ramesh Reddy**, *manuscript under preparation.*

5. Development of simple, facile and multi-step one-pot synthesis of substituted quinoline derivatives from the Baylis-Hillman adducts.
   D. Basavaiah, **K. Ramesh Reddy** and B. Satpal Singh *to be communicated*.

6. A novel substitution dependant stereochemical control in the Johnson-Claisen rearrangement of Baylis-Hillman adducts: An interesting competition between [1,3] and [1,2] interactions in transition state.
   D. Basavaiah, T. Satyanarayana, B. Devendar, P. Anupama, **K. Ramesh Reddy** and K. Padmaja *to be communicated*.

7. Facile transformation of the Baylis-Hillman adducts into substituted (1*H*)-quinolin-2-ones and substituted quinolines *via* a novel one-pot multi-reaction strategy.
   D. Basavaiah, T. Satyanarayana, B. Devendar and **K. Ramesh Reddy** *manuscript under preparation.*