THE BAYLIS-HILLMAN BROMIDES AND CARBONATES IN ORGANIC SYNTHESIS: DEVELOPMENT OF NOVEL METHODOLOGIES FOR SPIROOXINDOLES CONTAINING DIHYDROFURAN, EPOXIDE AND NITRONE FRAMEWORKS

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A THESIS SUBMITTED FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY

BY

SATPAL SINGH BADSARA

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"In memory of my Grandfather and Uncle"

This thesis is dedicated to my beloved Parents and family members

CONTENTS

STATEMENT

I hereby declare that the matter embodied in this thesis is the result of investigations carried out by me in the School of Chemistry, University of Hyderabad, Hyderabad, under the supervision of **Professor D. BASAVAIAH**.

In keeping with the general practice of reporting scientific observations, due acknowledgements have been made wherever the work described is based on the findings of other investigators.

HYDERABAD

April, 2013 **SATPAL SINGH BADSARA**

CERTIFICATE

Certified that the work embodied in this thesis entitled **The Baylis-Hillman Bromides and Carbonates in Organic Synthesis: Development of Novel Methodologies for Spirooxindoles containing Dihydrofuran, Epoxide, and Nitrone Frameworks**" has been carried out by **Mr. Satpal Singh Badsara,** under my supervision and the same has not been submitted elsewhere for a degree.

Professor D. BASAVAIAH
(THESIS SUPERVISOR)

DEAN
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ACKNOWLEDGEMENTS

In my ongoing journey, this thesis marks an important milestone. The making of this milestone is incomplete without the conceptual, technical, editorial, moral and financial help of many. Hence; I would like to record my gratitude for the guidance and support that I received in the making of this thesis.

It gives me great pleasure in expressing my deepest sense of gratitude to my research supervisor **Professor D. Basavaiah**, for excellent guidance and invaluable suggestions throughout my research tenure. My skills however limited as it maybe owes to the rigorous training and guidance of my supervisor.

I thank the present and former Deans and all the faculty members of the School of Chemistry for their timely help and cooperation during my Ph. D. program. I am thankful to Professors T. P. Radhakrishnan and S. Pal for their helpful discussions regarding the X-ray data analysis. It is great privilege to express my heartfelt regards to Professor T. R. Rao, Department of Chemistry, BHU and Professor B. Ananthakrishnan, S. N. School, UOH for their useful suggestions and help and helping me to handle moral panics as a student and researcher.

My special thank to Dr. P. Raghavaiah for his help on different occasion. I acknowledge the help and support provided by the technical and non-teaching staff of the School of Chemistry. I also thank Mr. S. Satyanarayana, Mr. V. Bhaskara Rao, Mrs. Asia Perwej, Mrs. Vijaya Laxmi, Mr. M. Shetty, Mr. Thurabuddin, Mr. Prasad, Mr. Durgesh for their timely and invaluable help.

National Single Crystal X-ray Facility and HRMS Facility funded by DST (New Delhi) in School of Chemistry and the financial assistance by CSIR (New Delhi) and DST (New Delhi) is gratefully acknowledged.

I am extremely thankful to my seniors Dr. K. Venkateswara Rao, Dr. J. Raju Reddy, Dr. Veerendhar, Dr. B. Devender, Dr. P. Anupama , Dr. K. Ramesh Reddy, Dr. Utpal Das, Dr. D. V. Lenin Babu, Dr. K. Aravindu, Dr. Suparna Roy, Dr. B. Sekhara Reddy and present labmates K. Santosh Kumar, D. Mallikarjuna Reddy, G. Veeraraghavaiah, G. Chandra Sekhar Reddy, Sutanuka Pal, B. Lingaiah, Ch. Sayanna, Harathi L., P. Thamizharasi, Dr. R. B. Singh, Dr. K. C. Bharadwaj for

their timely help and pleasant association and helping me to tide over emotional and academic turbulences. I thank my co-worker Dr. B. C. Sahu for his help and co-operation.

I am very thankful to all friends in School of Chemistry especially Rajeshwar, Monima, Mosumi, Naba, Tanmay, Vikarant, Ranjeet, Sanjeev, Tridip, Pawan, Srinivas Reddy, Phani, Suri, Rajesh, Dr. Jagadeesh, Laxman, Ramasuresh, Venu, Naveen, Anji, Thiru, Praveen, Ramesh, Pradeep, Ramesh, Gupta, Hari, Sekhar Reddy and so on…….

I am thankful to my friends in University of Hyderabad for creating a home away from home particularly Abhay, Shyam, Chetan, Sanjeev, Anand, Tejendra, Anshuman, Sachchida Nand, Naren and group, Sisuranjan and group, Mohit, Anjali, Moolchand, Taphan, Anjani, Rakesh, Venkat, Susil, Sandeep, Sai, Guru and group, Manish and my friends form different places, Sarwan, Madhu, Amantullah, Dhirendra, Shyam Raj, Badrinath, Gaurav Taneja, Shivakant, Sarita, Sarika, Samta, Susil, Prdeep, Motilal, Tejpal, Rajpal, Alok, Surajbhan (IRS), Tinku, Hena, Kuldeep for their heartily support.

I express my deepest affection to my **mother** & **father, aunty** & **uncle** (late.), **Grandma** for their support, encouragement, deserves great appreciation. I would like to express my sincere gratitude to my **brothers** Jugmohan, Dr. Surendra, Kamlesh and my **sisters** Suman (Nunu) and Anu for their constant support, timely help, and supporting to my rest of family. I am also extremely thankful to ***my in-laws family*** and ***Bua's family*** for their love and affection. I would like to state my inexplicable gratitude for all the family members for suspending the family priorities for me to facilitate my research work. It is my journey - rather than the thesis - that matters to them and I hope I have not disappointed them.

Finally, I wish to place on record my gratitude for the person who deserve the real appreciation "my wife" ***MONA*** who stood firmly behind me guiding and assisting me to do my research. She was the source of strength and accommodated all my frustrations and anger in a graceful manner. The research could not have been completed if not for her silent but important role in my research.

Satpal Singh Badsara

ABBREVIATIONS

Ac	acetyl
AcOH	acetic acid
aq.	aqueous
Ar	aryl
Bn	benzyl
Boc	*tert*-butoxycarbonyl
Bs	benzenesulfonyl
Bu	*n*-butyl
^{t}Bu or Bu^{t}	*tert*-butyl
cat.	catalyst
Cbz	benzyloxycarbonyl
Conc.	concentrated
m-CPBA	*meta*-chloroperbenzoic acid
DABCO	1,4-diazabicyclo(2.2.2)octane
DBU	1,8-diazabicyclo(5.4.0)undec-7-ene
DCE	1,2-dichloroethane
DCM	dichloromethane
de	diastereomeric excesses
DEAD	diethyldiazadicarboxylate
$(DHQD)_2PYR$	hydroquinidine-2,5-diphenyl-4,6-pyrimidienyl diether
$(DHQD)_2AQN$	hydroquinineaneanthraxquinone-1,4-diyldiether
DIAD	diisopropyldiazadicarboxylate

DMAP	dimethylaminopyridine
DMF	*N,N*-dimethylformamide
DMSO	dimethyl sulfoxide
dr	diastereomeric ratio
ee	enantiomeric excesses
Eq.	equation
eq.	equivalent(s)
Et	ethyl
EWG	electron withdrawing group
Hex	hexyl
3-HQD	3-hydroxyquinuclidine
IBX	2-iodooxybenzoic acid
β-ICD	*β*-isocupreidine
LAH	lithium aluminum hydride
LDA	lithium diisopropylamide
Me	methyl
MP	melting point
Ms	mesyl
MVK	methyl vinyl ketone
MW	microwave
NHC	*N*-heterocyclic carbene
NMP	*N*-methyl 2-pyrrolidinone
Nu	nucleophile
ORTEP	Oak Ridge Thermal Ellipsoid Plot

PBN	α-phenyl-*tert*-butylnitrone
Pg	protecting group
Ph	phenyl
PMP	*p*-methoxyphenyl
^{i}Pr	*iso*-propyl
Pr	propyl
PTA	1,3,5-triaza-7-phosphaadamantane
rt	room temperature
TBAB	tetrabutylammonium bromide
TBAF	tetrabutylammonium fluoride
TBDMS/TBS	*tert*-butyldimethylsilyl
Tf	trifluoromethanesulfonyl
TFA	trifluoroacetic acid
TFAA	trifluoroacetic anhydride
TFSA	trifluoromethanesulfonic acid
THF	tetrahydrofuran
TMEDA	tetramethylethylenediamine
TMG	1,1,3,3-tetramethylguanidine
TMPDA	1,1,3,3-tetramethylpropane-1,3-diamine
TMS	trimethylsilyl
TMSOTf	trimethylsilyl trifluoromethanesulfonate
Tol	*p*-tolyl
Ts	*p*-toluenesulfonyl
TTMPP	*tris*(2,4,6-trimethoxyphenyl)phosphine

ABSTRACT

The Baylis-Hillman reaction which originated from a patent has now become one of the most popular C-C bond forming reaction as evidenced by large number of publications and several major and minor reviews. Baylis-Hillman reaction is an atom economy reaction which involves three components *i.e.* activated alkenes, electrophiles and catalyst or catalyst system and provides diverse classes of multifunctional molecules. These multifunctional molecules have been used for various organic transformations and also for synthesis of several hetero & carbocyclic frameworks including natural products as well as biologically active compounds. Our research group is working on this fascinating reaction from last 29 years and contributed significantly for the development of this reaction.

This thesis deals with the applications of the Baylis-Hillman adducts in synthesis of spiro-oxindole frameworks and densely functionalized epoxides and is divided into three chapters 1) Introduction 2) Objectives, Results & Discussion and 3) Experimental. The first chapter, *i.e.* Introduction describes a brief account of literature on the development of the reaction and also presents a briefly on the applications of the Baylis-Hillman adducts in various aspects of organic synthesis.

The second chapter describes the objectives, work plan and discussion of the experimental results. The thesis has the following objectives.

1) To utilize the Baylis-Hillman bromides as a source of 1,3-dipoles with a view to understand the reactivity profile of three stericlly different allyl bromides (**46-48**) [derived from i) Baylis-Hillman alcohol, obtained from HCHO and methyl

acrylate ii) Baylis-Hillman alcohols, obtained from aryl aldehydes and methyl acrylate iii) Baylis-Hillman alcohols, obtained from aromatic aldehydes and acrylonitrile] in dipolar addition reactions with isatin derivatives **59**.

2) To utilize the dipoles generated from Baylis-Hillman bromides **47, 48** for cyclo-addition reactions with ethyl glyoxalate and diethyl ketomalonate with a view to understand their reactivity profiles.
3) To utilize carbonates of Baylis-Hillman alcohols (derived from cyclohexenones and isatin derivatives) for synthesis of nitrone-spirooxindole-frameworks **79** in one pot operation.

The Baylis-Hillman Bromides as a Source of 1,3-Dipoles : Steric Factors Directed Synthesis of Oxindole Fused Spiro Oxirane and Dihydrofuran Frameworks

Spiro-oxindole moiety is one of the important structural frameworks frequently found in many natural products. Therefore development of simple synthetic strategies for obtaining spiro-oxindole derivatives has been and continues to be an attractive area in synthetic and medicinal chemistry.

It has been well documented in the literature that Baylis Hillman adducts (or their derivatives) containing ester group (prepared from alkyl acrylates) and nitrile group (prepared from acrylonitrile) showed remarkable opposite stereochemical directions in various chemical transformations. These stereochemical reversals have been mostly attributed to the steric differences between nitrile (smaller group) and ester functionality (larger group). To the best of our knowledge, there is no systematic study

in understanding the stereochemical directions in cycloaddition reactions of the Baylis-Hillman adducts (or their derivatives) containing ester group and nitrile group. Therefore, it occurred to us that the dipoles generated from Baylis-Hillman bromides containing ester and nitrile groups, should in principle show different reactivities in cycloaddition reactions with isatin derivatives. We have selected three sterically different Baylis-Hillman bromides **46-48** and various isatin derivatives (**59**) as reaction partners for our study.

In this direction we have carried out the cyclo-addition reaction of these sterically different allyl bromides **46-48** with isatin derivatives under the influence of Me_2S in the presence of Cs_2CO_3 in DMF at 15-20 ºC for 8 hr. It was interesting to note that the allyl bromide **46** on cycloaddition with isatin derivatives **59** provided five membered spiro-dihydrofuran-oxindole derivatives **61a-g** (Table 2), whereas the allyl bromide **47** provided three member spiro-epoxyoxindoles (**63a-j** & **64a-j**) as a separable mixture of diasteromers (Table 7). The allyl bromide **48** on cycloaddition reaction with isatin derivatives **59** under same conditions provided spiro-dihydrofuran-oxindole derivatives (**67a-f**) in diastereomerically pure form (Eq. 21, Table 10).

From these studies it is quite clear that steric factors direct cyclo-addition reactions between the dipoles generated from Baylis-Hillman bromides **46-48** and isatins **59** as dipolarophiles, thus providing an interesting methodologies for synthesis of spiro-epoxy-oxindoles (**63** & **64**) and spiro-dihydrofuran-oxindoles (**61** & **67**).

The Baylis-Hillman Bromides: Synthesis of Densely Functionalized Epoxides *via* Cyclo-addition strategy

After successfully examining the steric influences in cyclo-addition reactions of the isatin derivatives with three sterically different Baylis-Hillman bromides (**46-48**) we undertook to investigate cycloaddition reaction of allyl bromides (**47** & **48**) with reactive carbonyl compounds *i.e.* ethyl glyoxalate and diethyl ketomalonate with a view to understand the reactivity profile of these allyl bromides in these reactions.

In this direction we have employed the allyl bromide **47** for cycloaddition reaction with ethyl glyoxalate or diethyl ketomalonate under the influence of Me_2S/K_2CO_3 in CH_3CN/H_2O solvent system. In these reactions three membered ring *i.e.* densely functionalized epoxide derivatives **70a-f** were obtained (Eq. 23, Table 14). Similarly cycloaddition reactions using the allyl bromide **48** with ethyl glyoxalate or diethyl ketomalonate also resulted in the formation of three member ring *i.e;* epoxide derivatives **71a-g** (Eq. 24, Table 17). In these reactions we did not notice the formation of any dihydrofuran derivatives.

Facile One-pot Synthesis of Nitrone-spiro-oxindoles Frameworks using Carbonates of Baylis-Hillman alcohols

In recent years there has been increasing interest in understanding the free radical mediated oxidative damage to cells because it is considered to be one of the major factors responsible for many diseases such as neuro-degeneration, stroke, cancers *etc*. After the initial studies on the applications of PBN (α-phenyl-*tert*-butylnitrone) and its derivatives for trapping free radical in chemical systems, research work from various

leading laboratories has been directed toward examining the utility of nitrones as spin traps in biological systems and many significant results were achieved in this direction. In fact the present day synthetic and medicinal chemistry demand the design, synthesis of appropriate nitrone framework for addressing the problems of oxidative damage to tissues.

As mentioned above, spirooxindole skeleton is another unique structural framework that is present in several natural products and biologically active molecules. It occurred to us that molecules containing both nitrone skeleton and spirooxindole structural unit might show interesting biological activities.

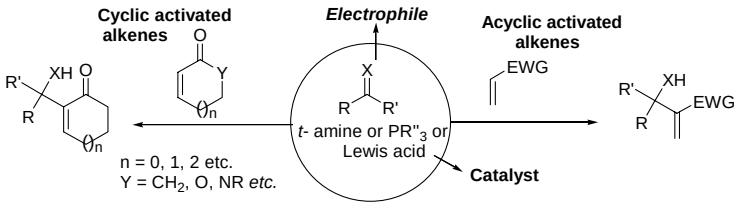
Accordingly we have developed a facile protocol for synthesis of nitrone-spiro-oxindoles frameworks (**79**) *via* the alkylation of nitromethane with the carbonates (**77**) of Baylis-Hillman alcohol (**76**) followed by reductive cyclization with Fe/HCl in EtOH according to the Scheme 63 (Table 22).

The third chapter provides detailed experimental procedures, physical constants like melting point, IR, ^{1}H & ^{13}C NMR, HRMS spectral data.

Introduction

Although there are umpteen number of reactions or methodologies available in the literature, development of novel and facile strategies for construction of carbon-carbon bonds has been and continuous to be challenging endeavor in organic synthesis because of its fundamental importance in organic chemistry.[1-2] The present day demands in organic synthesis emphasize the concepts like atom economy,[3] organocatalysis[4] and generation of functional groups[5] for development of any new strategy for construction of carbon-carbon bonds. The Baylis-Hillman reaction[6-29] is one such three component reaction (well equipped with and the concepts of atom-economy, organocatalysis and generation of functional groups) and has become very useful carbon-carbon bond forming reaction in recent years. It involves the coupling of α-position of activated alkenes with electrophiles under the influence of a catalyst or catalytic system producing densely functionalized molecules (Scheme 1).

Scheme 1



R = aryl, alkyl, heteroaryl; R' = H, COOR, alkyl; R'' = aryl, alkyl
X = O, NCOOR, NTs, NSO_2Ph, $NP(=O)R_2$, $NPPh_2$ etc.

EWG = electron withdrawing group : COR, CHO, CN, COOR, $PO(OEt)_2$, SO_3Ph, SO_2Ph, SOPh, $CONR_2$, COSR etc.

During the last three decades, Baylis-Hillman reaction has grown exponentially with respect to all the essential three components, offering diverse opportunities for its use in various synthetic transformations and methodologies. The growth of this reaction is evidenced by publications of large number of research papers and several major[8-14] and minor reviews.[15-24]

1 Activated alkenes/alkynes and electrophile and catalyst[8,10]

1.1 Activated alkenes/alkynes and electrophile and catalyst: Earlier developments[8,11, 14, 15, 17]

The list of commonly used activated alkenes/alkynes, electrophiles and catalysts are presented in Fig.1 indicating the growth and scope and expansion of this fascinating reaction.[8,11, 14, 15, 17]

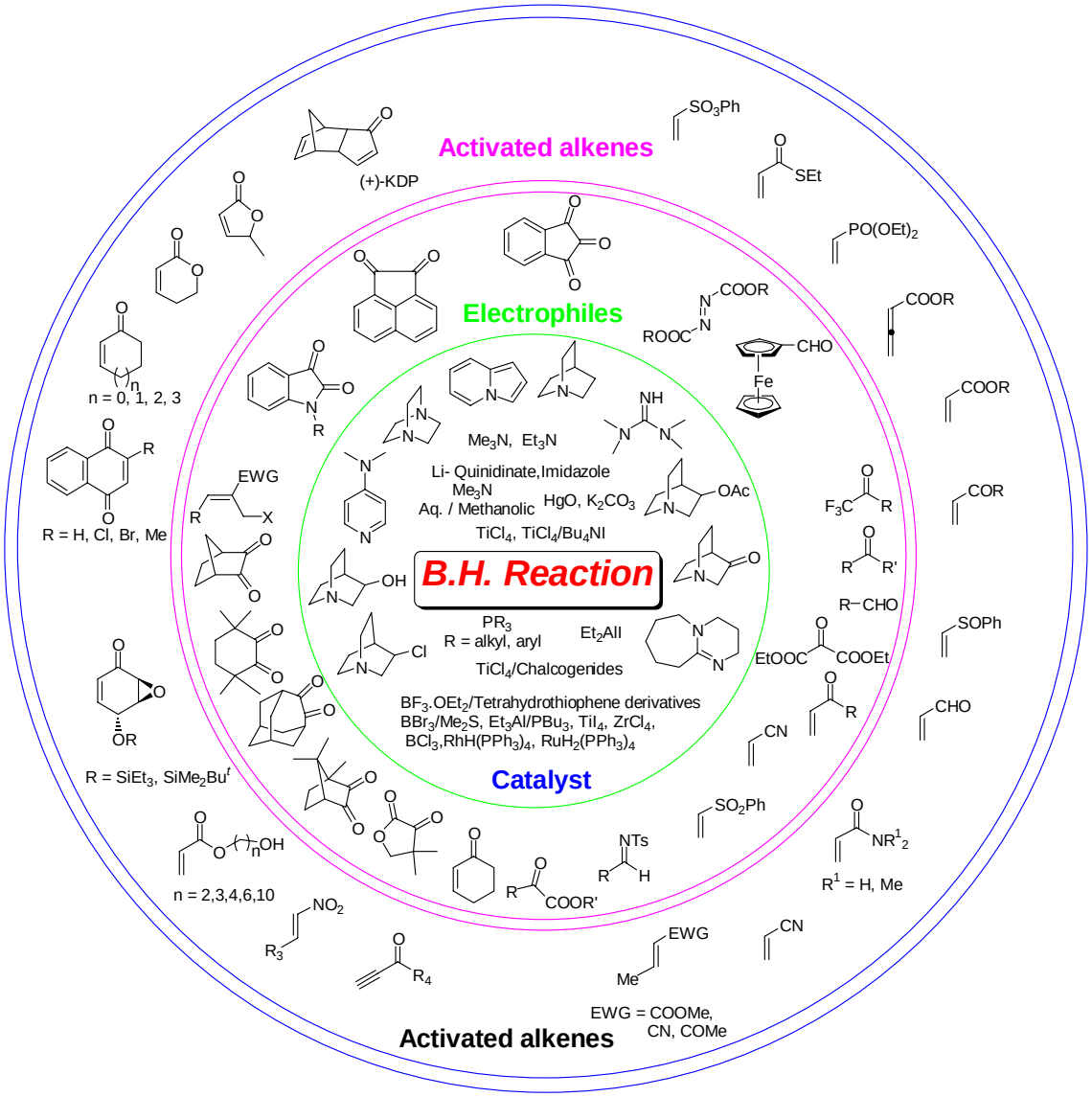


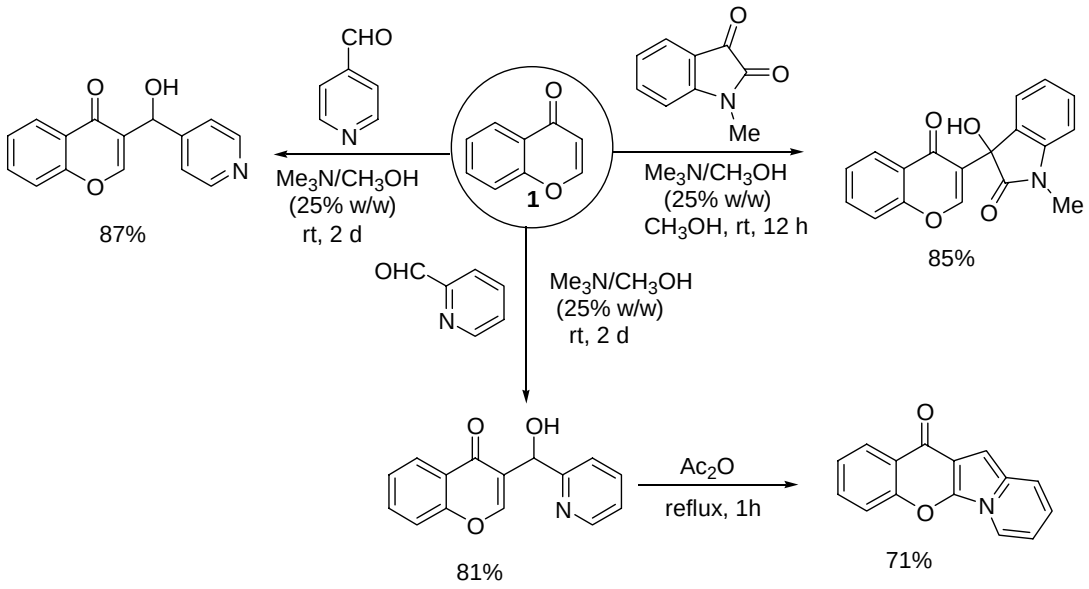
Figure-1: List of activated alkene/alkynes, electrophiles and catalysts known in literature

Some of the recent and important developments with respect to the essential components are described in this section.

1.2. Activated Alkenes: Recent developments

Our research group[30] demonstrated the application of 1-benzopyran-4(4*H*)-one derivatives as novel activated alkenes in the Baylis-Hillman coupling with reactive electrophiles such as heteroaromatic-aldehydes, nitro-benzaldehydes and isatin-derivatives (one example is shown in Scheme 2). Allyl alcohols thus obtained from pyridine-2-carboxaldehyde and 1-benzopyran-4(4*H*)-one derivatives (**1**) were successfully transformed into tetracyclic indolizine fused chromone frameworks following the reaction sequences as shown in Scheme 2 (one example is shown).

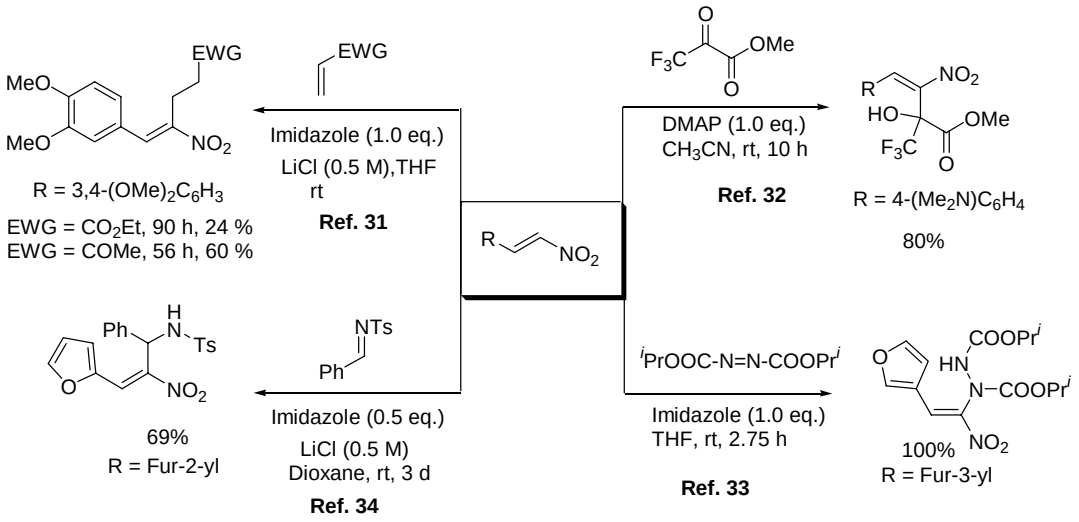
Scheme 2



Application of nitroalkene derivatives as activated alkenes for Baylis-Hillman coupling with α-keto esters, azadicarboxylates, aldimines & MVK, alkyl acrylate as electrophiles

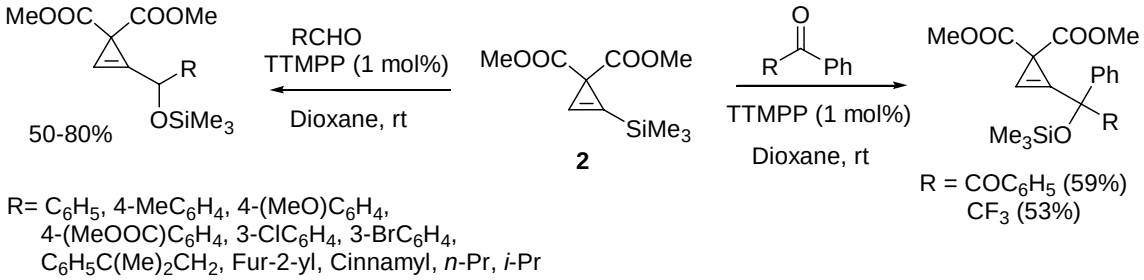
to provide the corresponding multi-functional molecules was reported by Namboothiri and co-workers[31-34] (Scheme 3). These reactions indeed indicate the importance of nitroalkene as activated alkene.

Scheme 3



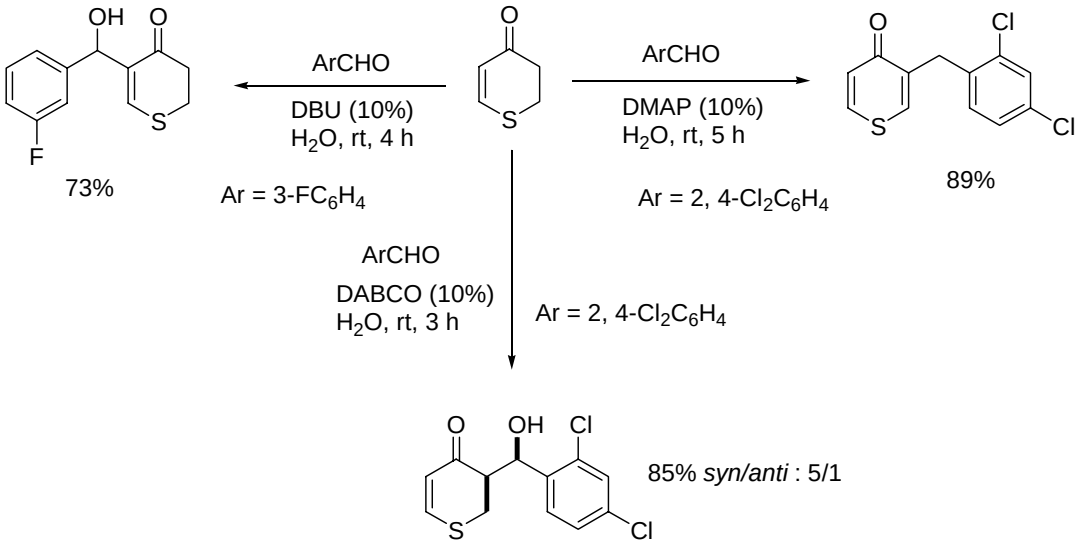
Gevorgyan and co-workers[35] have reported an interesting reaction of 1-silyl-substituted cyclopropenes (**2**) with aldehydes or ketones under the catalytic influence of TTMPP [*tris*(2,4,6-trimethoxyphenyl)phosphine] to produce the corresponding allyl silyl ether, (Baylis-Hillman type products) as shown in Scheme 4.

Scheme 4

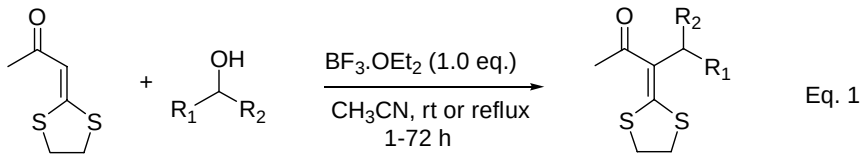


Abaee and co-workers[36] have reported an interesting coupling of dihydrothiopyran-4-one with aldehydes using amine as a catalyst in aqueous media. The product formation depends on the amine used, thus DBU provided the Baylis-Hillman products whereas DMAP and DABCO produced aldol condensation products and aldol products respectively, as shown in Scheme 5. Representative examples are presented.

Scheme 5



The Baylis-Hillman coupling of α-oxaketene-*S,S*-acetals with aryl alkyl carbinols in the presence of $BF_3.OEt_2$ was reported by Zhang and co-workers[37] to provide the corresponding α-alkylated products in excellent yields (Eq. 1).



Eq. 1

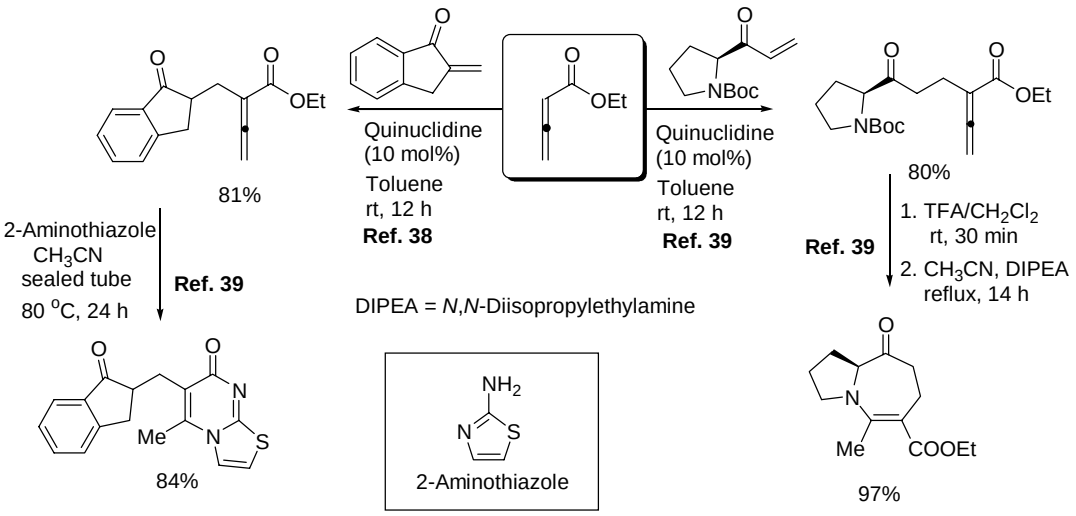
R_1 = C_6H_5, 4-$(MeO)C_6H_4$, 4-ClC_6H_4, 3,4$(OCH_2O)C_6H_3$, 4-$(Me_2N)C_6H_4$, 4-(Me)PhCH=CMe, Cinnamayl

R_2 = H, Me, Cinnamyl

1.3. Elecrophiles : Recent developments

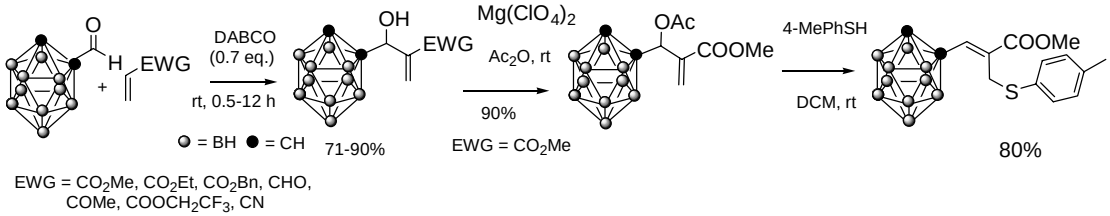
An interesting Baylis-Hillman coupling of allenic esters with α,β-unsaturated ketones (acyclic and cyclic) in the presence of quinuclidine as catalyst providing α-alkylated allenic esters in high yields was reported by Miller and co-workers.[38,39] Subsequently these compounds were efficiently used as synthons for obtaining bicyclic heterocyclic molecules following the reaction sequence as shown in Scheme 6. One example is presented.

Scheme 6



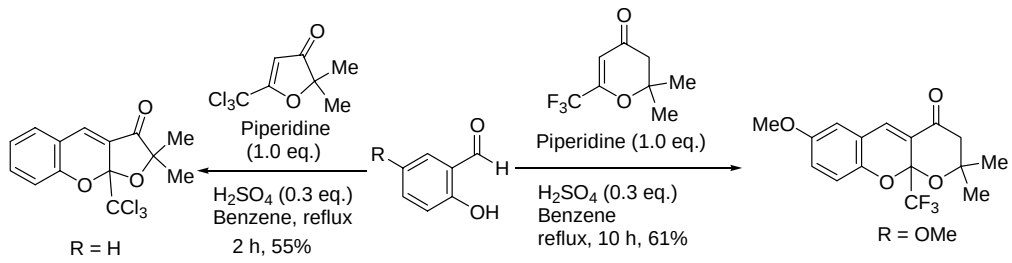
Carborane aldehydes have been successfully used as electrophiles for coupling with various activated alkenes to provide the corresponding alcohols by Reddy and co-workers.[40] Some such adducts were transformed into tri-substituted alkenes following the reaction sequence as shown in Scheme 7 (one example is presented).

Scheme 7



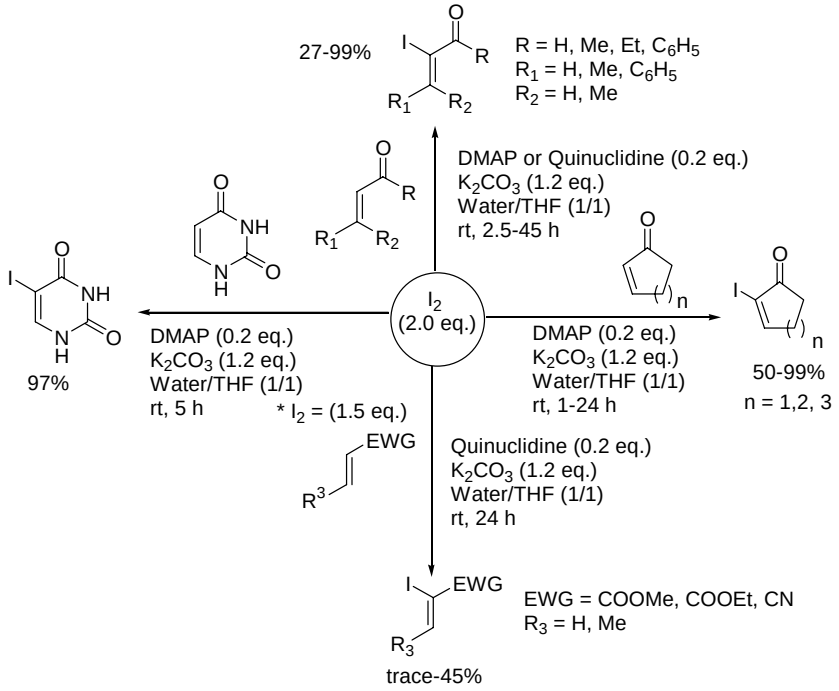
Sosnovskikh and co-workers[41] reported a facile coupling of polyhaloalkyl-substituted γ-pyrones, and β-furanones as activated alkenes with salicylaldehydes as electrophiles under the influence of organo-catalyst to produce the polycyclic oxygen heterocyclic compounds. Representative examples are shown in Scheme 8.

Scheme 8



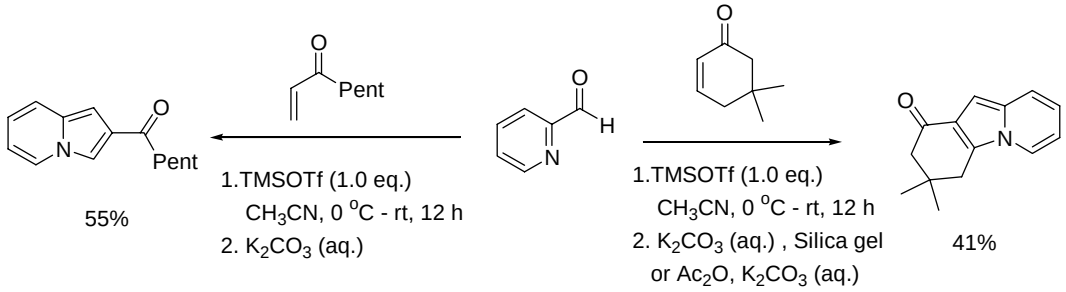
Krafft and Cran[42] have reported an interesting reaction of iodine with cyclic and acyclic enones in the presence of appropriate base to afford the corresponding α-iodinated enones. Similar iodination reaction with uracil provided the corresponding α-iodinated products following the reaction sequence as shown in Scheme 9.

Scheme 9



Our research group[43] reported, for the first time, the application of pyridine-2-carboxaldehyde acting as electrophile as well as catalyst in reaction with activated alkenes such as alkyl vinyl ketones and cyclic enones in the presence of trimethylsilyl trifluoromethanesulfonate (TMSOTf) leading to facile synthesis of indolizine derivatives in one-pot operation (Schemes 10, representative examples are presented).

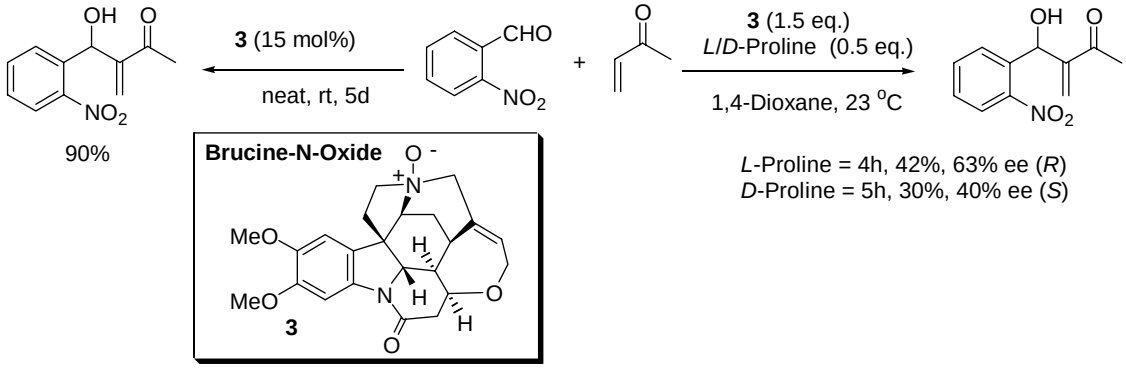
Scheme 10



1.4. Catalyst: Recent developments

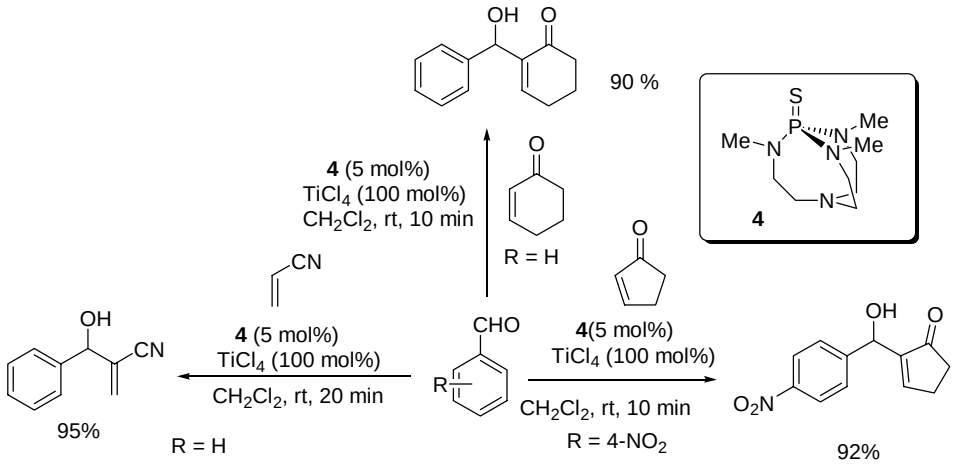
Oh and co-workers[44] described the brucine *N*-oxide (**3**) catalyzed Baylis-Hillman coupling between alkyl vinyl ketones with aldehydes. They have also observed that using proline as co-catalyst provided the resulting Baylis-Hillman adduct in reasonably good enantioselectivities (Scheme 11).

Scheme 11



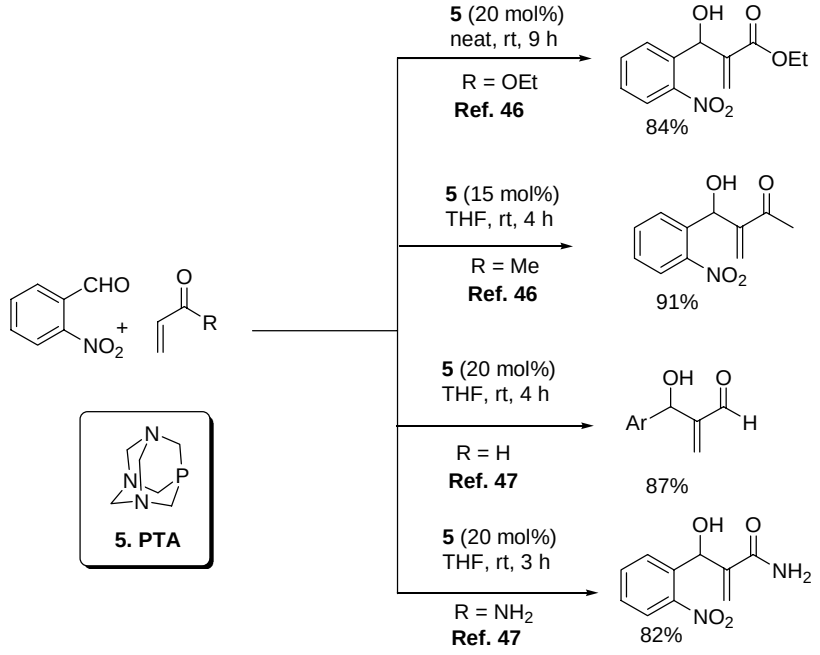
The bicyclic phosphorus compound **4** was used as catalyst in the presence of $TiCl_4$ for the Baylis-Hillman coupling between various cyclic/ acyclic activated alkenes and aldehydes by Verkade and co-workers.[45] In these reactions rate of reaction is observed to be faster. Representative examples are given in Scheme 12.

Scheme 12



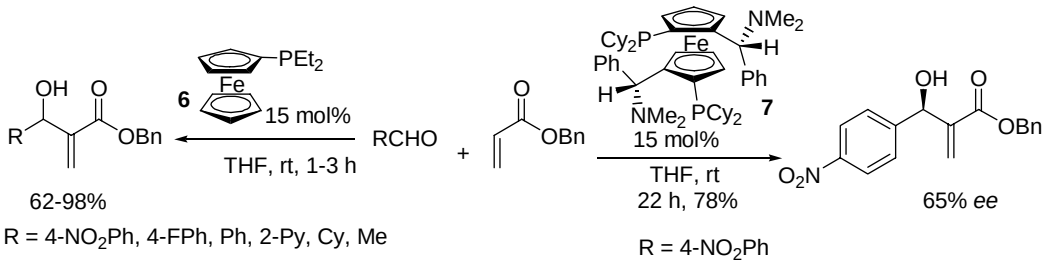
He and co-workers[46,47] have found 1,3,5,-triaza-7-phosphaadamantane (PTA) (**5**) as efficient Baylis-Hillman catalyst for the coupling of various activated alkenes with aldehydes to provide the resulting adducts in good yields. Selected examples are presented in Scheme 13.

Scheme 13



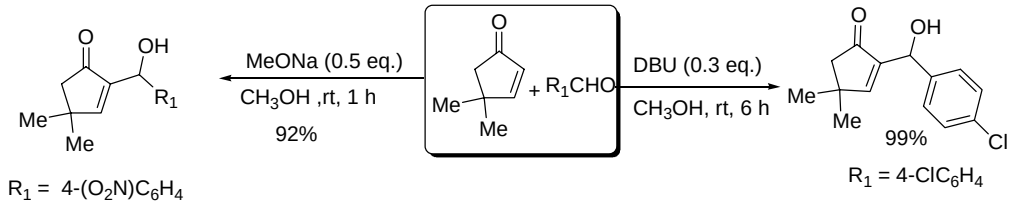
The ferrocenyldialkylphosphines (**6** &**7**) were reported to be useful catalysts for the Baylis-Hillman coupling between aldehydes and acrylates by Carretero and co-workers.[48] The resulting adducts were obtained in high yields and also at shorter reaction time. Representative examples are shown in Scheme 14.

Scheme 14



Cheng and co-workers[49] have reported an interesting Baylis-Hillman coupling between cyclic activated alkenes with various electrophiles under the influence of sodium methoxide or DBU in methanol or K_2CO_3 in methanol. Representative examples are described in Schemes 15.

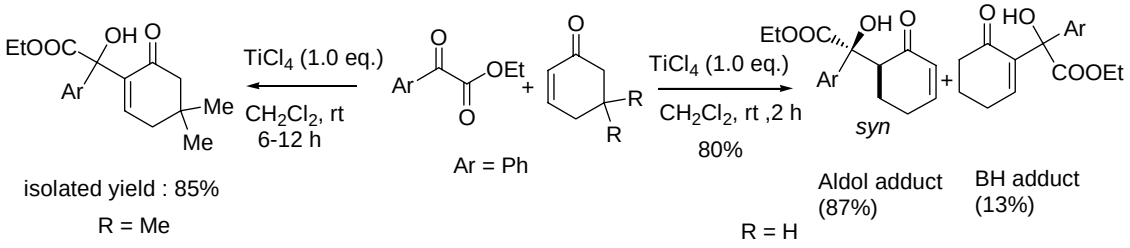
Scheme 15



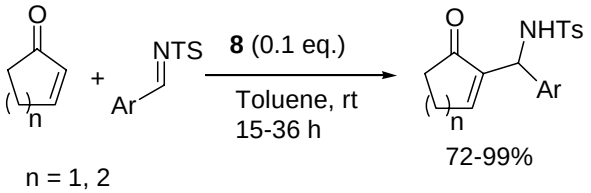
Our research group[50] used titanium tetrachloride as a medium to perform the Baylis-Hillman reaction of α-keto esters with 5,5-dimethylcyclohex-2-enone to provide the corresponding Baylis-Hillman adducts exclusively. Similar $TiCl_4$ mediated reaction of α-keto esters with cylclohex-2-enone furnished the corresponding aldol adducts (with high

syn-diastereoselectivity) as the major product (along with the Baylis-Hillman adducts as the minor product). These reactions clearly demonstrate the role of steric factors in directing the reaction pathway (Scheme 16).

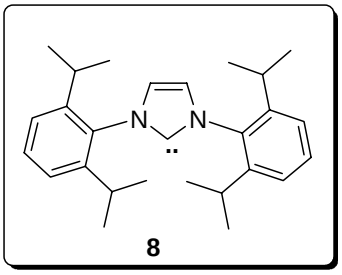
Scheme 16



Ye and co-workers[51] for the first time, reported the ingenious application of *N*-heterocyclic carbenes (NHCs) (**8**) as catalysts for performing Baylis-Hillman coupling between cyclic activated alkenes and *N*-tosylated imines according to Eq 2.



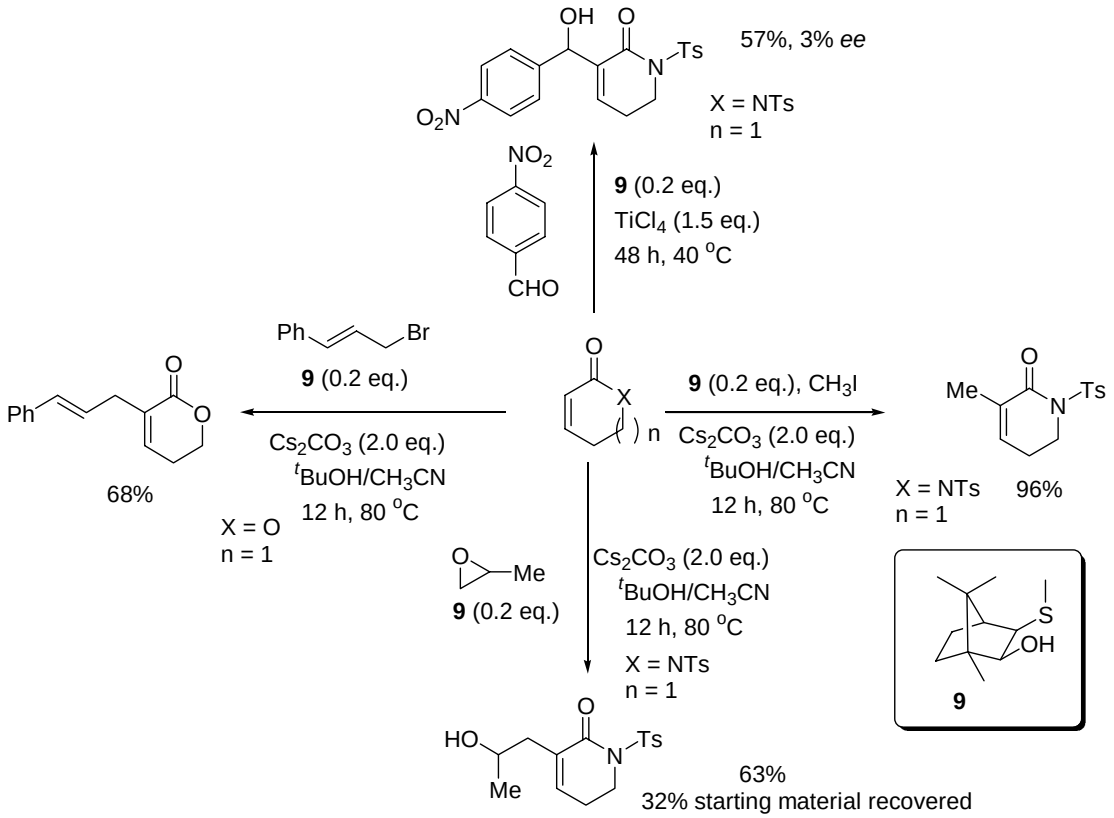
Eq. 2



Pe´rez-Castells and co-workers[52] have reported Baylis-Hillman coupling between alkyl halides or epoxides as electrophiles and lactones and lactams as activated alkenes using dialkyl sulfide (**9**) containing hydroxy functionality as a catalyst under basic conditions. This procedure works well with many alkyl halides, allyl halides and epoxides (Scheme

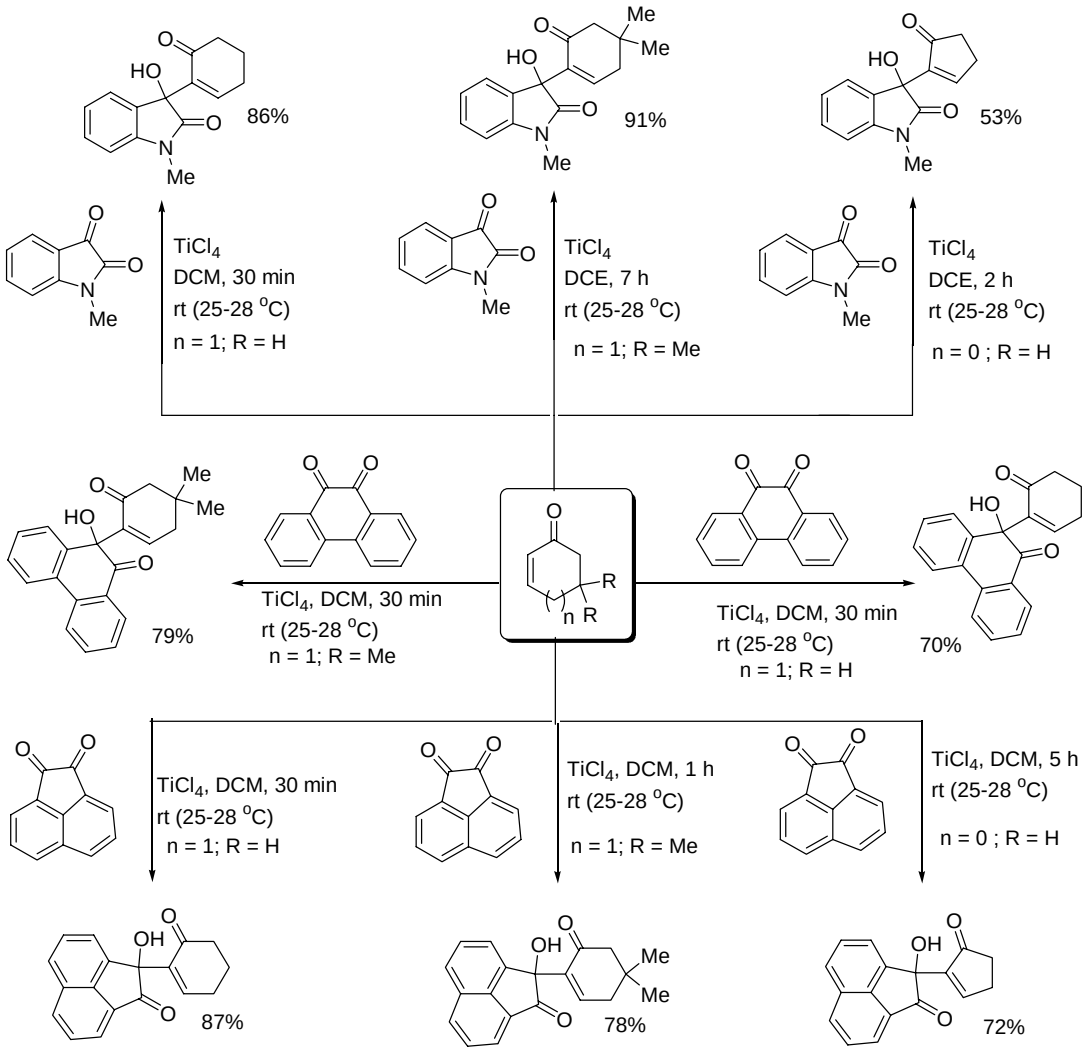
17). In the case of aldehydes this catalyst requires acidic condition to facilitate the coupling with activated alkenes. Similar reaction of aldehydes in basic conditions does not work.

Scheme 17



Our research group[53] have reported the Baylis-Hillman coupling between isatin/cyclic 1,2-diones as electrophiles and cyclic activated alkenes (cyclohex-2-enone, cyclopent-2-enone, 5,5-dimethylcyclohex-2-enone) under the influence of $TiCl_4$ to provide the corresponding Baylis-Hillman adduct according to the Scheme 18.

Scheme 18


86%
91%
53%
TiCl4
DCM, 30 min
rt (25-28 °C)
n = 1; R = H
TiCl4
DCE, 7 h
rt (25-28 °C)
n = 1; R = Me
TiCl4
DCE, 2 h
rt (25-28 °C)
n = 0 ; R = H
79%
TiCl4, DCM, 30 min
rt (25-28 °C)
n = 1; R = Me
TiCl4, DCM, 30 min
rt (25-28 °C)
n = 1; R = H
70%
TiCl4, DCM, 30 min
rt (25-28 °C)
n = 1; R = H
TiCl4, DCM, 1 h
rt (25-28 °C)
n = 1; R = Me
TiCl4, DCM, 5 h
rt (25-28 °C)
n = 0 ; R = H
87%
78%
72%

2. Asymmetric version of Baylis-Hillman reaction

2.1 Earlier developments:

There has been increasing interest in the development of asymmetric Baylis-Hillman reaction during the last two decades and significant results have been achieved with respect to chiral activated alkenes, chiral electrophiles and chiral catalysts.[8,11,17,19,20] A brief lists of some of the important chiral essential components that have been successfully employed in asymmetric Baylis-Hillman reaction are described in Figs.2-4.

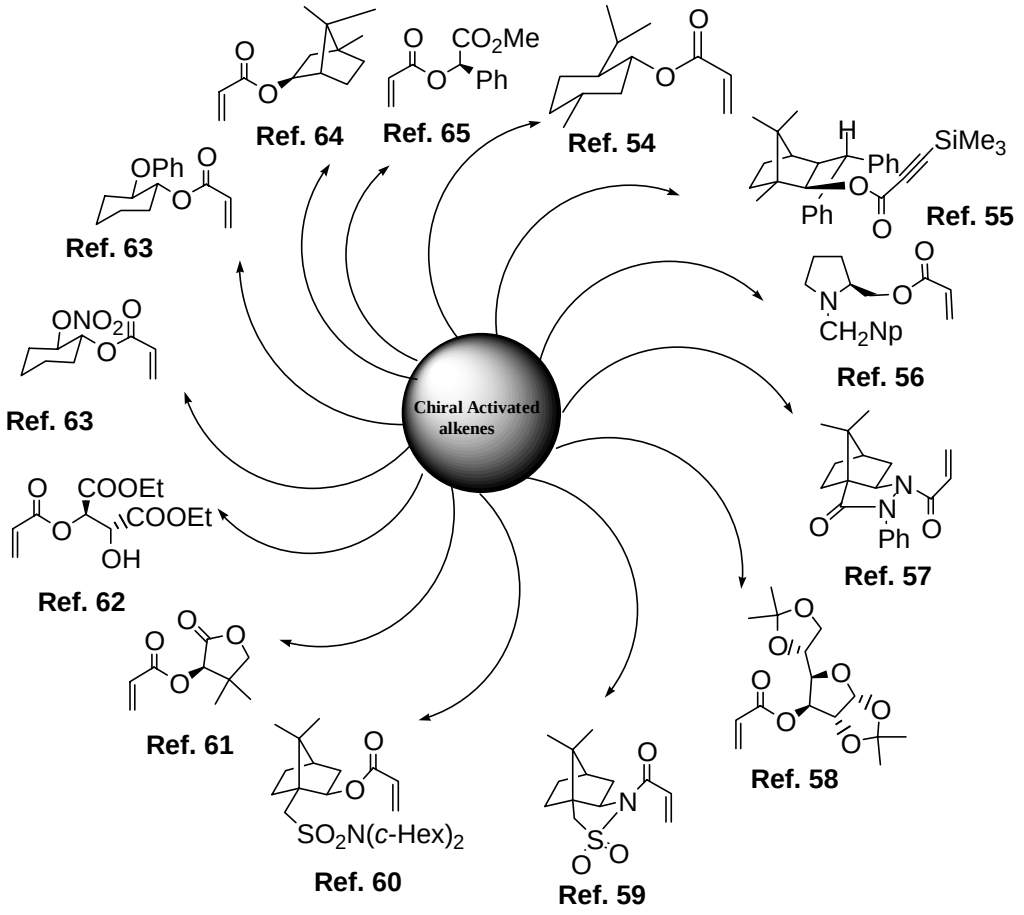


Figure 2 : Chiral activated alkenes

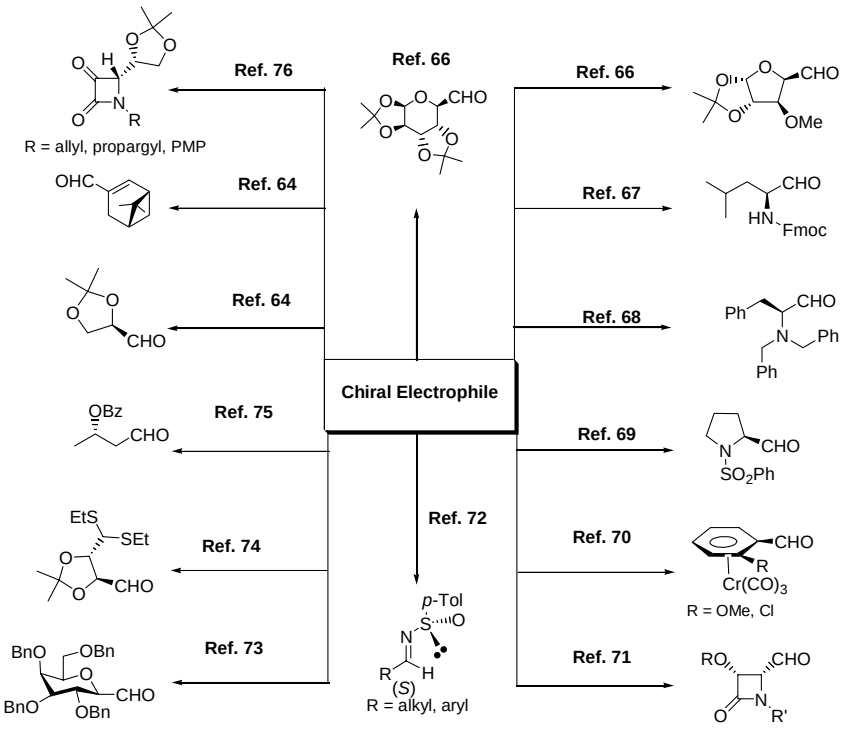


Figure 3: Chiral electrophiles

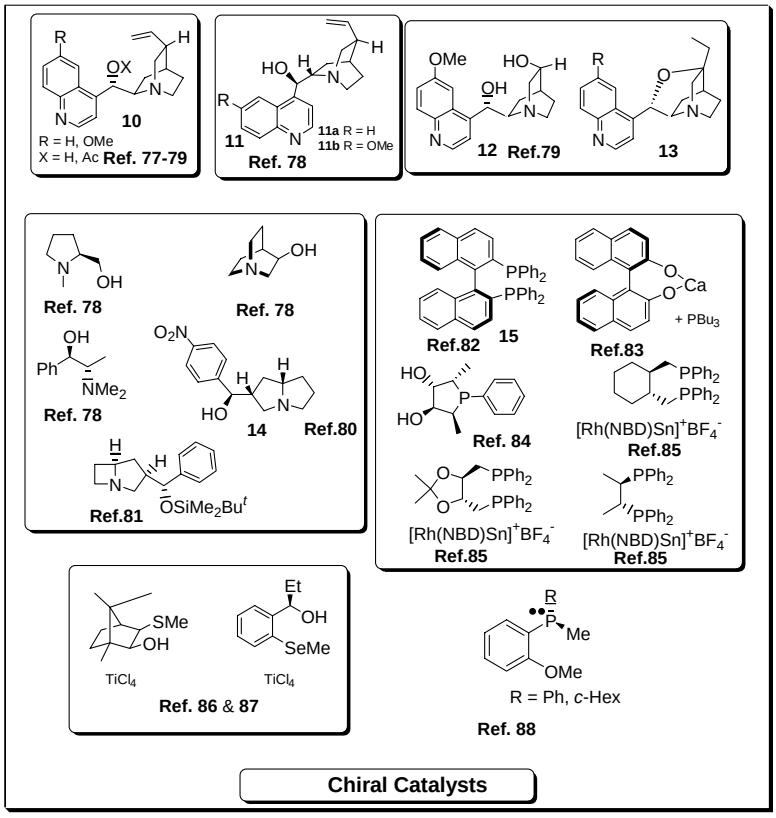
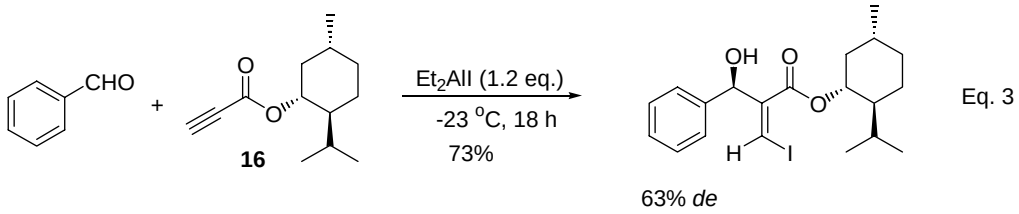


Figure 4: Chiral Catalysts

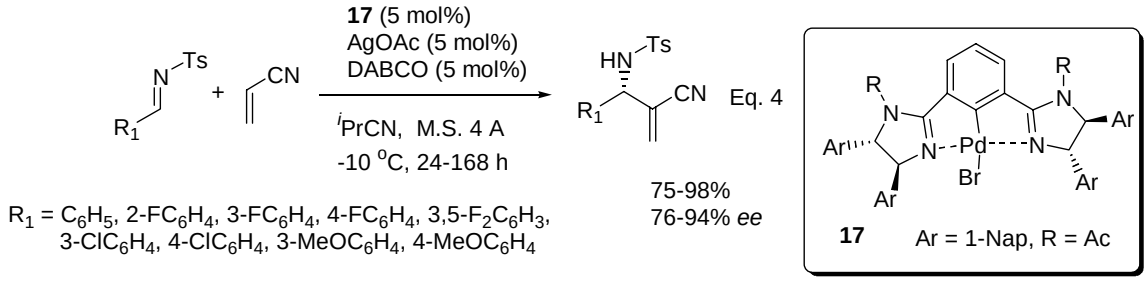
2.2 Recent developments:

Some of the most recent and relevant developments for asymmetric Baylis-Hillman reaction are described in this section.

Li and co-workers[89] reported a facile coupling of (*L*)-menthyl propiolate **16** as activated alkyne with various aromatic and aliphatic aldehydes under the influence of diethylaluminum iodide to provide the resulting adducts in 63% diastereoselectivity. One example is shown in Eq 3.

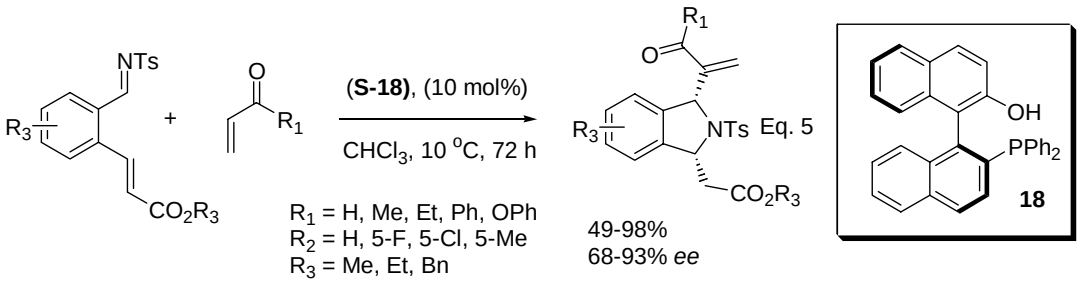


Hyodo and co-workers[90] have demonstrated application of chiral pincer complexes of 1,3-bis(imidazolin-2-yl)benzene bearing a bulky substituent and Pd II (**17**) as useful catalyst for Baylis-Hillman reaction of acrylonitrile with imines to provide resulting adducts in highly enantioselective purities, according to Eq. 4.



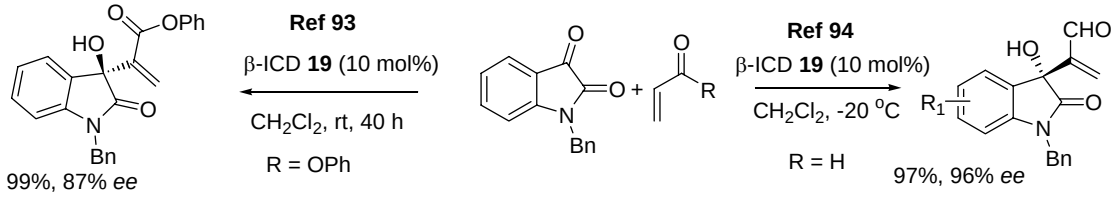
Sasai and co-workers[91] have developed an efficient methodology for the asymmetric synthesis of 1,3-disubstituted isoindolines *via* chiral phosphine (**18**) (developed by Shi)[92]

catalyzed Baylis-Hillman reaction of activated alkenes with *N*-tosylimines followed by intramolecular Michael reaction according to the Eq. 5.

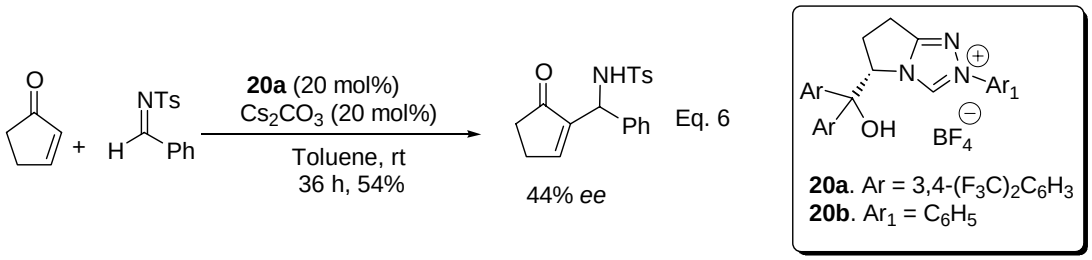


The asymmetric Baylis-Hillman reaction of isatin derivatives as electrophile with various activated alkenes under the influence of *β*-ICD (**19**) was independently reported by Shi and co-workers[93] and Zhou and co-workers[94] (Scheme 19).

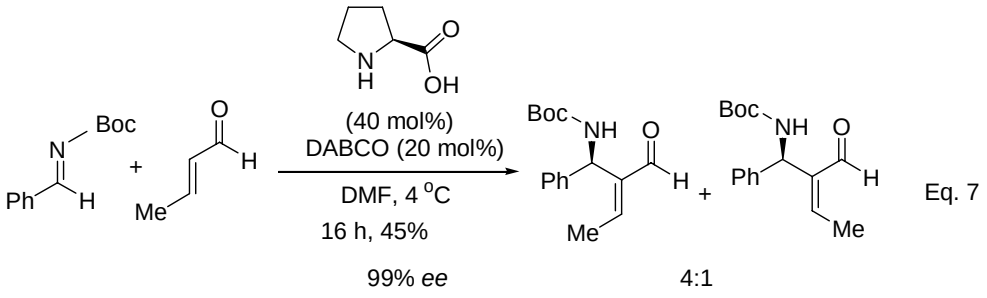
Scheme 19



Ye and co-workers[95] used carbene precursors (**20**) as chiral catalysts for Baylis-Hillman reaction between cyclopent-2-enone and phenyl-*N*-tosylamine in the presence of Cs_2CO_3 as a base. Highest enantioselectivity of 44% was achieved in the coupling of cyclohex-2-enone with phenyl-*N*-tosylamine (Eq 6).



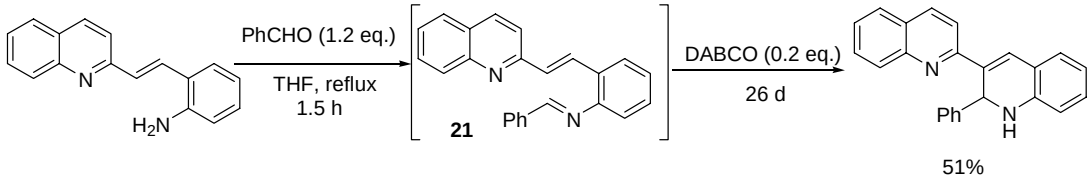
Cordova and co-workers[96] have reported a simple synthesis of *β*-substituted Baylis-Hillman adducts *via* proline mediated reaction between *β*-mono/disubstituted acrolein and aldimine derivatives under the influence of DABCO. However these adduct were obtained as a mixture of *E* and *Z*-isomers in high enantiomeric purities. Representative examples are shown in Eq 7.



3. Intramolecular Baylis-Hillman reaction

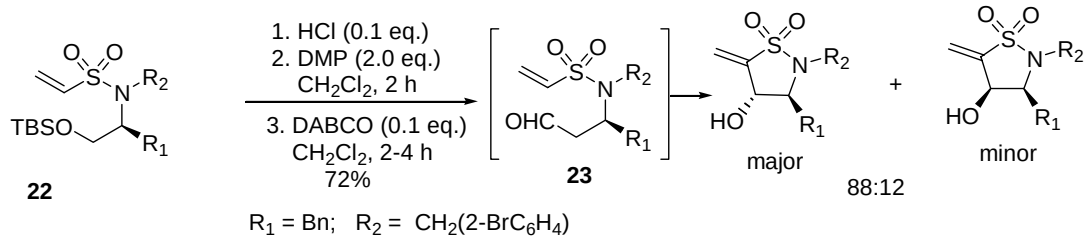
Trifonov and co-workers[97] reported an elegant intramolecular Baylis-Hillman reaction of (**21**) under the influence of DABCO leading to formation of an interesting 1′,2′-dihydro-2,3′-biquinolines, following the reaction sequence as shown in Scheme 20.

Scheme 20



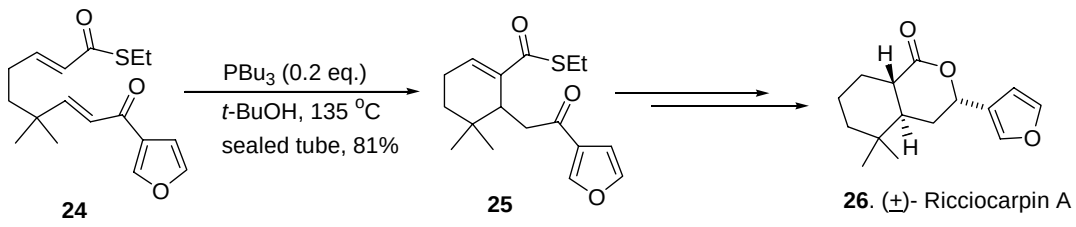
Zhou and Hanson[98] have transformed vinyl sulphamide (**22**) derived from amino alcohols into cyclic sulfones with good to excellent diastereoselectivity, following the reaction sequence as shown in Scheme 21. These reactions proceed *via* intramolecular Baylis-Hillman reaction of *insitu* formed aldehydes (**23**).

Scheme 21

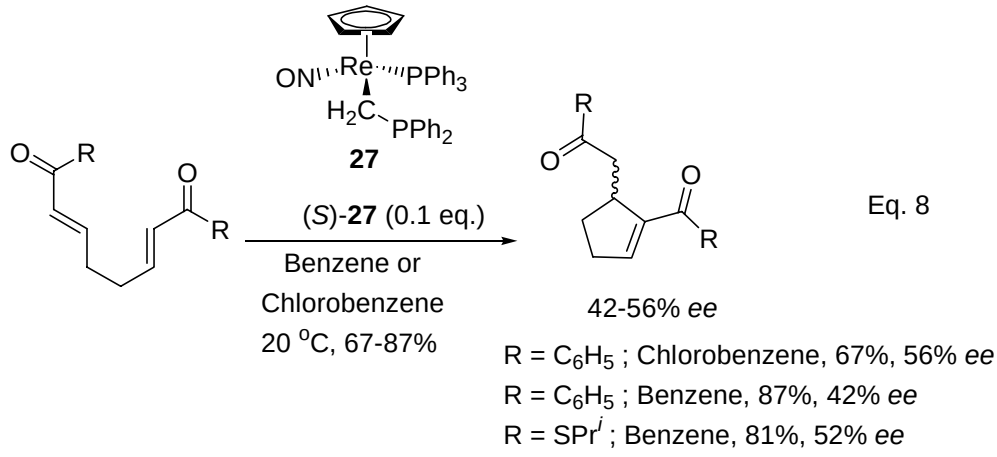


Agapiou and Krische[99] have reported a facile tributyl phosphine catalyzed intramolecular Baylis-Hillman reaction of (**24**) to provide cyclohexene derivative (**25**) which was subsequently transformed into (±)-ricciocarpin A (**26**), an interesting bioactive compound (Scheme 22).

Scheme 22



Seidel and Gladysz[100] have reported an intramolecular Baylis-Hillman reaction of dienones using (*S*)-rhenium-containing phosphine catalyst [(*S*)-**27**] to provide the resulting carbocyclic compounds in moderate enantioselectivities. Representative examples are shown in Eq 8.



Eq. 8

4. Application of Baylis-Hillman adducts

4.1 Earlier developments:

Due to the presence of several functional groups in proximity, the Baylis-Hillman adducts and derivatives offer enormous opportunity for their diverse use in organic transformations including for the synthesis of various carbocyclic/heterocyclic compounds as bioactive compounds. Earlier developments (Baylis-Hillman alcohols; Fig. 5),[101-112] (Baylis-Hillman acetates; Fig. 6),[113-123] (Baylis-Hillman bromides; Fig. 7)[124-133] are briefly presented in this section.

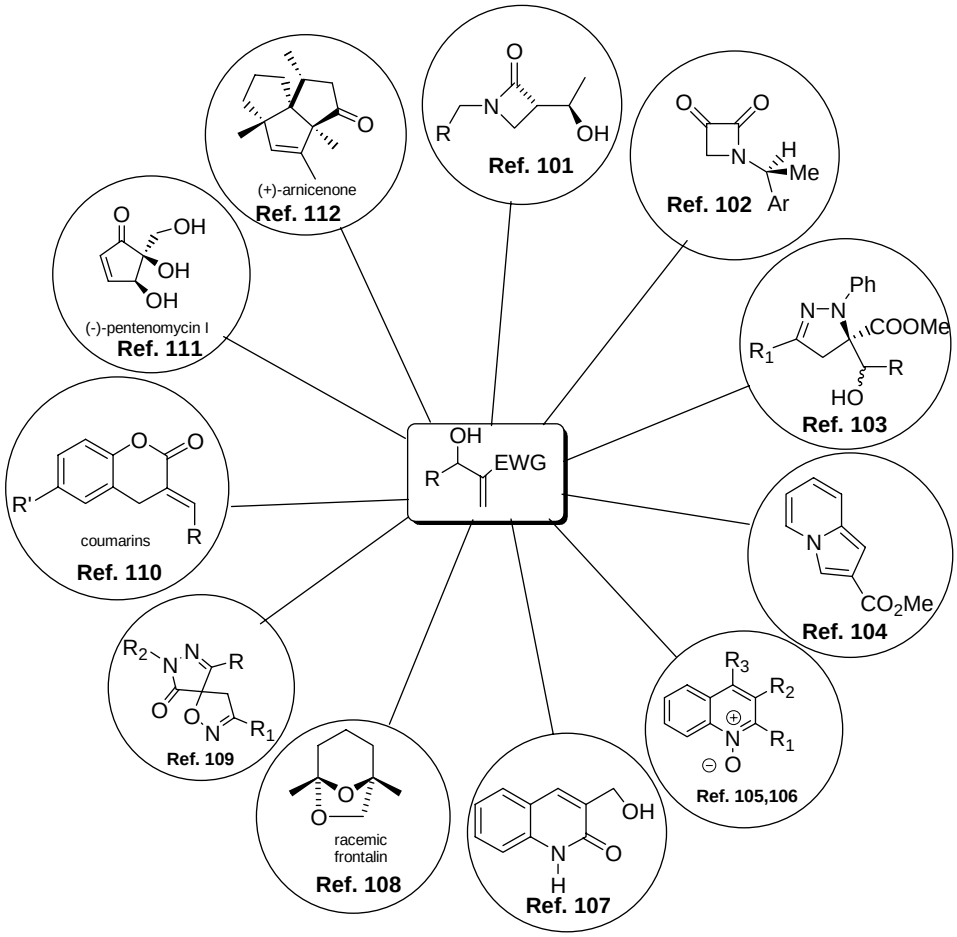


Figure-5

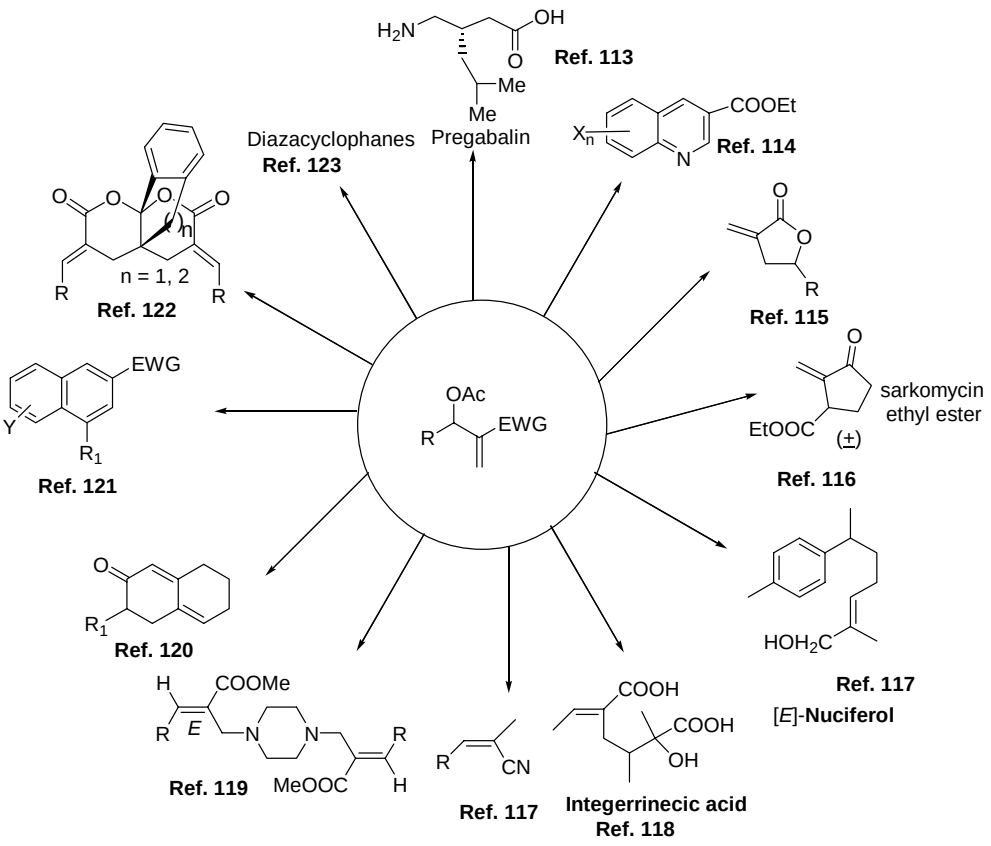


Figure-6

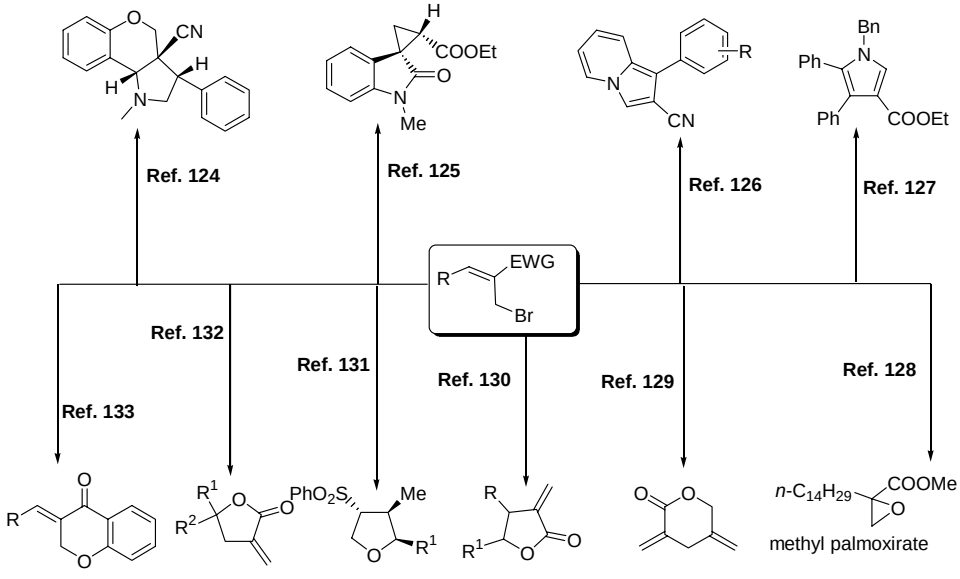


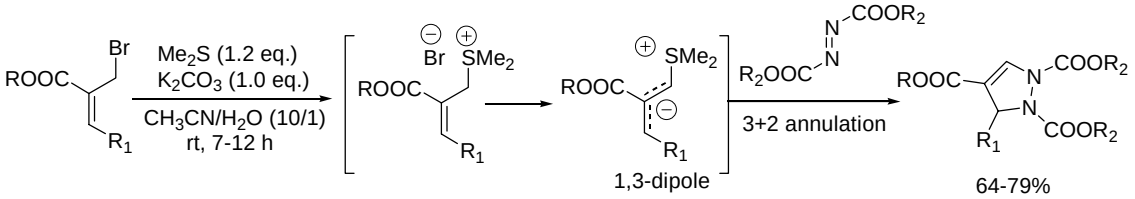
Figure-7

4.2 : Recent developments

Some of the important recent relevant applications of Baylis-Hillman adducts are presented in this section.

Our research group[134] has reported a facile methodology for obtaining functionalized dihydropyrazole derivatives *via* [3+2] annulations strategy thus demonstrating the Baylis-Hillman bromides as a valuable source of 1,3-dipoles under the influence of dimethyl sulfide in the presence of potassium carbonate for cycloaddition reaction with dialkyl azodicarboxylates (dipolarophiles) (Scheme 23).

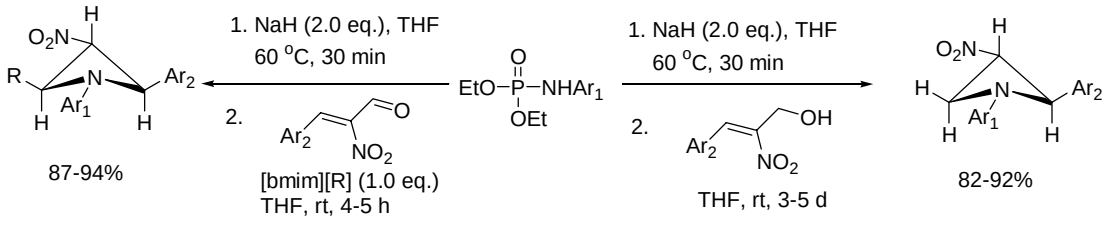
Scheme 23



R_1 = C_6H_5, 4-MeC_6H_4, 3-ClC_6H_4, 4-ClC_6H_4, 4-BrC_6H_4
R = Me, Et, *i*-Bu & R_2 = Et, *i*-Pr

Rai and Yadav[135] have developed an one-pot procedure for a highly diastereo-selective synthesis of 1,2,3-tri- and 1,2,3,4-tetrasubstituted azetidines from Baylis-Hillman alcohols and their aldehydes, respectively as shown in Scheme 24.

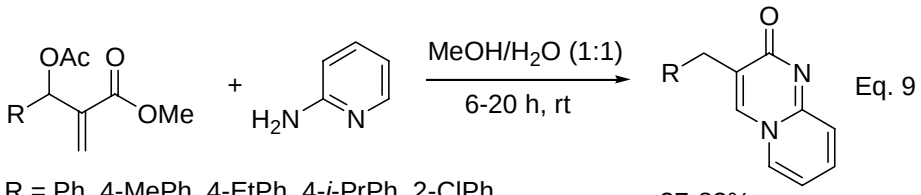
Scheme 24



Ar_2 = C_6H_5, 4-ClC_6H_4, 2-ClC_6H_4, 4-$MeOC_6H$, 3-Furyl
Ar_1 = C_6H_5, Ts
R = SCN, SC_6H_5, NO_3, TfO,

Ar_2 = C_6H_5, 4-ClC_6H_4, 2-ClC_6H_4, 4-$MeOC_6H$, 3-Furyl
Ar_1 = C_6H_5, 4-FC_6H_4, Ts

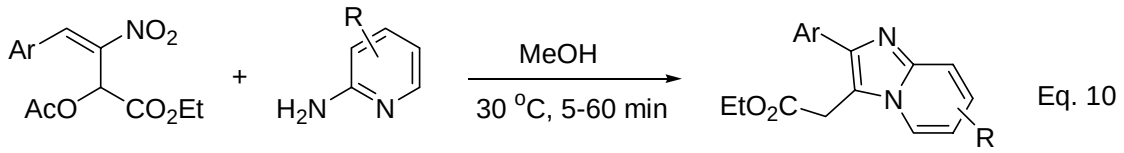
A facile one pot methodology for the synthesis of fused pyrimidones *via* the reaction of 2-aminopyridine with Baylis-Hillman acetates following the reaction as shown in Eq. 9, was reported by our research group.[136]



R = Ph, 4-MePh, 4-EtPh, 4-*i*-PrPh, 2-ClPh, 4-ClPh, 3-MeOPh, 4-MeOPh, *n*-Pent

37-83%

Namboothiri and co-workers[137] have reported one-pot synthesis of functionalized imidazopyridines through reagent-free reaction between Baylis-Hillman acetates of nitroalkenes and 2-aminopyridines. They have also proposed a reasonable mechanism for this transformation (Eq.10).



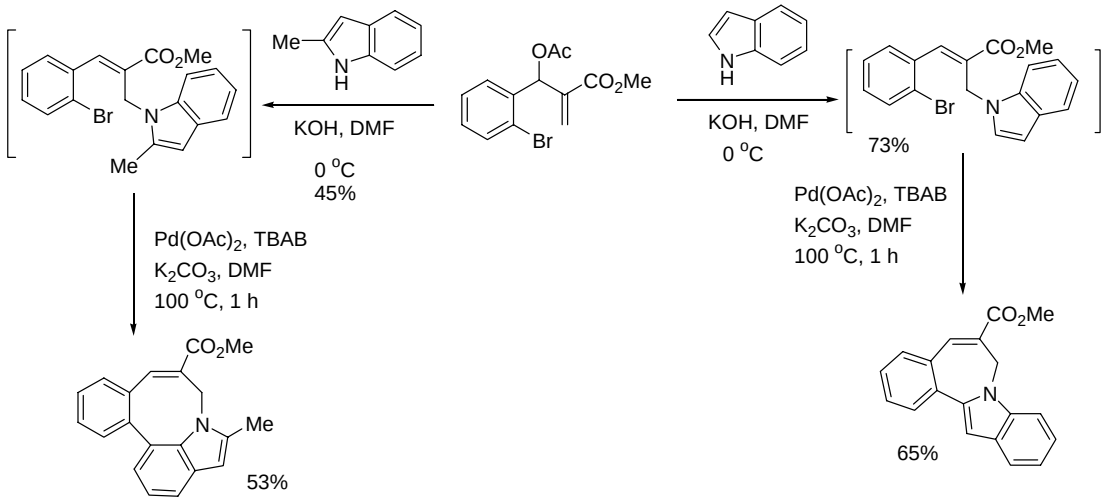
Ar = Ph, 4-MePh, 4-ClPh, 3-BrPh, 2-NO_2Ph, 3,4-$(OMe)_2$Ph, 3,4, 5-$(OMe)_3$Ph, 2-furyl, 2-thienyl, Cinamyl, 2-MeO-cinnamyl

R = 3-Me, 4-Me, 5-Cl, 5-Br, 3-OTBDMS

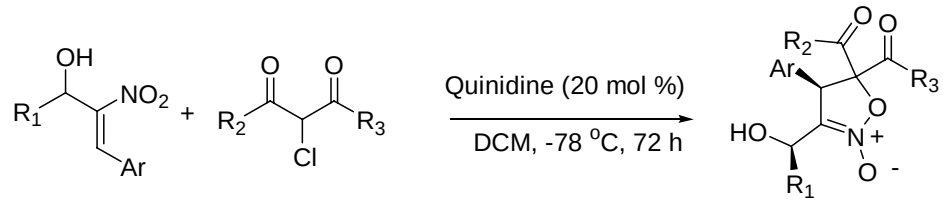
62-96 %

Kim and co-workers[138] have developed a facile methodology for synthesis of tetracyclic fused indole derivatives from the Baylis-Hillman acetates *via* the Michael addition of indole derivatives followed by Heck cyclization of the *in situ* formed intermediate as shown in Scheme 25.

Scheme 25



Guo et all[139] have elegantly transformed the Baylis-Hillman adducts (obtained *via* the coupling between nitrostyrene and ethyl glyoxalate or formaldehyde) into multifunctional isoxazoline *N*-oxides *via* enantioselective [4 + 1] annulations with 2-halo-1,3-dicarbonyl compounds using quinidine as catalyst (Eq. 11).



Ar = C_6H_5, 2-ClC_6H_4, 4-ClC_6H_4, 4-BrC_6H_4, 4-FC_6H_4, 4-MeC_6H_4, 4-$MeOC_6H_4$, 4-$CF_3C_6H_4$, 2-Furanyl
R_1 = H, CO_2Et ; R_2 = Me, OEt ; R_3 = Me

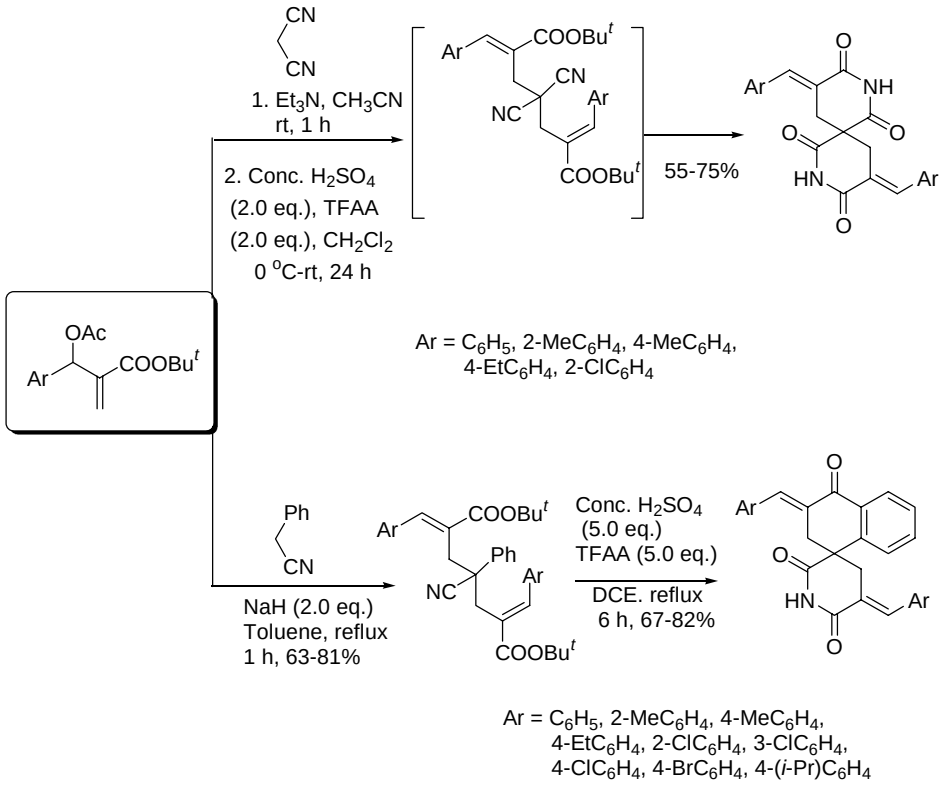
55-97 %
58-92 % *ee*
dr : 94:6 - >99:1

Eq. 11

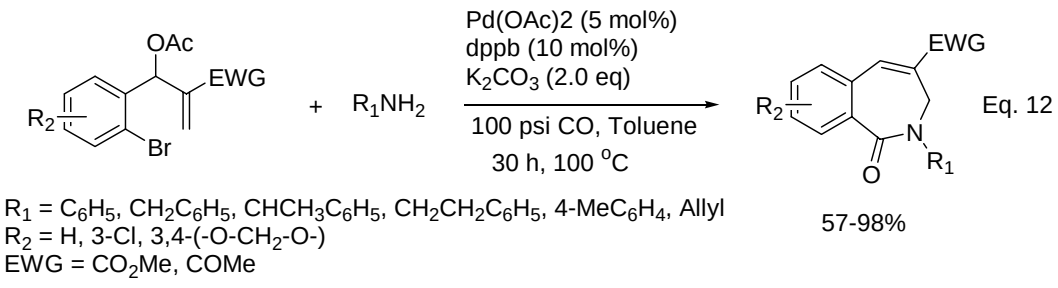
Our research group[140] has developed a simple and convenient synthesis of di(*E*)-arylidene-tetralone-spiro-glutarimides from Baylis-Hillman acetates *via* an interesting bisalkylation of phenylcyanide following biscyclization strategy involving facile C-C and C-N bond formations following the reaction sequence as described in Scheme 26. A simple one-pot multi step transformation of the Baylis-Hillman acetates into di(*E*)-

arylidene-spiro-bisglutarimides was also reported by our research group *via* bisalkylation of malononitrile followed by biscyclization strategy as shown in Scheme 26.

Scheme 26



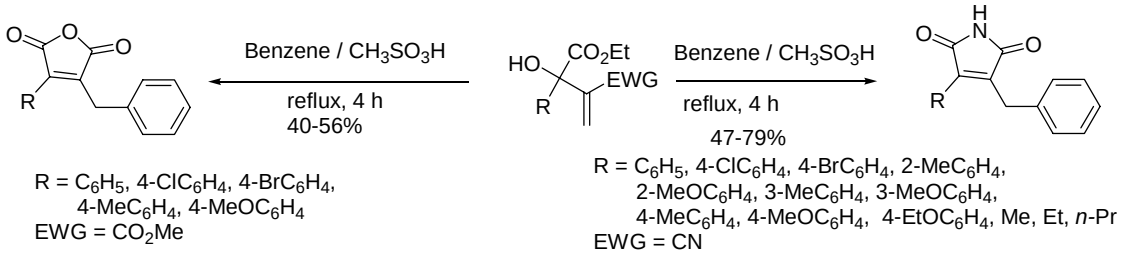
Alper and co-workes[141] have transformed the Baylis-Hillman adducts into benzazenone derivatives *via* hydroamination with amines, followed by intramolecular cyclocarbonylation (Eq 12).



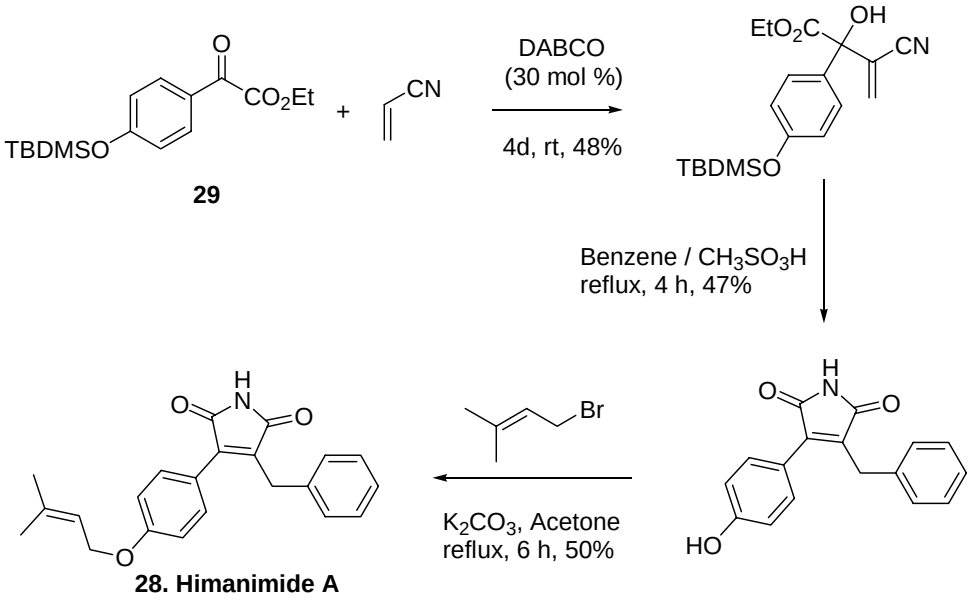
Eq. 12

Our research group[142] has developed one-pot procedure for the synthesis of unsymmetrical 3,4-disubstituted maleimide and maleic anhydride derivatives from Baylis-Hillman alcohols (derived from α-keto esters) as shown in Scheme 27. This strategy has been extended to the synthesis of Himanimide A (**28**), an important bioactive molecule using the Baylis-Hillman alcohol obtained *via* the coupling of *α*-keto-ester (**29**) with acrylonitrile as a key starting material, according to the Scheme 28.

Scheme 27

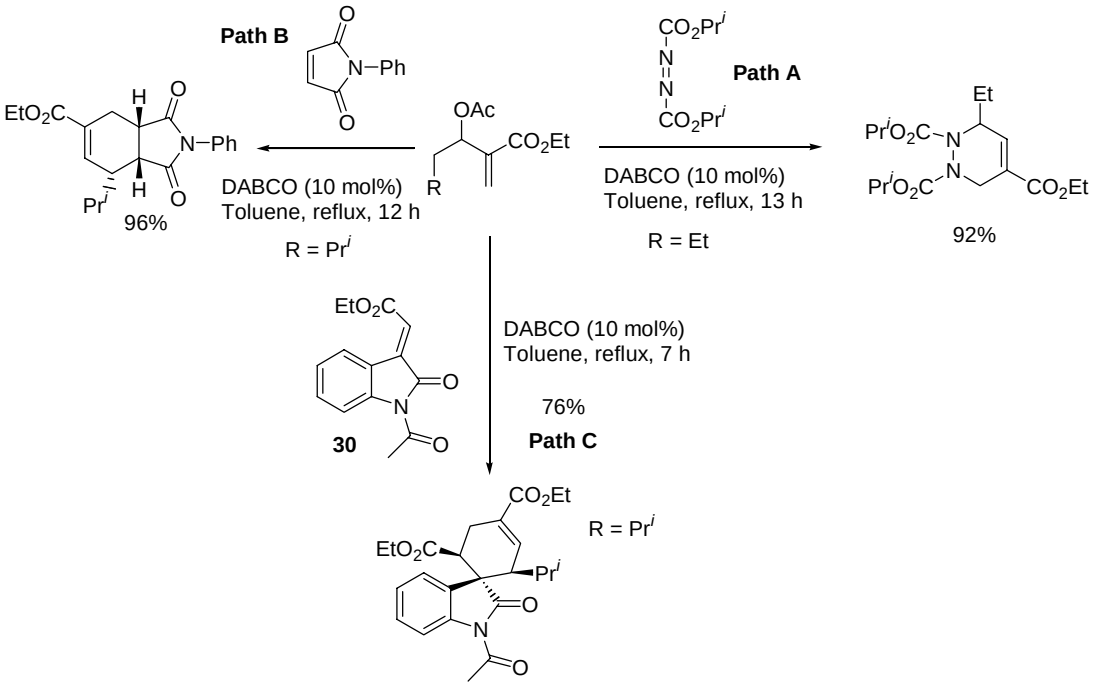


Scheme 28



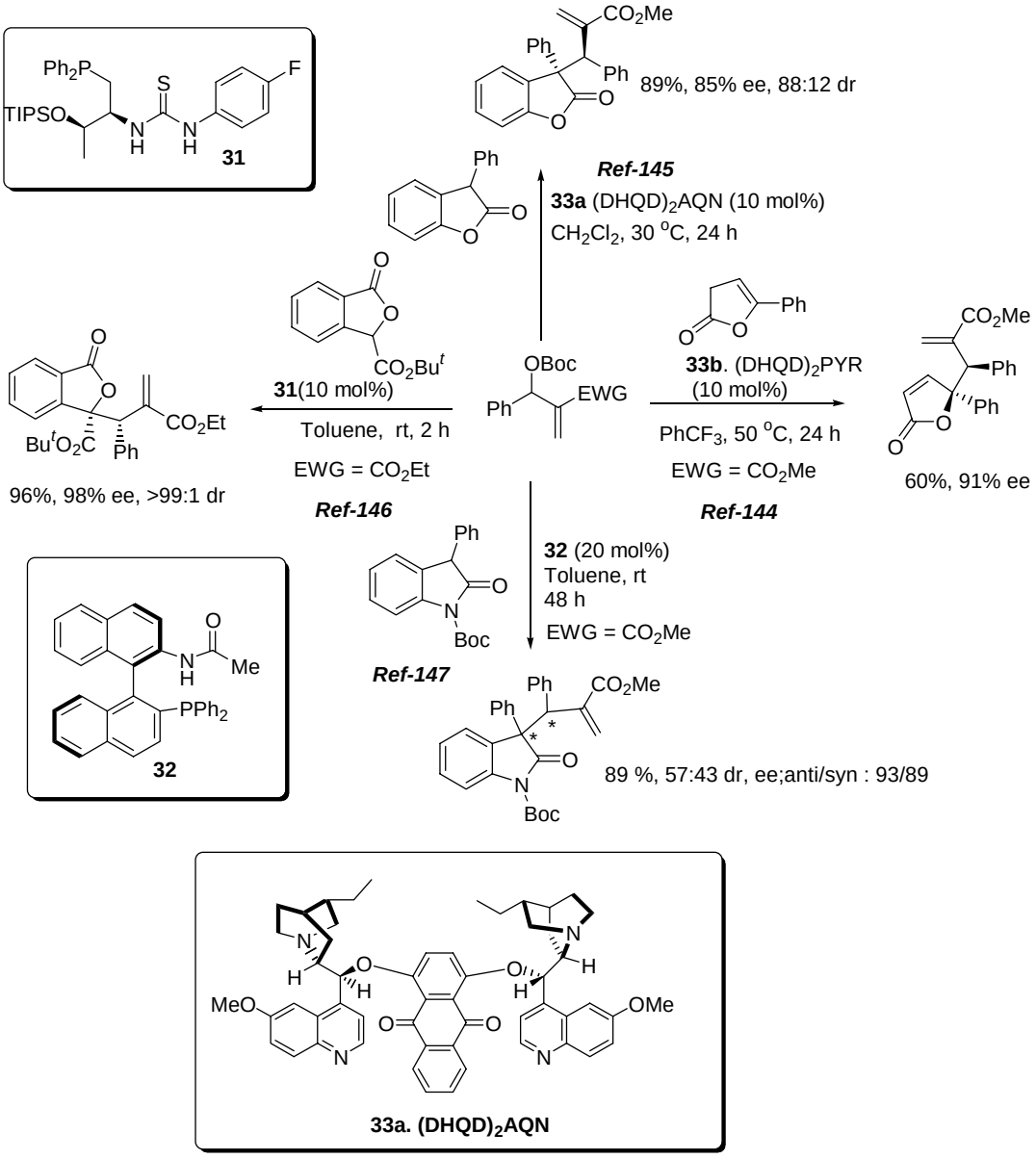
He and co-workers[143] have developed an amine-catalyzed [4+2] annulation reaction of Baylis-Hillman acetates with electron-deficient alkenes and maleimide to provide highly functionalized cyclohexenes (Path A) and tetrahydropyridazines (Path B) respectively. Similar reaction with 2-oxaindole derivative (**30**) provided spirooxindole derivatives (Path C), as shown in Scheme 29.

Scheme 29

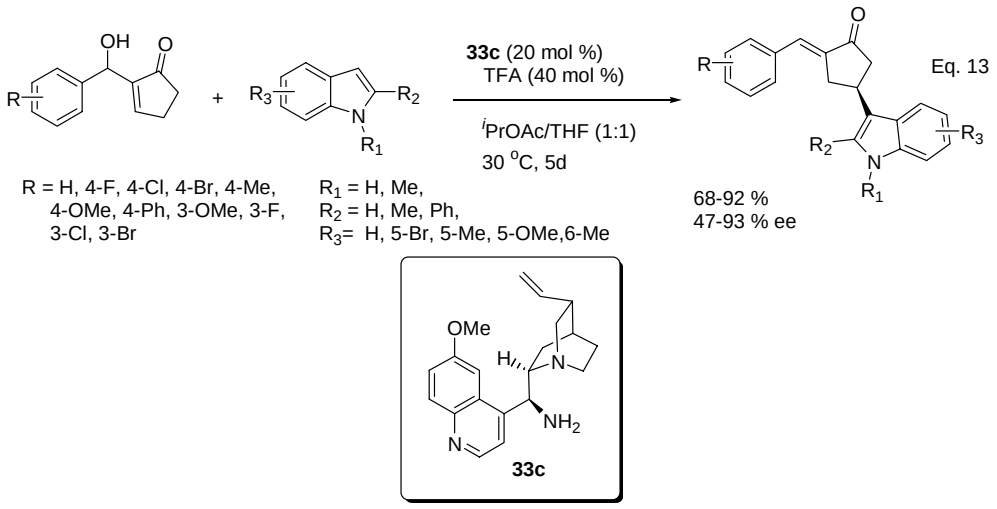


Chen and co-workers[144] have reported an elegant enantioselective synthesis of *γ*,*γ*-disubstituted butenolides containing adjacent chiral centers *via* allylic alkylation of *γ* ,*γ*-butenolides with Baylis-Hillman carbonates using chiral catalyst **31**. Later on Cheng and co-workers[145], Lu and co-workers[146] and Shi and co-workers[147] have also reported the similar kind of transformations using different catalyst **31, 32, 33** respectively as shown in Scheme 30.

Scheme 30

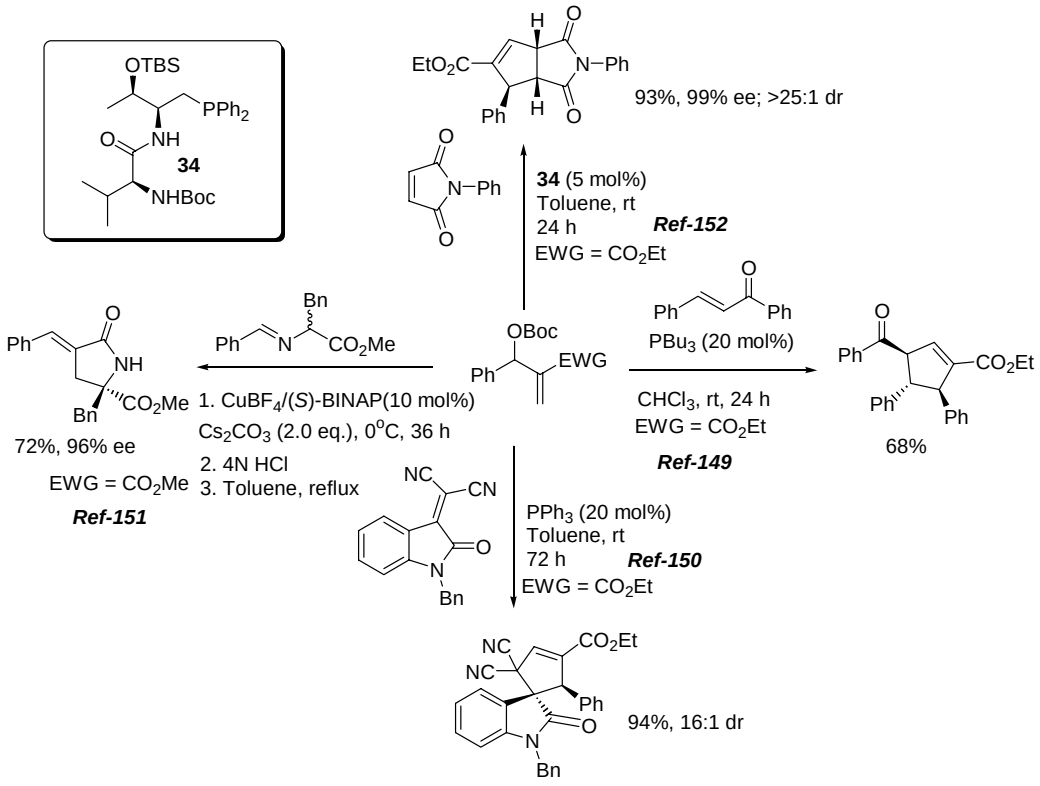


Chen et all[148] reported enantioselective nucleophilic substitution of cyclic Baylis-Hillman alcohols with indoles (under organocatalysis condition) using a chiral primary amine as the catalyst in combination with a Brønsted acid as the co-catalyst. They have obtained unexpected *δ*-products with exclusive regioselectivity and high enantioselectivity (Eq. 13).



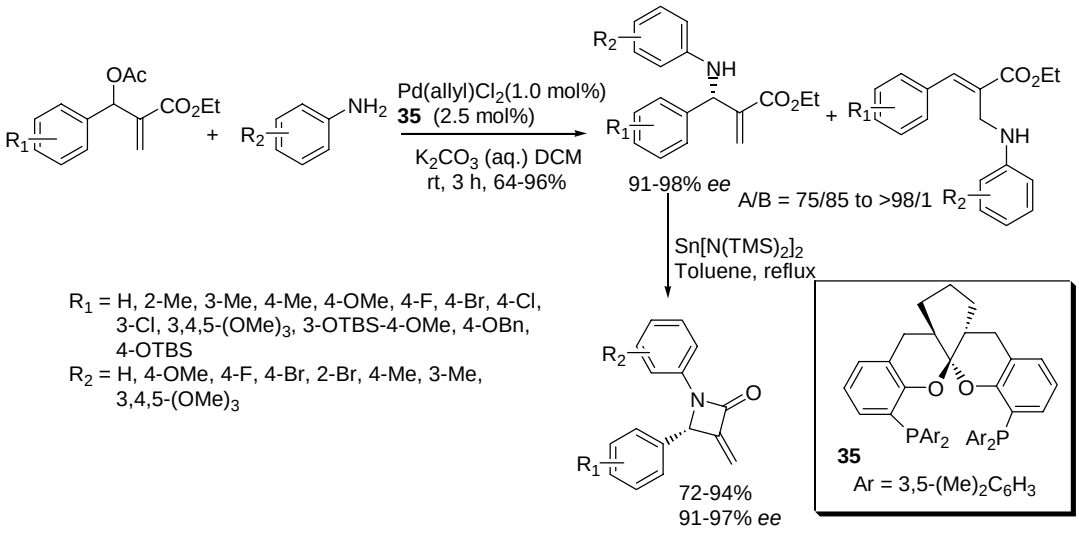
The Baylis-Hillman carbonates have been transformed into various cyclic compounds both in racemic form as well as enantiomeric enriched form according to Scheme 31 by various research groups.[149-152]

Scheme 31



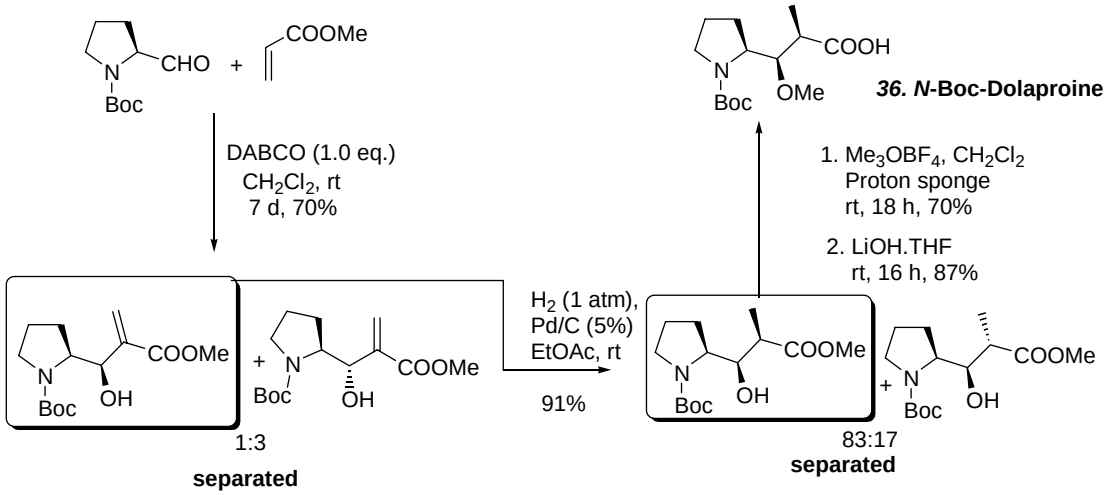
Wang et all[153] have reported a facile enantioselective allylic amination of the Baylis-Hillman acetates with aromatic amines using the chiral phosphine catalyst (**35**) (optically pure spiro-2,2'-bischromane derivatives) which provided the corresponding *β*-arylamino acid esters in good yields with enantioselectivities. The resultant *β*-arylamino acid esters were subsequently transformed into *β*-lactam derivatives (Scheme 32).

Scheme 32



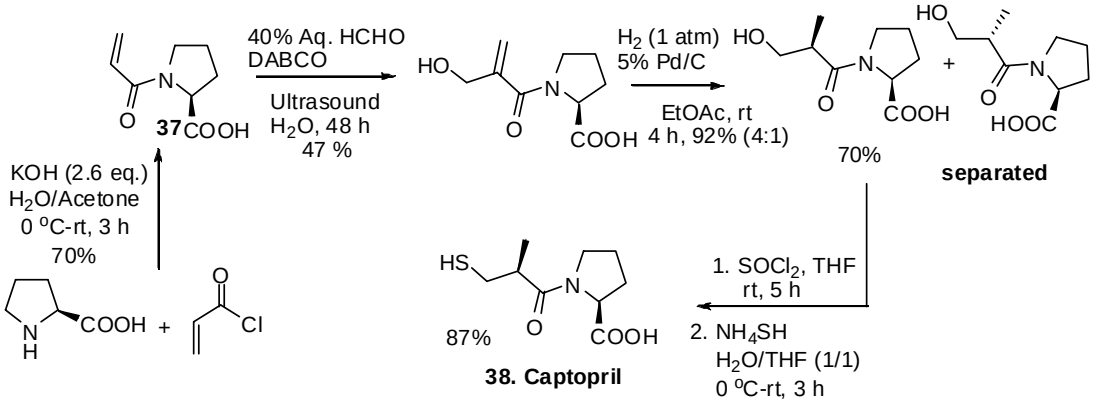
Almeida and Coelho[154] have reported an interesting strategy for synthesis of *N*-Boc-dolaproine (**36**) starting from the Baylis-Hillman adduct obtained *via* the coupling between *N*-protected prolinal and methyl acrylate, following the reaction sequence as shown in Scheme 33.

Scheme 33



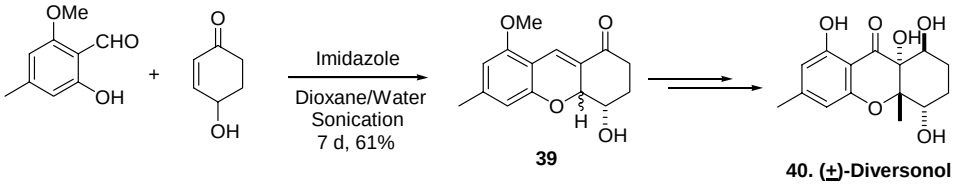
A simple synthesis of potent and orally available inhibitor of ACE, captopril (**38**), from the Baylis-Hillman alcohol, derived from *N*-acryloylproline (**37**) *via* the reaction with formaldehyde was reported by Feltrin and Almeida[155] following the reaction sequence as shown in Scheme 34.

Scheme 34



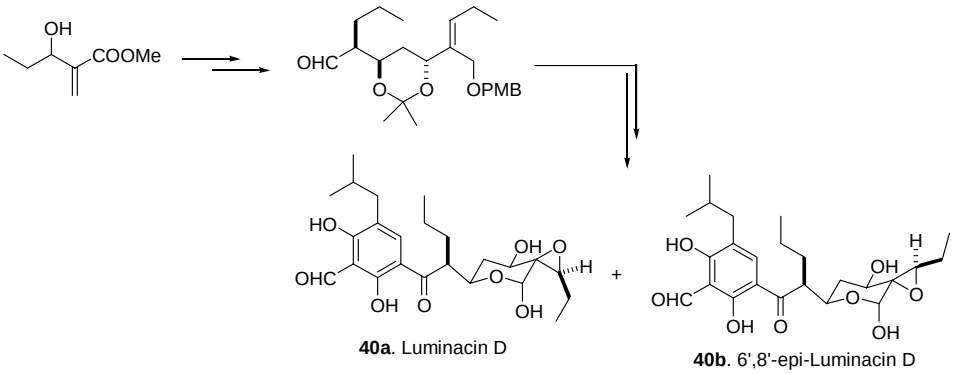
Brase and co-workers[156] have successfully used the Baylis-Hillman alcohols (**39**) obtained *via* the reaction between 2-hydroxy-6-methoxy-4-methyl benzaldehyde and 4-hydroxy-cyclohex-2-enone for synthesis of diversonol (**40**) in 14 synthetic steps, following the reaction sequence as shown in Scheme 35.

Scheme 35



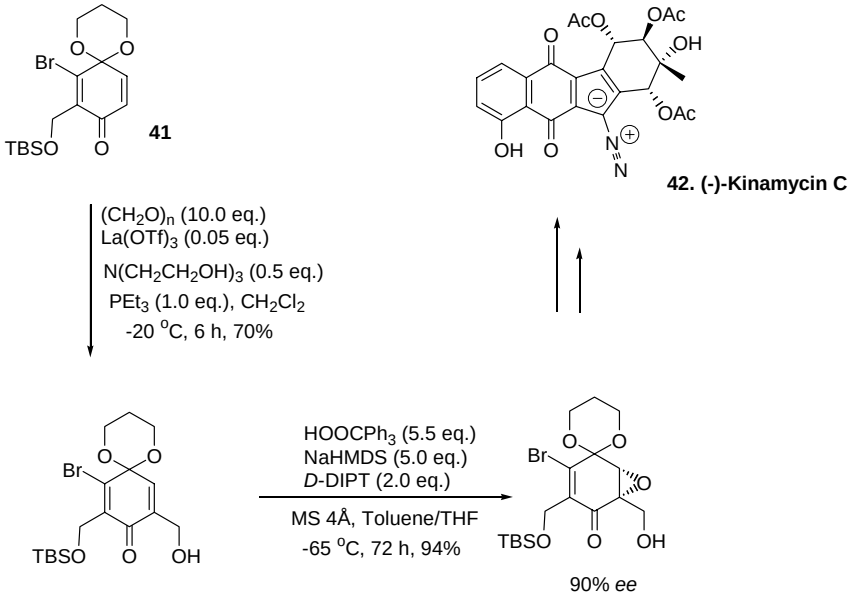
Jogireddy and Maier[157] have developed a novel route for total synthesis of luminacin D (**40a**) and its 6′,8′-epimer (**40b**) using Baylis-Hillman alcohol methyl 3-hydroxy-2-methylenepentanoate as the key starting material according to the reaction sequence as shown in Scheme 36.

Scheme 36



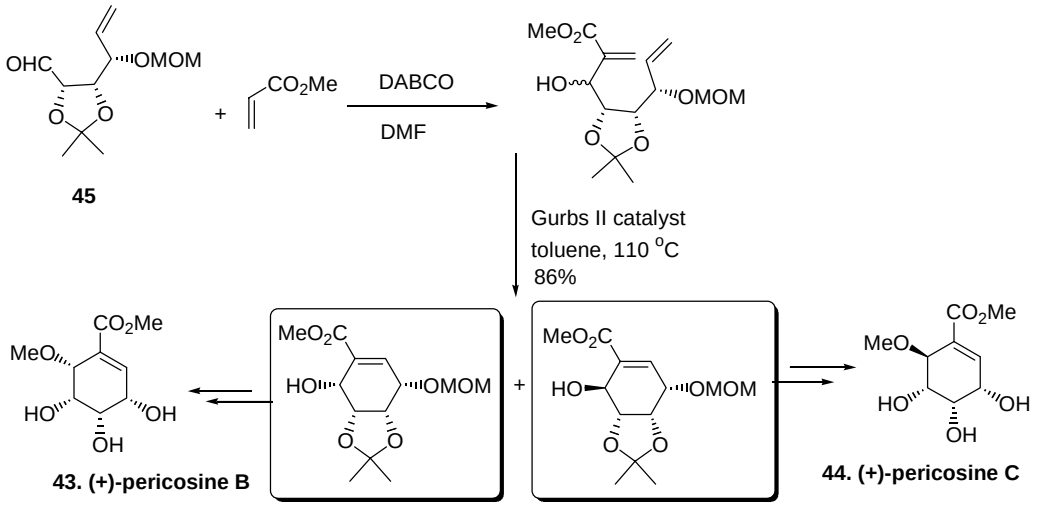
Lei and Porco Jr.[158] have developed a facile methodology for synthesis of antibiotic (-)-kinamycin C (**42**), starting from the Baylis-Hillman adduct derived from the substituted quinine monoketal (**41**) and formaldehyde, according to the reaction sequence as shown in Scheme 37.

Scheme 37



Vankar and co-worker[159] have developed a simple and divergent route for the synthesis of (+)-pericosine B (**43**) and (+)-pericosine C (**44**) using Baylis-Hillman adduct obtained via the reaction of **45** with methyl acrylate followed by ring-closing metathesis according to the reaction strategy as shown in Scheme 38.

Scheme 38



OBJECTIVES, RESULTS AND DISCUSSION

From the preceding section it is quite evident that the Baylis-Hillman reaction is very useful carbon-carbon bond forming reaction providing diverse classes of densely functionalized molecules which have been extensively and systematically employed in a variety of organic transformation methodologies as well as in the synthesis of natural products and bioactive compounds. Our research group has been working on various aspects of the Baylis-Hillman reaction for the last several years with view to develop this reaction into a powerful carbon-carbon bond forming reaction so as to be useful in different aspects of organic chemistry in particular and in organic synthesis, in particular. We have also used these Baylis-Hillman adducts in various organic transformations and also as synthons for obtaining a variety of carbocyclic and heterocyclic frameworks of medicinal importance. We have undertaken thesis work with the following main objectives.

OBJECTIVES

1) To utilize the Baylis-Hillman bromides as a source of 1,3-dipoles with a view to understand the reactivity profile of three stericlly different allyl bromides (**46-48**) [derived from i) Baylis-Hillman alcohol, obtained from HCHO and methyl acrylate ii) Baylis-Hillman alcohols, obtained from aryl aldehydes and methyl acrylate iii)

Baylis-Hillman alcohols, obtained from aromatic aldehydes and acrylonitrile] in dipolar addition reactions with isatin derivatives.

2) To utilize the dipoles generated from Baylis-Hillman bromides **47**, **48** (obtained from the Baylis-Hillman alcohols of aromatic aldehydes and methyl acrylate or acrylonitrile) for cyclo-addition reactions with ethyl glyoxalate and diethyl ketomalonate with a view to understand their reactivity profile.

3) To utilize *t*-Boc derivatives **77** of Baylis-Hillman alchols derived from cyclohexenones and isatin derivatives for synthesis of nitrone-spirooxindole-frameworks **79** in a one pot operation.

RESULTS AND DISCUSSION

The Baylis-Hillman Bromides as a Source of 1,3-Dipoles : Steric Factors Directed Synthesis of Oxindole Fused Spiro Oxirane and Dihydrofuran Frameworks

Spiro-oxindole moiety is one of the important structural frameworks frequently found in many natural products[160-168] (Fig. 8). Therefore development of simple synthetic strategies for obtaining spiro-oxindole derivatives has been and continues to be an attractive area in synthetic and medicinal chemistry.[169-179]

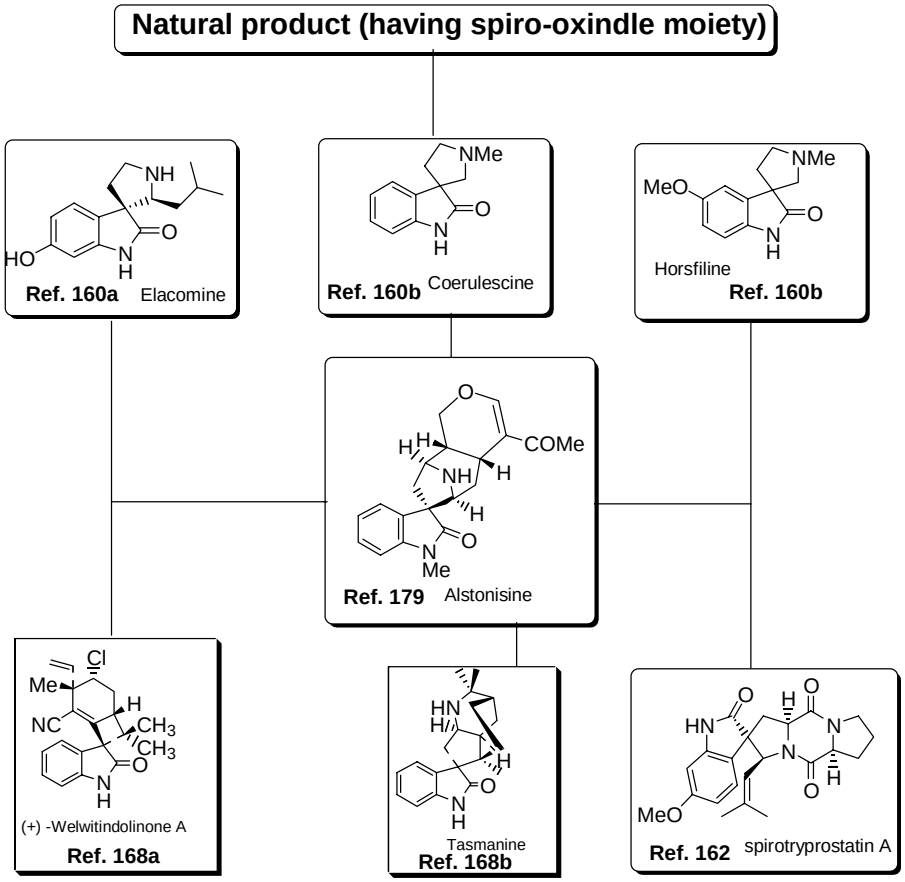
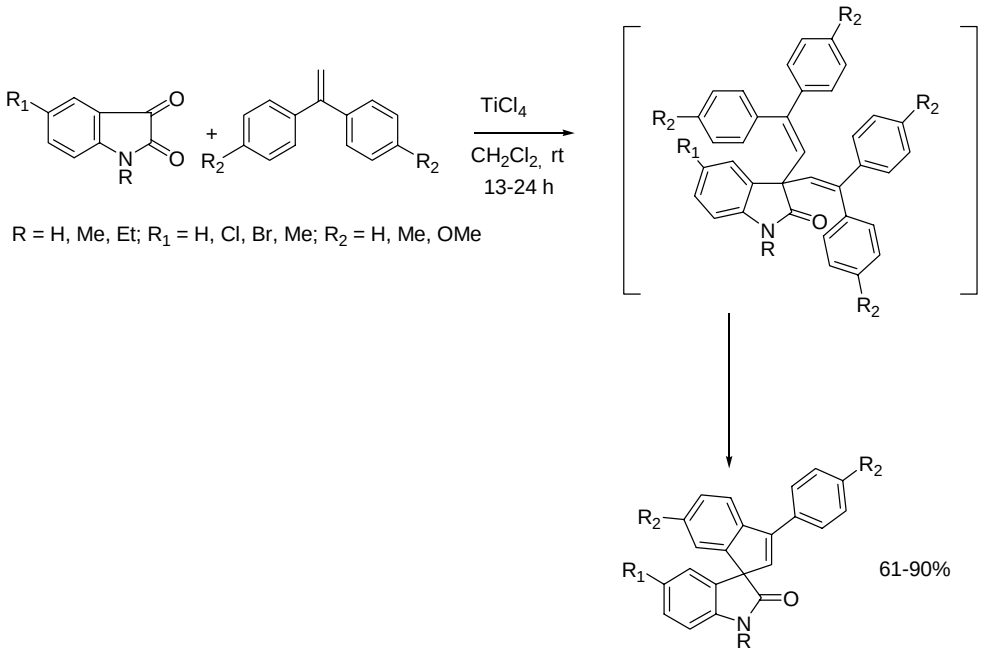


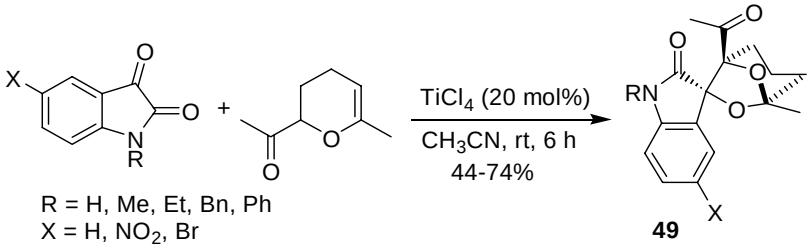
Figure 8: Natural products

Accordingaly, several synthetic methedologies have been developed by various research groups for obtaining spiro-oxindoles. Our research group[175] has reported a simple and one-pot protocol for the synthesis of indene-spiro-oxindole derivatives *via* $TiCl_4$-mediated reaction between 1,1-diarylethylenes and isatin derivatives involving construction of two carbon-carbon bonds through tandem Prins and intramolecular Friedel-Crafts (PFC) reactions (Scheme 39).

Scheme 39



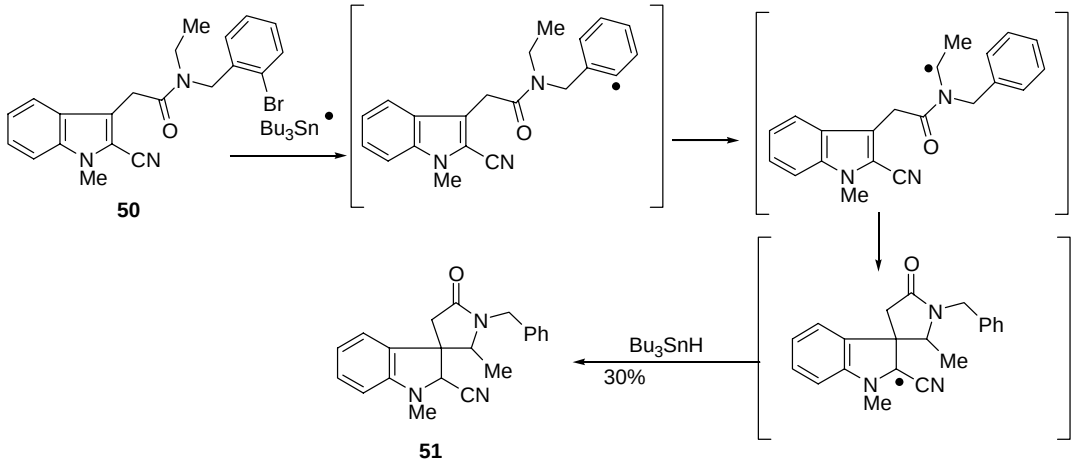
We have also developed simple, atom economical, convenient, one-pot stereoselective methodology[178] for synthesis of spiro-oxindoles [{1-acetyl-5-methyl-6,8-dioxabic-yclo(3.2.1)octane}-7-spiro-3′-(indolin-2′-one) framework] (**49**) *via* the $TiCl_4$ induced reaction between isatin derivatives and 2-acetyl-6-methyl-2,3-dihydro-4*H*-pyran as described in Eq. 14



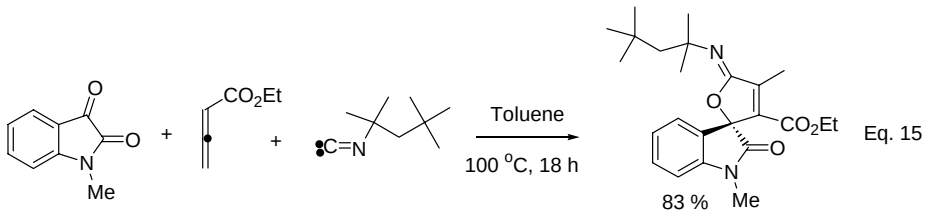
Eq. 14

Jones and co-workers[179] reported an interesting methodology for synthesis of spiro-oxindole derivatives (**51**), *via* tributylstannane mediated radical cyclization of amide (**50**) following the reaction sequence as described in the Scheme 40.

Scheme 40

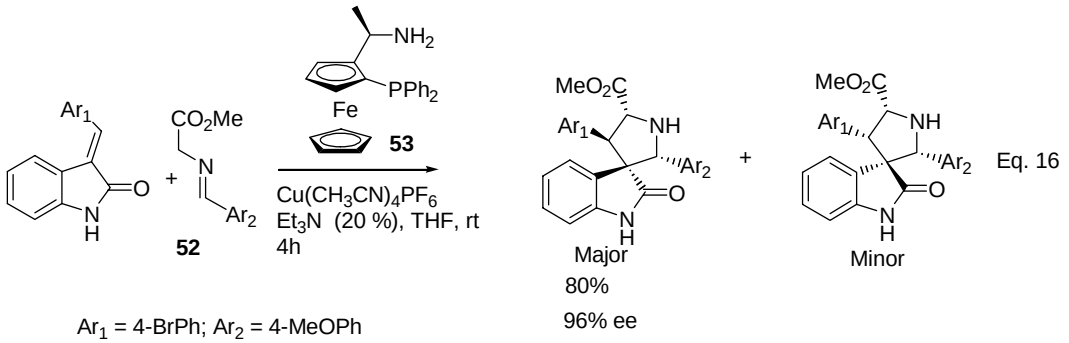


Li and co-workers[172] have described a novel three-component [2+2+1] cycloaddition reaction for obtaining functionalized spirocyclic oxindole-butenolides from simple and readily available starting materials, 1,1,3,3-tetramethylbutyl isocyanide, ethyl 2,3-butadienoate, and 1-methylisatin in an efficient and atom economical manner following the reaction sequence as shown in Eq. 15. One example is shown.



Eq. 15

Waldmann and co-workers[173] reported a highly enantioselective synthesis of spiro-oxindoles *via* chiral phosphine (**53**) catalyzed 1,3-dipolar cycloaddition reaction between 3-methylene-2-oxindoles and azomethine ylides (generated from imine) (**52**) following the reaction sequence as shown in Eq. 16.

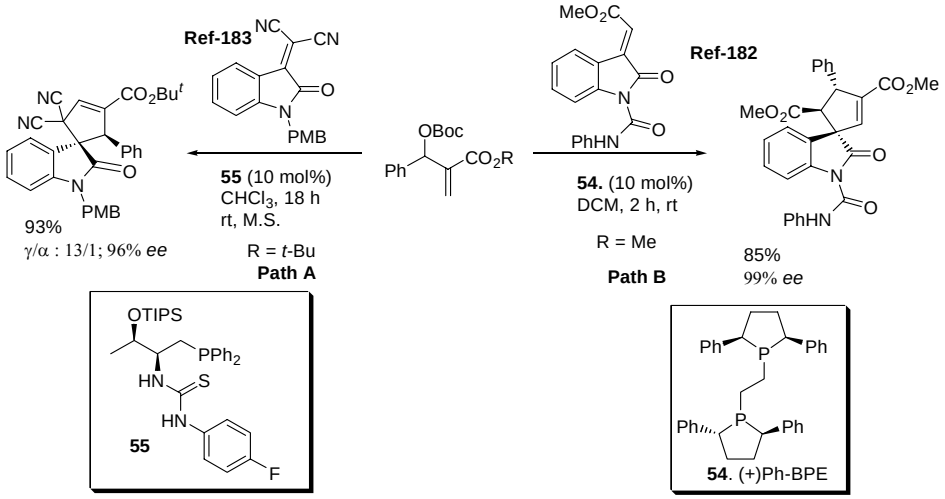


The Baylis-Hillman adducts and their derivatives have also been successfully employed in [3+2] cyclo-addition reactions as dipolarophiles (with benzonitrile oxide[103] and azomethine ylides[180,181] *etc*. as dipoles) and also a source for generating dipoles (with methyleneindolinones[182] isatylidene malononitriles,[183] *N*-phenylmaleimide,[184,185] enones,[149] DEAD/DIAD,[134] propargyl sulfones[186] *etc*. as dipolarophiles) producing a variety of heterocylic and carbocylic compounds of medicinal importance.

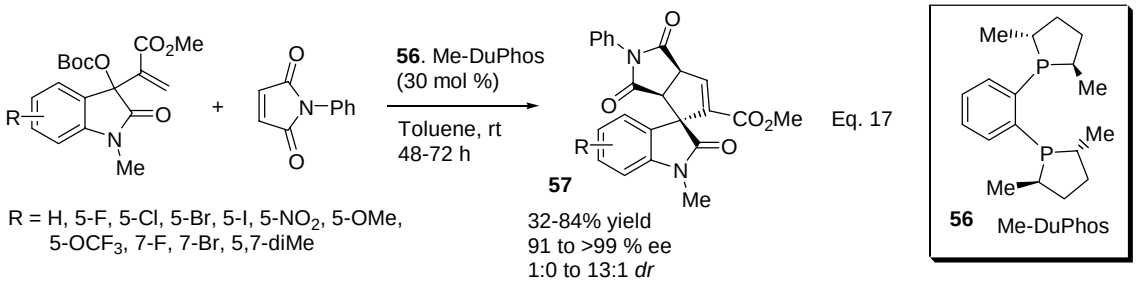
Barbas III and co-workers[182] have reported chiral phosphine **54** catalyzed [3+2] cycloaddition reaction of Baylis-Hillman carbonates with methyleneindolinones to provide spirocyclopenteneoxindoles in high enantioselectivities (Path A, Scheme 41). A similar cycloaddition reaction was reported by Lu and co-workers[183] using *L*-threonine

derived phophine (**55**) as catalyst as shown in Path B, Scheme 41 (One example each is presented).

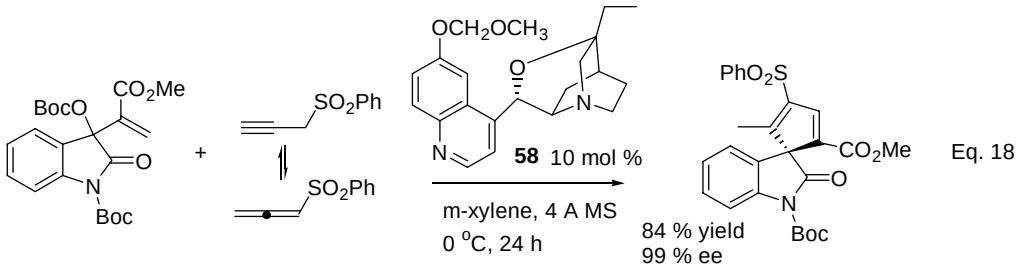
Scheme 41



An interesting and highly enantioselective and diastereoselective synthesis of spiro-oxindole frameworks (**57**) was reported by Liu and co-workers[184] *via* the 1,3-dipolar cycloaddition reaction between the carbonates of Baylis-Hillman adducts (derived from isatins and methyl acrylate) and maleimide derivatives using the chiral catalyst (**56**), according to the reaction sequence as shown in Eq. 17.



Chen *et al* [186] have developed the highly chemo and enantioselective synthesis of spiro-oxindole *via* [3 + 2] annulations of carbonates of Baylis-Hillman alcohols derived from isatins with propargyl sulfones using *β*-ICD O-MOM ether (**58**) as catalysis according to the reaction sequences shown in Eq. 18. The reaction is believed to proceed *via* formal dipolar cycloaddition of *in situ* generated allylic *N*-ylide with allenyl sulfone followed by a C=C bond isomerization.

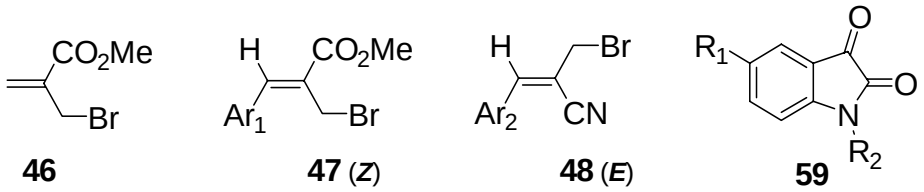


Eq. 18

Our objectives

It has been well documented in the literature that Baylis-Hillman adducts (or their derivatives) containing ester group (prepared from alkyl acrylates) and nitrile group (prepared from acrylonitrile) showed remarkable opposite stereochemical directions in various chemical transformations.[187-197] These stereochemical reversals have been mostly attributed to the steric differences between nitrile (smaller group) and ester functionality (larger group). To the best of our knowledge, there is no systematic study in understanding the stereochemical directions in cycloaddition reactions of the Baylis-Hillman adducts (or their derivatives) containing ester group and nitrile group. Therefore, it occurred to us that

the dipoles generated from Baylis-Hillman bromides containing ester and nitrile groups, should in principle show different reactivities in cycloaddition reactions with isatin derivatives. We have selected three strically different Baylis-Hillman bromides **46, 47, 48** and various isatin derivatives (**59**) (Fig. 9) as reaction partners for our study.

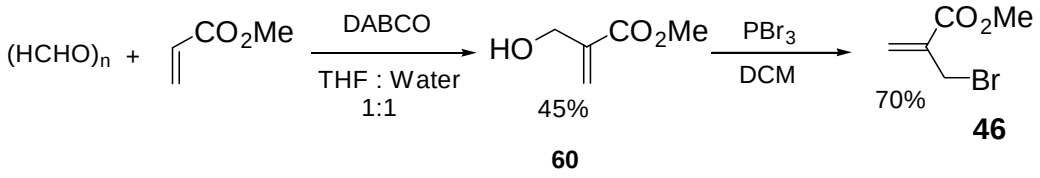


46 **47** (***Z***) **48** (***E***) **59**

Figure 9: Starting materials for cycloaddition reaction

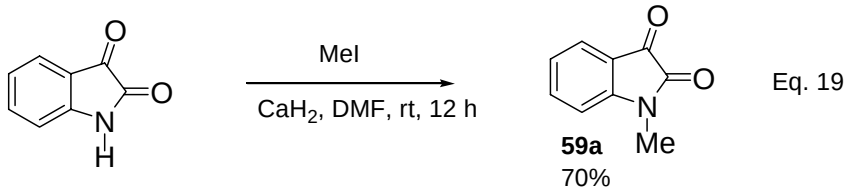
At first we have selected the simple allyl bromide **46** for an study. The required allyl bromide was obtained *via* the reaction of Baylis-Hillman alcohol **60** with PBr_3. The Baylis-Hillman alcohol **60** was obtained following the known literature procedure *i.e. via* the coupling between HCHO and methyl acrylate under the influence of DABCO following the reaction sequence as shown in Scheme 42. Structures of allyl alcohol (**60**) and allyl bromide **46** were established by Spectral data (IR, ^{1}H, ^{13} C NMR).

Scheme 42



60 **46**

We have initally selected *N*-methylisatin **59a** as a dipolarophile for an study. This was prepared *via* the alkylation of commercially avilable isatin with methyl iodide in persence of CaH_2 according to the known procedure[198] (Eq. 19). Structure of *N*-methylisatin was confirmed by spectral data (IR, ^1H, ^{13}C NMR).

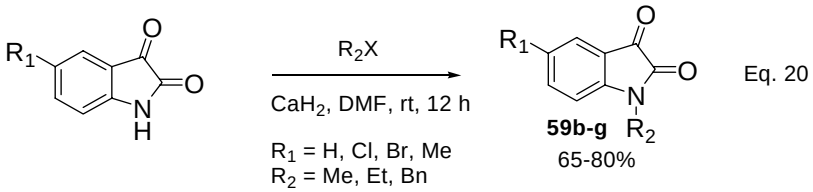


Eq. 19

We have then performed the cyclo-addition reaction between Baylis-Hillman bromide methyl 2-(bromomethyl)prop-2-enoate (**46**) and 1-methylisatin (**59a**). In the initial studies the reaction between **46** and **59a** under the influence of Me_2S in the presence of K_2CO_3 in DMF gave spiro-dihydrofuran-oxindole (**61a**) in 74% isolated yield (Table 1, entry 1).The structure of the product **61a** was confirmed by IR, ^1H & ^{13}C NMR data and HRMS data analysis. Structure of **61a** was further confirmed by single crystal X-ray data analysis. ORTEP digram for **61a** is shown in Fig. 10. For optimization we have performed this reaction under different conditions (Table 1). The best results were obtained when the allyl bromide **46** (3 mmol) was treated with **59a** (2 mmol) in DMF (5 mL) at 15-20 °C in the presence of Cs_2CO_3 (4 mmol) for 8 h thus providing desired spiro-dihydrofuran-oxindole (**61a**) in 83% isolated yield (Table 1, entry 5).

To understand the generality of this methodology we have selected a representative class of *N*-substituted isatins **59b-g**. Required *N*-substitutated isatins **59b-g** were prepared *via*

the alkylation of commercially available isatins with alkyl or aryl halides in presence of CaH_2 according to the known procedure[198] as in the case of *N*-methylisatin according to Eq. 20. Structures of all of the isatin derivatives were established by Spectral data (IR, ^1H, ^{13}C NMR).



We have then subjected these *N*-substituted-isatins **59b-g** to the cycloaddition reaction with Baylis-Hillman bromide **46** as in the case of **61a**. The resulting spiro-dihydrofuran-oxindoles **61b-g** were obtained in 78-86% isolated yields (Table 2). Structures of the dihydrofuranes **61b-g** were confirmed by IR, ^1H & ^{13}C NMR data and HRMS data. A plausible mechanism for the formation of **61a-g** from allyl bromide **46** and *N*-substituted isatins **59a-g** is presented in Scheme 43 taking **61a** as a model case.

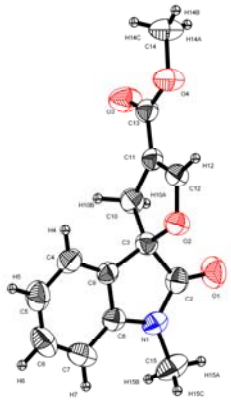
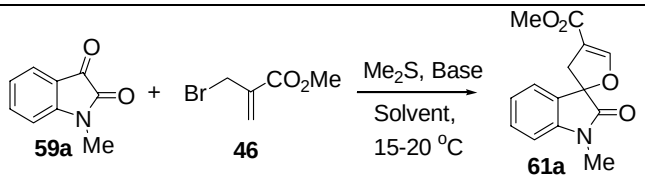


Fig. 10: ORTEP diagram of the compound **61a**

Table 1. *Optimization: Treatment of methyl 2-(bromomethyl)-prop-2-enoate (**46**) (3 mmol) with 1-methylisatin (**59a**) (2 mmol) under the influence of Me_2S (4 mmol) and base (4 mmol) to provide the spirodihydrofuran-oxindole (**61a**)*



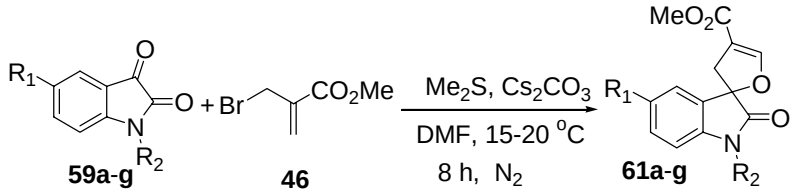
Entry	Base	Solvent (5 mL)	Time [hrs]	Yield (%)
1	K_2CO_3	DMF	48	74
2	K_2CO_3	$CHCl_3$	72	38
3	K_2CO_3	CH_3CN	36	43
4	K_2CO_3	THF	60	38
5	**Cs_2CO_3**	**DMF**	**8**	**83**
6	Cs_2CO_3	THF	24	65
7	Cs_2CO_3	DMF	12	78[a]
8	Cs_2CO_3	CH_3CN	24	71
9	NaOH	DMF	14	76

[a] One equivalent of base was used

Next we have turned our attention to examine the application of Baylis-Hillman bromide, methyl (2*Z*)-2-bromomethyl-3-phenylprop-2-enoate (**47a**) (containing sterically bulky phenyl group trans to the ester group) in the cycloaddition reaction with 1-methylisatin (**59a**) under similar conditions. The desired allyl bromide methyl (2*Z*)-2-bromomethyl-3-phenylprop-2-enoate **(47a)** was obtained from the Baylis-Hillman alcohol methyl 3-hydroxy-2-methylene-3-phenylpropanoate (**62a**) *via* the reaction with HBr in the presence

of H_2SO_4 following the litrature procedure. The Baylis-Hillman alchol was obtained *via* the coupling of benzaldehyde with methyl acrylate under the influence of DABCO (Scheme 44) Structures of allyl bromide **47a** & Baylis-Hillman alcohol **62a** were confirmed by spectral data (IR, ^1H, ^{13}C NMR).

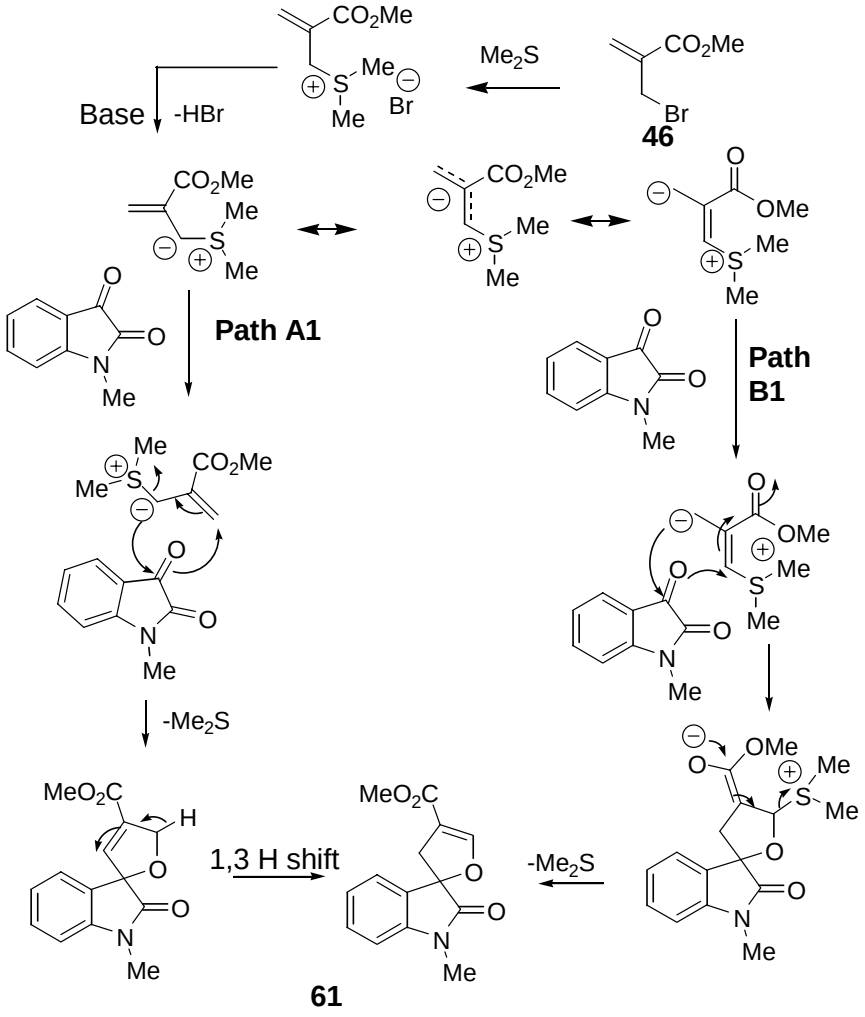
Table 2. Synthesis of spirodihydrofuran - oxindoles ***61a-g*** *[a]*



Entry	R_1	R_2	Isatin	Product[b]	Yield (%)[c]	M.P.(°C)
1	H	Me	**59a**	**61a**[d]	83	124-126
2	H	Et	**59b**	**61b**	78	102-104
3	Cl	Me	**59c**	**61c**	78	113-115
4	Cl	Et	**59d**	**61d**	82	102-104
5	Br	Me	**59e**	**61e**	86	120-122
6	Br	Et	**59f**	**61f**	81	126-128
7	Me	Bz	**59g**	**61g**	80	116-118

[a] All reactions were carried out on a 3 mmol scale of Baylis-Hillman bromide (**46**) with 2 mmol of isatins (**59a-g**) in the presence of Me_2S (4 mmol) and Cs_2CO_3 (4 mmol) in DMF (5 mL) at 15-20 °C. [b] All the compounds were obtained as solids and fully characterized by IR, ^1H, ^{13}C NMR and HRMS data analysis. [c] Isolated yields were based on the isatins. [d] Structure of this compound was further confirmed by single crystal X-ray data analysis.

Scheme 43. *Plasuable Mechanism for the formation of spiro-dihydrofuran-oxindole (**61**)*



Scheme 44

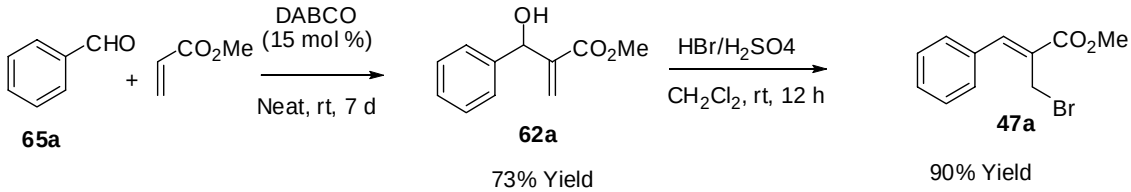
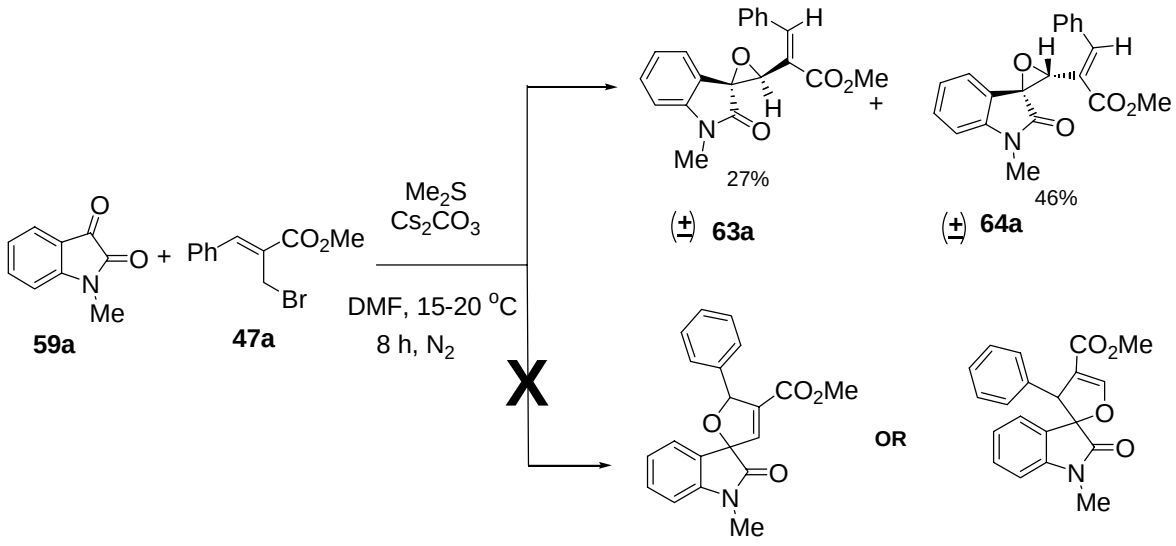


Table 3. *Crystal data and structure refinement for* **61a.**

Identification code	: **61a**	
Empirical formula	: $C_{14}\ H_{13}\ N\ O_4$	
Formula weight	: 259.25	
Temperature	: 298(2) K	
Wavelength	: 0.71073 Å	
Crystal system	: Monoclinic	
Space group	: P 21/c	
Unit cell dimensions	: a = 14.048(2) Å	α= 90°.
	: b = 8.8043(14) Å	β= 97.373(15)°.
	: c = 10.5431(17) Å	γ = 90°.
Volume	: 1293.2(3) $Å^3$	
Z	: 4	
Density (calculated)	: 1.332 Mg/m^3	
Absorption coefficient	: 0.099 mm^{-1}	
F(000)	: 544	
Crystal size	: 0.48 x 0.36 x 0.24 mm^3	
Theta range for data collection	: 2.92 to 26.39°.	
Index ranges	: -15<=h<=17, -10<=k<=6, -13<=l<=13	
Reflections collected	: 4888	
Independent reflections	: 2624 [R(int) = 0.0201]	
Completeness to theta = 26.39°	: 99.2 %	
Absorption correction	: Semi-empirical from equivalents	
Max. and min. transmission	: 0.9767 and 0.9542	
Refinement method	: Full-matrix least-squares on F^2	
Data / restraints / parameters	: 2624 / 0 / 178	
Goodness-of-fit on F^2	: 1.022	
Final R indices [I>2sigma(I)]	: R1 = 0.0442, wR2 = 0.1170	
R indices (all data)	: R1 = 0.0751, wR2 = 0.1265	
Largest diff. peak and hole	: 0.191 and -0.156 $e.Å^{-3}$	

We have then performed the reaction between **47a** and *N*-methylisatin **59a** in the presence of SMe_2/K_2CO_3, We did not obtain the expected spiro-dihydrofuran-oxindole, instead spiro-epoxyoxindoles (**63a** & **64a**) (27:46) were obtained (separated by column chromatography) in over all 73% isolated yield (Scheme 45. Table 7, entry 1). Structures of the products **63a** & **64a** were confirmed by IR, ^{1}H & ^{13}C NMR data and HRMS data analysis as well as by single crystal X-ray data analysis. ORTEP digram for **63a** & **64a** are shown in Figs. 11 & 12 repectively. It is interesting to note that the allyl bromide **46** provided spiro-dihydrofuran oxindoles (**61**) while sterically more demanding allyl bromide **47a** gave spiro-epoxyoxindoles (**63a** & **64a**). This reaction clearly indicates the influence of steric factors in directing the reaction path way thus leading to the formation of different products.

Scheme 45



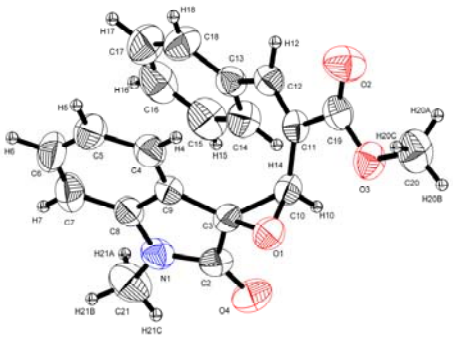


Fig. 11: ORTEP diagram of the compound **63a**

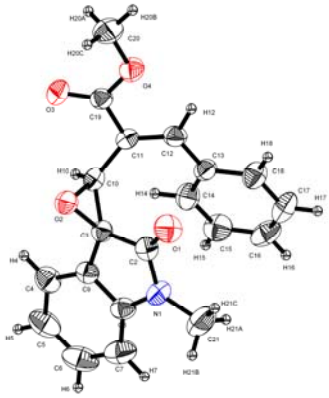


Fig. 12: ORTEP diagram of the compound **64a**

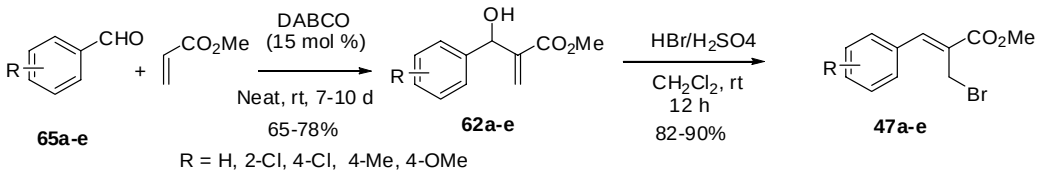
We have then extended this strategy to selected Baylis-Hillman bromides **47b-e** (which were prepared from the Baylis-Hillman alcohols (**62b-f,** Table 5) for cycloaddition reactions with representative isatin derivatives (**59a**, **c**, **e**). The resulting spiro-epoxyoxindoles (**63b-j**& **64a-j**) were obtained as separable mixtures of diastereomers in 65-75% isolated yields (Table 7). Structures of the products **63b-j & 64b-j** were confirmed by IR, ^{1}H & ^{13}C NMR data and HRMS data analysis.

Table 4. *Crystal data and structure refinement for* **63a**

Identification code	: **63a**	
Empirical formula	: $C_{20}\ H_{17}\ N\ O_4$	
Formula weight	: 335.35	
Temperature	: 298(2) K	
Wavelength	: 0.71073 Å	
Crystal system	: Monoclinic	
Space group	: C2/c	
Unit cell dimensions	: a = 21.667(5) Å	α= 90°.
	: b = 9.338(2) Å	β= 95.438(4)°.
	: c = 16.828(4) Å	γ = 90°.
Volume	: 3389.3(14) $Å^3$	
Z	: 8	
Density (calculated)	: 1.314 Mg/m^3	
Absorption coefficient	: 0.092 mm^{-1}	
F(000)	: 1408	
Crystal size	: 0.36 x 0.29 x 0.19 mm^3	
Theta range for data collection	: 1.89 to 26.04°.	
Index ranges	: -26<=h<=26, -11<=k<=11, -20<=l<=20	
Reflections collected	: 16063	
Independent reflections	: 3296 [R(int) = 0.0311]	
Completeness to theta = 26.04°	: 98.1 %	
Absorption correction	: Semi-empirical from equivalents	
Max. and min. transmission	: 0.9827 and 0.9676	
Refinement method	: Full-matrix least-squares on F^2	
Data / restraints / parameters	: 3296 / 0 / 233	
Goodness-of-fit on F^2	: 1.065	
Final R indices [I>2sigma(I)]	: R1 = 0.0425, wR2 = 0.1189	
R indices (all data)	: R1 = 0.0533, wR2 = 0.1276	
Extinction coefficient	: 0.0036(5)	
Largest diff. peak and hole	: 0.182 and -0.161 $e.Å^{-3}$	

The structures of **63h** & **64h** were further confiremed by single crystal X-ray data analysis. ORTEP digram for **63h & 64h** are shown in Figs. 13 & 14 repectively. Structures of allyl bromide **47b-e** and B.H. alcohols (**62a-e**) were confirmed by confirmed by IR, ^{1}H & ^{13}C NMR data).

Table 5 : *Syntheis of Baylis-Hillman alcohols* ***62a-e*** *and bromides* ***47a-e***[199-200]



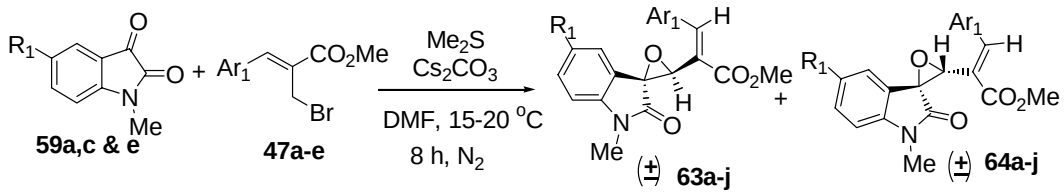
Entry	Aldehyde	R	B.H. Alcohol[a]	EWG	Yield[b,c] (%)	B.H. Bromide	Yield (%)[d,e,f]
1	**65a**	H	**62a**	CO_2Me	73	**47a**	90
2	**65b**	2-Cl	**62b**	CO_2Me	78	**47b**	86
3	**65c**	4-Cl	**62c**	CO_2Me	78	**47c**	86
4	**65d**	4-Me	**62d**	CO_2Me	76	**47d**	82
5	**65g**	4-OMe	**62e**	CO_2Me	65	**47e**	83

[a]. All reactions were carried out on 100 mmol scale of various aldehydes with methyl acrylate (150 mmol), under the influence of DABCO (15 mmol) at rt. [b].All compounds were well characterized by IR, ^{1}H NMR, ^{13}C NMR spectral data. [c]. Yields are based on aldehydes. [d]. All reactions were carried out on 50 mmol scale of Baylis-Hillman alcohols and HBr (100 mmol)/H_2SO_4 (50 mmol) in DCM. [e] All compounds were well characterized by IR, ^{1}H NMR, ^{13}C NMR spectral data. [f]. Yields are based on Baylis-Hillman alcohols.

Table 6. *Crystal data and structure refinement for* **64a.**

Identification code	: **64a**	
Empirical formula	: C_{20} H_{17} N O_4	
Formula weight	: 335.35	
Temperature	: 298(2) K	
Wavelength	: 0.71073 Å	
Crystal system	: Monoclinic	
Space group	: P2(1)/c	
Unit cell dimensions	: a = 8.5133(10) Å	α= 90°.
	: b = 16.889(2) Å	β= 104.600(2)°.
	: c = 11.8434(14) Å	γ = 90°.
Volume	: 1647.9(3) $Å^3$	
Z	: 4	
Density (calculated)	: 1.352 Mg/m^3	
Absorption coefficient	: 0.095 mm^{-1}	
F(000)	: 704	
Crystal size	: 0.28 x 0.20 x 0.14 mm^3	
Theta range for data collection	: 2.15 to 25.35°.	
Index ranges	: -10<=h<=10, -20<=k<=20, -14<=l<=14	
Reflections collected	: 16044	
Independent reflections	: 3013 [R(int) = 0.0640]	
Completeness to theta = 25.35°	: 99.9 %	
Absorption correction	: Semi-empirical from equivalents	
Max. and min. transmission	: 0.9869 and 0.9740	
Refinement method	: Full-matrix least-squares on F^2	
Data / restraints / parameters	: 3013 / 0 / 232	
Goodness-of-fit on F^2	: 1.178	
Final R indices [I>2sigma(I)]	: R1 = 0.0784, wR2 = 0.1473	
R indices (all data)	: R1 = 0.1015, wR2 = 0.1571	
Largest diff. peak and hole	: 0.255 and -0.179 $e.Å^{-3}$	

Table-7. *Synthesis of spiro-epoxy-oxindoles* **(63a-j & 64a-j)** [*a,b, c*]



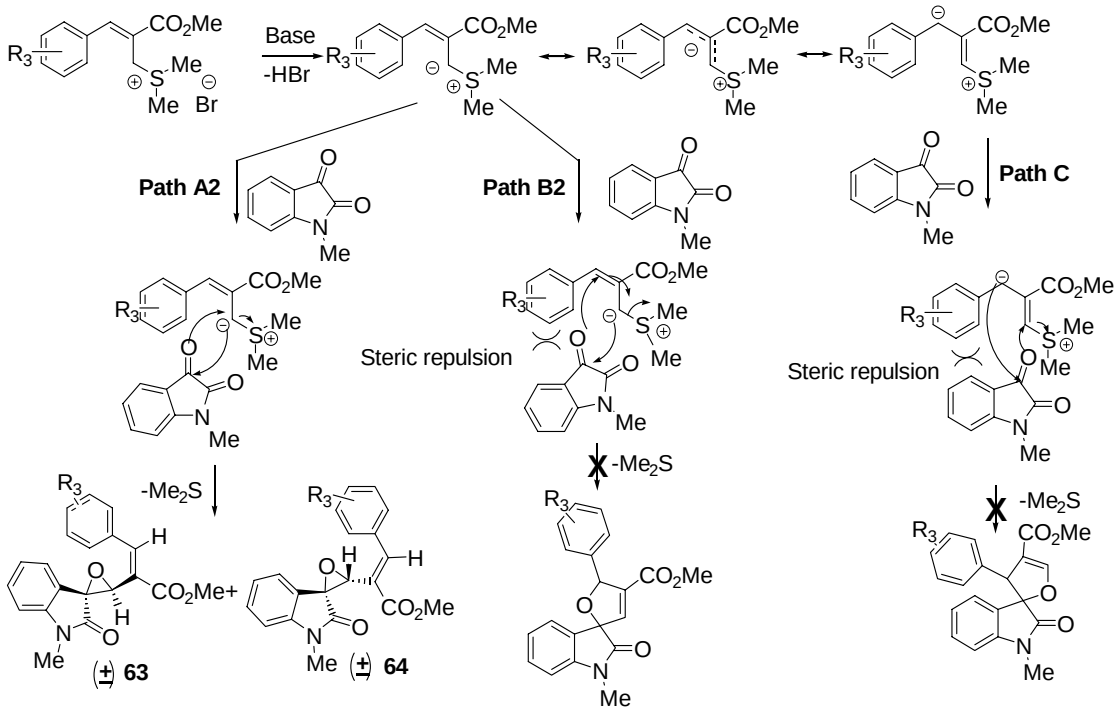
Entry	Isatin	R_1	B.H. Br	Ar_1	Product **63**	Yield (%)	M.P (^oC)	Product **64**	Yield (%)	M.P (^oC)
1	**59a**	H	**47a**	C_6H_5	**63a**[d]	27	136-138	**64a**[d]	46	160-162
2	**59e**	Br	**47a**	C_6H_5	**63b**	30	161-163	**64b**	43	132-134
3	**59a**	H	**47b**	4-ClC_6H_4	**63c**	19	111-113	**64c**	52	117-119
4	**59a**	H	**47c**	4-MeC_6H_4	**63d**	30	152-154	**64d**	43	136-138
5	**59c**	Cl	**47c**	4-MeC_6H_4	**63e**	25	170-172	**64e**	42	168-170
6	**59a**	H	**47d**	2-ClC_6H_4	**63f**	25	156-158	**64f**	50	164-166
7	**59e**	Br	**47d**	2-ClC_6H_4	**63g**	26	191-193	**64g**	42	158-160
8	**59a**	H	**47e**	4-$MeOC_6H_4$	**63h**[d]	41	127-129	**64h**[d]	29	123-125
9	**59c**	Cl	**47e**	4-$MeOC_6H_4$	**63i**	36	117-119	**64i**	31	142-144
10	**59e**	Br	**47e**	4-$MeOC_6H_4$	**63j**[e]	41	--	**64j**	24	142-144

[a] All reactions were carried out on a 3 mmol scale of Baylis-Hillman bromides (**47a-e**) with 2 mmol of isatins (**59**a,**c**,**e**) in the presence of Me_2S (4 mmol) and Cs_2CO_3 (4 mmol) in DMF (5 mL) at 15-20 ^oC. [b]

Pure diastereomers **63** and **64** were separated and obtained as solids and fully characterized by IR, ^{1}H, ^{13}C NMR and HRMS data analysis. [c] Isolated yields were based on the isatins. [d] Structures of these compounds were further confirmed by single crystal X-ray data analysis. [e] This was obtained as viscous liquid.

A plausible mechanism for the formation of spiro-epoxy-oxindoles derivatives (**63** & **64**) from the Baylis-Hillman bromides **47** and isatin derivatives **59** is presented in Scheme 46.

Scheme 46. Plasuable Mechanism for the formation of spiro-epoxyoxindoles **(63 & 64)**



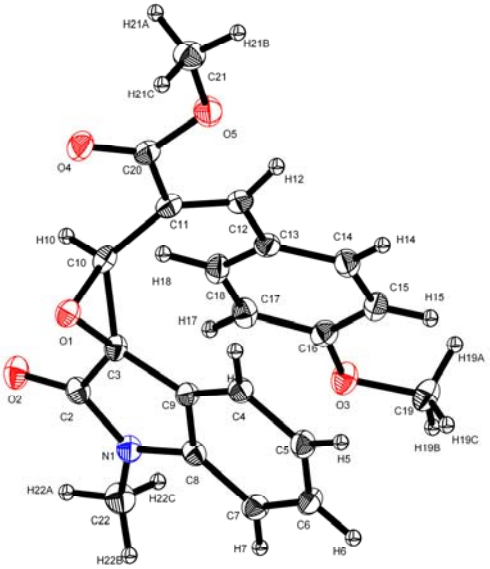


Fig.13 ORTEP diagram of the compound **63h**

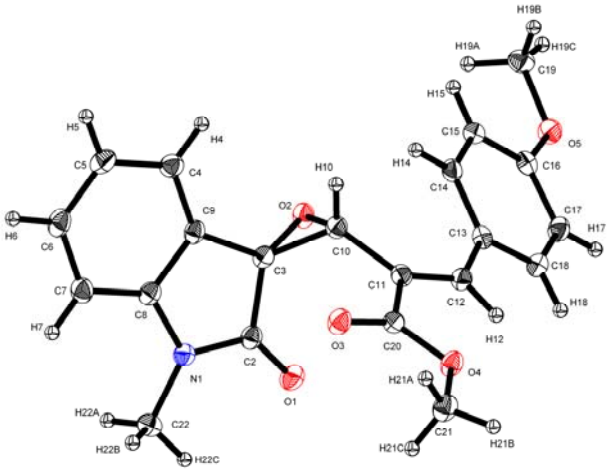


Fig. 14 ORTEP diagram of the compound **64h**

Table 8. *Crystal data and structure refinement for* **63h.**

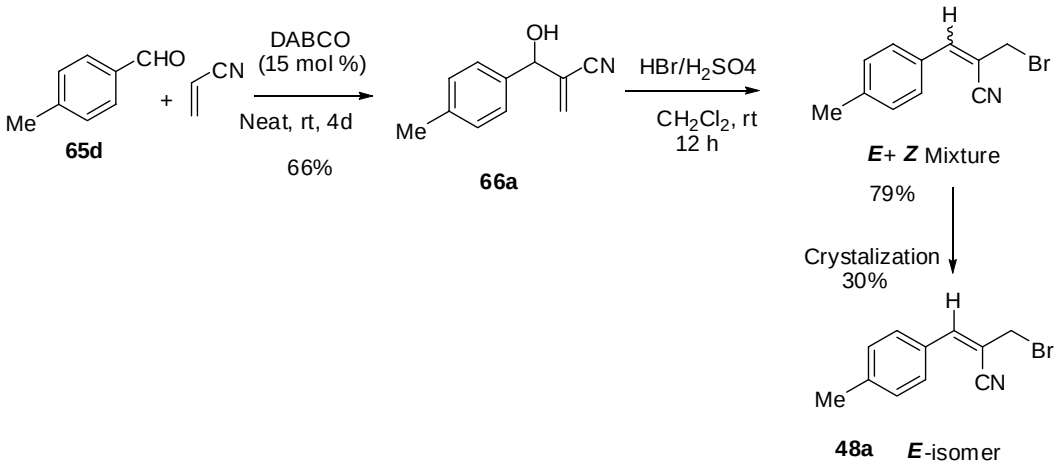
Identification code	: **63h**	
Empirical formula	: C_{21} H_{19} N O_5	
Formula weight	: 365.38	
Temperature	: 100(2) K	
Wavelength	: 0.71073 Å	
Crystal system	: Monoclinic	
Space group	: P2(1)/n	
Unit cell dimensions	: a = 8.6930(8) Å	α= 90°.
	: b = 16.1202(14) Å	β= 102.8320(10)°.
	: c = 13.0192(11) Å	γ = 90°.
Volume	: 1778.9(3) $Å^3$	
Z	: 4	
Density (calculated)	: 1.364 Mg/m^3	
Absorption coefficient	: 0.098 mm^{-1}	
F(000)	: 768	
Crystal size	: 0.28 x 0.22 x 0.10 mm^3	
Theta range for data collection	: 2.04 to 26.05°.	
Index ranges	: -10<=h<=10, -19<=k<=19, -16<=l<=16	
Reflections collected	: 17922	
Independent reflections	: 3496 [R(int) = 0.0276]	
Completeness to theta = 26.05°	: 99.4 %	
Absorption correction	: Empirical	
Max. and min. transmission	: 0.9903 and 0.9731	
Refinement method	: Full-matrix least-squares on F^2	
Data / restraints / parameters	: 3496 / 0 / 252	
Goodness-of-fit on F^2	: 1.060	
Final R indices [I>2sigma(I)]	: R1 = 0.0366, wR2 = 0.0916	
R indices (all data)	: R1 = 0.0392, wR2 = 0.0936	
Extinction coefficient	: 0.0070(10)	
Largest diff. peak and hole	: 0.294 and -0.208 $e.Å^{-3}$	

Table 9. *Crystal data and structure refinement for* **64h.**

Identification code	: **64h**	
Empirical formula	: C_{21} H_{19} N O_5	
Formula weight	: 365.38	
Temperature	: 100(2) K	
Wavelength	: 0.71073 Å	
Crystal system	: Monoclinic	
Space group	: P2(1)/c	
Unit cell dimensions	: a = 14.4870(9) Å	α= 90°.
	: b = 6.8565(4) Å	β= 99.9040(10)°.
	: c = 17.8691(11) Å	γ = 90°.
Volume	: 1748.49(18) $Å^3$	
Z	: 4	
Density (calculated)	: 1.388 Mg/m^3	
Absorption coefficient	: 0.100 mm^{-1}	
F(000)	: 768	
Crystal size	: 0.28 x 0.24 x 0.10 mm^3	
Theta range for data collection	: 1.43 to 26.02°.	
Index ranges	: -17<=h<=17, -8<=k<=8, -22<=l<=22	
Reflections collected	: 17367	
Independent reflections	: 3449 [R(int) = 0.0252]	
Completeness to theta = 26.02°	: 99.9 %	
Absorption correction	: Empirical	
Max. and min. transmission	: 0.9901 and 0.9726	
Refinement method	: Full-matrix least-squares on F^2	
Data / restraints / parameters	: 3449 / 0 / 251	
Goodness-of-fit on F^2	: 1.064	
Final R indices [I>2sigma(I)]	: R1 = 0.0381, wR2 = 0.0972	
R indices (all data)	: R1 = 0.0396, wR2 = 0.0986	
Largest diff. peak and hole	: 0.283 and -0.297 e.$Å^{-3}$	

The significant reactivity differences between the allyl bromides **46** & **47** in these reactions have lead us to investigate the reaction of (2*E*)-2-bromomethyl-3-(4-methylphenyl)-prop-2-enenitrile (**48a**)[201] with 5-chloro-1-methylisatin (**59c**) under similar conditions. The required allyl bromides, (2*E*)-2-bromomethyl-3-(4-methylphenyl)-prop-2-enenitrile (**48a)** was prepared from the Baylis-Hillman alcohol (**66a**) similarly as allyl bromide **47a** (Scheme 47). These Baylis-Hillman bromides **48a** were obtained as a mixture of *E/Z*-isomer. However we could obtain the pure **48a** *E*-allyl bromide by careful crystallization.

Scheme 47

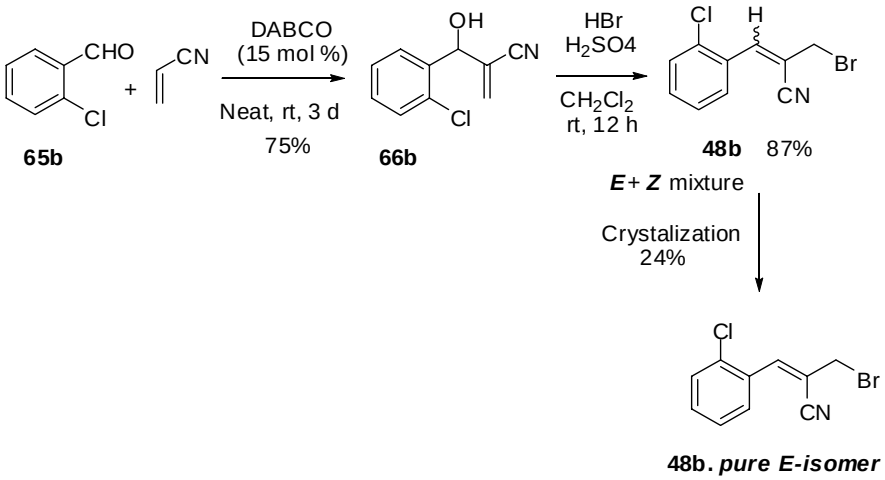


Now we have carried out the reaction of (2*E*)-2-bromomethyl-3-(4-methylphenyl)-prop-2-enenitrile (**48a**) with 5-chloro-1-methylisatin (**59c**) under similar conditions. In this case spiro-epoxyoxindole was not obtained. In stead spirodihydrofuran-oxindole **67a** [3*R*(2′*R*), 5′*R*]/ [3*S*(2′*S*), 5′*S*]-(1-methyl-5-chloroindolin-2-one)-3-spiro-2′-[4′-cyano-5′-(4-methyl-phenyl)-2′, 5′-dihydrofuran] was isolated as a single diastereomer (Table 10, entry 1). We

were pleased to see the high stereoselectivity in this reaction. To understand the applicablity of this strategy we have subjected allyl bromide **48a** to the reaction with isatin derivatives **59d** & **59e** which gave spirodihydrofuran-oxindoles **67b** & **67c** in 73 and 67% yields respectively.

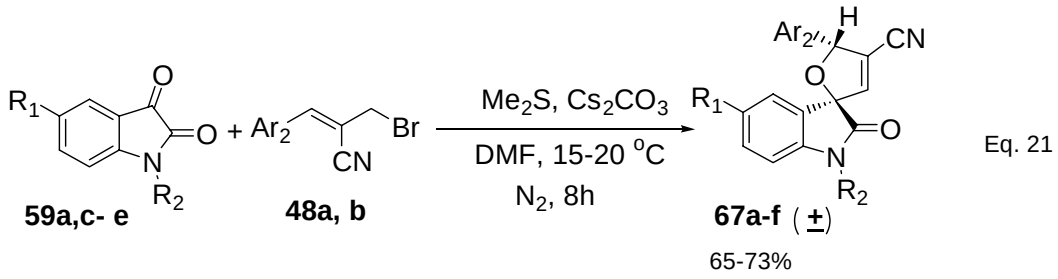
In order to understand the generality of this reaction we have selected another allyl bromide (2*E*)-2-bromomethyl-3-(2-chlorophenyl)-prop-2-enenitrile (**48b)**.[201] This was obtained as *E/Z* mixture from the corresponding Bayis-Hilman alcohol (**66b**) accoding to the similar procedure **47a**. Carefull crystilzation provided the pure (2*E*)-2-bromomethyl-3-(2-chlorophenyl)-prop-2-enenitrile (**48b**) (Scheme 48). Structures of the Baylis-Hillman alcohols **66b** and allyl bromide **48b** were confirmed by IR, ^{1}H & ^{13}C NMR data analysis.

Scheme 48



Similarly reaction of allyl bromide **48b** with isatin derivatives **59a,c, e** provided the desired spiro-dihydrofuran-oxindoles **67d-f** in 65-71% isolated yields (Eq. 21). Structures of the products **67a-f** were confirmed by IR, ^{1}H & ^{13}C NMR data and HRMS data analysis and

the structures of **67d** & **67e** were further confiremed by single crystal X-ray data analysis. ORTEP digram for **67d** & **67e** are shown in Figs. 15 & 16 repectively.

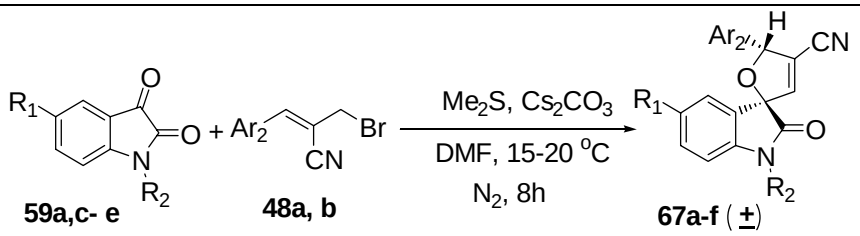


Eq. 21

A possible mechanastic path way for formation spiro-dihydrofuran-oxindoles **67a-f** is described in Scheme 49.

The different reactivities of the allyl bromides **46**, **47** & **48** might be attributed to the steric factors as shown in the machanistic path way (Schemes 43, 46 & 49). Thus, in the case of allyl bromides **47a-e** spirodihydrofuran-oxindoles were not formed. This is probably due to the (*Z*)-stereochemistry of the bromide that might prevent the attack of oxygen anion on the olefinic carbon α-to aryl group (due to steric hinderance) thus leading to the formation of oxirane ring. In the case of allyl bromide **48a**,**b** (*E*)- stereochemistry might facilitate the formation of spirodihydrofuran-oxindole framework with high diastereoselectivity (Scheme 49).

Table 10. *Synthesis of spirodihydrofuran-oxindoles* **67a-f** [a]



59a,c- e **48a, b** **67a-f** (±)

Entry	Isatins	R_1	R_2	B.H. Bromide	Ar_2	Product[b]	Yield[c] (%)	M.P (^oC)
1	**59c**	Cl	Me	**48a**	4-MeC_6H_4	**67a**	66	210-212
2	**59d**	Cl	Et	**48a**	4-MeC_6H_4	**67b**	73	186-188
3	**59e**	Br	Me	**48a**	4-MeC_6H_4	**67c**	67	206-208
4	**59a**	H	Me	**48b**	2-ClC_6H_4	**67d**[d]	69	166-168
5	**59c**	Cl	Me	**48b**	2-ClC_6H_4	**67e**[d]	65	204-206
6	**59e**	Br	Me	**48b**	2-ClC_6H_4	**67f**	71	182-184

[a] All reactions were carried out on a 3 mmol scale of BH bromides (**48a,b**) with 2 mmol of isatins (**59a,c-e**) in the presence of Me_2S (4 mmol) and Cs_2CO_3 (4 mmol) in DMF (5 mL) at 15-20 ^oC.

[b] All the compounds were obtained as solids and fully characterized by IR, ^1H, ^{13}C and HRMS data analysis.

[c] Isolated yields were based on the isatins.

[d] Structures of these compounds were further confirmed by single crystal X-ray data analysis.

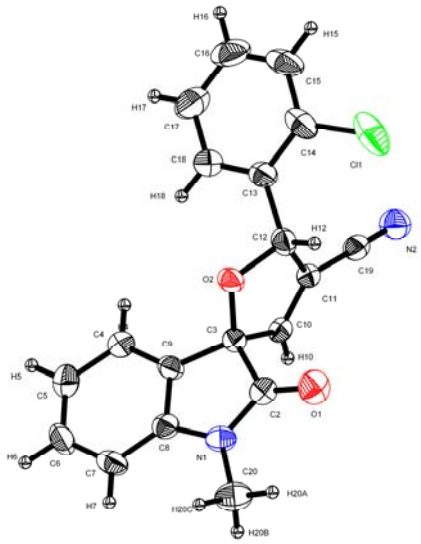


Fig. 15 ORTEP diagram of the compound **67d**

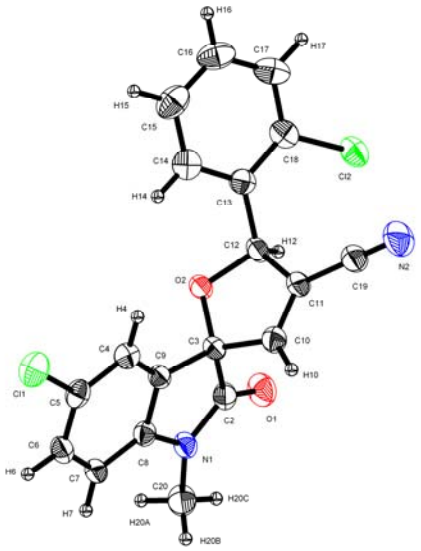


Fig. 16 ORTEP diagram of the compound **67e**

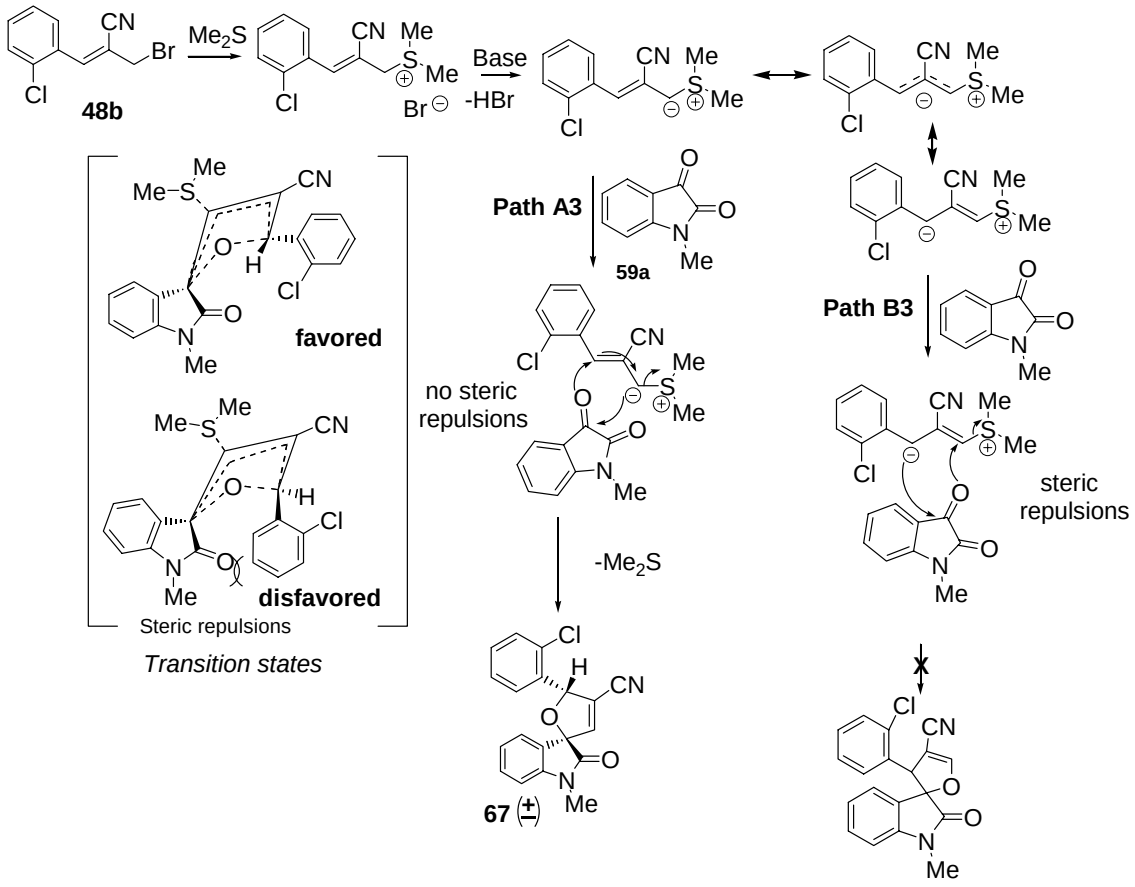
Table 11. *Crystal data and structure refinement for* **67d.**

Identification code	: **67d**	
Empirical formula	: C_{19} H_{13} Cl N_2 O_2	
Formula weight	: 336.76	
Temperature	: 373(2) K	
Wavelength	: 0.71073 Å	
Crystal system	: Orthorhombic	
Space group	: Pna2(1)	
Unit cell dimensions	: a = 24.913(12) Å	α= 90°.
	: b = 5.730(3) Å	β= 90°.
	: c = 11.248(6) Å	γ = 90°.
Volume	: 1605.5(14) $Å^3$	
Z	: 4	
Density (calculated)	: 1.393 Mg/m^3	
Absorption coefficient	: 0.251 mm^{-1}	
F(000)	: 696	
Crystal size	: 0.24 x 0.21 x 0.08 mm^3	
Theta range for data collection	: 1.63 to 26.17°.	
Index ranges	: -30<=h<=30, -7<=k<=7, -13<=l<=13	
Reflections collected	: 14703	
Independent reflections	: 3154 [R(int) = 0.0739]	
Completeness to theta = 26.17°	: 98.9 %	
Absorption correction	: Semi-empirical from equivalents	
Max. and min. transmission	: 0.9802 and 0.9421	
Refinement method	: Full-matrix least-squares on F^2	
Data / restraints / parameters	: 3154 / 1 / 222	
Goodness-of-fit on F^2	: 1.032	
Final R indices [I>2sigma(I)]	: R1 = 0.0608, wR2 = 0.1530	
R indices (all data)	: R1 = 0.0673, wR2 = 0.1576	
Absolute structure parameter	: 0.50(11)	
Largest diff. peak and hole	: 0.316 and -0.228 $e.Å^{-3}$	

Table 12. *Crystal data and structure refinement for* **67e.**

Identification code	: **67e**	
Empirical formula	: C_{19} H_{12} Cl_2 N_2 O_2	
Formula weight	: 371.21	
Temperature	: 100(2) K	
Wavelength	: 0.71073 Å	
Crystal system	: Monoclinic	
Space group	: P2(1)/c	
Unit cell dimensions	: a = 10.964(6) Å	α= 90°.
	: b = 17.387(10) Å	β= 101.439(9)°.
	: c = 9.109(5) Å	γ = 90°.
Volume	: 1702.0(16) $Å^3$	
Z	: 4	
Density (calculated)	: 1.449 Mg/m^3	
Absorption coefficient	: 0.396 mm^{-1}	
F(000)	: 760	
Crystal size	: 0.32 x 0.28 x 0.24 mm^3	
Theta range for data collection	: 1.90 to 24.71°.	
Index ranges	: -12<=h<=12, -20<=k<=20, -10<=l<=10	
Reflections collected	: 11840	
Independent reflections	: 2853 [R(int) = 0.0633]	
Completeness to theta = 24.71°	: 98.4 %	
Absorption correction	: Semi-empirical from equivalents	
Max. and min. transmission	: 0.9109 and 0.8837	
Refinement method	: Full-matrix least-squares on F^2	
Data / restraints / parameters	: 2853 / 0 / 231	
Goodness-of-fit on F^2	: 1.087	
Final R indices [I>2sigma(I)]	: R1 = 0.0623, wR2 = 0.1782	
R indices (all data)	: R1 = 0.0648, wR2 = 0.1813	
Largest diff. peak and hole	: 0.394 and -0.470 $e.Å^{-3}$	

Scheme 49. *Plausible Mechanism for the formation of spiro-dihydrofuran-oxindole* **(67)**



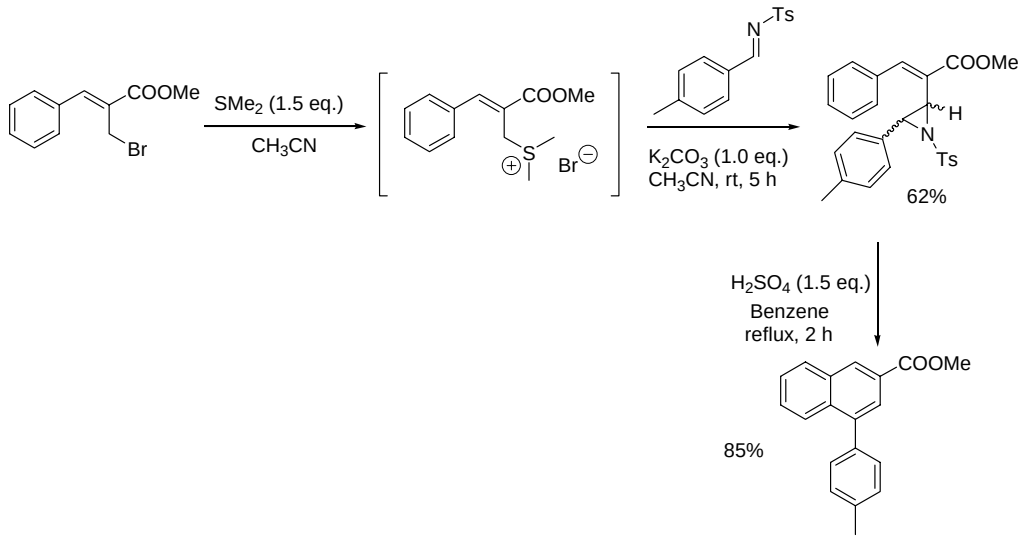
In conclusion, we have demonstrated steric factors directed cyclo-addition reactions between the dipoles generated from Baylis-Hillman bromides **46-48** and isatins **59** as dipolarophiles, thus providing an interesting methodologies for synthesis of spiro-epoxy-oxindoles (**63** & **64**) and spiro-dihydrofuran-oxindoles (**61** & **67**).

The Baylis-Hillman Bromides: Synthesis of Densely Functionalized Epoxides *via* Cyclo-addition strategy

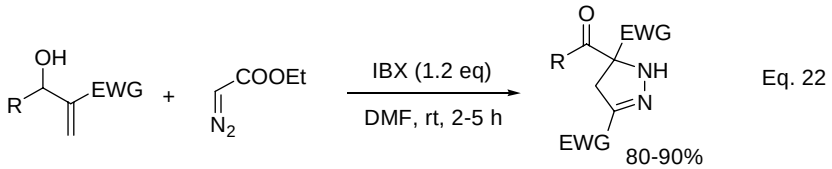
After successfully examined the steric influence in cyclo-addition reaction of the isatin derivatives with sterically different Baylis-Hillman bromides (**46-48**) we undertook to investigate cycloaddition reaction of allyl bromide (**47** & **48**) with reactive carbonyl compounds *i.e.* ethyl glyoxylate and diethyl ketomalonate with a view to understand the reactivity profile of the allyl bromides in these reactions. Literature survey reveals that aldimine derivatives /DEAD/DIAD have been used for cycloaddition reaction with allyl bromide with various research groups.

Kim and co-workers[202] reported an interesting synthesis of arylnaphthalene derivatives *via* the reaction of Baylis-Hillman bromides with *N*-tosylamine in presence of SMe_2 following the reaction sequence as shown in Scheme 50. This reaction is believed to proceed through cycloaddition reaction of Baylis-Hillman bromide with *N*-tosylamine to provide aziridine which on treatment with H_2SO_4 provided naphthalene derivatives (One example is presented).

Scheme 50



Yadav and co-workers[203] have reported a facile synthesis of pyrazolines *via* the 1,3-dipolar cycloaddition reaction of Baylis-Hillman alcohols with ethyl diazoacetate in the presence of 2-iodooxybenzoic acid (IBX) (Eq. 22).

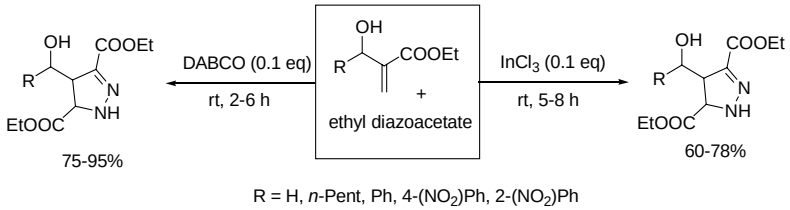


Eq. 22

R = *n*-Pent, prop-1-enyl, *c*-Hex., Ph, 4-ClPh, 3-BrPh, 4-FPh, 4-(OMe)Ph, 2,5-$(OMe)_2$Ph 3-(OPh)Ph, 4-MePh, *trans*-cinnamyl
EWG = COOMe, COOEt

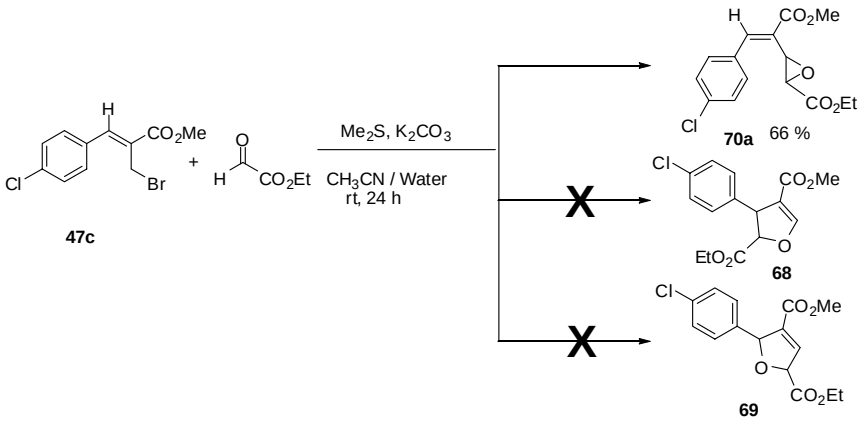
Subsequently Krishna and co-workers[204] have reported an $InCl_3$ or DABCO mediated 1,3-dipolar cycloaddition of Baylis-Hillman alcohols with ethyl diazoacetate to afford 3,5-disubstituted pyrazolines in moderate to good yield, under solvent free conditions (Scheme 51).

Scheme 51



We have first subjected (2*Z*)-2-bromomethyl-3-(4-chlorophenyl)prop-2-enoate (**47c**) for cyclo-addition reaction with ethyl glyoxylate under the influence of Me_2S using K_2CO_3 as a base in CH_3CN/H_2O solvent system. We could not obtain the expected five membered ring *i.e.* Furan derivative (**68** & **69**) instead a three membered product *i.e* epoxide derivative (**70a**) was obtained in 66% yield as white solid (Scheme 52). The structure of this product was confirmed by IR, ^1H, ^{13}C NMR, HRMS and single crystal X-ray data analysis.

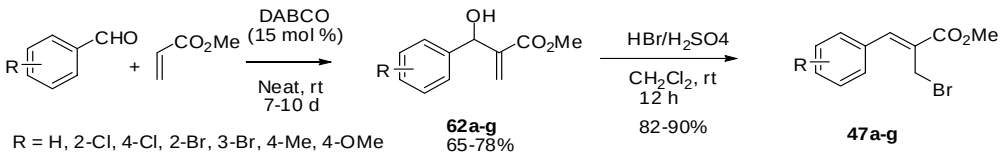
Scheme 52



With view to understand the generality of this reaction we have prepared various Baylis-Hillman alcohols (**62a-g**), from the respective aldehydes (**65a-g**) and methyl acrylate. These alcohols were subsequently converted into their corresponding Baylis-Hillman

bromides **47a-g** (Table 18). Structures of the products **62a-g** & **47a-g** were confirmed by IR, ^{1}H & ^{13}C NMR data analysis.

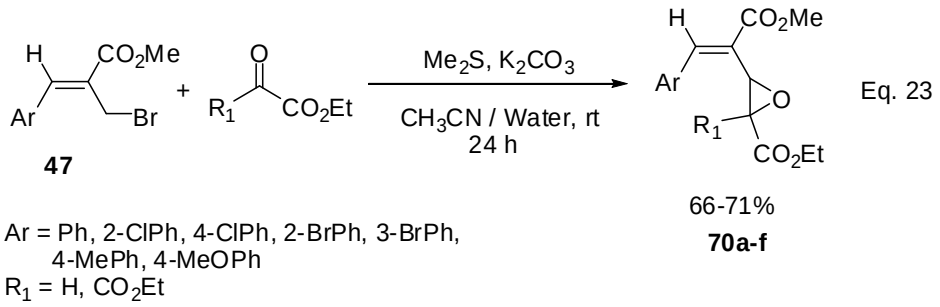
Table 13



Entry	Aldehyde	R	B.H. Alcohol	Yield (%)[a,b,c]	B.H. Bromide	Yield (%)[d,e,f]
1	**65a**	H	**62a**	73	**47a**	90
2	**65b**	2-Cl	**62b**	78	**47b**	86
3	**65c**	4-Cl	**62c**	78	**47c**	86
4	**65d**	4-Me	**62d**	76	**47d**	82
5	**65e**	4-OMe	**62e**	65	**47e**	83
6	**65f**	2-Br	**62f**	78	**47f**	86
7	**65g**	3-Br	**62g**	76	**47g**	86

[a]. All reactions were carried out on 100 mmol scale of various aldehydes with methyl acrylate (150 mmol), under the influence of DABCO (15 mmol) at rt. [b].All compounds were well characterized by IR, ^{1}H, ^{13}C NMR spectral data. [c]. Yields are based on aldehydes. [d]. All reactions were carried out on 50 mmol scale of Baylis-Hillman alcohols and HBr (100 mmol)/H_2SO_4 (50 mmol) in DCM. [e] All compounds were well characterized by IR, ^{1}H NMR, ^{13}C NMR spectral data. [f]. Yields are based on Baylis-Hillman alcohols.

We have then treated the Baylis-Hillman bromides with ethyl glyoxylate/diethyl ketomalonate under the influence of Me_2S and K_2CO_3 as a base in CH_3CN/H_2O solvent system to provide multifunctional epoxides **70a-f** in good yields as shown in Eq.-23, Table-14. All the compounds were well characterized using IR, ^1H, ^{13}C NMR and HRMS data analysis and structure of compound **70a** was further confirmed by single crystal x-ray data analysis. ORTEP diagram for **70a** is shown in Fig. 17.



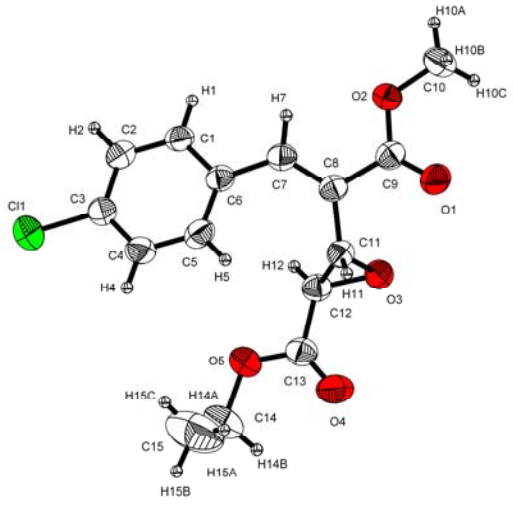
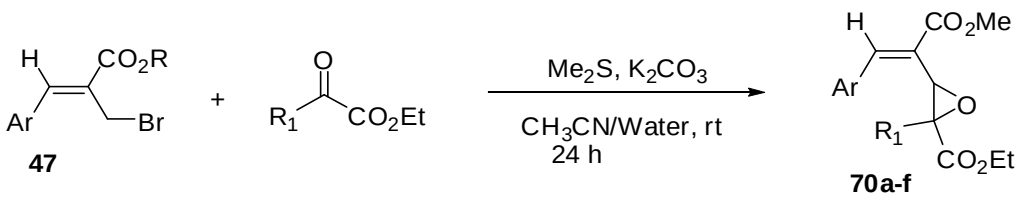


Fig.17: ORTEP diagram for compound **70a**

Table-14 *: Syntheis of epoxides* ***70a-f***[a,b]



Entry	B.H. Bromide	Ar	R_1	Product[c]	Yield (%)
1	**47c**	4-ClPh	H	**70a**[d]	66
2	**47a**	Ph	CO_2Et	**70b**	67
3	**47b**	2-ClPh	CO_2Et	**70c**	69
4	**47d**	4-MePh	CO_2Et	**70d**	66
5	**47e**	2-BrPh	CO_2Et	**70e**	68
6	**47f**	3-BrPh	CO_2Et	**70f**	71

[a]. All the reactions were carried out on the 2.0 mmol of Baylis-Hillman bromide **47** and 3.0 mmol of ethyl glyoxylate/diethyl ketomalonate under the influence of Me_2S (2.4 mmol)/K_2CO_3 (2.0 mmol) in CH_3CN/H_2O system.

[b]. Isolated yields are based on Baylis-Hillman bromides.

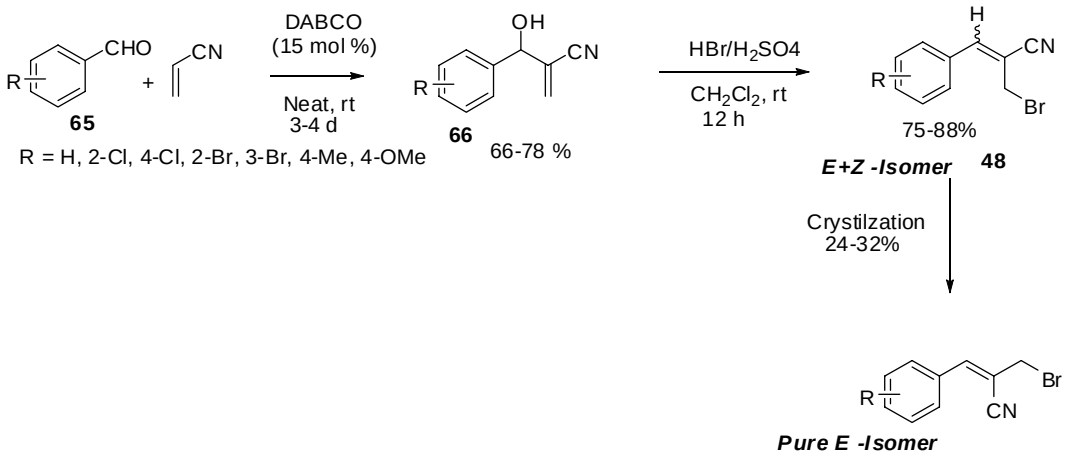
[c]. All the compounds were obtained as colorless liquid and well characterized using IR, ^1H, ^{13}C and HRMS data analysis. [d]. This was obtained as low melting solid and structure of this compound was further confirmed by single crystal X-ray data analysis.

Table 15. *Crystal data and structure refinement for* ***70a***

Identification code	**70a**	
Empirical formula	C_{15} H_{15} Cl O_5	
Formula weight	310.72	
Temperature	298(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P21/c	
Unit cell dimensions	a = 13.9223(6) Å	a= 90°.
	b = 15.0031(7) Å	b= 93.229(4)°.
	c = 7.0605(3) Å	g = 90°.
Volume	1472.44(11) $Å^3$	
Z	4	
Density (calculated)	1.402 Mg/m^3	
Absorption coefficient	0.278 mm^{-1}	
F(000)	648	
Crystal size	0.38 x 0.32 x 0.19 mm^3	
Theta range for data collection	2.93 to 24.70°.	
Index ranges	-16<=h<=16, -17<=k<=17, -7<=l<=8	
Reflections collected	5638	
Independent reflections	2510 [R(int) = 0.0190]	
Completeness to theta = 24.70°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9491 and 0.9018	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2510 / 0 / 200	
Goodness-of-fit on F^2	0.875	
Final R indices [I>2sigma(I)]	R1 = 0.0457, wR2 = 0.1204	
R indices (all data)	R1 = 0.0613, wR2 = 0.1343	
Largest diff. peak and hole	0.445 and -0.266 e.$Å^{-3}$	

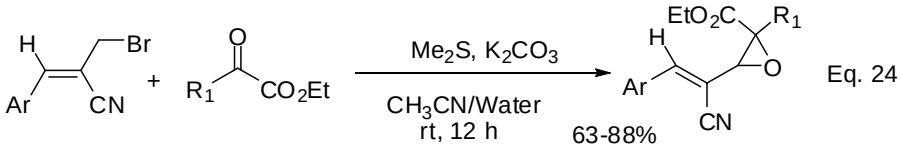
With a view to understand the influence of stereochemistry of allyl bromide, we have prepared various Baylis-Hillman bromides **48** from the Baylis-Hillman alcohols **66a-f** (Scheme 53, Table 21). These Baylis-Hillman alcohols were prepared from the respective aldehydes **65** and acrylonitrile. The Baylis-Hillman bromides obtained as a mixture of *E/Z*-isomer, the pure *E*-isomers were obtained by careful crystallization.

Scheme 53



R = H, 2-Cl, 4-Cl, 2-Br, 3-Br, 4-Me, 4-OMe

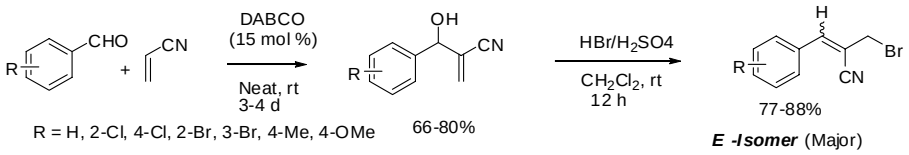
Then we have employed these Baylis-Hillman bromides **48a-e** for similar cycloaddition reaction with ethyl glyoxylate/diethyl ketomalonate under the influence of Me_2S and K_2CO_3 as a base in CH_3CN /H_2O solvent system to provide multifunctional epoxides **71a-g** in good yields as shown in Eq.-24, Table-17. All the compounds were well characterized using IR, ^1H, ^{13}C NMR and HRMS data analysis structure of compound **71b** was further confirmed by single crystal X-ray data analysis. ORTEP diagram for compound **71b** is shown in Fig 18.



Ar = Ph, 2-ClPh, 4-ClPh, 2-BrPh, 4-MePh, 4-MeOPh
R_1 = H, CO_2Et

71a-g

Table 16



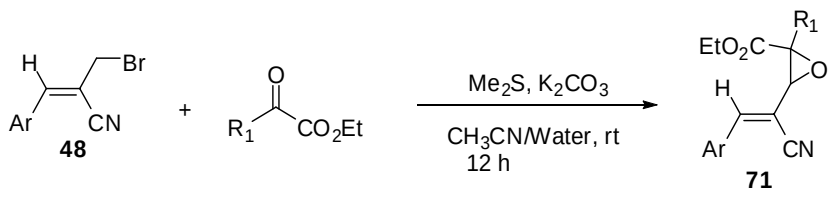
R = H, 2-Cl, 4-Cl, 2-Br, 3-Br, 4-Me, 4-OMe

66-80%

Entry	Aldehyde	R	B.H. Alcohol[a,b]	Yield[c] (%)	B.H. Bromide[d,e]	Yield (%)[f]
1	**65d**	4-Me	**66a**	66	**48a**	79
2	**65b**	2-Cl	**66b**	75	**48b**	87
3	**65c**	4-Cl	**66c**	80	**48c**	77
4	**65e**	4-OMe	**66d**	66	**48d**	79
5	**65f**	2-Br	**66e**	78	**48e**	87
6	**65a**	H	**66f**	72	**48f**	78

[a]. All reactions were carried out on 100 mmol scale of various aldehydes with acrylonitrile (150 mmol), under the influence of DABCO (15 mmol) at rt. [b].All compounds were well characterized by IR, ^{1}H NMR, ^{13}C NMR spectral data. [c]. Yields are based on aldehydes. [d]. All reactions were carried out on 50 mmol scale of Baylis-Hillman alcohols and HBr (100 mmol)/H_2SO_4 (50 mmol) in DCM. [e] All compounds were well characterized by IR, ^{1}H NMR, ^{13}C NMR spectral data. [f]. Yields are based on Baylis-Hillman alcohols.

Table-17: *Synthesis of epoxides* **71a-g**[a,b]



Entry	B.H. Bromide	Ar	R_1	Product[c]	Yield (%)
1	**48a**	4-MePh	H	**71a**	63
2	**48a**	4-MePh	CO_2Et	**71b**[d]	81
3	**48b**	2-ClPh	CO_2Et	**71c**	77
4	**48c**	4-ClPh	CO_2Et	**71d**	82
5	**48d**	4-OMePh	CO_2Et	**71e**	85
6	**48e**	2-BrPh	CO_2Et	**71f**	79
7	**48f**	Ph	CO_2Et	**71g**	88

[a]. All the reactions were carried out on the 2.0 mmol of Baylis-Hillman bromide **48** and 3.0 mmol of ethyl glyoxylate / diethyl ketomalonate under the influence of Me_2S/K_2CO_3 in CH_3CN/H_2O system.

[b]. Isolated yields are based on Baylis-Hillman bromides.

[c]. All the compounds were obtained as colorless liquid and well characterized using IR, ^1H, ^{13}C and HRMS data analysis. [d]. This was obtained as a solid and structure of this compound was further confirmed by single crystal X-ray data analysis.

Table 18. *Crystal data and structure refinement for* **71b.**

Identification code	**71b**	
Empirical formula	C_{18} H_{19} N O_5	
Formula weight	329.34	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclnic	
Space group	P-1	
Unit cell dimensions	a = 8.1530(5) Å	a= 103.338(7)°.
	b = 10.4533(9) Å	b= 93.835(6)°.
	c = 21.8360(19) Å	g = 103.672(6)°.
Volume	1744.9(2) $Å^3$	
Z	4	
Density (calculated)	1.254 Mg/m^3	
Absorption coefficient	0.092 mm^{-1}	
F(000)	696	
Crystal size	0.39 x 0.38 x 0.32 mm^3	
Theta range for data collection	2.87 to 24.71°.	
Index ranges	-9<=h<=9, -12<=k<=10, -25<=l<=25	
Reflections collected	11544	
Independent reflections	5955 [R(int) = 0.0248]	
Completeness to theta = 24.71°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9712 and 0.9650	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5955 / 0 / 448	
Goodness-of-fit on F^2	1.028	
Final R indices [I>2sigma(I)]	R1 = 0.0681, wR2 = 0.1628	
R indices (all data)	R1 = 0.0907, wR2 = 0.1803	
Extinction coefficient	0.054(3)	
Largest diff. peak and hole	0.546 and -0.604 e.$Å^{-3}$	

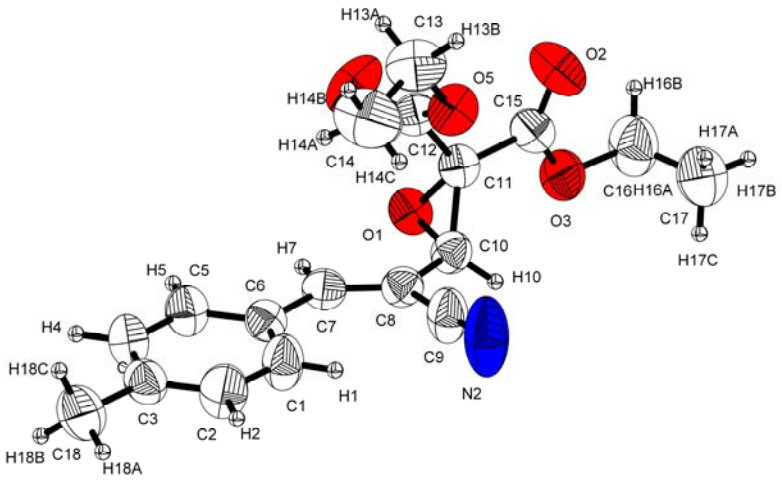


Fig. 18: ORTEP diagrame for compound **71b**

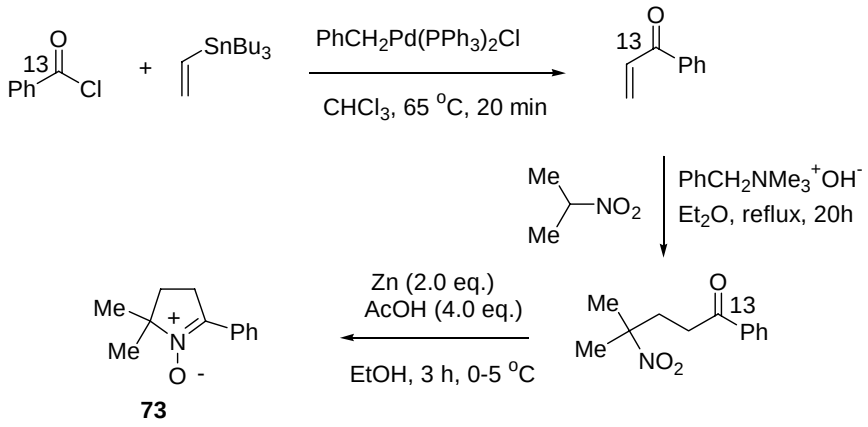
In Conclusion, we have developed a facile one pot strategy for the synthesis of densely functionalized epoxides **70** & **71** *via* cycloaddition reaction using Baylis-Hillman bromides as dipoles and ethyl glyoxalate or diethyl ketomalonoate as dipolarophiles.

Facile one-pot synthesis of nitrone-spiro-oxindoles frameworks using carbonates of Baylis-Hillman alcohols

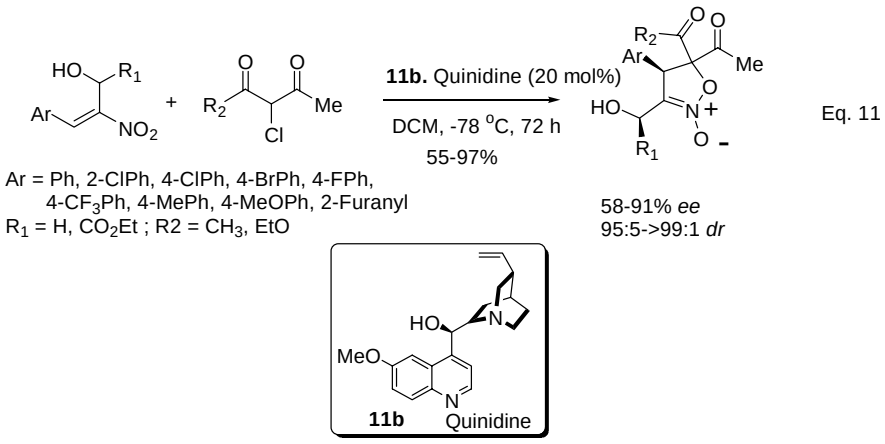
In recent years there has been increasing interest in understanding the free radical mediated oxidative damage to cells because it is considered to be one of the major factors responsible for many diseases such as neuro-degeneration, stroke, cancers *etc*.[205-211] After the initial studies on the applications of PBN (α-phenyl-*tert*-butylnitrone) (**72**)and its derivatives for trapping free radical in chemical systems, research work from various leading laboratories has been directed toward examining the utility of nitrones as spin traps in biologically systems and many significant results were achieved in this direction.[212-217] In fact the present day synthetic and medicinal chemistry demand the design, synthesis of appropriate nitrile oxide framework for addressing the problems of oxidative damage to tissues.[218-220]

Janzen et all[220] have synthesized 2-phenyl-5,5-dimethyl-1-pyrroline *N*-oxide (nitronyl-^{13}C) **73** according to the reaction sequence shown in Scheme 54 and used them for enhanced radical addend recognition and spin adduct persistence.

Scheme 54

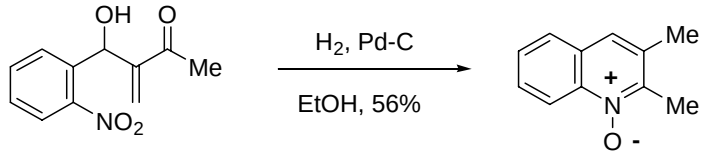


There are some reports are in literature for the synthesis of *N*-oxides from the Baylis-Hillman adducts. Zhu and co-workers[139] have reported an interesting synthesis of *N*-oxides via [4+1] annulations of 1,3-dicarbonyl compounds with Baylis-Hillman adducts, catalyzed by organo-catalyst **11b** (Eq. 11).



Eq. 11

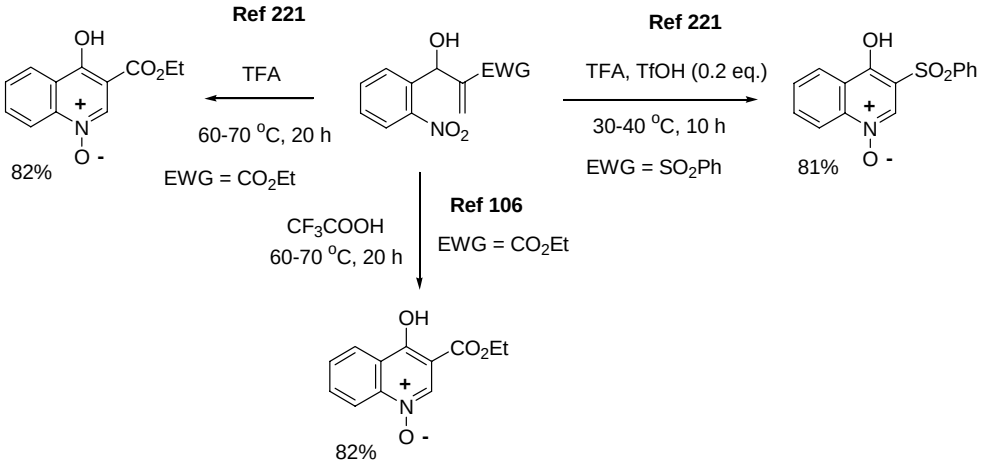
A facile synthesis of quinoline *N*-oxide derivatives *via* the reduction of Baylis-Hillman adduct obtained from 2-nitrobenzaldehyde with H_2/Pd-C as shown in Eq. 25 was reported by Kaye and co-workers.[104,105]



Eq. 25

Kim and co-workers[106, 221] have also reported a facile synthesis of quinoline *N*-oxide derivatives *via* the treatment of Baylis-Hillman adducts obtained from 2-nitrobenzaldehyde with TFA or TFA/TfOH or CF_3COOH according to the Scheme 55.

Scheme 55

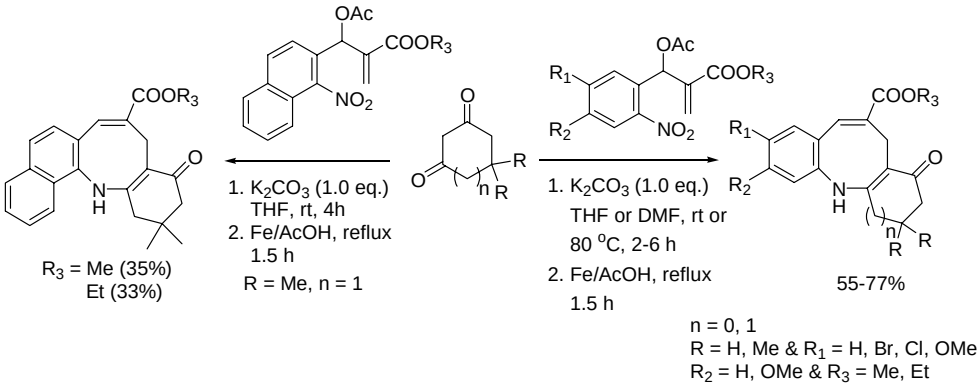


Spirooxindole skeleton is another unique structural framework that is present in several natural products and biologically active molecules; therefore development of efficient and simple protocols for obtaining spirooxindole derivatives represents an attractive area of

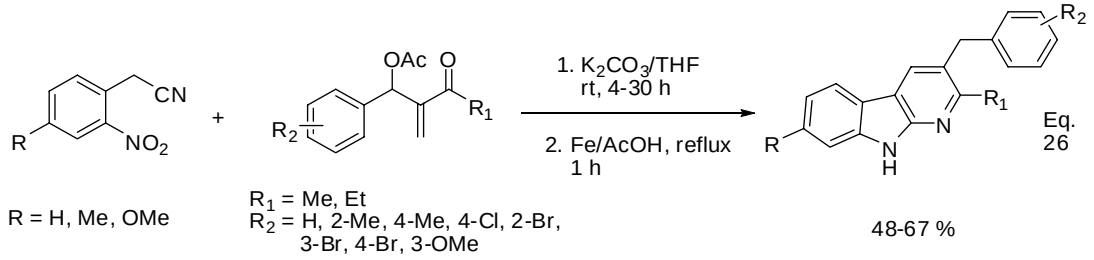
research in synthetic chemistry. It occurred to us that molecules containing both nitrone skeleton and spirooxindole structural units might show interesting biological activities. For synthesis of spirooxindoles please see Schemes 39-41 & eqs. 16-18.

Our research group[222] has successfully transformed Baylis-Hillman acetates into tri-/ tetracyclic heterocyclic frameworks containing an important azocine moiety *via* a facile and operationally simple one-pot multi-step protocol involving alkylation, reduction, and cyclization sequence, following the sequence as shown in Scheme 56.

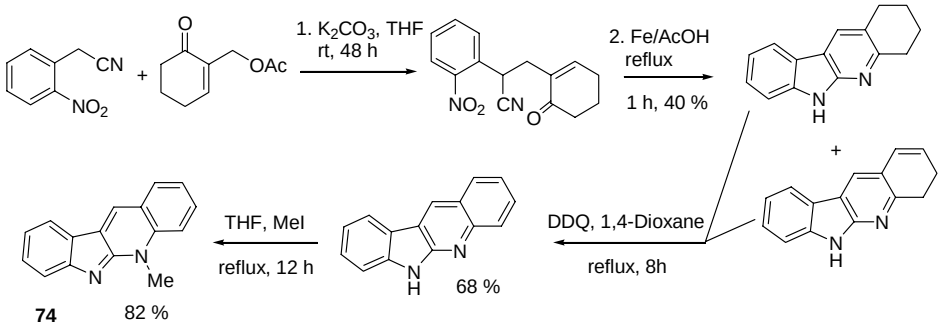
Scheme 56



Very recently our research group[223] has also developed facile one-pot methodology for the synthesis of *α*-carbolines *via* monoalkylation of Baylis-Hillman acetates with 2-nitroarylacetonitriles followed by reductive cyclization using Fe/AcOH according to the eq. 26. We have also utilized this methodology for the concise synthesis of a bioactive alkaloid *neocryptolepine* **(74)** as shown in Scheme 57.

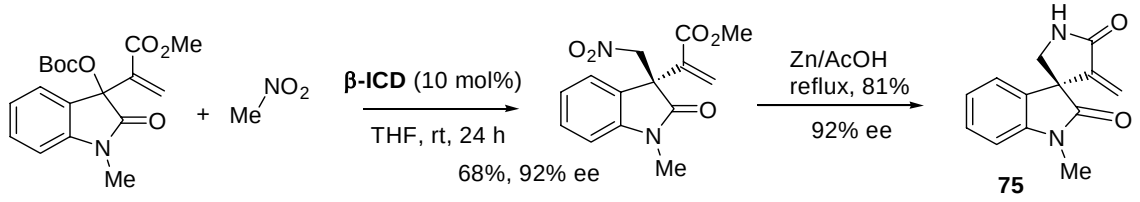


Scheme 57



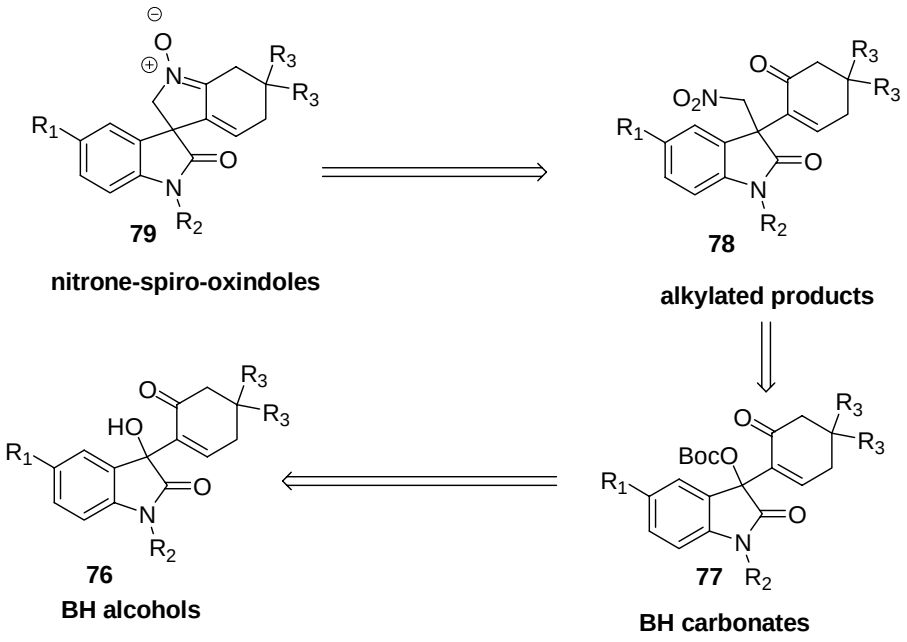
It is worth mentioning here that recently Lu and co-workers[224] have reported asymmetric allylic alkylation of isatin derived Baylis-Hillman carbonates with nitro alkanes and one of the alkylated product was then converted into spirooxindole derivatives **75** using Zn/AcOH as reducing agent as shown in Scheme 58.

Scheme 58



Based on the above information, we have directed our study towards development of a simple synthetic procedure for obtaining nitrone-spiro-oxindole frameworks following the retro synthetic strategy as presented in Scheme 59.

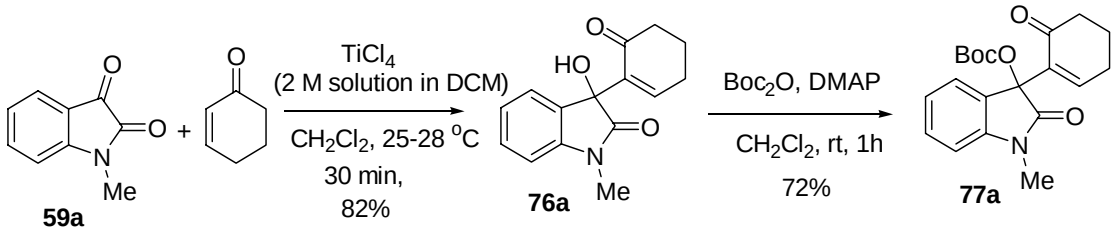
Scheme 59



On the basis of our experience in understanding the versatility of BH adducts, we envisaged that the Baylis-Hillman carbonates (**77**) would serve as appropriate alkylators for obtaining the nitro-enone dertivatives **78** which in turn can be transformed into an interesting class of compounds (**79**) containing both the spirooxindole and nitrone frameworks as shown in the retro synthetic strategy (Scheme 59).

Accordingly, first we have selected 3-(*tert*-butoxycarbonyloxy)-3-(cyclohex-2-enon-2-yl)-1-methylindolin-2-one **77a** for our study for alkylation with nitromethane. This was prepared from the 3-hydroxy-3-(cyclohex-2-enon-2-yl)-1-methylindolin-2-one (Baylis-Hillman alcohol **76a** *via* the treatment with Boc_2O under the catalytic influence of DMAP in CH_2Cl_2 as solvent for 1h under N_2 atmosphere according to the known procedure which provided the boc-derivative in 72% yield as brown solid. The Baylis-Hillman alcohol 3-hydroxy-3-(cyclohex-2-enon-2-yl)-1-methylindolin-2-one was prepared *via* the coupling between 1-methylisatin and cyclohex-2-enone under the influence of $TiCl_4$ in 82%, according to procedure developed in our laboratory (Scheme 60). The structures of Baylis-Hillman alcohol **76a** and Boc-derivative **77a** were confirmed by IR, ^1H, ^{13}C data analysis.

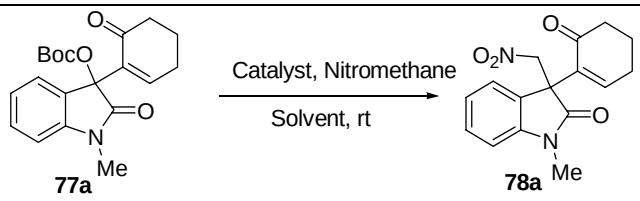
Scheme 60



In the initial studies 3-(*tert*-butoxycarbonyloxy)-3-(cyclohex-2-enon-2-yl)-1-methylindolin-2-one (**77a**) was treated with nitromethane under the influence of DMAP in CH_3CN as a solvent in N_2 atmosphere for 48 hr to obtain the nitro-enone derivative **78a** in 50% isolated yield. For optimization of this reaction we have used various nucleophilic catalyst/base and solvents and found that DMAP as catalyst in DCM provided the

alkylated product **78a** in 80% isolated yield (Table 19). Structure of nitro-enone derivative **78a** was confirmed by IR, ^{1}H, ^{13}C, HRMS data analysis.

Table 19: *Optimization: Alkylation of nitromethane with BH-carbonate* ***78a***[a]

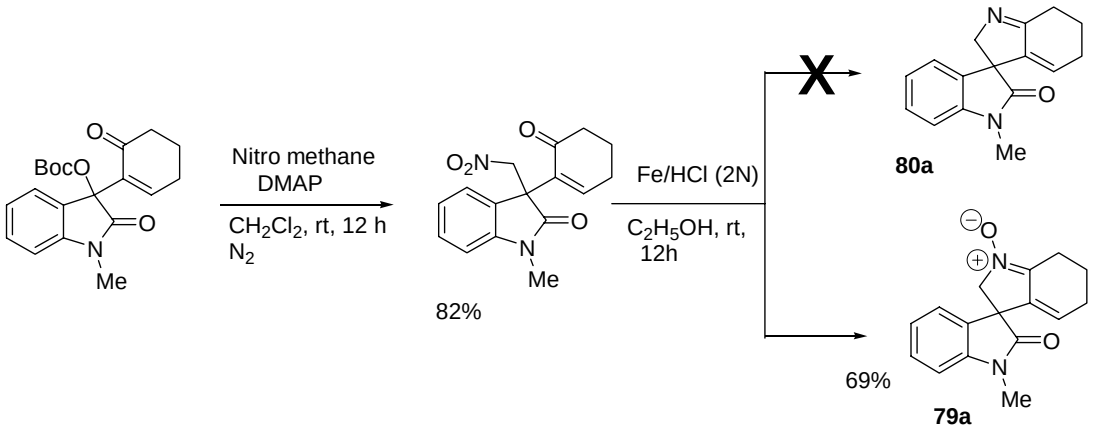


Entry	Catalyst	Solvent	Time	Yield (%)
1	DABCO	DCM	48	N. R.
2	PPh_3	DCM	48	N. R.
3	Me_2S	DCM	48	N. R.
4	DMAP	Toluene	48	53
5	DMAP	CH_3CN	48	50
6	**DMAP**	**DCM**	**12**	**82**[b]
7	DMAP	DCM	24	75[c]

[a] All reactions were carried out on a 2.0 mmol scale of Baylis-Hillman carbonates (**77a**) with 3.0 mmol of nitromethane in the presence of various nucleophiles (bases) (2.0 mmol) in different solvents at room temperature under N_2 atmosphere. [b] Reaction was also carried out on a 4.0 mmol scale of Baylis-Hillman carbonates (**77a**) with 6.0 mmol of nitromethane in the presence of DMAP (4.0 mmol) in anhydrous DCM at room temperature under N_2 atmosphere. [c] 1.0 mmol of DMAP was used.

Reductive cyclization of nitro-enone, 3-nitromethyl-3-(cyclohex-2-enon-2-yl)-1-methylindolin-2-one (**78a**) using the Fe/HCl in EtOH provided five member nitrone-spiro-oxiindole derivative, [1-methylindolin-2-one]-3-spiro-3′-[2′,5′,6′,7′-tetrahyroindole 1′-oxide] (**79a**) was obtained in 69% yield (overall yield 57% starting from **77a**), according to Scheme 61. The structures of nitro-enone **78a** and cyclized product **79a** were confirmed by IR, ^{1}H, ^{13}C and HRMS data analysis. Interestingly no trace of spirooxindole derivative **80a** was formed in this reaction.

Scheme 61



At this stage it occurred to us that it would be useful and interesting if these two steps are performed in one-pot procedure as it will avoid one isolation step. Accordingly, we have treated the Baylis-Hillman carbonate **77a** (2 mmol) with nitromethane (3 mmol) in the presence of DMAP (2 mmol) in DCM at room temperature for 12 h and the resulting reaction mixture (after the solvent was removed under reduced pressure) was subsequently treated with Fe powder (12 mmol) and 2N HCl (2 mL) in ethanol for 12 h at room

temperature to provide the desired nitrone-spirooxindole **79a** in 59% overall yield (after usual work-up followed by purification of the crude product, thus obtained, by silica gel column chromatography). The Spectral (IR, ^{1}H & ^{13}C NMR, HRMS) data and M.P. of this product was identical with that of the compound, obtained in a two step protocol.

This is indeed a very encouraging result. We therefore have selected one-pot procedure to understand the generality of this methodology. We have prepared a representative class of the Baylis-Hillman adducts (**76a-l**) from selected isatins and cyclohexenone & 5,5-dimethylcyclohexenone and converted them into their carbonate derivatives (**77a-l)** according to Scheme 62 (Tables 20 & 21). Structures of these compounds were in complete agreement with IR, ^{1}H NMR, ^{13}C NMR and HRMS data.

Scheme 62

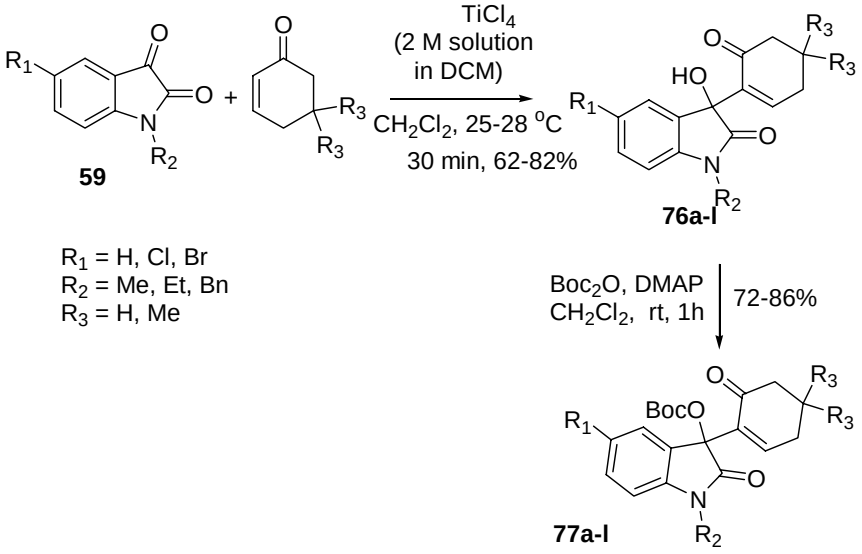
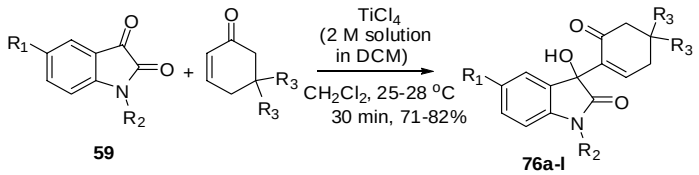


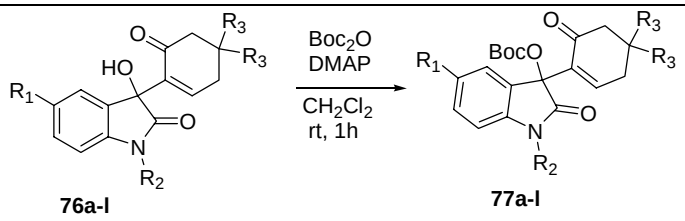
Table 20. *Synthesis of Baylis-Hillman alcohols* **76**[a]



Isatins	R_1	R_2	R_3	Product[b]	Yield (%)[c]	M.P. (ºC)
59a	H	Me	H	**76a**	82	134-136
59b	H	Et	H	**76b**	79	140-142
59h	H	Bz	H	**76c**	76	154-158
59c	Cl	Me	H	**76d**	80	166-168
59d	Cl	Et	H	**76e**	71	178-180
59i	Cl	Bz	H	**76f**	80	204-206
59e	Br	Me	H	**76g**	82	162-164
59f	Br	Et	H	**76h**	62	170-172
59j	Br	Bz	H	**76i**	74	210-212
59c	Cl	Me	Me	**76j**	78	180-182
59e	Br	Me	Me	**76k**	75	178-180
59d	Cl	Et	Me	**76l**	68	194-196

[a]. All reactions were carried out on 30 mmol scale of various isatins with cyclohex-2-enone or 5,5-dimethyl cyclohex-2-enone (30 mmol), under the influence of $TiCl_4$ (30 mmol, 15 ml of 2M solution in CH_2Cl_2) at 25-28 ºC for 30 min. [b].All compounds were obtained as solids and gave satisfactory IR, ^1H NMR, ^{13}C NMR spectral data. [c]. Yields are based on isatins.

Table 21. *Synthesis of Carbonates of Baylis-Hillman adducts*[a,b,c]



76a-l **77a-l**

BH-Alchol	R_1	R_2	R_3	Product	Yield (%)	M.P. (ºC)
76a	H	Me	H	**77a**	72	130-132
76b	H	Et	H	**77b**	70	140-142
76c	H	Bz	H	**77c**	83	124-126
76d	Cl	Me	H	**77d**	71	162-164
76e	Cl	Et	H	**77e**	78	172-174
76f	Cl	Bz	H	**77f**	79	160-162
76g	Br	Me	H	**77g**	80	162-164
76h	Br	Et	H	**77h**	74	174-176
76i	Br	Bz	H	**77i**	76	170-172
76j	Cl	Me	Me	**77j**	75	158-160
76k	Br	Me	Me	**77k**	86	140-142
76l	Cl	Et	Me	**77l**	79	168-170

[a] All reactions were carried out on 20 mmol scale of Baylis-Hillman alcohols with 22 mol of Boc_2O under the influence of DMAP in CH_2Cl_2 at 0º C for 1 h. [b] All compounds were obtained as solids and gave satisfactory IR, ^1H NMR, ^{13}C NMR and HRMS data. [c] Yields are based on Baylis-Hillman alcohols.

We have then subjected these carbonates (**77a-l**) first to the reaction with nitromethane and then *in situ* produced alkylated products (**78a-l**) with Fe/HCl as in the case of **79a** to produce the resulting nitrone-spiro-oxindoles (**79a-l**) in 56-65% isolated yields (Scheme 63). All compounds were obtained as solids and gave satisfactory IR, ^{1}H NMR, ^{13}C NMR and HRMS data and the structures of compounds **79b** and **79j** was further confirmed by single crystal X-ray data analysis. ORTEP diagrams for **79b** and **79j** are shown in Figs 19 & 20 respectively.

Scheme 63

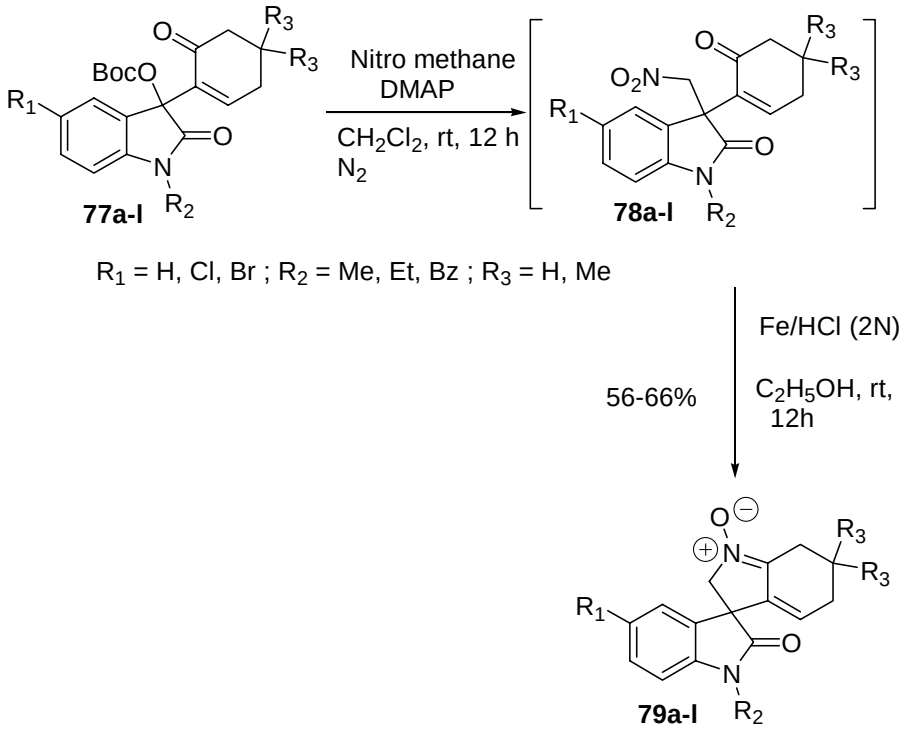
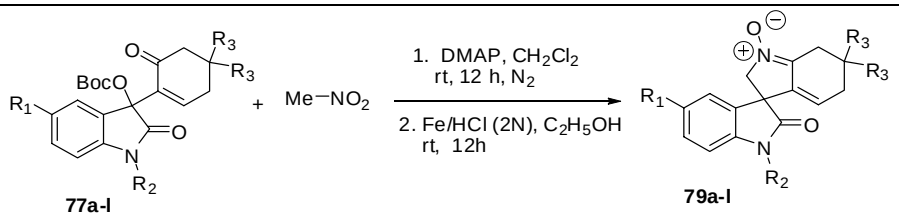


Table 22. *Synthesis of Nitrone-spirooxindole derivatives* **79a-l**[a]



B.H. Carbonates	R_1	R_2	R_3	R_4	Product[b]	Yield[c] (%)	M.P.(ºC)
77a	H	Me	H	H	**79a**	59	180-182
77b	H	Et	H	H	**79b**	64[d]	162-164
77c	H	Bz	H	H	**79c**	60	162-164
77d	Cl	Me	H	H	**79d**	61	202-204
77e	Cl	Et	H	H	**79e**	56	154-156
77f	Cl	Bz	H	H	**79f**	62	100-102
77g	Br	Me	H	H	**79g**	65	198-200
77h	Br	Et	H	H	**79h**	60	182-184
77i	Br	Bz	H	H	**79i**	64	186-188
77j	Cl	Me	Me	H	**79j**	63[d]	186-188
77k	Br	Me	Me	H	**79k**	58	194-196
77l	Cl	Et	Me	H	**79l**	61	184-186

[a]. All reactions were carried out on 2.0 mmol scale of Baylis-Hillman carbonates **77a-l** and nitro alkane (3.0 mmol) under the influence of DMAP (2.0 mmol) in CH_2Cl_2 at 0º C for 1 h, followed by treatment with Fe powder (6.0 mmol), HCl (2.0 mL of 2N HCl) in EtOH (10.0 mL). [b]. All compounds were obtained as solids and gave satisfactory IR, ^{1}H NMR, ^{13}C NMR and HRMS data. [c].Yields are based on boc-derivatives. [d]. Structures of compound **79b**, **79j** was further confirmed by single crystal data-analysis.

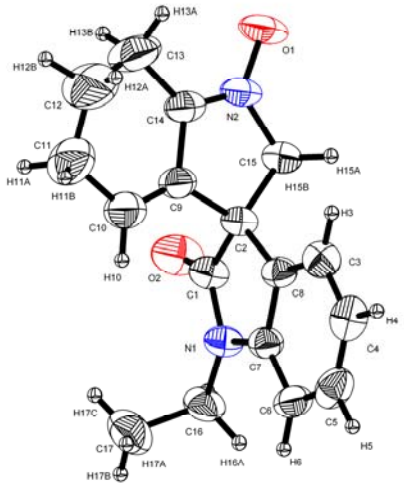


Fig. 19: ORTEP diagram of compound **79b**

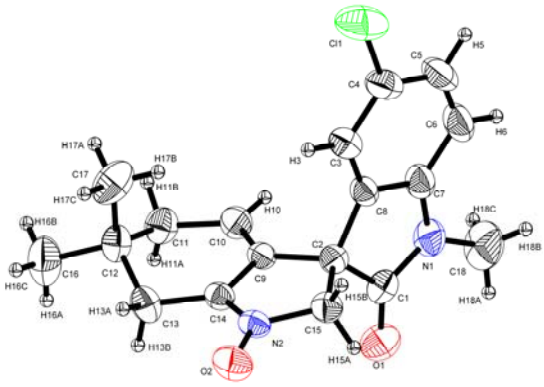


Fig. 20: ORTEP diagram of compound **79j**

Table 23. *Crystal data and structure refinement for* **79b**

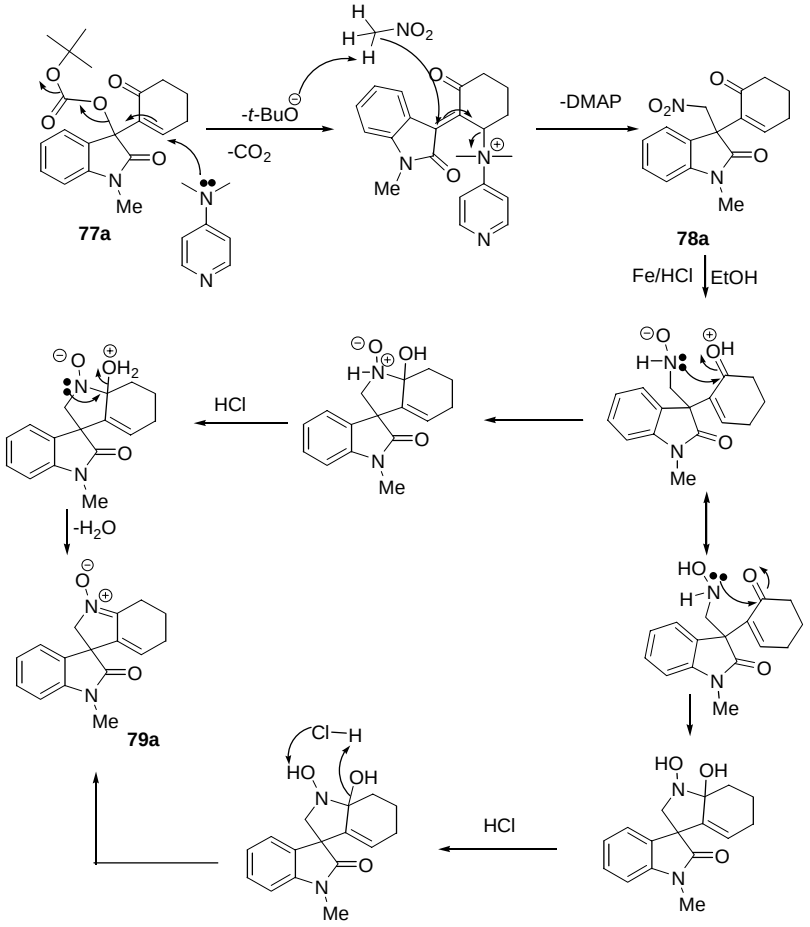
Identification code	: **79b**	
Empirical formula	: C_{17} H_{18} N_2 O_2	
Formula weight	: 282.33	
Temperature	: 298(2) K	
Wavelength	: 0.71073 Å	
Crystal system	: Triclinic	
Space group	: P-1	
Unit cell dimensions	: a = 8.4050(6) Å	α= 92.5970(10)°.
	: b = 8.7609(6) Å	β= 109.0770(10)°.
	: c = 11.2366(8) Å	γ = 108.3070(10)°.
Volume	: 732.23(9) $Å^3$	
Z	: 2	
Density (calculated)	: 1.281 Mg/m^3	
Absorption coefficient	: 0.085 mm^{-1}	
F(000)	: 300	
Crystal size	: 0.36 x 0.28 x 0.25 mm^3	
Theta range for data collection	: 1.94 to 25.00°.	
Index ranges	: -9<=h<=9, -10<=k<=10, -13<=l<=13	
Reflections collected	: 7053	
Independent reflections	: 2568 [R(int) = 0.0229]	
Completeness to theta = 25.00°	: 99.5 %	
Absorption correction	: Empirical	
Max. and min. transmission	: 0.9791 and 0.9701	
Refinement method	: Full-matrix least-squares on F^2	
Data / restraints / parameters	: 2568 / 0 / 192	
Goodness-of-fit on F^2	: 1.057	
Final R indices [I>2sigma(I)]	: R1 = 0.0493, wR2 = 0.1404	
R indices (all data)	: R1 = 0.0531, wR2 = 0.1454	
Extinction coefficient	: 0.22(2)	
Largest diff. peak and hole	: 0.323 and -0.332 $e.Å^{-3}$	

Table 24. *Crystal data and structure refinement for* **79j**

Identification code	: **79j**	
Empirical formula	: C_{18} H_{19} Cl N_2 O_2	
Formula weight	: 330.81	
Temperature	: 298(2) K	
Wavelength	: 0.71073 Å	
Crystal system	: Monoclinic	
Space group	: C2/c	
Unit cell dimensions	: a = 15.6727(8) Å	α= 90°.
	: b = 10.8206(5) Å	β= 103.779(5)°.
	: c = 19.7503(11) Å	γ = 90°.
Volume	: 3253.0(3) $Å^3$	
Z	: 8	
Density (calculated)	: 1.351 Mg/m^3	
Absorption coefficient	: 0.246 mm^{-1}	
F(000)	: 174	
Crystal size	: 0.28 x 0.20 x 0.18 mm^3	
Theta range for data collection	: 2.91 to 26.37°.	
Index ranges	: -9<=h<=19, -13<=k<=7, -24<=l<=23	
Reflections collected	: 6118	
Independent reflections	: 3331 [R(int) = 0.0256]	
Completeness to theta = 26.37°	: 99.9 %	
Absorption correction	: Semi-empirical from equivalents	
Max. and min. transmission	: 0.9945 and 0.9914	
Refinement method	: Full-matrix least-squares on F^2	
Data / restraints / parameters	: 3331 / 0 / 211	
Goodness-of-fit on F^2	: 1.006	
Final R indices [I>2sigma(I)]	: R1 = 0.0491, wR2 = 0.1134	
R indices (all data)	: R1 = 0.0752, wR2 = 0.1282	
Largest diff. peak and hole	: 0.196 and -0.290 $e.Å^{-3}$	

A plausible mechanism for obtaining nitrone-spiro-oxindoles (**79**) is presented in Scheme 64 taking **79a** as a model case.

Scheme 64 *: Plausible mechanism for the synthesis of nitrone-spirooxindole derivatives* **79**



In conclusion, we have developed an efficient one-pot methodology for the synthesis of nitrone-spiro-oxindoles (**79**) *via* alkylation of nitromethane with Baylis-Hillman carbonates **77** followed by reductive cyclization of the *in situ* generated nitro-enones **78** using Fe/HCl /EtOH in encouraging yields.

Conclusions

All the objectives mentioned in the beginning of the chapter have been achieved with considerable success. We have successfully demonstrated the steric factors directed cycloaddition reactions between dipoles that are generated from Baylis-Hillman bromides **46-48** and isatins **59** as dipolarophiles, thus the allyl bromide **46** provided the spirodihydrofurane-oxindole frameworks **61** **[**(1-alkylindolin-2-one)-3-spiro-2′-(4′-methoxycarbonyl-2′, 3′-dihydrofuran)]. The allyl bromides **47** provided separable mixture of diasteromer of spiroepoxy oxindoles (**63)** [3*R*(2′*R*), 3′*S*]/ [3*S*(2′S), 3′*R*]-(1-alkylindolin-2-one)-3-spiro-2′-[3′-{(*E*)-1-methoxycarbon-yl-2-aryl}ethenyloxirane] & **64** **[**3*S*(2′*S*), 3′*S*]/ [3*R*(2′*R*), 3′*R*]-(1-alkyl-5-bromoindolin-2-one)-3-spiro-2′-[3′-{(*E*)-1-methoxycarbonyl -2-aryl}ethenyloxirane], whereas the allyl bromide **48** provided dihydrofurane derivatives **67** [3*R*(2′*R*), 5′*R*]/ [3*S*(2′*S*), 5′*S*]-(1-alkylndolin-2-one)-3-spiro-2′-[4′-cyano-5′-(4-aryl)-2′, 5′-dihydrofuran].

We have also studies the role of steric factors of Baylis-Hillman bromides **47** & **48** in the cyclo-addition reaction with ethyl glyoxalate and diethyl ketomalonoate and developed a facile one pot strategy for the synthesis of densely functionalized epoxides **70** & **71**.

We developed a facile one pot strategy for obtaining nitrone-spirooxindole frameworks **79** [1-alkylindolin-2-one]-3-spiro-3′-[2′,5′,6′,7′-tetrahyroindole 1′-oxide] using the carbonates **77** of Baylis-Hillman adducts **76** as alkylater for nitromethane under the

influence of DMAP, followed by reductive cyclization using Fe/HCl in ethanol as reagent system.

Our studies clearly demonstrated the importance of the Baylis-Hillman adducts as a valuable source in organic transformation methodologies, particularly for one-pot multi-step/reaction strategies.

EXPERIMENTAL

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.

Chromatography: All reactions were monitored using Thin Layer Chromatography (TLC). Analytical Thin Layer Chromatography (TLC) was performed on glass plates (7×2 cm) coated with Acme's silica gel GF 254 (254 mμ) containing 13% calcium sulfate as a binder. The spots were visualized by short exposure to UV light or iodine vapor. Column chromatography was carried out using Acme's silica gel (60-120 mesh or 100-200 mesh).

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, peaks are reported in cm^{-1}.

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

Nuclear Magnetic Resonance Spectra: Proton magnetic resonance spectra and carbon-13 magnetic resonance spectra were recorded on BRUKER-AVANCE-400 or 500 spectrometers. ^{1}H NMR (400/500 MHz) spectra for all the samples were measured in chloroform-*d* with TMS (δ = 0 ppm) as an internal standard. ^{13}C NMR (100 MHz) spectra for all the samples were measured in chloroform-*d* 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 =

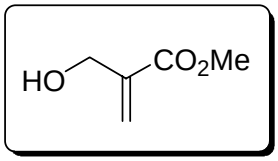
triplet, q = quartet, m = multiplet, dd = doublet of doublet, bs = broad singlet, dABq = doublet of AB quartet, (3) number of hydrogens integrated for the signal, (4) coupling constant *J* in Hertz.

X-ray Crystallographic Study: Single crystal X-ray data for all the 11 compounds (**61a, 63a, 64a, 63h, 64h, 67d, 67e, 70a, 71b, 79b and 79j)** were collected on a Bruker SMART APEX CCD area detector system [λ(Mo-Kα) = 0.71073 Å] at 298K graphite monochromator with a ω scan width of 0.3^{o}, crystal-detector distance 60 mm, collimator 0.5 mm. The SMART software (Version 5.630) was used for the intensity data acquisition and the SAINTPLUS Software (Version 6.45) was used for the data extraction. In each case, absorption correction was performed with the help of SADABS program, an empirical absorption correction using equivalent reflections was performed with the program. An empirical absorption correction using spherical harmonics was implemented in ‘‘SCALE3 ABSPACK’’ scaling algorithm. The structurs wwer solved using SHELXS-97, and full-matrix least-squares refinement against F^2 was carried out using SHELXL-97. All non-hydrogen atoms were refined anisotropically. The software used to prepare the material is *WinGx* v1.70.01 (L. Farrugia, 2005). The DIAMOND (Version 2.1e) software was used for molecular graphics.

HRMS Analysis: HRMS spectra were recorded on Bruker maXis ESI-TOF spectrometer.

Methyl 3-hydroxy-2-methylene-propanoate (60)

To a stirred solution of paraformaldehyde (100 mmol, 3.03 g), methyl acrylate (150 mmol, 12.91g) in THF:Water (1:1) added DABCO (30 mol%, 3.36 g). After stirring for 2 days at room temperature, the reaction mixture was extracted with diethyl ether (3 x 50 mL), the combined organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and the crude product thus obtained was purified by column chromatography which afforded the title compound (methyl 3-hydroxy-2-methylene-propanoate) in 45% yield as colorless liquid.



Yield (%) : 45 (5.22 g)

IR (neat) : ν 3435, 1720, 1637 cm^{-1}

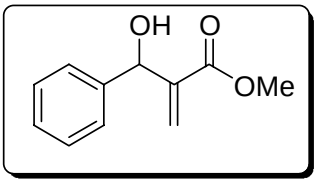
^1H NMR (400 MHz) : δ 2.92 (bs, 1H), 3.79 (s, 3H), 4.33 (s, 2H), 5.86 (d, 2H, J = 1.6 Hz), 6.27 (d, 1H, J = 0.4 Hz)

^{13}C NMR (100 MHz) : δ 51.93, 62.14, 125.77, 139.35, 166.82

Methyl 3-hydroxy-2-methylene-3-phenylpropanoate (62a)

A solution of benzaldehyde (100 mmol, 10.612 g), methyl acrylate (150 mmol, 12.913 g) and DABCO (15 mol%, 1.682 g) was kept at room temperature. After 7 days the reaction mixture was diluted with ether (100 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 residue thus obtained was purified by column chromatography (10%

EtOAc in hexanes, silica gel) to provide the title compound (methyl 3-hydroxy-2-methylene-3-phenylpropanoate) in 73% yield as a colorless liquid.



Yield (%) : 73 (14.07 g)

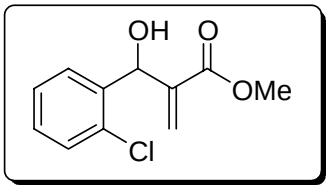
IR (neat) : ν 3468, 1720, 1631 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.71 (s, 3H), 5.55 (s, 1H), 5.84 (s, 1H), 6.33 (s, 1H), 7.24-7.39 (m, 5H)

^{13}C NMR (100 MHz) : δ 52.01, 73.25, 126.19, 126.64, 127.88, 128.48, 141.29, 141.99, 166.83

Methyl 3-(2-chlorophenyl)-3-hydroxy-2-methylenepropanoate (62b):

This compound was prepared as colorless liquid *via* the DABCO catalyzed coupling between 2-chlorobenzaldehyde and methyl acrylate following the similar procedure as described for **62a** as colorless liquid.



Reaction time : 8 days

Yield (%) : 78 (8.79 g)

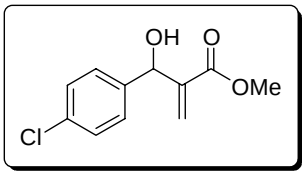
IR (neat) : ν 3437, 1724, 1631 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.77 (s, 3H), 5.58 (s, 1H), 5.97 (s, 1H), 6.33 (s, 1H), 7.21-7.38 (m, 3H), 7.56 (dd, 1H, J = 1.6 Hz & 8.0 Hz)

^{13}C NMR (100 MHz) : δ 52.07, 69.08, 126.92, 126.97, 128.12, 128.96, 129.40, 132.78, 138.33, 140.67, 166.92

Methyl 3-(4-chlorophenyl)-3-hydroxy-2-methylenepropanoate (62c):

This compound was prepared *via* the DABCO catalyzed Baylis-Hillman reaction between 4-chlorobenzaldehyde and methyl acrylate following the similar procedure as described for **62a** as colorless liquid.



Reaction time : 8 days

Yield (%) : 78

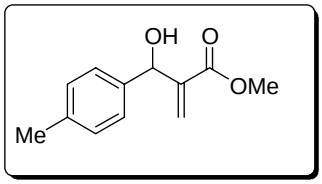
IR (neat) : ν 3422, 1716, 1633 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.10 (d, 1H, J = 5.6 Hz), 3.73 (s, 3H), 5.53 (d, 1H, J = 5.6 Hz) 5.83 (s, 1H), 6.34 (s, 1H), 7.32 (s, 4H)

^{13}C NMR (100 MHz) : δ 51.99, 72.34, 126.16, 128.03, 128.51, 133.49, 139.86, 141.68, 166.56

Methyl 3-hydroxy -2-methylene-3-(4-methylphenyl)propanoate (62d):

DABCO catalyzed Baylis-Hillman reaction between 4-methylbenzaldehyde and methyl acrylate following the similar procedure as described for **62a**, provided the compound as colorless liquid.



Reaction time : 10 days

Yield (%) : 76

IR (KBr) : ν 3503, 1712, 1626 cm^{-1}

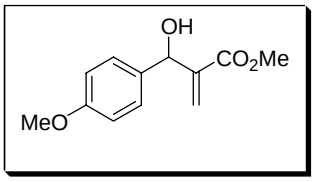
^{1}H NMR (400 MHz) : δ 2.33 (s, 3H), 2.92 (d, 1H, J = 5.6 Hz), 3.71 (s, 3H), 5.53 (d, 1H, J = 5.6 Hz), 5.84 (s, 1H), 6.32 (s, 1H), 7.15 (d, 2H, J = 8.0 Hz), 7.26 (d, 2H, J = 8.0 Hz)

^{13}C NMR (100 MHz) : δ 21.14, 51.91, 73.00, 125.78, 126.57, 129.13, 137.52, 138.41, 142.11, 166.78

Methyl 3-hydroxy-3-(4-methoxyphenyl)-2-methylenepropanoate (62e):

This was prepared according to the procedure developed in our laboratory.

A mixture of 4-methoxybenzaldehyde (50 mmol, 6.80 g), DABCO (15 mol%, 7.5 mmol, .840 g), methyl acrylate (75 mmol, 6.456 g), silica gel {(>200 mesh), (12.5-13.75 g)} were mixed thoroughly and kept at room temperature for 10 days. The reaction mixture was washed thoroughly with ethyl acetate (4 x 50 mL). Combined organic layer was dried over anhydrous Na_2SO_4 and solvent was evaporated. The residue thus obtained was purified by column chromatography (silica gel, 10% ethyl acetate in hexanes) to provide the **62e** as colorless viscous liquid.



Yield (%) : 65

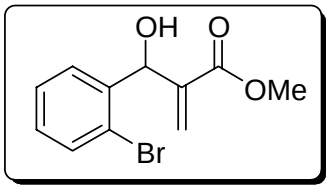
IR (KBr) : ν 3344, 1714, 1610 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.88 (s, 1H), 3.72 (s, 3H), 3.80 (s, 3H), 5.52 (s, 1H), 5.84 (s, 1H), 6.32 (s, 1H), 6.88 (d, 2H, J = 8.8 Hz), 7.29 (d, 2H, J = 8.8 Hz)

^{13}C NMR (100 MHz) : δ 51.92, 55.25, 72.66, 113.82, 125.54, 127.94, 133.51, 142.22, 159.20, 166.79

Methyl 3-(2-bromophenyl)-3-hydroxy-2-methylenepropanoate (62f):

This compound was prepared *via* the DABCO catalyzed Baylis-Hillman reaction between 2-bromobenzaldehyde and methyl acrylate following the similar procedure as described for **62a** as colorless liquid.



Reaction time : 7 days

Yield : 78 %

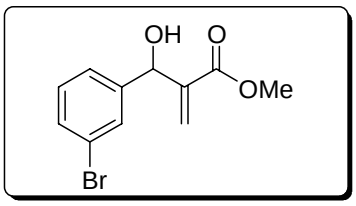
IR (neat) : ν 3427, 1712, 1633 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.80 (s, 3H), 5.57 (s, 1H), 5.95 (s, 1H), 6.36 (s, 1H), 7.13-7.22 (m, 1H), 7.36 (t, 1H, J = 7.6 Hz), 7.56 (d, 1H, J = 8.0 Hz)

^{13}C NMR (100 MHz) : δ 52.21, 71.43, 123.15, 127.21, 127.70, 128.43, 129.38, 132.19, 139.87, 140.68, 167.04.

Methyl 3-(3-bromophenyl)-3-hydroxy-2-methylenepropanoate (62g)

This compound was prepared *via* the DABCO catalyzed Baylis-Hillman reaction between 3-bromobenzaldehyde and methyl acrylate following the similar procedure as described for **62a** as colorless liquid.



Reaction time : 7 days

Yield (%) : 76

IR (neat) : ν 3412, 1712, 1631 cm^{-1}

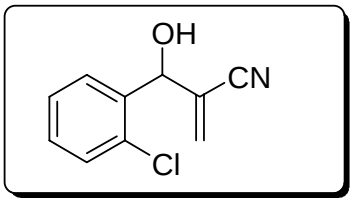
^{1}H NMR (400 MHz) : δ 3.74 (s, 3H), 5.52 (s, 1H), 5.85 (s, 1H), 6.37 (s, 1H), 7.11-7.45 (m, 3H), 7.54 (s, 1H)

^{13}C NMR (100 MHz) : δ 52.07, 72.40, 122.50, 123.28, 126.60, 129.64, 129.96, 130.84, 141.36

3-(2-Chlorophenyl)-3-hydroxy-2-methylene-propanenitrile (66b)

A solution of 2-chlorobenzaldehyde (50 mmol, 7.02g), acrylonitrile (75 mmol, 3.975g), and DABCO (15 mol%, 7.5 mmol, 0.841g) was kept at room temperature for 3 days. The reaction mixture was diluted with 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 residue thus obtained was purified by column chromatography to provide the desired product as colorless liquid.

Reaction time : 3 days



Yield (%) : 75 (7.26 g)

IR (KBr) : ν 3456, 2229, 1615 cm^{-1}

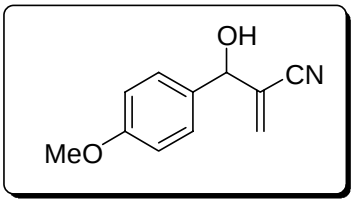
^{1}H NMR (400 MHz) : δ 2.64 (s, 1H), 5.77 (s, 1H), 6.07 (s, 2H), 7.27-7.43 (m, 3H), 7.62 (dd, 1H, J = 1.6 Hz & 7.6 Hz)

^{13}C NMR (100 MHz) : δ 70.32, 116.70, 124.51, 127.51, 127.91, 129.66, 129.93, 131.51, 132.49, 136.43

3-Hydroxy-3-(4-methoxyphenyl)-2-methylene-propanenitrile (66d)

This compound was prepared *via* the DABCO catalyzed Baylis-Hillman reaction of 4-methoxybenzaldehyde with acrylonitrile following the similar procedure as described for **66b** as colorless liquid.

Reaction time : 4 days



Yield (%) : 66

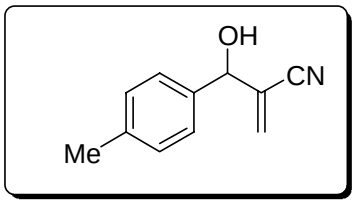
IR (neat) : ν 3445, 2227, 1610 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.38 (bs, 1H), 3.81 (s, 3H), 5.25 (s, 1H), 6.02 (s, 1H), 6.11 (s, 1H), 6.92 (d, 2H, J = 8.8 Hz), 7.31 (d, 2H, J = 8.8 Hz)

^{13}C NMR (100 MHz) : δ 55.29, 73.56, 114.22, 117.10, 126.31, 127.92, 129.59, 131.36, 159.85

3-Hydroxy-2-methylene-3-(4-methylphenyl)propanenitrile (66a)

This compound was prepared via the DABCO catalyzed Baylis-Hillman reaction between 4-methylbenzaldehyde and acrylonitrile following the similar procedure as described for **66b** as colorless liquid.



Reaction time : 4 days

Yield (%) : 66

IR (neat) : ν 3445, 2227, 1614 cm^{-1}

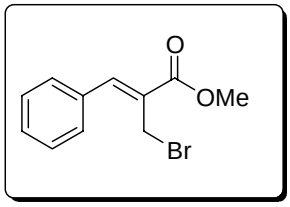
^{1}H NMR (400 MHz) : δ 2.35 (s, 3H), 2.83 (bs, 1H), 5.22 (s, 1H), 5.99 (s, 1H), 6.07 (s, 1H), 7.19 (d, 2H, J = 8.0 Hz), 7.25 (d, 2H, J = 8.0 Hz)

^{13}C NMR (100 MHz) : δ 21.10, 73.74, 117.05, 126.25, 126.44, 129.46, 129.71, 136.22, 138.61

Methyl (2*Z*)-2-bromomethyl-3-phenylprop-2-enoate (47a)

To a stirred solution of methyl 3-hydroxy-2-methylene-3-phenylpropanoate (50 mmol, 9.61 g) in CH_2Cl_2 (100 mL) was added HBr (48 %, 100 mmol, 8.091 g) followed by dropwise addition of conc. H_2SO_4 (50 mmol, 4.90 g) at 0 ^{o}C. After stirring at room

temperature for 12 h, reaction mixture was poured into ice-cold water (20 mL). Organic layer was separated and the aqueous layer was extracted with ether (3 x 25 mL). Combined organic layer was washed with water, saturated $NaHCO_3$ solution and water and dried over anhydrous Na_2SO_4. Solvent was evaporated and the crude product, thus obtained, was purified by column chromatography (silica gel, 2 % ethyl acetate in hexanes) , to afford the allyl bromide as a colorless liquid in 90% isolated yield (11.51 g).



IR (neat) : ν 1720, 1626 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.88 (s, 3H), 4.39 (s, 2H), 7.38-7.51 (m, 3H), 7.58, (d, 2H, J = 7.2 Hz), 7.83 (s, 1H)

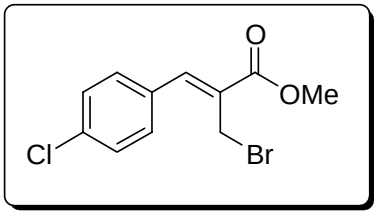
^{13}C NMR (100 MHz) : δ 26.73, 52.38, 128.57, 128.56, 129.56, 134.12, 142.86, 166.50

Methyl (2*Z*)-2-bromomethyl-3-(4-chlorophenyl)prop-2-enoate (47c)

This compound was prepared *via* the treatment of methyl 3-(4-chlorophenyl)-3-hydroxy-2-methylenepropanoate with HBr (48%) in the presence of conc. H_2SO_4, following the similar procedure as described for **47a** as a colorless liquid.

Reaction time : 12 h

Yield (%) : 86



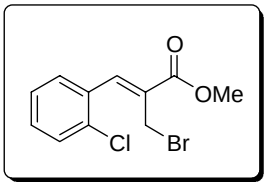
IR (Neat) : ν 1720, 1626 cm^{-1}

^1H NMR (400 MHz) : δ 3.89 (s, 3H), 4.36 (s, 2H), 7.44 (d, 2H, J = 8.4 Hz), 7.52 (d, 2H, J = 8.4 Hz), 7.76 (s, 1H)

^{13}C NMR (100 MHz) : δ 26.38, 52.66, 129.29, 131.01, 132.70, 135.84, 141.63, 166.48

Methyl (2*Z*)-2-bromomethyl-3-(2-chlorophenyl)prop-2-enoate (47b)

Treatment of Methyl 3-(2-chlorophenyl)-3-hydroxy-2-methylenepropanoate with HBr (48%) in the presence of conc. H_2SO_4, following the similar procedure as described for **47a**, provided the allyl bromide as colorless viscous liquid.



Reaction time : 12 h

Yield (%) : 86

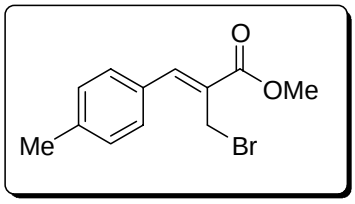
IR (neat) : ν 1716, 1624 cm^{-1}

^1H NMR (400 MHz) : δ 3.90 (s, 3H), 4.27 (s, 2H), 7.32-7.42 (m, 2H), 7.43-7.47 (m, 1H), 7.71 (dd, 1H, J = 2.0 Hz & 7.2 Hz) 7.92 (s, 1H)

^{13}C NMR (100 MHz) : δ 26.24, 52.58, 127.02, 129.56, 129.83, 130.48, 130.59, 132.84, 134.50, 139.51, 166.05

Methyl (2Z)-2-bromomethyl-3-(4-methylphenyl)prop-2-enoate (47d)

This compound was prepared as a colorless liquid via the reaction of methyl 3-hydroxy -2-methylene-3-(4-methylphenyl) propanoate with HBr (48%) in the presence of conc. H_2SO_4, following the similar procedure as described for **47a.**



Reaction time : 12 h

Yield (% : 82

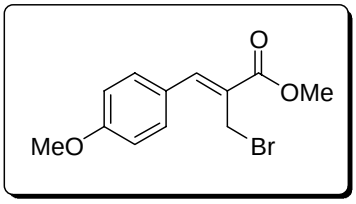
IR (neat) : ν 1716, 1626 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.40 (s, 3H), 3.88 (s, 3H), 4.42 (s, 2H), 7.27 (d, 2H, J = 8.0 Hz), 7.49 (d, 2H, J = 8.0 Hz), 7.80 (s, 1H)

^{13}C NMR (100 MHz) : δ 21.50, 27.16, 52.45, 127.68, 129.69, 129.91, 131.42, 140.16, 143.19, 166.83

Methyl (2*Z*)-2-bromomethyl-3-(4-methoxyphenyl)prop-2-enoate (47e)

Reaction of methyl 3-(4-methoxyphenyl)-3-hydroxy-2-methylenepropanoate with HBr (48 %) in the presence of conc. H_2SO_4, following the similar procedure as described for **47a**, afforded the title compound as colorless liquid.



Reaction time : 12 h

Yield (%) : 83

IR (neat) : ν 1705, 1611 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.86 (s, 3H), 3.87 (s, 3H), 4.44 (s, 2H), 6.99 (d, 2H, J = 8.8 Hz), 7.58 (d, 2H, J = 8.8 Hz), 7.78 (s, 1H)

^{13}C NMR (100 MHz) : δ 27.58, 52.38, 55.39, 114.45, 126.11, 126.72, 132.01, 142.96, 160.86, 166.94

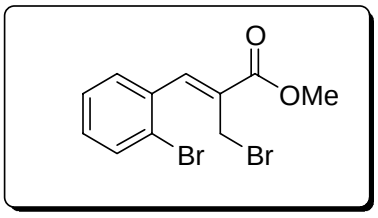
Methyl (2*Z*)-2-bromomethyl-3-(2-bromophenyl)prop-2-enoate (47f)

Treatment of Methyl 3-(2-bromophenyl)-3-hydroxy-2-methylenepropanoate with HBr (48%) in the presence of conc. H_2SO_4, following the similar procedure as described for **47a**, provided the allyl bromide as colorless viscous liquid.

Reaction time : 12 h

Yield (%) : 86

IR (neat) : ν 1712, 1626 cm^{-1}

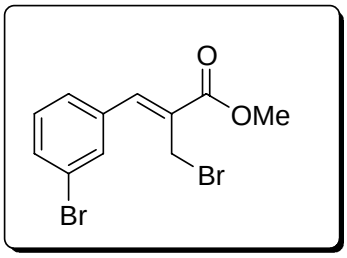


^{1}H NMR (400 MHz) : δ 3.91 (s, 3H), 4.25 (s, 2H), 7.24-7.31 (m, 1H), 7.44 (d, 1H, J = 7.2 Hz), 7.65 (d, 1H, J = 8.0 Hz), 7.69 (d, 1H, J = 8.0 Hz), 7.86 (s, 1H)

^{13}C NMR (100 MHz) : δ 26.25, 52.65, 124.48, 127.64, 129.64, 130.26, 130.72, 133.05, 134.73, 141.74, 166.08

Methyl (2Z)-2-bromomethyl-3-(3-bromophenyl)prop-2-enoate (47g)

Treatment of Methyl 3-(3-bromophenyl)-3-hydroxy-2-methylenepropanoate with HBr (48%) in the presence of conc. H_2SO_4, following the similar procedure as described for **47a**, provided the allyl bromide as colorless viscous liquid.



Reaction time : 12 h

Yield (%) : 86 (7.49 g)

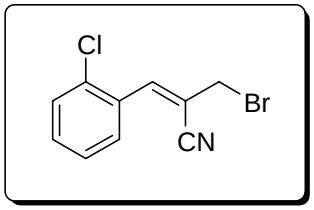
IR (neat) : ν 1712, 1622 cm^{-1}

^1H NMR (400 MHz) : δ 3.89 (s, 3H), 4.35 (s, 2H), 7.31-7.37 (m, 1H), 7.50-7.57 (m, 2H), 7.70 (s, 1H), 7.75 (s, 1H)

^{13}C NMR (100 MHz) : δ 26.06, 52.67, 122.96, 127.87, 130.03, 130.44, 132.34, 132.50, 136.23, 141.09, 166.22

2-(Bromomethyl)-3-(2-chlorophenyl)prop-2-enenitrile (48b)

This compound was prepared *via* the treatment of 3-(2-chlorophenyl)-3-hydroxy-2-methylenepropanenitrile with HBr (48%) in the presence of conc. H_2SO_4, following the similar procedure as described for **47a**. The product was obtained as mixture of *E:Z* isomers, which were subjected to crystallization to afford the one pure *E*- isomer.



Reaction time : 12 h

Yield (%) : 87

IR (KBr) : ν 2212, 1618 cm^{-1}

^{1}H NMR (400 MHz) : δ 4.25 (s, 2H), 7.34-7.51 (m, 3 H), 7.60 (s, 1H), 8.01-8.08 (m, 1H)

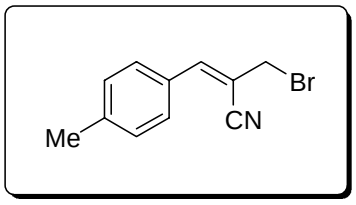
^{13}C NMR (100 MHz) : δ 31.88, 111.27, 116.42, 127.34, 129.24, 129.96, 130.72, 132.07, 134.59, 142.69

2-(Bromomethyl)-3-(4-methylphenyl)prop-2-enenitrile (48a)

This compound was prepared *via* the treatment of 3-Hydroxy-2-methylene-3-(4-methyl phenyl)propanenitrile with HBr (48%) in the presence of conc. H_2SO_4, following the similar procedure as described for **47a**. The product was obtained as mixture of *E:Z* isomer, which were subjected to crystallization to afford the one pure *E*- isomer.

Reaction time : 12 h

Yield (%) : 79



IR (KBr) : ν 2212, 1604 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.40 (s, 3H), 4.22 (s, 2H), 7.17 (s, 1H), 7.25 (d, 2H, J = 8.0 Hz), 7.70 (d, 2H, J = 8.0 Hz)

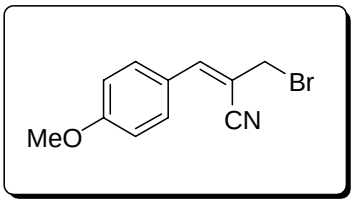
^{13}C NMR (100 MHz) : δ 21.61, 33.14, 106.56, 117.34, 129.28, 129.66, 129.74, 142.15, 146.58

2-(Bromomethyl)-3-(4-methoxyphenyl)prop-2-enenitrile (48d)

This compound was prepared *via* the treatment of 3-Hydroxy-2-methylene-3-(4-methoxy phenyl)propanenitrile with HBr (48%) in the presence of conc. H_2SO_4, following the similar procedure as described for **47a**. The product was obtained as mixture of *E:Z* isomer, which were subjected to crystallization to afford the one pure *E*- isomer.

Reaction time : 12 h

Yield (%) : 79



IR (KBr) : ν 2214, 1601 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.86 (s, 3H), 4.22 (s, 2H), 6.95 (d, 2H, J = 8.8 Hz), 7.13 (s, 1H), 7.79 (d, 2H, J = 8.8 Hz)

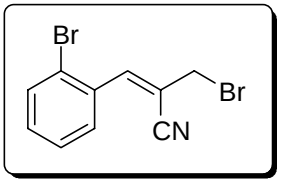
^{13}C NMR (100 MHz) : δ 33.59, 55.40, 104.45, 114.34, 117.64, 124.98, 131.17, 146.14, 161.94

2-(Bromomethyl)-3-(2-bromophenyl)prop-2-enenitrile (48e)

This compound was prepared *via* the treatment of 3-hydroxy-2-methylene-3-(2-bromophenyl)propanenitrile with HBr (48%) in the presence of conc. H_2SO_4, following the similar procedure as described for **47a**. The product was obtained as mixture of *E:Z* isomer, which were subjected to crystallization to afford the one pure *E*- isomer.

Reaction time : 12 h

Yield (%) : 87



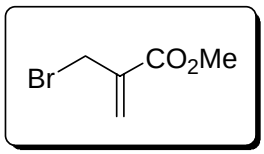
IR (KBr) : ν 2218, 1618 cm^{-1}

^1H NMR (400 MHz) : δ 4.25 (s, 2H), 7.28-7.34 (m, 1H), 7.43 (t, 1H, J = 7.6 Hz), 7.55 (s, 1H), 7.65 (d, 1H, J = 8.0 Hz), 7.98 (d, 1H, J = 8.0 Hz)

^{13}C NMR (100 MHz) : δ 31.69, 111.41, 116.31, 124.71, 127.92, 129.53, 132.12, 132.49, 133.18, 145.22

Methyl 2-(bromomethyl)prop-2-enoate (46)

Methyl 2-(hydroxymethyl)prop-2-enoate (60 mmol, 6.96) was dissolved in DCM (50 mL) and PBr_3 (150 mmol, 40.6 g) was added drop wise with stirring at room temperature. After 12 h, the reaction mixture was poured into ice cold water. Then the reaction mixture was extracted with ether (3 x 40 mL). The combined organic layer was dried over anhydrous Na_2SO_4, solvent was evaporated and the crude product thus obtained was purified by distillation.



Yield (%) : 70 (7.5g)

IR (neat) : ν 1739 cm^{-1}

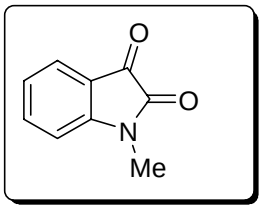
^1H NMR (400 MHz) : δ 3.82 (s, 3H), 4.19 (s, 2H), 5.97 (s, 1H), 6.34 (s, 1H)

^{13}C NMR (100 MHz) : δ 29.22, 52.20, 129.15, 137.24, 165.20

1-Methylisatin (59a)

This compound was prepared following the known procedure[198]

A stirred suspension of isatin (100 mmol, 14.713 g) and powdered CaH_2 (300 mmol, 12.6 g) in DMF (100 mL) was heated at 40-50 ^oC for 20 minutes. Methyl iodide (500 mmol, 70.9 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 solution and aq. NaCl solution was added. Reaction mixture was extracted with ethyl acetate (3 X 100 mL), combined organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and the crude product thus obtained was subjected to crystallization which afforded the desired product in 70% yield as brick red solid.



Yield (%) : 70

M.P : 131-133 ºC (lit.[198] 133-134 ºC)

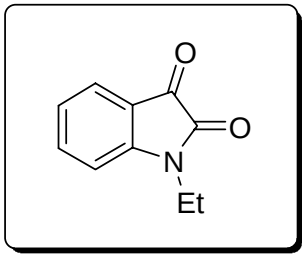
IR (KBr) : ν 1745, 1726, 1606 cm^{-1}

^1H NMR (400 MHz) : δ 3.26 (s, 3H), 6.90 (d, 1H, J = 7.6 Hz), 7.10-7.18 (m, 1H), 7.58-7.66 (m, 2H)

^{13}C NMR (100 MHz) : δ 25.90, 109.90, 116.94, 123.52, 124.68, 138.35, 151.10, 157.87, 183.11

1-Ethylisatin (59b)

This compound was obtained *via* the reaction between isatin and ethyl bromide in the presence of CaH_2, following the similar procedure as described for the compound **59a**, as orange solid.



Reaction time : 12 h

M.P : 86-88 ºC (lit[198] 86-87 ºC)

Yield (%) : 80

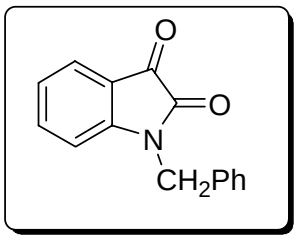
IR (KBr) : *v* 1734, 1720, 1608 cm^{-1}

^1H NMR (400 MHz) : δ 1.32 (t, 3H, *J* = 7.2 Hz), 3.80 (q, 2H, *J* = 7.2 Hz), 6.92 (d, 1H, *J* = 7.6 Hz), 7.08-7.13 (m, 1H), 7.56-7.63 (m, 2H)

^{13}C NMR (100 MHz) : δ 12.26, 34.69, 109.99, 117.22, 123.39, 125.01, 138.31, 150.37, 157.59, 183.49

1-Benzylisatin (59h)

This compound was obtained *via* the reaction between isatin and benzyl bromide in the presence of CaH_2, following the similar procedure as described for the compound **59a**, as orange solid.



Reaction time : 12 h

M.P : 128-130 ºC (lit[198] 133-134 ºC)

Yield (%) : 69

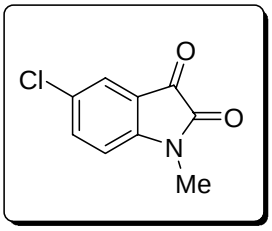
IR (KBr) : ν 1731, 1611 cm^{-1}

^{1}H NMR (400 MHz) : δ 4.94 (s, 2H), 6.80 (d, 1H, J = 8.0 Hz), 7.08-7.13 (m, 1H), 7.27-7.38 (m, 5H), 7.47-7.52 (m, 1H), 7.60 (d, 1H, J = 7.2 Hz)

^{13}C NMR (100 MHz) : δ 44.00, 111.04, 117.62, 123.87, 125.37, 127.42, 128.14, 129.03, 134.50, 138.38, 150.69, 158.27, 183.26

5-Chloro-1-methylisatin (59c)

Reaction between 5-chloroisatin and methyl iodide in the presence of CaH_2, following the similar procedure as described for the compound **59a**, provided the desired product as red solid.



Reaction time : 12 h

M.P : 170-172 ºC (lit[198] 172-174 ºC)

Yield (%) : 72

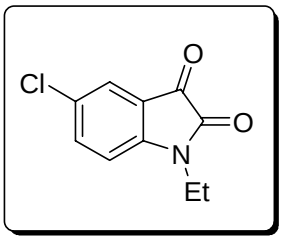
IR (KBr) : ν 1745, 1734, 1608 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.25 (s, 3H), 6.86 (d, 1H, J = 8.8 Hz), 7.55-7.62 (m, 2H)

^{13}C NMR (100 MHz) : δ 26.37, 111.34, 118.17, 125.09, 129.60, 137.80, 149.70, 157.65, 182.36

5-Chloro -1-ethylisatin (59d)

This compound was obtained *via* the treatment of 5-chloroisatin with ethyl bromide in the presence of CaH_2, following the similar procedure as described for the compound **59a**, as brick red solid.



Reaction time : 12 h

M.P : 131-133 ºC

Yield (%) : 72

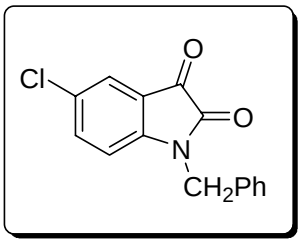
IR (KBr) : *v* 1736, 1608 cm^{-1}

^1H NMR (400 MHz) : δ 1.31 (t, 3H, *J* = 7.2 Hz), 3.79 (q, 2H, *J* = 7.2 Hz), 6.88 (d, 1H, *J* = 9.2 Hz), 7.52-7.59 (m, 2H)

^{13}C NMR (100 MHz) : δ 12.28, 28.99, 111.44, 118.18, 124.98, 129.13, 137.64, 148.80, 157.14, 182.58

5-Chloro -1-benzylisatin (59i)

This compound was obtained *via* the treatment of 5-chloroisatin with benzyl bromide in the presence of CaH_2, following the similar procedure as described for the compound **59a**, as brick red solid.



Reaction time : 12 h

M.P : 140-142 ºC

Yield (%) : 65

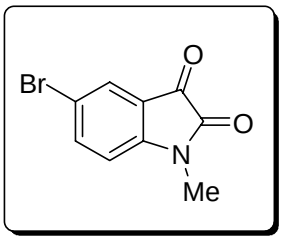
IR (KBr) : ν 1753, 1736, 1600 cm^{-1}

^1H NMR (400 MHz) : δ 4.93 (s, 2H), 6.72 (d, 1H, J = 8.4 Hz), 7.27-7.40 (m, 5H), 7.43 (dd, 1H, J = 0.4 Hz & 8.4 Hz), 7.58 (d, 1H, J = 2.0 Hz)

^{13}C NMR (100 MHz) : δ 44.22, 112.38, 118.53, 125.32, 127.44, 128.39, 129.20, 129.78, 134.10, 137.72, 148.99, 157.77, 182.30

5-Bromo-1-methylisatin (59e)

This compound was obtained *via* the reaction between 5-bromoisatin and methyl iodide in the presence of CaH_2, following the similar procedure as described for the compound **59a**, as red solid.



Reaction time : 12 h

Yield (%) : 72

M.P : 180-182 ºC

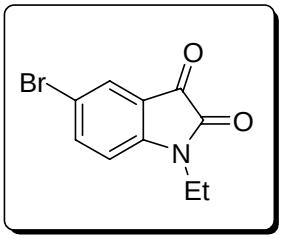
IR (KBr) : ν 1749, 1724, 1606 cm^{-1}

^1H NMR (400 MHz) : δ 3.26 (s, 3H), 6.81 (dd, 1H, J = 0.4 Hz & 8.0 Hz), 7.68-7.73 (m, 2H)

^{13}C NMR (100 MHz) : δ 26.45, 111.68, 116.77, 118.69, 128.19, 140.67, 150.22, 157.58, 182.23

5-Bromo -1-ethylisatin (59f)

This compound was obtained *via* the reaction between 5-bromoisatin and ethyl bromide in the presence of CaH_2, following the similar procedure as described for the compound **59a**, as red solid.



Reaction time : 12 h

Yield (%) : 72

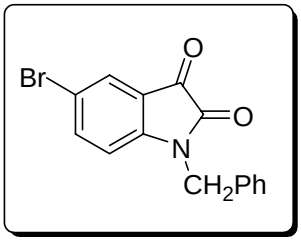
IR (KBr) : *v* 1734, 1602 cm^{-1}

^1H NMR (400 MHz) : δ 1.31 (t, 3H, *J* = 7.2 Hz), 3.79 (q, 2H, *J* = 7.2 Hz), 6.83 (d, 1H, *J* = 8.4 Hz), 7.71 (s, 2H)

^{13}C NMR (100 MHz) : *δ* 12.41, 35.11, 111.82, 116.38, 118.72, 128.13, 140.56, 149.34, 157.11, 182.52

5-Bromo -1-benzylisatin (59j)

This compound was obtained *via* the treatment of 5-bromoisatin with benzyl bromide in the presence of CaH_2, following the similar procedure as described for the compound **59a**, as brick red solid.



Reaction time : 12 h

Yield (%) : 68%

M.P : 150-152 ºC

IR (KBr) : ν 1753, 1731, 1600 cm^{-1}

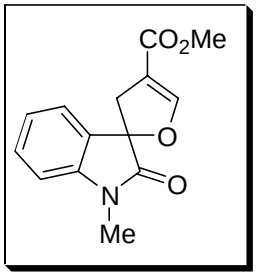
^{1}H NMR (400 MHz) : δ 4.92 (s, 2H), 6.68 (d, 1H, J = 8.4 Hz), 7.28-7.39 (m, 5H), 7.58 (dd, 1H, J = 0.4 Hz & 8.4 Hz), 7.69 (d, 1H, J = 2.0 Hz)

^{13}C NMR (100 MHz) : δ 44.19, 112.79, 116.80, 118.85, 127.43, 128.18, 128.39, 129.19, 134.05, 140.57, 149.40, 157.56, 182.13

Representative procedure: Synthesis of (1-Methylindolin-2-one)-3-spiro-2´-[4´-methoxycarbonyl -2´, 3´-dihydrofuran] (61a)

To a stirred solution of methyl 2-(bromomethyl)prop-2-enoate **46** (3.0 mmol, 0.537 g) in DMF (5 mL) were added dimethyl sulfide (4.0 mmol, 0.248 g, 0.3 mL), Cs_2CO_3 (4.0 mmol, 1.303 g) and 1-methylisatin **59a** (2.0 mmol, 0.322 g) at 15- 20 $^{\circ}$C. After stirring for 8 h at the same temperature the reaction mixture was diluted with water (3 mL) and extracted with EtOAc (3x10 mL). Combined organic layer was washed with water (2 x 5 mL) and dried over anhydrous Na_2SO_4. Solvent was evaporated and the crude, thus obtained was purified by column chromatography (silica gel, 20% ethyl acetate in hexanes) to provide **61a** in 83% (0.431 g) yield as a white solid.

Reaction time : 8 h



Yield (%) : 83

M.P. :124-126 ^{o}C

IR (KBr) : *v* 1732, 1708, 1631, 1612 cm^{-1}

^{1}H NMR ($CDCl_3$, 400 MHz) : δ 3.11 & 3.37 (dABq, 2H, *J* = 2.0 & 15.2 Hz), 3.21 (s, 3H), 3.76 (s, 3H), 6.83-6.87 (m, 1H), 7.08-7.14 (m, 1H), 7.34-7.41 (m, 3H)

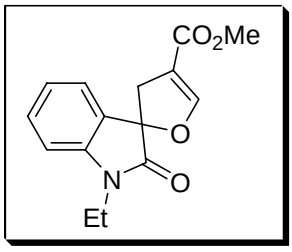
^{13}C NMR ($CDCl_3$, 100 MHz) : δ 26.36, 37.06, 51.30, 86.98, 108.68, 109.01, 123.61, 123.93, 128.66, 130.97, 143.42, 155.70, 164.50, 173.75

HRMS calc'd for $C_{14}H_{13}NO_4$ + Na (M + Na), 282.0742; Found: 282.0697.

(1-Ethylindolin-2-one)-3-spiro-2´-[4´-methoxycarbonyl-2´, 3´-dihydrofuran] (61b)

This compound was prepared *via* [3+2] Cycloaddition reaction between 1-ethylisatin with methyl 2-(bromomethyl)prop-2-enoate, following the similar procedure described for **61a** as a white solid.

Reaction time : 8 h



Yield (%) :78

M.P :102-104 ^{o}C

IR (KBr) : *v* 1720, 1705, 1631, 1612 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.29 (t, 3H, J = 7.2 Hz), 3.10 & 3.37 (dABq, 2H, J = 1.6 & 15.2 Hz), 3.68-3.81 (m*, 5H), 6.87 (d, 1H, J = 8.0 Hz), 7.06-7.12 (m, 1 H), 7.34-7.42 (m, 3 H)

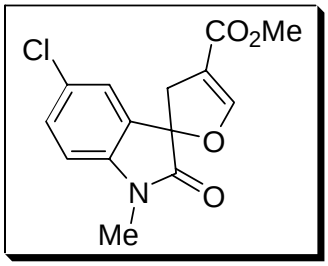
^{13}C NMR (100 MHz) : δ 12.52, 34.99, 37.13, 51.36, 87.05, 108.86, 109.07, 123.47, 124.21, 128.98, 130.96, 142.60, 155.77, 164.60, 173.45

HRMS calc'd for $C_{15}H_{15}NO_4$ + Na (M + Na), 296.0899 ; Found , 296.0899.

* This multiplet contains one singlet for three protons and a multiplet for two protons.

(1-Methyl-5-chloroindolin-2-one)-3-spiro-2´-[4´-methoxycarbonyl-2´,3´-dihydrofuran] (61c)

This compound was prepared *via* [3+2] Cycloaddition reaction between 5-chloro-1-methylisatin with methyl 2-(bromomethyl)prop-2-enoate, following the similar procedure described for **61a** as a white solid.



Reaction time : 8 h

Yield (%) : 78

M.P. :113-115 ^{o}C

IR (KBr) : ν 1741, 1705, 1630, 1614 cm^{-1}

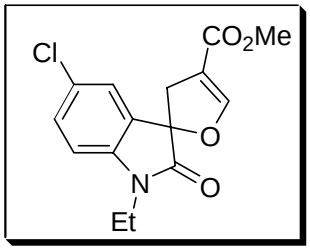
^{1}H NMR (400 MHz) : δ 3.09 & 3.37 (dABq, 2H, J = 2.0 & 15.2 Hz), 3.21 (s, 3H), 3.77 (s, 3 H), 6.78 (d, 1H, J = 7.6 Hz), 7.31-7.42, (m, 3 H)

^{13}C NMR (100 MHz) : δ 26.50, 37.17, 51.37, 86.54, 109.07, 109.75, 124.45, 128.85, 130.11, 130.79, 141.90, 155.44, 164.23, 173.29

HRMS calc'd for $C_{14}H_{12}ClNO_4$ + Na (M + Na), 316.0353 ; Found: 316.0355.

(1-Ethyl–5-chloroindolin-2-one)-3-spiro-2´-[4´-methoxycarbonyl-2´,3´-dihydrofuran] (61d)

This compound was prepared *via* [3+2] Cycloaddition reaction between 5-chloro-1-ethylisatin with methyl 2-(bromomethyl)prop-2-enoate, following the similar procedure described for **61a** as a white solid.



Reaction time : 8 h

Yield (%) : 82%

M.P. :102-104 ^{o}C

IR (KBr) : ν 1728, 1705, 1633, 1614 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.28 (t, 3H, J = 7.2 Hz), 3.08 & 3.97 (dABq, 2H, J = 2.0 & 15.2 Hz), 3.67-3.80 (m*, 5H), 6.80 (d, 1H, J = 8.4 Hz), 7.30-7.41 (m, 3H)

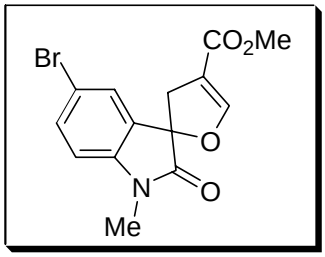
^{13}C NMR (100 MHz) : δ 12.33, 35.06, 37.16, 51.30, 86.52, 109.04, 109.83, 124.61, 128.61, 130.38, 130.70, 141.02, 155.42, 164.20, 172.89

HRMS calc'd for $C_{15}H_{14}ClNO_4$ + Na (M + Na), 330.0509; Found: 330.0493.

*This multiplet contains one singlet for three protons and multiplet for two protons

(1-Methyl-5-bromoindolin-2-one)-3-spiro-2´-[4´-methoxycarbonyl-2´,3´-dihydrofuran] (61e)

This compound was prepared *via* [3+2] Cycloaddition reaction between 5-bromo-1-methylisatin with methyl 2-(bromomethyl)prop-2-enoate, following the similar procedure described for **61a** as a white solid.



Reaction time : 8 h

Yield (%) : 86%

M.P. :120-122 ^{o}C

IR (KBr) : ν 1739, 1703, 1628, 1610 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.09 & 3.37 (dABq, 2H, J = 2.0 & 15.2 Hz), 3.20 (s, 3H), 3.77 (s, 3 H), 6.74 (dd, 1H, J = 2.0 & 6.8 Hz), 7.38, (t, 1H, J = 2.0 Hz), 7.49 (s, 1H), 7.50 (dd*, 1H, J = 2.0 & 7.2 Hz)

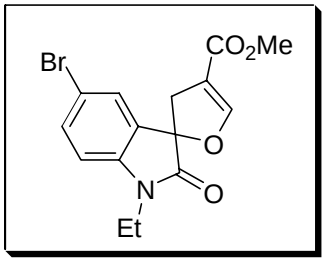
^{13}C NMR (100 MHz) : δ 26.44, 37.14, 51.32, 86.43, 109.03, 110.20, 115.92, 127.12, 130.41, 133.65, 142.37, 155.38, 164.16, 173.11

HRMS calc'd for $C_{14}H_{12}BrNO_4$ + Na (M + Na), 359.9847; Found: 359.9849.

*One of the peaks of dd merged with singlet at δ 7.49.

(1-Ethyl-5-bromoindolin-2-one)-3-spiro-2´[4´-methoxycarbonyl-2´,3´-dihydrofuran] (61f)

This compound was prepared *via* [3+2] Cycloaddition reaction between 5-bromo-1-ethylisatin with methyl 2-(bromomethyl)prop-2-enoate, following the similar procedure described for **61a** as a white solid.



Reaction time : 8 h

Yield (%) : 81%

M.P. :126-128 ^{o}C

IR (KBr) : *v* 1730, 1712, 1637, 1608 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.27 (t, 3H, *J* = 7.2 Hz), 3.09 & 3.37 (dABq, 2H, *J* = 1.6 & 15.2 Hz), 3.68-3.79 (m*, 5H), 6.76 (d, 1H, *J* = 8.0 Hz), 7.38 (t, 1H, *J* = 2.0 Hz)**,** 7.48 (d, 1H, *J* = 2.0 Hz), 7.50 (s, 1H)

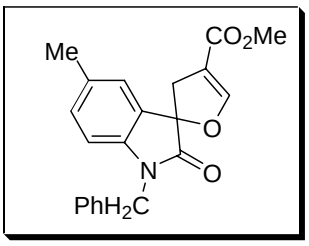
^{13}C NMR (100 MHz) : δ 12.41, 35.14, 37.26, 51.42, 86.54, 109.14, 110.37, 115.86, 127.47, 130.84, 133.70, 141.60, 155.50, 164.31, 172.89

HRMS calc'd for $C_{15}H_{14}BrNO_4$ + Na (M + Na), 374.0004; Found: 374.0006.

* This multiplet contains one singlet for three protons and multiplet for two protons.

(1-Benzyl-5-methylindolin-2-one)-3-spiro-2´-[4´-methoxycarbonyl-2´, 3´-dihydrofuran] (61g)

This compound was prepared *via* [3+2] Cycloaddition reaction between 5-methyl-1-benzylisatin with methyl 2-(bromomethyl)prop-2-enoate, following the similar procedure described for **61a** as a white solid.



Reaction time : 8 h

Yield (%) : 80%

M.P. : 116-118 ^{o}C

IR (KBr) : *v* 1722, 1705, 1628, 1610 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.29 (s, 3H), 3.14 & 3.44 (dABq, 2H, *J* = 2.0 & 15.2 Hz), 3.77 (s, 3H), 4.84 & 4.90 (ABq, 2H, *J* = 15.6 Hz), 6.60 (d, 1H, *J* = 8.0 Hz), 7.03 (dd, 1H, *J* = 0.8 & 8.0 Hz), 7.21 (d, 1H, *J* = 0.4 Hz), 7.24-7.36 (m, 5 H), 7.43, (t, 1H, *J* = 2.0 Hz)

^{13}C NMR (100 MHz) : δ 20.91, 37.29, 43.88, 51.33, 87.24, 109.09, 109.51, 124.79, 127.20, 127.78, 128.71, 128.85, 131.10, 133.44, 135.13, 140.08, 155.76, 164.56, 173.95

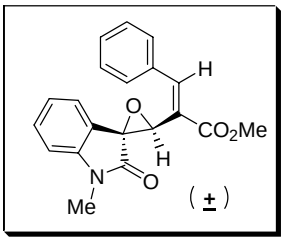
HRMS calc'd for $C_{21}H_{19}NO_4$ + Na (M + Na), 372.1212; Found , 372.1254.

NOTE: We have kept [3R(2´R), 3´S]/ [3S(2´S), 3´R]- before the names of the compounds 63a-j and [3S(2´S), 3´S]/ [3R(2´R), 3´R]- before the names of the compounds 64a-j to indicate the racemic nature and also stereochemistry.

Representative procedure: Synthesis of 63 and 64

To a stirred solution of methyl (2*Z*)-2-bromomethyl-3-phenylprop-2-enoate **47a** (3.0 mmol, 0.765 g) in DMF (5 mL) were added dimethyl sulfide (4.0 mmol, 0.248 g, 0.30 mL), Cs_2CO_3 (4.0 mmol, 1.303 g) and 1-methylisatin **59a** (2.0 mmol, 0.322 g) at 15-20 °C. After stirring for 8 h at same temperature the reaction mixture was diluted with water (3 mL) and extracted with EtOAc (3x10 mL). Combined organic layer was washed with water (2 x 5 mL) and dried over anhydrous Na_2SO_4. Solvent was evaporated and the crude, thus obtained was purified by careful column chromatography (silica gel, 20 % ethyl acetate in hexanes) to provide **63a** (27%, 0.180 g), and **64a** (46%, 0.310 g) as white solids (73% overall yield).

[3*R*(2´*R*), 3´*S*]/ [3*S*(2´S), 3´*R*]-(1-Methylindolin-2-one)-3-spiro-2´-[3´-{(*E*)-1-methoxy-carbonyl-2-phenyl}ethenyloxirane] (63a)



Yield (%) : 27; white solid

M.P. :136-138 °C

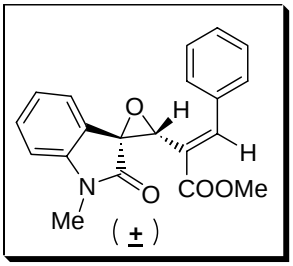
IR (KBr) : *ν* 1738, 1707, 1620 cm^{-1}

^{1}H NMR (400 MHz) : *δ* 3.19 (s, 3H), 3.69 (s, 3H), 4.67 (d, 1H, *J* = 1.6 Hz), 6.65 (d, 1H, *J* = 7.6 Hz), 6.79 (dd, 1H, *J* = 0.8 & 7.6 Hz), 6.84-6.91 (m, 1H), 7.15-7.36 (m, 6H), 7.91 (s, 1H)

^{13}C NMR (100 MHz) : *δ* 26.40, 52.16, 60.52, 62.61, 108.30, 120.59, 122.29, 122.92, 124.13, 128.04, 129.49, 129.66, 129.93, 133.38, 144.41, 145.00, 166.37, 171.18

HRMS calc'd for $C_{20}H_{17}NO_4$ + Na (M + Na), 358.1055 ; Found: 358.1065.

[3*S*(2´*S*), 3´*S*]/ [3*R*(2´*R*), 3´*R*]-(1-Methylindolin-2-one)-3-spiro-2´-[3´-{(*E*)-1-methoxy-carbonyl-2-phenyl}ethenyloxirane] (64a)



Yield (%) : 46; white solid

M.P. : 160-162 ^oC

IR (KBr) : ν 1724, 1620 cm^{-1}

^1H NMR (400 MHz) : δ 2.89 (s, 3H), 3.83 (s, 3H), 4.54 (d, 1H, J = 1.2 Hz), 6.78 (d, 1H, J = 8.0 Hz), 7.06-7.13 (m, 1H), 7.16-7.30 (m, 4H), 7.33-7.41 (m, 3H), 7.93 (s, 1H)

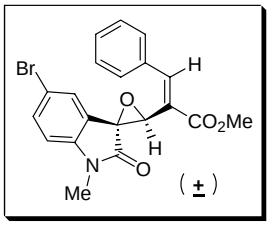
^{13}C NMR (100 MHz) : δ 26.02, 52.04, 61.08, 62.23, 108.37, 121.57, 122.37, 122.42, 123.44, 128.09, 129.31, 129.94, 130.26, 133.80, 144.20, 144.61, 166.38, 169.46

HRMS calc'd for $C_{20}H_{17}NO_4$+ Na (M + Na), 358.1055; Found: 358.1063.

63b &64b:-

These compounds were prepared *via* cycloaddition reaction between 5-bromo-1-methylisatin with methyl (2*Z*)-2-bromomethyl-3-phenylprop-2-enoate, following the similar procedure described for **63a & 64a**.

[3*R*(2´*R*), 3´*S*]/ [3*S*(2´*S*), 3´*R*]-(1-Methyl-5-bromoindolin-2-one)-3-spiro-2´-[3´-{(*E*)-1-methoxycarbonyl-2-phenyl}ethenyloxirane] (63b)



Yield (%) : 30; white solid

M.P. : 161-163 ^{o}C

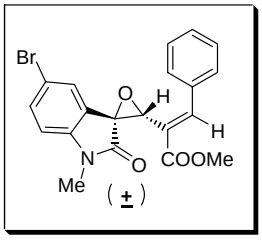
IR (KBr) : ν 1722, 1640 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.16 (s, 3H), 3.78 (s, 3H), 4.66 (d, 1H, J = 1.2 Hz), 6.48 (d, 1H, J = 8.4 Hz), 6.87 (d, 1H, J = 2.0 Hz), 7.18-7.23 (m, 5H), 7.28 (dd, 1 H, J = 2.0 & 8.4 Hz), 7.95 (s, 1H)

^{13}C NMR (100 MHz) : δ 26.49, 52.35, 60.80, 62.05, 109.72, 114.95, 122.76, 123.82, 126.00, 128.09, 129.40, 129.51, 132.61, 133.49, 143.38, 145.19, 166.15, 170.56

HRMS calc'd for $C_{20}H_{16}BrNO_4$ + Na (M + Na), 436.0160; Found: 436.0176.

[3*S*(2´*S*), 3´*S*]/ [3*R*(2´*R*), 3´*R*]-(1-Methyl-5-bromoindolin-2-one)-3-spiro-2´-[3´-{(*E*)-1-methoxycarbonyl-2-phenyl}ethenyloxirane] (64b)



Yield (%) : 43; white solid

M.P. : 132-134 ^{o} C

IR (KBr) : ν 1720, 1640 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.87 (s, 3H), 3.81 (s, 3H), 4.51 (d, 1H, J = 1.2 Hz), 6.66 (d, 1H, J = 8.0 Hz), 7.18-7.31 (m, 3H), 7.32 (d, 1H, J = 2.0

Hz), 7.37 (d, 2H, *J* = 7.2 Hz), 7.47 (dd, 1H, *J* = 2.0 & 8.0 Hz), 7.94 (s, 1H)

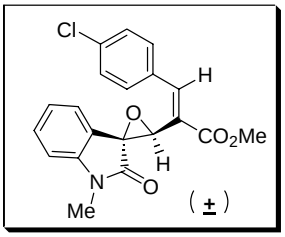
^{13}C NMR (100 MHz) : δ 26.32, 52.26, 61.45, 62.00, 109.95, 115.19, 123.13, 124.73, 125.00, 128.30, 129.57, 130.08, 133.12, 133.87, 143.77, 144.75, 166.39, 169.09

HRMS calc'd for $C_{20}H_{16}BrNO_4$ +Na (M + Na), 436.0160 ; Found: 436.0182.

63c & 64c:-

These compounds were prepared *via* cycloaddition reaction between 1-methylisatin with methyl (2*Z*)-2-bromomethyl-3-(4-chlorophenyl)prop-2-enoate, following the similar procedure described for **63a & 64a**.

[3*R*(2´*R*), 3´*S*]/ [3*S*(2´*S*), 3´*R*]-(1-Methylindolin-2-one)-3-spiro-2´-[3´-{(*E*)-1-methoxy-carbonyl -2-(4-chlorophenyl)}ethenyloxirane] (63c)



Yield (%) : 19; white solid

M.P. : 111-113 ^{o}C

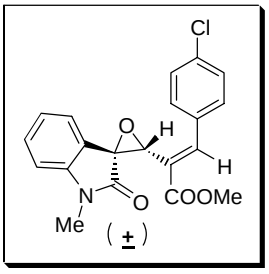
IR (KBr) : *v* 1726, 1703, 1616 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.21 (s, 3H), 3.68 (s, 3H), 4.62 (s, 1H), 6.70 (d, 1H, *J* = 8.0 Hz), 6.75 (d, 1H, *J* = 7.2 Hz), 6.84-6.93 (m, 1H), 7.13-7.31 (m, 5H), 7.86 (s, 1H)

^{13}C NMR (100 MHz) : δ 26.58, 52.39, 60.48, 62.80, 108.45, 120.61, 122.53, 123.04, 124.95, 128.42, 130.24, 130.97, 131.96, 135.72, 143.73, 144.56, 166.23, 171.15

HRMS calc'd for $C_{20}H_{16}ClNO_4$ + Na (M + Na), 392.0666 ; Found: 392.0661.

[3*S*(2´*S*), 3´*S*]/ [3*R*(2´*R*), 3´*R*]-(1-Methylindolin-2-one)-3-spiro -2´-[3´-{(*E*)-1-methoxy-carbonyl -2-(4-chlorophenyl)}ethenyloxirane] (64c)



Yield (%) : 52; brown solid

M.P. : 117-119 ^{o}C

IR (KBr) : ν 1732, 1712, 1620 cm^{-1}

^{1}H NMR ($CDCl_3$, 400 MHz) : δ 2.97 (s, 3H), 3.81 (s, 3H), 4.49 (d, 1H, J = 1.2 Hz), 6.84 (d, 1H, J = 8.0 Hz), 7.06-7.14 (m, 1H), 7.17-7.21 (m, 3H), 7.34 (d, 2H, J = 8.4 Hz), 7.36-7.43 (m, 1H), 7.88 (s, 1H)

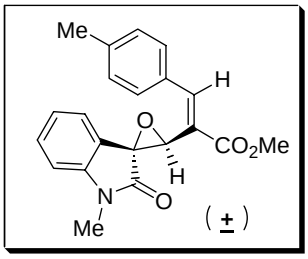
^{13}C NMR ($CDCl_3$, 100 MHz) : δ 26.32, 52.37, 61.14, 62.49, 108.62, 121.87, 122.46, 122.76, 124.27, 128.55, 130.62, 131.45, 132.57, 135.59, 143.12, 144.86, 166.36, 169.66

HRMS calc'd for $C_{20}H_{16}ClNO_4$ + Na (M + Na), 392.0666 ; Found: 392.0667.

63d &64d:

These compounds were prepared *via* cycloaddition reaction between 1-methylisatin with methyl (2*Z*)-2-bromomethyl-3-(4-methylphenyl)prop-2-enoate, following the similar procedure described for **63a & 64a**.

[3*R*(2´*R*), 3´*S*]/ [3*S*(2´*S*), 3´*R*]-(1-Methylindolin-2-one)-3-spiro-2´-[3´-{(*E*)-1-methoxycarbonyl-2-(4-methylphenyl)}ethenyloxirane] (63d)



Yield (%) : 30; white solid

M.P. : 152-154 ^{o}C

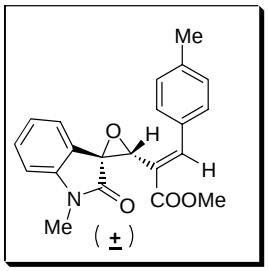
IR (KBr) : *v* 1720, 1697, 1614 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.31 (s, 3H), 3.21 (s, 3H), 3.63 (s, 3H), 4.66 (d, 1H, *J* = 1.2 Hz), 6.69 (d, 1H, *J* = 8.0 Hz), 6.79 (d, 1H, *J* = 7.6 Hz), 6.84-6.91 (m, 1H), 7.05 (d, 2H, *J* = 8.0 Hz), 7.16-7.23 (m, 1H), 7.22-7.32 (m, 2H), 7.90 (s, 1H)

^{13}C NMR (100 MHz) : δ 21.47, 26.58, 52.18, 60.74, 62.96, 108.25, 120.96, 122.47, 123.14, 128.99, 130.03, 130.10, 130.70, 140.25, 144.60, 145.32, 166.67, 171.44;

HRMS calc'd for $C_{21}H_{19}NO_4$+ Na (M + Na), 372.1212 ; Found: 372.1211.

[3*S*(2´*S*), 3´*S*]/ [3*R*(2´*R*), 3´*R*]-(1-Methylindolin-2-one)-3-spiro-2´-[3´-{(*E*)-1-methoxycarbonyl-2-(4-methylphenyl)}ethenyloxirane] (64d)



Yield (%) : 43; white solid

M.P. : 136-138 ^{o}C

IR (KBr) : *v* 1730, 1699, 1620 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.31 (s, 3H), 2.92 (s, 3H), 3.80 (s, 3H), 4.51 (d, 1H, *J* = 1.6 Hz), 6.79 (d, 1H, *J* = 7.6 Hz), 7.02 (d, 2H, *J* = 8.4 Hz), 7.07-7.13 (m, 1H), 7.22 (d, 1H, *J* = 7.2 Hz), 7.29 (d, 2H, *J* = 8.4 Hz), 7.33-7.41 (m, 1H), 7.91 (s, 1H)

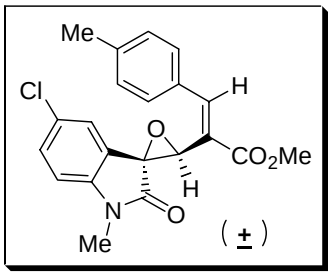
^{13}C NMR (100 MHz) : δ 21.37, 26.21, 52.16, 61.39, 62.54, 108.37, 121.81, 122.58, 122.68, 122.73, 129.01, 130.27, 130.37, 131.25, 139.88, 144.55, 144.90, 166.73, 169.74

HRMS calc'd for $C_{21}H_{19}NO_4$ + Na (M + Na), 372.1212 ; Found: 372.1211.

63e & 64e:

These compounds were prepared *via* cycloaddition reaction between 4-chloro-1-methylisatin with methyl (2*Z*)-2-bromomethyl-3-(4-methylphenyl)prop-2-enoate, following the similar procedure described for **63a & 64a**.

[3*R* (2´*R*), 3´*S*]/ [3*S* (2´*S*), 3´*R*]-(1-Methyl-5-chloroindolin-2-one)-3-spiro-2´-[3´-{(*E*)-1-methoxycarbonyl -2-(4-methylphenyl)}ethenyloxirane] (63e)



Yield (%) : 25; brown solid

M.P. : 170-172 ^{o}C

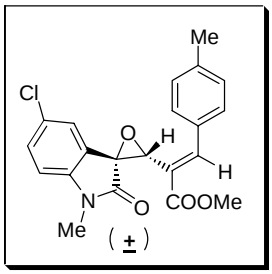
IR (KBr) : ν 1726, 1695, 1616 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.30 (s, 3H), 3.19 (s, 3H), 3.72 (s, 3H), 4.65 (d, 1H, J = 1.2 Hz), 6.57 (d, 1H, J = 8.4 Hz), 6.74 (d, 1H, J = 2.0 Hz), 7.04 (d, 2H, J = 8.0 Hz), 7.16 (dd, 1H, J = 2.0 & 8.4 Hz), 7.21 (d, 2H, J = 8.0 Hz), 7.93 (s, 1H)

^{13}C NMR (100 MHz) : δ 21.46, 26.67, 52.35, 61.03, 62.52, 109.13, 122.80, 122.85, 123.53, 128.01, 129.01, 129.82, 129.86, 130.77, 140.29, 143.11, 145.51, 166.43, 170.96

HRMS calc'd for $C_{21}H_{18}ClNO_4$ + Na (M + Na), 406.0822 ; Found: 406.0821.

[3*S* (2´*S*), 3´*S*]/ [3*R* (2´*R*), 3´*R*]-(1-Methyl-5-chloroindolin-2-one)-3-spiro-2´-[3´-{(*E*)-1-methoxycarbonyl -2-(4-methylphenyl)}ethenyloxirane] (64e)



Yield (%) : 42; brown solid

M.P. : 168-170 ^{o}C

IR (KBr) : ν 1722, 1620 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.33 (s, 3H), 2.92 (s, 3H), 3.80 (s, 3H), 4.50 (d, 1H, J = 1.2 Hz), 6.73 (d, 1H, J = 8.4 Hz), 7.05 (d, 2H, J = 8.0 Hz), 7.20 (d, 1H, J = 2.0 Hz), 7.30 (d, 2H, J = 8.0 Hz), 7.35 (dd, 1H, J = 2.0 & 8.0 Hz), 7.92 (s, 1H);

^{13}C NMR (100 MHz) : δ 21.38, 26.33, 52.19, 61.52, 62.24, 109.37, 122.16, 122.30, 124.47, 128.06, 129.04, 130.22, 131.06, 140.05, 143.32, 144.90, 166.56, 169.29

HRMS calc'd for $C_{21}H_{18}ClNO_4$ + Na (M + Na), 406.0822 ; Found: 406.0824.

63f & 64f:

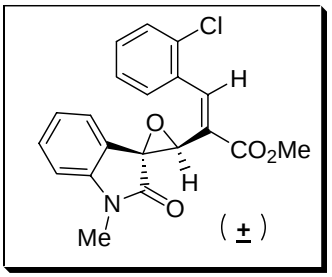
These compounds were prepared *via* cycloaddition reaction between 1-methylisatin with methyl (2*Z*)-2-bromomethyl-3-(2-chlorophenyl)prop-2-enoate, following the similar procedure described for **63a & 64a**.

[3*R* (2´*R*), 3´*S*]/ [3*S* (2´*S*), 3´*R*]-(1-Methylindolin-2-one)-3-spiro-2´-[3´-{(*E*)-1-methoxy-carbonyl-2-(2- chlorophenyl)}ethenyloxirane] (63f)

Yield (%) : 25; white solid

M.P. :. 156-158 ^oC

IR (KBr) : ν 1726, 1703, 1614 cm^{-1}

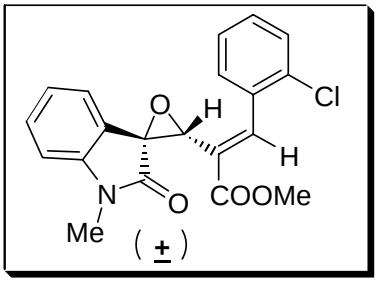


^{1}H NMR (400 MHz) : δ 3.17 (s, 3H), 3.74 (s, 3H), 4.65 (d, 1H, J = 1.6 Hz), 6.66 (d, 1H, J = 7.6 Hz), 6.88 (d, 1H, J = 7.2 Hz), 6.91-6.98 (m, 1H), 7.13-7.25 (m, 4H), 7.33-7.40 (m, 1H), 8.15 (s, 1H)

^{13}C NMR (100 MHz) : δ 26.57, 52.50, 60.78, 62.34, 108.36, 120.43, 122.90, 123.37, 126.17, 126.25, 129.42, 130.05, 130.25, 130.55, 132.37, 134.32, 141.62, 144.45, 165.81, 171.17

HRMS calc'd for $C_{20}H_{16}ClNO_4$ + Na (M + Na), 392.0666; Found: 392.0670

[3*S*(2´*S*), 3´*S*]/ [3*R*(2´*R*), 3´*R*]-(1-Methylindolin-2-one)-3-spiro-2´-[3´-{(*E*)-1-methoxy-carbonyl-2-(2- chlorophenyl)}ethenyloxirane] (64f)



Yield (%) : 50; white solid

M.P. : 164-166 ^{o}C

IR (KBr) : ν 1722, 1618 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.97(s, 3H), 3.81 (s, 3H), 4.48 (s, 1H), 6.76 (d, 1H, J = 7.6 Hz), 7.01 (d, 1H, J = 8.4 Hz), 7.05 (d, 1H, J = 7.6 Hz), 7.14 (d, 1H, J = 7.6 Hz), 7.16-7.24 (m, 1H), 7.30-7.41 (m, 3H), 8.11 (s, 1H)

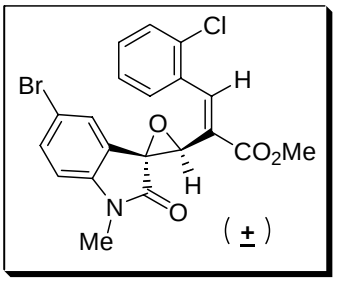
^{13}C NMR (100 MHz) : δ 26.33, 52.36, 61.47, 61.76, 108.47, 121.79, 122.41, 122.55, 125.73, 126.12, 129.50, 130.23, 130.37, 130.53, 132.76, 134.48, 141.12, 144.77, 166.01, 169.53

HRMS calc'd for $C_{20}H_{16}ClNO_4$ +Na (M + Na), 392.0666 ; Found: 392.0674.

63g & 64g

These compounds were prepared *via* cycloaddition reaction between 5-bromo-1-methylisatin with methyl (2*Z*)-2-bromomethyl-3-(2-chlorophenyl)prop-2-enoate, following the similar procedure described for **63a & 64a**.

[3*R*(2´*R*), 3´*S*]/ [3*S*(2´*S*), 3´*R*]-(1-Methyl-5-bromoindolin-2-one)-3-spiro-2´-[3´-{(*E*)-1-methoxycarbonyl -2-(2- chlorophenyl)}ethenyloxirane] (63g)



Yield (%) : 26; white solid

M.P. : 191-193 ^{o}C

IR (KBr) : *v* 1730, 1705, 1612 cm^{-1}

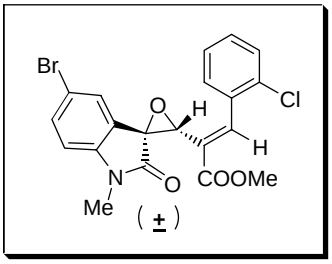
^{1}H NMR (400 MHz) : δ 3.13 (s, 3H), 3.82 (s, 3H), 4.64 (d, 1H, *J* = 1.2 Hz), 6.51 (d, 1H, *J* = 8.4 Hz), 6.97 (d, 1H, *J* = 2.0 Hz), 7.12-7.24 (m, 3H), 7.28 (d, 1H, *J* = 7.6 Hz),* 7.33 (dd, 1H, *J* = 2.0 & 8.4 Hz), 8.15 (s, 1H)

^{13}C NMR (100 MHz) : δ 26.63, 52.64, 61.15, 61.86, 109.71, 115.73, 122.48, 125.82, 126.07, 126.43, 129.44, 130.13, 130.59, 132.23, 132.93, 134.38, 141.93, 143.42, 165.58, 170.59

HRMS calc'd for $C_{20}H_{15}BrClNO_4$ + Na (M + Na), 469.9771; Found: 469.9773.

* One of the peaks merged with $CDCl_3$ peak.

[3*S*(2´*S*), 3´*S*]/ [3*R*(2´*R*), 3´*R*]-(1-Methyl-5-bromoindolin-2-one)-3-spiro-2´-[3´-{(*E*)-1-methoxycarbonyl -2-(2-chlorophenyl)}ethenyloxirane] (64g)



Yield (%) : 42; white solid

M.P. : 158-160 ^{o}C

IR (KBr) : ν 1726, 1614 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.99 (s, 3H), 3.82 (s, 3H), 4.47 (d, 1H, J = 1.2 Hz), 6.66 (d, 1H, J = 8.4 Hz), 7.01-7.13 (m, 1H), 7.21-7.29 (m, 2H), 7.35-7.42 (m, 2H), 7.46 (dd, 1H, J = 2.0 & 8.0 Hz), 8.13 (s, 1H)

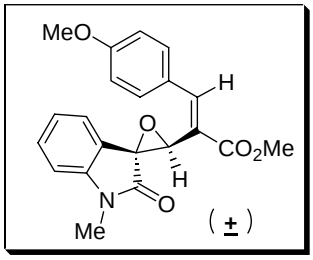
^{13}C NMR (100 MHz): δ 26.54, 52.49, 61.44, 61.80, 109.99, 115.31, 124.68, 125.18, 125.42, 126.25, 129.66, 130.40, 130.53, 132.80, 133.19, 134.56, 141.63, 143.85, 165.95, 169.10

HRMS calc'd for $C_{20}H_{15}BrClNO_4$ + Na (M + Na), 469.9771 ; Found: 469.9778.

63h &64h:

These compounds were prepared *via* cycloaddition reaction between 1-methylisatin with methyl (2*Z*)-2-bromomethyl-3-(4-methoxyphenyl)prop-2-enoate, following the similar procedure described for **63a & 64a**.

[3*R*(2´*R*), 3´*S*]/ [3*S*(2´*S*), 3´*R*]-(1-Methylindolin-2-one)-3-spiro-2´-[3´-{(*E*)-1-methoxy-carbonyl-2-(4-methoxyphenyl)}ethenyloxirane] (63h)



Yield (%) : 41; white solid

M.P. : 127-129 ^{o}C

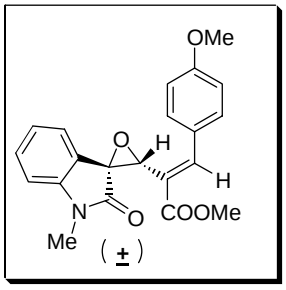
IR (KBr) : *v* 1718, 1699, 1618 cm^{-1};

^{1}H NMR (400 MHz) : *δ* 3.24 (s, 3H), 3.60 (s, 3H), 3.80 (s, 3H), 4.65 (s, 1H), 6.71 (d, 1H, *J* = 7.6 Hz), 6.75-6.83 (m, 3H), 6.84-6.92 (m, 1H), 7.17-7.24 (m, 1H), 7.39 (d, 2H, *J* = 8.0 Hz), 7.88 (s, 1H)

^{13}C NMR (100 MHz) : *δ* 26.46, 51.91, 55.24, 60.56, 62.92, 108.25, 113.65, 120.87, 121.34, 122.31, 122.90, 125.93, 129.93, 132.02, 144.47, 144.84, 160.85, 166.63, 171.32

HRMS calc'd for $C_{21}H_{19}NO_5$ + H (M +H), 366.1341 ; Found: 366.1343.

[3*S*(2´*S*), 3´*S*]/ [3*R*(2´*R*),3´*R*]-(1-Methylindolin-2-one)-3-spiro-2´-[3´-{(*E*)-1-methoxy-carbonyl-2-(4-methoxyphenyl)}ethenyloxirane] (64h)



Yield (%) : 29; white solid

M.P. : 123-125 ^{o}C

IR (KBr) : *v* 1726, 1685, 1615 cm^{-1};

^{1}H NMR (400 MHz) : δ 2.97 (s, 3H), 3.78 (s, 3H), 3.79 (s, 3H), 4.50 (d, 1H, J = 1.2 Hz), 6.75 (d, 2H, J = 8.8 Hz), 6.82 (d, 1H, J = 7.6 Hz), 7.07-7.14 (m, 1H), 7.23 (dd, 1H, J = 0.4 & 7.6 Hz), 7.34-7.43 (m, 3H), 7.89 (s, 1H)

^{13}C NMR (100 MHz) : δ 26.13, 51.93, 55.23, 61.20, 62.54, 108.37, 113.66, 120.98, 121.66, 122.48, 122.63, 126.45, 130.28, 132.12, 144.19, 144.75, 160.64, 166.72, 169.70

HRMS calc'd for $C_{21}H_{19}NO_5$ + Na (M + Na), 388.1161 ; Found: 388.1162.

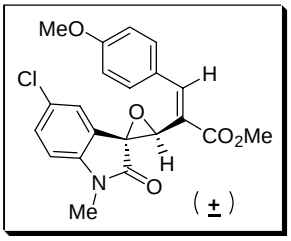
63i & 64i:

These compounds were prepared *via* cycloaddition reaction between 5-chloro-1-methylisatin with methyl (2*Z*)-2-bromomethyl-3-(4-methoxyphenyl)prop-2-enoate, following the similar procedure described for **63a & 64a**.

[3*R*(2′*R*), 3′*S*]/ [3*S*(2′*S*), 3′*R*]-(1-Methyl-5-chloroindolin-2-one)-3-spiro-2′-[3′-{(*E*)-1-metho-xycarbonyl-2-(4-methoxyphenyl)}ethenyloxirane] (63i)

Yield (%) : 36; white solid

M.P. : 117-119 ^{o}C



IR (KBr) : ν 1730, 1695, 1604 cm^{-1}

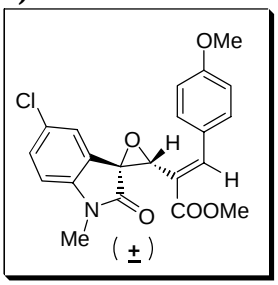
^{1}H NMR (400 MHz) : δ 3.21 (s, 3H), 3.69 (s, 3H), 3.79 (s, 3H), 4.64 (d, 1H, J = 1.2 Hz), 6.62 (d, 1H, J = 8.4 Hz), 6.75 (d, 1H, J = 2.0 Hz),

6.77 (d, 2H, *J* = 8.4 Hz), 7.17 (dd, 1H, *J* = 2.0 & 8.4 Hz), 7.33 (d, 2H, *J* = 8.0 Hz), 7.91 (s, 1H)

^{13}C NMR (100 MHz) : δ 26.67, 52.18, 55.36, 60.94, 62.59, 109.25, 113.77, 121.12, 122.82, 123.36, 126.03, 127.90, 129.80, 131.89, 143.08, 145.15, 160.97, 166.50, 170.95

HRMS calc'd for $C_{21}H_{18}ClNO_5$ + Na (M + Na), 422.0771; Found: 422.0773.

[3*S*(2´*S*), 3´*S*]/ [3*R*(2´*R*), 3´*R*]-(1-Methyl-5-chloroindolin-2-one)-3-spiro-2´-[3´-{(*E*)-1-methoxycarbonyl -2-(4-methoxyphenyl)}ethenyloxirane] (64i)



Yield (%) : 31; white solid

M.P : 142-144 ^{o}C

IR (KBr) : ν 1722, 1601 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.96 (s, 3H), 3.77 (s, 3H), 3.79 (s, 3H), 4.48 (s, 1H), 6.75 (d, 1H, *J* = 8.4 Hz), 6.78 (d, 2H, *J* = 8.8 Hz), 7.21 (d, 1H, *J* = 1.6 Hz), 7.34 (dd, 1H, *J* = 2.0 & 8.4 Hz), 7.40 (d, 2H, *J* = 8.4 Hz), 7.89 (s, 1H)

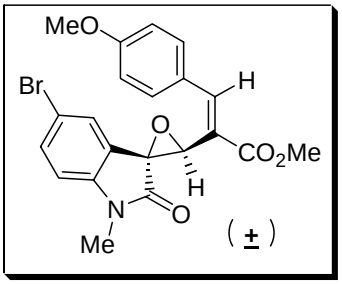
^{13}C NMR (100 MHz) : δ 26.41, 52.11, 55.38, 61.51, 62.39, 109.46, 113.84, 120.61, 122.33, 124.59, 126.45, 128.10, 130.21, 132.26, 143.37, 144.68, 160.87, 166.72, 169.42

HRMS calc'd for $C_{21}H_{18}ClNO_5$ + Na (M + Na), 422.0771 ; Found: 422.0772.

63j &64j:

These compounds were prepared *via* cycloaddition reaction between 5-bromo-1-methylisatin with methyl (2*Z*)-2-bromomethyl-3-(4-methoxyphenyl)prop-2-enoate, following the similar procedure described for **63a & 64a**.

[3*R*(2´*R*), 3´*S*]/ [3*S*(2´*S*), 3´*R*]-(1-Methyl-5-bromoindolin-2-one)-3-spiro-2´-[3´-{(*E*)-1-methoxycarbonyl -2-(4-methoxyphenyl)}ethenyloxirane] (63j)



Yield (%) : 41

Colourless viscous liquid

IR (neat) : *v* 1732, 1604 cm^{-1}

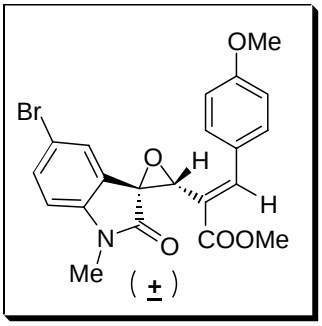
^{1}H NMR (400 MHz) : δ 3.21 (s, 3H), 3.70 (s, 3H), 3.79 (s, 3H), 4.64 (s, 1H), 6.57 (d, 1H, *J* = 8.0 Hz), 6.78 (d, 2H, *J* = 8.0 Hz), 6.89 (s, 1H), 7.32 (d, 3H, *J* = 7.6 Hz),* 7.92 (s, 1H)

^{13}C NMR (100 MHz) : δ 26.65, 52.20, 55.36, 60.95, 62.47, 109.71, 113.76, 115.07, 121.11, 123.13, 126.08, 131.85, 132.70, 143.53, 145.17, 160.94, 166.50, 170.82

HRMS calc'd for $C_{21}H_{18}BrNO_5$ + Na (M + Na), 466.0266 ; Found: 466.0268.

*It contains two doublets (one for two protons and the other for one) and one of the peaks of the one doublet merges with one of the peaks of the other doublet.

[3*S*(2´*S*), 3´*S*]/ [3*R*(2´*R*), 3´*R*]-(1-Methyl-5-bromoindolin-2-one)-3-spiro-2´-[3´-{(*E*-)1-methoxycarbonyl -2-(4-methoxyphenyl)}ethenyloxirane] (64j)



Yield (%) : 24; white solid

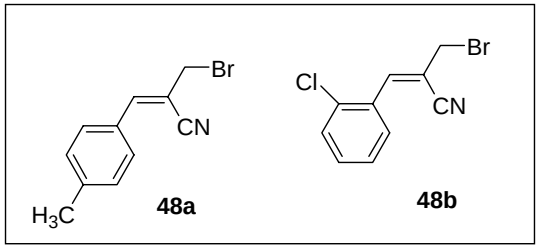
M.P. : 142-144 ^{o}C

IR (KBr) : ν 1724, 1615 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.95 (s, 3H), 3.76 (s, 3H), 3.78 (s, 3H), 4.48 (s, 1H), 6.70 (d, 1H, J = 8.0 Hz), 6.78 (d, 2H, J = 8.8 Hz) , 7.33 (d, 1H, J = 2.0 Hz), 7.40 (d, 2H, J = 8.8 Hz), 7.48 (dd, 1H, J = 2.0 & 8.0 Hz), 7.88 (s, 1H)

^{13}C NMR (100 MHz) : δ 26.35, 52.05, 55.35, 61.51, 62.27, 109.92, 113.84, 115.18, 120.61, 124.95, 125.02, 126.44, 132.24, 133.08, 143.86, 144.65, 160.87, 166.67, 169.28

HRMS calc'd for $C_{21}H_{18}BrNO_5$ + Na (M + Na), 466.0266; Found: 466.0262.



The allyl bromides (2E) 2-bromomethyl-3- (4-methylphenyl)prop-2-enenitrile (48a) and (2E) 2-bromomethyl-3-(2-chlorophenyl)prop-2-enenitrile (48b) were prepared according to the known procedure.[201] Pure (E)- isomers were obtained by careful crystallization.

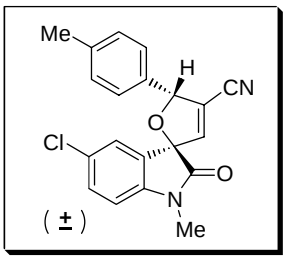
NOTE: We have kept [3R(2´R), 5´R]/ [3S(2´S), 5´S] before the names of the compounds 67a-c and [3R(2´R), 5´S]/ [3S(2´S), 5´R]- before the names of the compounds 67d-f to indicate the racemic nature and also stereochemistry.

Representative procedure: Synthesis of [3*R*(2´*R*), 5´*R*]/ [3*S*(2´*S*), 5´*S*]-(1-Methyl-5-chloroindolin-2-one)-3-spiro-2´-[4´-cyano-5´-(4-methylphenyl)-2´, 5´-dihydrofuran] (67a)

To a stirred solution of (2*E*) 2-bromomethyl-3- (4-methylphenyl)prop-2-enenitrile (**48a**) (3 mmol, 0.708 g) in DMF (5 mL) were added dimethyl sulfide (4.0 mmol, 0.248 g, 0.30 mL), Cs_2CO_3 (4.0 mmol, 1.303 g) and 1-methyl-5-chloroisatin (**59c**) (2.0 mmol, 0.380 g) at 15-20 ^{0}C. Stirring was continued for 8 h at the same temperature and the reaction mixture was diluted with water (3 mL) and extracted with EtOAc (3x10 mL). Combined organic layer was washed with water (2x 5 mL) and dried over anhydrous Na_2SO_4. Solvent was evaporated and the crude, thus obtained was purified by column chromatography (silica gel, 20 % ethyl acetate in hexanes) to provide 0.465 g of **67a** (66% yield).

Reaction time : 8 h

Yield (%) : 66; white solid



M.P. : 210-212 °C

IR (KBr) : *v* 2229, 1726, 1614 cm^{-1}

^{1}H NMR (400 MHz) : *δ* 2.39 (s, 3H), 3.16 (s, 3H), 6.30 (d, 1H, *J* = 2.0 Hz), 6.55 (d, 1H, *J* = 2.4 Hz), 6.77 (d, 1H, *J* = 8.0 Hz), 7.24-7.30 (m, 3H)*, 7.32-7.38 (m, 3H)

^{13}C NMR (100 MHz) : *δ* 21.29, 26.70, 88.28, 90.50, 110.03, 112.35, 121.10, 125.96, 126.84, 127.65, 128.97, 129.87, 131.29, 133.47, 139.73, 141.38, 142.39, 172.59

HRMS calc'd for $C_{20}H_{15}ClN_2O_2$ + Na (M + Na), 373.0720 ; Found: 373.0725**.**

*It actually contains one doublet at δ 7. 28 (2H, *J* = 8.8 Hz) and another doublet at δ 7. 27 (1H, *J* = 2.0 Hz).

[3*R*(2´*R*), 5´*R*]/ [3*S*(2´*S*), 5´*S*]-(1-Ethyl-5-chloroindolin-2-one)-3-spiro-2´-[4´-cyano-5´-(4-methylphenyl)-2´, 5´-dihydrofuran] (67b)

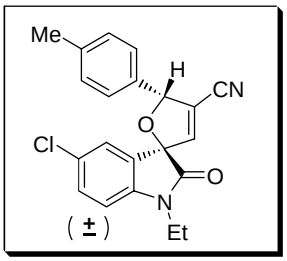
This compound was prepared *via* [3+2] cycloaddition reaction between 5-chloro-1-ethylisatin with (2*E*) 2-bromomethyl-3- (4-methylphenyl)prop-2-enenitrile, following the similar procedure described for **67a.**

Reaction time : 8 h

Yield (%) : 73; white solid

M.P. : 186-188 °C

IR (KBr) : *v* 2227, 1718, 1610 cm^{-1}



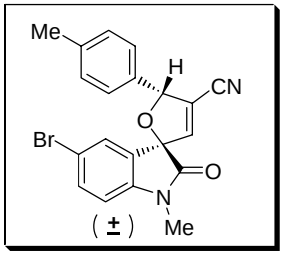
^{1}H NMR (400 MHz) : δ 1.27 (t, 3H, J = 7.2 Hz), 2.40 (s, 3H), 3.64-3.82 (m, 2H), 6.32 (d, 1H, J = 2.0 Hz), 6.57 (d, 1H, J = 2.4 Hz), 6.81 (d, 1H, J = 8.4 Hz), 7.26-7.32 (m, 3H), 7.33-7.39 (m, 3H)

^{13}C NMR (100 MHz) : δ 12.40, 21.29, 35.37, 88.28, 90.51, 110.14, 112.36, 121.05, 126.19, 126.85, 127.92, 128.78, 129.87, 131.25, 133.49, 139.72, 141.44, 141.52, 172.23

HRMS calc'd for $C_{21}H_{17}ClN_2O_2$ + H (M + H), 365.1057 ; Found: 365.1056.

[3*R*(2´*R*), 5´*R*]/ [3*S*(2´*S*), 5´*S*]-(1-Methyl-5-bromoindolin-2-one)-3-spiro-2´-[4´-cyano-5´-(4-methylphenyl)-2´, 5´-dihydrofuran] (67c)

This compound was prepared *via* [3+2] cycloaddition reaction between 5-bromo-1-methylisatin with methyl (2*E*) 2-bromomethyl-3- (4-methylphenyl)prop-2-enenitrile, following the similar procedure described for **67a.**



Reaction time : 8 h

Yield (%) : 67; white solid

M.P. : 206-208 ^{o}C

IR (KBr) : v 2229, 1726, 1610 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.39 (s, 3H), 3.18 (s, 3H), 6.31 (d, 1H, J = 2.4 Hz), 6.56 (d, 1H, J = 2.4 Hz), 6.74 (d, 1H, J = 8.4 Hz), 7.28 (d, 2H, J =

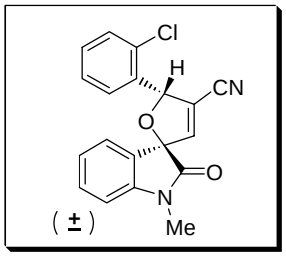
8.0 Hz), 7.35 (d, 2H, *J* = 8.0 Hz), 7.40 (d, 1H, *J* = 2.0 Hz), 7.51 (dd, 1H, *J* = 2.0 & 8.0 Hz)

^{13}C NMR (100 MHz) : δ 21.33, 26.73, 88.32, 90.45, 110.52, 112.37, 116.18, 121.18, 126.88, 128.01, 128.77, 129.91, 133.46, 134.25, 139.78, 141.38, 142.90, 172.54

HRMS calc'd for $C_{20}H_{15}BrN_2O_2$ + Na (M + Na), 417.0215 ; Found: 417.0209.

[3*R*(2´*R*), 5´*S*]/ [3*S*(2´*S*), 5´*R*]-(1-Methylindolin-2-one)-3-spiro-2´-[4´-cyano-5´-(2-chlorophe-nyl)-2´, 5´-dihydrofuran] (67d)

This compound was prepared prepared *via* [3+2] cycloaddition reaction between 1-methylisatin with (2*E*) 2-bromomethyl-3- (2-chlorophenyl)prop-2-enenitrile, following the similar procedure described for **67a.**



Reaction time : 8 h

Yield (%) : 69; white solid

M.P. : 166-168 ^{o}C

IR (KBr) : *v* 2227, 1718, 1612 cm^{-1}

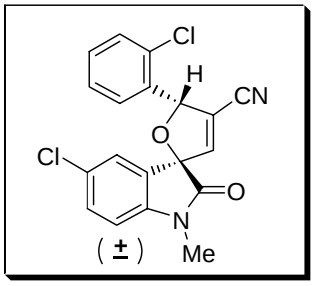
^{1}H NMR (400 MHz) : δ 3.21 (s, 3H), 6.63 (d, 1H, *J* = 2.0 Hz), 6.85 (d, 1H, *J* = 2.4 Hz), 6.87 (d, 1H, *J* = 8.0 Hz), 7.10-7.17 (m, 1H), 7.30-7.49 (m, 5H), 7.57 (dd, 1H, *J* = 2.0 & 7.6 Hz)

^{13}C NMR (100 MHz) : δ 26.66, 84.60, 90.85, 109.12, 112.35, 120.05, 123.69, 125.56, 125.91, 127.53, 128.12, 130.30, 130.68, 131.65, 133.76, 134.29, 142.98, 144.04, 172.70

HRMS calc'd for $C_{19}H_{13}ClN_2O_2$ + Na (M + Na), 359.0563 ; Found: 359.0570.

[3*R*(2′*R*), 5′*S*]/ [3*S*(2′*S*), 5′*R*]-(1-Methyl-5-chloroindolin-2-one)-3-spiro-2′-[4′-cyano-5′-(2-chlorophenyl)- 1′, 5′-dihydrofuran] (67e)

This compound was prepared *via* [3+2] cycloaddition reaction between 5-chloro-1-methylisatin with (2*E*) 2-bromomethyl-3- (2-chlorophenyl)prop-2-enenitrile, following the similar procedure described for **67a**.



Reaction time : 8 h

Yield (%) : 65; white solid

M.P. : 204-206 ^{o}C

IR (KBr) : ν 2229, 1722, 1612 cm^{-1}

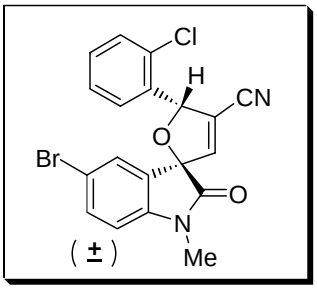
^{1}H NMR (400 MHz) : δ 3.18 (s, 3H), 6.63 (d, 1H, J = 2.4 Hz), 6.79 (d, 1H, J = 8.4 Hz), 6.82 (d, 1H, J = 2.0 Hz), 7.28 (d, 1H, J = 2.0 Hz), 7.34-7.49 (m, 4H), 7.53 (d, 1H, J = 7.6 Hz)

^{13}C NMR (100 MHz) : δ 26.73, 84.73, 90.44, 110.12, 112.07, 120.35, 125.96, 127.26, 127.64, 128.07, 128.96, 130.31, 130.85, 131.47, 133.74, 133.80, 142.36, 142.51, 172.20

HRMS calc'd for $C_{19}H_{12}Cl_2N_2O_2$ + Na (M + Na), 393.0173 ; Found: 393.0172.

[3*R*(2´*R*), 5´*S*]/ [3*S*(2´*S*), 5´*R*]-(1-Methyl-5-bromoindolin-2-one)-3-spiro-2´-[4´-cyano-5´-(2-chlorophenyl)- 1´ 5´-dihydrofuran] (67f)

This compound was prepared *via* [3+2] cycloaddition reaction between 5-bromo-1-methylisatin with (2*E*) 2-bromomethyl-3- (2-chlorophenyl)prop-2-enenitrile, following the similar procedure described for **67a.**



Reaction time : 8 h

Yield (%) : 71; white solid

M.P. :182-184 ^{o}C

IR (KBr) : *v* 2229, 1736, 1610 cm^{-1};

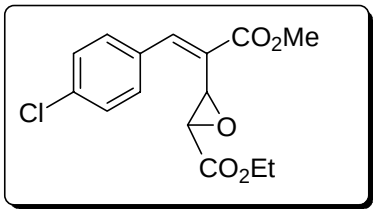
^{1}H NMR (400 MHz) : δ 3.21 (s, 3H), 6.63 (d, 1H, *J* = 2.4 Hz), 6.77 (d, 1H, *J* = 8.4 Hz), 6.84 (d, 1H, *J* = 2.4 Hz), 7.35-7.57 (m, 6H)

^{13}C NMR (100 MHz) : δ 26.79, 84.84, 90.41, 110.61, 112.12, 116.20, 120.53, 127.69, 128.15, 128.84, 130.43, 130.93, 133.84, 133.89, 134.45, 142.35, 143.08, 172.19

HRMS calc'd for $C_{19}H_{12}BrClN_2O_2$ + Na (M + Na), 436.9668 ; Found: 436.9666.

Ethyl (4*E*)-5-(4-chlorophenyl)-4-methoxycarbonyl-2, 3-epoxy-pent-4-enoate (70a)

To a stirring solution of methyl-(2*Z*) 2-bromomethyl-3(4-chlorophenyl)-prop-2-enoate (**47c**) (2.0 mmol, 0.579 g) in CH_3CN (3 mL) and water (0.3 mL) added, dimethyl sulfide (2.4 mmol, 0.148 g, 0.18 mL). The reaction mixture was stirred for 2 h untill all the conversion of Baylis-Hillman bromide into salt (monitored by TLC). Then K_2CO_3 and ethyl glyoxalate (3.0 mmol) were added successively at room temperature. After stirring at room temperature for 22 h, solvent was removed under reduced pressure and the residue was diluted water extracted with EtOAc (3 x 10 mL). Combined organic layer was dried over anhydrous Na_2SO_4 and solvent was evaporated. The crude product thus obtained was purified by column chromatography (silica gel, 15% ethyl acetate in hexanes) to afforded the desired product in 66% isolated yield as white solid.



Reaction time : 2 h+22 h

Yield (%) : 66 (0.410 g)

IR (KBr) : ν 1747, 1718, 1637 cm^{-1}

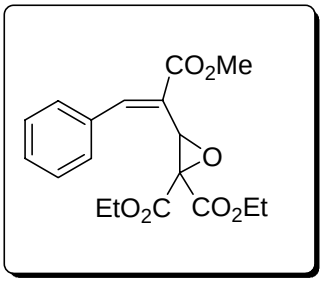
^{1}H NMR (400 MHz) : δ 1.32 (t, 3H, J = 7.2 Hz), 3.48 (d, 1H, J = 2.0 Hz), 3.86 (s, 3H), 4.04 (t, 1H, J = 1.6 Hz), 4.28 (q, 2H, J = 7.2 Hz), 7.32-7.493 (m, 4H), 7.84 (s, 1H)

^{13}C NMR (100 MHz) : δ 14.24, 52.56, 53.59, 55.60, 61.96, 126.31, 129.02, 131.50, 131.79, 136.22, 143.74 , 163.31 , 168.32

HRMS calc'd for $C_{15}H_{15}ClO_5$ +Na (M + Na), 333.0506 ; Found, 333.0477

Ethyl (4*E*)-2-ethoxycarbonyl-4-methoxycarbonyl-5-phenyl-2, 3-epoxy-pent-4-enoate (70b)

This compound was obtained as a colorless viscous liquid *via* the treatment of 2 (Z) 2-bromomethyl-3-phenyl-prop-2-enoate (**47a**) with diethyl ketomalonate in the presence of dimethyl sulphide and K_2CO_3, following a similar procedure described for the molecule **70a**.



Reaction time : 2 h+22 h

Yield (%) : 67

IR (neat) : *v* 1745, 1716, 1635 cm^{-1}

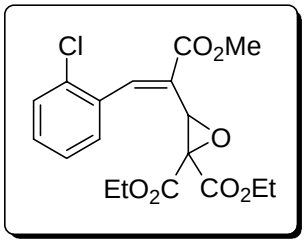
^{1}H NMR (400 MHz) : δ 1.10 (t, 3H, *J* = 7.2 Hz), 1.32 (t, 3H, *J* = 7.2 Hz), 3.85 (s, 3H), 3.90-4.01 (m, 1 H), 4.04-4.14 (m, 1H), 4.32 (q, 2H, *J* = 7.2 Hz), 4.52 (d, 1H, *J* = 1.2 Hz), 7.36-7.45 (m, 3H), 7.49-7.55 (m, 2H),7.81 (s, 1H)

^{13}C NMR (100 MHz) : δ 13.76, 14.00, 52.34, 58.48, 62.16, 62.44, 62.65, 123.27, 128.50, 129.98, 130.39, 133.13, 144.23, 163.77, 165.18, 166.29

HRMS calc'd for $C_{18}H_{20}O_7$ + Na (M + Na), 371.1107 ; Found , 371.1099

Ethyl (4*E*)-5-(2-chlorophenyl)-2-ethoxycarbonyl-4-methoxycarbonyl-2, 3-epoxy-pent-4-enoate (70c)

This compound was obtained as a colorless viscous liquid *via* the treatment of 2 (*Z*) 2-bromomethyl-3-(2-chlorophenyl)prop-2-enoate (**47b**) with diethyl ketomalonate in the presence of dimethyl sulphide and K_2CO_3, following a similar procedure described for the molecule **70a**.



Reaction time : 2 h+22 h

Yield (%) : 69

IR (neat) : *v* 1747, 1643 cm^{-1}

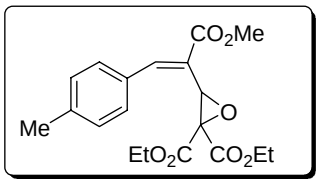
^{1}H NMR (400 MHz) : δ 1.19 (t, 3H, *J* = 7.2 Hz), 1.29 (t, 3H, *J* = 7.2 Hz), 3.87 (s, 3H), 4.14 (q, 2H, *J* = 7.2 Hz), 4.23-4.32 (m, 2H), 4.48 (d, 1H, *J* = 1.2 Hz), 7.28-7.35 (m, 2H), 7.38-7.43 (m, 1H), 7.45-7.50 (m, 1H), 7.99 (s, 1H)

^{13}C NMR (100 MHz) : δ 13.86, 14.00, 52.53, 58.68, 62.07, 62.33, 62.79, 125.57, 126.50, 129.40, 130.70, 130.91, 132.09, 134.19, 140.96, 163.49, 165.06, 165.57

HRMS calc'd for $C_{18}H_{19}ClO_7$ + Na (M + Na), 405.0717 ; Found , 405.0661

Ethyl (4*E*)-2-ethoxycarbonyl-4-methoxycarbonyl-5-(4-methylphenyl)-2, 3-epoxy-pent-4-enoate (70d)

This compound was obtained as a colorless viscous liquid *via* the treatment of 2 (*Z*) 2-bromomethyl-3-(4-methylphenyl)prop-2-enoate (**47d**)with diethyl ketomalonate in the presence of dimethyl sulphide and K_2CO_3, following a similar procedure described for the molecule **70a**.



Reaction time : 2 h+22 h

Yield (%) : 66

IR (neat) : *v* 1747, 1722, 1633 cm^{-1}

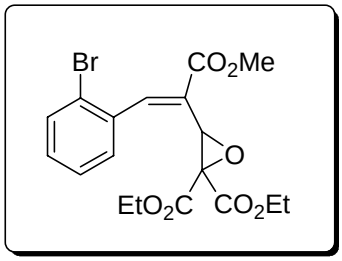
^{1}H NMR (400 MHz) : δ 1.09 (t, 3H, *J* = 7.2 Hz), 1.32 (t, 3H, *J* = 7.2 Hz), 2.37 (s, 3H), 3.83 (s, 3H), 3.89-4.00 (m, 1H), 4.04-4.14 (m, 1H), 4.32 (q, 2H, *J* = 7.2 Hz), 4.51 (d, 1H, *J* = 0.8 Hz) 7.21 (d, 2H, *J* = 8.0 Hz), 7.43 (d, 2H, *J* = 8.0 Hz), 7.77 (s, 1H)

^{13}C NMR (100 MHz) : δ 13.73, 13.99, 21.49, 52.24, 58.53, 62.10, 62.52, 62.59, 122.14 , 129.25, 130.33, 130.52, 140.46, 144.28, 163.80, 165.22, 166.43

HRMS calc'd for $C_{19}H_{22}O_7$ (M + Na), 385.1263 ; Found , 385.1258

Ethyl (4*E*)-5-(2-bromophenyl)-2-ethoxycarbonyl-4-methoxycarbonyl-2, 3-epoxy-pent-4-enoate (70e)

This compound was obtained as a colorless viscous liquid *via* the treatment of 2 (*Z*) 2-bromomethyl-3-(2-bromo-phenyl)prop-2-enoate (**47e**) with diethyl ketomalonate in the presence of dimethyl sulphide and K_2CO_3, following a similar procedure described for the molecule **70a**.



Reaction time : 2 h+22 h

Yield (%) : 68

IR (neat) : *v* 1745, 1728, 1643 cm^{-1}

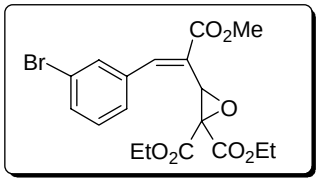
^{1}H NMR (400 MHz) : δ 1.20 (t, 3H, *J* = 7.2 Hz), 1.29 (t, 3H, *J* = 7.2 Hz), 3.87 (s, 3H), 4.15(q, 2H, *J* = 7.2 Hz), 4.23-4.32 (m, 2H), 4.46 (d, 1H, *J* = 1.2 Hz), 7.19-7.25 (m, 1H), 7.31-7.38 (m, 1H), 7.46 (dd, 1H, *J* = 1.2 & 7.6 Hz), 7.59 (dd, 1H, *J* = 1.2 & 8.4 Hz), 7.93 (s, 1H)

^{13}C NMR (100 MHz) : δ 13.90, 13.99, 52.49, 58.60, 61.99, 62.35, 62.74, 124.19, 125.41, 127.08, 130.75, 130.97, 132.56, 133.94, 143.09, 163.44, 165.06, 165.51

HRMS calc'd for $C_{18}H_{19}BrO_7$ + Na (M + Na), 449.0212 ; Found , 449.0202

Ethyl (4*E*)-5-(3-bromophenyl)-2-ethoxycarbonyl-4-methoxycarbonyl-2, 3-epoxy-pent-4-enoate (70f)

This compound was obtained as a colorless viscious liquid *via* the treatment of 2 (*Z*) 2-bromomethyl-3-(3-bromophenyl)prop-2-enoate (**47f**) with diethyl ketomalonate in the presence of dimethyl sulfide and K_2CO_3, following a similar procedure described for the molecule **70a**.



Reaction time : 24 h

Yield (%) : 71

IR (neat) : *v* 1732, 1639 cm^{-1}

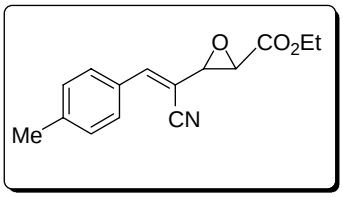
^{1}H NMR (400 MHz) : δ 1.13 (t, 3H, *J* = 7.2 Hz), 1.33 (t, 3H, *J* = 7.2 Hz), 3.85 (s, 3H), 3.93-4.04 (m, 1H), 4.06-4.17 (m, 1H), 4.32 (q, 2H, *J* = 7.2 Hz), 4.51 (s, 1H), 7.24-7.32 (m, 1H), 7.44 (d, 1H, *J* = 7.6 Hz), 7.51(d, 1H, *J* = 7.6 Hz), 7.62 (s, 1H), 7.72, (s, 1H)

^{13}C NMR (100 MHz) : *δ* 13.71, 13.93, 52.40, 58.17, 62.18, 62.23, 62.71, 122.40 , 124.80, 128.65, 129.90, 132.63, 132.78, 135.13, 142.24, 163.54, 164.88, 165.73

HRMS calc'd for $C_{18}H_{19}BrO_7$ +Na (M + Na), 449.0212 ; Found , 449.0202

Ethyl (4*Z*)-4-cyano-5-(4-methylphenyl)-2,3-epoxy-pent-4-enoate (71a)

This compound was obtained as a white solid *via* the treatment of 2 (*E*) 2-bromomethyl-3-(4-methyl-phenyl)propenenitrile (**48a**) with ethyl glyoalate in the presence of dimethyl sulphide and K_2CO_3, following a similar procedure described for the molecule **70a**.



Reaction time : 2 h + 10 h

Yield (%) : 63

M.P. : 96-98 ºC

IR (KBr) : *v* 2216, 1755, 1626 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.34 (t, 3H, *J* = 7.2 Hz), 2.40 (s, 3H), 3.76 (d, 1H, *J* = 2.0 Hz), 3.87 (d, 1H, *J* = 1.6 Hz), 4.23-4.36 (m, 2H), 7.25 (d, 2H, *J* = 8.0 Hz) , 7.28 (s, 1H), 7.70 (d, 2H, *J* = 8.4 Hz)

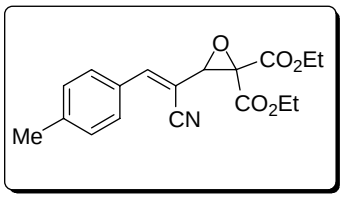
^{13}C NMR (100 MHz) : δ 14.12, 21.65, 53.69, 57.58, 62.20, 104.80, 115.31, 129.42, 129.56, 129.83, 142.42, 147.58, 167.39

HRMS calc'd for $C_{15}H_{15}NO_3$ +Na (M + Na), 280.0950 ; Found, 280.0955

Ethyl (4*Z*)-4-cyano-2-ethoxycarbonyl-5-(4-methylphenyl)-2, 3-epoxy-pent-4-enoate (71b)

This compound was obtained as a white solid *via* the treatment of 2 (*E*) 2-bromomethyl-3-(4-methylphenyl) propenenitrile (**48a**) with diethyl ketomalonate in the presence of

dimethyl sulphide and K_2CO_3, following a similar procedure described for the molecule **70a**.



Reaction time : 2 h + 10 h

Yield (%) : 81

M.P. :54-56 ºC

IR (KBr) : ν 2218, 1749, 1606 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.23 (t, 3H, J = 7.2 Hz), 1.35 (t, 3H, J = 7.2 Hz), 2.40 (s, 3H), 4.19-4.30 (m, 3H), 4.33 (q, 2H, J = 7.4 Hz), 7.23 (s, 1H), 7.24 (d, 2H, J = 6.8 Hz), 7.68 (d, 2H, J = 8.0 Hz)

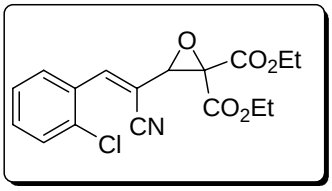
^{13}C NMR (100 MHz) : δ 13.91, 13.98, 21.58, 60.11, 62.04, 62.54, 63.25, 100.87, 115.75, 129.27, 129.48, 129.76, 142.39, 146.39, 162.78, 164.40

HRMS calc'd for $C_{18}H_{19}NO_5$ +Na (M + Na), 352.1161 ; Found, 352.1095

Ethyl (4*Z*)-5-(2-chlorophenyl)-4-cyano-2-ethoxycarbonyl-2, 3-epoxy-pent-4-enoate (71c)

This compound was obtained as a colorless vicious liquid *via* the treatment of 2 (*E*) 2-bromomethyl-3-(2-chlorophenyl)propenenitrile (**48b**) with diethyl ketomalonate in the presence of dimethyl sulphide and K_2CO_3, following a similar procedure described for the molecule **70a**.

Reaction time : 2 h + 10 h



Yield (%) : 77

IR (neat) : ν 2222, 1747, 1622 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.28 (t, 3H, J = 7.2 Hz), 1.35 (t, 3H, J = 7.2 Hz), 4.26-4.38 (m, 5H), 7.29-7.48 (m, 3H), 7.68 (s, 1H), 7.94 (dd, 1H, J = 1.6 & 7.6 Hz)

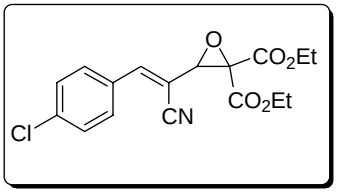
^{13}C NMR (100 MHz) : δ 13.81, 13.85, 59.72, 61.95, 62.58, 63.26, 106.35, 114.65, 127.20, 129.05, 129.97, 130.41, 132.18, 134.62, 143.17, 162.49, 164.17

HRMS calc'd for $C_{17}H_{16}ClNO_5$ +Na (M + Na), 372.0615; Found, 372.0604

Ethyl (4Z)-2-ethoxycarbonyl-4-cyano-5-(4-chlorophenyl)-2,3-epoxy-pent-4-enoate (71d)

This compound was obtained as a colorless viscious liquid *via* the treatment of 2 (*E*) 2-bromomethyl-3-(4-chlorophenyl)propenenitrile (**48c**) with diethyl ketomalonate in the presence of dimethyl sulfide and K_2CO_3, following a similar procedure described for the molecule **70a**.

Reaction time : 2 h + 10 h



Yield (%) : 82

IR (neat) : ν 2219, 1742, 1621 cm^{-1}

^1H NMR (400 MHz) : δ 1.23 (t, 3H, J = 7.2 Hz), 1.35 (t, 3H, J = 7.2 Hz), 4.21-4.38 (m, 5H), 7.24 (s, 1H), 7.41 (d, 2H, J = 8.8 Hz), 7.71 (d, 2H, J = 8.8 Hz)

^{13}C NMR (100 MHz) : δ 13.92, 14.01, 59.82, 62.10, 62.66, 63.36, 103.00, 115.29, 129.41, 130.39, 130.62, 137.65, 144.93, 162.69, 164.22

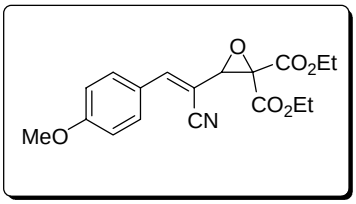
HRMS calc'd for $C_{17}H_{16}ClNO_5$ +Na (M + Na), 372.0615 ; Found, 372.0601

Ethyl (4Z)-4-cyano-2-ethoxycarbonyl-5-(4-metoxyphenyl)-2, 3-epoxy-pent-4-enoate (71e)

This compound was obtained as a colorless viscous liquid *via* the treatment of 2 (*E*) 2-bromomethyl-3-(4-methoxyphenyl) propenenitrile (**48d**) with diethyl ketomalonate in the presence of dimethyl sulphide and K_2CO_3, following a similar procedure described for the molecule **70a**.

Reaction time : 2 h + 10 h

Yield (%) : 85



IR (neat) : ν 2216, 1749, 1601 cm^{-1}

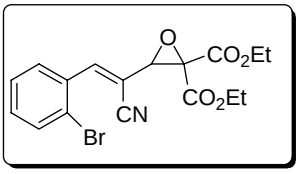
^{1}H NMR (400 MHz) : δ 1.23 (t, 3H, J = 7.2 Hz), 1.34 (t, 3H, J = 7.2 Hz), 3.84 (s, 3H), 4.20-4.37 (m, 5H), 6.93 (d, 2H, J = 8.8 Hz), 7.20 (s, 1H), 7.76 (d, 2H, J = 8.8 Hz)

^{13}C NMR (100 MHz) : δ 13.79, 13.85, 55.34, 60.20, 61.91, 62.38, 63.09, 98.73, 114.34, 115.93, 124.66, 131.40, 145.90, 162.12, 162.76, 164.38

HRMS calc'd for $C_{18}H_{19}NO_6$ +Na (M + Na), 368.1110 ; Found, 368.1094

Ethyl (4*Z*)-5-(2-bromophenyl)-4-cyano-2-ethoxycarbonyl-2, 3-epoxy-pent-4-enoate (71f)

This compound was obtained as a colorless vicious liquid *via* the treatment of 2 (*E*) 2-bromomethyl-3-(2-bromophenyl)propenenitrile (**48e**) with diethyl ketomalonate in the presence of dimethyl sulphide and K_2CO_3, following a similar procedure described for the molecule **70a**.



Reaction time : 2 h + 10 h

Yield (%) : 79

IR (neat) : ν 2222, 1749, 1622 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.29 (t, 3H, J = 7.2 Hz), 1.35 (t, 3H, J = 7.2 Hz), 4.26-4.38 (m, 5H), 7.28-7.34 (m, 1H), 7.36-7.43 (m, 1H),7.61 (s, 1H), 7.60 (dd, 1H, J = 0.8 & 8.0 Hz), 7.89 (dd, 1H, J = 0.8 & 8.0 Hz)

^{13}C NMR (100 MHz) : δ 13.91, 13.97, 59.75, 62.00, 62.70, 63.36, 106.54, 114.66, 124.82, 127.88, 129.42, 132.31, 133.32, 145.80, 162.57, 164.28

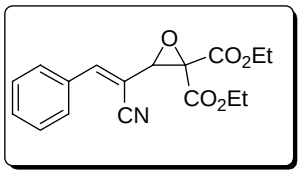
HRMS calc'd for $C_{17}H_{16}BrNO_5$ +Na (M + Na), 416.0110 ; Found, 416.0071

Ethyl (4Z)-4-cyano-2-ethoxycarbonyl-5-phenyl-2, 3-epoxy-pent-4-enoate (71g)

This compounds **71gi** & **71gii** were obtained as colorless viscous liquids *via* the treatment of mixture of 2 (*E*)/2(*Z*) 2-bromomethyl-3-phenyl-prop-2-enenitrile (**48f**) with diethyl ketomalonate in the presence of dimethyl sulphide and K_2CO_3, following a similar procedure described for the molecules **70a**, as separable mixture.

***Ethyl (4Z)-2-ethoxycarbonyl-4-cyano-5-phenyl-2,3-epoxy-pent-4-enoate* (71gi)**

Reaction time : 2 h+10 h



Yield (%) : 64

IR (neat) : ν 2220, 1743, 1620 cm^{-1}

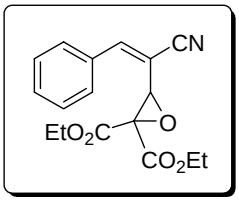
^{1}H NMR (400 MHz) : δ 1.23 (t, 3H, J = 7.2 Hz), 1.35 (t, 3H, J = 7.2 Hz), 4.21-4.31 (m, 3H), 4.34 (q, 2H, J = 7.2 Hz), 7.28 (s, 1H), 7.39-7.49 (m, 3H), 7.72-7.82 (m, 2H)

^{13}C NMR (100 MHz) : δ 13.92, 13.98, 59.58, 62.05, 62.61, 63.32, 102.33, 115.52, 129.06, 129.40, 131.59, 131.92, 146.45, 162.74, 164.34

HRMS calc'd for $C_{17}H_{17}NO_5$ +Na (M + Na), 338.1004 ; Found,338.0983

Ethyl (4E)-2-ethoxycarbonyl-4-cyano-5-phenyl-2,3-epoxy-pent-4-enoate **(71gii)**

Yield (%) : 24



IR (neat) : v 2222, 1759, 1610 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.31 (t, 3H, J = 7.2 Hz), 135 (t, 3H, J = 7.2 Hz) *, 4.29 (d, 1H, J = 1.2 Hz), 4.31-4.40 (m, 4H), 7.39-7.51 (m, 5H), 7.57 (d, 1H, J = 0.8 Hz) * One of the peak of triplet (having lowest shift value) merged with one of the peak of other triplet (having highest chemical shift value).

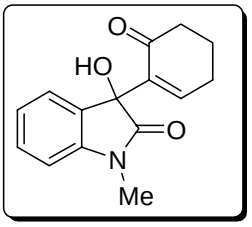
^{13}C NMR (100 MHz) : δ 13.82, 14.00, 57.36, 61.43, 62.93, 63.23, 108.04, 115.84, 129.09, 129.76, 131.11, 132.33, 150.30, 163.09, 164.35

HRMS calc'd for $C_{17}H_{17}NO_5$ +Na (M + Na), 338.1004 ; Found,338.0946

3-(Cyclohex-2-enon-2-yl)-3-hydroxy-1-methylindolin-2-one (76a)

This molecule was prepared according to the procedure which has developed in our laboratory.

To a stirring solution of 1-methylisatin (30 mmol, 4.83 g) and cyclohex-2-enone (30 mmol, 2.88g, 2.9 mL) in dichloromethane (30 mL), $TiCl_4$ (30 mmol, 15 mL of 2M solution in dichloromethane) was added at 0 ^oC. After stirring for 30 minutes at room temperature (25-28 ^oC), the reaction was quenched with water (50 mL). Reaction mixture was extracted with dichloromethane (3 x 100 mL). Combined organic layer was washed with saturated aqueous Na_2CO_3 solution and dried over anhydrous Na_2SO_4. Solvent was evaporated and the crude product thus obtained was purified by column chromatography (silica gel, 60% EtOAc/Hexanes) to provide the title compound in 82% (6.59 g) yield as white solid.



M.P. : 134-136 ºC

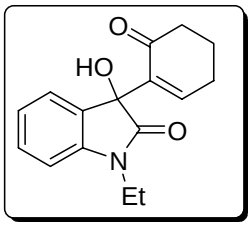
IR (KBr) : *v* 3347, 1704, 1671, 1605 cm^{-1}

^1H NMR (400 MHz) : δ 1.90-2.09 (m, 2H), 2.27-2.42 (m, 2H), 2.43-2.53 (m, 2H), 3.23 (s, 3H),4.02 (s, 1H), 6.84 (d, 1H, *J* = 7.6 Hz), 7.01 (t, 1H, *J* = 7.6 Hz), 7.14 (d, 1H, *J* = 7.2 Hz), 7.30 (t, 1H, *J* = 7.6 Hz), 7.35-7.44 (m, 1H)

^{13}C NMR (100 MHz) : δ 22.39, 25.83, 26.41, 38.38, 76.03, 108.59, 122.82, 123.60, 129.93, 130.07, 138.28, 144.37, 147.74, 176.59, 198.33

3-(Cyclohex-2-enon-2-yl)-3-hydroxy-1-ethylindolin-2-one (76b)

This compound was prepared by the similar procedure as described for **76a** *via* the Baylis-Hillman coupling of 1-ethylisatin with cyclohex-2-enone under the influence of $TiCl_4$ as brown solid.



Reaction time : 30 min

Yield (%) : 79 (6.41 g)

M.P. : 140-142 ºC

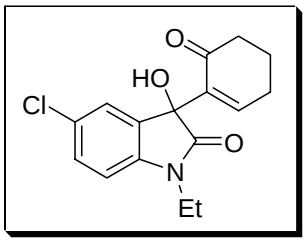
IR (KBr) : *v* 3331, 1704, 1660, 1605 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.34 (t, 3H, J = 7.2 Hz), 1.92-2.08 (m, 2H), 2.31-2.56 (m, 4H), 3.58 (s, 1H), 3.65-3.92 (m, 2H), 6.88 (d, 1H, *J* = 8.0 Hz), 7.00 (t, 1H, *J* = 7.2 Hz), 7.17 (d, 1H, *J* =7.2 Hz), 7.25-7.34 (m, 1H), 7.35-7.42 (m, 1H)

^{13}C NMR (100 MHz) : δ 12.12, 22.38, 25.80, 34.84, 38.33, 75.87, 108.70, 122.57, 123.70, 129.82, 130.31, 138.38, 143.42, 147.67, 176.22, 198.11

5-Chloro-3-(cyclohex-2-enon-2-yl)-3-hydroxy-1-ethylindolin-2-one (76e)

This compound was prepared by the similar procedure as described for **76a** *via* the Baylis-Hillman coupling of 5-chloro-1-ethylisatin with cyclohex-2-enone under the influence of $TiCl_4$ as brown solid.



Reaction time : 30 min

Yield (%) : 71%

M.P. : 178-180 ºC

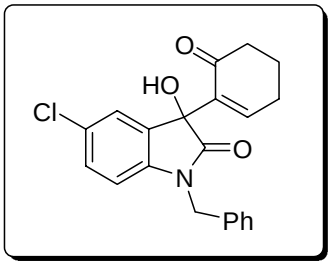
IR (KBr) : *v* 3315, 1701, 1665 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.30 (t, 3H, *J* = 7.2 Hz), 1.88-2.06 (m, 2H), 2.25-2.43 (m, 2H), 2.44-2.56 (m, 2H), 3.58-3.88 (m, 2H), 4.19 (s, 1H), 6.78 (d, 1H, *J* = 8.4 Hz), 7.07 (d, 1H, *J* = 2.0 Hz), 7.24 (dd, 1H, *J* = 2.0 & 8.0 Hz), 7.48 (t, 1H, *J* = 4.0 Hz)

^{13}C NMR (100 MHz) : δ 11.95, 22.33, 25.79, 34.97, 38.16, 75.47, 109.63, 124.18, 127.77, 129.54, 132.05, 138.11, 142.03, 148.08, 175.97, 197.79

5-Chloro-3-(cyclohex-2-enon-2-yl)-3-hydroxy-1-benzylindolin-2-one (76f)

This compound was prepared by the similar procedure as described for **76a** *via* the Baylis-Hillman coupling of 5-chloro-1-benzylisatin with cyclohex-2-enone under the influence of $TiCl_4$ as brown solid.



Reaction time : 30 min

Yield (%) : 80%

M.P. : 204-206 ºC

IR (KBr) : *v* 3311, 1702, 1682, 1612 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.88-2.07 (m, 2H), 2.27-2.54 (m, 4H), 4.24 (s, 1H), 4.81 & 4.97 (ABq, 2H, J = 16.0 Hz), 6.54 (d, 1H, J = 8.4 Hz), 7.05-7.12 (m, 2H), 7.22-7.28 (m, 1H), 7.29-7.35 (m, 2H), 7.40 (d, 2H, J = 7.2 Hz), 7.50 (t, 1H, J = 4.0 Hz)

^{13}C NMR (100 MHz) : δ 22.36, 25.83, 38.17, 44.17, 75.61, 110.82, 124.05, 127.16, 127.68, 128.16, 128.86, 129.57, 131.83, 135.15, 137.94, 142.10, 148.49, 176.67, 197.83

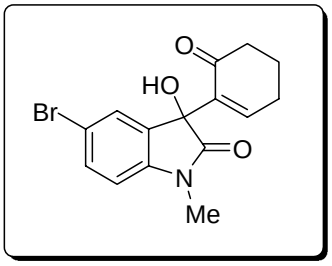
5-Bromo-3-(cyclohex-2-enon-2-yl)-3-hydroxy-1-methylindolin-2-one (76g)

This compound was prepared by the similar procedure as described for **76a** *via* the Baylis-Hillman coupling of 5-bromo-1-methylisatin with cyclohex-2-enone under the influence of $TiCl_4$ as brown solid.

Reaction time : 30 min

Yield (%) : 82%

M.P. : 162-164 ºC



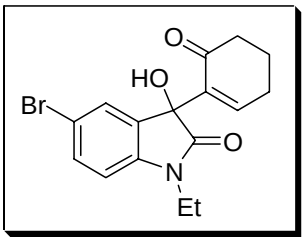
IR (KBr) : ν 1707, 1668, 1604 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.96-2.07 (m, 2H), 2.31-2.46 (m, 2H), 2.47-2.56 (m, 2H), 3.22 (s, 3H), 3.75 (s, 1H), 6.74 (d, 1H, J = 8.0 Hz), 7.25 (d, 1H, J = 2.0 Hz), 7.38-7.48 (m, 2H)

^{13}C NMR (100 MHz) : δ 22.23, 25.70, 26.40, 38.02, 75.26, 110.01, 115.17, 126.53, 132.13, 132.38, 137.89, 143.33, 148.32, 176.32, 197.80

5-Bromo-3-(cyclohex-2-enon-2-yl)-3-hydroxy-1-ethylindolin-2-one (76h)

This compound was prepared by the similar procedure as described for **76a** *via* the Baylis-Hillman coupling of 5-bromo-1-ethylisatin with cyclohex-2-enone under the influence of $TiCl_4$ as brown solid.



Reaction time : 30 min

Yield (%) : 62%

M.P. : 170-172 ºC

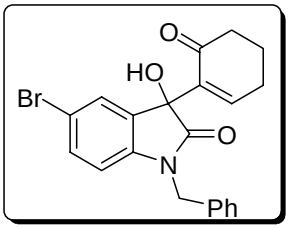
IR (KBr) : ν 3320, 1698, 1665, 1610 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.30 (t, 3H, J = 7.2 Hz), 1.88-2.06 (m, 2H), 2.25-2.43 (m, 2H), 2.44-2.56 (m, 2H), 3.60-3.88 (m, 2H), 4.01 (s, 1H), 6.74 (d, 1H, J = 8.4 Hz), 7.22 (d, 1H, J = 2.0 Hz), 7.40 (dd, 1H, J = 2.0 & 8.0 Hz), 7.47 (t, 1H, J = 4.0 Hz)

^{13}C NMR (100 MHz) : δ 11.99, 22.35, 25.83, 35.01, 38.20, 75.52, 110.21, 115.14, 126.98, 132.33, 132.55, 138.12, 142.57, 148.13, 175.86, 197.87

5-Bromo-3-(cyclohex-2-enon-2-yl)-3-Hydroxy-1-benzylindolin-2-one (76i)

This compound was prepared by the similar procedure as described for **76a** *via* the Baylis-Hillman coupling of 5-bromo-1-benzylisatin with cyclohex-2-enone under the influence of $TiCl_4$ as brown solid.



Reaction time : 30 min

Yield (%) : 74%

M.P. : 210-212 ºC

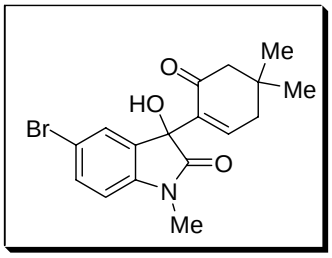
IR (KBr) : *v* 3309 1698, 1687, 1649, 1605cm^{-1}

^{1}H NMR (400 MHz) : δ 1.88-2.05 (m, 2H), 2.27-2.54 (m, 4H), 4.31 (s, 1H), 4.80 & 4.96 (ABq, 2H, J = 16.0 Hz), 6.49 (d, 1H, J = 8.4 Hz), 7.18-7.28 (m, 3H), 7.30-7.35 (m, 2H), 7.39 (d, 2H, J = 7.2 Hz), 7.50 (t, 1H, J = 4.0 Hz)

^{13}C NMR (100 MHz) : δ 22.33, 25.81, 38.13, 44.13, 75.49, 111.31, 115.45, 126.72, 127.14, 127.66, 128.84, 132.19, 132.43, 135.10, 137.91, 142.58, 148.55, 176.60, 197.77

5-Bromo-3-(5,5-dimethylcyclohex-2-enon-2-yl)-3-hydroxy-1-methylindolin-2-one (76k)

This compound was prepared by the similar procedure as described for **76a** *via* the Baylis-Hillman coupling of 5-bromo-1-methylisatin with 5,5-dimethylcyclohex-2-enone under the influence of $TiCl_4$ as brown solid.



Reaction time : 30 min

Yield (%) : 75%

M.P. : 178-180 ºC

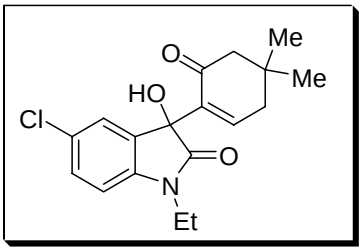
IR (KBr) : *v* 3311, 1707, 1666, 1598 cm^{-1}

^{1}H NMR (400 MHz) : δ 0.99 (s, 3H), 1.02 (s, 3H), 2.15 & 2.22 (ABq, 2H, *J* = 16.0 Hz), 2.38 (d, 2H, *J* = 4.0 Hz), 3.19 (s, 3H), 4.30 (s, 1H), 6.72 (d, 1H, *J* = 8.0 Hz), 7.19 (d, 1H, *J* = 2.0 Hz), 7.33 (t, 1H, *J* = 4.0 Hz), 7.41 (dd, 1H, *J* = 8.4 & 2.0 Hz)

^{13}C NMR (100 MHz) : δ 26.50, 28.09, 28.15, 34.03, 39.83, 51.73, 75.45, 110.14, 115.34, 126.61, 132.08, 132.58, 137.07, 143.48, 145.99, 176.29, 198.07

5-Chloro-3-(5,5-dimethylcyclohex-2-enon-2-yl)-3-hydroxy-1-ethylindolin-2-one (76l)

This compound was prepared by the similar procedure as described for **76a** *via* the Baylis-Hillman coupling of 5-chloro-1-ethylisatin with 5,5-dimethylcyclohex-2-enone under the influence of $TiCl_4$ as brown solid.



Reaction time : 30 min

Yield (%) : 68%

M.P**.** **:** 194-196 ºC

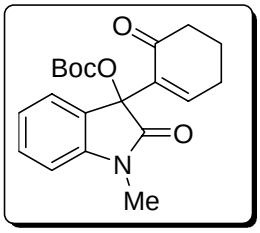
IR (KBr) : *v* 3309, 1704, 1665, 1600 cm^{-1}

^{1}H NMR (400 MHz) : δ 0.99 (s, 3H), 1.03 (s, 3H), 1.30 (t, 3H, *J* = 7.2 Hz), 2.15 & 2.23 (ABq, 2H, *J* = 16.0 Hz), 2.38 (d, 2H, *J* = 4.4 Hz), 3.59-3.71 (m, 1H), 3.76-3.87 (m, 1H), 4.25 (s, 1H), 6.78 (d, 1H, *J* = 8.0 Hz), 7.06 (d, 1H, *J* = 2.0 Hz), 7.25 (dd, 1H, *J* = 8.0 & 2.0 Hz), 7.35 (t, 1H, *J* = 4.0 Hz)

^{13}C NMR (100 MHz) : δ 11.96, 27.99, 28.27, 34.02, 34.98, 39.84, 51.74, 75.46, 109.72, 124.06, 127.85, 129.59, 132.04, 137.22, 142.08, 145.80, 176.01, 197.90

Repersentative procedure: Synthesis of 3-(*tert*-butoxycarbonyloxy)-3-(cyclohex-2-enon-2-yl)-1-methylindolin-2-one (77a)

To a stirring solution of 3-(cyclohex-2-enon-2-yl)-3-hydroxy-1-methylindolin-2-one (**76a**) (20 mmol, 5.14 g) in anhydrous CH_2Cl_2 (40 mL) at 0 ºC were added Boc_2O (22 mmol, 4.8 g, 5.0 mL) and DMAP (1.0 mmol, 0.122 g) in anhydrous CH_2Cl_2 (40 mL) dropwise slowly (over half an hour) at the same temperature. After the addition, the stirring was continued at room temperature (25-30 ºC) for 1 h. The reaction mixture was washed with aqueous hydrochloric acid (2N, 2mL) followed by saturated aqueous sodium bicarbonate solution (10 mL). Organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated. The crude product, thus obtained, was purified by column chromatography (40% ethyl acetate in hexanes) to provide the title compound as a brown solid in 72% (5.15 g) yield.



Reaction time : 0.5 h (0 ºC)+1 h (RT)

Yield (%) : 72

M.P. :130-132 ºC

IR (KBr) : *ν* 1749, 1728, 1674, 1610 cm^{-1}

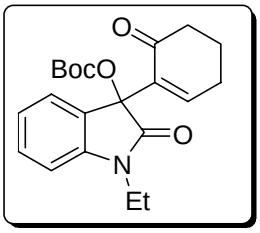
^1H NMR (400 MHz) : *δ* 1.33 (s, 9H), 1.88-2.07 (m, 2H), 2.23-2.39 (m, 2H), 2.46-2.61 (m, 2H), 3.30 (s, 3H), 6.85 (d, 1H, *J* = 8.0 Hz), 6.92-6.99 (m, 1H), 7.11 (dd, 1H, *J* = 0.8 & 7.2 Hz)*, 7.29-7.35 (m, 1H), 7.64 (t, 1H, *J* = 4.0 Hz), *not properly resolved

^{13}C NMR (100 MHz) : δ 22.09, 25.88, 26.61, 27.49, 38.52, 79.49, 83.13, 108.16, 122.14, 122.74, 126.97, 130.11, 136.02, 145.70, 148.25, 149.77, 173.16, 195.81

HRMS calcd for $C_{20}H_{23}NO_5$ + Na (M + Na), 380.1474; Found, 380.1488.

3-(*tert*-Butoxycarbonyloxy)-3-(cyclohex-2-enon-2-yl)-1-ethylindolin-2-one (77b)

The title compound was prepared by the similar procedure as described for **77a** *via* the treatment of Baylis-Hillman alcohol, 3-(cyclohex-2-enon-2-yl)-3-hydroxy-1-ethylindolin-2-one with Boc_2O and DMAP as brown solid.



Reaction time : 0.5 h (0 ºC)+1 h (RT)

Yield (%) : 74

M.P. . 140-142 ºC

IR (KBr) : ν 1755, 1728, 1678, 1608 cm^{-1}

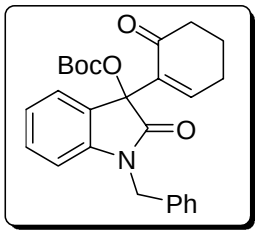
^{1}H NMR (400 MHz) : δ 1.33 (s, 9H), 1.35 (t, 3H, J = 7.2 Hz)*, 1.88-2.05 (m, 2H), 2.23-2.40 (m, 2H), 2.46-2.57 (m, 2H), 3.70-3.82 (m, 1H), 3.86-3.96 (m, 1H), 6.86 (d, 1H, J = 7.6 Hz), 6.91-6.98 (m, 1H), 7.11 (dd, 1H, J = 0.8 & 7.2 Hz), 7.27-7.33 (m, 1H), 7.62 (t, 1H, J = 4.0 Hz), * one of the peak merged with singlet at δ 1.33

^{13}C NMR (100 MHz) : δ 11.59, 22.03, 25.80, 27.42, 34.86, 38.47, 79.49, 82.86, 108.13, 121.78, 122.90, 127.13, 129.92, 135.99, 144.78, 148.04, 149.67, 172.44, 195.57

HRMS calcd for $C_{21}H_{25}NO_5$ + Na (M + Na), 394.1630; Found, 394.1634

3-(*tert*-Butoxycarbonyloxy)-3-(cyclohex-2-enon-2-yl)-1-benzylindolin-2-one (77c)

The title compound was prepared by the similar procedure as described for **77a** *via* the treatment of Baylis-Hillman alcohol, 3-(cyclohex-2-enon-2-yl)-3-hydroxy-1-benzylindolin-2-one with Boc_2O and DMAP as white solid.



Reaction time : 0.5 h (0 ºC)+1 h (RT)

Yield (%) : 83

M.P. : 124-126 ºC

IR (KBr) : ν 1758, 1735, 1683, 1612 cm^{-1}

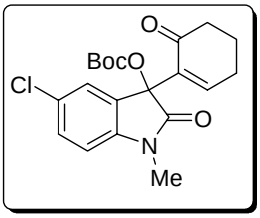
^{1}H NMR (400 MHz) : δ 1.40 (s, 9H), 1.86-2.10 (m, 2H), 2.25-2.46 (m, 2H), 2.49-2.62 (m, 2H), 5.05 (s, 2H), 6.63 (d, 1H, J = 8.0 Hz), 6.89-6.98 (m, 1H), 7.11-7.20 (m, 2H), 7.25-7.32 (m, 1H), 7.33-7.41 (m, 2H), 7.57 (d, 2H, J = 7.2 Hz), 7.69 (t, 1H, J = 4.0 Hz)

^{13}C NMR (100 MHz) : δ 22.14, 25.96, 27.61, 38.57, 44.79, 79.60, 83.11, 109.43, 122.19, 122.84, 127.05, 127.22, 127.36, 128.54, 129.98, 135.94, 136.14, 145.22, 148.34, 149.93, 173.40, 195.74

HRMS calcd for $C_{26}H_{27}NO_5$ + H (M + H), 434.1967; Found, 434.1968.

5-Chloro-3-(*tert*-butoxycarbonyloxy)-3-(cyclohex-2-enon-2-yl)-1-methylindolin-2-one (77d)

The title compound was prepared by the similar procedure as described for **77a** *via* the treatment of Baylis-Hillman alcohol, 5-chloro-3-(cyclohex-2-enon-2-yl)-3-hydroxy-1-methylindolin-2-one with Boc_2O and DMAP as brown solid.



Reaction time : 0.5 h (0 ºC)+1 h (RT)

Yield (%) : 71

M.P. : 162-164 ºC

IR (KBr) : ν 1761, 1726, 1678, 1612 cm^{-1}

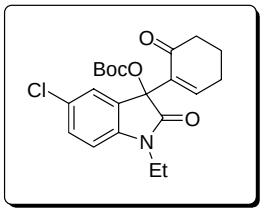
^{1}H NMR (400 MHz) : δ 1.36 (s, 9H), 1.90-2.03 (m, 2H), 2.25-2.40 (m, 2H), 2.50-2.58 (m, 2H), 3.29 (s, 3H), 6.77 (d, 1H, J = 8.0 Hz), 7.07 (d, 1H, J = 2.0 Hz), 7.28 (dd, 1H, J = 2.0 & 8.4 Hz)*, 7.65 (t, 1H, J = 4.4 Hz), *one of the peak of dd merged with $CHCl_3$ peak

^{13}C NMR (100 MHz) : δ 22.06, 25.93, 26.75, 27.55, 38.48, 79.05, 83.51, 109.16, 123.26, 127.31, 128.69, 129.93, 135.68, 144.46, 148.81, 149.79, 172.76, 195.81

HRMS calcd for $C_{20}H_{22}ClNO_5$ + Na (M + Na), 414.1084; Found, 414.1087.

5-Chloro-3-(*tert*-butoxycarbonyloxy)-3-(cyclohex-2-enon-2-yl)-1-ethylindolin-2-one (77e)

The title compound was prepared by the similar procedure as described for **77a** *via* the treatment of Baylis-Hillman alcohol, 5-chloro-3-(cyclohex-2-enon-2-yl)-3-hydroxy-1-ethylindolin-2-one with Boc_2O and DMAP as brown solid.



Reaction time : 0.5 h (0 ºC)+1 h (RT)

Yield (%) : 78

M.P. : 172-174 ºC

IR (KBr) : ν 1747, 1726, 1671, 1610 cm^{-1}

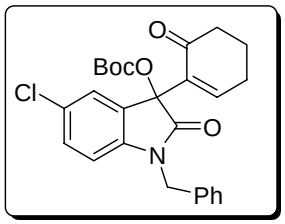
^{1}H NMR ($CDCl_3$, 400 MHz) : δ 1.31 (t, 3H, J = 7.2 Hz), 1.34 (s, 9H), 1.87-2.03 (m, 2H), 2.22-2.38 (m, 2H), 2.45-2.54 (m, 2H), 3.67-3.77 (m, 1H), 3.78-3.91 (m, 1H), 6.77 (d, 1H, J = 8.0 Hz), 7.07 (d, 1H, J = 2.0 Hz), 7.23 (dd, 1H, J = 2.0 & 8.4 Hz), 7.60 (t, 1H, J = 4.4 Hz)

^{13}C NMR (100 MHz) : δ 11.52, 22.01, 25.87, 27.49, 35.08, 38.43, 79.05, 83.29, 109.15, 123.40, 126.97, 128.89, 129.78, 135.63, 143.54, 148.68, 149.71, 172.09, 195.65

HRMS calcd for $C_{21}H_{24}ClNO_5$ + H (M + H), 406.1421; Found, 406.1418.

5-Chloro-3-(*tert*-butoxycarbonyloxy)-3-(cyclohex-2-enon-2-yl)-1-benzylindolin-2-one (77f)

The title compound was prepared by the similar procedure as described for **77a** *via* the treatment of Baylis-Hillman alcohol, 5-chloro-3-(cyclohex-2-enon-2-yl)-3-hydroxy-1-benzylindolin-2-one with Boc_2O and DMAP as white solid.



Reaction time : 0.5 h (0 ºC)+1 h (RT)

Yield (%) : 79

M.P. : 160-162 ºC

IR (KBr) : ν 1758, 1728, 1672, 1610 cm^{-1}

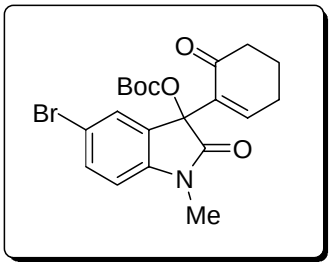
^{1}H NMR (400 MHz) : δ 1.39 (s, 9H), 1.88-2.08 (m, 2H), 2.27-2.44 (m, 2H), 2.49-2.62 (m, 2H), 4.96 & 5.02 (ABq, 2H, J = 16.0 Hz), 6.51 (d, 1H, J = 8.0 Hz), 7.08-7.12 (m, 2H), 7.24-7.39 (m, 3H),* 7.51 (d, 2H, J = 7.2 Hz), 7.67 (t, 1H, J = 4.0 Hz), * It contains $CHCl_3$ peak

^{13}C NMR (100 MHz) : δ 22.16, 26.06, 27.70, 38.57, 44.96, 79.21, 83.63, 110.50, 123.36, 127.41, 127.48, 127.53, 128.71, 128.82, 129.91, 135.56, 135.83, 143.92, 149.04, 149.98, 173.08, 195.89

HRMS calcd for $C_{26}H_{26}ClNO_5$ + H (M + H), 468.1578; Found, 468.1575.

5-Bromo-3-(*tert*-butoxycarbonyloxy)-3-(cyclohex-2-enon-2-yl)-1-methylindolin-2-one (77g)

The title compound was prepared by the similar procedure as described for **77a** *via* the treatment of Baylis-Hillman alcohol, 5-bromo-3-(cyclohex-2-enon-2-yl)-3-hydroxy-1-methylindolin-2-one with Boc_2O and DMAP as brown solid.



Reaction time : 0.5 h (0 ºC)+1 h (RT)

Yield (%) : 80

M.P. : 162-164 ºC

IR (KBr) : ν 1759, 1726, 1678, 1610 cm^{-1}

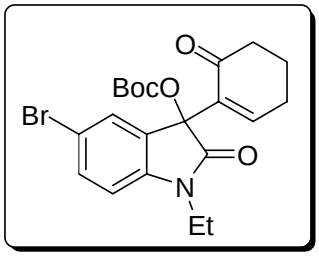
^{1}H NMR (400 MHz) : δ 1.36 (s, 9H), 1.90-2.06 (m, 2H), 2.25-2.41 (m, 2H), 2.49-2.58 (m, 2H), 3.28 (s, 3H), 6.73 (d, 1H, J = 8.0 Hz), 7.20 (d, 1H, J = 2.0 Hz), 7.42 (dd, 1H, J = 2.0 & 8.0 Hz), 7.64 (t, 1H, J = 4.0 Hz)

^{13}C NMR (100 MHz): δ 22.07, 25.95, 26.76, 27.57, 38.48, 78.97, 83.60, 109.73, 114.57, 125.96, 129.01, 132.88, 135.67, 144.94, 148.94, 149.79, 172.71, 195.92

HRMS calcd for $C_{20}H_{22}BrNO_5$ + Na (M + Na), 458.0579; Found, 458.0584.

5-Bromo-3-(*tert*-butoxycarbonyloxy)-3-(cyclohex-2-enon-2-yl)-1-ethylindolin-2-one (77h)

The title compound was prepared by the similar procedure as described for **77a** *via* the treatment of Baylis-Hillman alcohol, 5-bromo-3-(cyclohex-2-enon-2-yl)-3-hydroxy-1-ethylindolin-2-one with Boc_2O and DMAP as brown solid.



Reaction time : 0.5 h (0 ºC)+1 h (RT)

Yield (%) : 74

M.P. : 174-176 ºC

IR (KBr) : ν 1758, 1725, 1676, 1605 cm^{-1}

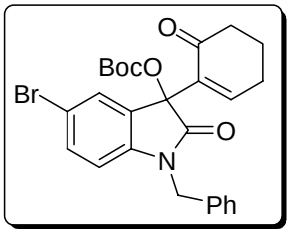
^{1}H NMR (400 MHz) : δ 1.33 (t, 3H, J = 7.2 Hz), 1.36 (s, 9H), 1.89-2.06 (m, 2H), 2.25-2.41 (m, 2H), 2.49-2.56 (m, 2H), 3.69-3.80 (m, 1H), 3.81-3.94 (m, 1H), 6.75 (d, 1H, J = 8.0 Hz), 7.21 (d, 1H, J = 2.0 Hz), 7.41 (dd, 1H, J = 2.0 & 8.4 Hz), 7.62 (t, 1H, J = 4.0 Hz)

^{13}C NMR (100 MHz) : δ 11.61, 22.11, 25.99, 27.60, 35.17, 38.53, 79.07, 83.47, 109.77, 114.31, 126.20, 129.33, 132.80, 135.74, 144.13, 148.83, 149.79, 172.11, 195.81

HRMS calcd for $C_{21}H_{24}BrNO_5$ + Na (M + Na), 472.0736; Found, 472.0740.

5-Bromo-3-(*tert*-butoxycarbonyloxy)-3-(cyclohex-2-enon-2-yl)-1-benzylindolin-2-one (77i)

The title compound was prepared by the similar procedure as described for **77a** *via* the treatment of Baylis-Hillman alcohol, 5-bromo-3-(cyclohex-2-enon-2-yl)-3-hydroxy-1-benzylindolin-2-one with Boc_2O and DMAP as yellow solid.



Reaction time : 0.5 h (0 ºC)+1 h (RT)

Yield (%) : 76

M.P. : 170-172 ºC

IR (KBr) : ν 1753, 1730, 1672, 1605 cm^{-1}

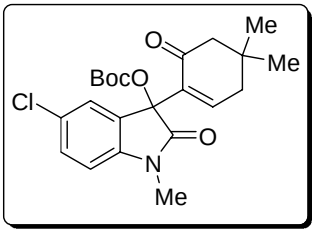
^{1}H NMR (400 MHz) : δ 1.39 (s, 9H), 1.91-2.08 (m, 2H), 2.28-2.44 (m, 2H), 2.49-2.62 (m, 2H), 4.96 & 5.02 (ABq, 2H, J = 16.0 Hz), 6.47 (d, 1H, J = 8.4 Hz), 7.21 (d, 1H, J = 2.0 Hz), 7.23-7.30 (m, 2H),* 7.31-7.36 (m, 2H), 7.51 (d, 2H, J = 7.2 Hz), 7.67 (t, 1H, J = 4.0 Hz), * It contains $CHCl_3$ peak

^{13}C NMR (100 MHz) : δ 22.15, 26.06, 27.71, 38.56, 44.94, 79.12, 83.65, 111.03, 114.79, 126.05, 127.41, 127.48, 128.71, 129.17, 132.81, 135.52, 135.84, 144.42, 149.05, 149.98, 172.97, 195.89

HRMS calcd for $C_{26}H_{26}BrNO_5$ + H (M + H), 512.1073; Found, 512.1069.

5-Chloro-3-(*tert*-butoxycarbonyloxy)-3-(5,5-dimethylcyclohex-2-enon-2-yl)-1-methyl-indolin-2-one (77j)

The title compound was prepared by the similar procedure as described for **77a** *via* the treatment of Baylis-Hillman alcohol, 5-chloro-3-(5,5-dimethylcyclohex-2-enon-2-yl)-3-hydroxy-1-methylindolin-2-one with Boc_2O and DMAP as yellow solid.



Reaction time : 0.5 h (0 ºC)+1 h (RT)

Yield (%) : 75

M.P. : 158-160 ºC

IR (KBr) : ν 1752, 1736, 1676, 1615, cm^{-1}

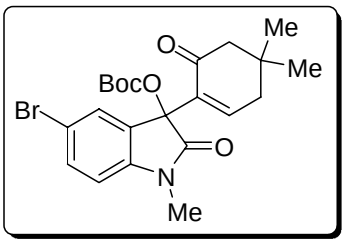
^{1}H NMR (400 MHz) : δ 0.99 (s, 3H), 1.02 (s, 3H), 1.36 (s, 9H), 2.15 & 2.18 (ABq, 2H, J = 16.0 Hz), 2.42 (d, 2H, J = 4.4 Hz), 3.28 (s, 3H), 6.77 (d, 1H, J = 8.4 Hz), 7.07 (d, 1H, J = 2.0 Hz), 7.27 (dd, 1H, J = 2.0 & 8.4 Hz), 7.51 (t, 1H, J = 4.4 Hz)

^{13}C NMR (100 MHz) : δ 26.83, 27.61, 27.96, 28.17, 33.79, 39.96, 52.10, 79.07, 83.62, 109.24, 123.13, 127.40, 128.70, 130.03, 134.73, 144.56, 146.58, 149.82, 172.69, 196.15

HRMS calcd for $C_{22}H_{26}ClNO_5$ + Na (M + Na), 442.1397; Found, 442.1397.

5-Bromo-3-(*tert*-butoxycarbonyloxy)-3-(5,5-dimethylcyclohex-2-enon-2-yl)-1-methyl-indolin-2-one (77k)

The title compound was prepared by the similar procedure as described for **77a** *via* the treatment of Baylis-Hillman alcohol, 5-bromo-3-(5, 5-dimethylcyclohex-2-enon-2-yl)-3-hydroxy-1-methylindolin-2-one with Boc_2O and DMAP as yellow solid.



Reaction time : 0.5 h (0 ºC)+1 h (RT)

Yield (%) : 86

M.P. : 140-142 ºC

IR (KBr) : ν 1750, 1732, 1682, 1618, 1605 cm^{-1}

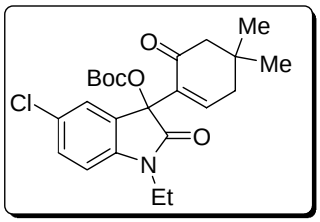
^{1}H NMR (400 MHz) : δ 0.99 (s, 3H), 1.02 (s, 3H), 1.36 (s, 9H), 2.15 & 2.20 (ABq, 2H, J = 16.0 Hz), 2.42 (d, 2H, J = 4.4 Hz), 3.28 (s, 3H), 6.74 (d, 1H, J = 8.4 Hz), 7.20 (d, 1H, J = 2.0 Hz), 7.43 (dd, 1H, J = 2.0 & 8.0 Hz), 7.51 (t, 1H, J = 4.4 Hz)

^{13}C NMR (100 MHz): δ 26.80, 27.61, 27.92, 28.21, 33.79, 39.95, 52.09, 78.97, 83.63, 109.77, 114.58, 125.82, 129.03, 132.93, 134.73, 145.04, 146.58, 149.80, 172.57, 196.15

HRMS calcd for $C_{22}H_{26}ClNO_5$ + H (M + H), 464.1073; Found, 464.1074.

5-Chloro-3-(*tert*-butoxycarbonyloxy)-3-(5,5-dimethylcyclohex-2-enon-2-yl)-1-ethyl-indolin-2-one (77l)

The title compound was prepared by the similar procedure as described for **77a** *via* the treatment of Baylis-Hillman alcohol, 5-chloro-3-(5, 5-dimethylcyclohex-2-enon-2-yl)-3-hydroxy-1-methylindolin-2-one with Boc_2O and DMAP as brown solid.



Reaction time : 0.5 h (0 ºC)+1 h (RT)

Yield (%) : 79

M.P. : 168-170 ºC

IR (KBr) : ν 1750, 1676, 1610 cm^{-1};

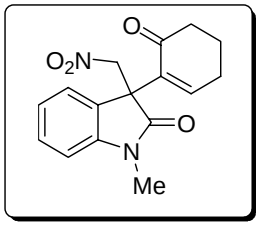
^{1}H NMR (400 MHz) : δ 0.99 (s, 3H), 1.02 (s, 3H), 1.33 (t, 3H, J = 7.2 Hz), 1.36 (s, 9H), 2.16 & 2.20 (ABq, 2H, J = 16.0 Hz), 2.39 & 2.45 (dABq, 2H, J = 4.4 & 15.2 Hz), 3.68-3.80 (m, 1H), 3.81-3.94 (m, 1H), 6.79 (d, 1H, J = 8.4 Hz), 7.06 (d, 1H, J = 2.0 Hz), 7.22 (dd, 1H, J = 8.4 & 2.4 Hz),* 7.50 (t, 1H, J = 4.4 Hz), * It contains $CHCl_3$ peak

^{13}C NMR (100 MHz) : δ 11.63, 27.63, 28.09, 33.79, 35.21, 39.99, 52.13, 79.16, 83.48, 109.30, 123.35, 127.15, 129.01, 129.95, 134.81, 143.74, 146.47, 149.81, 172.10, 196.04

HRMS calcd for $C_{23}H_{28}ClNO_5$ + Na (M + Na), 456.1554; Found, 456.1558.

3-(Cyclohex-2-enon-2-yl)-3-nitromethyl-1-methylindolin-2-one (78a)

To a stirring solution of 3-(*tert*-butoxycarbonyloxy)-3-(cyclohex-2-enon-2-yl)-1-methylindolin-2-one (**77a**) (4.0 mmol, 1.430 g) and nitromethane (6.0 mmol, 0.366 g, 0.33 mL) in anhydrous DCM (10 mL) was added DMAP (4.0 mmol, 0.488 g) at room temperature (25-30 ºC). After strring for 12 h at room temperature under N_2 atmosphere, solvent was removed and crude product thus obtained was purified by column chromatogaraphy (40% EtOAc in hexanes), to provide the desired product in 82% (0.985 g) as a white solid.



Reaction time : 12 h

Yield (%) : 82

M.P. : 140-142 ºC

IR (KBr) : ν 1709, 1676, 1630 1610 cm^{-1}

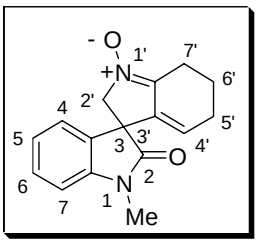
^{1}H NMR (400 MHz) : δ 1.84-2.06 (m, 2H), 2.30-2.55 (m, 4H), 3.31 (s, 3H), 5.03 & 5.60 (ABq, 2H, J = 13.6 Hz), 6.88 (d, 1H, J = 8.0 Hz), 6.94 (t, 1H, J = 4.4 Hz), 7.00-7.09 (m, 1H), 7.28-7.36 (m, 1H), 7.50 (dd, 1H, J = 0.8 & 7.6 Hz)

^{13}C NMR (100 MHz) : δ 21.87, 26.39, 26.71, 39.22, 54.36, 76.54, 108.65, 122.90, 124.83, 127.70, 129.11, 134.70, 143.80, 149.38, 175.22, 197.69

HRMS calcd for $C_{16}H_{16}N_2O_4$ + H (M + H), 301.1188; Found, 301.1191.

[1-Methylindolin-2-one]-3-spiro-3´-[2´,5´,6´,7´-tetrahyroindole 1´-oxide] (79a)

To a stirring solution of 3-nitromethyl-3-(cyclohex-2-enon-2-yl)-1-methylindolin-2-one **78a** (2.0 mmol, 0.600 g) in dry ethanol (10 mL) at room temperature (25-30 ºC) were added Fe powder (12.0 mmol, 0.672 g) and 2N HCl (2.0 mL). After strirring at room temperature (25-30 °C) for 12 h the reaction mixture was diluted with ethyl acetate (20 mL) and stirred for a few minutes and filtered to remove iron impurities. The residue was washed with ethyl acetate (20 mL). The combined organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and the crude product thus obtained was subjected to column chromatography (silica gel, 2% EtOH in EtOAc) to provide **79a** in 69% (0.370 g) isolated yield as a brown solid.



Reaction time : 12 h

Yield (%) : 69

M.P. :180-182 ºC

IR (KBr) : ν 1718, 1610, 1587 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.71-1.92 (m, 2H),* 2.08-2.27 (m, 2H), 2.69-2.80 (m, 2H), 3.26 (s, 3H), 4.21 & 4.47 (ABq, 2H, J = 14.0 Hz), 5.39

(t, 1H, J = 4.4 Hz), 6.90 (d, 1H, J = 8.0 Hz), 7.08-7.18 (m, 2H), 7.32-7.38 (m, 1H), *It contains moisture peak

^{13}C NMR (100 MHz) : δ 20.02, 21.28, 24.59, 26.57, 51.29, 68.66, 108.48, 122.85, 123.48, 123.86, 129.06, 130.94, 137.42, 143.44, 143.91, 175.95

HRMS calcd for $C_{16}H_{16}N_2O_2$ + H (M + H), 269.1290 ; Found, 269.1290.

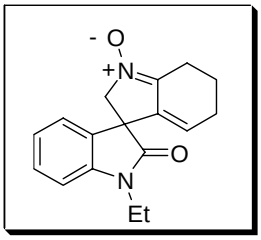
Representative one-pot procedure: [1-Methylindolin-2-one]-3-spiro-3´-[2´,5´,6´,7´-tetrahyroindole 1´-oxide] (79a)

To a stirring solution of 3-(*tert*-butoxycarbonyloxy)-3-(cyclohex-2-enon-2-yl)-1-methylindolin-2-one (**77a**) (2.0 mmol, 0.715 g) and nitromethane (3.0 mmol, 0.183 g, 0.16 mL) in anhydrous CH_2Cl_2 (5 mL) at room temperature (25-30 ºC) was added DMAP (2.0 mmol, 0.244 g). After stirring at the same temperature for 12 h under N_2 atmosphere, the solvent was removed under reduced pressure. The resulting residue was dissolved in dry ethanol (10 mL) and Fe powder (12.0 mmol, 0.672 g) and 2N HCl (2.0 mL) were added. After strirring at room temperature (25-30 ºC) for 12 h the reaction mixture was diluted with ethyl acetate (20 mL) and stirred for a few minutes and filtered to remove iron impurities. The residue was washed with ethyl acetate (20 mL). The combined organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and the crude product thus obtained was subjected to column chromatography (silica gel, 2% EtOH in EtOAc) to provide **79a** in 59% (0.319 g) isolated yield as brown solid.

Note: - The Spectral (IR,^{1}H & ^{13}C NMR, HRMS) data and melting point of this product was identical with that of the compound, obtained in a two step protocol.

[1-Ethylindolin-2-one]-3-spiro-3´-[2´,5´,6´,7´-tetrahyroindole 1´-oxide] (79b)

The title compound was prepared by the similar procedure as described for **79a** *via* the treatment of 3-(*tert*-butoxycarbonyloxy)-3-(cyclohex-2-enon-2-yl)-1-ethylindolin-2-one (**77b**) with nitromethane and subsequently reduction of *in situ* generated nitro-enone with Fe/HCl in EtOH, as brown solid.



Reaction time :12 h + 12 h

Yield (%) : 64

M.P. : 162-164 ºC

IR (KBr) : *v* 1709, 1612, 1583 cm^{-1}

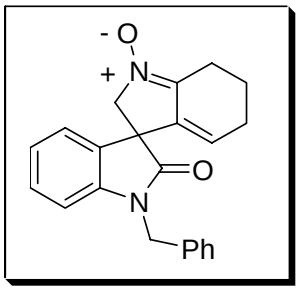
^{1}H NMR (400 MHz) : δ 1.31 (t, 3H, *J* = 7.2 Hz), 1.72-1.94 (m, 2H),$^{\#}$ 2.08-2.28 (m, 2H), 2.75 (t, 2H, *J* = 6.8 Hz), 3.69-3.92 (m, 2H), 4.22 & 4.48 (ABq, 2H, *J* = 14.0 Hz), 5.37 (t, 1H, *J* = 4.4 Hz), 6.92 (d, 1H, *J* = 8.0 Hz), 7.07-7.12 (m, 1H), 7.14-7.19 (m, 1H), 7.31-7.37 (m, 1H),* $^{\#}$It contains moisture peak. *Unresolved dd

^{13}C NMR (100 MHz) : δ 12.52, 20.00, 21.26, 24.59, 34.97, 51.22, 68.53, 108.60, 123.01, 123.25, 123.67, 128.97, 131.25, 137.58, 142.46, 143.95, 175.49

HRMS calcd for $C_{17}H_{18}N_2O_2$ + Na (M + Na), 305.1266; Found, 305.1232.

[1-Benzylindolin-2-one]-3-spiro-3´-[2´,5´,6´,7´-tetrahyroindole 1´-oxide] (79c)

The title compound was prepared by the similar procedure as described for **79a** *via* the treatment of 3-(*tert*-butoxycarbonyloxy)-3-(cyclohex-2-enon-2-yl)-1-benzylindolin-2-one (**77c**) with nitromethane and subsequently reduction of *in situ* generated nitro-enone with Fe/HCl in EtOH, as white solid.



Reaction time : 12 h + 12 h

Yield (%) : 60

M.P. : 162-164 ºC

IR (KBr) : *v* 1709, 1616, 1589 cm^{-1}

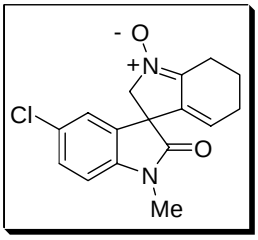
^{1}H NMR (400 MHz) : δ 1.73-1.96 (m, 2H),[#] 2.09-2.30 (m, 2H), 2.76 (t, 2H, *J* = 6.8 Hz), 4.26 & 4.54 (ABq, 2H, *J* = 14.0 Hz), 4.77 & 5.09 (ABq, 2H, *J* = 15.6 Hz), 5.40 (t, 1H, *J* = 4.4 Hz), 6.79 (d, 1H, *J* = 8.0 Hz), 7.03-7.09 (m, 1H), 7.16 (dd, 1H, *J* = 0.8 & 7.2 Hz)*, 7.18-7.23 (m, 1H), 7.26-7.38 (m, 5H), [#]It contains moisture peak. *unresolved dd

^{13}C NMR (100 MHz) : *δ* 20.02, 21.28, 24.67, 43.97, 51.29, 68.74, 109.46, 122.93, 123.48, 123.62, 127.11, 127.69, 128.70, 128.93, 130.98, 135.23, 137.68, 142.53, 143.75, 176.05

HRMS calcd for $C_{22}H_{20}N_2O_2$ + Na (M + Na), 367.1422; Found, 367.1406.

[1-Methyl-5-chlorolindolin-2-one]-3-spiro-3´-[2´,5´,6´,7´-tetrahyroindole 1´-oxide] (79d)

The title compound was prepared by the similar procedure as described for **79a** *via* the treatment of 3-(*tert*-butoxycarbonyloxy)-3-(cyclohex-2-enon-2-yl)-5-chloro-1-methylindolin-2-one (**77d**) with nitromethane and subsequently reduction of *in situ* generated nitro-enone with Fe/HCl in EtOH, as brown solid.



Reaction time : 12 h + 12 h

Yield (%) : 61

M.P. : 202-204 ºC

IR (KBr) : *v* 1720, 1610, 1589 cm^{-1}

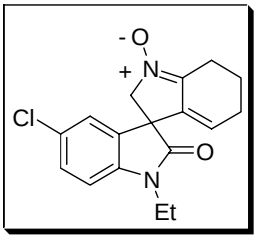
^{1}H NMR (400 MHz) : δ 1.74-1.94 (m, 2H), 2.11-2.28 (m, 2H), 2.75 (t, 2H, *J* = 6.8 Hz), 3.25 (s, 3H), 4.19 & 4.47 (ABq, 2H, *J* = 14.0 Hz), 5.40 (t, 1H, *J* = 4.4 Hz), 6.83 (d, 1H, *J* = 8.0 Hz), 7.15 (d, 1H, *J* = 2.0 Hz), 7.32 (dd, 1H, *J* = 2.0 & 8.0 Hz)

^{13}C NMR (100 MHz) : δ 20.12, 21.46, 24.81, 26.90, 51.52, 68.61, 109.61, 123.68, 124.53, 128.93, 129.19, 132.66, 137.04, 142.18, 144.13, 175.63

HRMS calc'd for $C_{16}H_{15}ClN_2O_2$ + H (M + H), 303.0900; Found, 303.0900.

[1-Ethyl-5-chlorolindolin-2-one]-3-spiro-3´-[2´,5´,6´,7´-tetrahyroindole 1´-oxide] (79e)

The title compound was prepared by the similar procedure as described for **79a** *via* the treatment of 3-(*tert*-butoxycarbonyloxy)-3-(cyclohex-2-enon-2-yl)-5-chloro-1-ethylindolin-2-one (**77e**) with nitromethane and subsequently reduction of *in situ* generated nitro-enone with Fe/HCl in EtOH, as brown solid.



Reaction time : 12 h + 12 h

Yield (%) : 56

M.P. : 154-156 ºC

IR (KBr) : ν 1713, 1607, 1585 cm^{-1}

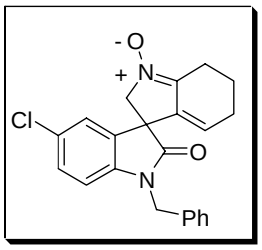
^{1}H NMR (500 MHz) : δ 1.29 (t, 3H, J = 7.0 Hz), 1.76-1.94 (m, 2H),[#] 2.12-2.28 (m, 2H), 2.75 (t, 2H, J = 7.0 Hz), 3.68-3.78 (m, 1H), 3.79-3.88 (m, 1H), 4.19 & 4.47 (ABq, 2H, J = 14.0 Hz), 5.38 (t, 1H, J = 4.5 Hz), 6.85 (d, 1H, J = 8.0 Hz), 7.15 (d, 1H, J = 2.0 Hz), 7.30 (dd, 1H, J = 2.0 & 8.5 Hz), [#]It contains moisture peak

^{13}C NMR (100 MHz) : δ 12.68, 20.22, 21.53, 24.90, 35.42, 51.52, 68.64, 109.74, 123.87, 123.94, 128.79, 129.15, 133.17, 137.40, 141.31, 143.87, 175.26

HRMS calcd for $C_{17}H_{17}ClN_2O_2$ + H (M + H), 317.1057; Found, 317.1056.

[1-Benzyl-5-chlorolindolin-2-one]-3-spiro-3´-[2´,5´,6´,7´-tetrahyroindole 1´-oxide] (79f)

The title compound was prepared by the similar procedure as described for **79a** *via* the treatment of 3-(*tert*-butoxycarbonyloxy)-3-(cyclohex-2-enon-2-yl)-5-chloro-1-benzylindolin-2-one (**77f**) with nitromethane and subsequently reduction of *in situ* generated nitro-enone with Fe/HCl in EtOH, as white solid.



Reaction time :12 h + 12 h

Yield (%) : 62

M.P. : 100-102 ºC

IR (KBr) : *v* 1715, 1610, 1583 cm^{-1}

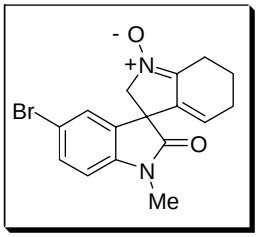
^{1}H NMR (400 MHz) : δ 1.68-1.88 (m, 2H), [#] 2.06-2.24 (m, 2H), 2.69 (t, 2H, *J* = 6.8 Hz), 4.15 & 4.45 (ABq, 2H, *J* = 14.0 Hz), 4.68 & 4.99 (ABq, 2H, *J* = 15.6 Hz), 5.34 (t, 1H, *J* = 4.4 Hz), 6.63 (d, 1H, *J* = 8.4 Hz), 7.07 (d, 1H, *J* = 2.0 Hz), 7.11 (dd, 1H, *J* = 2.0 & 8.4 Hz), 7.17-7.31 (m, 5H)*, [#]It contains moisture peak. *It contains $CHCl_3$ peak

^{13}C NMR (100 MHz) : δ 19.93, 21.28, 24.70, 44.10, 51.32, 68.44, 110.53, 123.52, 124.35, 127.07, 127.86, 128.72, 128.80, 128.91, 132.46, 134.79, 137.05, 141.08, 143.94, 175.56

HRMS calcd for $C_{20}H_{19}ClN_2O_2$ + H (M + H), 379.1213; Found, 379.1210.

[1-Methyl-5-bromoindolin-2-one]-3-spiro-3´-[2´,5´,6´,7´-tetrahyroindole 1´-oxide] (79g)

The title compound was prepared by the similar procedure as described for **79a** *via* the treatment of 3-(*tert*-butoxycarbonyloxy)-3-(cyclohex-2-enon-2-yl)-5-bromo-1-methylindolin-2-one (**77g**) with nitromethane and subsequently reduction of *in situ* generated nitro-enone with Fe/HCl in EtOH, as brown solid.



Reaction time : 12 h + 12 h

Yield (%) : 65

M.P. : 198-200 ºC

IR (KBr) : ν 1716, 1604, 1585 cm^{-1}

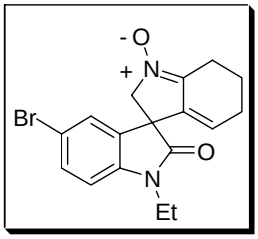
^{1}H NMR (400 MHz) : δ 1.76-1.93 (m, 2H), 2.11-2.28 (m, 2H), 2.75 (t, 2H, J = 6.0 Hz), 3.24 (s, 3H), 4.19 & 4.46 (ABq, 2H, J = 14.0 Hz), 5.40 (t, 1H, J = 4.4 Hz), 6.78 (d, 1H, J = 8.4 Hz), 7.28 (d, 1H, J = 2.0 Hz), 7.47 (dd, 1H, J = 2.0 & 8.4 Hz)

^{13}C NMR (100 MHz) : δ 20.13, 21.46, 24.82, 26.87, 51.44, 68.65, 110.08, 116.10, 124.37, 126.38, 132.08, 133.05, 137.05, 142.67, 143.96, 175.52

HRMS calcd for $C_{16}H_{15}BrN_2O_2$ + Na (M + Na), 369.0215; Found, 369.0184.

[1-Ethyl-5-bromoindolin-2-one]-3-spiro-3´-[2´,5´,6´,7´-tetrahyroindole 1´-oxide] (79h)

The title compound was prepared by the similar procedure as described for **79a** *via* the treatment of 3-(*tert*-butoxycarbonyloxy)-3-(cyclohex-2-enon-2-yl)-5-bromo-1-ethylindolin-2-one (**77h**) with nitromethane and subsequently reduction of *in situ* generated nitro-enone with Fe/HCl in EtOH, as brown solid.



Reaction time : 12 h + 12 h

Yield (%) : 60

M.P. : 182-184 ºC

IR (KBr): *v* 1715, 1605, 1589 cm^{-1}

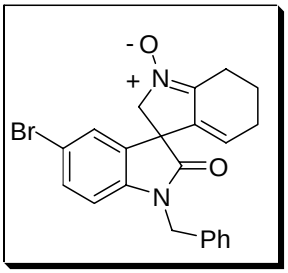
^{1}H NMR (400 MHz) : δ 1.29 (t, 3H, *J* = 7.2 Hz), 1.74-1.94 (m, 2H),[#] 2.12-2.29 (m, 2H), 2.75 (t, 2H, *J* = 6.8 Hz), 3.67-3.88 (m, 2H), 4.19 & 4.47 (ABq, 2H, *J* = 14.4 Hz), 5.38 (t, 1H, *J* = 4.8 Hz), 6.80 (d, 1H, *J* = 8.4 Hz), 7.29 (d, 1H, *J* = 2.0 Hz), 7.46 (dd, 1H, *J* = 8.4 & 2.0 Hz), [#]It contains moisture peak

^{13}C NMR (100 MHz) : δ 12.69, 20.20, 21.53, 24.90, 35.41, 51.45, 68.63, 110.24, 115.96, 124.18, 126.63, 132.07, 133.51, 137.33, 141.79, 144.01, 175.17

HRMS calcd for $C_{17}H_{17}BrN_2O_2$ + Na (M + Na), 383.0371; Found, 383.0364.

[1-Benzyl-5-bromoindolin-2-one]-3-spiro-3´-[2´,5´,6´,7´-tetrahyroindole 1´-oxide] (79i)

The title compound was prepared by the similar procedure as described for **79a** *via* the treatment of 3-(*tert*-butoxycarbonyloxy)-3-(cyclohex-2-enon-2-yl)-5-bromo-1-benzylindolin-2-one (**77i**) with nitromethane and subsequently reduction of *in situ* generated nitro-enone with Fe/HCl in EtOH, as white solid.



Reaction time : 12 h + 12 h

Yield (%) : 64

M.P. : 186-188 ºC

IR (KBr) : *v* 1715, 1610, 1589 cm^{-1}

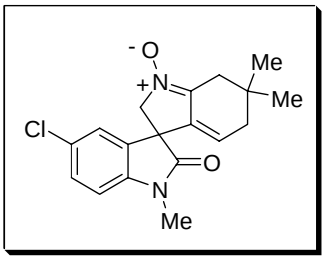
^{1}H NMR (400 MHz) : δ 1.75-1.95 (m, 2H),[#] 2.12-2.31 (m, 2H), 2.76 (t, 2H, *J* = 6.8 Hz), 4.23 & 4.53 (ABq, 2H, *J* = 14.0 Hz), 4.75 & 5.06 (ABq, 2H, *J* = 15.6 Hz), 5.41 (t, 1H, *J* = 4.4 Hz), 6.66 (d, 1H, *J* = 8.4 Hz), 7.24-7.36 (m, 7H),* [#] It contains moisture peak. *It contains $CHCl_3$ peak

^{13}C NMR (100 MHz) : δ 20.08, 21.40, 24.84, 44.23, 51.37, 68.66 111.08, 116.10, 124.11, 126.36, 127.19, 128.01, 128.94, 131.91, 133.04, 134.86, 137.24, 141.68, 143.75, 175.56

HRMS calcd for $C_{22}H_{19}BrN_2O_2$ + H (M +H), 423.0708; Found, 423.0704.

[1-Methyl-5-chloroindolin-2-one]-3-spiro-3´-[6´,6´-dimethyl-2´,5´,6´,7´-tetrahyroindole 1´-oxide] (79j)

The title compound was prepared by the similar procedure as described for **79a** *via* the treatment of 3-(*tert*-butoxycarbonyloxy)-3-(5,5-dimethylcyclohex-2-enon-2-yl)-5-chloro-1-methylindolin-2-one (**77j**) with nitromethane and subsequently reduction of *in situ* generated nitro-enone with Fe/HCl in EtOH, as white solid.



Reaction time : 12 h + 12 h

Yield (%) : 63

M.P. : 186-188 ºC

IR (KBr) : ν 1722, 1588 cm^{-1}

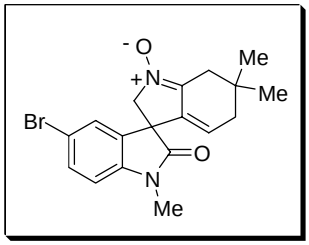
^{1}H NMR (400 MHz) : δ 1.03 (s, 3H), 1.06 (s, 3H), 2.00 & 2.07 (dABq, 2H, J = 4.8 & 18.0 Hz), 2.55 (s, 2H),* 3.25 (s, 3H), 4.22 & 4.49 (ABq, 2H, J = 14.0 Hz), 5.29 (t, 1H, J = 4.8 Hz), 6.84 (d, 1H, J = 8.4 Hz), 7.14 (d, 1H, J = 2.0 Hz), 7.33 (dd, 1H, J = 2.0 & 8.0 Hz), *It may be unresolved Abq

^{13}C NMR (100 MHz) : δ 26.97, 28.55, 28.64, 30.96, 34.91, 39.33, 51.33, 69.16, 109.66, 122.37, 123.58, 129.03, 129.26, 132.73, 136.47, 142.27, 144.35, 175.67

HRMS calcd for $C_{18}H_{19}ClN_2O_2$ + H (M + H), 331.1213; Found, 331.1209.

[1-Methyl-5-bromoindolin-2-one]-3-spiro-3´-[6´,6´-dimethyl-2´,5´,6´,7´-tetrahyroindole 1´-oxide] (79k)

The title compound was prepared by the similar procedure as described for **79a** *via* the treatment of 3-(*tert*-butoxycarbonyloxy)-3-(5,5-dimethylcyclohex-2-enon-2-yl)-5-bromo-1-methylindolin-2-one (**77k**) with nitromethane and subsequently reduction of *in situ* generated nitro-enone with Fe/HCl in EtOH, as white solid.



Reaction time : 12 h + 12 h

Yield (%) : 58

M.P. :194-196 ºC

IR (KBr) : ν 1704, 1616, 1578 cm^{-1}

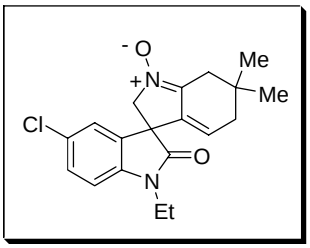
^{1}H NMR (400 MHz) : δ 1.03 (s, 3H), 1.06 (s, 3H), 2.05 & 2.07 (dABq, 2H, J = 4.8 & 18.0 Hz), 2.47-2.62 (m, 2H),* 3.24 (s, 3H), 4.21 & 4.49 (ABq, 2H, J = 14.0 Hz), 5.29 (t, 1H, J = 4.8 Hz), 6.79 (d, 1H, J = 8.0 Hz), 7.28 (d, 1H, J = 2.0 Hz), 7.48 (dd, 1H, J = 2.0 & 8.4 Hz), *Unresolved Abq

^{13}C NMR (100 MHz) : δ 26.97, 28.56, 28.71, 30.99, 34.96, 39.39, 51.30, 69.24, 110.15, 116.23, 122.30, 126.37, 132.19, 133.17, 136.52, 142.80, 144.30, 175.59

HRMS calcd for $C_{18}H_{19}BrN_2O_2$ + H (M + H), 375.0708; Found, 375.0712

[1-Ethyl-5-chloroindolin-2-one]-3-spiro-3´-[6´,6´-dimethyl-2´,5´,6´,7´-tetrahyroindole 1´-oxide] (79l)

The title compound was prepared by the similar procedure as described for **79a** *via* the treatment of 3-(*tert*-butoxycarbonyloxy)-3-(5,5-dimethylcyclohex-2-enon-2-yl)-5-chloro-1-ethylindolin-2-one (**77j**) with nitromethane and subsequently reduction of *in situ* generated nitro-enone with Fe/HCl in EtOH, as white solid.



Reaction time : 12 h + 12 h

Yield (%) : 61

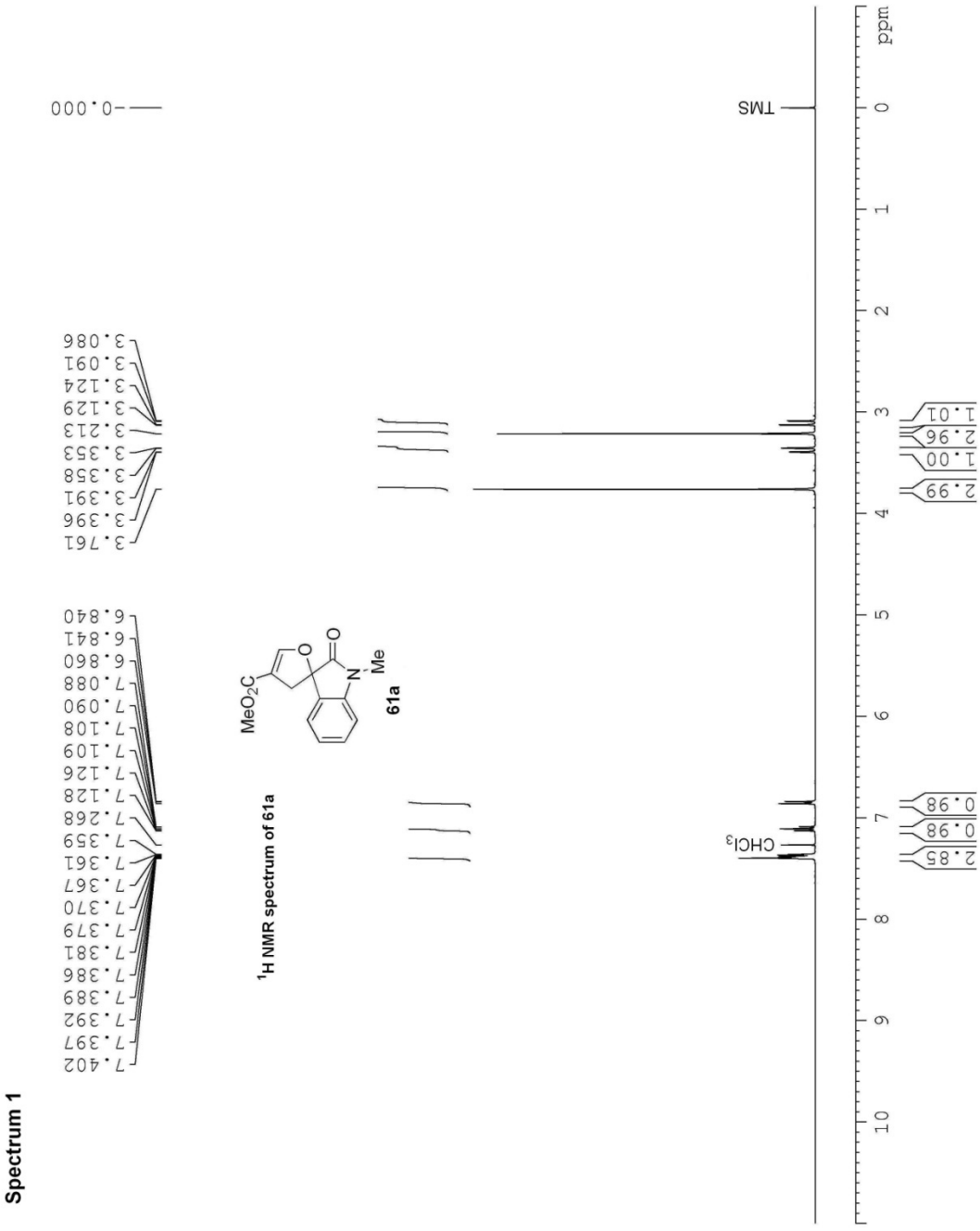
M.P. : 184-186 ºC

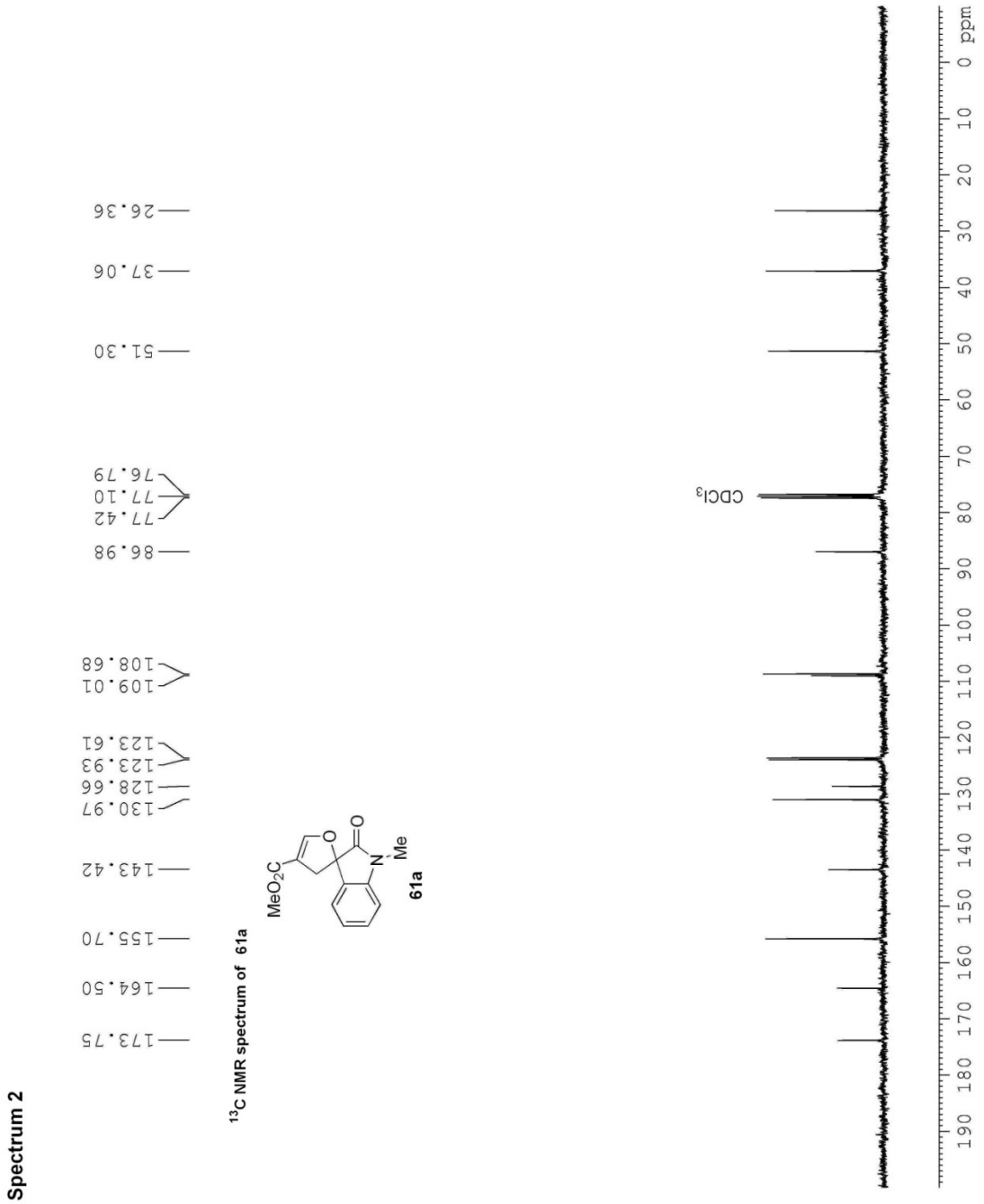
IR (KBr) : ν 1704, 1605, 1582 cm^{-1}

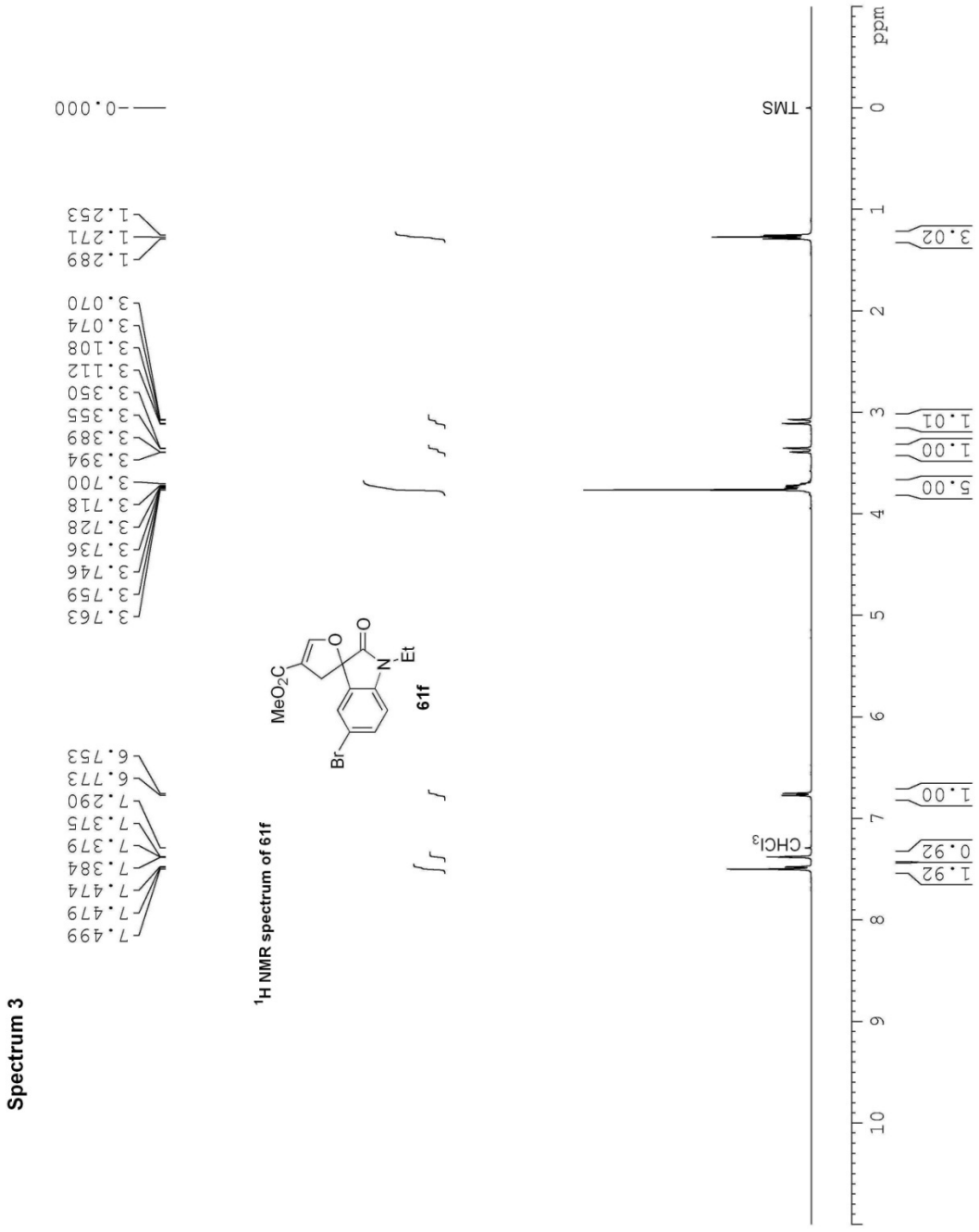
^{1}H NMR (500 MHz) : δ 1.02 (s, 3H), 1.07 (s, 3H), 1.29 (t, 3H, J = 7.5 Hz), 2.00 & 2.07 (dABq, 2H, J = 4.5 & 18.0 Hz), 2.54 (s, 2H),* 3.68-3.88 (m, 2H), 4.22 & 4.50 (ABq, 2H, J = 14.5 Hz), 5.26 (t, 1H, J = 4.5 Hz), 6.84 (d, 1H, J = 8.5 Hz), 7.14 (d, 1H, J = 2.0 Hz), 7.31 (dd, 1H, J = 2.0 & 8.0 Hz), * Unresolved ABq

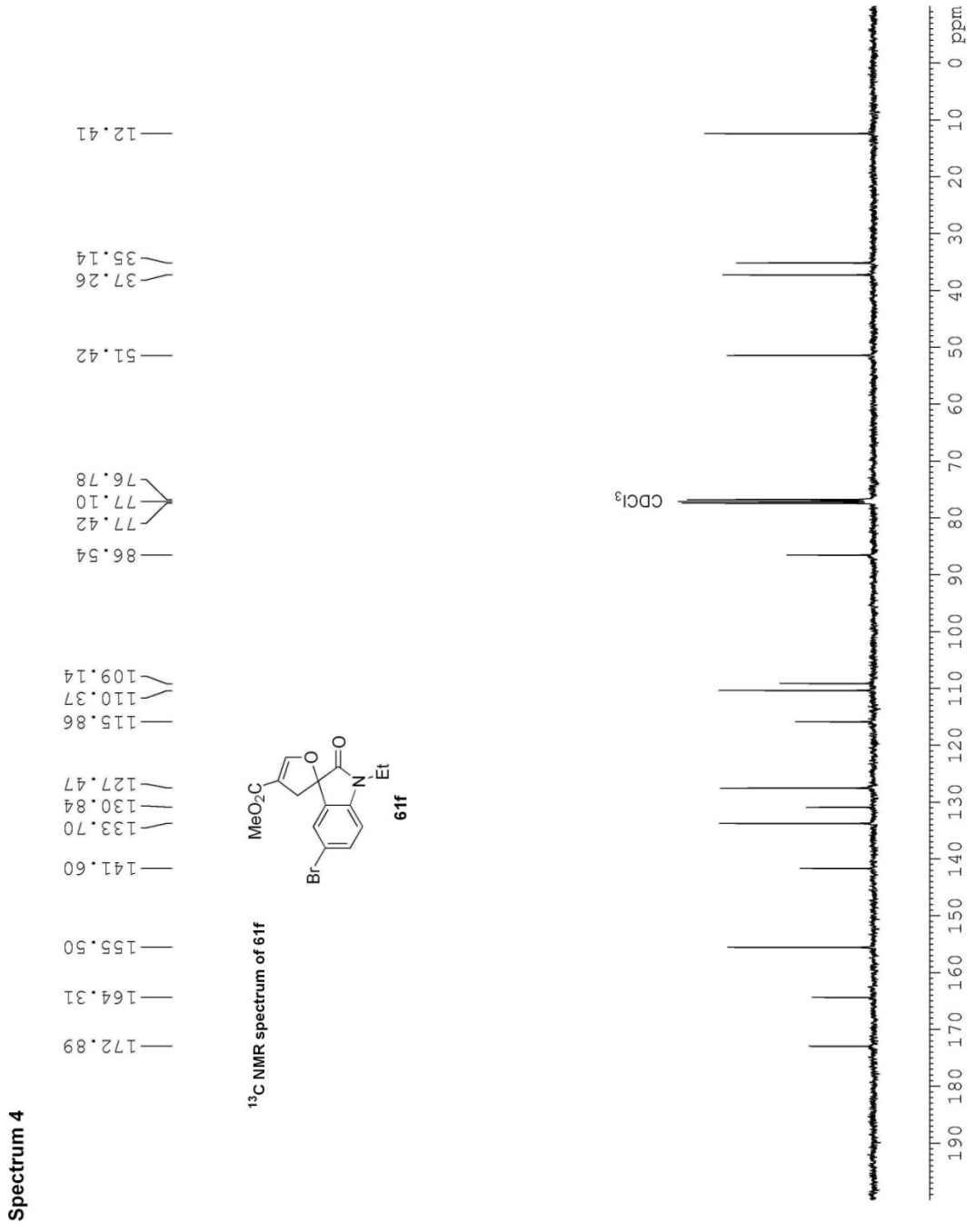
^{13}C NMR (100 MHz) : δ 12.65, 28.53, 28.64, 30.94, 34.90, 35.38, 39.33, 51.25, 69.07, 109.76, 121.87, 123.67, 128.76, 129.15, 133.13, 136.70, 141.30, 144.14, 175.19

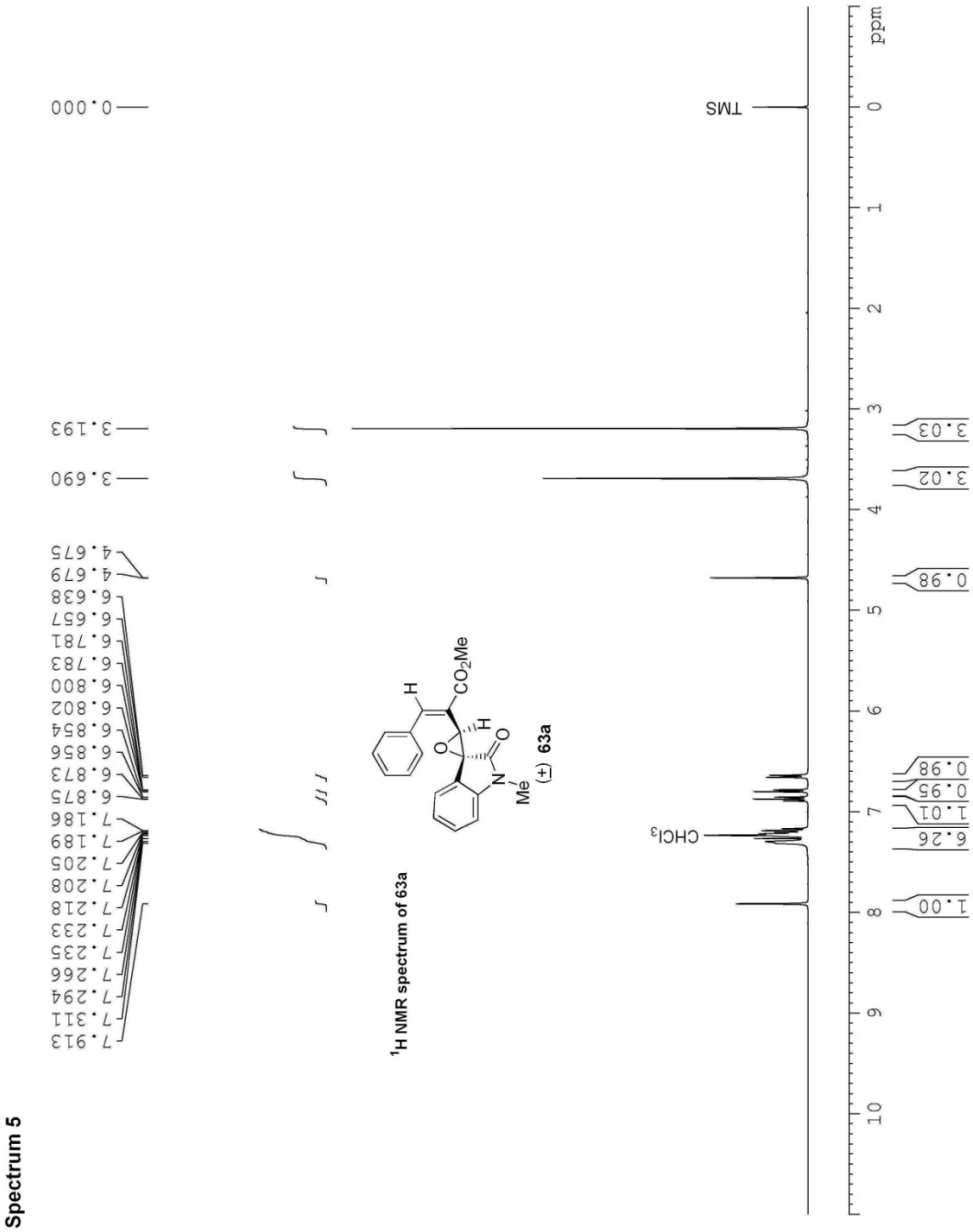
HRMS calcd for $C_{19}H_{21}ClN_2O_2$ + H (M + H), 345.1370; Found, 345.1377.


Spectrum 1
7.402
7.397
7.392
7.389
7.386
7.381
7.379
7.370
7.367
7.361
7.359
7.268
7.128
7.126
7.109
7.108
7.090
7.088
6.860
6.841
6.840
3.761
3.396
3.391
3.358
3.353
3.213
3.129
3.124
3.091
3.086
0.000
TMS
CHCl3
2.85
0.98
0.98
2.99
1.00
2.96
1.01
ppm
MeO2C
O
O
N
Me
61a
1H NMR spectrum of 61a

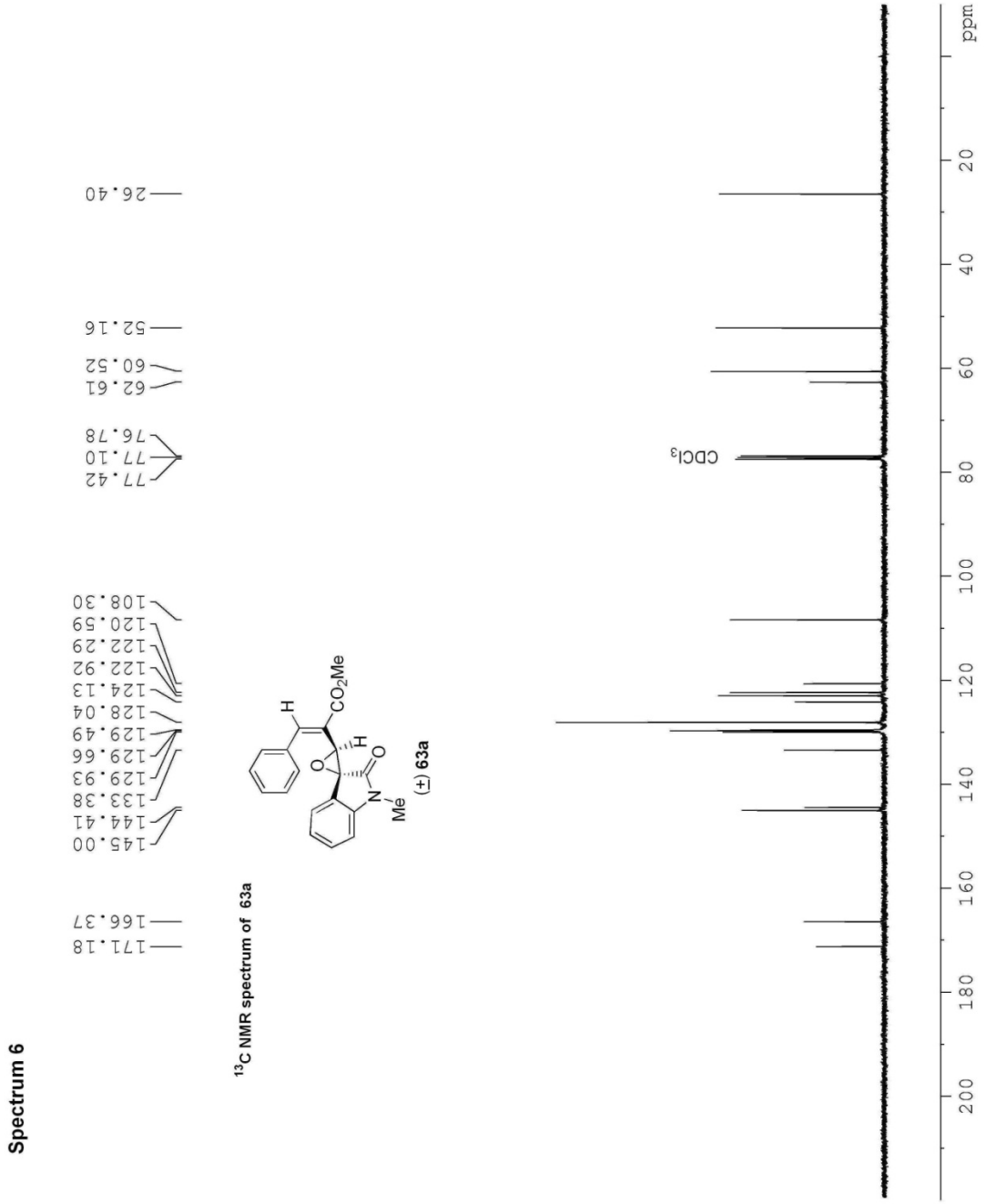

Spectrum 2
^{13}C NMR spectrum of 61a
MeO2C
O
O
N
Me
61a
173.75
164.50
155.70
143.42
130.97
128.66
123.93
123.61
109.01
108.68
86.98
77.42
77.10
76.79
51.30
37.06
26.36
CDCl3
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


Spectrum 3
7.499
7.479
7.474
7.384
7.379
7.375
7.290
6.773
6.753
3.763
3.759
3.746
3.736
3.728
3.718
3.700
3.394
3.389
3.355
3.350
3.112
3.108
3.074
3.070
1.289
1.271
1.253
0.000
^{1}H NMR spectrum of 61f
MeO$_2$C
Br
O
O
N
Et
61f
CHCl$_3$
TMS
1.92
0.92
1.00
3.02
5.00
1.00
1.01
ppm

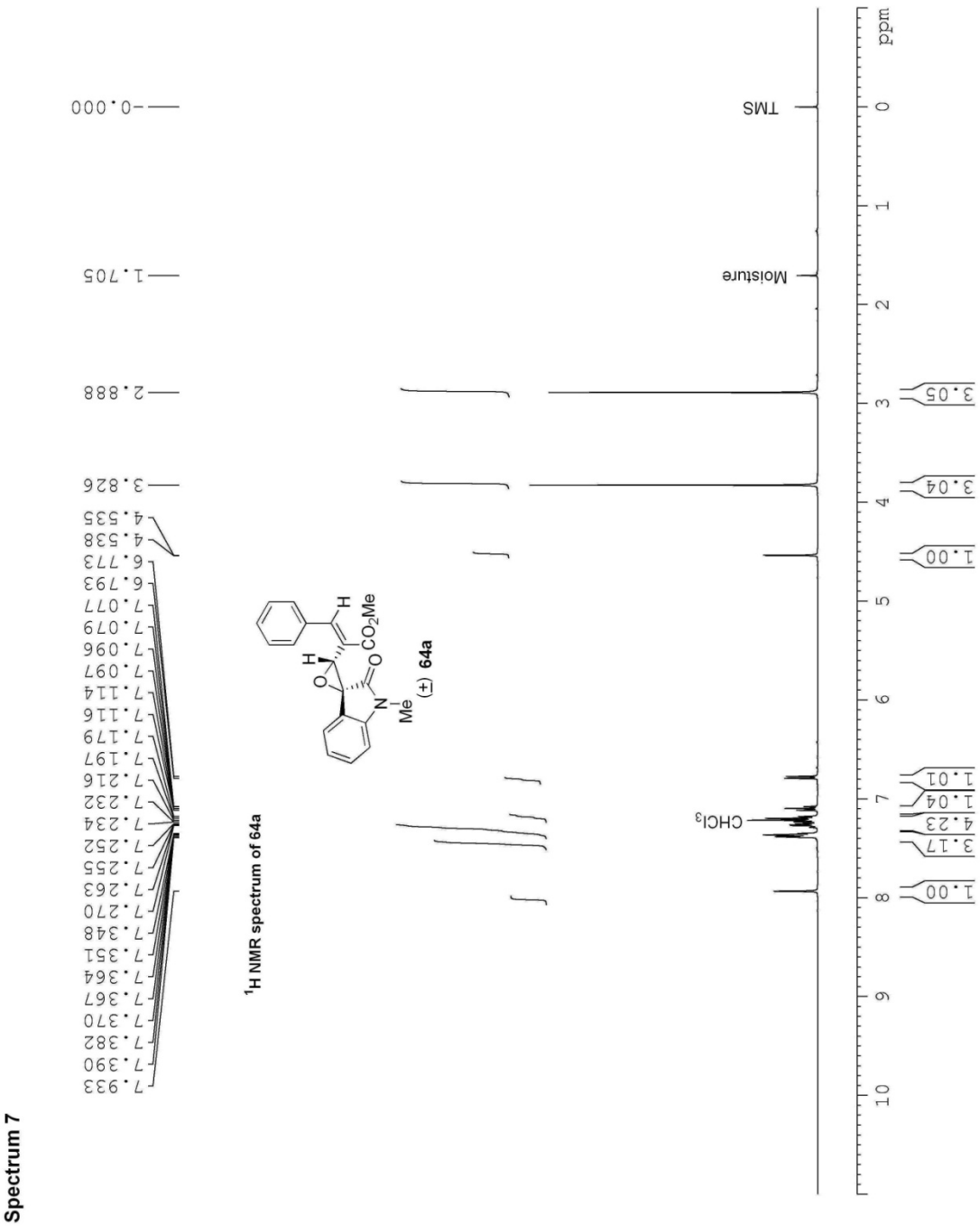

Spectrum 4
^{13}C NMR spectrum of 61f
MeO2C
Br
O
O
N
Et
61f
CDCl3
172.89
164.31
155.50
141.60
133.70
130.84
127.47
115.86
110.37
109.14
86.54
77.42
77.10
76.78
51.42
37.26
35.14
12.41
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


Spectrum 5
0.000
3.193
3.690
4.675
4.679
6.638
6.657
6.781
6.783
6.800
6.802
6.854
6.856
6.873
6.875
7.186
7.189
7.205
7.208
7.218
7.233
7.235
7.266
7.294
7.311
7.913
TMS
CHCl3
1.00
6.26
1.01
0.95
0.98
0.98
3.02
3.03
ppm
0 1 2 3 4 5 6 7 8 9 10
CO2Me
H
H
O
O
N
Me
(±) 63a
1H NMR spectrum of 63a

Spectrum 6



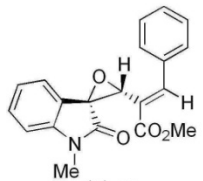
^{13}C NMR spectrum of 63a


Spectrum 7
^{1}H NMR spectrum of 64a
(±) 64a
TMS
Moisture
CHCl$_3$
ppm
0
1
2
3
4
5
6
7
8
9
10
3.05
3.04
1.00
1.01
1.04
4.23
3.17
1.00
-0.000
1.705
2.888
3.826
4.535
4.538
6.773
6.793
7.077
7.079
7.096
7.097
7.114
7.116
7.179
7.197
7.216
7.232
7.234
7.252
7.255
7.263
7.270
7.348
7.351
7.364
7.367
7.370
7.382
7.390
7.933

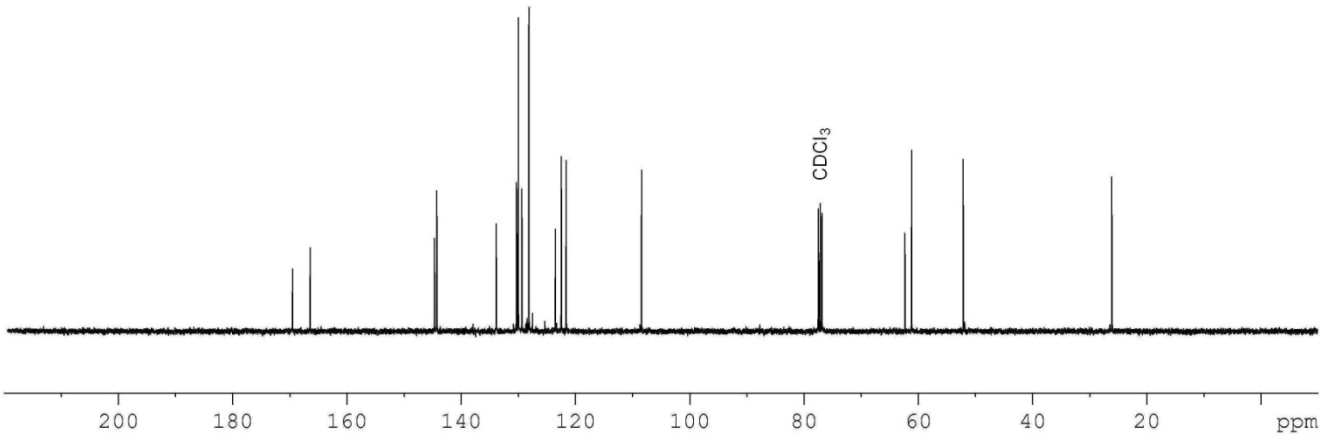
Spectrum 8

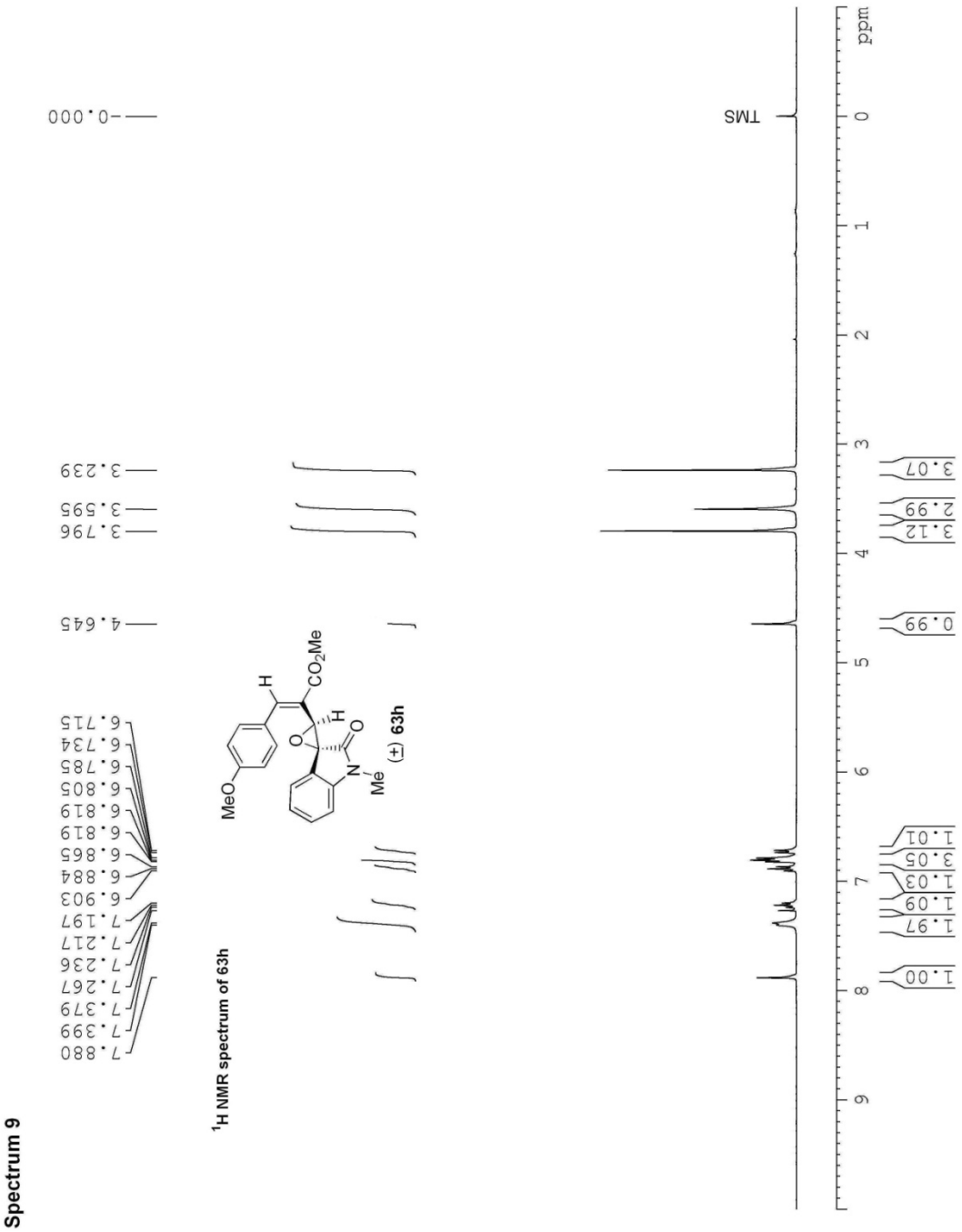
169.46
166.38
144.61
144.20
133.80
130.26
129.94
129.31
128.09
123.44
122.42
122.37
121.57
108.37
77.42
77.10
76.78
62.23
61.08
52.04
26.02

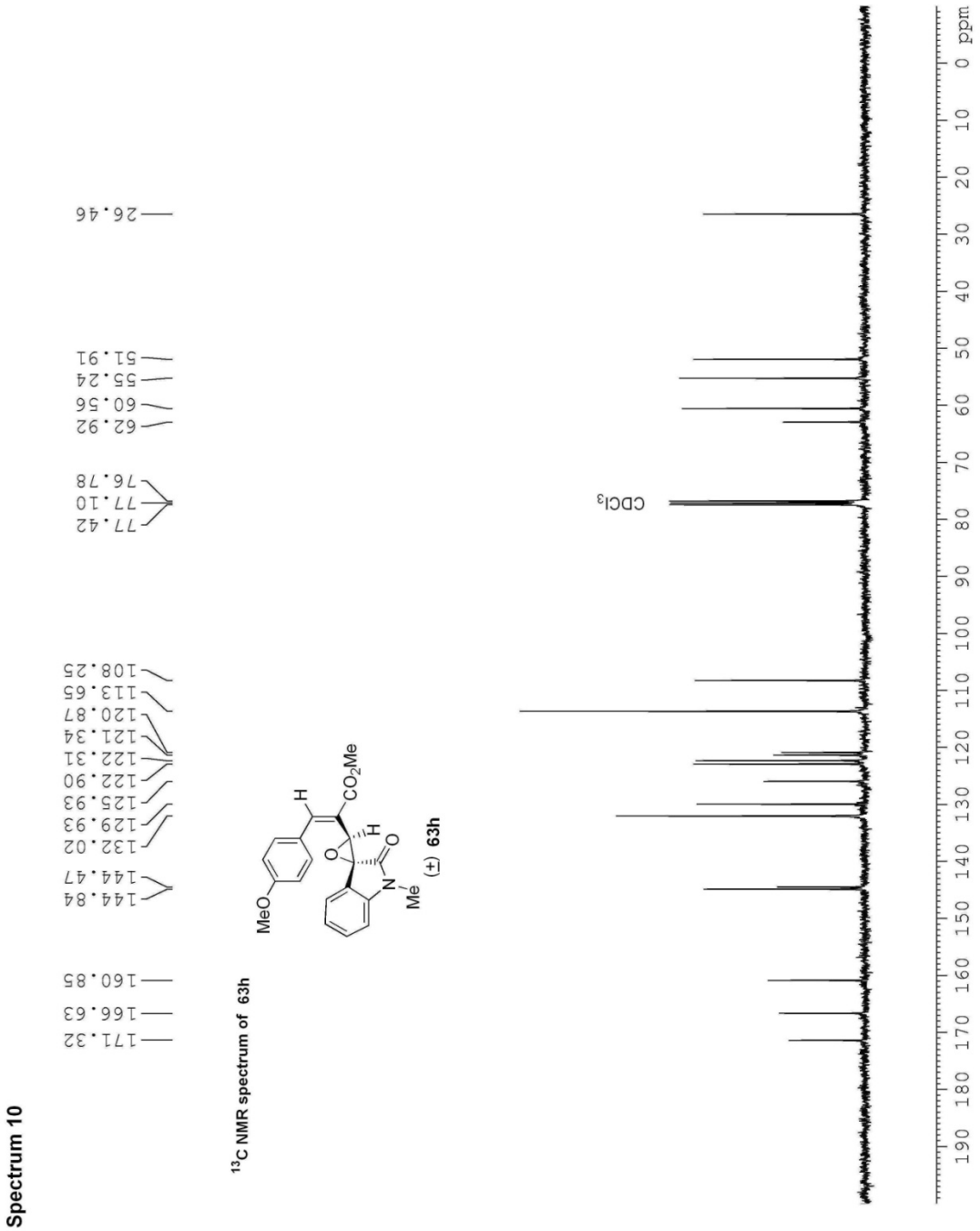
^{13}C NMR spectrum of 64a

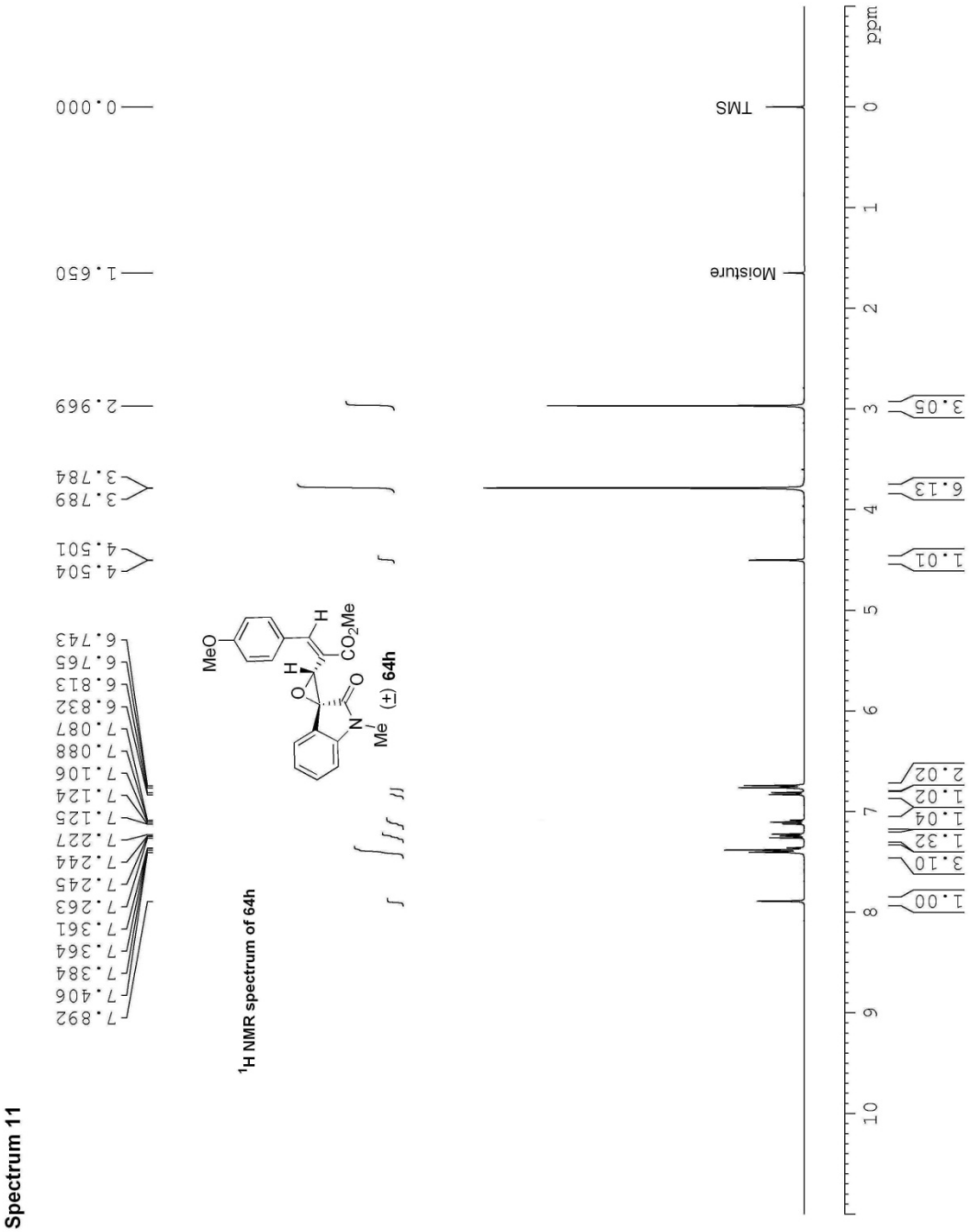


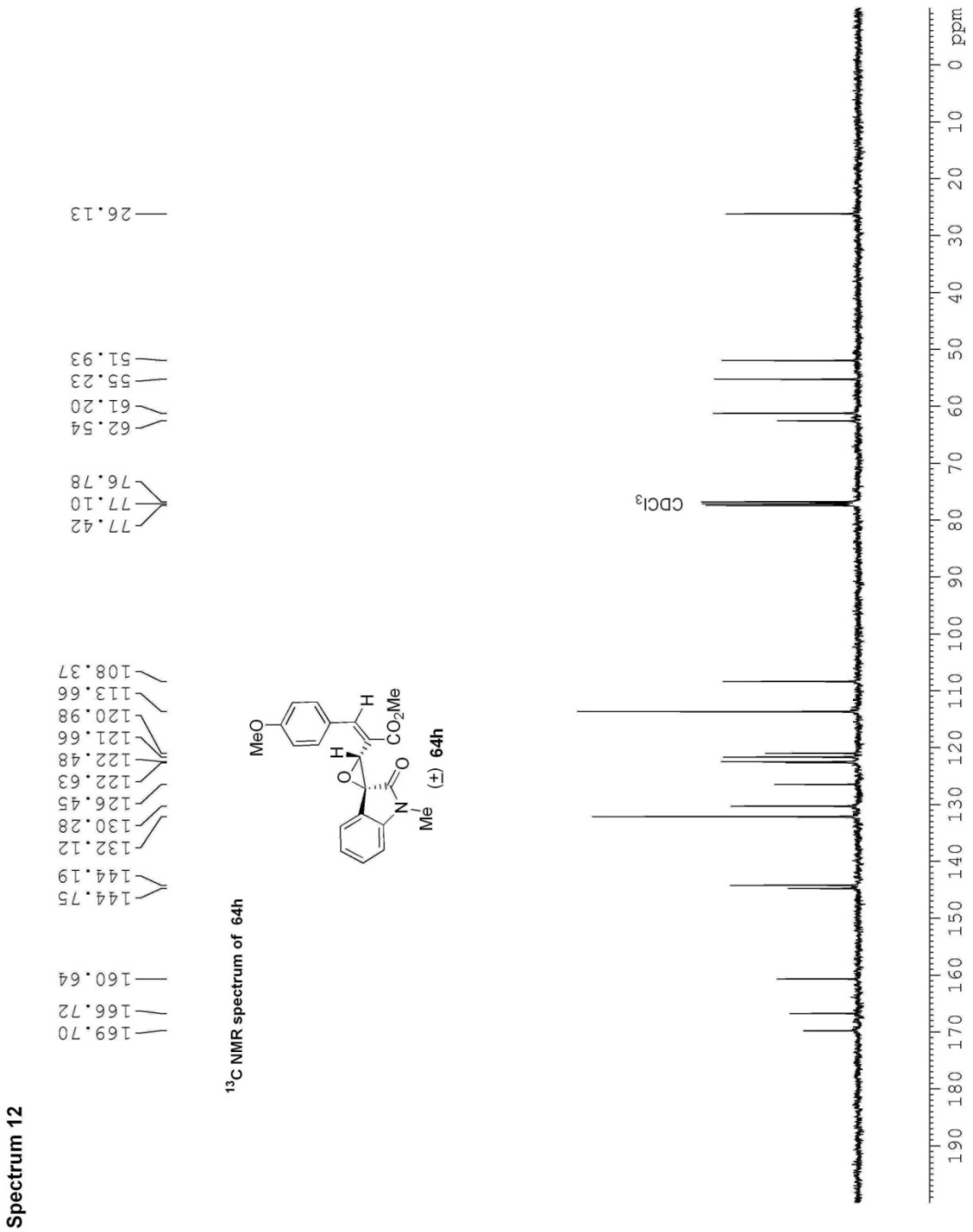
(±) **64a**

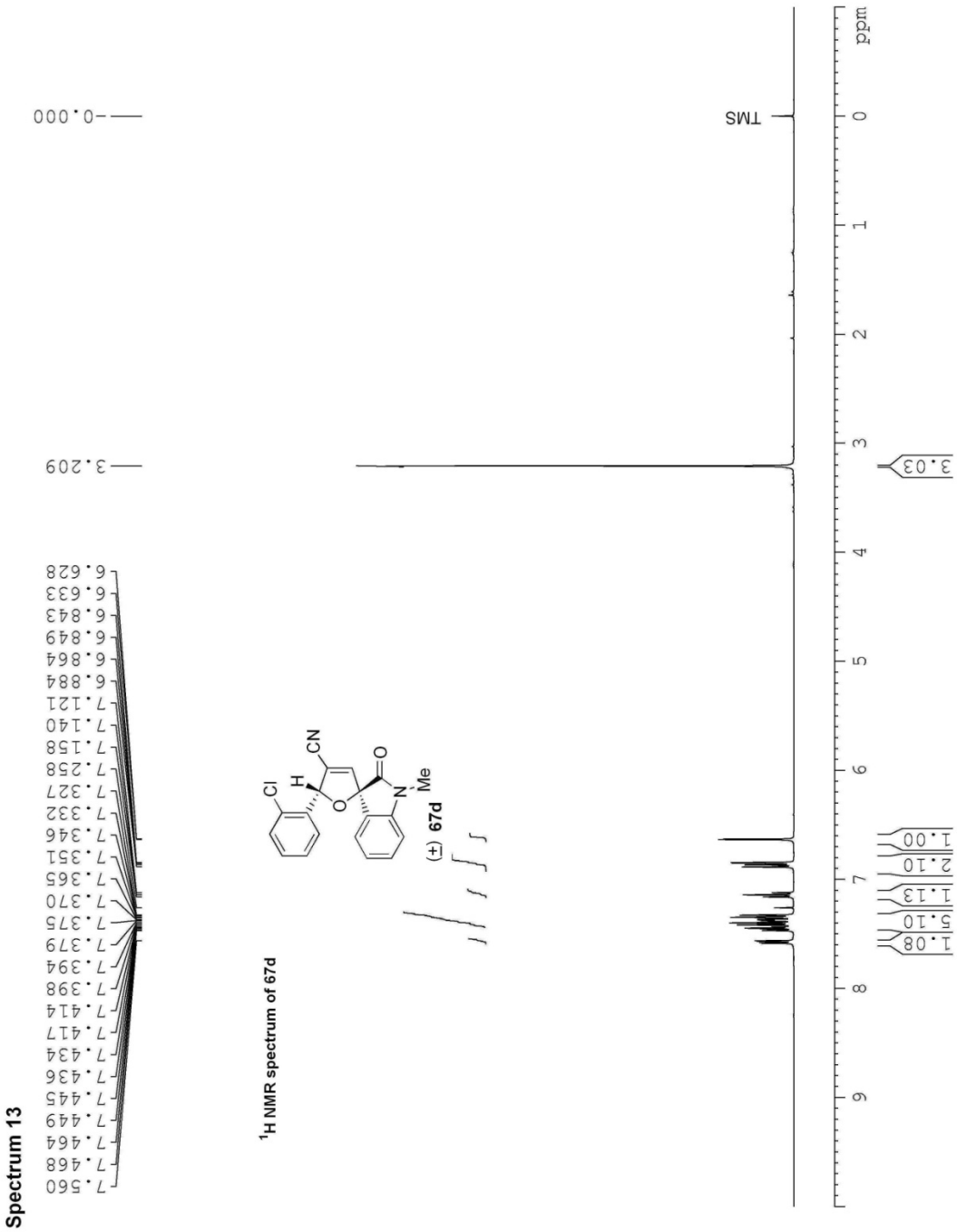


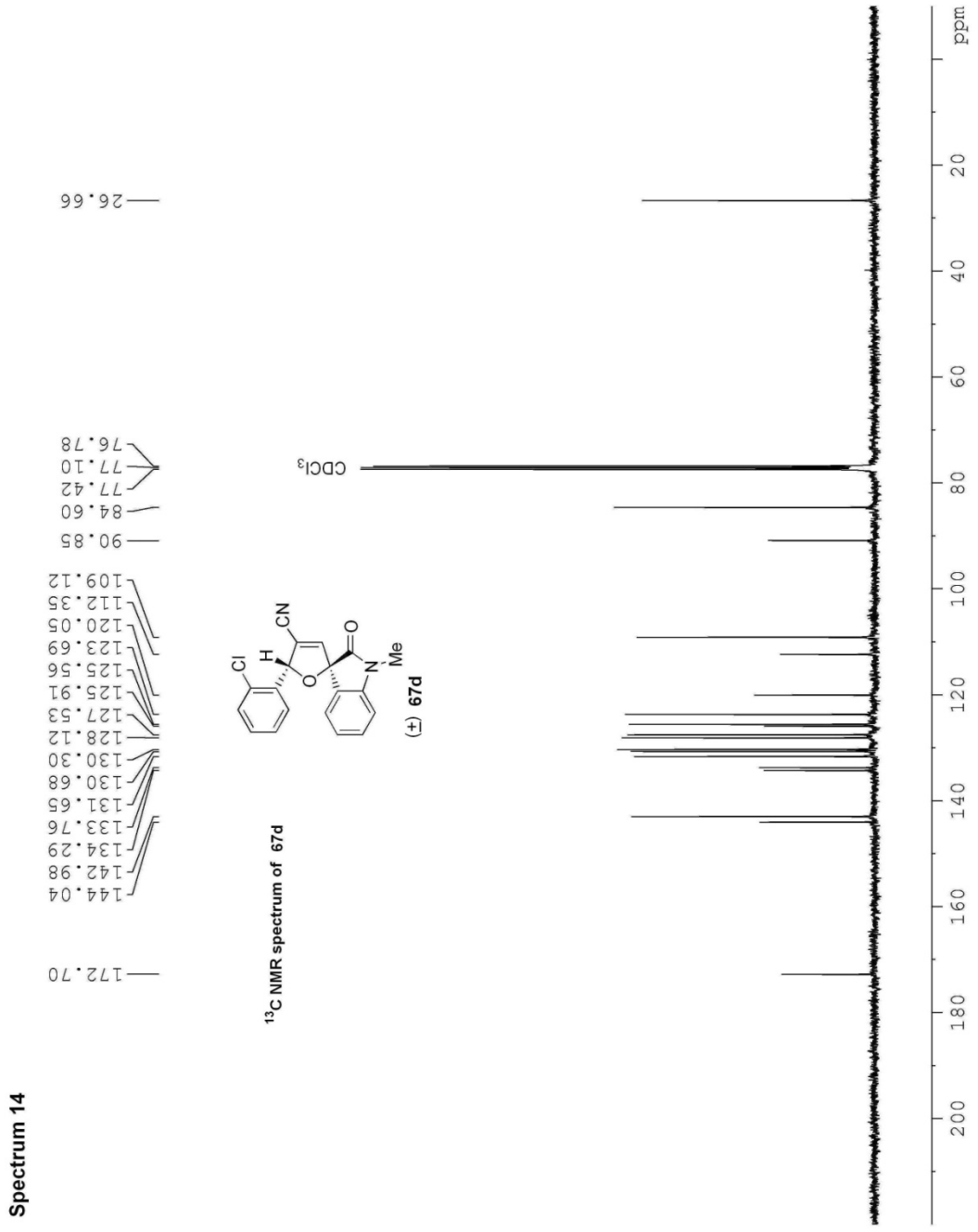

Spectrum 9
0.000
7.880
7.399
7.379
7.267
7.236
7.217
7.197
6.903
6.884
6.865
6.819
6.819
6.805
6.785
6.734
6.715
4.645
3.796
3.595
3.239
TMS
1.00
1.97
1.09
1.03
3.05
1.01
0.99
3.12
2.99
3.07
ppm
0
1
2
3
4
5
6
7
8
9
MeO
H
CO2Me
H
O
O
N
Me
(±) 63h
1H NMR spectrum of 63h

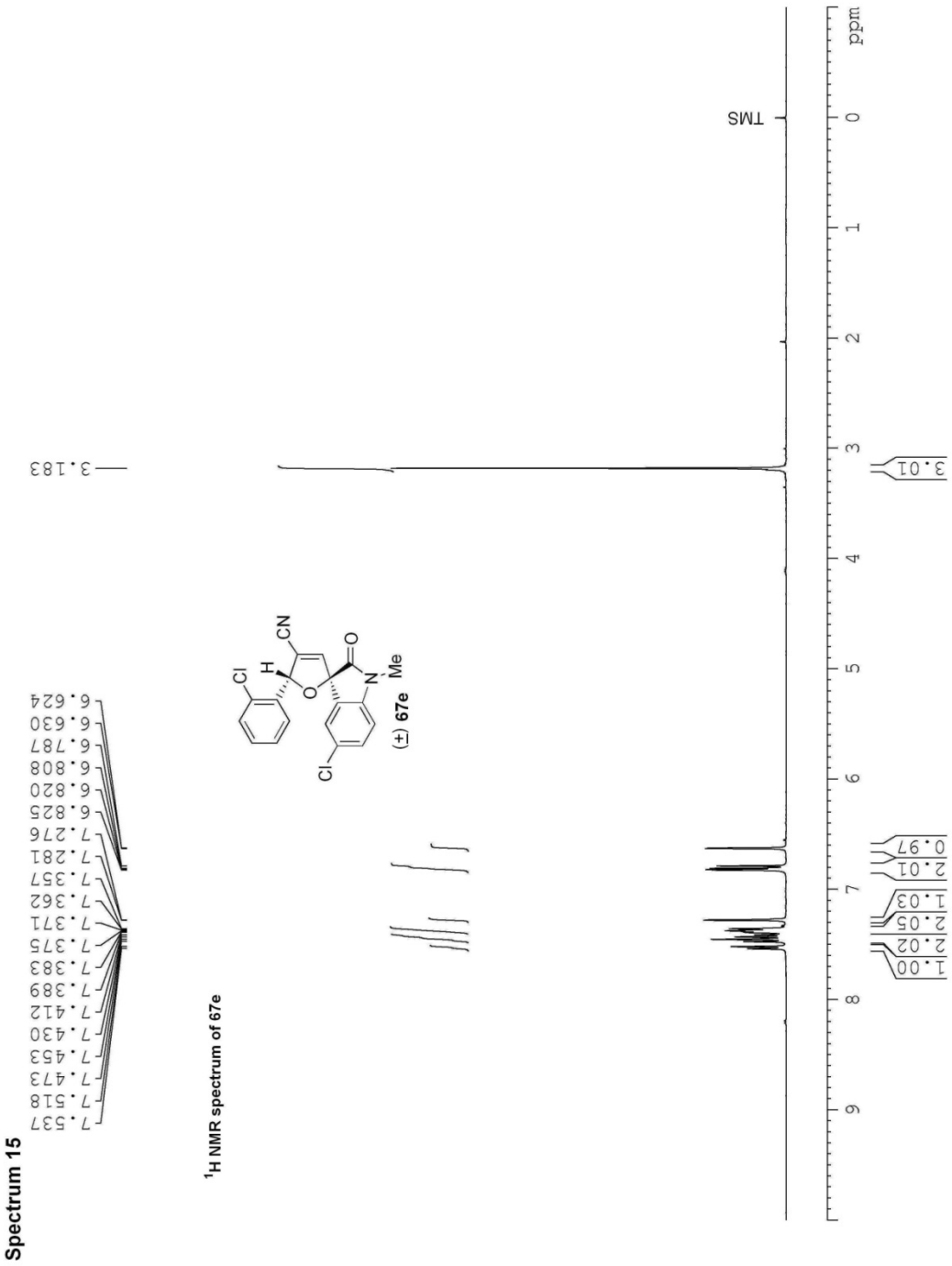

Spectrum 10
^{13}C NMR spectrum of 63h
(±) 63h
MeO
Me
CO2Me
CDCl3
171.32
166.63
160.85
144.84
144.47
132.02
129.93
125.93
122.90
122.31
121.34
120.87
113.65
108.25
77.42
77.10
76.78
62.92
60.56
55.24
51.91
26.46
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

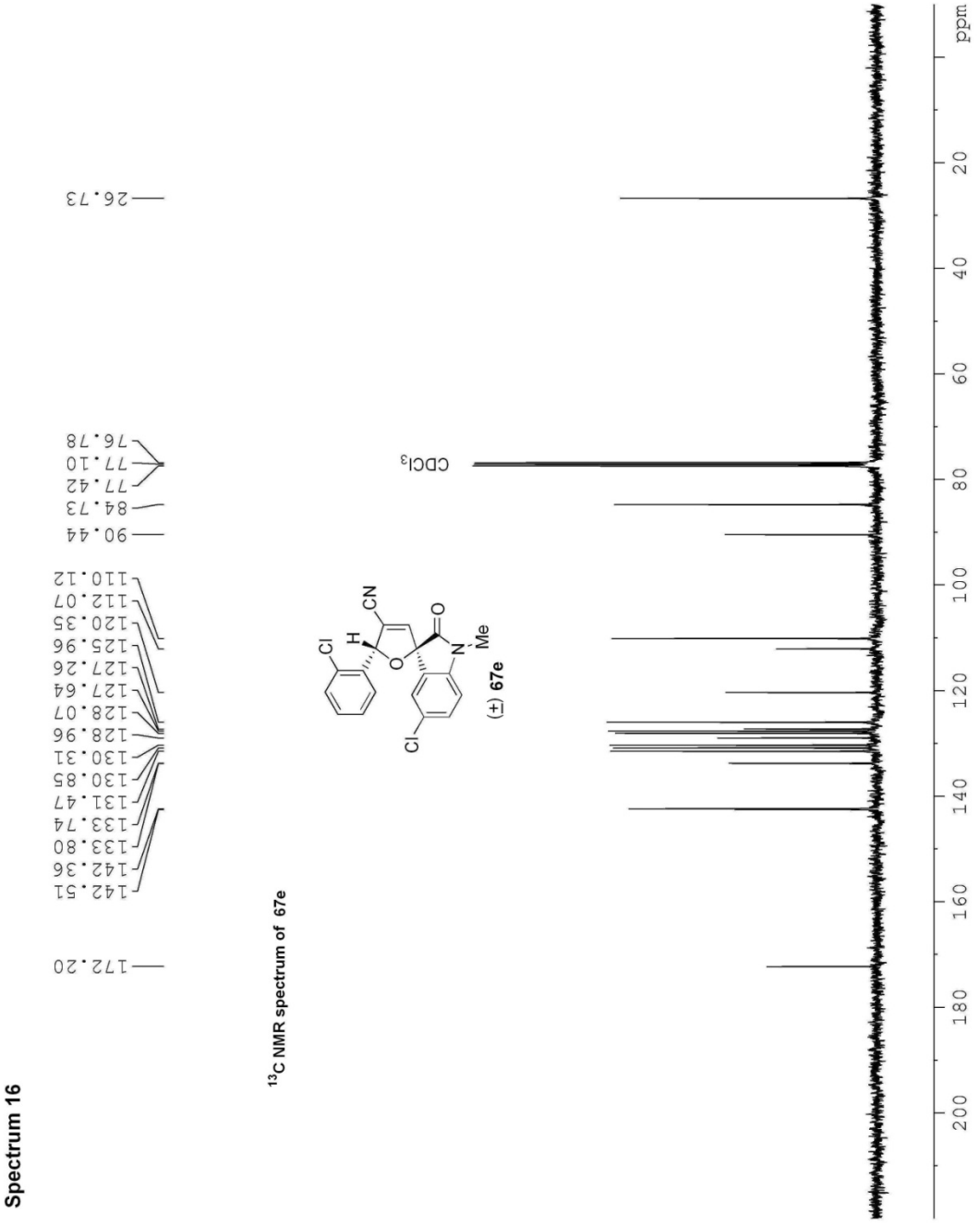

Spectrum 11
7.892
7.406
7.384
7.364
7.361
7.263
7.245
7.244
7.227
7.125
7.124
7.106
7.088
7.087
6.832
6.813
6.765
6.743
4.504
4.501
3.789
3.784
2.969
1.650
0.000
TMS
Moisture
1.00
3.10
1.32
1.04
1.02
2.02
1.01
6.13
3.05
ppm
MeO
H
O
H
CO2Me
O
N
Me
(±) 64h
1H NMR spectrum of 64h

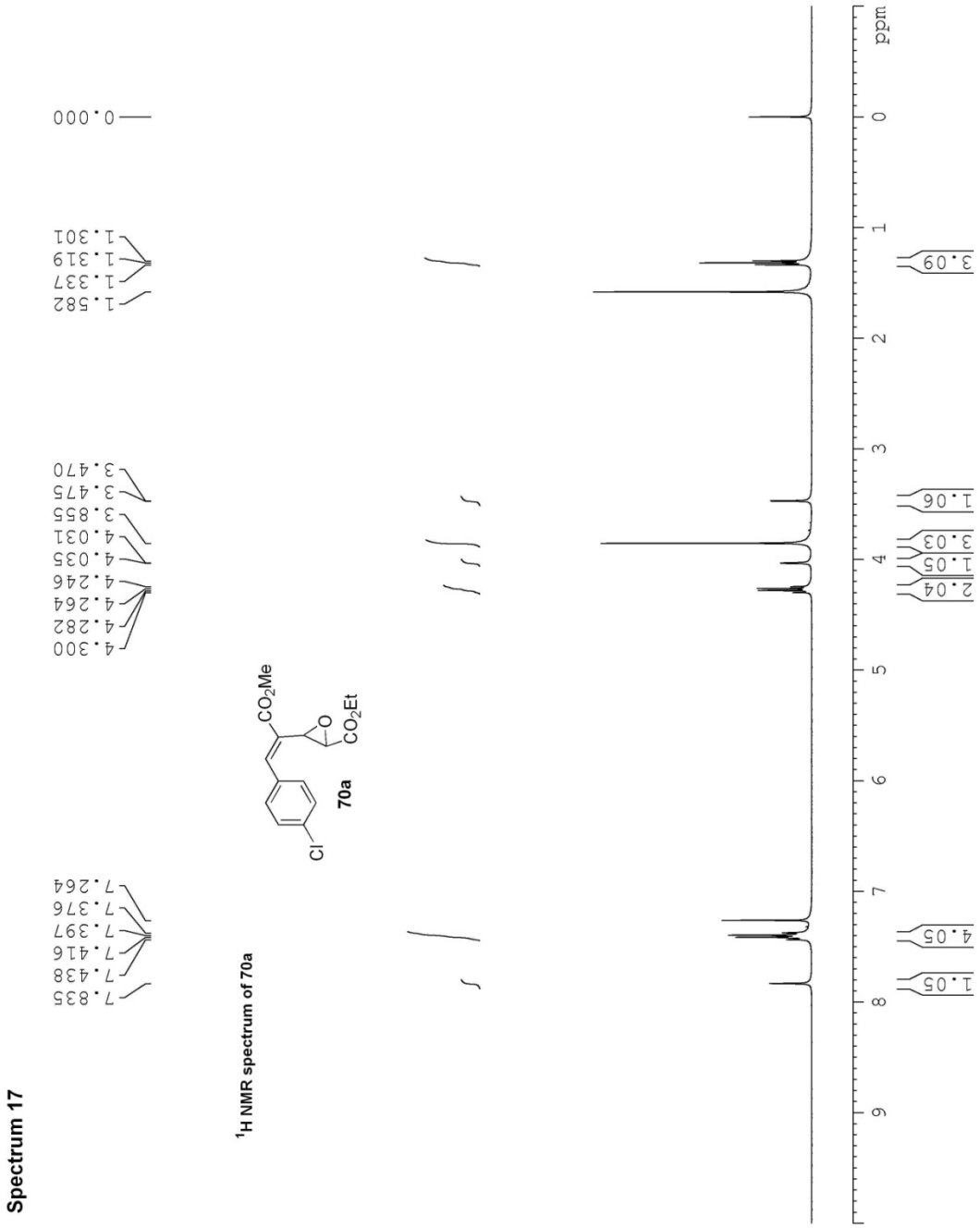

Spectrum 12
^{13}C NMR spectrum of 64h
MeO
CO2Me
H
O
O
N
Me
(±) 64h
CDCl3
ppm

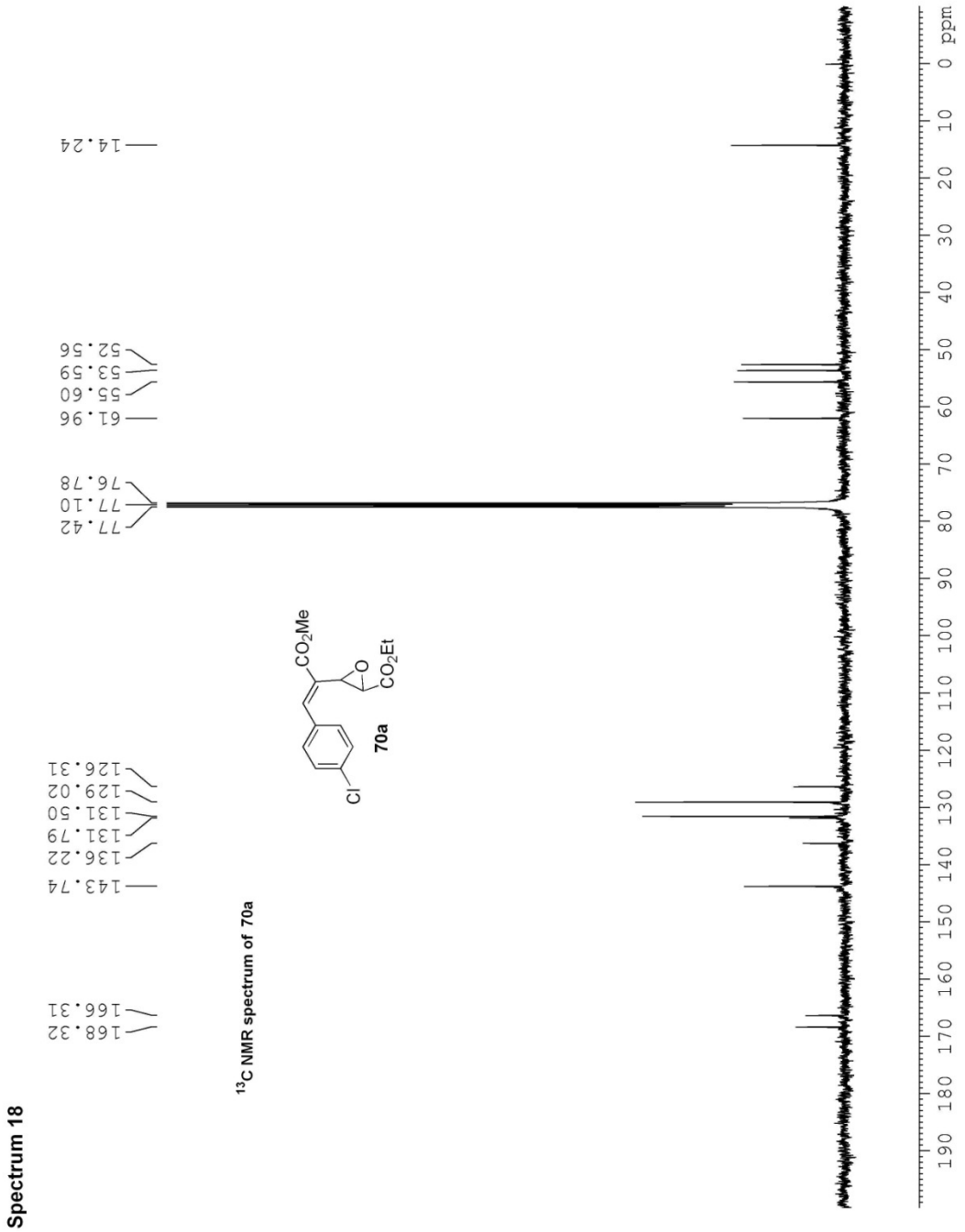

Spectrum 13
7.560
7.468
7.464
7.449
7.445
7.436
7.434
7.417
7.414
7.398
7.394
7.379
7.375
7.370
7.365
7.351
7.346
7.332
7.327
7.258
7.158
7.140
7.121
6.884
6.864
6.849
6.843
6.633
6.628
3.209
-0.000
TMS
3.03
1.08
5.10
1.13
2.10
1.00
ppm
0
1
2
3
4
5
6
7
8
9
Cl
H
CN
O
N
Me
(±) 67d
1H NMR spectrum of 67d

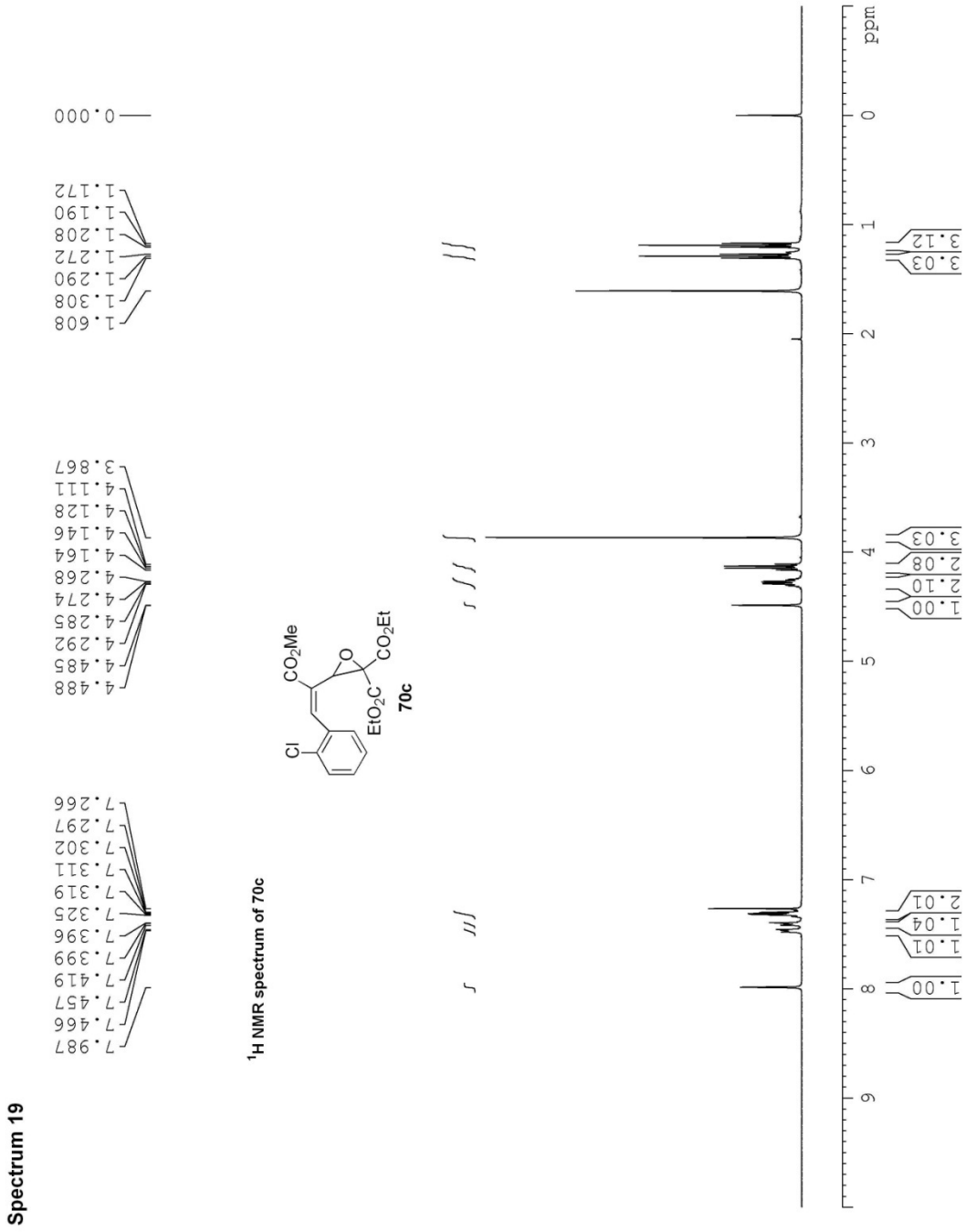

Spectrum 14
26.66
76.78
77.10
77.42
84.60
90.85
109.12
112.35
120.05
123.69
125.56
125.91
127.53
128.12
130.30
130.68
131.65
133.76
134.29
142.98
144.04
172.70
CDCl3
ppm
20
40
60
80
100
120
140
160
180
200
13C NMR spectrum of 67d
(±) 67d
Cl
H
CN
O
N
Me

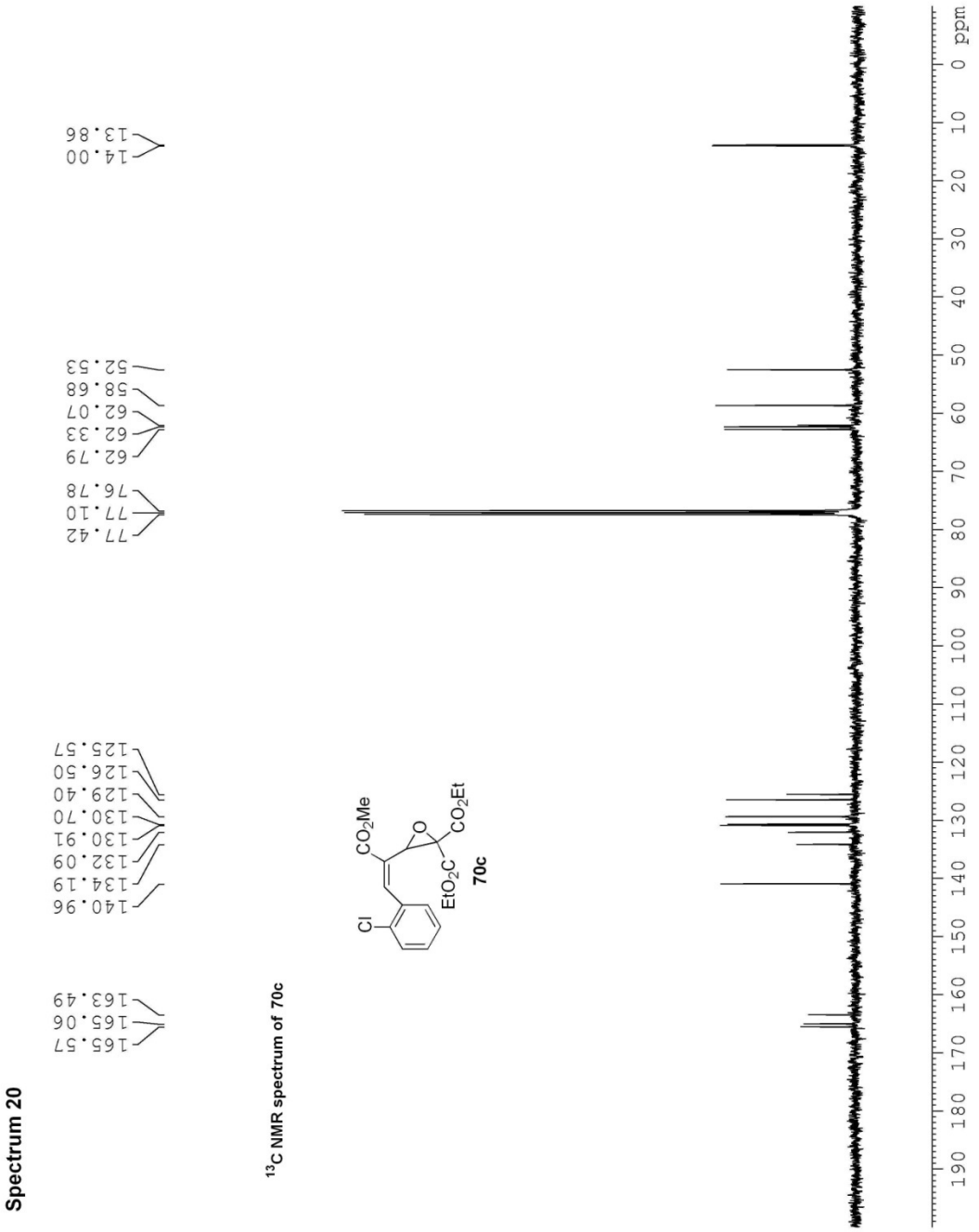

Spectrum 15
7.537
7.518
7.473
7.453
7.430
7.412
7.389
7.383
7.375
7.371
7.362
7.357
7.281
7.276
6.825
6.820
6.808
6.787
6.630
6.624
3.183
TMS
ppm
0
1
2
3
4
5
6
7
8
9
3.01
1.00
2.02
2.05
1.03
2.01
0.97
Cl
H
O
CN
O
N
Me
Cl
(±) 67e
1H NMR spectrum of 67e


Spectrum 16
13C NMR spectrum of 67e
(±) 67e
CDCl3
ppm
26.73
76.78
77.10
77.42
84.73
90.44
110.12
112.07
120.35
125.96
127.26
127.64
128.07
128.96
130.31
130.85
131.47
133.74
133.80
142.36
142.51
172.20


Spectrum 17
7.835
7.438
7.416
7.397
7.376
7.264
4.300
4.282
4.264
4.246
4.035
4.031
3.855
3.475
3.470
1.582
1.337
1.319
1.301
0.000
1.05
4.05
1.06
3.03
1.05
2.04
3.09
ppm
0
1
2
3
4
5
6
7
8
9
^{1}H NMR spectrum of 70a
70a
CO2Me
CO2Et
O
Cl

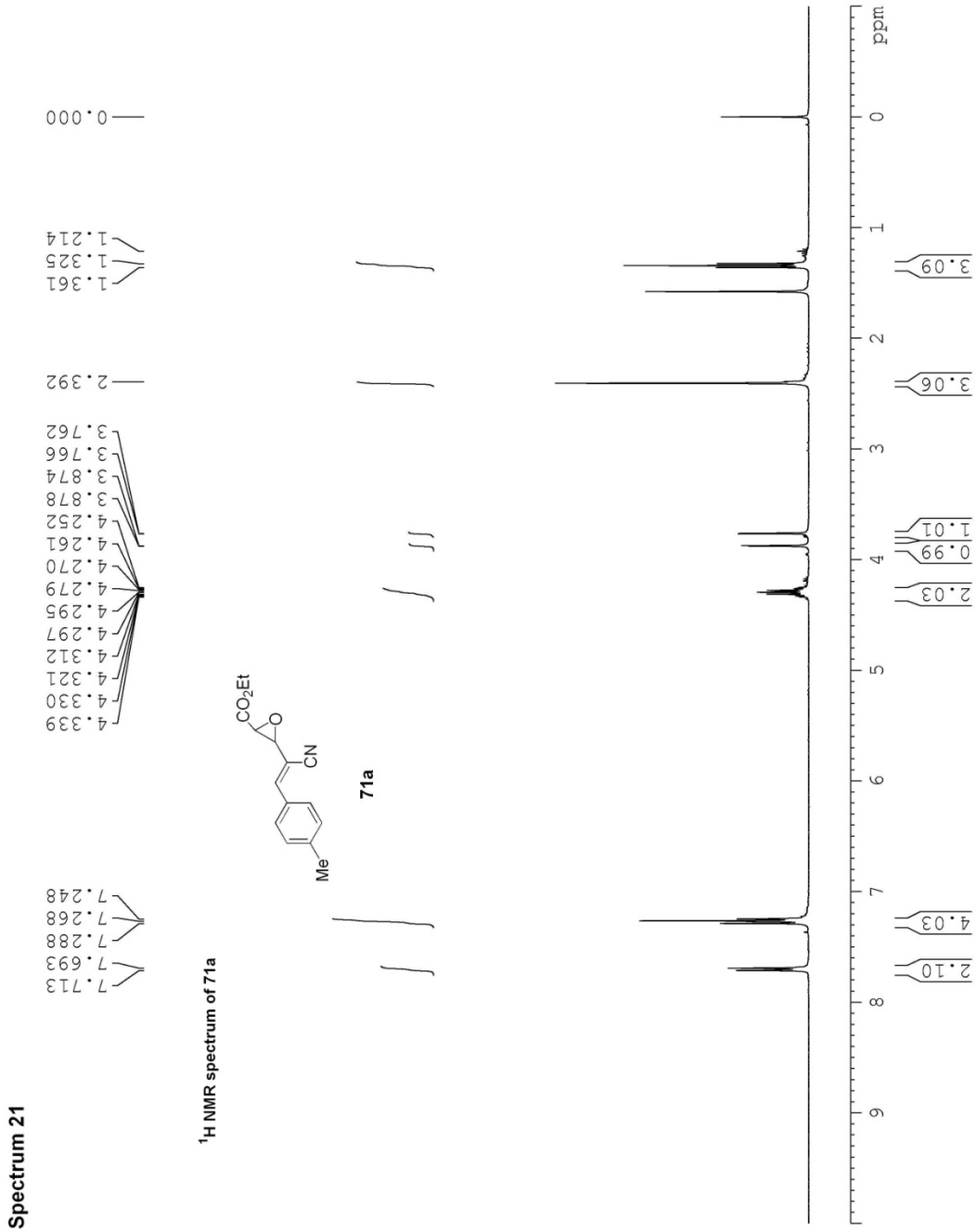

Spectrum 18
^{13}C NMR spectrum of 70a
CO2Me
O
CO2Et
Cl
70a
168.32
166.31
143.74
136.22
131.79
131.50
129.02
126.31
77.42
77.10
76.78
61.96
55.60
53.59
52.56
14.24
ppm

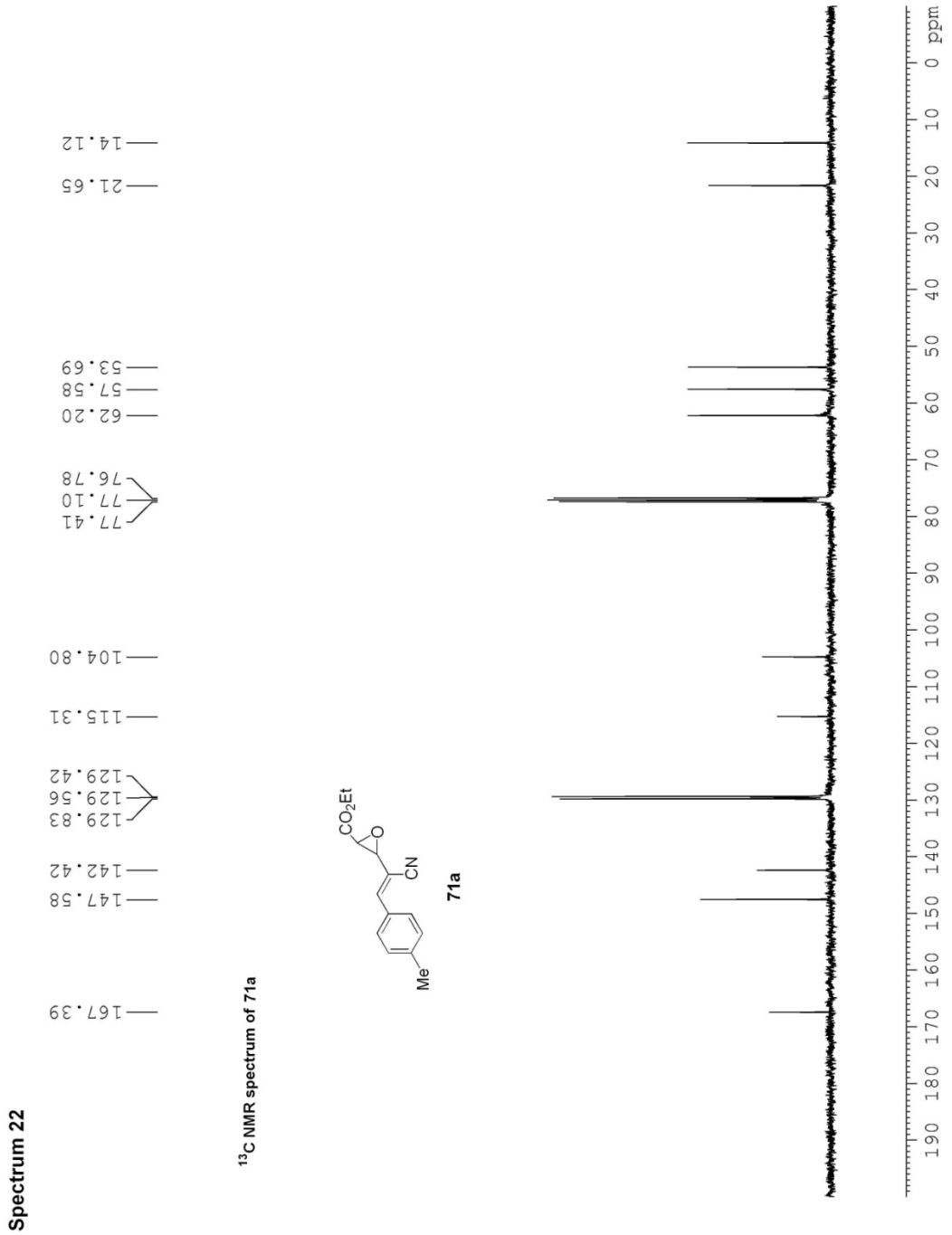

Spectrum 19
7.987
7.466
7.457
7.419
7.399
7.396
7.325
7.319
7.311
7.302
7.297
7.266
4.488
4.485
4.292
4.285
4.274
4.268
4.164
4.146
4.128
4.111
3.867
1.608
1.308
1.290
1.272
1.208
1.190
1.172
0.000
1H NMR spectrum of 70c
CO2Me
CO2Et
EtO2C
Cl
70c
1.00
1.01
1.04
2.01
1.00
2.10
2.08
3.03
3.03
3.12
ppm

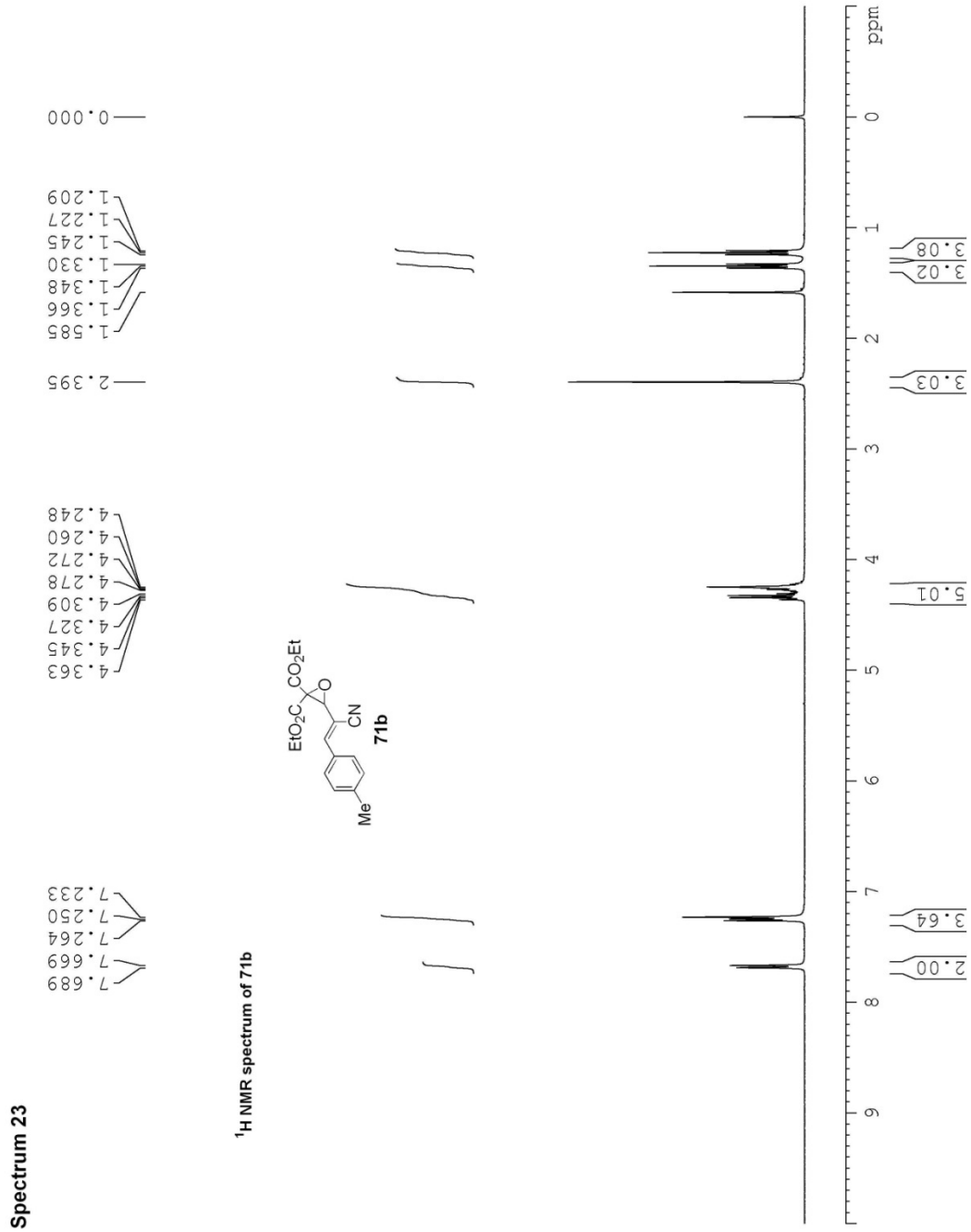


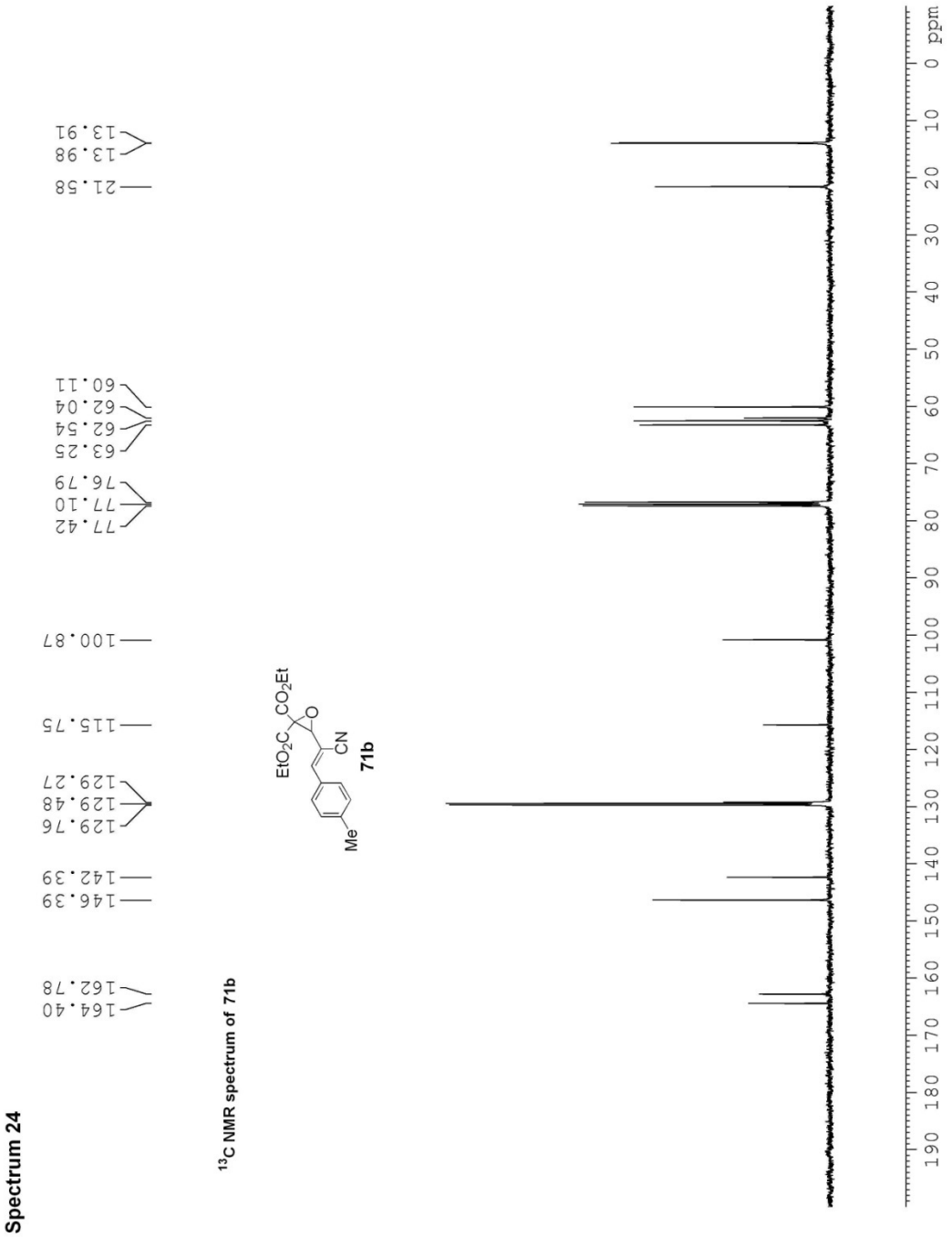
^{13}C NMR spectrum of 70c

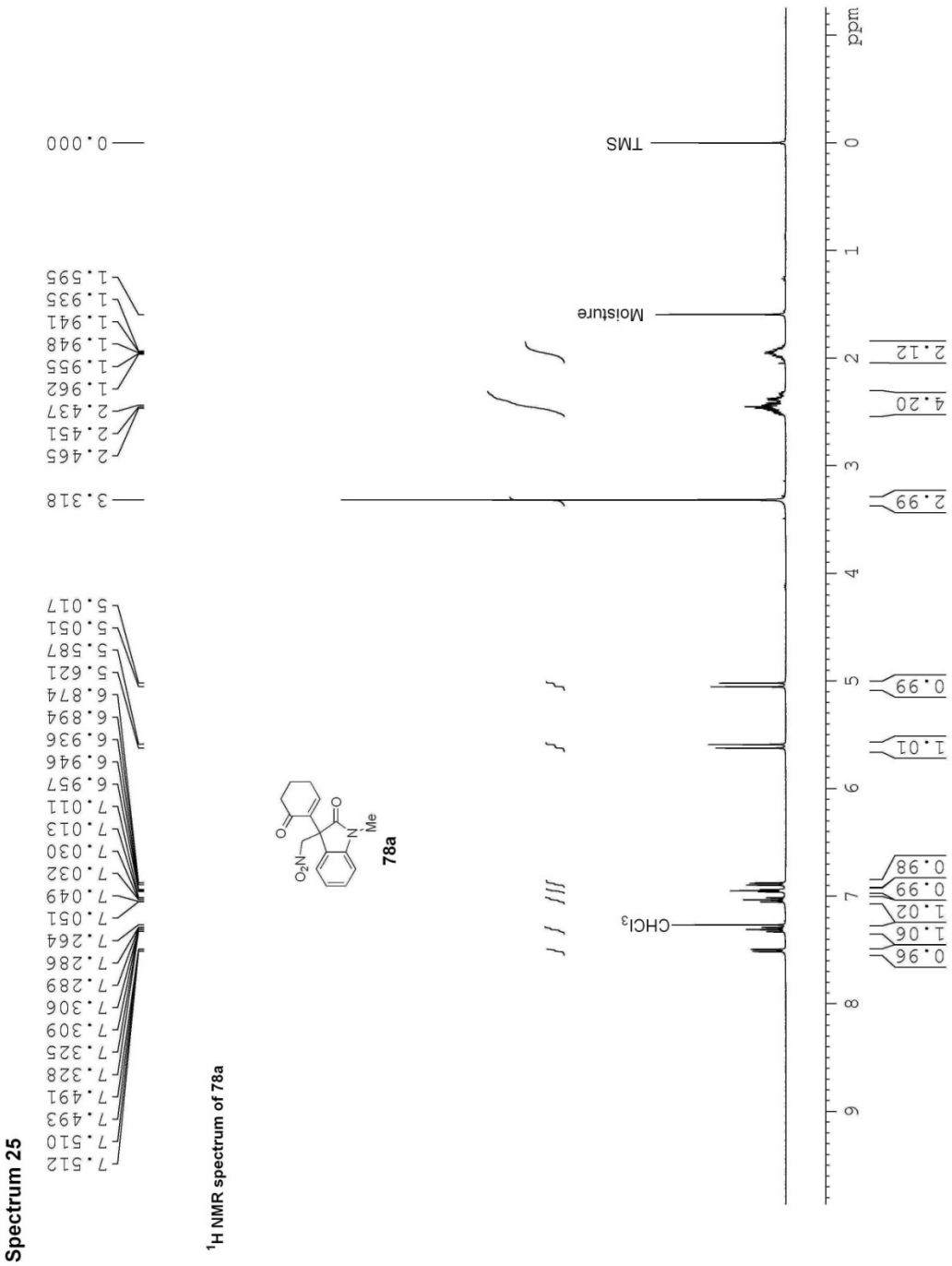
70c


Spectrum 21
^{1}H NMR spectrum of 71a
71a
CO2Et
CN
Me
7.713
7.693
7.288
7.268
7.248
4.339
4.330
4.321
4.312
4.297
4.295
4.279
4.270
4.261
4.252
3.878
3.874
3.766
3.762
2.392
1.361
1.325
1.214
0.000
2.10
4.03
2.03
0.99
1.01
3.06
3.06
3.09
ppm

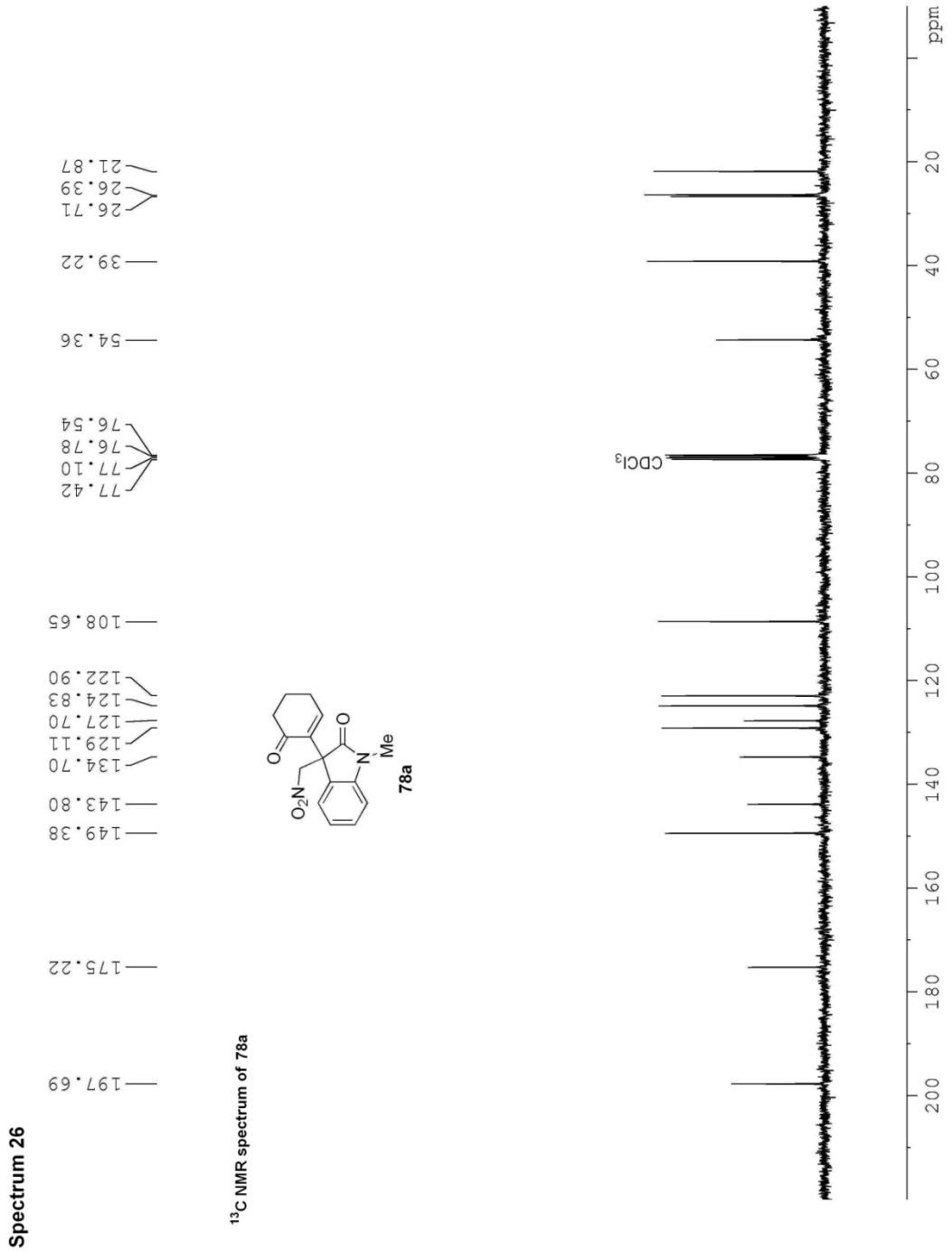

Spectrum 22
^{13}C NMR spectrum of 71a
CO2Et
O
CN
Me
71a
167.39
147.58
142.42
129.83
129.56
129.42
115.31
104.80
77.41
77.10
76.78
62.20
57.58
53.69
21.65
14.12
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

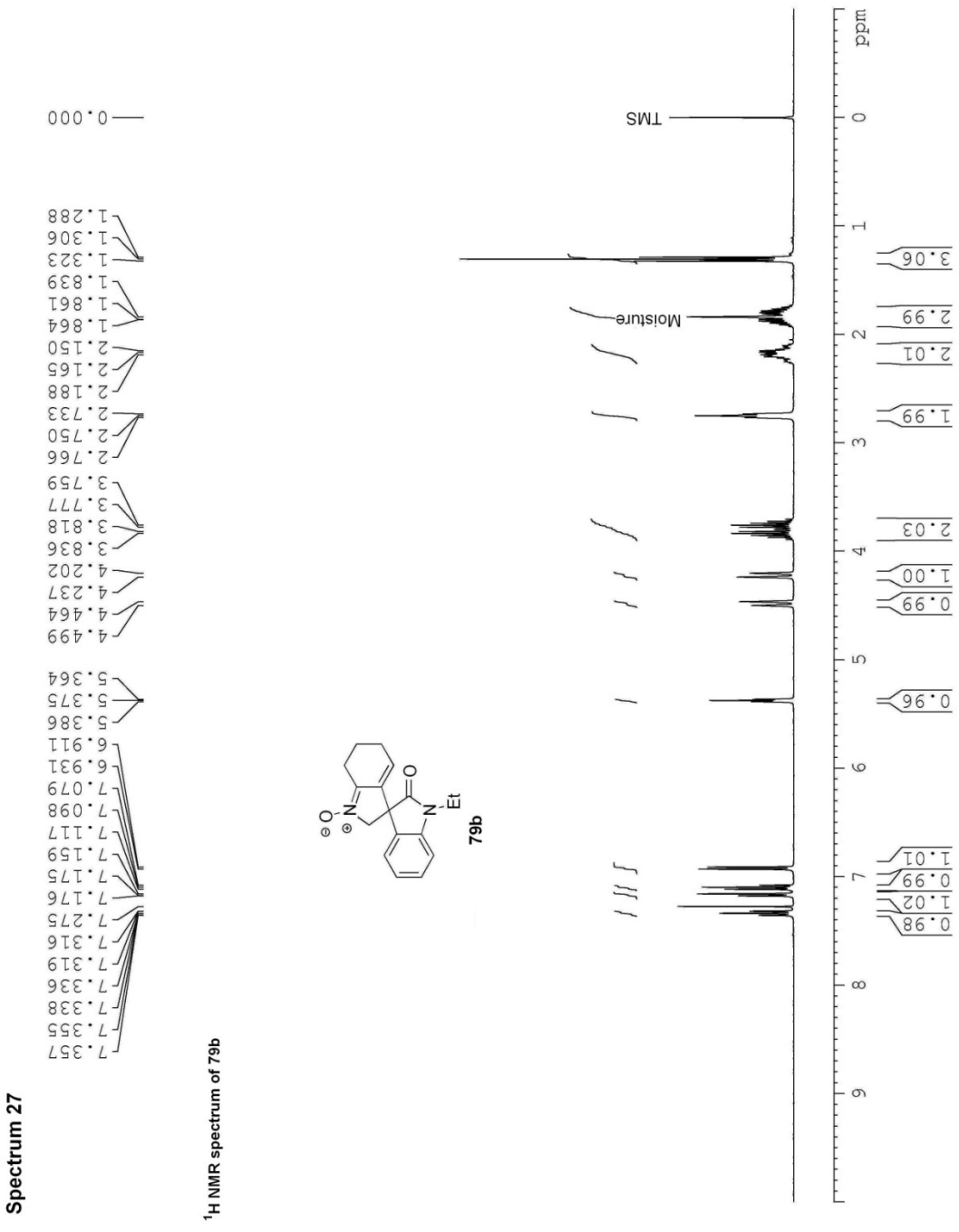

Spectrum 23
7.689
7.669
7.264
7.250
7.233
4.363
4.345
4.327
4.309
4.278
4.272
4.260
4.248
2.395
1.585
1.366
1.348
1.330
1.245
1.227
1.209
0.000
^{1}H NMR spectrum of 71b
EtO2C
CO2Et
O
CN
Me
71b
ppm
2.00
3.64
5.01
3.03
3.02
3.08


Spectrum 24
^{13}C NMR spectrum of 71b
EtO2C
CO2Et
O
CN
Me
71b
164.40
162.78
146.39
142.39
129.76
129.48
129.27
115.75
100.87
77.42
77.10
76.79
63.25
62.54
62.04
60.11
21.58
13.98
13.91
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

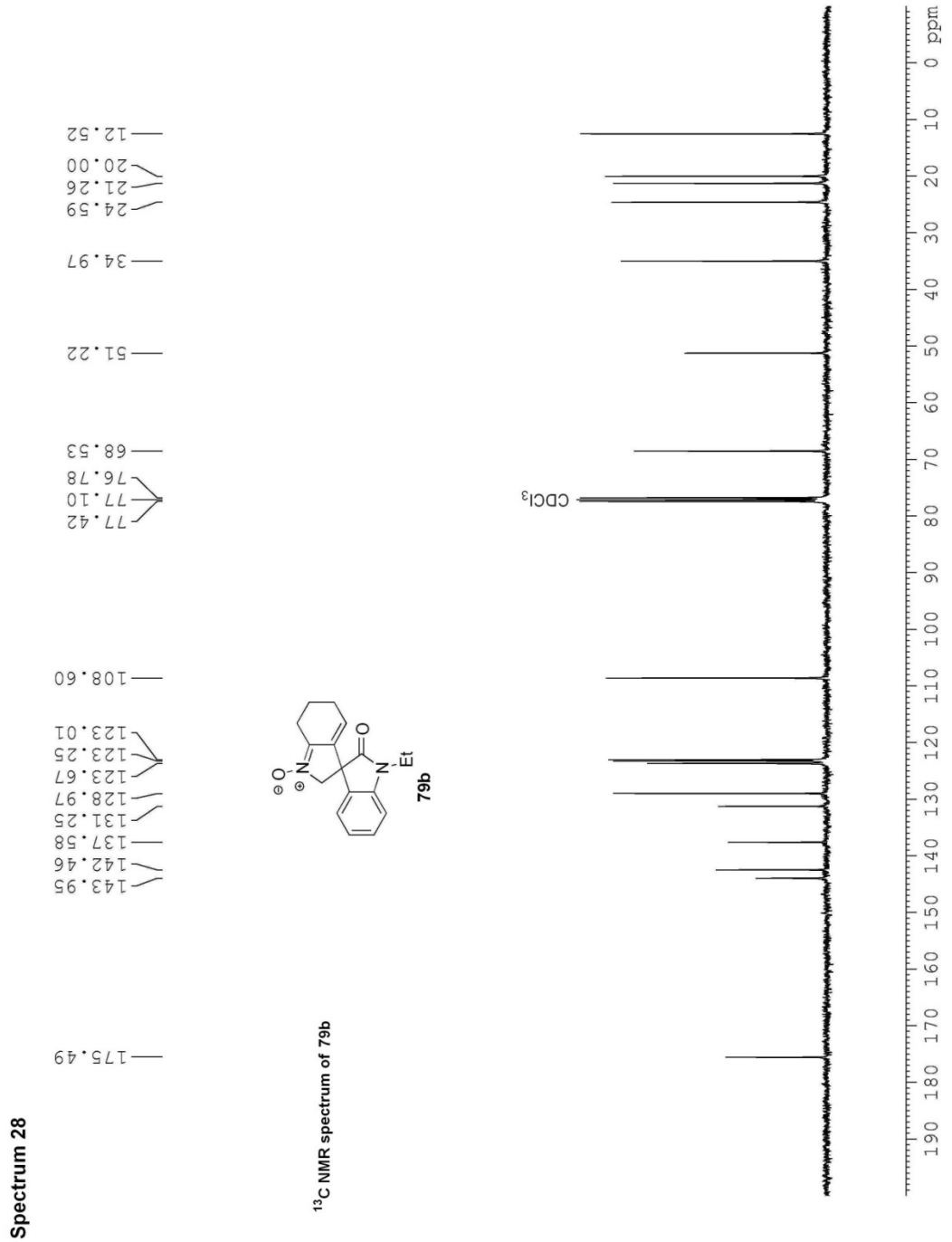


^{1}H NMR spectrum of 78a


Spectrum 26
^{13}C NMR spectrum of 78a
197.69
175.22
149.38
143.80
134.70
129.11
127.70
124.83
122.90
108.65
77.42
77.10
76.78
76.54
54.36
39.22
26.71
26.39
21.87
CDCl3
O
O
N
Me
O2N
78a
200
180
160
140
120
100
80
60
40
20
ppm

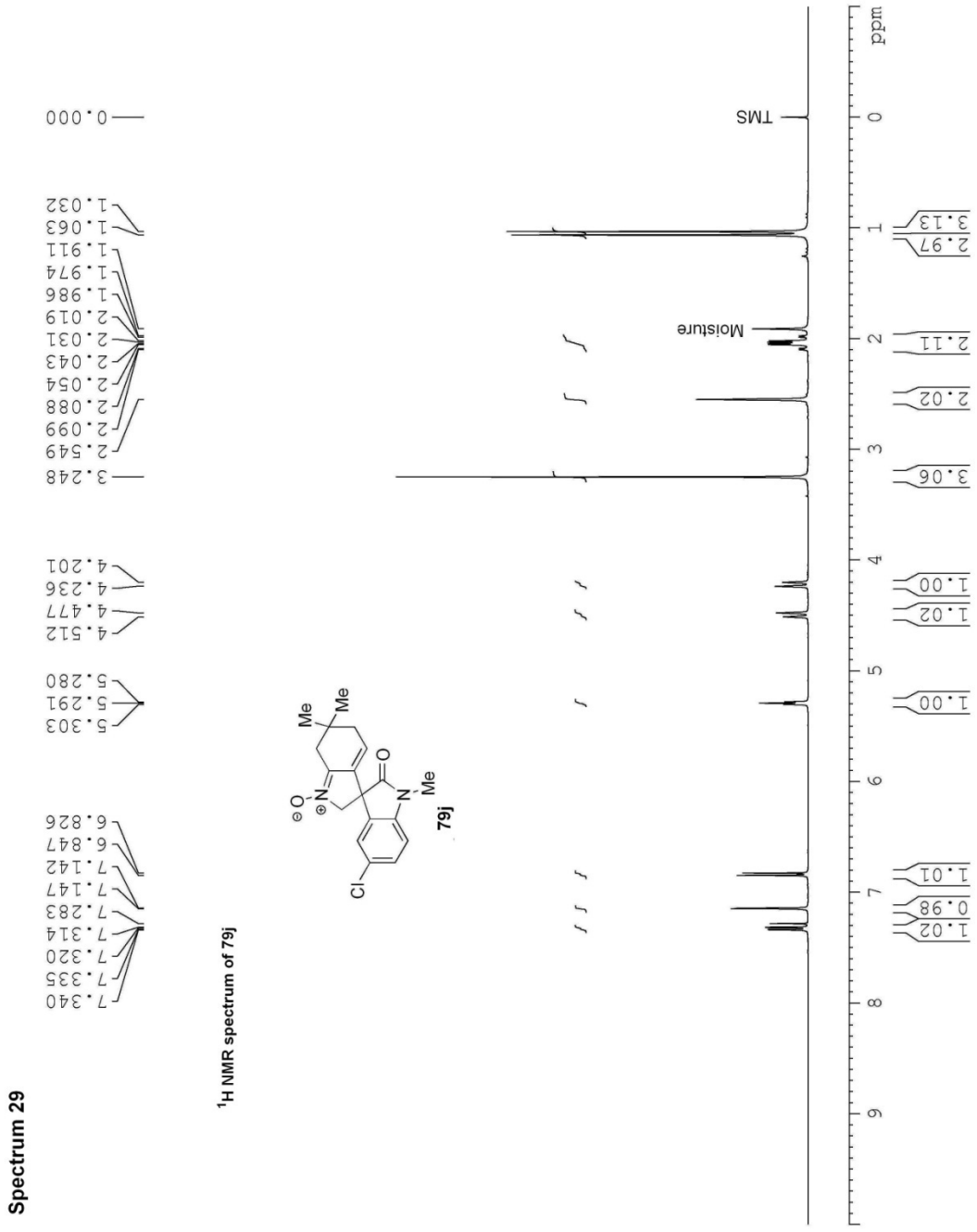


^{1}H NMR spectrum of 79b

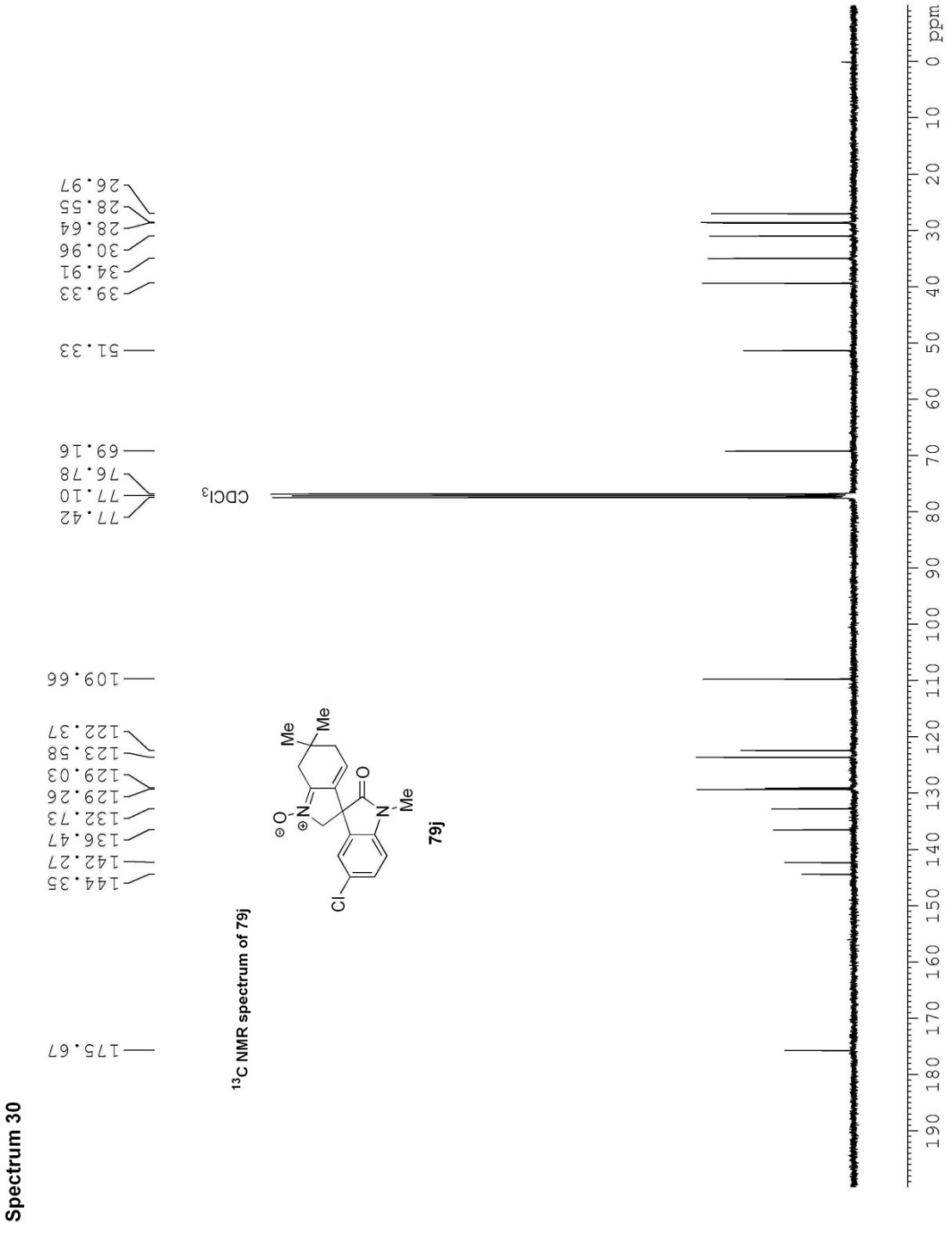


^{13}C NMR spectrum of 79b

79b



^{1}H NMR spectrum of 79j



^{13}C NMR spectrum of 79j

79j

APPENDIX
(X-RAY CRYSTALLOGRAPHIC DATA)

Table I. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **61a**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
C(2)	6457(1)	10002(2)	10772(2)	49(1)
C(3)	7234(1)	9644(2)	9894(2)	42(1)
C(4)	7674(1)	6945(2)	9082(2)	54(1)
C(5)	7476(2)	5398(2)	9148(2)	64(1)
C(6)	6806(2)	4876(2)	9894(2)	67(1)
C(7)	6296(2)	5870(2)	10587(2)	59(1)
C(8)	6488(1)	7417(2)	10502(2)	42(1)
C(9)	7175(1)	7948(2)	9763(2)	40(1)
C(10)	8223(1)	10338(2)	10387(2)	48(1)
C(11)	8425(1)	11318(2)	9283(2)	40(1)
C(12)	7671(1)	11287(2)	8382(2)	45(1)
C(13)	9308(1)	12209(2)	9292(2)	45(1)
C(14)	10174(1)	13977(3)	8173(2)	70(1)
C(15)	5335(1)	8495(3)	11948(2)	71(1)
N(1)	6075(1)	8646(2)	11100(1)	48(1)
O(1)	6244(1)	11266(2)	11127(1)	72(1)
O(2)	6935(1)	10390(1)	8649(1)	50(1)
O(3)	9946(1)	12206(2)	10169(1)	71(1)
O(4)	9337(1)	13029(2)	8226(1)	62(1)

Table II. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **63a**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
C(2)	3481(1)	2872(2)	75(1)	56(1)
C(3)	3439(1)	2780(1)	967(1)	46(1)
C(4)	2683(1)	4150(2)	1815(1)	54(1)
C(5)	2247(1)	5241(2)	1778(1)	67(1)
C(6)	2098(1)	5969(2)	1083(1)	73(1)
C(7)	2362(1)	5635(2)	391(1)	65(1)
C(8)	2790(1)	4545(2)	428(1)	47(1)
C(9)	2960(1)	3824(1)	1139(1)	44(1)
C(10)	4009(1)	2392(2)	1475(1)	49(1)
C(11)	4156(1)	3044(2)	2273(1)	45(1)
C(12)	4212(1)	4454(2)	2393(1)	48(1)
C(13)	4176(1)	5594(2)	1793(1)	49(1)
C(14)	4425(1)	5442(2)	1071(1)	61(1)
C(15)	4386(1)	6541(2)	523(1)	76(1)
C(16)	4099(1)	7791(2)	680(1)	80(1)
C(17)	3855(1)	7966(2)	1389(1)	82(1)
C(18)	3897(1)	6884(2)	1950(1)	67(1)
C(19)	4287(1)	2094(2)	2975(1)	50(1)
C(20)	4494(1)	-285(2)	3400(1)	77(1)
C(21)	3063(1)	4512(2)	-1000(1)	80(1)
N(1)	3105(1)	3971(1)	-191(1)	56(1)
O(1)	3491(1)	1422(1)	1361(1)	59(1)
O(2)	4368(1)	2500(1)	3652(1)	75(1)
O(3)	4324(1)	729(1)	2766(1)	61(1)
O(4)	3808(1)	2165(2)	-317(1)	84(1)

Table III. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **64a**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
C(2)	5874(4)	1592(2)	5942(3)	40(1)
C(3)	5067(3)	1632(2)	4656(2)	34(1)
C(4)	5323(4)	644(2)	3035(3)	50(1)
C(5)	6154(5)	-15(2)	2812(4)	66(1)
C(6)	7332(5)	-348(2)	3681(4)	69(1)
C(7)	7713(4)	-52(2)	4803(4)	60(1)
C(8)	6875(4)	600(2)	5018(3)	42(1)
C(9)	5695(3)	945(2)	4141(3)	37(1)
C(10)	4577(3)	2379(2)	4033(3)	35(1)
C(11)	4730(3)	3160(2)	4608(2)	36(1)
C(12)	6101(3)	3472(2)	5238(3)	40(1)
C(13)	7748(3)	3152(2)	5474(3)	39(1)
C(14)	8290(4)	2684(2)	4695(3)	48(1)
C(15)	9848(4)	2397(2)	4972(3)	55(1)
C(16)	10882(4)	2565(2)	6014(3)	59(1)
C(17)	10383(4)	3037(2)	6799(3)	63(1)
C(18)	8833(4)	3333(2)	6523(3)	51(1)
C(19)	3190(3)	3600(2)	4371(3)	37(1)
C(20)	1719(4)	4629(2)	4924(4)	66(1)
C(21)	8106(5)	803(2)	7167(3)	77(1)
N(1)	6995(3)	1000(2)	6067(2)	46(1)
O(1)	5596(3)	1989(1)	6715(2)	56(1)
O(2)	3401(2)	1850(1)	4301(2)	43(1)
O(3)	2047(2)	3457(1)	3581(2)	51(1)
O(4)	3206(2)	4193(1)	5113(2)	53(1)

Table IV. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **63h**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
C(2)	9180(1)	3484(1)	2210(1)	20(1)
C(3)	8140(1)	3566(1)	3003(1)	18(1)
C(4)	6308(1)	2446(1)	3558(1)	20(1)
C(5)	5900(1)	1608(1)	3453(1)	22(1)
C(6)	6628(2)	1086(1)	2855(1)	24(1)
C(7)	7755(1)	1376(1)	2333(1)	22(1)
C(8)	8137(1)	2208(1)	2444(1)	19(1)
C(9)	7447(1)	2736(1)	3061(1)	18(1)
C(10)	8633(1)	4173(1)	3868(1)	19(1)
C(11)	8434(1)	3995(1)	4952(1)	20(1)
C(12)	9078(1)	3333(1)	5522(1)	21(1)
C(13)	10085(1)	2693(1)	5220(1)	20(1)
C(14)	10068(1)	1893(1)	5633(1)	22(1)
C(15)	10954(1)	1254(1)	5347(1)	22(1)
C(16)	11889(1)	1407(1)	4628(1)	20(1)
C(17)	11977(1)	2210(1)	4242(1)	22(1)
C(18)	11103(1)	2842(1)	4542(1)	22(1)
C(19)	12850(2)	13(1)	4699(1)	26(1)
C(20)	7554(1)	4640(1)	5401(1)	20(1)
C(21)	6448(2)	5043(1)	6821(1)	27(1)
C(22)	10155(2)	2298(1)	1313(1)	26(1)
N(1)	9170(1)	2662(1)	1958(1)	20(1)
O(1)	7249(1)	4309(1)	3042(1)	20(1)
O(2)	9938(1)	4032(1)	1909(1)	25(1)
O(3)	12778(1)	830(1)	4262(1)	24(1)
O(4)	7184(1)	5302(1)	4979(1)	26(1)
O(5)	7248(1)	4423(1)	6327(1)	25(1)

Table V. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3)for **64h**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
C(2)	1725(1)	-455(2)	9261(1)	18(1)
C(3)	1672(1)	1439(2)	8809(1)	16(1)
C(4)	175(1)	3146(2)	8052(1)	20(1)
C(5)	-803(1)	3047(2)	7908(1)	22(1)
C(6)	-1272(1)	1568(2)	8220(1)	23(1)
C(7)	-786(1)	132(2)	8683(1)	20(1)
C(8)	182(1)	243(2)	8815(1)	17(1)
C(9)	662(1)	1728(2)	8508(1)	17(1)
C(10)	2362(1)	3027(2)	8996(1)	17(1)
C(11)	3096(1)	2954(2)	9694(1)	17(1)
C(12)	4030(1)	2827(2)	9747(1)	17(1)
C(13)	4611(1)	2753(2)	9155(1)	17(1)
C(14)	4313(1)	3369(2)	8408(1)	17(1)
C(15)	4896(1)	3275(2)	7869(1)	18(1)
C(16)	5797(1)	2520(2)	8068(1)	17(1)
C(17)	6119(1)	1930(2)	8815(1)	20(1)
C(18)	5538(1)	2069(2)	9350(1)	19(1)
C(19)	6115(1)	3026(2)	6810(1)	22(1)
C(20)	2659(1)	3098(2)	10384(1)	17(1)
C(21)	2849(1)	3352(2)	11710(1)	23(1)
C(22)	554(1)	-2833(2)	9592(1)	22(1)
N(1)	820(1)	-1024(1)	9258(1)	18(1)
O(1)	2429(1)	-1318(1)	9557(1)	23(1)
O(2)	2401(1)	1747(1)	8364(1)	19(1)
O(3)	1816(1)	3160(1)	10356(1)	23(1)
O(4)	3270(1)	3172(1)	11036(1)	21(1)
O(5)	6407(1)	2310(1)	7570(1)	20(1)

Table VI. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **77d.** U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
C(2)	4400(1)	9024(5)	9396(3)	32(1)
C(3)	4055(1)	6896(5)	8996(3)	28(1)
C(4)	3588(1)	3911(7)	10414(3)	39(1)
C(5)	3515(2)	3288(7)	11598(4)	47(1)
C(6)	3767(2)	4522(7)	12485(3)	45(1)
C(7)	4094(1)	6425(7)	12234(3)	39(1)
C(8)	4152(1)	7044(6)	11063(3)	32(1)
C(9)	3907(1)	5810(5)	10158(3)	31(1)
C(10)	4380(1)	5484(5)	8133(3)	27(1)
C(11)	4188(1)	5803(5)	7063(3)	28(1)
C(12)	3706(1)	7437(6)	7084(3)	35(1)
C(13)	3230(1)	6408(7)	6439(3)	37(1)
C(14)	3098(2)	7109(8)	5302(3)	49(1)
C(15)	2697(2)	5976(10)	4672(4)	64(1)
C(16)	2428(2)	4145(11)	5173(4)	72(2)
C(17)	2548(2)	3470(11)	6301(4)	68(1)
C(18)	2945(2)	4580(9)	6921(4)	56(1)
C(19)	4382(1)	4838(6)	5973(3)	33(1)
C(20)	4769(2)	10548(7)	11275(4)	49(1)
N(1)	4442(1)	8922(5)	10592(3)	35(1)
N(2)	4531(1)	4106(6)	5090(3)	46(1)
O(1)	4591(1)	10458(4)	8744(3)	47(1)
O(2)	3599(1)	7642(4)	8324(2)	34(1)
Cl(1)	3440(1)	9385(2)	4620(1)	71(1)

Table VII. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **77e.** U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
C(2)	6741(3)	2036(2)	6371(4)	32(1)
C(3)	7434(3)	1352(2)	5792(3)	28(1)
C(4)	6416(3)	310(2)	3851(3)	30(1)
C(5)	5295(3)	98(2)	2939(3)	32(1)
C(6)	4215(3)	520(2)	2874(3)	31(1)
C(7)	4220(3)	1187(2)	3724(3)	29(1)
C(8)	5329(3)	1396(2)	4627(3)	27(1)
C(9)	6405(3)	964(2)	4708(3)	26(1)
C(10)	8507(3)	1640(2)	5157(3)	32(1)
C(11)	9544(3)	1473(2)	6094(4)	31(1)
C(12)	9277(3)	1062(2)	7480(3)	29(1)
C(13)	10034(3)	348(2)	7933(3)	31(1)
C(14)	9594(3)	-381(2)	7475(4)	38(1)
C(15)	10284(4)	-1034(2)	7916(4)	47(1)
C(16)	11457(4)	-962(2)	8797(4)	46(1)
C(17)	11922(3)	-250(2)	9261(4)	42(1)
C(18)	11201(3)	398(2)	8845(3)	34(1)
C(19)	10768(3)	1634(2)	5850(4)	38(1)
C(20)	4628(3)	2604(2)	5774(5)	42(1)
N(1)	5561(2)	2040(1)	5571(3)	30(1)
N(2)	11731(3)	1756(2)	5598(4)	56(1)
O(1)	7190(2)	2478(1)	7352(3)	45(1)
O(2)	7979(2)	872(1)	7023(2)	31(1)
Cl(1)	5246(1)	-729(1)	1837(1)	45(1)
Cl(2)	11793(1)	1295(1)	9510(1)	43(1)

Table VIII. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **70a** U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
Cl(1)	8900(1)	-992(1)	10452(1)	77(1)
O(2)	3592(1)	1228(1)	5677(2)	46(1)
O(1)	5885(1)	1502(1)	2292(2)	51(1)
O(5)	4137(1)	2367(1)	3983(2)	56(1)
C(1AA)	6203(2)	-367(2)	8837(3)	41(1)
C(2AA)	6289(2)	432(2)	7849(3)	38(1)
C(3AA)	5405(2)	828(2)	6983(3)	41(1)
C(4AA)	7641(2)	1454(2)	2847(3)	46(1)
C(5AA)	6992(2)	-800(2)	9651(3)	44(1)
C(6AA)	4292(2)	1721(2)	4967(3)	40(1)
O(4)	7778(1)	2103(1)	1912(3)	62(1)
C(8AA)	7201(2)	804(2)	7768(3)	47(1)
C(9AA)	8001(2)	370(2)	8577(3)	51(1)
O(3)	8332(1)	914(1)	3574(3)	68(1)
C(1BA)	7887(2)	-430(2)	9494(3)	46(1)
C(2BA)	6680(2)	1117(2)	3346(3)	42(1)
C(3BA)	5272(2)	1374(2)	5495(3)	38(1)
C(4BA)	6023(2)	1726(2)	4272(3)	39(1)
C(5BA)	2626(2)	1539(2)	5302(4)	58(1)
C(10)	9308(2)	1148(3)	3216(5)	88(1)
C(11)	9738(3)	1696(4)	4677(7)	135(2)

Table IX. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **71b.** U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
O	6335(2)	7983(2)	3219(1)	56(1)
O(2)	7322(3)	10712(2)	3312(1)	71(1)
O(5)	2235(3)	8481(2)	3269(1)	68(1)
C	3354(4)	7970(3)	2958(1)	55(1)
C(0AA)	5127(3)	8767(3)	3244(1)	49(1)
C(1AA)	3658(4)	4971(3)	4096(1)	53(1)
C(2AA)	5838(4)	8491(3)	3820(1)	53(1)
C(3AA)	4566(4)	6128(3)	3882(1)	54(1)
C(4AA)	4827(4)	7464(3)	4116(1)	52(1)
C(5AA)	3549(4)	3678(3)	3730(2)	63(1)
O(1)	4759(3)	10624(3)	2855(1)	86(1)
O(6)	3032(3)	7001(3)	2520(1)	89(1)
C(6AA)	5707(4)	10150(3)	3112(2)	57(1)
C(7AA)	2752(4)	2535(3)	3910(2)	68(1)
C(8AA)	2015(4)	2620(3)	4457(2)	62(1)
C(9AA)	4153(5)	8056(3)	4661(2)	71(1)
C(0BA)	2917(5)	5056(3)	4653(2)	75(1)
C(1BA)	445(4)	7776(4)	3080(2)	82(1)
N(2)	3642(6)	8585(3)	5087(2)	120(2)
C(2BA)	2119(5)	3899(4)	4822(2)	78(1)
C(3BA)	8029(6)	12052(4)	3200(2)	95(1)
C(4BA)	1121(5)	1368(4)	4645(2)	87(1)
O(7)	5490(3)	6661(2)	916(1)	62(1)
C(5BA)	8279(3)	6149(3)	924(1)	46(1)
O(9)	8165(3)	5710(2)	371(1)	71(1)
O(8)	9356(3)	5981(2)	1353(1)	69(1)

O(11)	7132(3)	9117(2)	1881(1)	79(1)
C(6BA)	5652(4)	6234(3)	1485(1)	55(1)
C(7BA)	4601(4)	3811(3)	884(2)	56(1)
C(8BA)	5279(4)	4745(3)	1421(1)	54(1)
C(9BA)	4128(4)	2334(3)	751(1)	55(1)
C(0CA)	7151(3)	6954(3)	1250(1)	48(1)
C(1CA)	7882(4)	8435(3)	1567(2)	61(1)
C(2CA)	3043(4)	-515(3)	462(2)	63(1)
C(3CA)	5684(5)	4436(3)	2008(2)	70(1)
C(4CA)	2956(4)	1603(3)	233(2)	64(1)
C(5CA)	4788(4)	1599(4)	1116(2)	69(1)
O(10)	9398(4)	8854(3)	1426(2)	143(2)
C(6CA)	2416(4)	210(4)	93(2)	69(1)
C(7CA)	10546(4)	5178(4)	1142(2)	73(1)
N(1)	6043(6)	4274(4)	2491(2)	107(1)
C(8CA)	4250(4)	207(4)	969(2)	72(1)
C(9CA)	2418(5)	-2034(4)	314(2)	92(1)
C(0DA)	10258(9)	10633(8)	1629(3)	150(3)
C(10)	7984(6)	13100(4)	3740(2)	102(1)
C(13)	10277(6)	4033(5)	1423(3)	110(2)
C(11)	-81(5)	6775(5)	3442(3)	116(2)
C(12)	10997(9)	10404(7)	2117(3)	151(2)

Table X. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **79b**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
C(1)	6186(2)	7282(2)	2016(2)	47(1)
C(2)	4276(2)	7201(2)	1873(2)	41(1)

C(3)	3003(2)	9560(2)	1334(2)	48(1)
C(4)	3454(3)	11198(2)	1217(2)	55(1)
C(5)	5196(3)	12113(2)	1363(2)	56(1)
C(6)	6531(2)	11439(2)	1621(2)	50(1)
C(7)	6066(2)	9814(2)	1745(1)	40(1)
C(8)	4322(2)	8880(2)	1615(1)	39(1)
C(9)	3933(2)	6871(2)	3110(2)	46(1)
C(10)	4741(3)	7767(3)	4265(2)	66(1)
C(11)	4131(4)	7231(3)	5345(2)	89(1)
C(12)	2422(5)	5936(5)	4961(3)	122(1)
C(13)	1757(4)	4714(3)	3829(3)	82(1)
C(14)	2470(2)	5370(2)	2836(2)	51(1)
C(15)	2822(2)	5727(2)	893(2)	48(1)
C(16)	9007(2)	9334(2)	2060(2)	56(1)
C(17)	10321(3)	9843(4)	3402(2)	81(1)
N(1)	7145(2)	8835(2)	1988(1)	45(1)
N(2)	1863(2)	4721(2)	1636(2)	48(1)
O(1)	563(2)	3370(1)	1069(1)	65(1)
O(2)	6743(2)	6152(2)	2131(2)	71(1)

Table XI. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **79J**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
C(1)	1670(1)	-1768(2)	695(1)	50(1)
C(2)	2156(1)	-698(2)	687(1)	42(1)
C(3)	3052(1)	-800(2)	858(1)	35(1)
C(4)	3462(1)	-1924(2)	1031(1)	43(1)

C(5)	2975(2)	-2987(2)	1036(1)	57(1)
C(6)	2075(2)	-2898(2)	869(1)	58(1)
C(7)	3749(1)	169(2)	886(1)	35(1)
C(8)	4598(1)	-593(2)	1069(1)	44(1)
C(9)	5011(2)	-2780(2)	1353(2)	76(1)
C(10)	3658(1)	925(2)	209(1)	41(1)
C(11)	3659(1)	2335(2)	1085(1)	34(1)
C(12)	3757(1)	1166(2)	1431(1)	32(1)
C(13)	3829(1)	1079(2)	2113(1)	41(1)
C(14)	3794(1)	2216(2)	2541(1)	47(1)
C(15)	3322(1)	3320(2)	2127(1)	46(1)
C(16)	3644(1)	3510(2)	1458(1)	46(1)
C(17)	2335(2)	3073(2)	1931(1)	72(1)
C(18)	3509(2)	4488(2)	2575(1)	74(1)
N(1)	4374(1)	-1785(2)	1165(1)	50(1)
N(2)	3599(1)	2213(1)	419(1)	36(1)
O(1)	5337(1)	-212(1)	1118(1)	63(1)
O(2)	3504(1)	3070(1)	-44(1)	51(1)
Cl(1)	537(1)	-1674(1)	485(1)	80(1)

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LIST OF PUBLICATIONS

1. Recent contributions from the Baylis-Hillman reaction to organic chemistry

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2. Baylis-Hillman Bromides as a Source of 1,3-Dipoles: Sterically Directed Synthesis of Oxindole-Fused Spirooxirane and Spirodihydrofuran Frameworks

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

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