BAYLISHILLMAN ADDUCTS AS VALUABLE SYNTHONS: DEVELOPMENT OF SIMPLE METHODOLOGIES FOR SYNTHESIS OF SUBSTITUTED MALEIMIDES, MALEIC ANHYDRIDES, BENZOFURANONES, INDOLIZINES AND BENZOFUSED INDOLIZINES

A THESIS SUBMITTED FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY

BY
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Dedicated

To

Parents, Brothers
& Jyothsna

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
AUGUST, 2008 **BADUGU DEVENDAR**

CERTIFICATE

Certified that the work embodied in this thesis entitled "**Baylis-Hillman adducts as valuable synthons: Development of simple methodologies for synthesis of substituted maleimides, maleic anhydrides, benzofuranones, indolizines and bezofused indolizines**" has been carried out by **Mr. Badugu Devendar**, under my supervision and the same has not been submitted elsewhere for a degree.

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(THESIS SUPERVISOR)

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SCHOOL OF CHEMISTRY
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ABBREVIATIONS

Ac	acetyl
aq.	aqueous
BINOL	1,1′-bi-2-naphthol
Bu	butyl
t-Bu or Bu^t	*tertiar*y butyl
Bn	benzyl
Boc	butoxycarbonyl
Bp	boiling point
Cp	cyclopentyl
CPME	cyclopentyl methyl ether
cat.	Catalyst
Cbz	benzyloxycarbonyl
DABCO	1,4-diazabicyclo(2.2.2)octane
dba	dibenzylideneacetone
DBU	1,8-diazabicyclo(5.4.0)undec-7-ene
DCC	1,3-dicyclohexylcarbodiimide
DCE	1,2-dichloroethane
DCM	dichloromethane
de	diastereomeric excess
dec.	decompose
DMF	*N*,*N*-dimethylformamide
DMAP	4-(dimethylamino)pyridine
DMSO	dimethyl sulfoxide
ee	enantiomeric excess
EWG	electron withdrawing group
Et	ethyl
eq.	equation

3-HQD	3-hydroxyquinuclidine
HMT	hexamethylenetetramine
HMDS	hexa methyl disilazane
LAH	lithium aluminum hydride
Me	methyl
Mp	melting point
MS	molecular sieves
MVK	methyl vinyl ketone
m-CPBA	*meta*-chloroperbenzoic acid
NCS	*N*-chlorosuccinamide
NMO	*N*-methylmorpholine *N*-oxide
PCC	pyridinium chlorochromate
PDC	pyridinium dichromate
PAP	polymer bound 4-(*N*-benzyl-*N*-methylamino) pyridine
PTA	1,3,5-triaza-7-phosphaadamantane
Pr	propyl
Ph	phenyl
Pent	pentyl
i-Pr or Pr^i	*iso*-propyl
rt	room temperature
RCM	ring-closing metathesis
TBAF	tetrabutylammonium fluoride
TBDMSCl	*tert*-butyldimethylsilyl chloride
TEA	triethylamine
TMEDA	tetramethylethylenediamine
TMG	1,1,3,3-tetramethylguanidine
THF	tetrahydrofuran
p-TsOH	*para*-toluenesulfonic acid

ABSTRACT

In recent years the Baylis-Hillman reaction has become a powerful synthetic tool for construction of C-C bond providing multifunctional molecules in one-pot atom economical process. These multifunctional molecules are usually referred to as the Baylis-Hillman adducts and have been extensively used in various organic transformation methodologies and also in synthesis of several biologically active molecules and natural products. Our research group has been working on various aspects of this fascinating reaction for the last several years with a view to develop Baylis-Hillman adducts as a valuable source for stereoselective processes and also for one-pot multistep synthesis.

This thesis deals with applications of Baylis-Hillman adducts in synthesis of heterocyclic compounds and consists of three chapters (1). Introduction (2). Objectives, Results & Discussion. (3). Experimental section. The first chapter, *i.e.*, Introduction presents the recent and relevant literature on the Baylis-Hillman reaction and also on applications of the Baylis-Hillman adducts.

The second chapter presents the objectives, and discussion of the experimental results. The thesis has the following objectives.

1) To develop a facile one-pot methodology for transformation of the Baylis-Hillman adducts into unsymmetrical disubstituted maleimide and maleic anhydride frameworks.

2) To develop a facile one-pot procedure for obtaining benzofuran-2-one frameworks from the Baylis-Hillman adducts *i.e.*, 2-hydroxy-2-aryl-2-(5,5-dimethylcyclohex-2-en-1-on-2-yl)ethanoates and 2-hydroxy-2-phenyl-2-cyclohex-2-en-1-on-2-yl)-ethanoate

3) To develop the Baylis-Hillman bromides as versatile synthons, for a facile one-pot synthesis of indolizine and benzofused indolizine frameworks.

Synthesis of disubstituted maleimdes

Development of efficient and convenient methodologies for synthesis of 3,4-disubstituted maleimide and maleic anhydride derivatives has been and continues to be an attractive and challenging endeavor in organic and medicinal chemistry because of the presence of these frameworks in a number of bio-active natural products, and also because several of their derivatives have been known to exhibit various biological activities such as cytotoxicity, angiogenesis, [some of these derivatives are known to be inhibitors of CaMKIIδ (calmodulin-dependant protien kinase)], cell death and vascular endothelial proliferation. Medicinal importance of both maleimide and maleic anhydride frameworks has fascinated us. We have, therefore, developed one-pot procedure for synthesis of disubstituted maleimdes (3-benzyl-4-aryl-1*H*-pyrrole-2,5-diones) (**101a-i**) *via* the treatment of 3-ethoxycarbonyl-3-hydroxy-3-aryl-2-methylenepropanenitrile (Baylis-Hillman adducts), (**100a-i**) with benzene in the presence of methanesulfonic acid (eq. 36 & Table 2).

The desired Baylis-Hillman adducts (**100a-i**) were obtained *via* the reaction of α-keto-esters with acrylonitrile in the presence of catalytic amount of DABCO (eq.35 & Table 1).

Synthesis of disubstituted maleic anhydrides

We have also developed simple methodology for transformation of the Baylis-Hillman adducts *i.e.*, (3-ethoxycarbonyl-3-hydroxy-3-aryl-2-methylenepropanoate) (**102a-c**) into disubstituted maleic anhydrides (3-benzyl-4-arylmaleic anhydrides) (**103a-c**) *via* the treatment with benzene in the presence of methanesulfoinc acid (Table 3)

The desired Baylis-Hillman alcohols (3-ethoxycarbonyl-3-hydroxy-3-aryl-2-methylene-propanoates) (**102a-c**) were prepared *via* the coupling of α-keto-esters with methyl acrylate under the influence of DABCO (eq. 38).

Development of simple methodology for benzofuranone derivatives

With a view to expand the scope of Baylis-Hillman adducts, we have also developed simple protocol for the transformation of the Baylis-Hillman adducts *i.e.*, [2-hydroxy-2-aryl-2-(5,5-dimethylcyclohex-2-en-1-on-2-yl)ethanoate (**112a-g**) & 2-hydroxy-2-phenyl-2-cyclohex-2-en-1-on-2-yl)ethanoate] (**114**), into corresponding benzofuranone derivatives *i.e.*, 6, 6-dimethyl-3-aryl-6*H*-benzofuran-2-one derivatives (**113a-g**) & 3-phenyl-3*H*-benzofuran-2-one (**115**) *via* the treatment with methanesulfonic acid (eq. 41 & Table 8 and eq 44).

The required Baylis-Hillman adducts (**112a-g & 114**), were prepared *via* the coupling of α-keto-esters with 5, 5 dimethylcyclohex-2-en-1-one and cyclohex-2-enone respectively (eq. 42 & eq. 43).

Synthesis of indolizine and benzofused indolizine derivatives

Indolizine framework has been and continues to be an interesting and structurally challenging nitrogen heterocyclic moiety because of the presence of this skeleton in a number of bioactive natural products. The biological and medicinal relevance of the indolizine derivatives has created a need for the development of efficient synthetic strategies for obtaining such derivatives. We have therefore developed a simple protocol for transformation of the Baylis-Hillman bromides *i.e.*, (2-bromomethyl-3-arylprop-2-enenitriles) (**126a-j**) into indolizine derivatives [1-aza-8-cyano-7-arylbicyclo-(4.3.0)nona-2,4,6,8-tetraenes] (**127a-j**) *via* the reaction with pyridine **(**eq. 51 & Table 11). The required Baylis-Hillman bromides (**126a-j**) were prepared from the corresponding Baylis-Hillman alcohols (**125a-j**), which in turn were obtained *via* the coupling of acrylonitrile with various aldehydes (Scheme 77 & Table 10).

We have also developed simple methodology for synthesis of benzofused-indolizine *i.e.* [pyrrolo(1,2-a)quinoline] derivatives [1-aza-12-cyano-11-aryltricyclo(8.3.-0.0^{2,7})trideca-2,-4, 6,8,10,12-hexaenes] (**128a-d 130**) *via* the treatment of Baylis-Hillman bromides (**126a-d, 126f**) with quinoline **(**eq. 52 & Table 12).

A simple methodology for synthesis of benzofused-indolizine *i.e.* [pyrrolo(1,2-a) isoquinoline] derivatives [1-aza-12-cyano-11-aryltricyclo(8.3.0.$0^{4,9}$)trideca-2,4,6,8,10,12-hexaenes] (**129a-d, 131**) was also developed *via* the reaction of Baylis-Hillman bromides (**126a-d, 126g**) with isoquinoline (Table 13).

The third chapter deals with the detailed experimental procedures, IR, ^{1}H NMR, ^{13}C NMR, Mass spectral data, microanalyses (CHN analysis), physical constants [melting points (Mp), and boiling points (Bp)].

LIST OF PUBLICATIONS

1) A Facile One-Pot Transformation of the Baylis-Hillman Adducts into Unsymmetrical Disubstituted Maleimide and Maleic Anhydride Frameworks.
Deevi Basavaiah,* **Badugu Devendar**, and Ainelly Veerendhar (*Submitted for publication).*

2) The Baylis-Hillman Bromides as Versatile Synthons: A Facile One–Pot Synthesis of Indolizine and Benzofused Indolizine Frameworks
Deevi Basavaiah,* **Badugu Devendar**, Dandamudi V.Lenin, and Tummanapally Satyanarayana (*Submitted for publication).*

3) A facile one-pot synthesis of benzofuran-2-one frameworks from the Baylis-Hillman adducts
Deevi Basavaiah* and **Badugu Devendar (***to be communicated).*

4) A Simple Protocol for the Synthesis of Piperidine-2,6-dione Framework from the Baylis-Hillman Adducts
Deevi Basavaiah,* Dandamudi V.Lenin, and **Badugu Devendar (***Submitted for publication).*

5) One-Pot Diastereoselective Synthesis of Spiro-Oxindoles Using the Baylis-Hillman Bromides
Deevi Basavaiah,* Ainelly Veerendhar, and **Badugu Devendar** (*Submitted for publication).*

6) A novel substitution dependant stereochemical control in the Johnson-Claisen rearrangement of Baylis-Hillman adducts: An interesting competition between [1,3] and [1,2] interactions in transition state
D. Basavaiah, T Satyanarayana, **Badugu Devendar,** P. Anupama, K. R. Reddy and K. Padmaja (*to be communicated*).

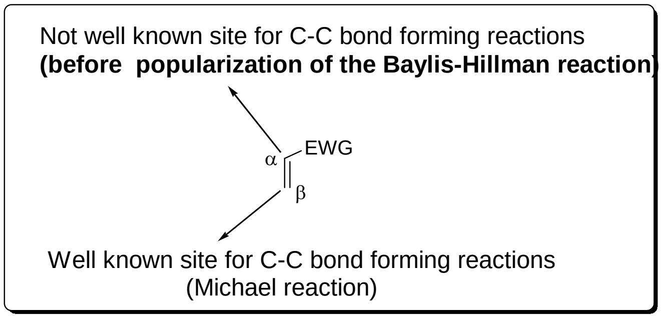
7) Facile transformation of the Baylis-Hillman adducts into substituted (1*H*)-quinolin-2-ones and substituted quinolines *via* a novel one-pot multi-reaction strategy
D. Basavaiah, T. Satyanarayana, **Badugu Devendar** and K. R. Reddy (*manuscript under preparation*).

CONTENTS

INTRODUCTION

The concept of selectivity plays a key role in every walk of life and in every aspect of science, particularly more in the field of organic chemistry. Construction of carbon-carbon bonds[1a,b] occupies unique place in organic chemistry because of its fundamental importance in assembling carbon framework. The present day challenges in organic chemistry create a need to develop methodologies for selective construction of carbon-carbon bonds at a particular place when there are more than one competing site for formation of carbon-carbon bonds. Let us consider α, β-unsaturated carbonyl (or containing other electron withdrawing groups such as ester or nitrile or nitro groups) compounds it is very easy to construct a C-C bond at β-position of these molecules *via* the well known Michael reaction (Fig. 1).[1c] But it was not that easy during the earlier times (few years before) to construct a C-C bond at α–position of α, β-unsaturated carbonyl compounds (activated alkenes). Also in recent years the concept of atom-economy and organo-catalysis have become increasingly important for developing any new organic reactions.

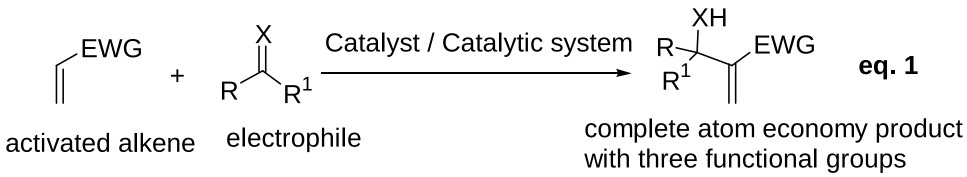
Figure 1



Baylis-Hillman reaction:

Recently the Baylis-Hillman reaction, a novel carbon-carbon bond forming reaction focusing on the concepts of (1) construction of carbon bonds at α–position of an activated alkenes (α, β-unsaturated carbonyl or other compounds), (2) atom-economy, and (3) organo-catalysis has been developed and in fact has also become one of the most popular and powerful synthetic tools in organic chemistry. Originating from a German patent[2] this reaction is essentially three component carbon-carbon bond forming reaction involving the coupling of the α–position of an activated alkene with carbon electrophile under the influence of catalyst or a catalytic system producing a variety of densely functionalized molecules with complete atom economy (eq. 1 & Fig. 2).[3-9] If the catalyst is organic compound like tertiary amines or phosphines this can be referred to as the organo-catalysis reaction.

Atom-economy reaction:



eq. 1

EWG = CHO, COR, CN, COOR, $PO(OEt)_2$, SOPh, SO_2Ph, SO_3Ph,

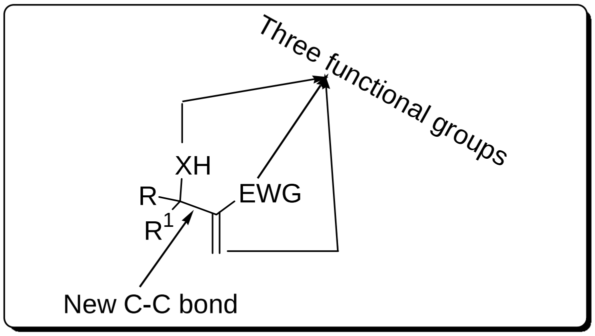
R = aryl, alkyl, heteroaryl, aralkyl

R^1 = H, COOR, Alkyl

X = O, NTs, NSO_2Ph, NCOOR

Catalyst / Catalytic system: 3^{o}amines, Lewis acids, phosphines, chalcogenides, *etc.*

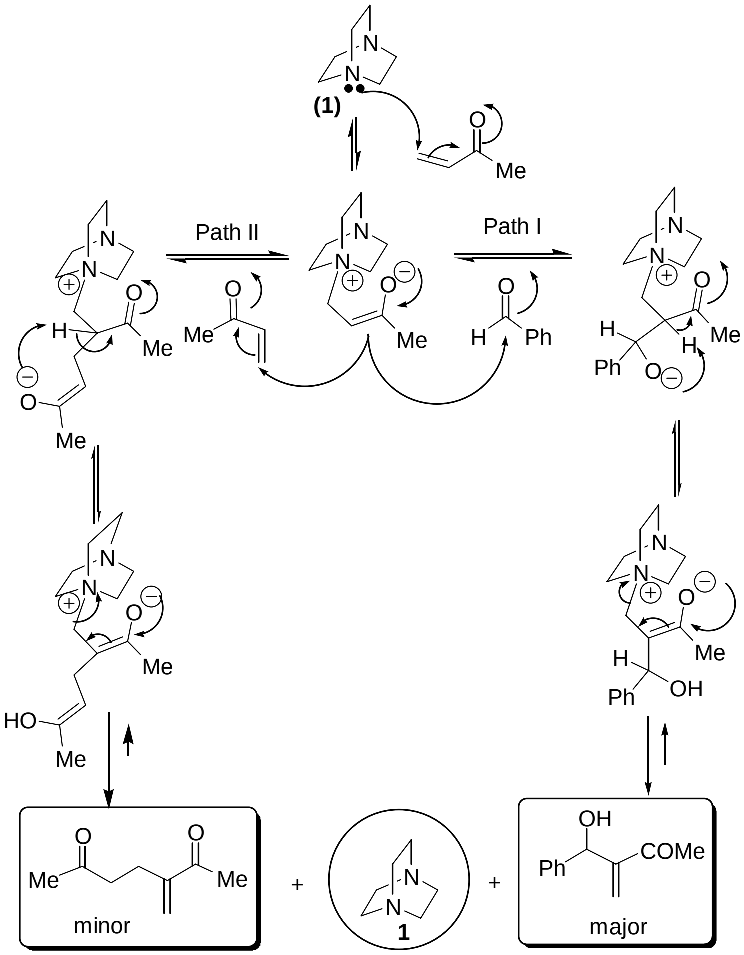
Figure 2



MECHANISM:

Based on the available evidence and literature, the most generally accepted mechanism[3-12] of the *tert*-amine catalyzed Baylis-Hillman reaction is described in the Scheme 1 considering the coupling of methyl vinyl ketone (as an activated olefin) with benzaldehyde (as an electrophile) under the catalytic influence of DABCO (**1**), as a model reaction. This mechanism is believed to proceed through the Michael, aldol addition-elimination sequence. In the first step DABCO (**1**) might add on to activated olefin (methyl vinyl ketone) in 1,4 addition (Michael addition) thus generating *in situ* a zwitterionic enolate, which would then add onto the electrophlie (benzaldehyde) in aldol fashion to produce zwitterion. Subsequent, proton migration followed by the release of catalyst would lead to the formation of densely functionalized molecules which are commonly known as the Baylis-Hillman adducts (Scheme 1, path I). In the case of reactive alkyl vinyl ketones (activated olefin) such as methyl vinyl ketone, Michael type dimers are formed as biproducts because these activated alkenes themselves act as electrophiles (Scheme 1; path-II)

Scheme 1



There has been a phenomenal growth of the Baylis-Hillman reaction during the last 20-25 years with respective to all the three essential components, *i.e.,* activated alkene, electrophile and catalyst as evidenced by plethora of research publications, five major reviews and several mini reviews.[3-9] Due to the presence of many (minimum of three) functional groups in proximity, the Baylis-Hillman adducts have been employed in various organic transformations and also used as substrates in several organic reactions.[3-9] Due to the large number of publications vast literature is now available on various aspects of this attractive reaction. It is therefore not possible to present each and every detail in this section. However, every attempt is made to present the recent and important developments, with respect to the all the essential components and also with respect to the applications of the Baylis-Hillman adducts in this section.

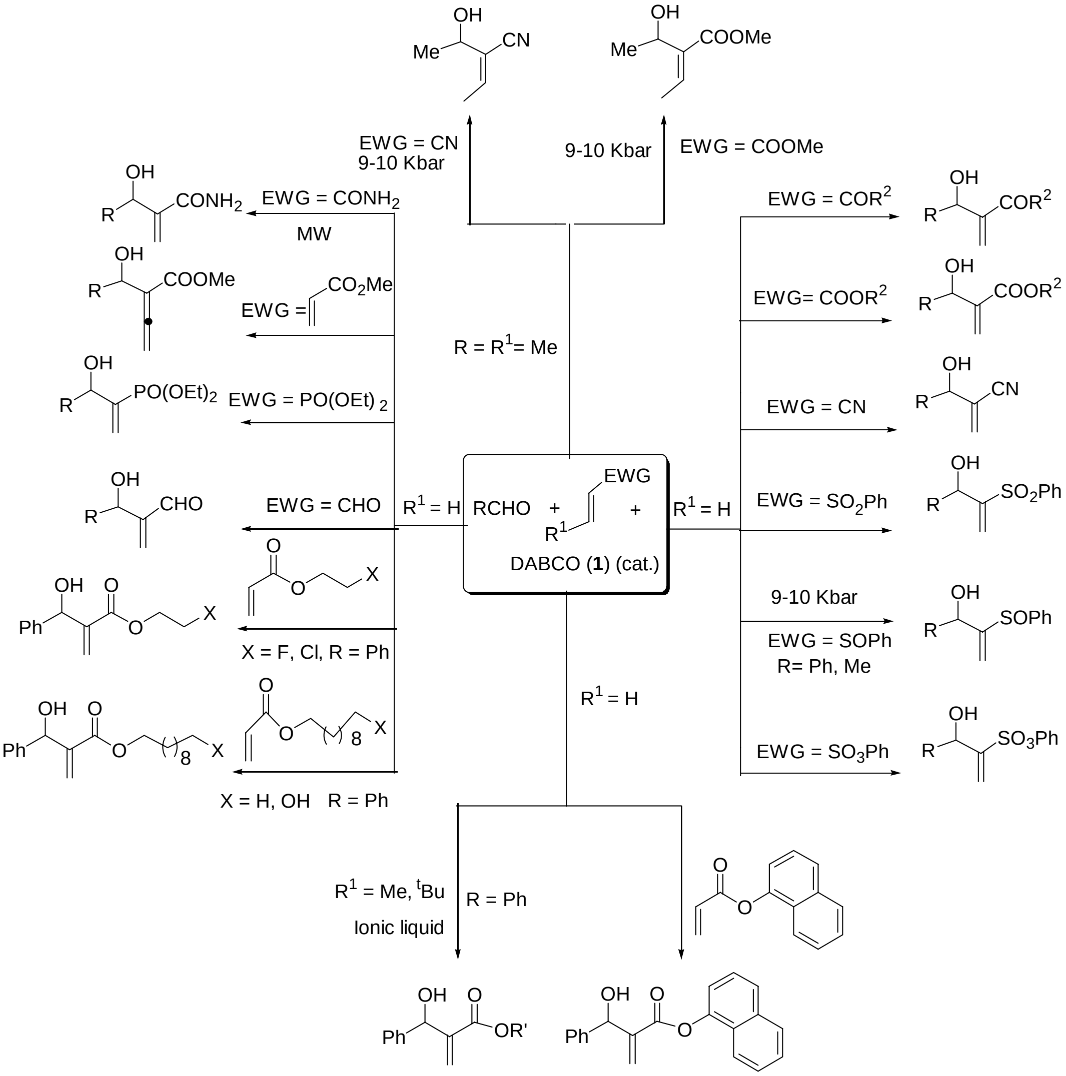
ACTIVATED ALKENES

Several acyclic and cyclic activated alkenes have been successfully used for coupling with various electrophiles under the influence of various catalysts / catalytic systems to provide a variety of densely functionalized molecules.

Acyclic alkenes: Earlier work

A number of acyclic activated alkenes such as alkyl vinyl ketones,[13-15] alkyl (aryl) acrylates,[12,16,17] acrylonitrile,[14,18] vinyl sulphones,[19] acrylamides,[20] allenic esters,[21,22] vinyl phosphonates,[23] vinyl sulphonates,[24] and acrolien[25, 26] have been effectively employed in the Baylis-Hillman coupling with a number of electrophiles to provide the desired densely functionalized molecules (Scheme 2). However, the activated alkenes having β-substituents such as crotononitrile[27,28]crotonic acid esters,[28] and less reactive alkenes like phenyl vinyl sulfoxide[29] do not participate in the Baylis-Hillman reaction with aldehydes. However they were brought into the scope of the reaction under high pressure conditions (Scheme 2).

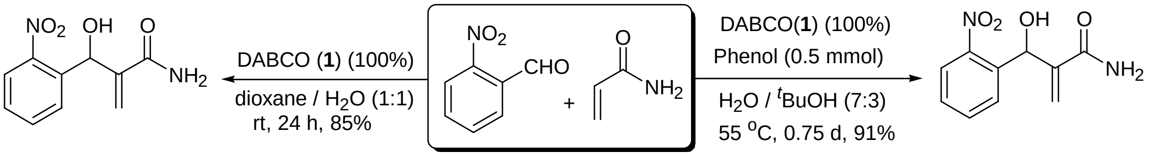
Scheme 2



Recent Developments:

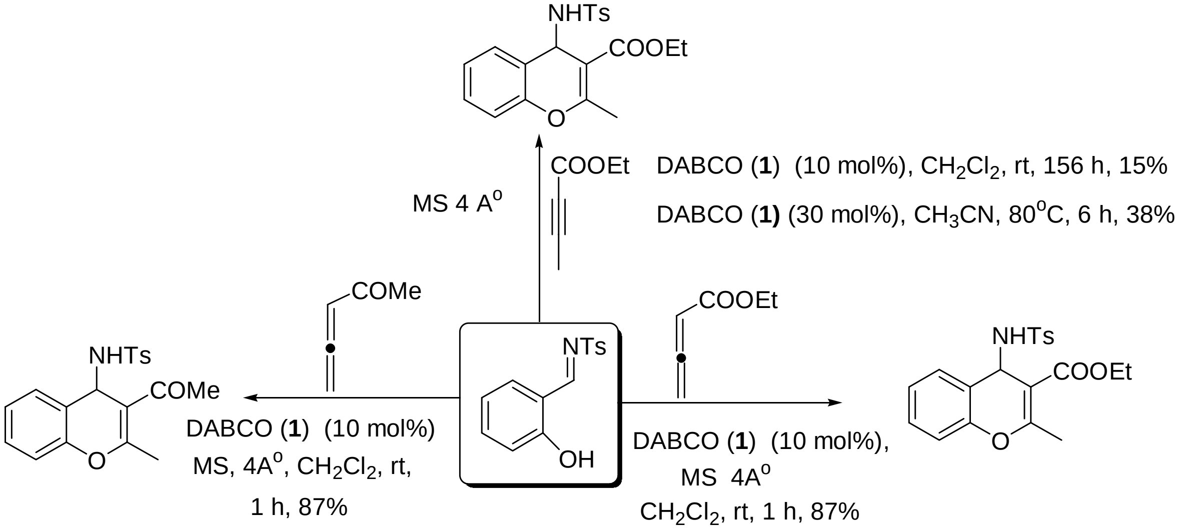
Hu[30] and Connon[31] independently employed less reactive activated alkene acrylamide for coupling with different types of aromatic aldehydes using DABCO as a catalyst in the presence of protic solvent system. One representative example is presented in Scheme 3.

Scheme 3



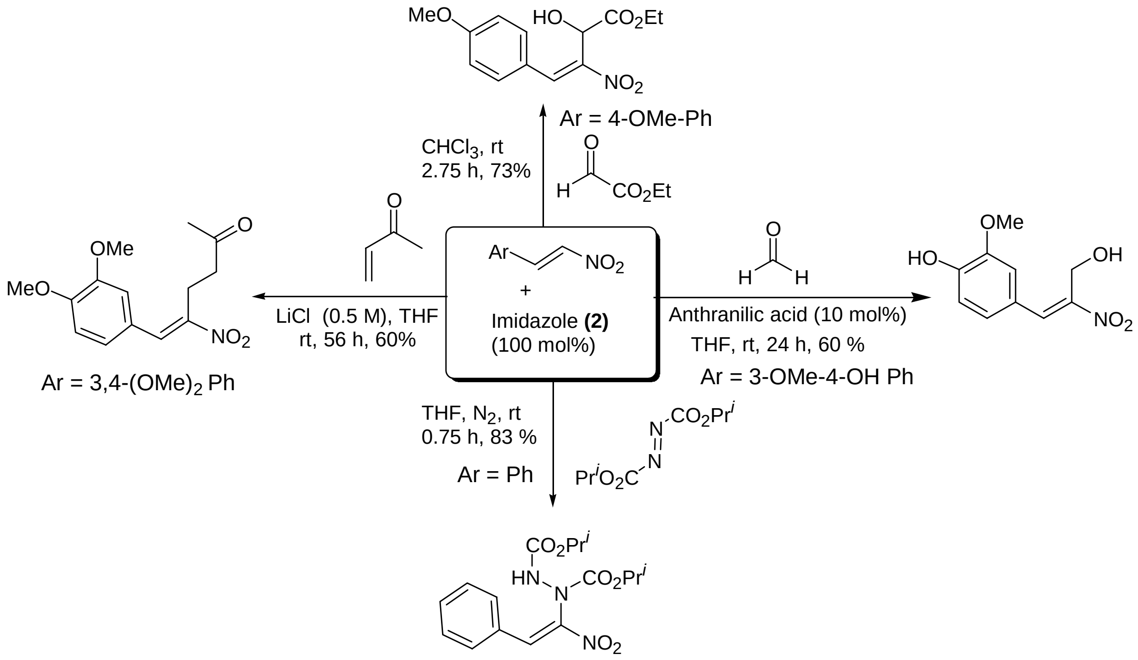
Shi and co-workers[32] have developed an interesting DABCO (**1**) catalyzed Baylis-Hillman reaction of salicyl-*N*-tosylimines (as electrophiles) with ethyl 2,3-butadienoate, ethylbut-2-ynoate and penta-3,4-dien-2-one (as activated alkenes and alkynes) at room temperature to provide the corresponding chromene derivatives in good to excellent yields. Representative examples are presented in Scheme 4.

Scheme 4

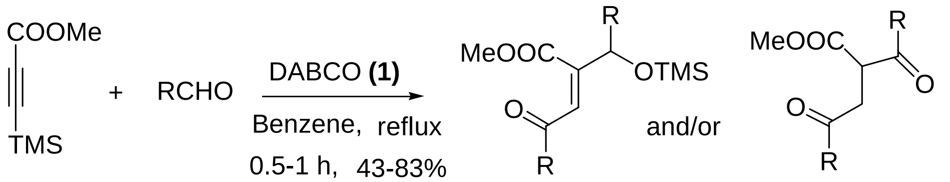


For the first time Namboothiri and co-workers[33-36] have elegantly and systematically studied the applications of conjugated nitroalkenes as activated alkenes in the Baylis-Hillman coupling with formaldehyde (formalin),[33] methyl vinyl ketone,[34] ethyl glyoxylate,[35] and diisopropyl azodicarboxylate[36] under the influence of imidazole (**2**) at room temperature. Representative examples are presented in Scheme 5.

Scheme 5



Nemoto and co-workers[37] have described an interesting reaction of methyl 3-trimethylsilylpropiolate with various aldehydes under the influence of DABCO leading to the formation of novel *β*-acylated Baylis-Hillman products involving simultaneous formation of two C-C bonds. Representative examples are presented in eq.2.



eq. 2

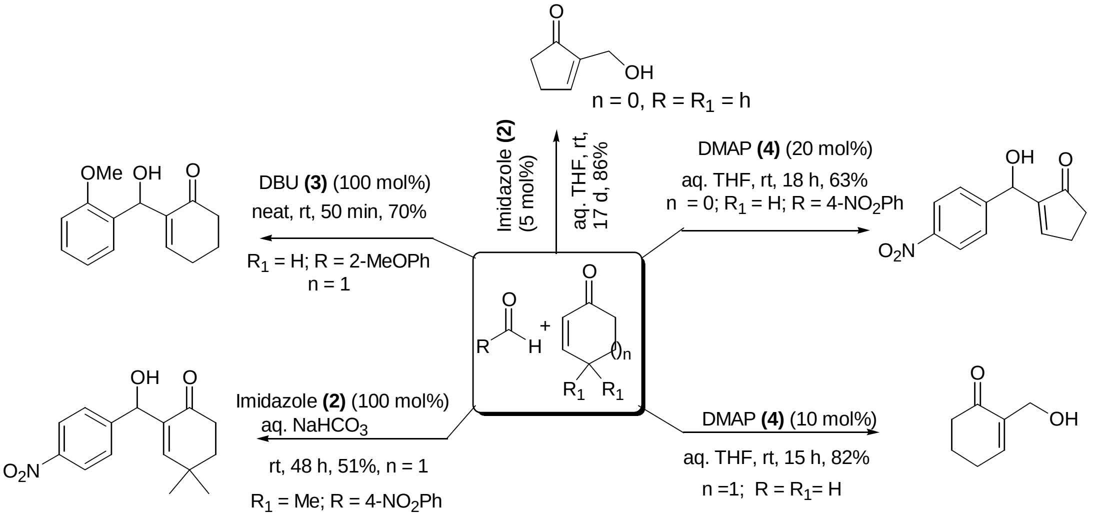
R = C_6H_5, 2-MeC_6H_4, 3-MeC_6H_4, 4-MeC_6H_4, 2-$OMeC_6H_4$, 3-$OMeC_6H_4$, 4-$OMeC_6H_4$, 4-ClC_6H_4, 1-naphthyl, 2-naphthyl, 2-Br, 4,5-$(OMe)_2$-C_6H_2

Ratio : 37-100 / 63-0

Cyclic activated alkenes: Earlier work

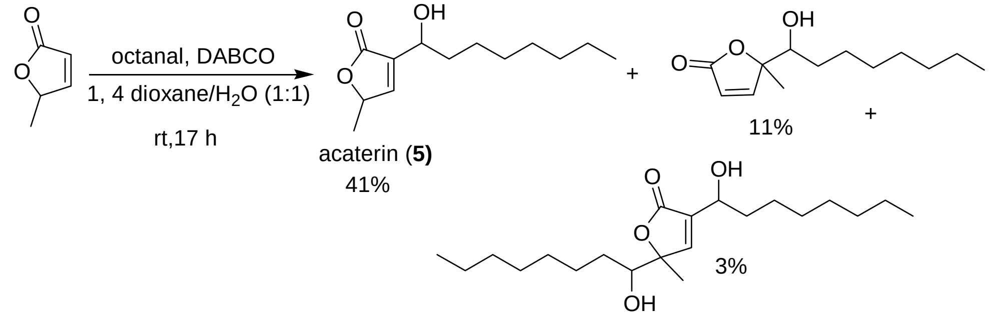
Various cyclic activated alkenes (cyclopent-2-enone, cyclohex-2-enone and their derivatives)[7,8] have been successfully used for coupling with number of aldehydes in the presence of variety of *tert*-amine catalysts, such as, DABCO (**1**),[38] imidazole (**2**),[2,39,40] DBU (**3**),[41] DMAP (**4**),[42,43] to provide multifunctional derivatives. Representative examples are presented in Scheme 6.

Scheme 6



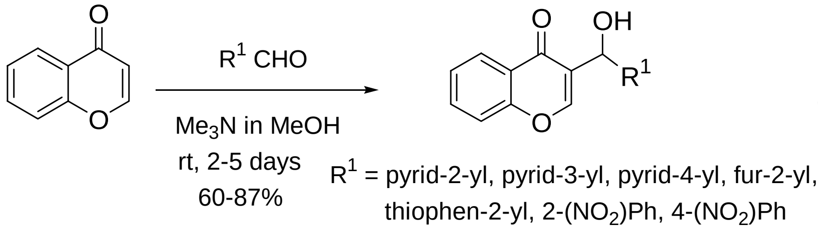
Recent Developments:

Franck and Figadere[44] have used δ-butyrolactone as activated alkene for Baylis-Hillman coupling with octanal leading to an interesting one-pot synthesis of racemic acaterin (**5**) (a natural product). This reaction also provides some undesired minor products (eq. 3).



eq. 3

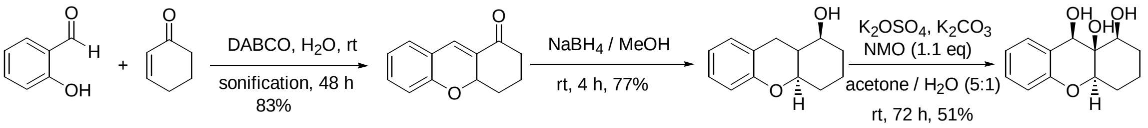
Our research group[45] has, for the first time, systematically studied the applications of 1-benzopyran-4(4*H*)-one, as activated olefine for coupling with various aromatic aldehydes in the presence of methanolic trimethylamine (**6**) (eq. 4).



eq. 4

Lesch and Brase [46] successfully developed a facile synthesis of tetrahydroxanthenones *via* the Baylis-Hillman reaction of salicylaldehydes with cyclohex-2-enones in the presence of DABCO under sonication, following the reaction sequence as shown in the Scheme 7.

Scheme 7

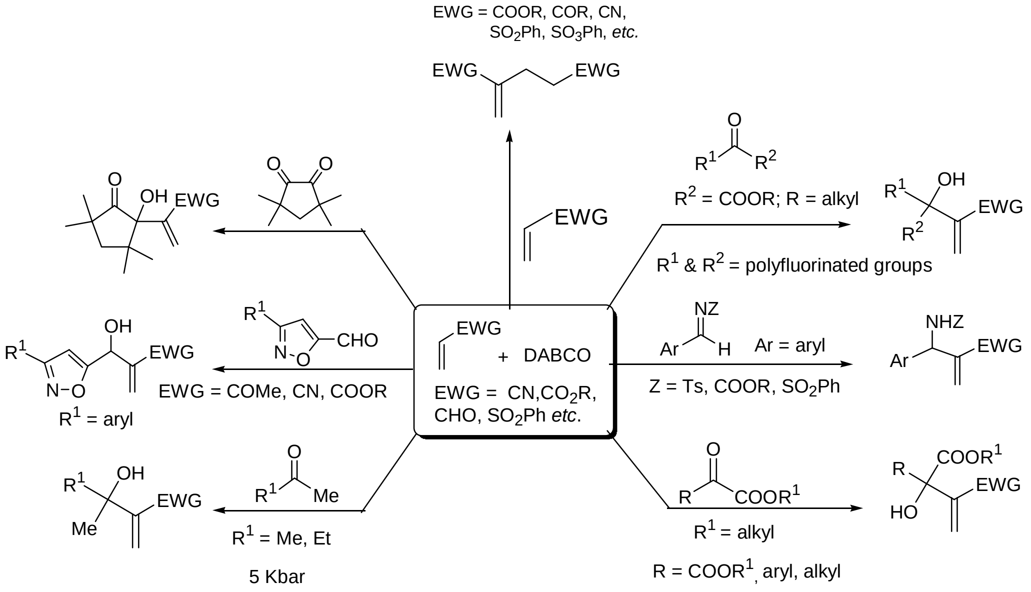


ELECTROPHILES

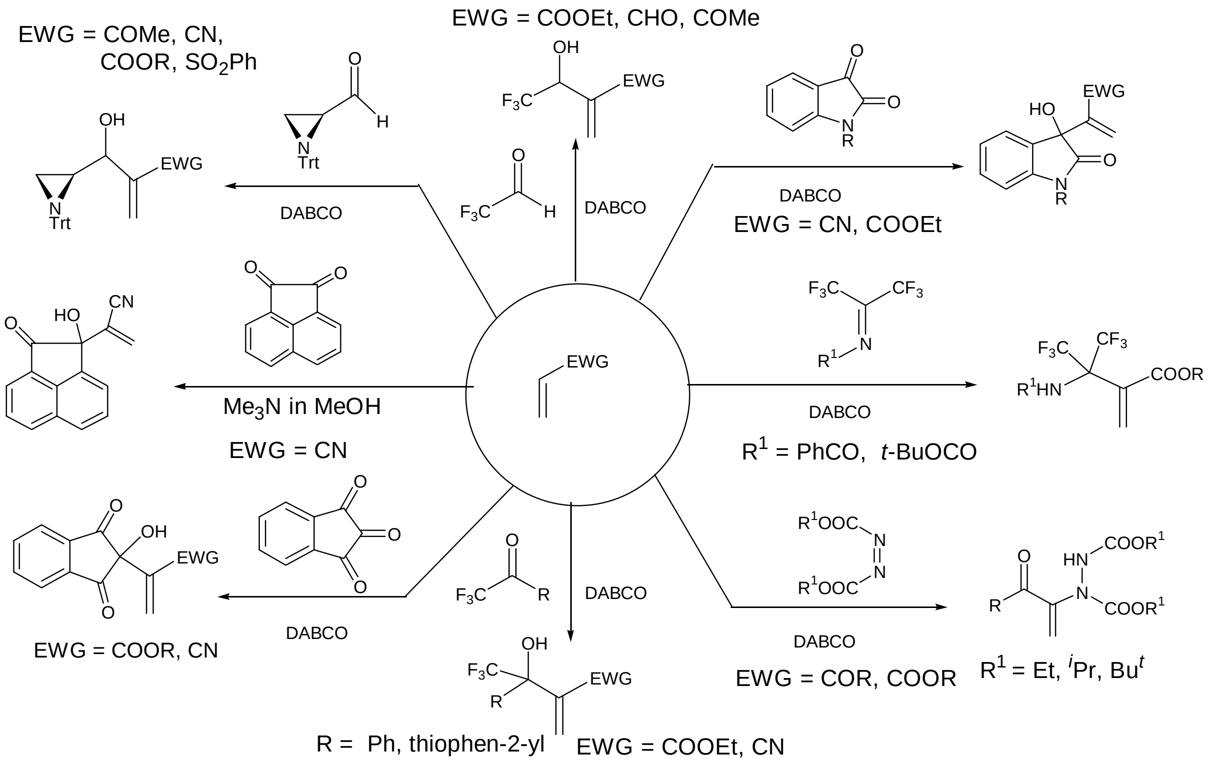
Earlier work

In addition to the aldehydes, other electrophiles such as α-keto esters,[47-49] fluoroketones,[50] aldimine derivatives,[51-54]activated alkenes,[55-58] non-enolizable 1,2- diketones[26] and isoxazole-5-carboxaldehydes[59] have also been effectively used in this reaction. However, simple ketones such as acetone & 2-butanone [25] being less reactive, do not participate in coupling with activated alkenes under normal conditions and require high pressure conditions for coupling with activated alkenes (Scheme 8). Recently, various isatin derivatives,[60,61] fluoroimines,[62] azodicarboxylates[63,64] fluorinated aldehydes & ketones,[65,66] *N*-trityl-aziridine-2-(*S*)-carboxaldehyde,[67] acenapthoquinone,[68] and ninhydrin,[35,61] have been comfortably employed as electrophiles in the Baylis-Hillman reaction. Selected examples are presented in Schemes 8 and 9.

Scheme 8



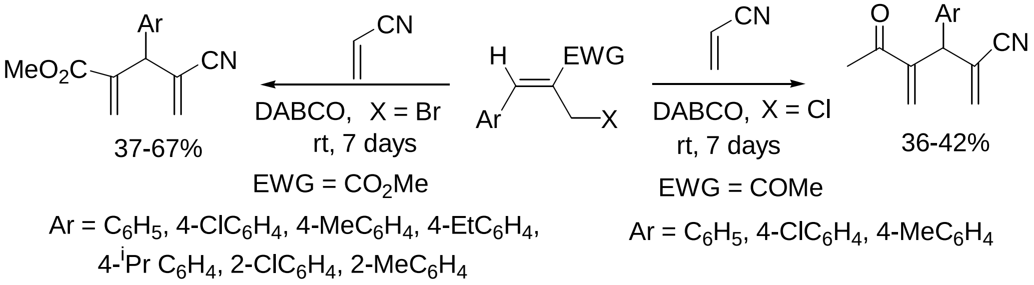
Scheme 9



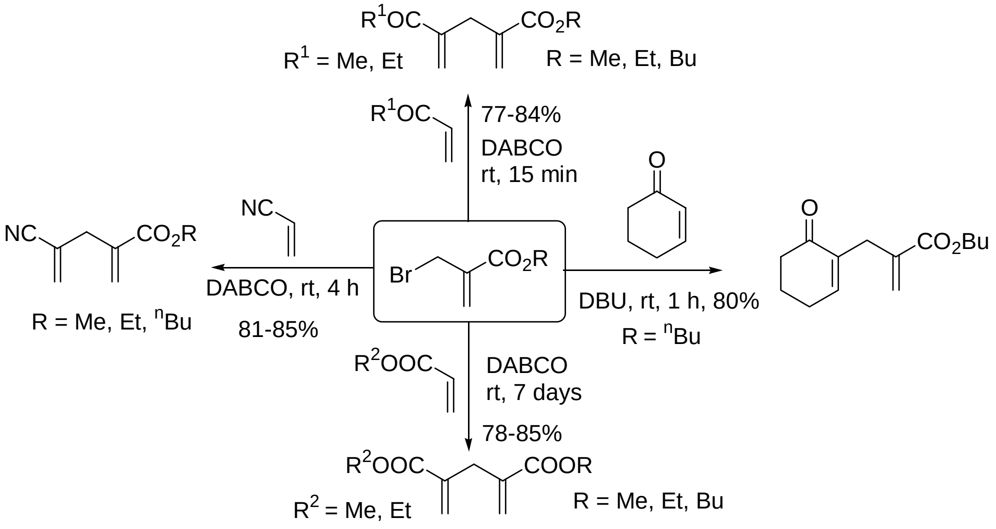
Recent Developments

The Baylis-Hillman bromides and chlorides have been for the first time employed, by our research group, as eletrophiles in the Baylis–Hillman coupling with various activated alkenes under the influence of DABCO to provide the corresponding substituted functionalized 1, 4-pentadienes (Schemes 10 and 11).[69, 70] We have also noticed that simple allyl halides do not participate in the Baylis-Hillman reaction with activated alkenes under these conditions.[69]

Scheme 10

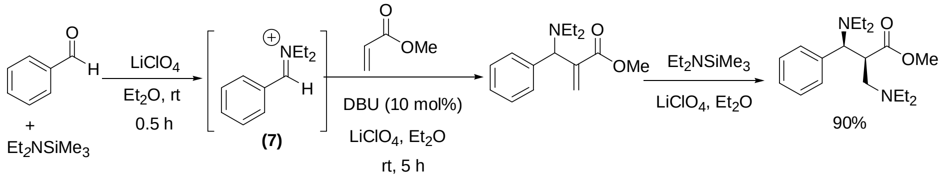


Scheme 11



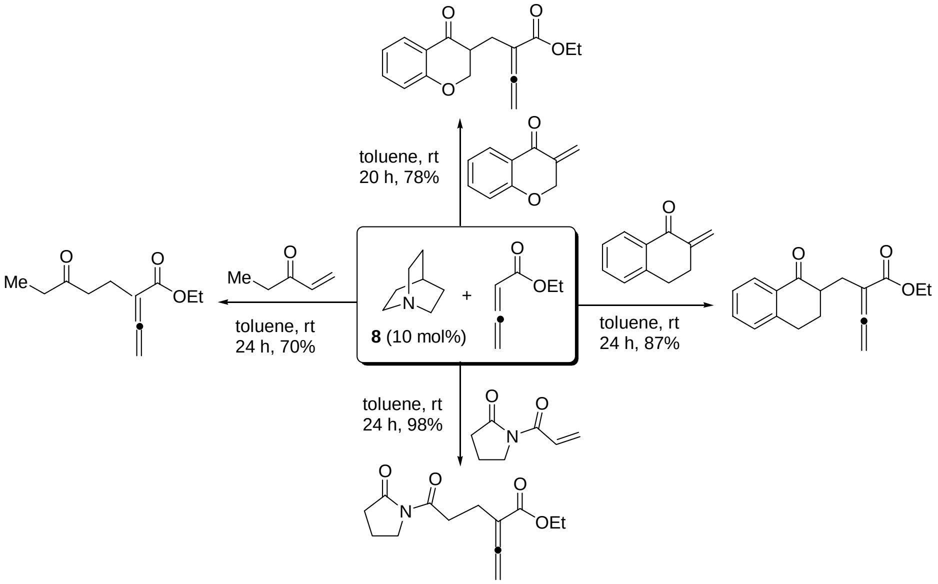
Saidi and co-workers[71] employed *in situ* generated iminium salts (**7**) (obtained *via* the treatment of the aldehydes with Et_2NSiMe_3) as electrophiles in the Baylis–Hillman reaction with methyl acrylate in the presence of DBU. The corresponding Baylis-Hillman adducts, thus obtained, further react with excess (trimethylsilyl)dialkylamines to give the diamines (Scheme 12).

Scheme 12



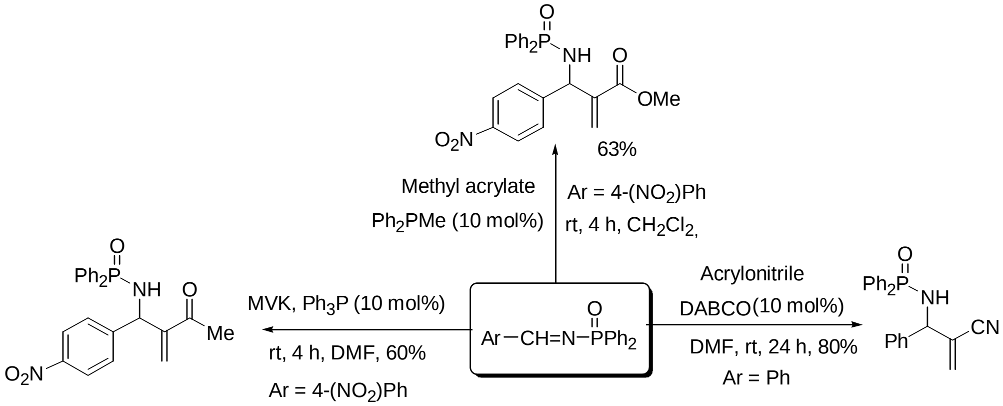
Miller and co-workers[72] reported an efficient quinuclidine (**8**) catalyzed coupling of allenic esters with α,β-unsaturated carbonyl compounds as electrophiles to provide the corresponding Baylis-Hillman adducts. Representative examples are presented in Scheme 13.

Scheme 13

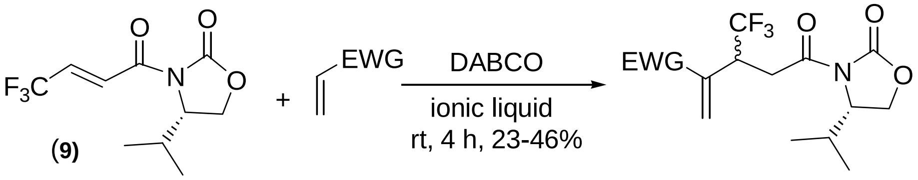


Shi and co-workers have successfully used N-arylidene-diphenylphosphinamides as electrophiles for coupling with various activated alkenes under the influence of DABCO and phosphines as catalysts. Representative examples are presented in Scheme 14.[73]

Scheme 14



Trifluoromethylprop-2-enamide (**9**) was employed as electrophile in the Baylis-Hillman reaction with activated olefines under the influence of DABCO in ionic liquids by Kitazume and co-workers (eq. 5) [74]



eq. 5

ionic liquid = [emim][OTf], [bmim][BF_4], [bmim][PF_6]
EWG = CO_2Me, CN, COMe

dr = 50:50 to 55:45

AMINE CATALYZED BAYLIS-HILLMAN REACTIONS:

Although the DABCO (**1**) was found to be catalyst of choice[1,38] variety of tertiary amines, such as, imidazole (**2**),[2,39,40,75] DBU (**3**),[41] DMAP (**4**),[42,43] methanolic-Me_3N (**6**),[45,68,76] quinuclidine (**8**),[2,77] indolizine (**10**),[2] HMT (**11**),[78,79] 3-hydroxyquinuclidine (**12**),[77,80] 3-acetoxyquinuclidine (**13**),[77,80] 3-chloroquinuclidine (**14**),[77] 3-quinuclidinone (**15**),[77] NMM (**16**),[79] TMPDA (**17**),[81] TMEDA (**18**),[82] TMG (**19**),[83,84] Et_3N (**20**),[27] aqueous-Me_3N (**21**),[85]

(Figure 3) and several polymer supported DMAP derivatives, such as, PAP [polymer-bound 4-(*N*-benzyl-*N*-methylamino)pyridine] (**22**),[86] DMAP-MSN [meso-porous silica nano-sphere] (**23**),[87] and ionic liquid (quinuclidine derivative) (**24**)[88] (Figure 4) have been successfully employed as catalysts in various Baylis-Hillman reactions. Representative examples are presented in Scheme15.

Figure 3

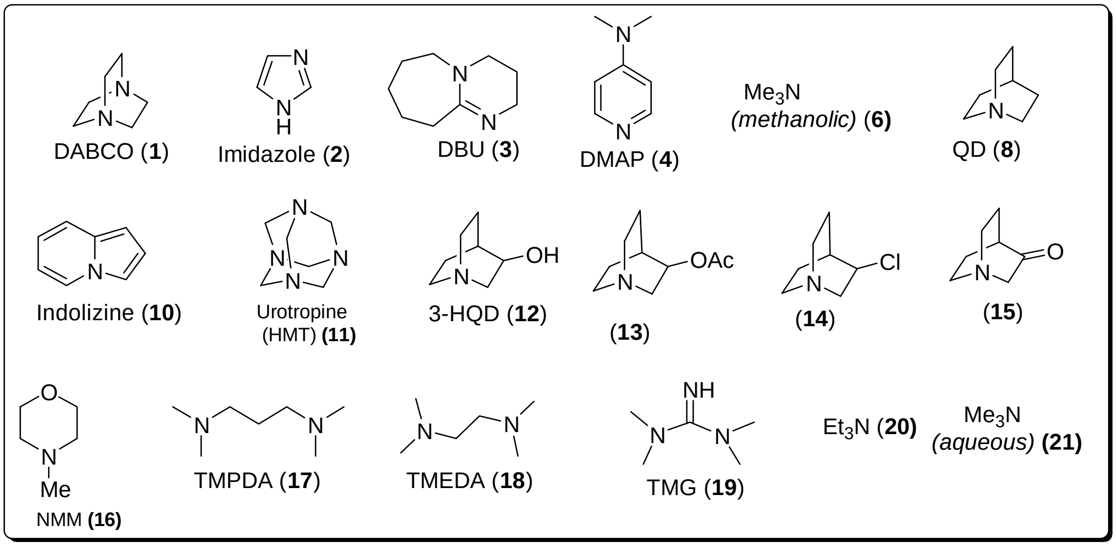
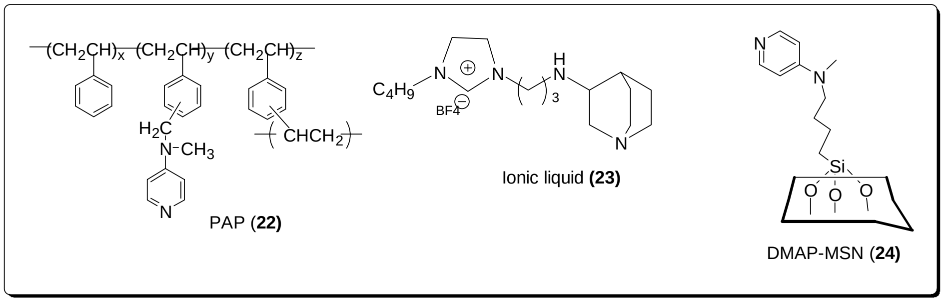
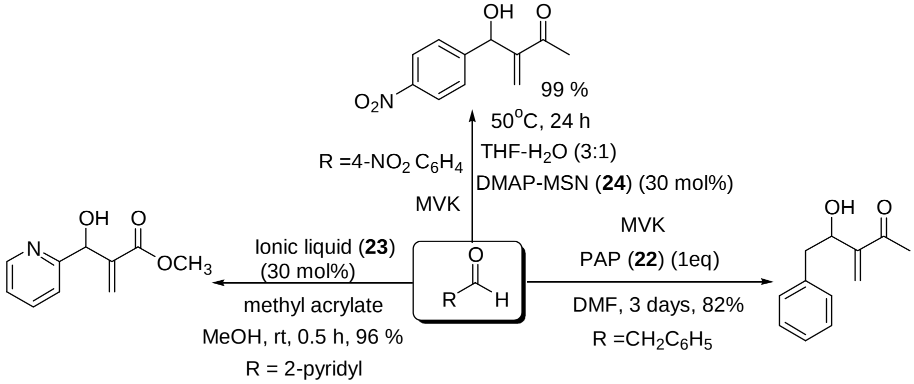


Figure 4



Scheme 15

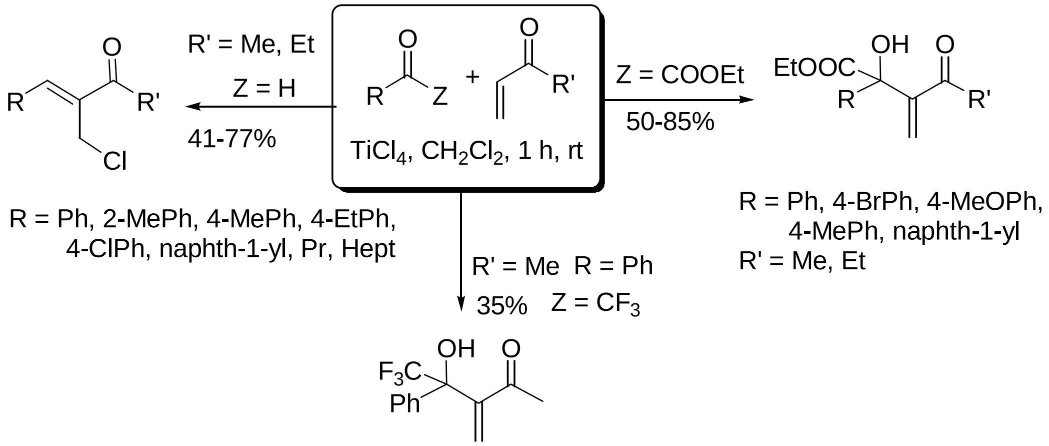


VARIOUS NON-AMINE CATALYSTS / CATALYTIC SYSTEMS EMPLOYED IN BAYLIS-HILLMAN REACTION:

In addition to the above mentioned amine catalysts a number of non-amine catalysts / catalytic systems, such as trialkyl phosphines,[89-91] triaryl phosphines,[92] and metal complexes like $RhH(PPh_3)_4$,[93,94] $RuH_2(PPh_3)_4$,[94,95] have been found to promote the coupling of various activated alkenes (acyclic and cyclic) with different types of aldehydes to provide the corresponding adducts. Also combination of Lewis acid with base such as $R_2S{-}TiCl_4$,[7,96-99] $TiCl_4$-R_4NX (X = halide),[7,100,101] $TiCl_4$-R_3N,[102] or Lewis acids such as $TiCl_4$,[103-105] $R_2X{-}BF_3$ (X = O, S),[106,107] and Et_2AlI[108,109] were also found to promote the Baylis-Hillman reaction. Representative recent and relevant examples are presented in Schemes 16-22.

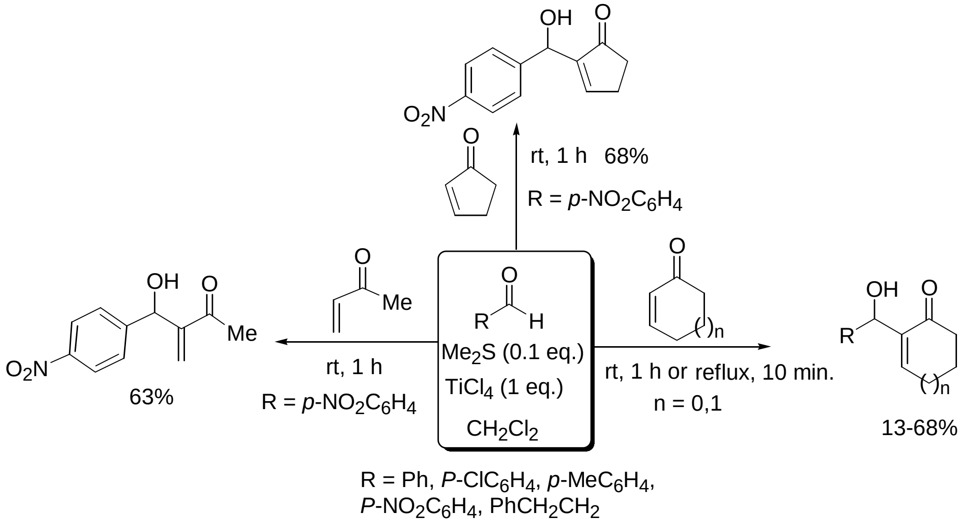
$TiCl_4$ promoted Baylis-Hillman coupling of α-keto esters and trifluoromethyl phenyl ketone with alkyl vinyl ketones to provide the desired Baylis-Hillman adducts has been reported by our research group.[104] Similar reaction with aldehydes provided the (*Z*)-allyl chlorides. Representative examples are presented in the Scheme16.

Scheme 16



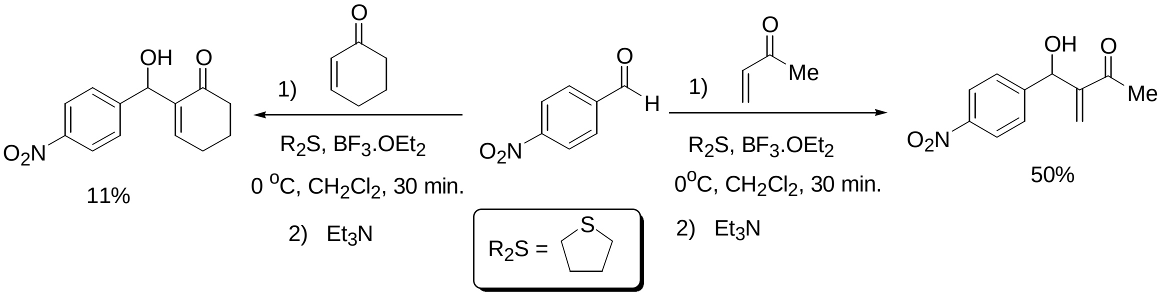
Kataoka and co-workers[97,98,110] developed an interesting class of chalcogenide promoted Baylis–Hillman reaction of various aldehydes with alkyl vinyl ketones in the presence of titanium tetrachloride. Representative examples are presented in Scheme 17.

Scheme 17



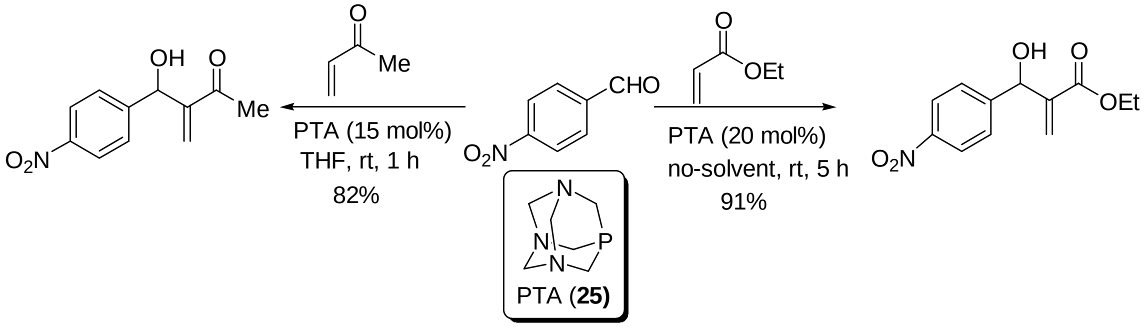
Goodman and co-workers[111] have subsequently used tetrahydrothiophene $BF_3 \bullet OEt_2$ as a catalytic system for the Baylis–Hillman reaction between aldehydes (electrophiles) and activated ketones (MVK and cyclohex-2-enone). Representative examples are described in Scheme 18.

Scheme 18

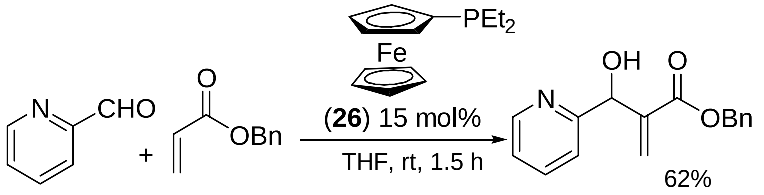


1, 3, 5-Triaza-7-phosphaadamantine (PTA) (**25**) has been successfully used as a catalyst for the Baylis-Hillman coupling of various aldehydes with different types of activated olefines by He and co-workers.[112] Representative examples are described in Scheme 19.

Scheme 19

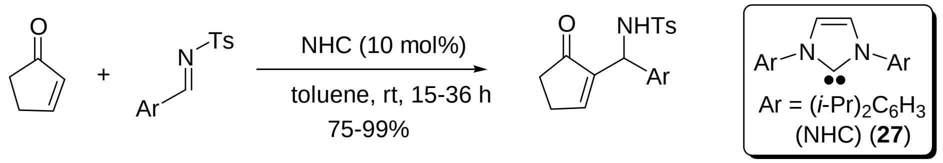


Carretero and co-workers[113] reported ferrocene diethylphosphine (**26**) as an air stable catalyst for the Baylis-Hillman reaction between various aldehydes and acrylates to afford the corresponding adducts in high yields. One representative example is presented in eq. 6.



eq. 6

Recently an interesting *N*-heterocyclic carbene (NHC **27**) catalyzed Baylis-Hillman reaction of cyclic enones with a variety of *N*-tosylimines, has been reported by He and co-workers to provide the corresponding adducts in high yields.[114] Representative examples are presented in eq.7.

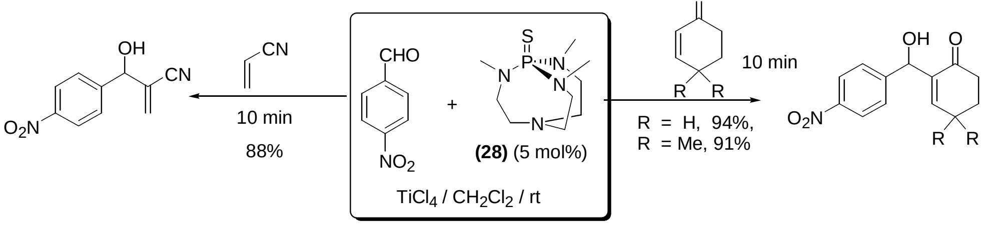


eq. 7

Ar = C_6H_5, 4-MeC_6H_4, 4-$MeOC_6H_4$,
4-ClC_6H_4, 4-FC_6H_4, 4-$NO_2C_6H_4$, 2-Furyl,
3-$MeOC_6H_4$, 3-ClC_6H_4, 2-$MeOC_6H_4$

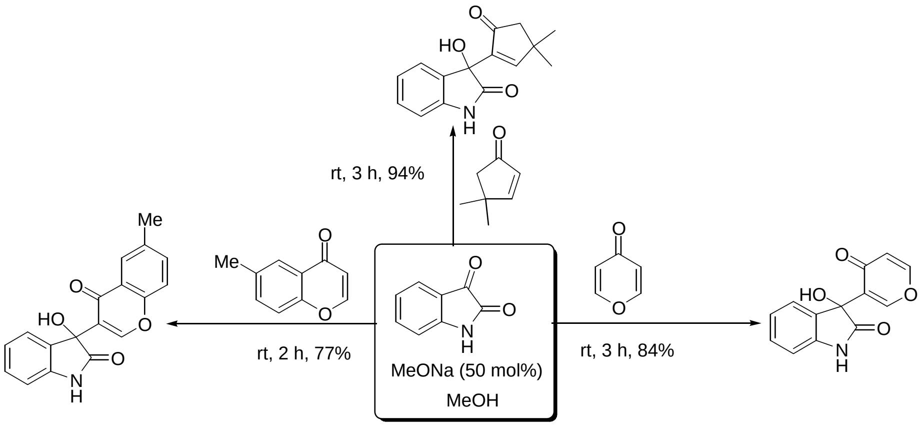
The aza-phosphine **28** has been found to be an excellent catalyst by Verkade and co-workers[115] for the Baylis-Hillman coupling between various acyclic/cyclic activated alkenes and different types of aldehydes to provide corresponding Baylis-Hillman adducts at a faster reaction rates and also in high yields. Some representative examples are presented in Scheme 20.

Scheme 20



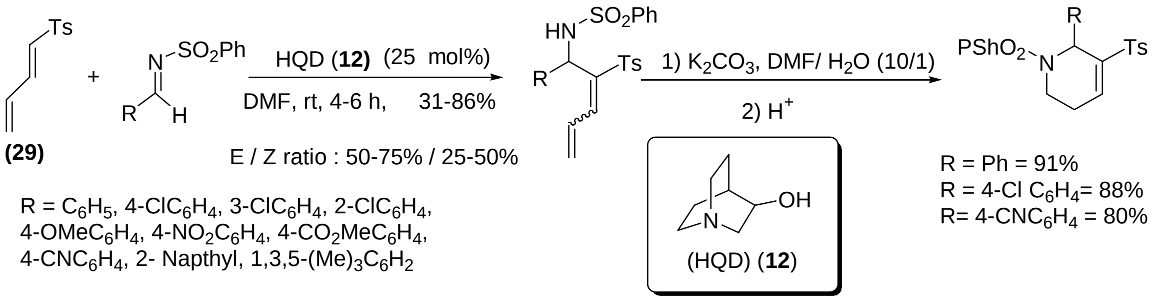
Cheng and co-workers[116] have developed methoxide ion in methanol to be a useful reagent to promote the Baylis-Hillman reactions of cyclic enones [such as cyclopent-2-enones, cyclohex-2-enones, γ- pyrone, and 1- benzopyran-4(4*H*)-ones] with various electrophiles. Representative examples are presented in Scheme 21.

Scheme 21



Back and co-workers[117] have successfully used (*p*-toluenesulfonyl)-1,3-butadiene (**29**) as activated alkene for coupling with aldimine derivatives in the presence of 3-hydroxyquinuclidine (HQD) (**12**) as catalyst to provide the corresponding Baylis-Hillman adducts which were subsequently transformed into tetrahydropyridine derivatives. Representative examples are presented in the Scheme 22.

Scheme 22

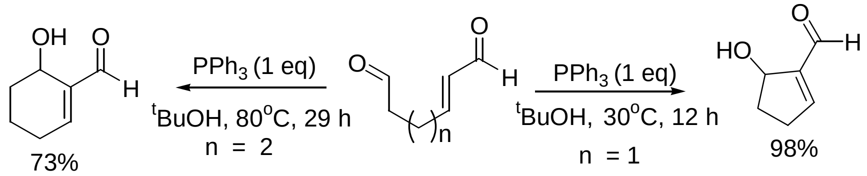


INTRAMOLECULAR BAYLIS-HILLMAN REACTIONS

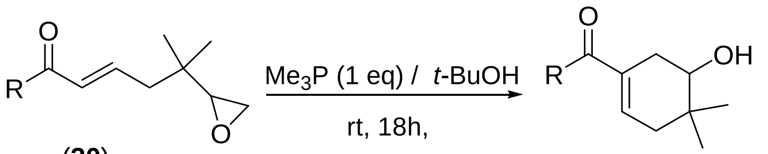
Although the Baylis-Hillman reaction has seen an exponential growth during the last several years the corresponding intra-molecular version did not grow in that proportion.[3-9] However in recent years this aspect has received more attention by the synthetic chemists and considerable progress has been achieved. Some important recent developments are given in the following schemes.

Koo *et* al.[118] have reported an efficient intramolecular Baylis-Hillman reaction of enal-aldehyde system using triphenylphosphine as a catalyst. Representative examples are shown in Scheme 23.

Scheme 23



Kraft and Wright[119] have described an interesting trialkylphosphine mediated intramolecular Baylis-Hillman reaction of enone-epoxide (**30**) framework to provide the corresponding carbocyclic derivatives. One representative example is shown in eq. 8.

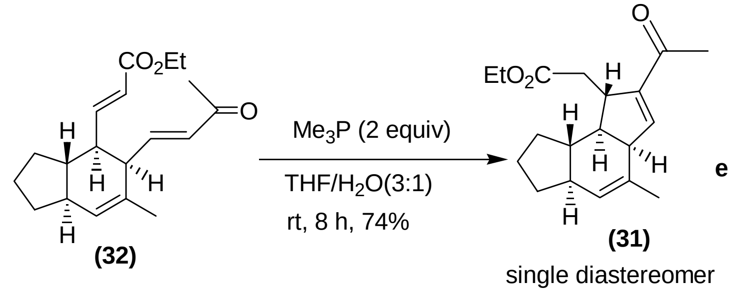


(**30**)

eq. 8

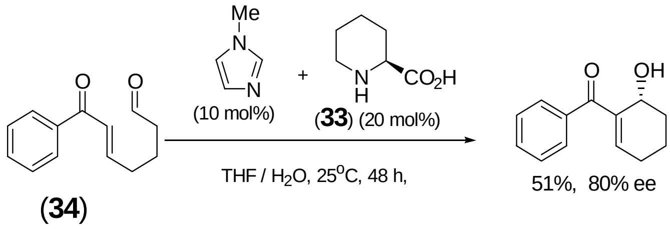
R = Me, 76%, R = Ph, 70%

Very recently, Methot and Roush[120] reported a facile synthesis of tricylic framework (**31**) *via* an interesting intramolecular Baylis-Hillman reaction of enone-ene-synthesis (**32**) in aqueous medium as described in eq.9.



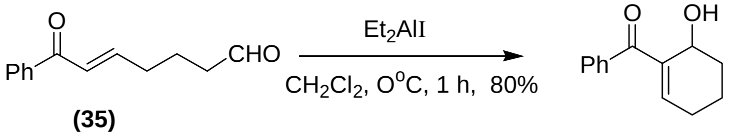
eq. 9

(*S*)-2-Pipecolinic acid (**33**) promoted asymmetric intramolecular Baylis-Hillman reaction of enone-aldehyde (**34**) frameworks in the presence of *N*-methylimidazole to provide the resulting adduct in good enantioselectivity was reported by Miller and co-workers.[121] One representive example is presented in eq. 10.



eq. 10

Enone-aldehyde (**35**) frameworks has been also successfully used as substrate for intramolecular Baylis-Hillman reaction under the influence of Et$_2$AlI by Oshima and co-workers.[122] One example is given in eq.11.



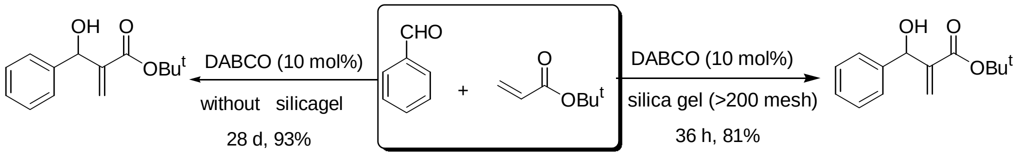
eq. 11

RATE ACCELARATION OF BAYLIS–HILLMAN REACTION

Most of the Baylis-Hillman reactions are slow reactions and require few days to few weeks for completion depending upon the reactivity of the three essential components. Several synthetic chemists addressed this problem and several attempts were made to surmount this problem with different strategies such as use of excess catalyst,[3-9] concept of hydrogen bonding (having a hydroxy group either in the catalyst or in the substrate),[80,123-125] aqueous medium,[126] microwave irradiation,[20] reactive activated alkens,[3-9,12,127] reactive electrophiles,[3-9] and high pressures [25,27,128] and considerable success has been achieved in these directions. In addition to the above efforts, recently organic chemists have employed some interesting strategies for rate acceleration in the Baylis–Hillman reaction.[129-131] Some of the important and interesting developments are discussed in this section.

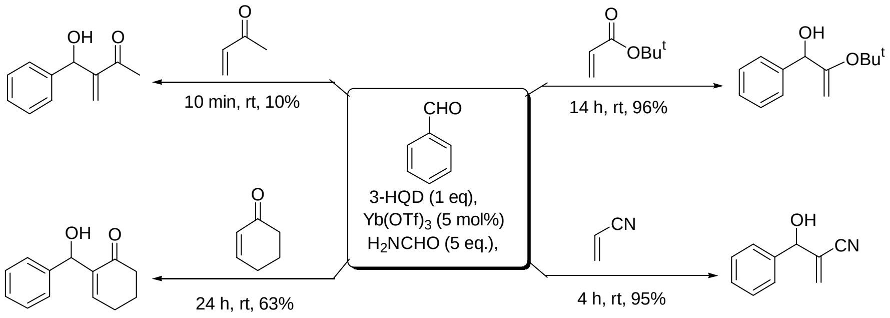
Our research group[129] has observed remarkable rate acceleration using silica gel as a solid phase medium in the Baylis–Hillman reaction. One example is presented in Scheme 24.

Scheme 24

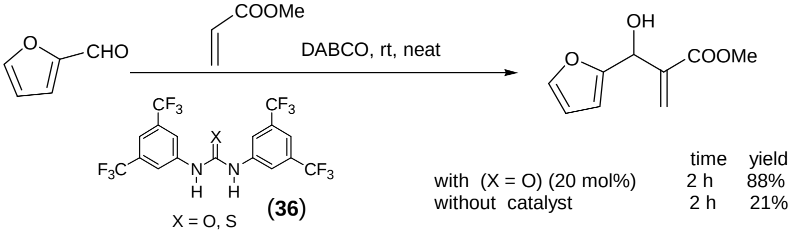


Recently, Aggarwal and co-workers[130] reported that polar solvents such as water and formamide accelerate the Baylis–Hillman reaction. They found that the presence of 5 equivalents of formamide gave better results (Scheme 25).

Scheme 25



Connon and co-workers[131] found that catalytic amount of bis-aryl (thio)ureas (**36**) accelerate the DABCO-promoted Baylis–Hillman reaction between aromatic aldehydes and methyl acrylate in the absence of solvent. One representative example is given in eq. 12.



eq. 12

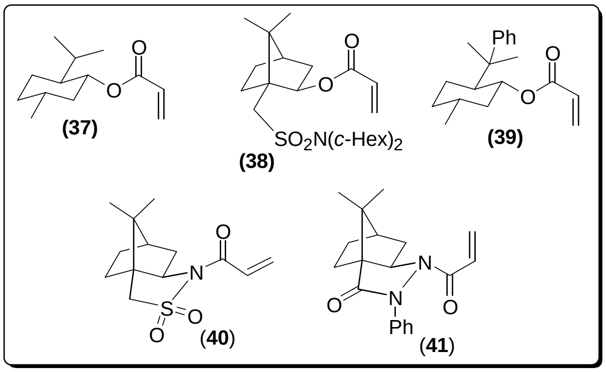
ASYMMETRIC BAYLIS-HILLMAN REACTION

In the case of prochiral electrophile the resulting Baylis-Hillman adduct contain a chiral center and hence there exists a possibility of developing its asymmetric version. The asymmetric version in principle can be achieved by having chirality either in activated alkene, electrophile, and catalysts or in the reaction medium (solvent or additives). Synthetic chemists have examined all these possibilities and achieved reasonable success in all these angles.

CHIRAL ACTIVATED ALKENES

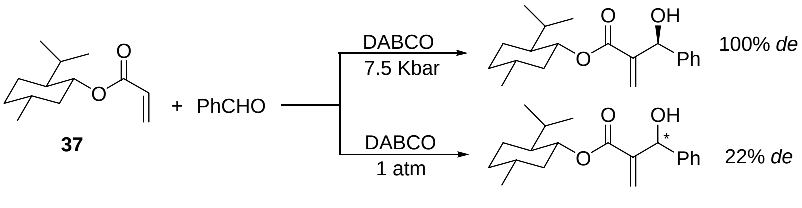
The chiral activated alkenes mostly acrylates or acrylamides derived from various chiral auxiliaries have been used for the Baylis-Hillman coupling with various electrophiles.[4,5] Representative chiral activated alkenes which provided reasonable selectivities are listed in Fig 5 and the selected applications are presented in Schemes 26-27 and eq 13-15.[132-138]

Figure 5

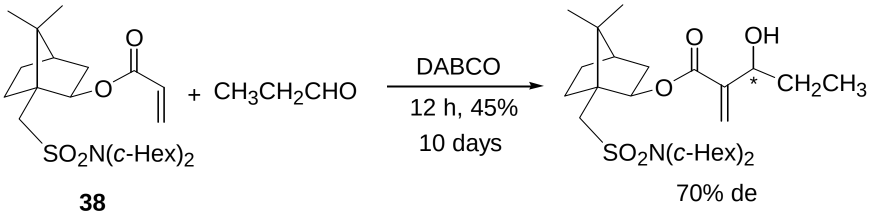


Menthyl acrylate was the first chiral activated alkene used for diastereoselective coupling reaction with aldehydes as early as 1986 by Brown.[132] Although the resulting products were obtained in low diastereoselectivities this strategy has become a guiding reaction for developing better chiral activated alkenes. Subsequently Gilbert and co-workers[133] found a remarkable increase in the diasteroselectivity in the coupling of (-)-menthyl acrylate (**37**) with benzaldehyde in the presence of DABCO at high pressure (7.5 Kbar) thus providing the required product with 100% *de*, while the same reaction at atmospheric pressure provides the desired adduct in 22% *de* only (Scheme 26).

Scheme 26

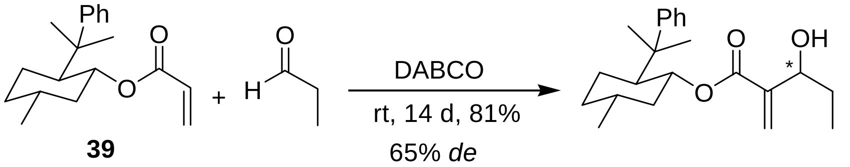


Our research group[134] has used chiral acrylates (**38**) as activated alkene for Baylis-Hillaman coupling with various aldehydes to provide the resulting adducts in low to moderate selectivity. One example is presented in eq. 13.



eq. 13

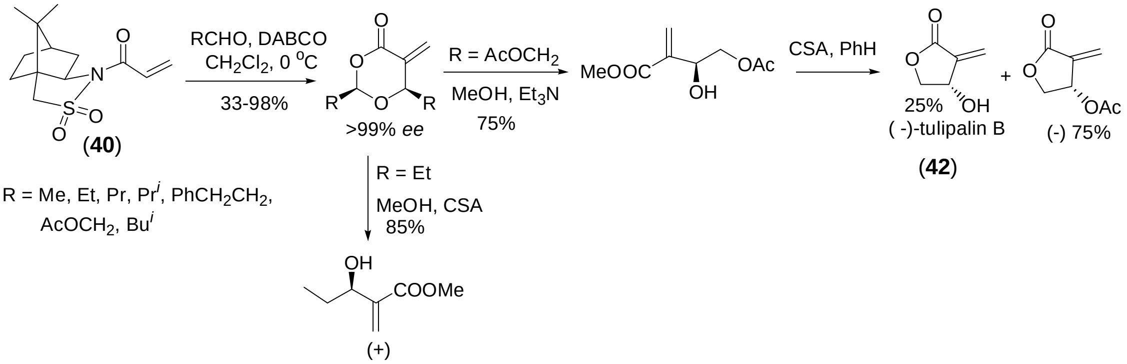
Later on Drewes and co-workers [135] employed (-)-8-phenylmenthyl acrylate (**39**) as a chiral activated alkene for Baylis-Hillman coupling with various aldehydes. The resulting adducts were obtained in moderate to good diastereoselectivities. One representative example is presented in the following eq.14



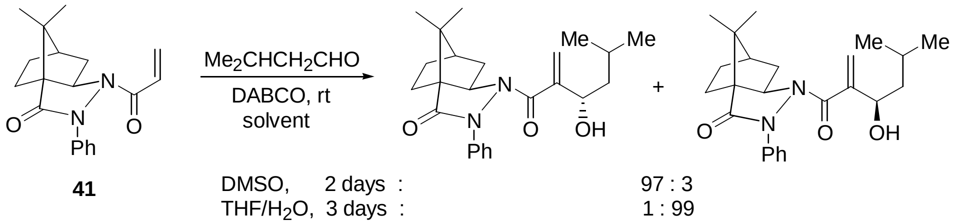
eq. 14

In the year 1997 Leahy and co-workers[136,137] have reported an interesting and high diastereoselective Baylis-Hillman coupling reaction using the enantiopure acrylamide (**40**), derived from camphorsulphonic acid, as activated alkene. They have also demonstrated the application of this methodology to the synthesis of (-)-tulipalin B (**42**), a biologically important natural product (Scheme 27).

Scheme 27



Yang and Chen[138] have used optically pure acryloylhydrazide (**41**) for the Baylis-Hillman coupling with various aldehydes (elctrophiles) under the influence of DABCO. The resulting Baylis-Hillman adducts were obtained in very high diastereoselectivities. They have also observed reversal in stereoselectivity by changing solvent system from DMSO to THF/H$_2$O. One representative example is presented in eq. 15.



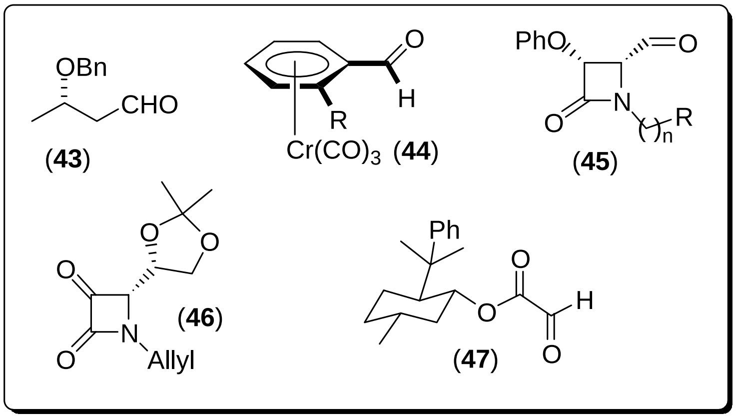
DMSO, 2 days : 97 : 3
THF/H$_2$O, 3 days : 1 : 99

eq.15

CHIRAL ELECTROPHILES

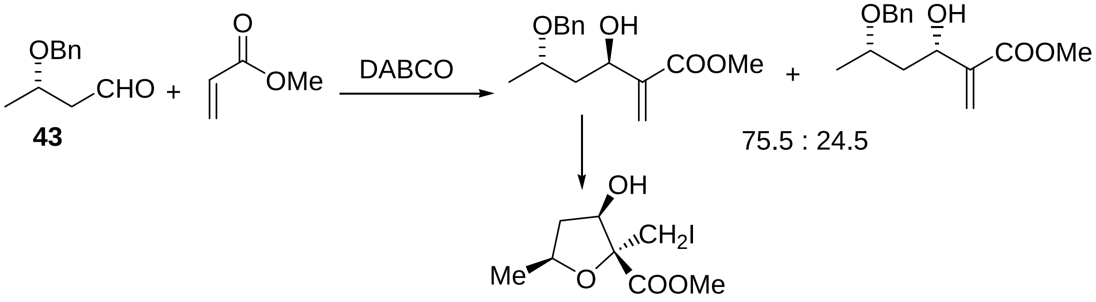
Various chiral electrophiles particularly aldehydes have been used for coupling with various activated alkenes to provide the resulting adduct in moderate to excellent diastereoselectivity. Representative chiral electrophiles (**43-47**)[139-143] are listed in Fig. 6 and some relevant examples are presented in the Scheme 28 and eqs 16-19.

Figure 6

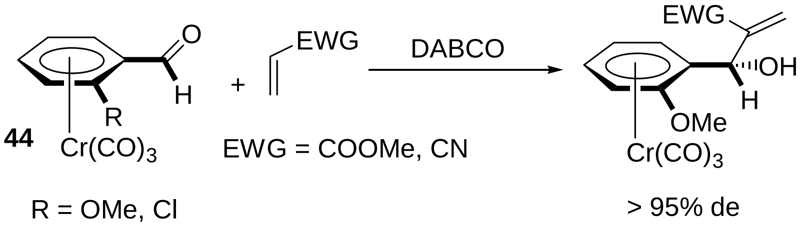


Drewes and co-workers[139] have used the (*S*)-3-benzyloxybuteraldehyde (**43**) as chiral electrophile for coupling with methyl acrylate under the influence of DABCO and the resulting major product was transformed into an useful tetrahydrofuran derivative (Scheme 28).

Scheme 28.



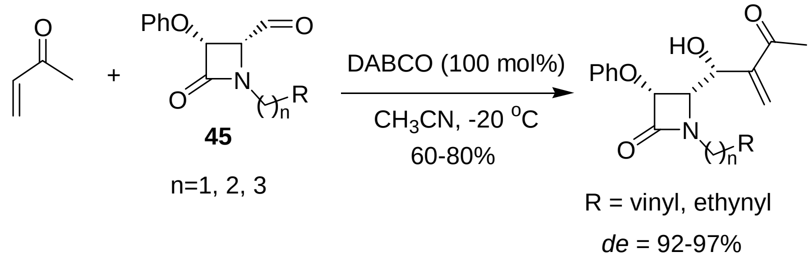
Racemic and non-recemic orthosubstituted benzaldehyde tricarbonyl chromium complexes (**44**) have been used as electrophiles in the DABCO catalyzed Baylis-Hillman reaction with methyl acrylate and acrylonitrile with high diastereoselectivity, by Kunding and co-workers.[140] Representative examples are presented in the eq.16



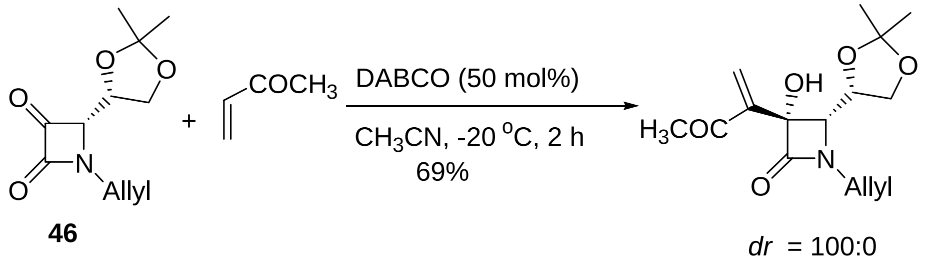
eq. 16

Enantiopure 1-alkenyl(alkynyl)-4-oxoazetidine-2-carbaldehydes (**45**)[141] were employed by Alcaide and co-workers, as chiral electrophiles in the Baylis-Hillman reaction with methyl vinyl ketone (MVK), thus providing the resulting Baylis-Hillman adducts with very high stereoselectivity (eq. 17). They have also successfully employed optically pure 3-oxo-2-

azetidinones (**46**) for coupling with activated alkenes under the influence of DABCO to provide the resulting Baylis-Hillman adducts in high diastereoselectivities (eq. 18).[142]

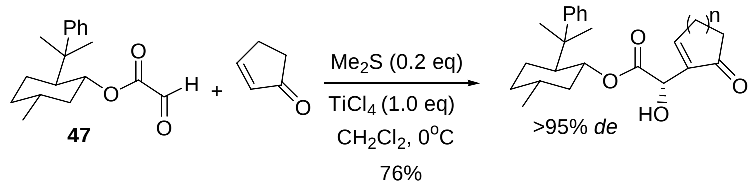


eq. 17



eq. 18

Bauer and Tarasiuk reported the Baylis–Hillman coupling of enantiopure aldehyde, *i.e*, (−)-8-phenylmenthylglyoxylate (**47**) with cyclic α,β-unsaturated ketones (cyclohex-2-enone and cyclopent-2-enone) under the catalytic influence of dimethyl sulfide in the presence of titanium tetrachloride to give the desired Baylis-Hillman adducts in high diastereo selectivities (eq 19).[143]

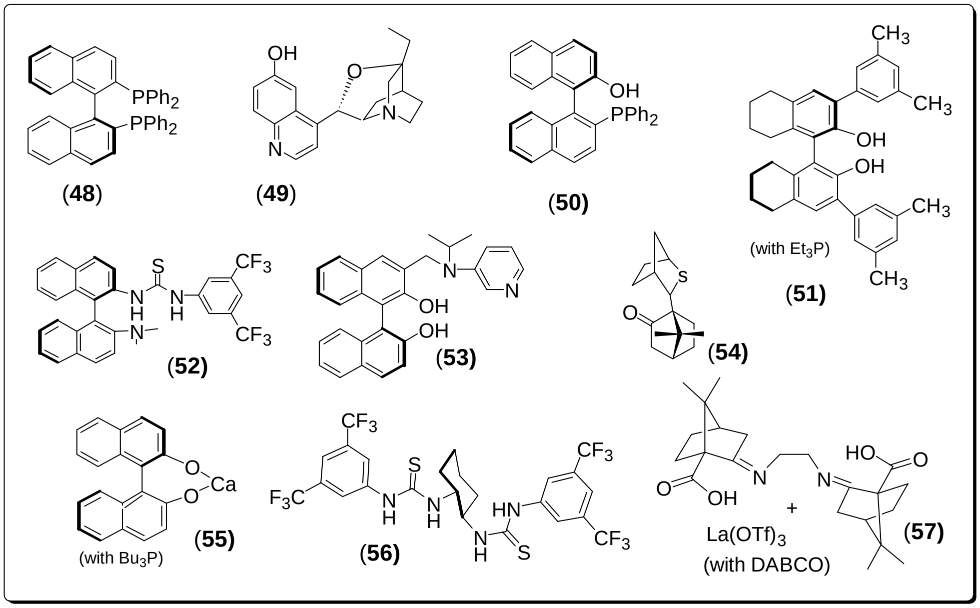


eq. 19

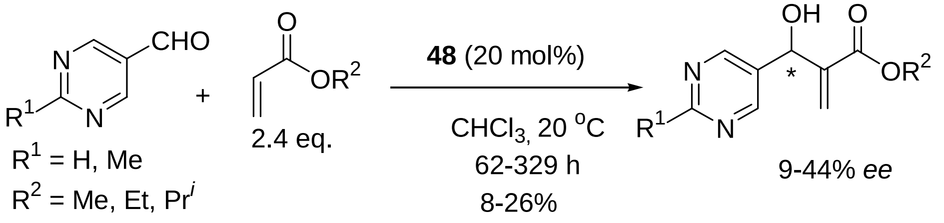
CHIRAL CATALYSTS & ADDITIVES / CATALYTIC SOURCES

The real challenge in achieving asymmetric version of the Baylis-Hillman reaction lies in the design of appropriate chiral catalysts and chiral additives (catalytic source), for performing the coupling reaction. Several chemists have directed their efforts in this direction and developed a number of chiral catalysts and chiral additives, to perform the asymmetric Baylis-Hillman reaction in high enantioselectivities. Some of the important and recent catalysts (**48-57**) [144-153] which gave respectable selectivities are listed in Fig. 7 and some relevant applications are presented in Scheme 29 and equations 20-28. [144-153]

Figure 7



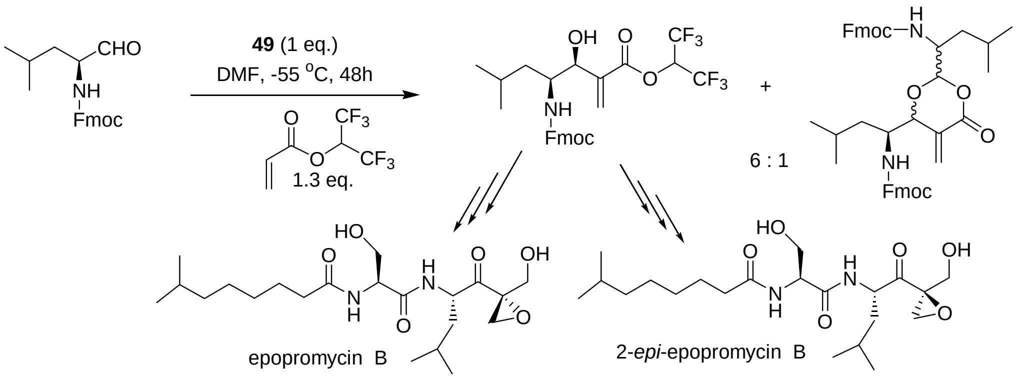
Soai and co-workers[144] have employed (S)-BINAP (**48**) as a chiral catalyst for coupling of pyrimidine-5-carboxaldehydes with acrylates to provide the resulting adducts upto 44% enantioselectivities (eq.20)



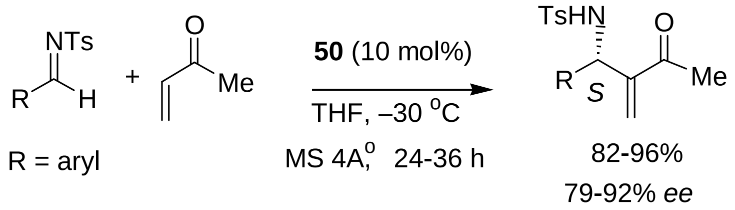
eq. 20

Hatakeyama and co-workers[145] developed an elegant catalyst (**49**) for the asymmetric Baylis-Hillman reaction and subsequently this strategy has been applied for synthesis of important biologically active molecules epopromycin B and 2-*epi*-epopromycin B following the reaction sequence as described in Scheme 29.

Scheme 29

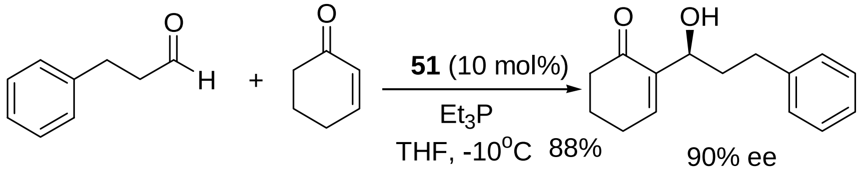


Shi and Chen[146] have reported an interesting asymmetric Baylis–Hillman reaction of *N*-sulfonated imines with methyl vinyl ketone using (*R*)-2′-diphenylphosphinyl-[1,1′]binaphthalenyl-2-ol as a chiral phosphine catalyst (**50**) providing the corresponding Baylis–Hillman adducts in high enantioselectivities. Representative examples are presented in the following eq.21.



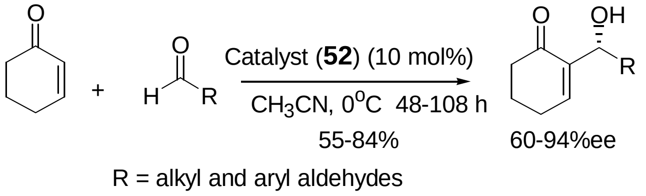
eq. 21

Schaus and co-workers[147] developed a highly enantioselective asymmetric Baylis-Hillman reaction of cyclohexenone with different aldehydes using the chiral catalyst (**51**). One representative example is presented in the following eq.22.



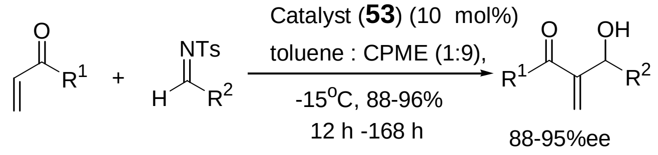
eq. 22

A new bifunctional binapthyl derived amine thiourea (**52**) was employed as organocatalyst by Wang and co-workers[148] to promote the enantioselective Baylis-Hillman reaction of cyclohex-2-enone with a variety of aldehydes to provide the resulting adducts in good yields with high enantioselectivities (eq. 23).



eq. 23

Sasai and co-workers[149] developed, an efficient and novel BINOL based bifunctional organocatalyst (**53**) containing 3-aminopyridine unit for high enantioselective Baylis-Hillman reaction of various *N*-tosylimines with MVK, EVK, and acrolien. Representative examples are presented in eq. 24.

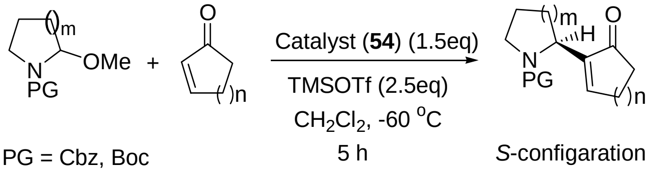


eq. 24

R^1 = Me, Et, H, Ph CPME = Cyclo pentyl methylether

R^2 = Ph, *p*-ClPh, *m*-ClPh, *p*-BrPh, *P*-MeOPh, 2-furyl, 2-napthyl, *p*-NO$_2$Ph,

Aggarwal and co-workers[150] reported an interesting asymmetric version of the Baylis-Hillman reaction between cyclic activated alkenes and *in situ* generated iminium ions as electrophiles in the presence of chiral sulfide (**54**) to produce the corresponding adducts in high enantioselectivities according to the reaction sequence presented in eq 25.

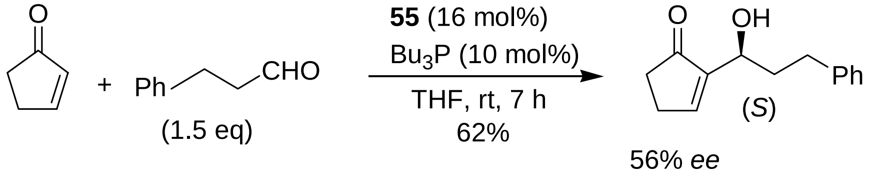


eq. 25

PG = Cbz, Boc
m, n = 1,2

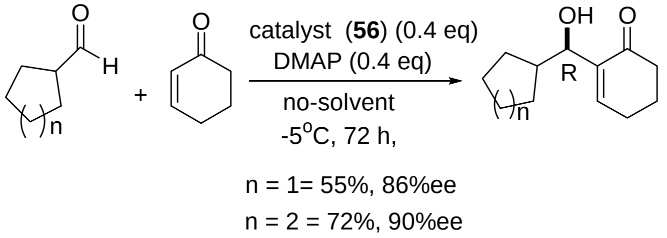
49 - 90%; 80 - 98% ee

Yamada and Ikaegami[151] reported an interesting asymmetric Baylis-Hillman reaction between hydrocinnamaldehyde and cyclopent-2-en-1-one using calcium salt of binaphthol (**55**) as a catalyst (eq.26).



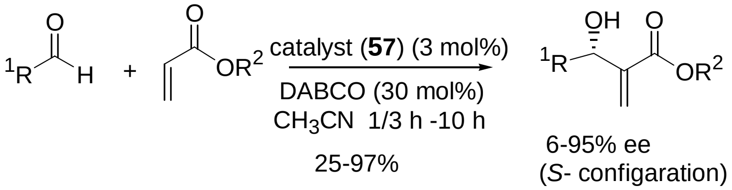
eq. 26

Nagasawa and co-workers[152] have reported a new chiral bis-thiourea organo-catalyst (**56**) for faster Baylis-Hillman reaction between 2-cyclohex-2-enone and various aldehydes in the presence of DMAP to provide the resulting adducts in high enantiomeric purities equation (27).



eq. 27

Chen and co-workers[153] reported an interesting asymmetric Baylis-Hillman reaction of various acrylates with several aldehydes using catalytic amount of camphor-derived ligand (**57**) in the presence of DABCO to provide the resulting adducts in moderate to high enantioselectivities. Representative examples are presented in eq.28.



eq. 28

R^1 = CH_3, CH_3CH_2, $(CH_3)_2CH$, C_6H_5, 4-$MeOC_6H_5$, 4-$NO_2C_6H_5$, $Ph(CH_2)_2CH_2$

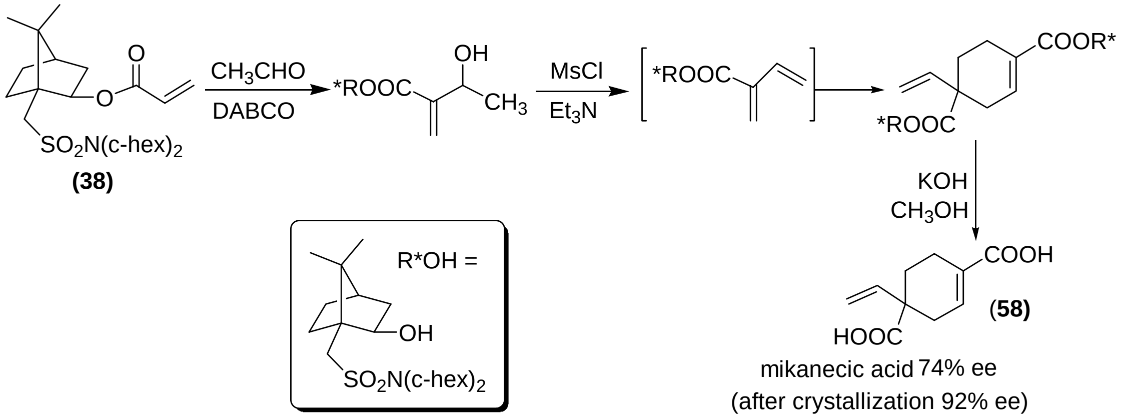
R^2 = CH_3, ^{t}Bu, Ph, Bn, 2-Naphthyl

APPLICATIONS OF THE BAYLIS-HILLMAN ADDUCTS

The Baylis-Hillman adducts play an important role in organic synthesis, as these adducts possess a minimum of three functional groups such as electron withdrawing group, methylene and hydroxyl groups in a proximity which in fact make them valuable substrates for various organic transformation methodologies. The Baylis-Hillman adducts have been also elegantly employed as valuable synthons in the synthesis of various tri substituted olefins, several important heterocycles, carbocycles, natural products and biologically active molecules[4-9]. Some of the important and recent developments in the application of these adducts are presented in this section.[153-174]

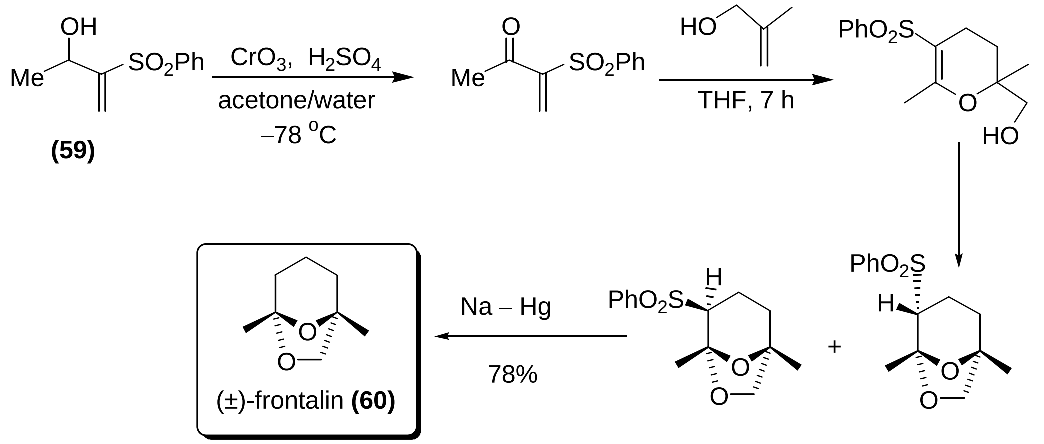
Our research group[154] has developed first enantioselective synthesis of mikanecic acid (**58**) (terpene dicarboxylic acid containing vinylic quaternary chiral center) from the Baylis–Hillman adduct derived from the chiral acrylate (**38**) following the reaction sequence as shown in Scheme 30.

Scheme 30



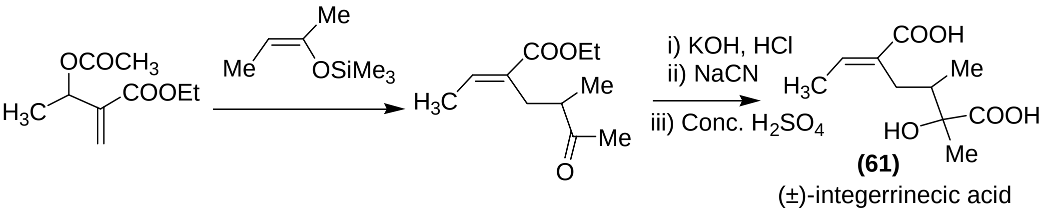
The Baylis–Hillman alcohol (**59**) (derived from phenyl vinyl sulphone as activated alkene and acetaldehyde as electrophile) has been transformed into racemic frontalin (**60**), an interesting biologically active molecule by Weichert and Hoffmann according to Scheme 31.[155]

Scheme 31



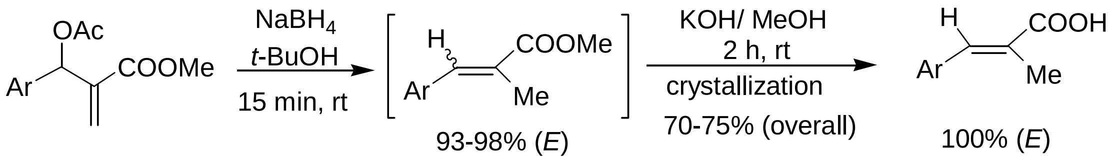
Drewes and co-workers[16] have synthesized intergerrinecic acid (**61**) from the acetate of the Baylis-Hillman alcohol, derived from acetaldehyde and ethyl acrylate, following the reaction sequence as described in Scheme 32.

Scheme 32



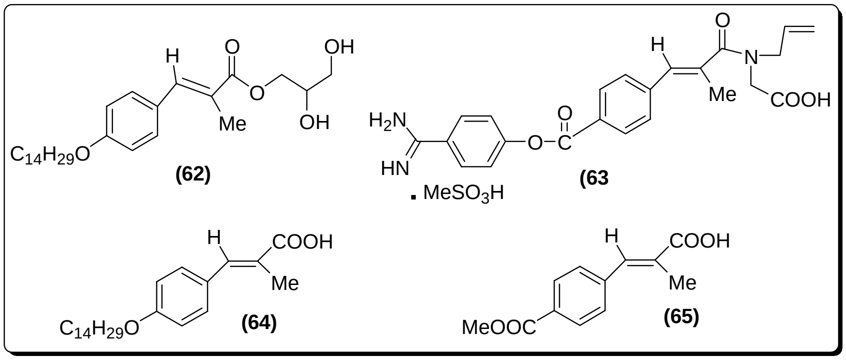
A simple one-pot and convenient methodology for the synthesis of (*E*)-α-methylcinnamic acids *via* the nucleophilic addition of hydride ion from $NaBH_4$ to the acetates of the Baylis–Hillman adducts, followed by hydrolysis and crystallization was reported by our research group (Scheme 33). This methodology was further extended to the synthesis of (*E*)-*p*-(myristyloxy)-α-methylcinnamic acid (**62**), a hypolipidemic active agent (useful precursor for another active hypolipidemic agent LK-903) (**63**) and [*E*]-*p*-(carbomethoxy)-α-methylcinnamic acid (**64**), a valuable synthon for an orally active serine protease inhibitor (**65**) (Figure 8).[156]

Scheme 33



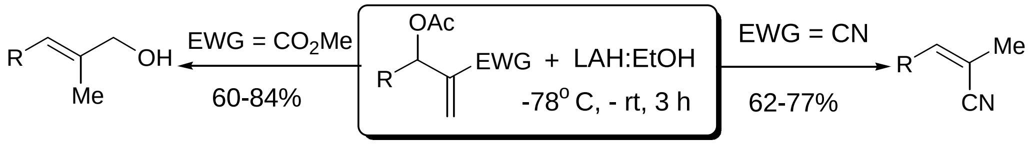
Ar= Ph, 4-ClPh, 4-(*i*-Pr)Ph, 4-MePh, 2,4-$(Cl)_2$Ph,
naphth-1-yl, 4-(tetradecyloxy)Ph

Figure 8



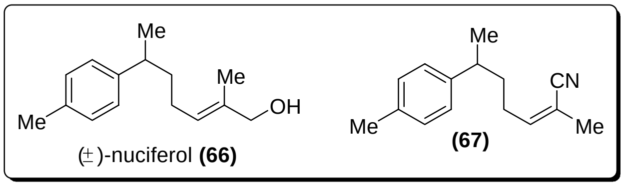
Our research group has reported a simple stereoselective synthesis of (2*E*)-2-methylalk-2-en-1-ols and (2*Z*)-2-methylalk-2-enenitriles *via* the treatment of the corresponding acetates of the Baylis-Hillman adducts with LAH:EtOH (Scheme 34). Subsequently, this methodology has been successfully applied for the synthesis of (*E*)-nuciferol (**66**), a biologically active terpene and precursor for (**67**) (*Z*)-nuciferol (Figure 9).[157]

Scheme 34



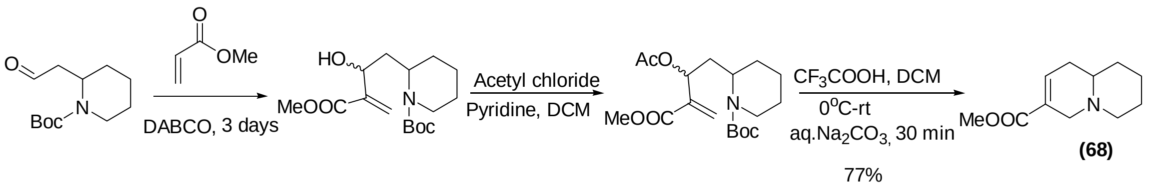
R = C_4H_9, C_5H_{11}, C_6H_{13}, C_6H_5, 4-MeC_6H_4, 3-(4-MeC_6H_4)Bu, 4-ClC_6H_4

Figure 9



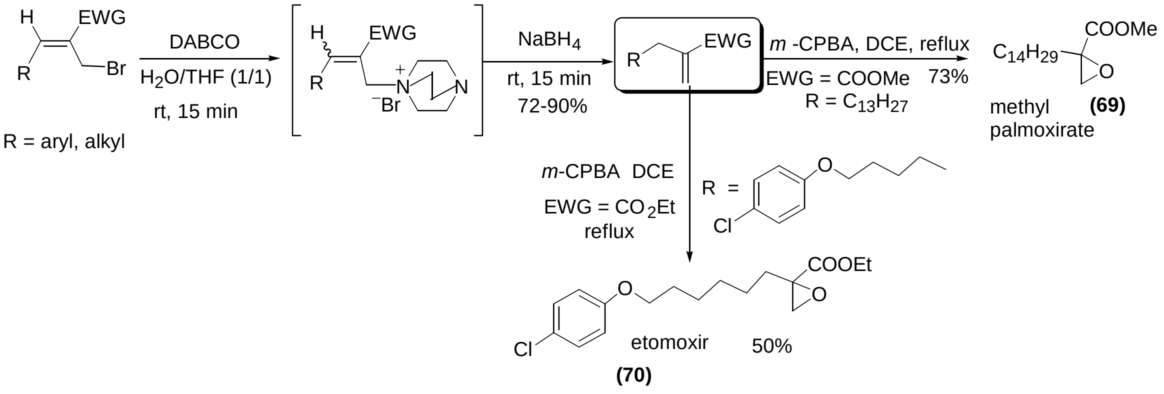
Clive and co-workers[158] have developed an interesting synthesis of hexahydroquinolizine framework (**68**) starting from N-protected amino aldehydes using the Baylis-Hillman reaction as the key step. One representative example is depicted in Scheme 35.

Scheme 35



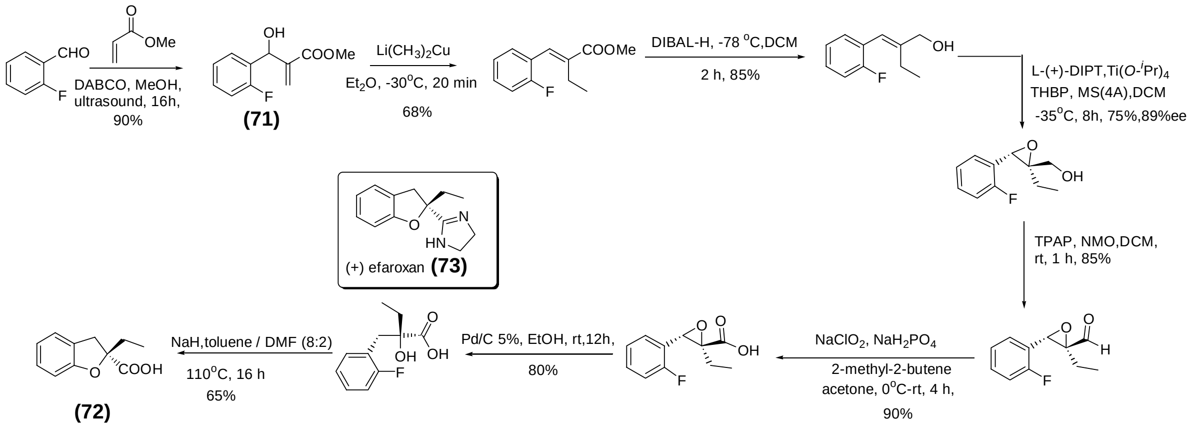
Our research group[159,160] has developed an interesting synthesis of 2-methylenealkanoates *via* the treatment of the Baylis-Hillman bromide with $NaBH_4$ in the presence of DABCO in aqueous media. These derivatives have been successfully transformed into hypoglycemic agents, methyl palmoxirate (**69**) and etomoxir (**70**) as described in Scheme 36.

Scheme 36

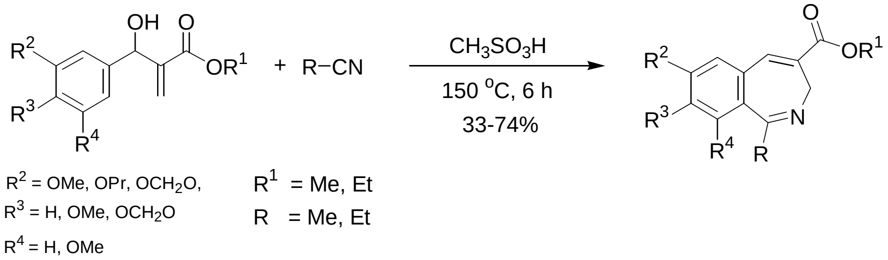


Coelho and co-workers[161] have used the Baylis-Hillman adduct (**71**) for synthesis of *R*-(+)-2-ethyl-2,3-dihydrobenzofuran carboxylic acid (**72**), a direct precursor of (+)-efroxan (**73**), according to Scheme 37.

Scheme 37



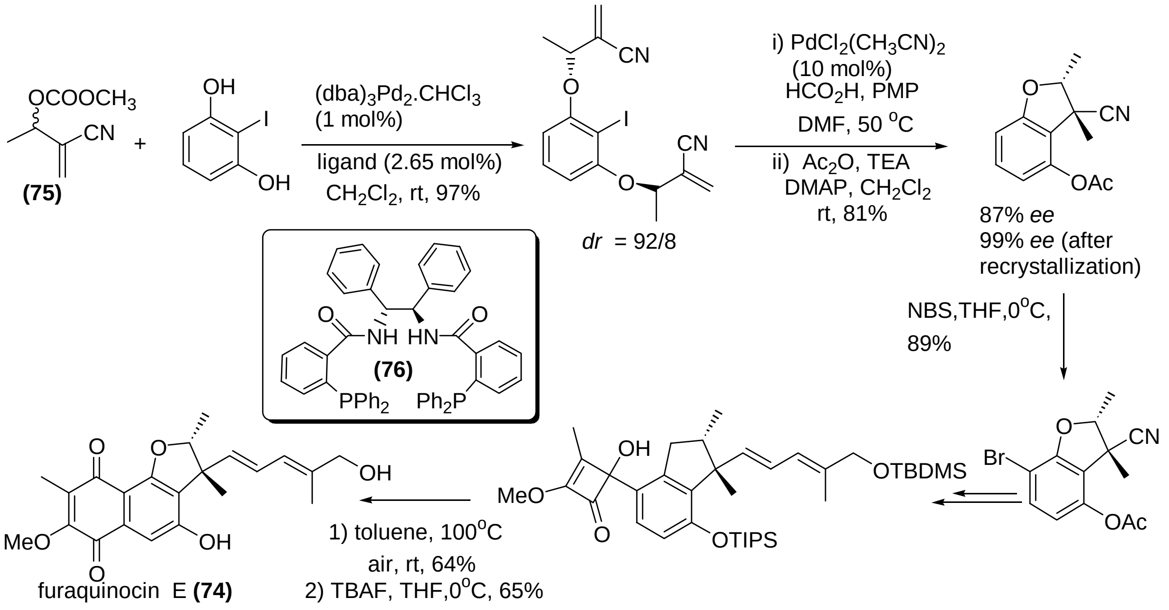
Our research group[162] has reported a novel strategy involving tandem constructuin of C-N and C-C bonds leading to a convenient one-pot procedure for the synthesis of 2-benzazepine derivatives from the Baylis-Hillman adducts. Representative examples were presented in eq.29.



eq. 29

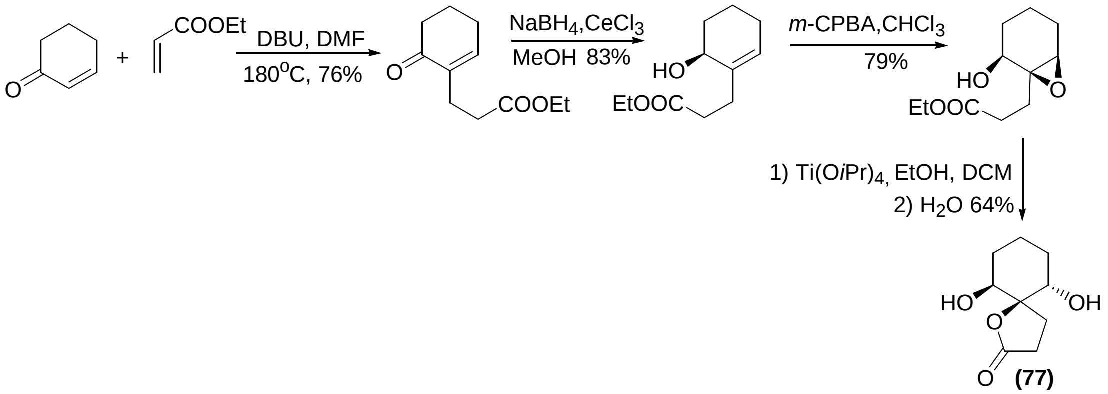
Trost *et.al.*[163] have reported a simple synthesis of Furaquinocin E (**74**) from the carbonate of Baylis-Hillman adduct (**75**) involving the principle of DYKAT using the chiral ligand (**76**) in the presence of (dba)$_3$ Pd$_2$.CHCl$_3$ following the reaction sequence as presented in Scheme 38.

Scheme 38



Maier *et.al.,*[164] reported the synthesis of spirolactone derivatives (**77**) using the Baylis-Hillman reaction as one of the key steps according to Scheme 39.

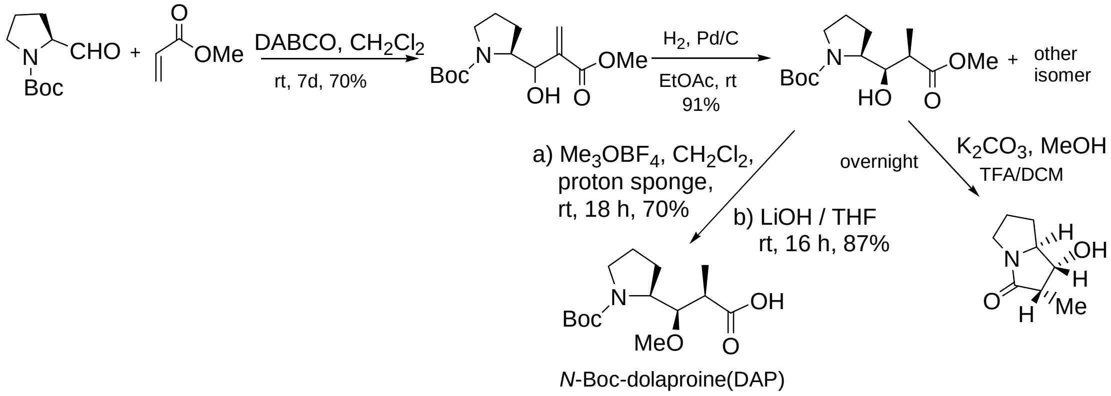
Scheme 39



(77)

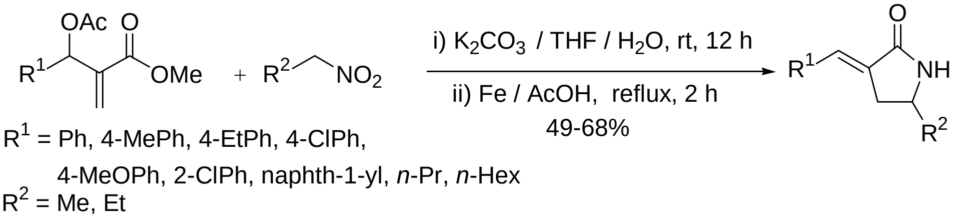
Almeida and Coelho[165] have reported the stereoselective synthesis of *N*-Boc-dolaproine (**78**) involving the Baylis-Hillman reaction as the key step.Following reaction sequence as shown in Scheme 40.

Scheme 40



N-Boc-dolaproine(DAP)
(78)

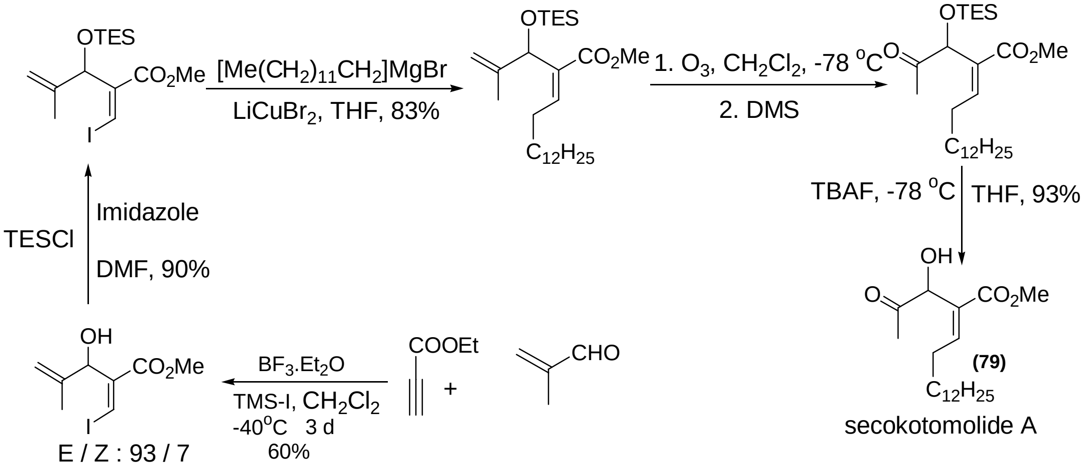
Our research group[166] reported a convenient one-pot synthesis of (*E*)-5-alkyl-3-arylidenepyrrolidin-2-one (γ-lactam) derivatives, *via* the treatment of Baylis-Hillman acetates with nitroalkanes in the presence of K_2CO_3, followed by reductive cyclization, using Fe/AcOH (eq. 30).



eq. 30

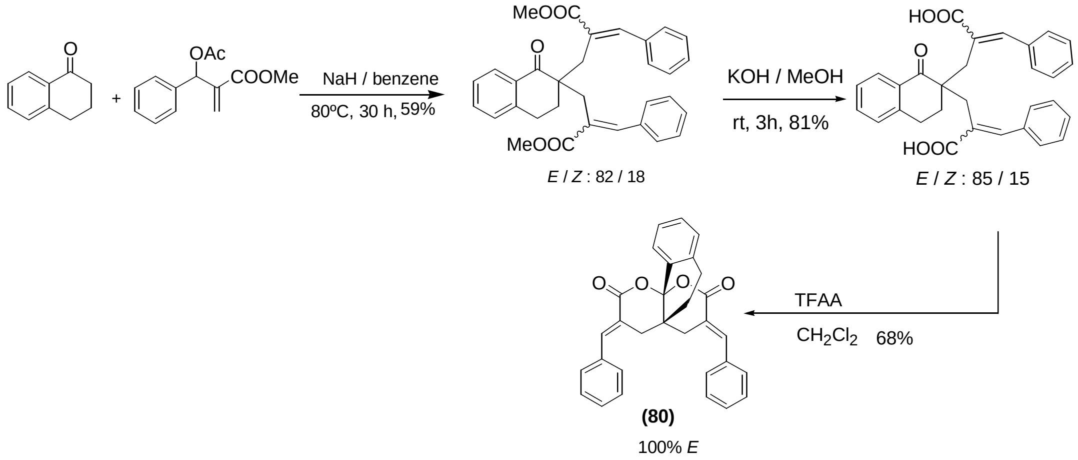
Ryu and co-workers[167] have successfully used the β-substituted Baylis-Hillman adducts for synthesis of secokotomolide A (**79**) an important biologically active compound (Scheme 41).

Scheme 41



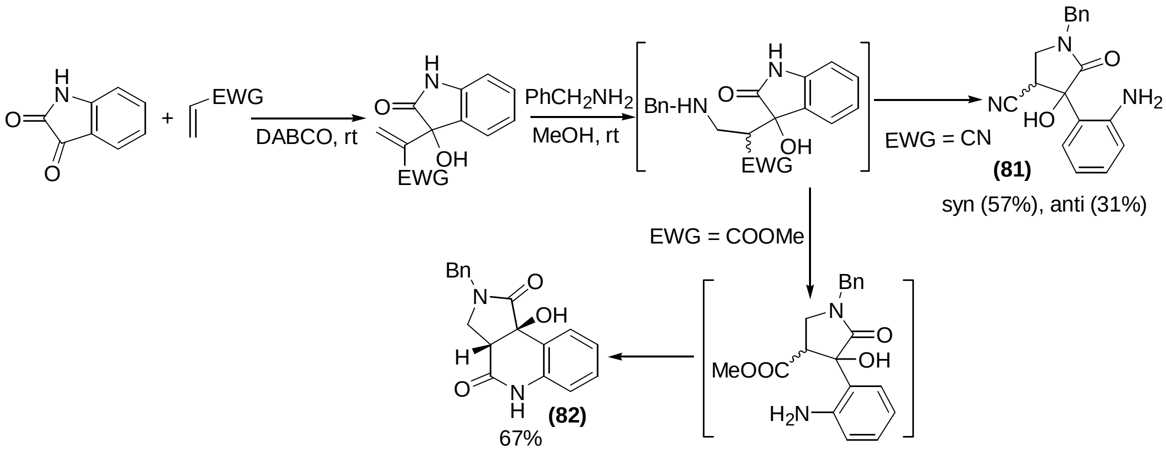
Our research group[168] has developed a facile methodology for synthesis of functionalized [4.4.4] propellano-bislactones (**80**) starting from the acetates of Baylis-Hillman adducts. One such example is presented in Scheme 42.

Scheme 42



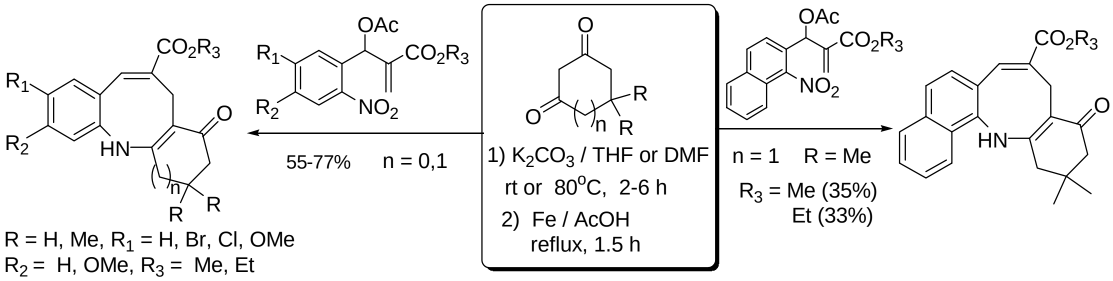
Kim has developed [169] a simple procedure for obtaining 3-aryl-3-hydroxypyrrolidin-2-ones (**81**) and tricyclic pyrrolo-quinoline framework (**82**) using the Baylis-Hillman adducts, derived from isatin derivatives. Representative example is presented in Scheme 43.

Scheme 43



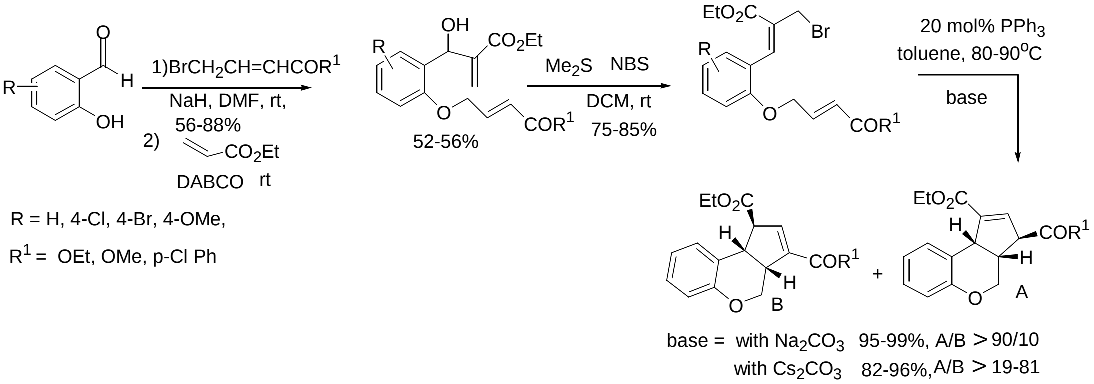
The Baylis-Hillman acetates have been elegantly transformed into functionalized tri / tetracyclic frameworks containing an important azocine moiety by our research group in an operationally simple one-pot procedure (Scheme 44).[170]

Scheme 44



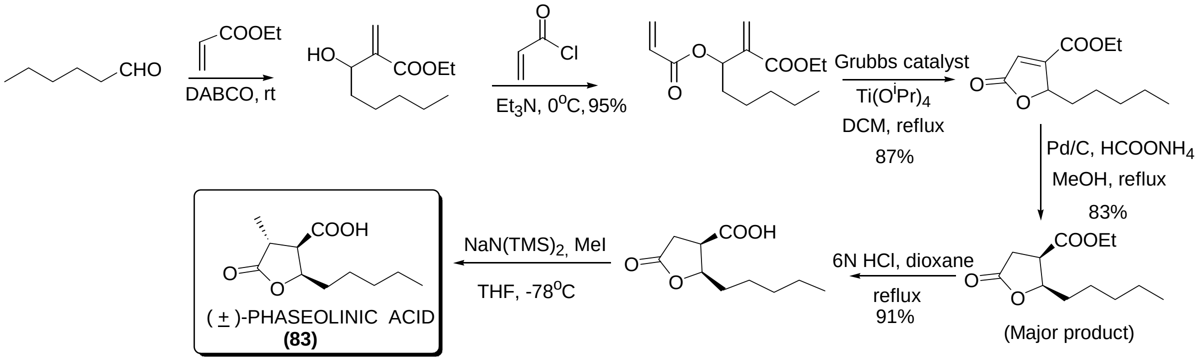
Tang *et.al.*[171] has described an interesting synthesis of benzobicyclo[4.3.0] compounds containing three continuous stereogenic centers using the Baylis-Hillman adducts following the reaction seqauence as presented in Scheme 45.

Scheme 45



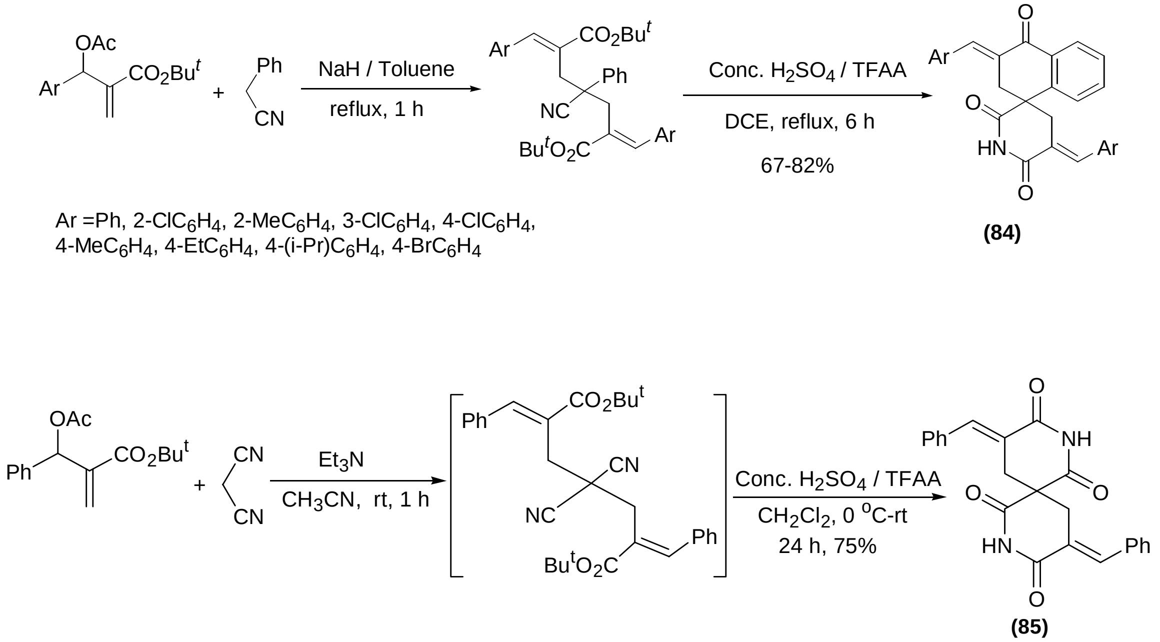
(±)Phaseolinic acid (**83**) an interesting natural product was synthesized by Selvakumar and co-workers,[172] which involves the Baylis-Hillman reaction and Grubbs RCM reaction as the key steps (Scheme 46).

Scheme 46



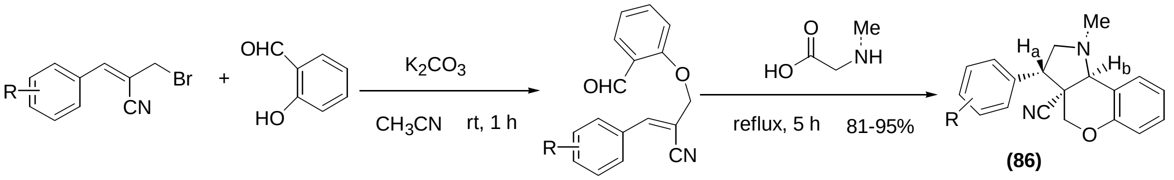
Recently our research group,[173] as developed a simple and convenient synthesis of di(*E*)-arylidene-tetralone-spiro-glutarimides (**84**) from Baylis–Hillman acetates *via* an interesting biscyclization strategy involving facile C–C and C–N bonds formation. Also, one-pot multistep transformation of the Baylis–Hillman acetates into di(*E*)-arylidene-spiro-bisglutarimides (**85**) is presented (Scheme 47).

Scheme 47



Bakthadoss and co-workers[174] have reported an interesting synthesis of tricyclic chromeno[4,3-b]pyrrolidine frameworks (**86**) using Baylis-Hillman bromides according to the reaction sequence presented in Scheme 48.

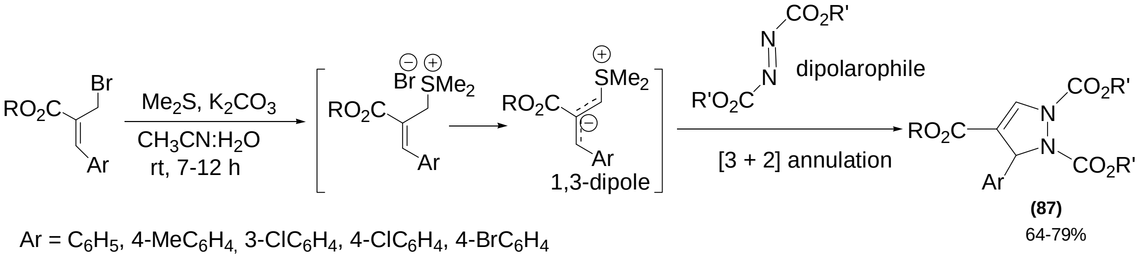
Scheme 48



R = H, 3,4-(OMe)$_2$, 3-Cl, 4-Cl, 2,4-(Cl)$_2$

Very recently, our reseach group[175] has demonstrated the Baylis-Hillman bromides as a valuable source of 1,3-dipoles for cyclo-addition onto dialkyl azodicarboxylates, as dipolarophiles, under the influence of Me$_2$S and K$_2$CO$_3$, to provide functionalized dihydropyrazole derivatives (**87**) in a simple one-pot [3+2] annulation strategy. Representative examples are presented Scheme 49.

Scheme 49



Ar = C$_6$H$_5$, 4-MeC$_6$H$_4$, 3-ClC$_6$H$_4$, 4-ClC$_6$H$_4$, 4-BrC$_6$H$_4$

R = Me, Et, Bu, Bu^t; R' = Et, Pr^i

OBJECTIVES, RESULTS AND DISCUSSION

Objectives

From the preceding chapter it is quite clear that the Baylis-Hillman adducts have been extensively used in various organic transformation methodologies and in synthesis of several natural and bioactive compounds.[4-9] With a view to expand further the scope of these adducts in organic synthesis and in continuation of on-going research program on this fascinating reaction, we have undertaken the thesis work with following objectives.

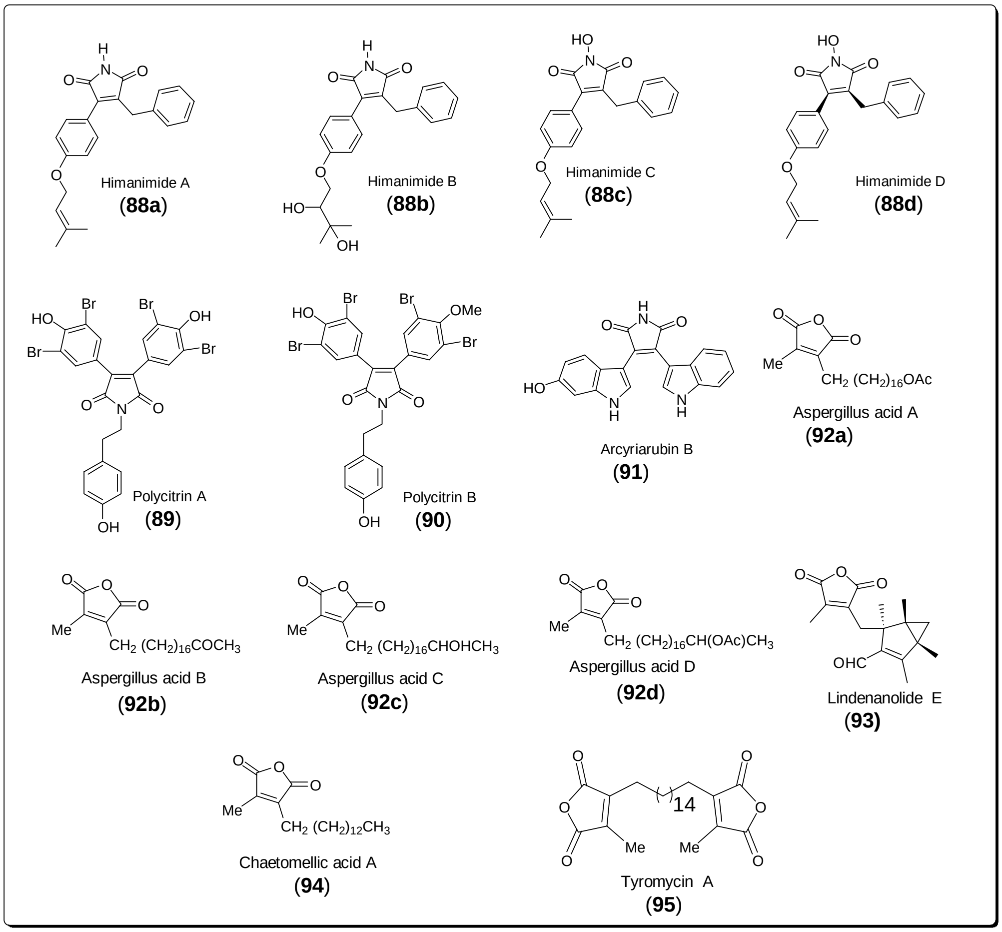
1) To develop a facile one-pot methodology for transformation of the Baylis-Hillman adducts into unsymmetrical disubstituted maleimide and maleic anhydride frameworks.
2) To develop a facile one-pot procedure for obtaining benzofuran-2-one frameworks from the Baylis-Hillman adducts *i.e.,* 2-hydroxy-2-aryl-2-(5,5-dime-thylcyclohex-2-en-1-one-2-yl)ethanoate, and 2-hydroxy-2-phenyl-2-cyclohex-2-en-1-one-2-yl)ethanoate.
3) To successfully employ the Baylis-Hillman bromides as versatile synthons, for a facile one-pot synthesis of indolizine and benzofused indolizine frameworks.

Results and Discussion

A Facile One-Pot Transformation of the Baylis-Hillman Adducts into Unsymmetrical Disubstituted Maleimide and Maleic Anhydride Frameworks

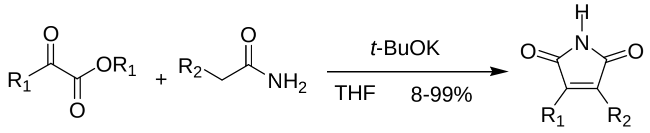
Development of efficient and convenient methodologies for synthesis of 3,4-disubstituted maleimide and maleic anhydride derivatives has been and continues to be an attractive and challenging endeavor in organic and medicinal chemistry because of the presence of these frameworks in a number of bio-active natural products such as himanimide A-D (**88 a-d**),[176] polycitrins A & B (**89 & 90**),[177] arcyriarubin-B (**91**),[178] aspergillus acid A-D (**92 a-d**),[179] lindenanolide E (**93**),[180] chaetomellic acid A (**94**),[181] tyromycin A (**95**),[182] (Fig.10) and also because several of their derivatives have been known to exhibit various biological activities such as cytotoxicity,[183] angiogenesis,[184] [some of these derivatives are known to be inhibitors of CaMKIIδ (calmodulin-dependant protien kinase)],[185] cell death and vascular endothelial proliferation.[186] Therefore several research groups have been working on deveolpment of simple methodologies for the synthesis of disubstituted maleimide and maleic anhydride derivatives and some of the recent and relevant methodologies have been provided in this section.

Figure 10



α-Keto esters and α-keto amides are the most frequently used synthons for the preparation of substituted maleimide derivatives. Representative examples are presented in the equations 31 & 32 and Schemes 50 & 51.

Faul and co-workers[187]

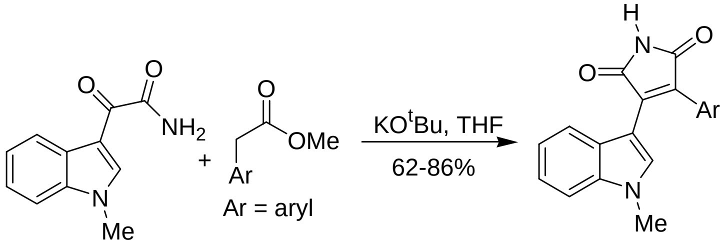


eq. 31

R_1 = 3-indolyl, *N*-methyl-3-indolyl, Ph, 2-thienyl, 2-furanyl, isopropyl

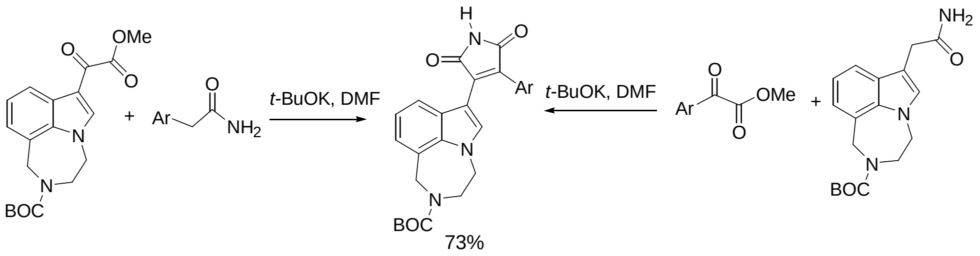
R_2 = Ph, *p*-BrC_6H_4, *p*-$MeOC_6H_4$, 1-naphthyl, 3-benzo[*b*]-thienyl, cyclohexyl, N-methyl-3-indolyl, 3-indolyl,

Gribble and co-workers[188]

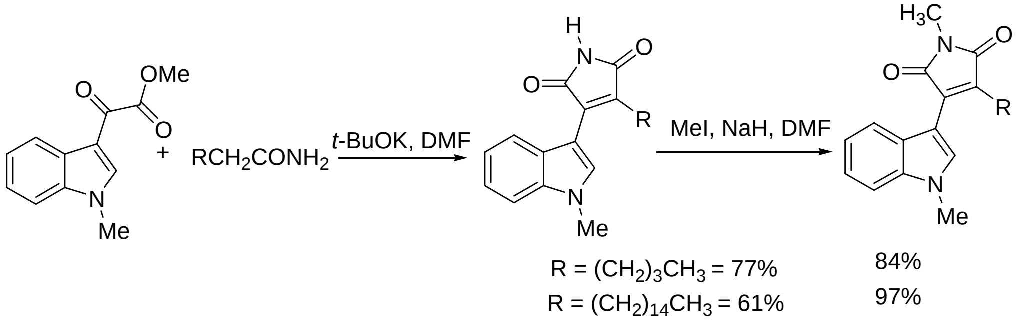


eq. 32

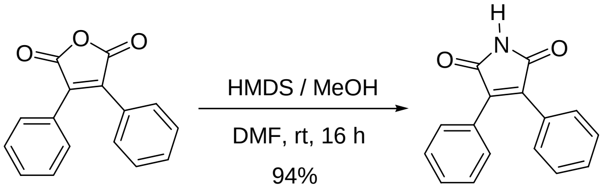
Scheme 50 *Engler and co-workers*[189]



Scheme 51 *Dodo and co-workers* [190]



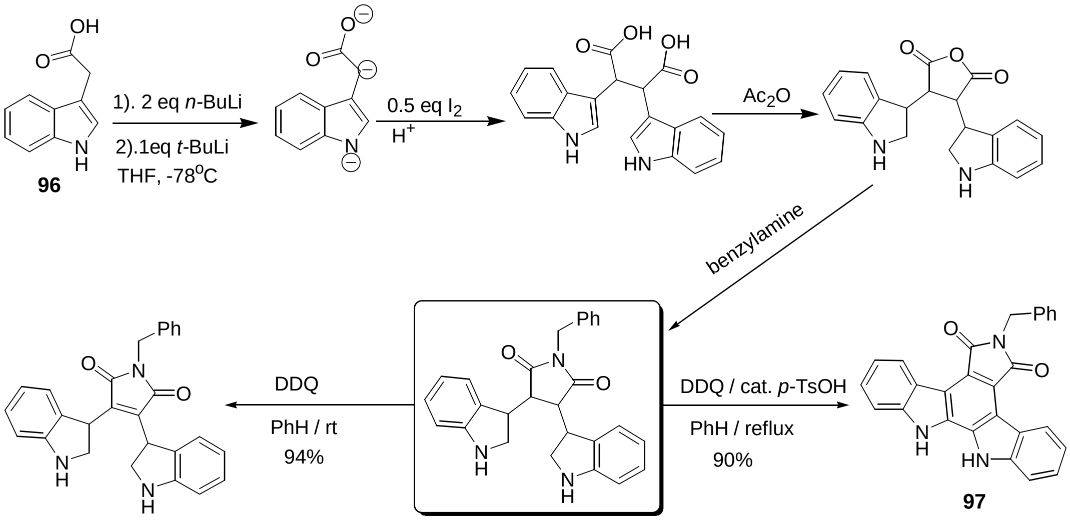
Maleic anhydride derivatives were easily converted into maleimides *via* the reaction with hexamethyldisilazane (HMDS) at room temperature in excellent yields by Davis and co-workers. One representative example is presented in equation 33.[191]



eq. 33

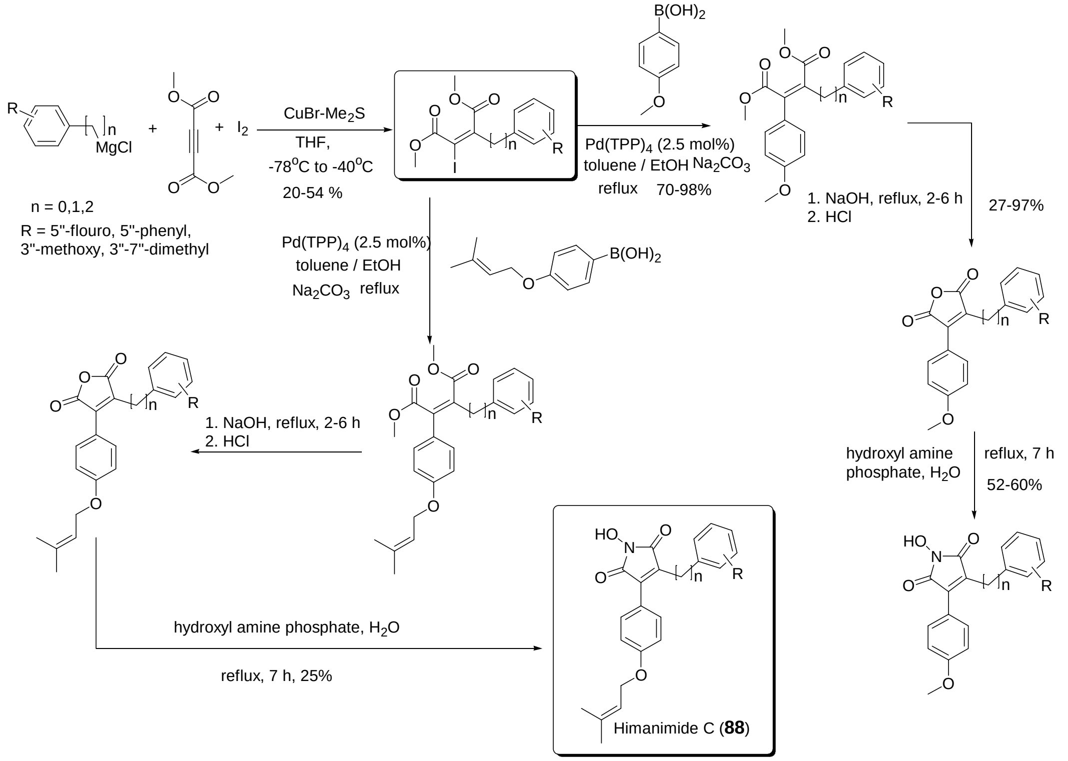
Bergman and Pelcman developed[192] an interesting synthesis of polycyclic maleimide (**97**) framework from indole acetic acid (**96**) following the reaction as shown in Scheme 52.

Scheme 52



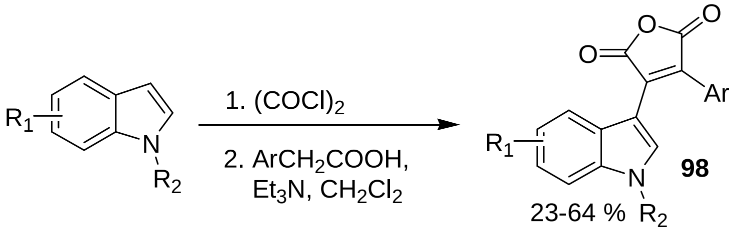
Selles[176] has reported an interesting stereoselective synthesis of new unnatural himanimide following the reaction strategy as described in Scheme 53.

Scheme 53



Himanimide C (**88**)

Davis and co-workers[193] reported a simple and convenient synthesis of bisindolyl and indolylarylmaleic anhydride derivatives (**98**) from the indoles following reaction strategy as shown in equation 34.



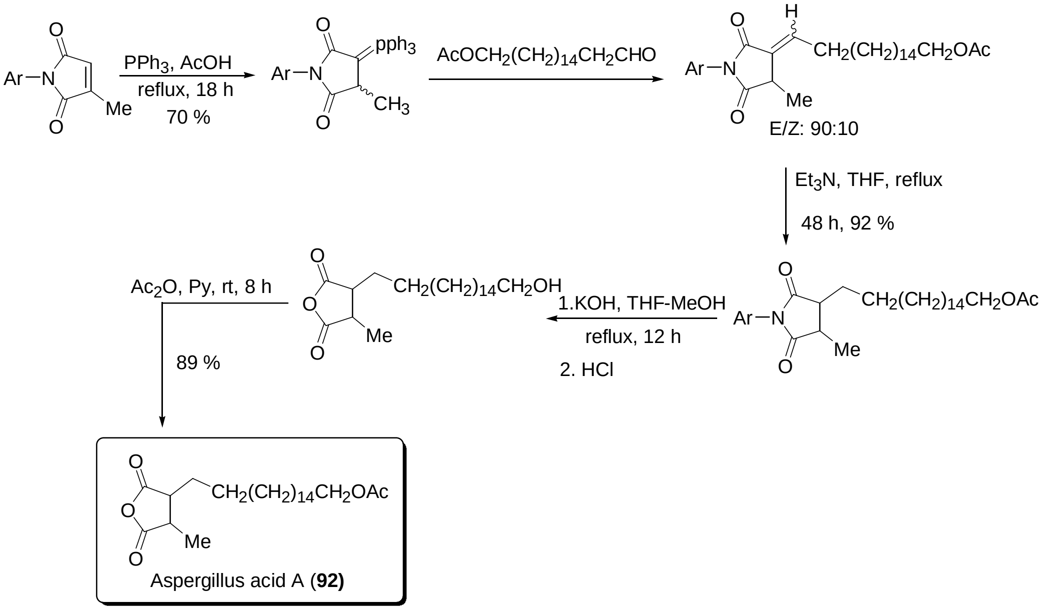
98 **eq. 34**

R_1 = H, 2-methyl, 5-(methoxycarbonyl) R_2 = methyl, 3-cyanophenyl, benzyl

Ar = 1-methyl-3-indolyl, 1-benzyl-3-indolyl,phenyl,
1-*p*-toluenesulphonyl-3-indolyl,
4-methoxyphenyl, 1-napthyl, 3-thienyl

Argade and co-workers[179] reported facile synthesis of Aspergillus acid A following reaction sequence as presented in Scheme 54.

Scheme 54

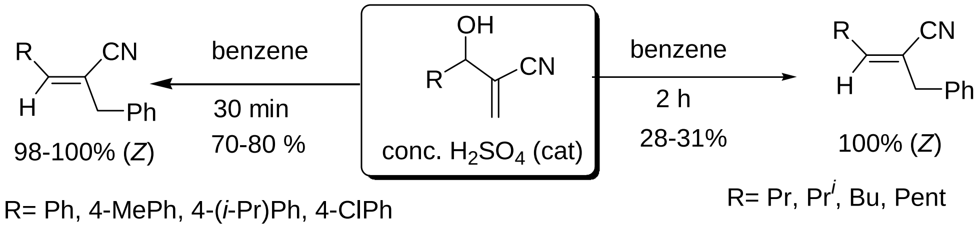


The medicinal importance of both maleimide and maleic anhydride frameworks has fascinated us. We have therefore undertaken a research program for developing convenient and one pot methodologies for synthesis of disubstituted maleimide and maleic anhydride derivatives from the Baylis-Hillman adducts.

Synthesis of disubstituted maleimide frameworks:

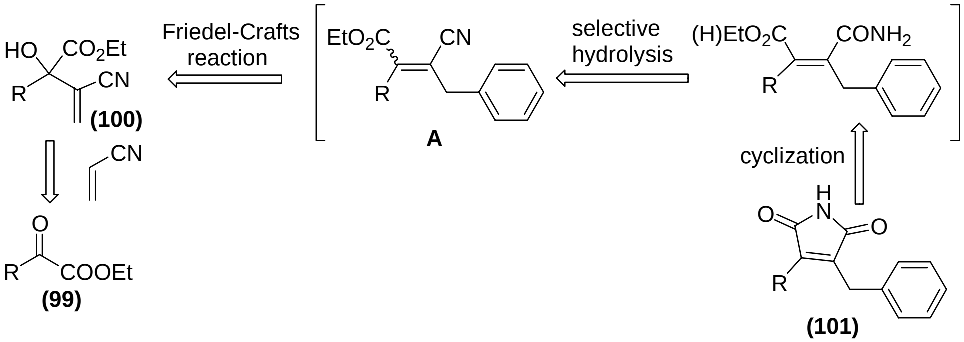
It is worth mentioning here our earlier work which describes the Friedel-Crafts reaction of 3-hydroxy-2-methylenealkanenitrile, the Baylis-Hillman adducts obtained *via* the reaction between aldehydes and acrylonitrile, with benzene providing a simple strategy for stereoselective synthesis of trisubstituted alkenes with nitrile group as substituent (Scheme 55).[194]

Scheme 55

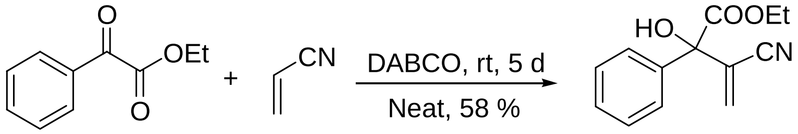


Based on this experience we felt that the Baylis-Hillman adducts, derived from α-keto esters as electrophiles and acrylonitrile as activated alkenes, could in principle serve as potential substrates for Friedel-Crafts reaction with benzene to provide the phenylated products *i.e.,* tetrasubstituted alkenes (**A**), containing ester and cyano groups (for retrosynthetic strategy see Scheme 56).

Scheme 56



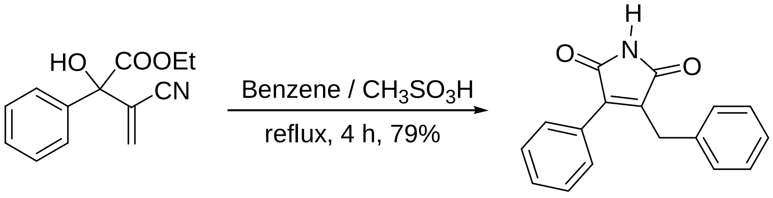
These tetrasubstituted alkenes **(A)** in principle on selective hydrolysis followed by cyclization would provide disubstituted maleimide. It also occurred to us that it would be very valuable and also interesting to perform all the three steps in one-pot. We also felt that it would be more interesting to perform all these three steps using a single reagent. Accordingly, we have first selected 3-ethoxycarbonyl-3-hydroxy-3-phenyl-2-methylene-propanenitrile (Baylis-Hillman adduct) (**100a**), as a substrate for the Friedel-Crafts reaction with benzene. The required Baylis-Hillman adduct was obtained *via* the reaction of ethyl benzoylformate with acrylonitrile under the catalytic influence of DABCO (eq 35).



(**99a**) (**100a**) **eq. 35**

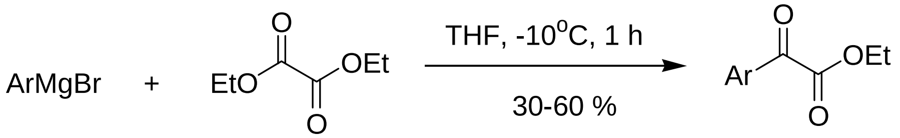
Next we have examined Friedel-Crafts reaction of Baylis-Hillman adduct (**100a**) with benzene under different conditions. The best results in this direction were obtained when 3-ethoxycarbonyl-3-hydroxy-3-phenyl-2-methylenepropanenitrile (**100a**) was treated with benzene in the presence of methanesulfonic acid at reflux for 4 h, thus providing the desired 3-benzyl-4-phenyl-1*H*-pyrrole-2,5-dione (**101a**) in 79% isolated yield after purification through column chromatography (Table 2). We were pleased to note that methanesulfonic acid has ingeniously performed all the three jobs (*i.e.,* Friedel-Crafts reaction, selective hydrolysis and cyclization) in one-pot operation (eq. 36).

Structure of this molecule was confirmed by IR, ^{1}H NMR (Spectrum 1), ^{13}C NMR (Spectrum 2), mass (LCMS) spectral data and elemental analysis. We have also obtained single crystal for this compound (**101a**) and further confirmed the structure by single crystal X-ray data (see Figure 11 for ORTEP diagram).



(**100a**) (**101a**) **eq. 36**

This strategy has indeed fascinated us because all the three reactions were carried out in one-pot and more interestingly all the reactions were meticulously performed by the single reagent, methanesulfonic acid. Encouraged by this result we have directed our attention towards understanding the generality of this methodology. Thus we have selected representative Baylis-Hillman alcohols (**100b-i**) as substrates for the preparation of disubstituted maleimide derivatives. The required Baylis-Hillman alcohols were obtained *via* the coupling of the corresponding α-keto esters (**99b-i**) with acrylonitrile (Table 1). The desired α-keto esters were prepared according to the eq. 37.

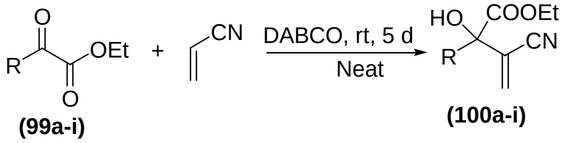


eq. 37

99 a-h

Ar = C_6H_5, 4-MeC_6H_4, 4-MeOC_6H_4, 3-MeC_6H_4, 3-MeOC_6H_4,
2-MeC_6H_4, 2-MeOC_6H_4, 4-EtOC_6H_4.

Table 1. Preparation of the Baylis-Hillman alcohols (adducts)[a]



Keto ester	R	Product[b]	Yield (%)[c]
99a	C_6H_5	**100a**	58
99b	4-MeC_6H_4	**100b**	71
99c	4-$MeOC_6H_4$	**100c**	42
99d	3-MeC_6H_4	**100d**	47
99e	3-$MeOC_6H_4$	**100e**	62
99f	2-MeC_6H_4	**100f**	44
99g	2-$MeOC_6H_4$	**100g**	61
99h	4-$EtOC_6H_4$	**100h**	50
99i	Methyl	**100i**	30

a). All reactions were carried out on 10 mmol scale of α-keto esters (**99a-i**) with acrylonitrile (20 mmol) under the catalytical influence of DABCO (30 mol%).

b) All the compounds (**100a-i**) were obtained as colorless solids and fully characterized by spectral data (IR, ^1H & ^{13}C NMR).

c) Isolated yields of the pure products based on the α-keto esters.

All these Baylis-Hillman adducts were successfully transformed into the desired 3,4-disubstituted maleimides (**101b-i**) in 54-76% isolated yields *via* the treatment with benzene under the influence of CH_3SO_3H at reflux for 4 h (Table 2). All the disubstituted maleimides (**101b-i**) were characterized by IR, ^{1}H & ^{13}C NMR {Spectrum 3 & 4 for compound **101b** ^{1}H & ^{13}C NMR respectively, Spectrum 5 & 6 for compound **101c** ^{1}H & ^{13}C NMR respectively, Spectrum 7 & 8 for compound **101d** ^{1}H & ^{13}C NMR respectively, ^{1}H NMR [Spectrum 9 (for compound **101f** at room temperature), Spectrum 10 (for compound **101f** at 5°C), Spectrum 11 (for compound **101f** at 40°C)], ^{13}C NMR (Spectrum 12 for compound **101f**), and Spectrum 13 & 14 for compound **101i** ^{1}H, & ^{13}C NMR respectively}. and mass (LCMS) spectral data and elemental analyses. We have also obtained single crystals for the compounds **101e,** and **101i** and further confirmed the structures by single crystal X-ray data (see Figure 12 & 13 for ORTEP diagrams).

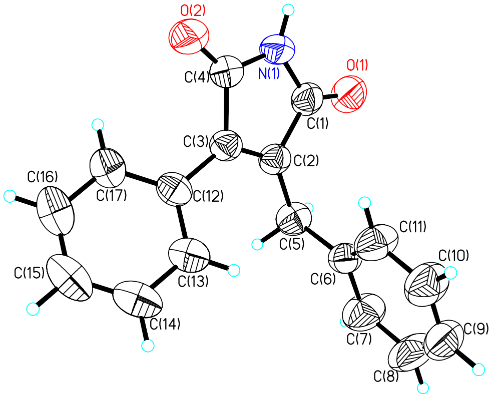
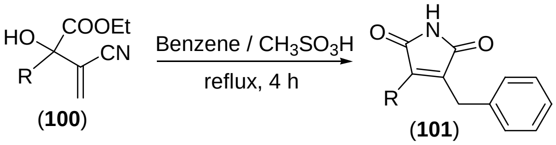


Figure 11 (ORTEP diagram of the compound 101a)

Table 2. Synthesis of 3,4-disubstituted maleimide derivatives from the Baylis-Hillman adducts[a]:



B-H alcohol	R	Product[b]	Yield (%)[c]	m.p (^{o}C)
100a	C_6H_5	**101a**[d]	79	118-120
100b	4-MeC_6H_4	**101b**	70	150-152
100c	4-MeOC_6H_4	**101c**	63	160-162
100d	3-MeC_6H_4	**101d**	76	70-72
100e	3-MeOC_6H_4	**101e**[d]	55	103-105
100f	2-MeC_6H_4	**101f**[π]	65	96-98
100g	2-MeOC_6H_4	**101g**	57	98-100
100h	4-EtOC_6H_4	**101h**	54	176-178
100i	Methyl	**101i**[d]	66	78-80

a) All reactions were carried out on 1 mmol scale of Baylis-Hillman alcohol (**100a-i**) with methanesulfonic acid (3 mmol) in benzene (6 mL) at reflux for 4 h.

b) All the compounds (**101a-i**) were obtained as colorless solids and fully characterized by spectral data (IR, ^{1}H & ^{13}C NMR, LCMS) and elemental analysis

c) Isolated yields of the pure products based on the Baylis-Hillman alcohols.

d) Structures of these molecules (**101a, 101e,** and **101i**) were also established from the single-crystal X-ray data

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[π] We have also recorded ^{1}H and ^{13}C NMR spectra at 5^{o}C and 40^{o}C with a view to understand the conformation stability of the molecule at different temperatures At 5^{o}C in ^{1}H NMR spectrum of **(101f)** benzylic protons appear as ABq at δ 3.56 & 3.68 (ABq, 2H, *J* = 14.2 Hz). At room temperature they appear as two singlets at δ 3.58 (s, 1H), 3.65 (s, 1H), while at 40^{o}C they appear as broad singlet at δ 3.68 (bs, 2H). However ^{13}C NMR is almost the same at these temperatures. From these spectral studies it is quite clear that there is conformational rigidity at 5^{o}C, while at room temperature and at 40^{o}C there is conformational flexibility.

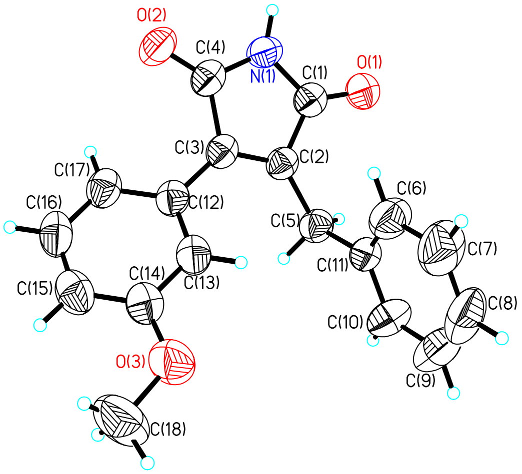


Figure 12 (ORTEP diagram of the compound 101e)

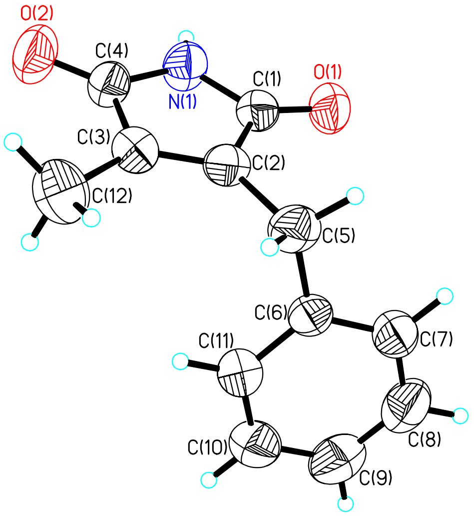


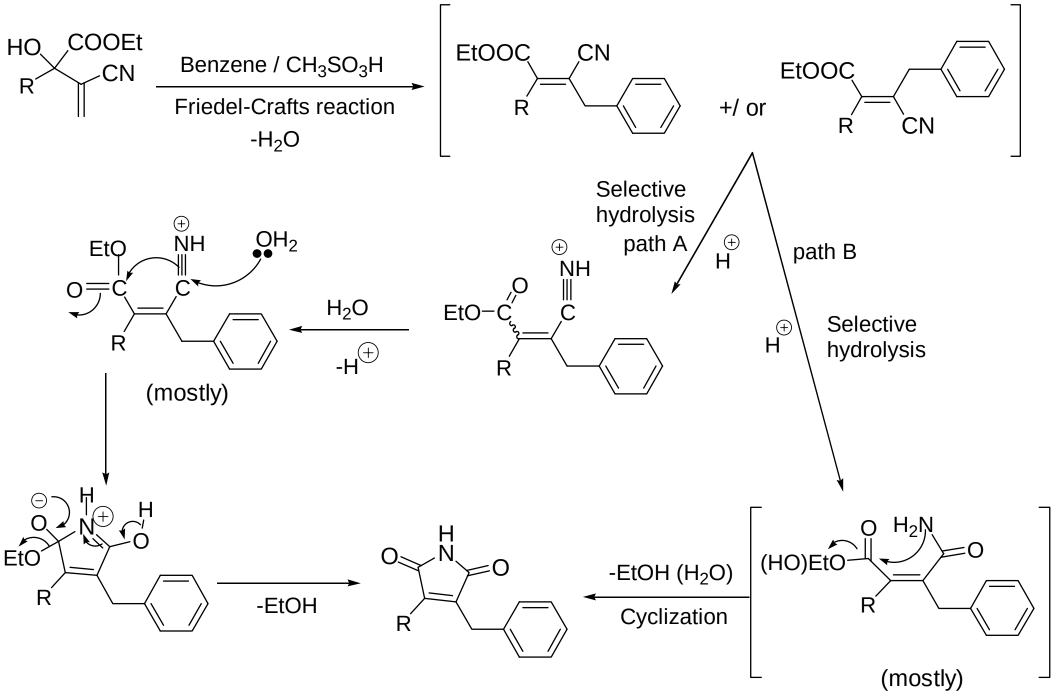
Figure 13 (ORTEP diagram of the compound 101i)

With a view to understand the applicability of this strategy to Baylis-Hillman adducts, derived from aliphatic α-keto esters, we have selected 3-ethoxycarbonyl-3-hydroxy-2-methylenebutanenitrile (**100i**) as a substrate. This alcohol was obtained *via* the Baylis-Hillman coupling of acrylonitrile with ethyl pyruvate (**99i**) under the influence of DABCO (Table 1). This tertiay alcohols was conveniently transformed into the corresponding maleimide (3-benzyl-4-phenyl-1*H*-pyrrole-2, 5-dione (**101a**) *via* the treatment with benzene in the presence of methanesulfonic acid.

Plausible mechanism for the transformation of Baylis-Hillman adducts in to maleimide derivatives is presented in Scheme 57.# The fact that the stereochemistry of the double bond in 3,4-disubstituted maleimide derivatives (Table 2) is (*Z*), clearly indicates that the amide-ester (acid) generated *in situ* should have (Z)-stereochemistry (mostly) (Scheme 57). This would mean that either the Friedel-Crafts reaction might provide the product with (*Z*)-stereochemistry (exclusively or predominately) or isomerization of (*E*)-product to (*Z*)-compound (to large extent) might be taking place during selective hydrolysis. Whatever may be the course of the reaction, the products isolated, clearly indicate that transient intermediate before the cyclization step had the (*Z*)–stereochemistry.

We can not completely rule out the formation of minor amounts of fumaric acid derivatives in these reactions as the yields of maleimide are not quantitaive

Scheme 57

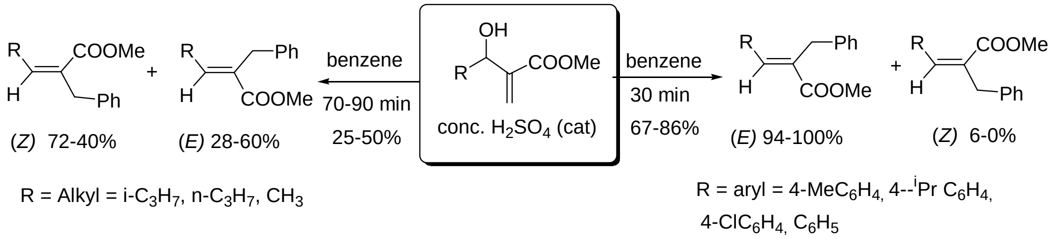


Synthesis of 3,4-disubstituted maleic anhydride frameworks:

After developing a simple one-pot methodology for the synthesis of unsymmetrical 3,4-disubstituted maleimide derivatives, we have directed our attention towards the synthesis of 3,4-disubstituted maleic anhydride derivatives.

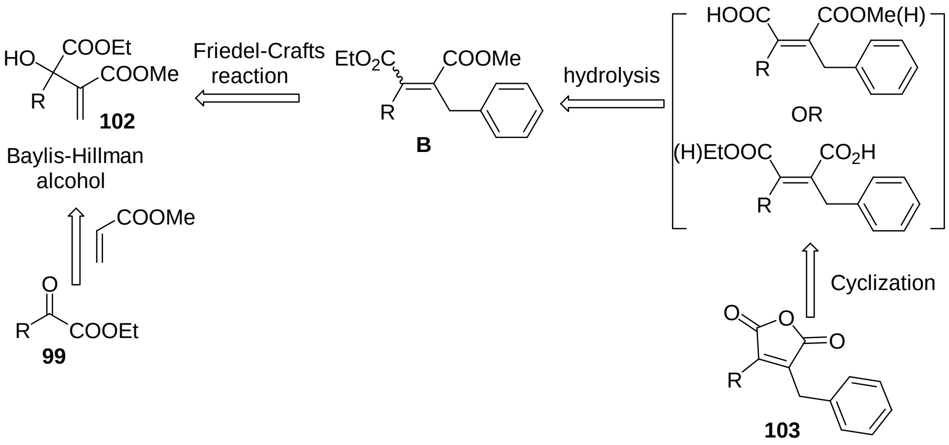
It is worth mentioning here our earlier work[194] which describes the Friedel-Craft reaction of 3-hydroxy-2-methylenealkanoates, the Baylis-Hillman adducts obtained *via* the reaction between aldehydes and methyl acrylate, with benzene providing a simple strategy for stereoselective synthesis of trisubstituted alkenes with ester group as a substituent (Scheme 58).

Scheme 58

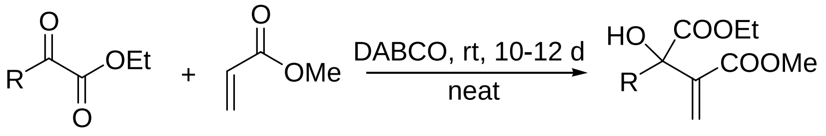


On the basis of this reaction strategy it occurred to us that the Baylis-Hillman adducts, derived from α-keto esters as electrophiles and methyl acrylate as activated alkenes, might serve as potential substrates for Friedel-Crafts reaction with benzene to provide the phenylated products *i.e.*, tetrasubstituted alkenes (**B**), containing two ester groups. These tetrasubstituted alkenes (**B)** in principle on selective hydrolysis followed by cyclization would provide disubstituted maleic anhydride framework (for retrosynthetic strategy see Scheme 59). On the basis of our work on the synthesis of maleimides we reasoned that it would be possible to perform all the three steps in one-pot using methanesulfonic acid as a magic reagent.

Scheme 59



We have first selected methyl 3-ethoxycarbonyl-3-hydroxy-3-phenyl-2-methylene-propanoate (**102a**), as a substrate for the Friedel-Crafts reaction with benzene in the presence of methanesulfonic acid. The desired Baylis-Hillman alcohol was prepared *via* the coupling of ethyl benzoylformate with methyl acrylate in the presence of DABCO as a catalyst (eq. 38).



eq. 38

99a-c

R = C_6H_5 47 % (**102a**)
$4\text{-}MeC_6H_4$ 57 % (**102b**)
$4\text{-}MeOC_6H_4$ 60 % (**102c**)

Then we have performed the Friedel-Crafts reaction of methyl 3-ethoxycarbonyl-3-hydroxy-3-phenyl-2-methylenepropanoate with benzene under various conditions. The best results were obtained when the Baylis-Hillman adduct (**102a)** was treated with benzene in the presence of methanesulfonic acid at reflux for 4 h providing the required 3-benzyl-4-phenylmaleic anhydride (**103a**) in 52% isolated yield. The structure of this molecule was confirmed by IR, ^{1}H NMR [Spectrum 15 (for compound **103a**)], & ^{13}C NMR [Spectrum 16 (for compound **103a**)], LCMS, and elemental analysis. The structure of this compound (**103a**) was further established by single crystal-X-ray data (for ORTEP diagram see Figure 14)

It is interesting to note that this (**103a**) is a natural product isolated from *aspergillus nidulans,*[195] and spectral data is in agreement with that literature data.

To understand the generality of this reaction strategy we have prepared representative Baylis-Hillman alcohols (**102b,c**) *via* the coupling of the α-keto esters with methyl acrylate (eq 38). These tertiary alcohols were subjected to the Friedel-Crafts reaction with benzene in the presence of methanesulfonic acid which directly provided 3,4-disubstituted maleic anhydride derivatives (**103b,c**) in 45 & 40 % isolated yields respectively (Table 3). The structures of these derivatives were established by the spectral data (IR, ^{1}H & ^{13}C NMR, LCMS), and elemental analysis.

Although the yields are inferior when compared to the corresponding maleimides, this reaction is still interesting in the sense that this methodology offers a simple procedure for synthesis of 3,4-disubsitituted maleic anhydride derivatives yet another important structural organization.

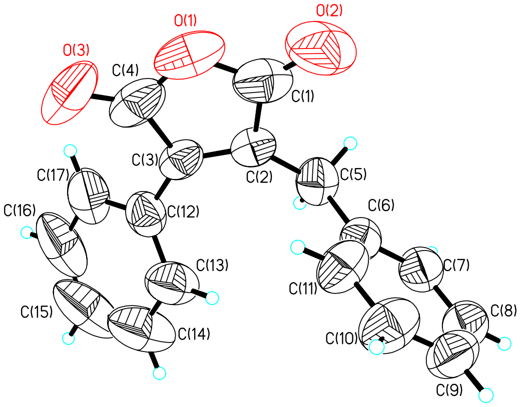
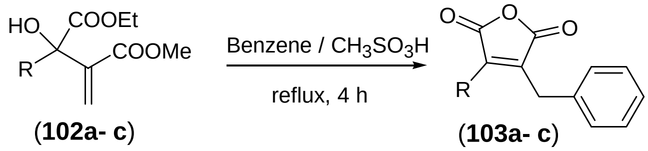


Figure 14. ORTEP diagram of compound **103a**

Table 3. **Synthesis of 3,4- disubstituted maleic anhydrides**[a]



B-H alcohol	R	Product[b]	Yield(%)[c]	m.p (°C)
102a	C_6H_5	**103a**[d]	52	56-58
102b	4-MeC_6H_4	**103b**	45	76-78
102c	4-MeOC_6H_4	**103c**	40	110-112

a) All reactions were carried out on 1 mmol scale of Baylis-Hillman alcohols (**102a-c**) with methanesulfonic acid (3 mmol) in benzene (6 mL) at reflux for 4 h.

b) All the compounds (**103a-c**) were obtained as colorless solids and fully characterized by spectral data (IR, ^{1}H & ^{13}C NMR, LCMS) and elemental analysis.

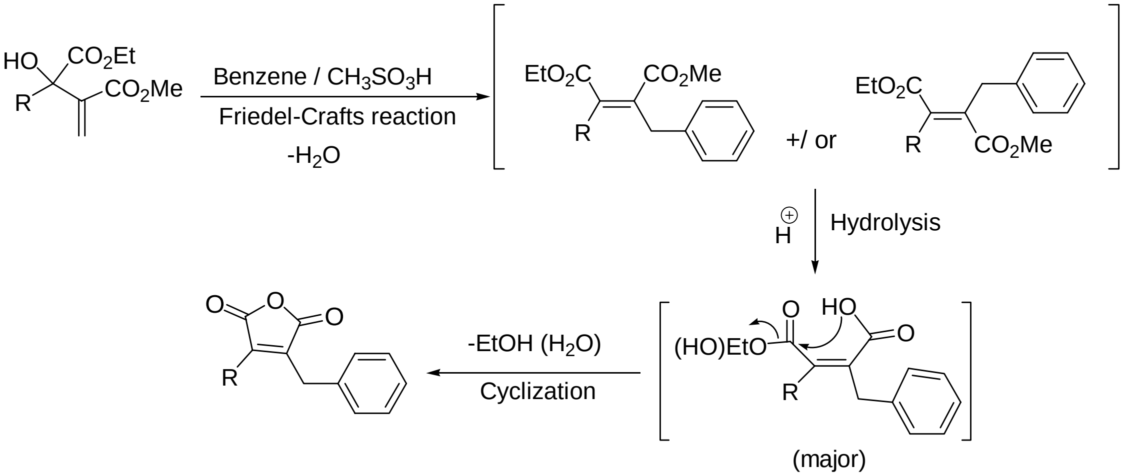
c) Isolated yields of the pure products based on the B-H alcohols.

d) Structure of this molecule (**103a**) was also established from single-crystal X-ray data.

In the case of 3,4-disubstituted maleic anhydrides, we noticed that substantial amounts (15-25 %) of starting material remain intact as evidenced by (TLC) analysis of the reaction mixture.[#] Hence the resulting products were obtained in low yields. However the results are still encouraging because the important 3,4-disubstituted maleic anhydride derivatives are synthesized in one-pot operation from the Baylis-Hillman adducts in reasonably good isolated yields. Studies are underway to understand the stereochemical course of the reaction. A plausible mechanism for the formation of maleic anhydride framework is given in Scheme 60.

[#] We also noticed that longer reaction times provide mixture of products as evidenced by TLC examination. Also, we can not completely rule out the possibility of the formation of the minor amounts of fumaric acid derivatives as the yields of maleic anhydride derivatives are low.

Scheme 60.



In conclusion, we have developed a convenient, operationally simple, 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 electrophiles), thus demonstrating the applications of Baylis-Hillman adducts, in synthetic organic chemistry.

Table 4: Crystal data collection and structure refinement for the compound **101a**

Empirical formula	: $C_{17}H_{13}NO_2$
Formula weight	: 263.28
Temperature	: 298 K
Wavelength	: 0.71073 Å
Crystal system	: Orthorhombic
Space group	: pbca (*International Table #14*)
Unit cell dimensions	: a = 15.379 (3) Å; α = 90.00 deg.
	: b = 6.8831 (14) Å; β = 90.00 deg.
	: c = 25.844 (5) Å; γ = 90.00 deg.
Volume	: 2735.7 (9) Å^3
Z, Calculated density	: Z = 8, 1.278 g / cm^3
Absorption coefficient	: 0.084 mm^{-1}
F(000)	: 1104
Crystal size	: 0.45 x 0.40 x 0.34 mm^3
Theta range for data collection	: 1.58 to 26.09 deg.
Limiting indices	: $-17 \le h \le 18$, $-8 \le k \le 8$, $-31 \le l \le 15$
Reflections collected / unique	: 16098 / 2708 [R(int) = 0.0331]
Completeness to theta = 26.09	: 99.6%
Absorption correction	: Multi-scan method (SADABS)
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 2708 / 0 / 185
Goodness-of-fit on F^2	: 1.046
Final R indices [I>2 sigma (I)]	: R1 = 0.0409, wR2 = 0.1159
R indices (all data)	: R1 = 0.0533, wR2 = 0.1098
Largest diff. peak and hole	: 0.164 and -0.223 e. Å^{-3}

Table 5: Crystal data collection and structure refinement for the compound **101e**

Empirical formula	: $C_{18} H_{15} NO_3$
Formula weight	: 293.31
Temperature	: 298 K
Wavelength	: 0.71073 Å
Crystal system	: Monoclinic
Space group	: P 21/n (*International Table #14*)
Unit cell dimensions	: a = 15.777(3) Å; α = 90 deg. b = 5.6522(9) Å; β = 93.257(3) deg. c = 16.639(3) Å; γ = 90 deg.
Volume	: 1481.3(4) $Å^3$
Z, Calculated density	: 4, 1.315 g / cm^3
Absorption coefficient	: 0.090 mm^{-1}
F(000)	: 616
Crystal size	: 0.42 x 0.28 x 0.16 mm^3
Theta range for data collection	: 1.73 to 26.02 deg.
Limiting indices	: $-19 \leq h \leq 19$, $-6 \leq k \leq 6$, $-19 \leq l \leq 20$
Reflections collected / unique	: 8883 / 2895 [R(int) = 0.0419]
Completeness to theta = 26.02	: 99.6 %
Absorption correction	: Multi-scan method (SADABS)
Max. and min. transmission	: 0.9857 and 0.9632
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 2895 / 0 / 204
Goodness-of-fit on F^2	: 0.870
Final R indices [I>2 sigma(I)]	: R1 = 0.0438, wR2 = 0.0822
R indices (all data)	: R1 = 0.0892, wR2 = 0.0939
Largest diff. peak and hole	: 0.113 and -0.143 e. $Å^{-3}$

Table 6: Crystal data collection and structure refinement for the compound **101i**

Empirical formula	: C_{12} H_{11} N O_2
Formula weight	: 201.22
Temperature	: 298 K
Wavelength	: 0.71073 Å
Crystal system	: Monoclinic
Space group	: P 21/n (*International Table #14*)
Unit cell dimensions	: a = 6.0246(10) Å; α = 90 deg. b = 7.9670(13) Å; β = 98.08 deg. c = 21.422(3) Å; γ = 90 deg.
Volume	: 1018.0(3) $Å^3$
Z, Calculated density	: 4, 1.313 g / cm^3
Absorption coefficient	: 0.090 mm^{-1}
F (000)	: 424
Crystal size	: 0.40 x 0.32 x 0.24 mm
Theta range for data collection	: 1.92 to 25.98 deg.
Limiting indices	: $-7\leq h\leq 7$, $-9\leq k\leq 9$, $-26\leq l\leq 26$
Reflections collected / unique	: 6026 / 1978 [R(int) = 0.0503]
Completeness to theta = 25.98	: 98.7 %
Absorption correction	: Multi-scan method (SADABS)
Max. and min. transmission	: 0.9787 and 0.9648
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 1978 / 0 / 141
Goodness-of-fit on F^2	: 0.911
Final R indices [I>2sigma(I)]	: R1 = 0.0445, wR2 = 0.0880
R indices (all data)	: R1 = 0.0766, wR2 = 0.0987
Largest diff. peak and hole	: 0.130 and -0.175 e. $Å^{-3}$

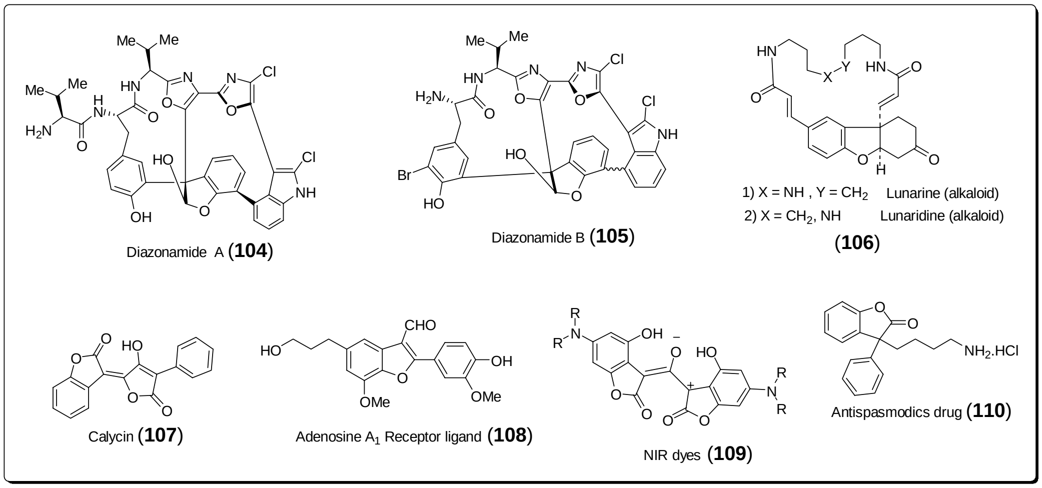
Table 7: Crystal data collection and structure refinement for the compound **103a**

Empirical formula	: C_{17} H_{12} O_3
Formula weight	: 264.27
Temperature	: 298 K
Wavelength	: 0.71073 Å
Crystal system	: Orthorhombic
Space group	: P 21 21 21(*International Table #14*)
Unit cell dimensions	: a = 5.6677(13) Å; α = 90 deg.
	b = 11.124(2) Å; β = 90 deg.
	c = 21.816(5) Å; γ = 90 deg.
Volume	: 1375.4(5) $Å^3$
Z, Calculated density	: 4, 1.276 g / cm^3
Absorption coefficient	: 0.087 mm^{-1}
F(000)	: 552
Crystal size	: 0.32 x 0.22 x 0.18 mm
Theta range for data collection	: 1.87 to 25.93 deg.
Limiting indices	: -6≤ h≤ 6, -13≤ k≤ 12, -24≤ l≤ 26
Reflections collected / unique	: 7702 / 1571 [R(int) = 0.0276]
Completeness to theta = 25.93	: 99.7 %
Absorption correction	: Multi-scan method (SADABS)
Max. and min. transmission	: 0.9844 and 0.9726
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 1571 / 0 / 181
Goodness-of-fit on F^2	: 1.047
Final R indices [I>2sigma(I)]	: R1 = 0.0447, wR2 = 0.1007
R indices (all data)	: R1 = 0.0654, wR2 = 0.1117
Absolute structure parameter	: 0(10)
Largest diff. peak and hole	: 0.118 and -0.143 e. $Å^{-3}$

A Facile One-Pot Synthesis of Benzofuran-2-one Derivatives

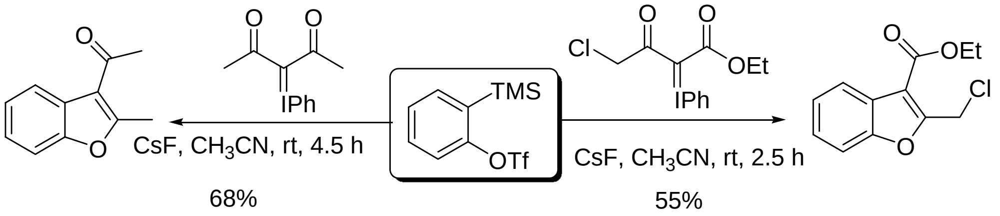
Benzofuran framework occupies a special place in heterocyclic chemistry due to the presence of this framework in a number of biological active molecules for example nominal diazonamide A & B (**104, 105**),[196] lunarine & lunaridine (**106**),[197] calycin (**107**),[198] adenosine A1 receptor ligand (**108**),[199] NIR dyes (**109**),[200] and antispasmodics drug (**110**)[201] (Fig. 15). Therefore development of simple strategies for obtaining this framework has become an attractive endeavor in synthetic organic chemistry. Some recent relevant literature reports are presented in the following Schemes 61-63, & eq.39.

Figure 15

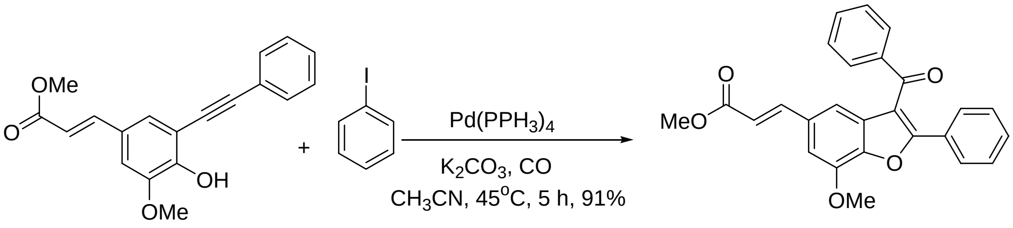

Diazonamide A (**104**)
Diazonamide B (**105**)
1) X = NH , Y = CH_2 Lunarine (alkaloid)
2) X = CH_2, NH Lunaridine (alkaloid)
(**106**)
Calycin (**107**)
Adenosine A_1 Receptor ligand (**108**)
NIR dyes (**109**)
Antispasmodics drug (**110**)

Li and co-workers[202] developed a general methodology for cycloaddition of benzyne with ylides leading to the synthesis of benzofuran derivatives. Representative examples are presented in Scheme 61.

Scheme 61



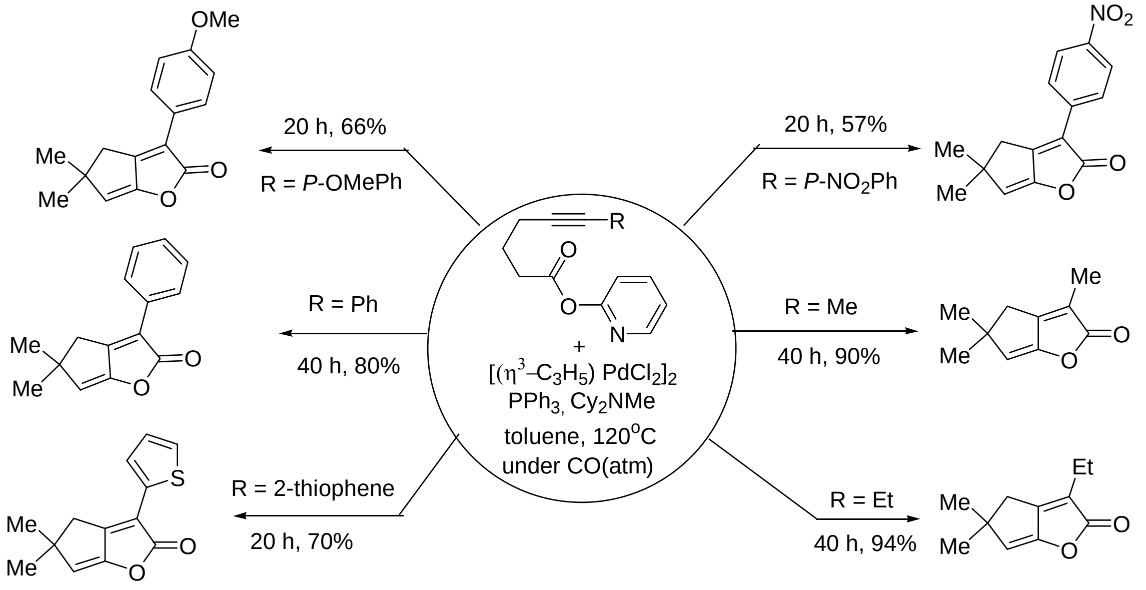
Appropriately substituted diarylacetylenes were elegantly transformed into benzofuran derivatives involving an interesting palladium catalyzed cyclo-carboylation strategies.[203,204] Reza Fathi and co-workers developed[203] a highly efficient synthetic approach for the carbonylative cyclization of *o*-alkynylphenols to the synthesis of corresponding 2-substituted-3-aroyl-benzo[*b*]furans. One example is presented in equation 39.



eq. 39

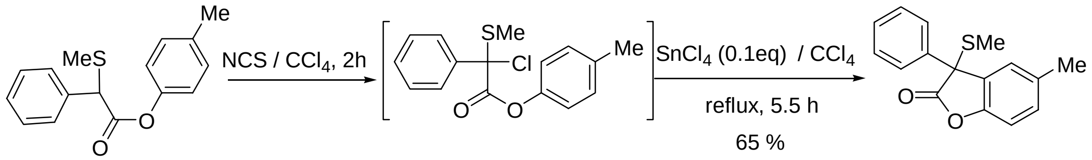
Chatani and co-workers [204] developed a facile methodology for the Pd-catalyzed cyclo-carbonylation of yne esters leading to the formation of γ-alkylidene α, β-unsaturated lactones. Representative examples are presented in Scheme 62.

Scheme 62



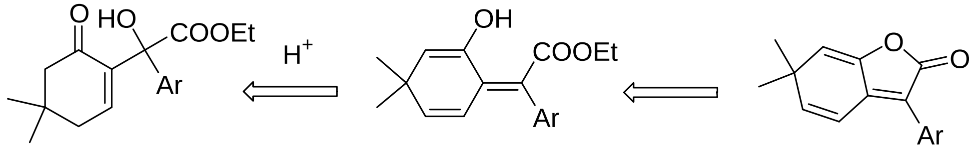
Philp Magnus[205] reported an intra-molecular Friedel-Craft reaction of *in situ* generated 2-thiomethyl-2-chloro-2-phenylacetyl aryl esters, with $SnCl_4$ leading to a synthesis of 3-thiomethyl-benzofuran-2-ones. Representative example is presented in Scheme 63.

Scheme 63

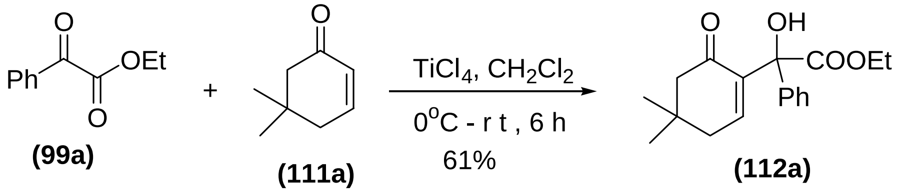


The medicinal relevance of the benzofuran derivatives has attracted our attention. We have therefore undertaken a research program for developing a convenient methodology for the synthesis of bezofuranone derivatives *via* the treatment of Baylis-Hillman tertiary alcohols with an appropriate acid according to retrosynthetic strategy Scheme 64.

Scheme 64



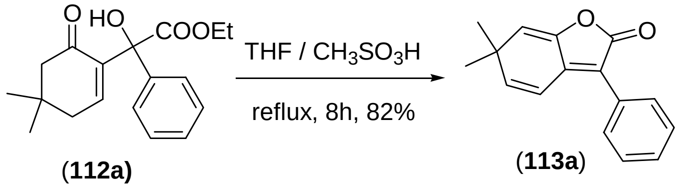
We have thus focused our attention towards the synthesis of 6, 6-dimethyl-3-aryl-6*H*-benzofuran-2-one derivatives. First we have selected ethyl 2-hydroxy-2-phenyl-2-(5,5-dimethylcyclohex-2-en-1-one-2-yl)ethanoate (**112a**) as a substrate towards understanding this strategy. The required Baylis-Hillman adduct (**112a**) was obtained *via* the coupling of ethyl phenylglyoxalate (**99a**) with 5,5-dimethylcyclohex-2-enone (**111a**) in the presence of $TiCl_4$ at room temperature for 6 h (eq. 40).



(99a) **(111a)** **(112a)**

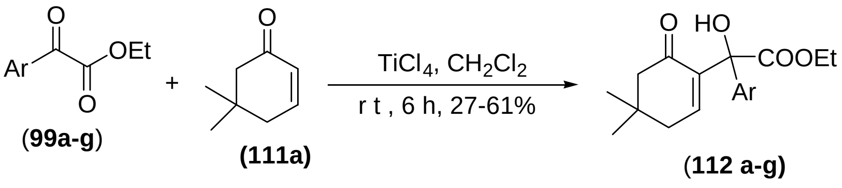
eq. 40

Then we have directed our efforts towards transformation of this adduct (**112a**) into the required lactone (**113a**) under different acidic conditions. The best results in this strategy were obtained when the Baylis-Hillman alcohol (**112a)**, was treated with methanesulfonic acid in THF at 90^{o}C for 8 h, thus providing 6, 6-dimethyl-3-phenyl-6*H*-benzofuran-2-one derivatives (**113a**) in 82 % isolated yield (eq 41). The structure of this molecule was confirmed by IR, ^{1}H NMR (Spectrum 17) & ^{13}C NMR (Spectrum 18), LCMS, and elemental analysis. We have also established the structure of this molecule (**113a**) by single crystal X-ray data (see Figure 16 for ORTEP diagram).



eq. 41

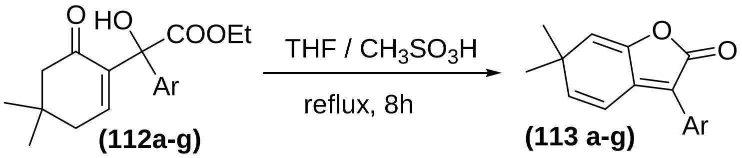
In order to understand the generality of the reaction, we have selected representative class of Baylis-Hillman adducts (**112a-g**) as substrates. These were prepared *via* the $TiCl_4$ mediated Baylis-Hillman reaction between ethyl arylglyoxalates (**99a-g**) with 5,5-dimethylcyclohex-2-enone (**111a**) at room temperature for 6 h (eq 42). These Baylis-Hillman alcohols (**112a-g**) were conveniently transformed into the lactones *via* the treatment with methanesulfonic acid in (62-83%) isolated yields (Table 8). Structures of all these derivatives (**113a-g**) were confirmed by IR, ^1H NMR & ^{13}C NMR [Spectrum 19 (for compound **113e**)] and [Spectrum 20 (for compound **113g**)] respectively, LCMS, and elemental analysis.



eq. 42

Ar = C_6H_5, 4-MeC_6H_4, 4-$MeOC_6H_4$, 3-MeC_6H_4, 3-$MeOC_6H_4$, 2-MeC_6H_4, 2-$MeOC_6H_4$

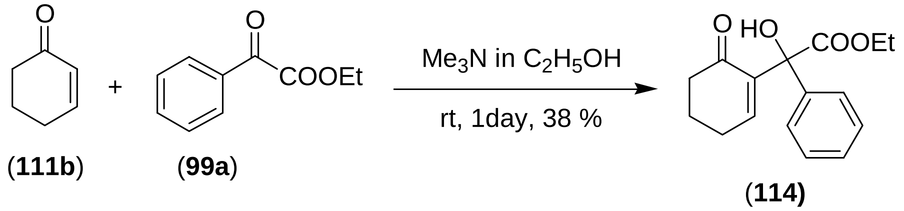
Table 8. Synthesis of 6, 6-Dimethyl-3-aryl-6*H*-benzofuran-2-one derivatives[a]



B-H alcohol	Ar	Product[b]	Yield(%)[c]	m.p (°C)
112a	C_6H_5	**113a**[d]	82	78-80
112b	4-MeC_6H_4	**113b**	81	86-88
112c	4-$MeOC_6H_4$	**113c**	79	90-92
112d	3-MeC_6H_4	**113d**	73	82-84
112e	3-$MeOC_6H_4$	**113e**	76	84-86
112f	2-MeC_6H_4	**113f**	83	108-110
112g	2-$MeOC_6H_4$	**113g**	62	102-104

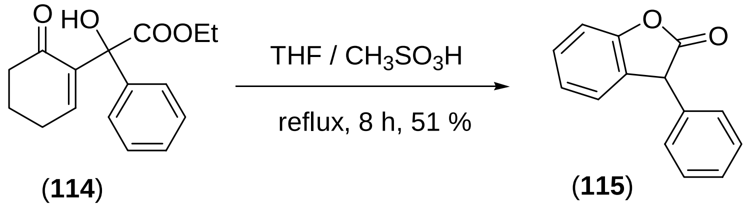
a) All reactions were carried out on 0.5 mmol scale of Baylis-Hillman alcohols (**112a-b**) with methanesulfonic acid (2.5 mmol) at 90°C for 8 h.
b) All the compounds (**113a-g**) were obtained as colorless solids and fully characterized by I R, ^1H & ^{13}C NMR, LCMS, and elemental analysis.
c) Isolated yields of the pure products based on the B-H alcohols.
d) Structure of this molecule (**113a**) was also established from single-crystal X-ray data.

We have then selected ethyl 2-hydroxy-2-phenyl-2-(cyclohex-2-en-1-on-2-yl)ethanoate (**114**) as a substrate to examine the generality of strategy. Required Baylis-Hillman adduct (**114**) was prepared *via* methanolic trimethylamine mediated coupling of ethyl phenylglyoxalate (**99a**) with cyclohex-2-enone (eq 43).



eq. 43

Then the Baylis-Hillman alcohol (**114**), was treated with methanesulfonic acid in THF for heating at 90°C for 8 h, providing 3-phenyl-3*H*-benzofuran-2-one (**115**) in 51 % isolated yield (eq 44). The structure of this molecule was confirmed by IR, ^{1}H NMR (Spectrum 21) & ^{13}C NMR (Spectrum 22), LCMS, and elemental analysis.



eq. 44

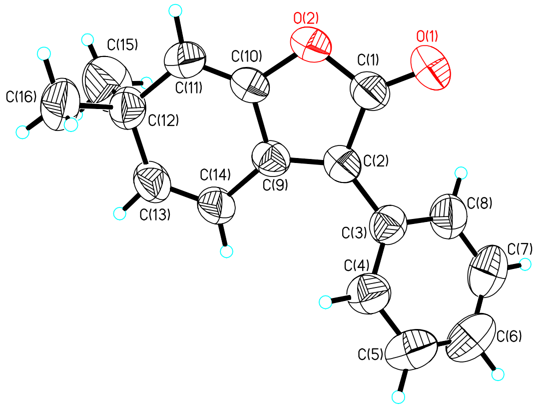
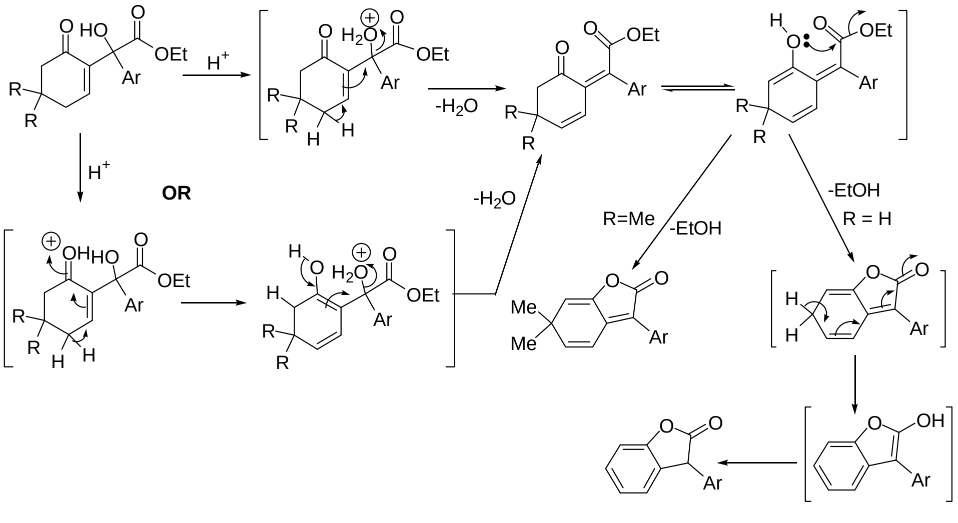


Figure 16. ORTEP diagram of compound **113a**

A plausible mechanism is presented in Scheme 65. The acid catalyzed reaction is believed to proceed through the protonation of tertiary hydroxyl group or carbonyl oxygen (or both) followed by the elimination of water molecule and ethanol to provide the 6, 6-dimethyl-3-aryl-6*H*-benzofuran-2-one derivatives. In the case of the Baylis-Hillman adduct derived from cyclohex-2-enone (R=H) the resulting triene will aromatize to provide the 3-phenyl-3*H*-benzofuran-2-one.

Scheme 65



In conclusion, we have developed operationally simple, one-pot procedure for the synthesis of 6, 6-dimethyl-3-aryl-6*H*-benzofuran-2-one and 3-phenyl-3*H*-benzofuran-2-one derivatives from the Baylis-Hillman alcohols thus demonstrating the applications of Baylis-Hillman adducts, in synthetic and medicinal chemistry.

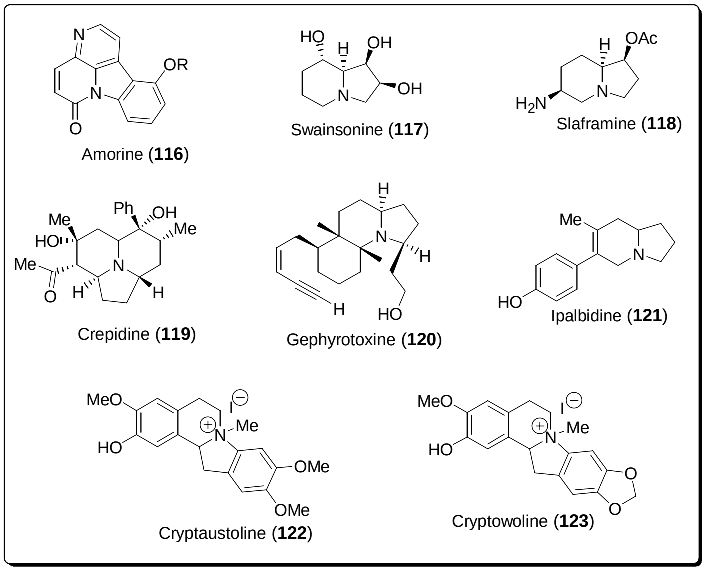
Table 9: Crystal data collection and structure refinement for the compound **113a**

Empirical formula	: $C_{16}H_{14}O_2$
Formula weight	: 238.27
Temperature	: 298 K
Wavelength	: 0.71073 Å
Crystal system	: Monoclinic
Space group	: P21/c (*International Table #14*)
Unit cell dimensions:	a = 10.7493(10) Å; α = 90 deg.
	b = 13.1617(12) Å; β = 108.285(2) deg.
	c = 9.6947(9) Å; γ = 90 deg.
Volume	: 1302.3(2) Å^3
Z, Calculated density	: 4, 1.215 g / cm^3
Absorption coefficient	: 0.079 mm^{-1}
F(000)	: 504
Crystal size	: 0.41 x 0.34 x 0.28 mm
Theta range for data collection	: 2.00 to 28.29 deg.
Limiting indices	: $-14 \leq h \leq 13$, $-17 \leq k \leq 17$, $-12 \leq l \leq 12$
Reflections collected / unique	: 14842 / 3136 [R(int) = 0.0285]
Completeness to theta = 28.29	: 96.8 %
Absorption correction	: Multi-scan method (SADABS)
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 3136 / 0 / 165
Goodness-of-fit on F^2	: 1.102
Final R indices [I>2 sigma (I)]	: R1 = 0.0684, wR2 = 0.1593
R indices (all data)	: R1 = 0.0964, wR2 = 0.1747
Largest diff. peak and hole	: 0.197 and -0.192 e. Å^{-3}

The Baylis-Hillman Bromides as Versatile Synthons: A Facile One-Pot Synthesis of Indolizine and Benzofused Indolizine Frameworks

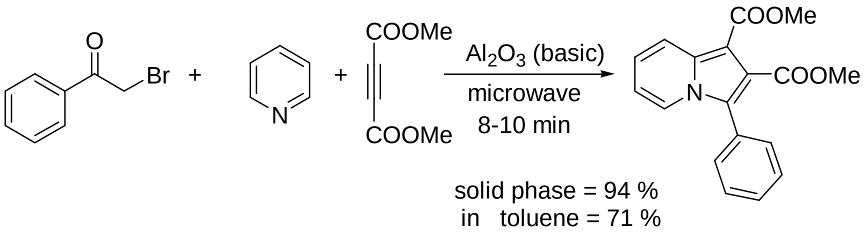
Indolizine framework has been and continues to be an interesting and structurally challenging nitrogen heterocyclic moiety because of the presence of this skeleton in a number of bioactive natural products such as amorine (**116**),[206] swainsonine (**117**),[206] slaframine (**118**),[206] crepidine (**119**),[206] gephyrotoxine (**120**),[206] ipalbidine (**121**),[206] cryptaustoline (**122**)[207a] and cryptowoline (**123**)[207b] (Fig. 17). Several indolizine derivatives, in fact, have been known to exhibit various biological activities such as antibacterial activity against mycobacterium tuberculosis,[208] inhibitors of phosphatase[209] and aromatase,[210] antioxidant,[211] calcium entry blockers,[212] 5-hydroxytryptamine (5-HT$_3$) receptor antagonists,[213] antidepressant[214] and antileukemic activities.[215]

Figure 17



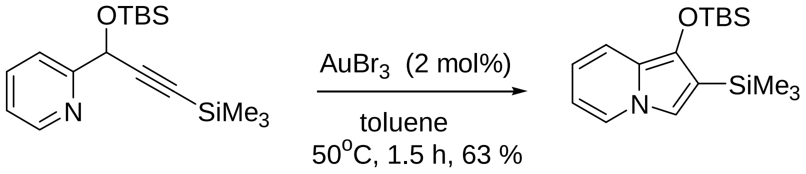
The biological and medicinal relevance of the indolizine derivatives has created a need for the development of efficient synthetic strategies for obtaining such derivatives and in fact, several systematic efforts have been made in this direction. Some of the recent reports are described in this section.

Boruah and co-workers[216] developed an interesting microwave mediated three-component reaction involving acyl bromide, pyridine, and acetylene in the presence of basic alumina for obtaining the corresponding indolizines. One representative example is presented in eq 45.



eq. 45

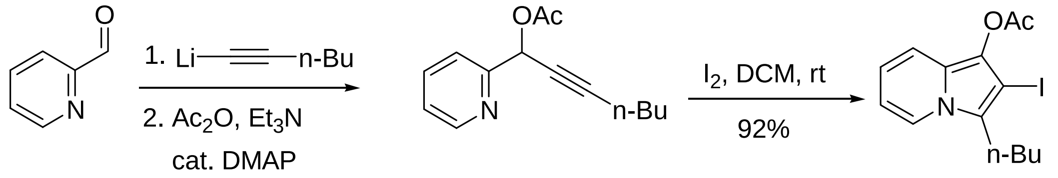
Gevorgyan and co-workers[217] developed a new protocol for mild cascade cycloismerisation of pyridine derivatives containing propargylic group into various types of N-fused pyrrolo-heterocycles in the presence of gold catalyst. One representative example is presented in eq 46.



eq.46

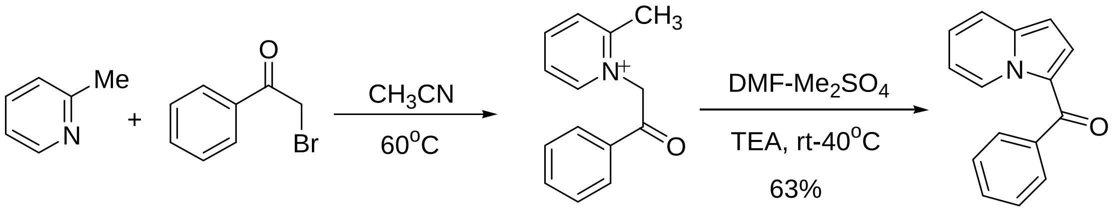
Kim and co-workers[218] reported a facile iodine mediated transformation of propargillic acetates containing pyridine moiety into functionalized indolizine derivatives. One representative example is presented in Scheme 66

Scheme 66



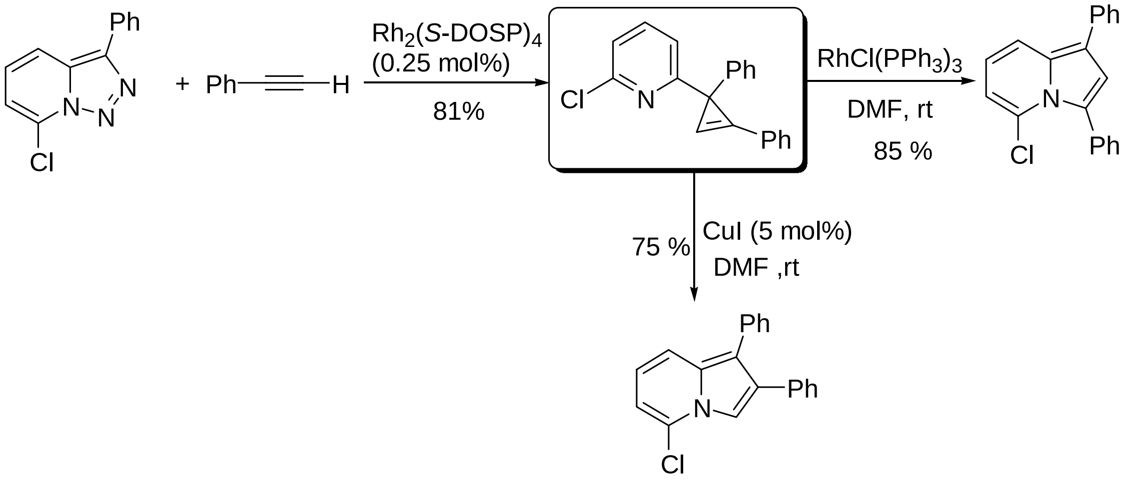
A simple methodology for synthesis of 3-acylated indolizines in good to excellent yields by using DMF-Me_2SO_4 as the key reagent following the reaction sequence as shown in Scheme 66 was developed by Lijun Sun and co-workers (one representative example is presented).[219]

Scheme 67



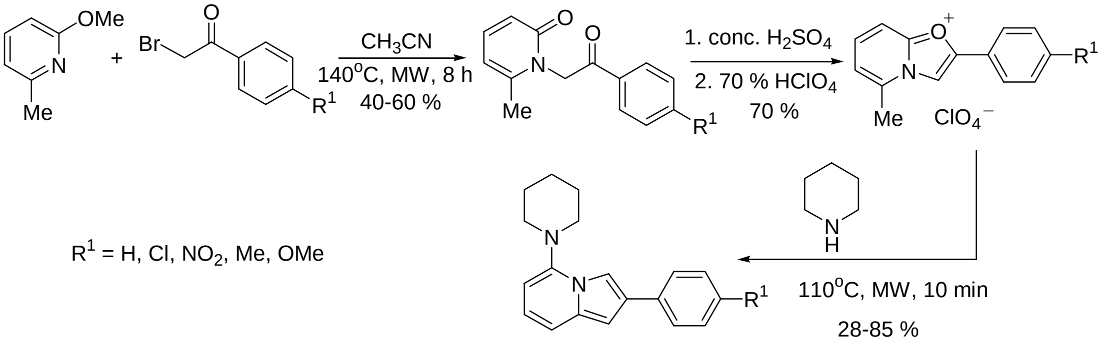
Gevorgyan and co-workers[220] reported a highly efficient regiodivergent method for the synthesis of indolizine derivatives *via* transition-metal-catalyzed rearrangement of *in situ* generated 3-iminocyclopropene systems following the reaction sequence as shown in Scheme 68. (One example is presented).

Scheme 68



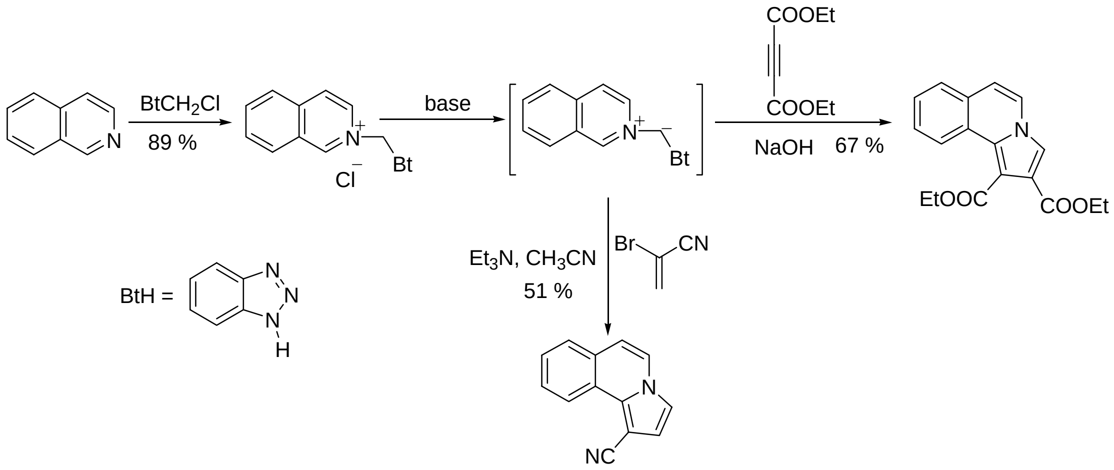
5-Aminoindolozines were prepared by Hoenke and co-workers[221]according to reaction sequence described in Scheme 69.

Scheme 69



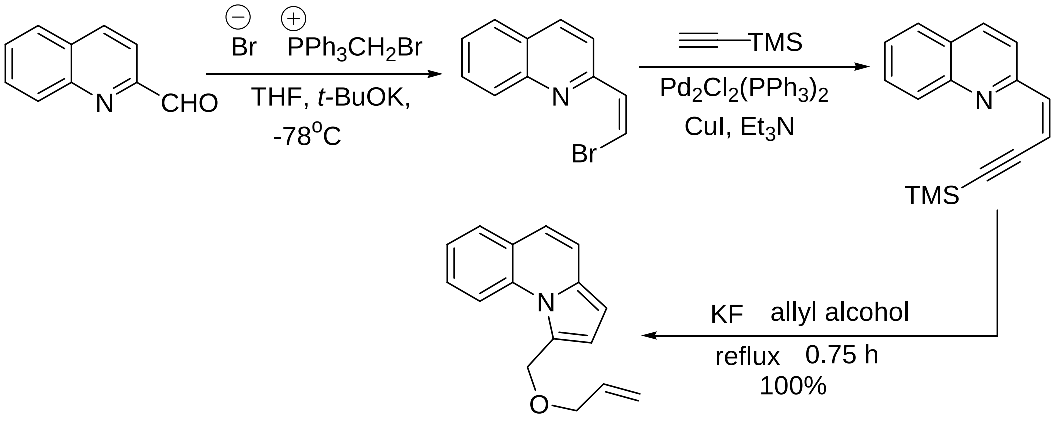
Kartritzaky and co-workers[222] reported an interesting protocol for synthesis of indolizines and pyrrolo[2,1-a]isoquinolines *via* 1,3-dipolar cycloadditions of pyridninum benzotriazolylmethylides or isoquinolinium benzotriazolylmethylides with ethylenes and acetylenes. One representative example is presented in Scheme 70.

Scheme 70

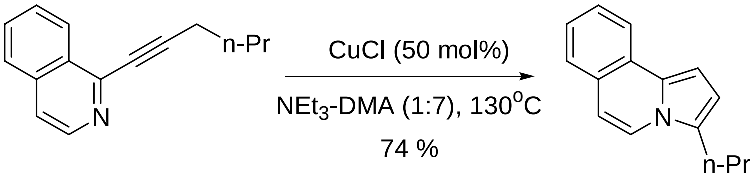


2-Quinolinecarboxaldehydes were conveniently transformed into substituted benzofused indolizine derivatives according to the sequence of reactions presented in Scheme 71 (one representative example is presented).[223]

Scheme 71

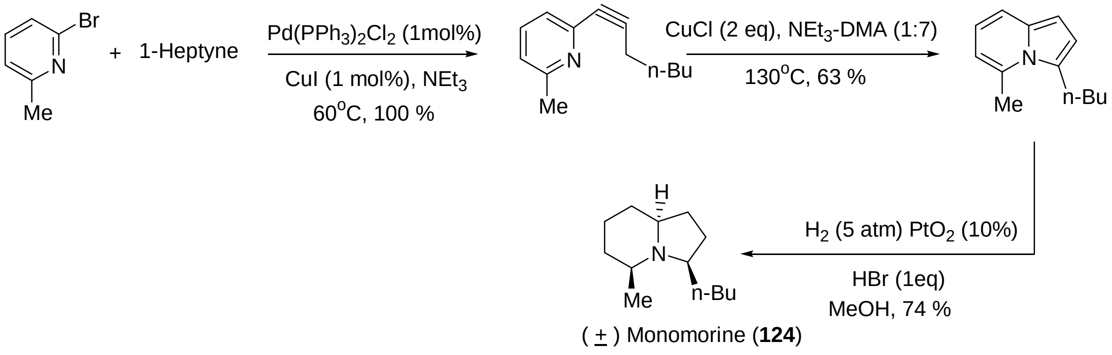


Gevorgyan and co-workers [224] developed a novel, general, and efficient Cu-assisted strategy for cycloisomerization of alkynyl imines into indolizine derivatives (eq. 47). This methodology has been extended to the synthesis of (±) monomorine Scheme 72.



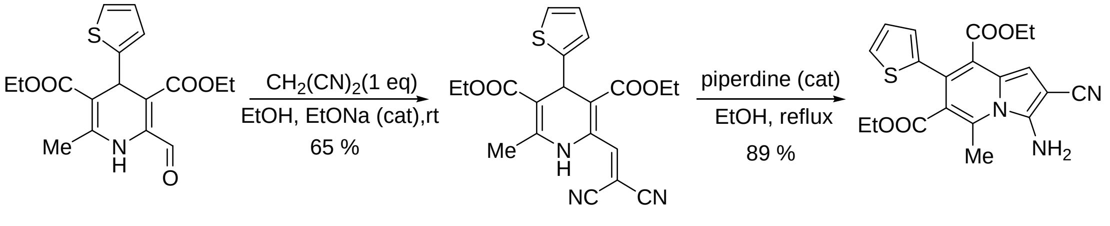
eq. 47

Scheme 72



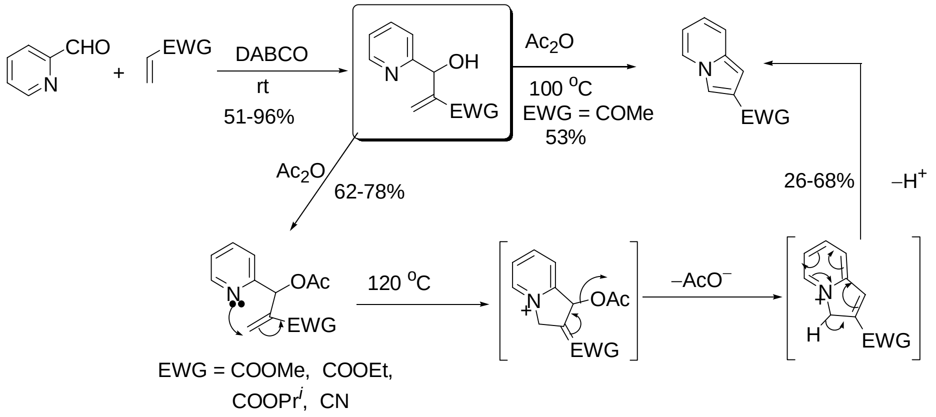
Simple synthesis of conjugated and thermodynamically stable indolizine derivatives starting from 2-formyl-1,4-dihydropiperidine system was reported by Daich and co-workers. One representative example is presented in Scheme 73.[225]

Scheme 73

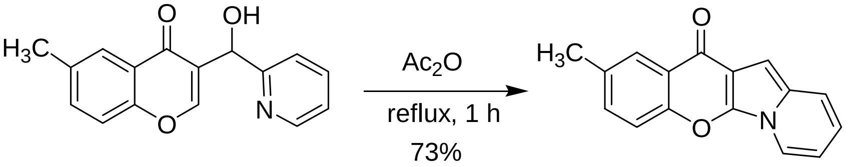


The Baylis-Hillman adducts have been successfully employed for synthesis of various indolizine frameworks by Bode and Kaye according to the Scheme 74.[226]

Scheme 74

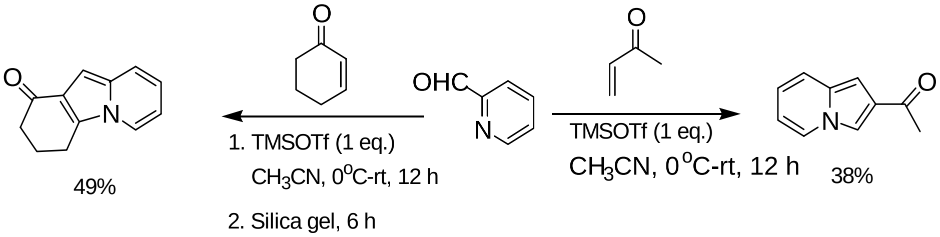


Our research group has developed an interesting methodology for obtaining fused indolizine derivatives from the Baylis-Hillman adducts derived from chromanone derivatives as activated alkenes (eq 48) in one-pot operation.[45] Our research group has also reported an interesting electrophile induced Baylis-Hillman reaction leading to the synthesis of indolizine frameworks following the reaction sequence as shown in Scheme 75.[227]

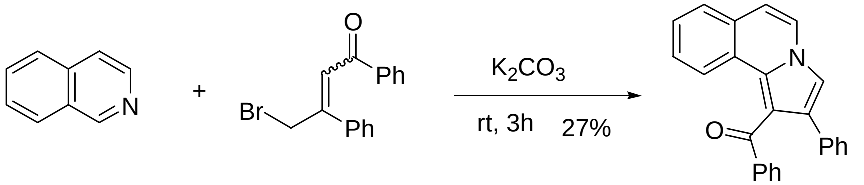


eq. 48

Scheme 75

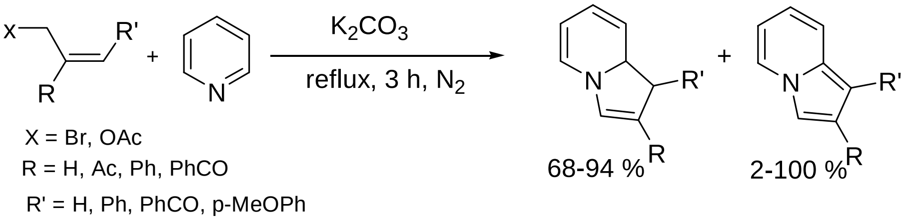


In 1972 Tamura and co-workers[228] reported an elegant conversion of 4-bromo-1,3-diphenylbut-2-en-1-one (involving 1,5-cyclization of nitrogen ylides) into the corresponding indolizine and pyrrolo(1,2-a)isoquinoline derivatives *via* the treatment with pyridine and isoquinoline derivatives respectively in the presence of potassium carbonate. One example is presented in eq 49.



eq. 49

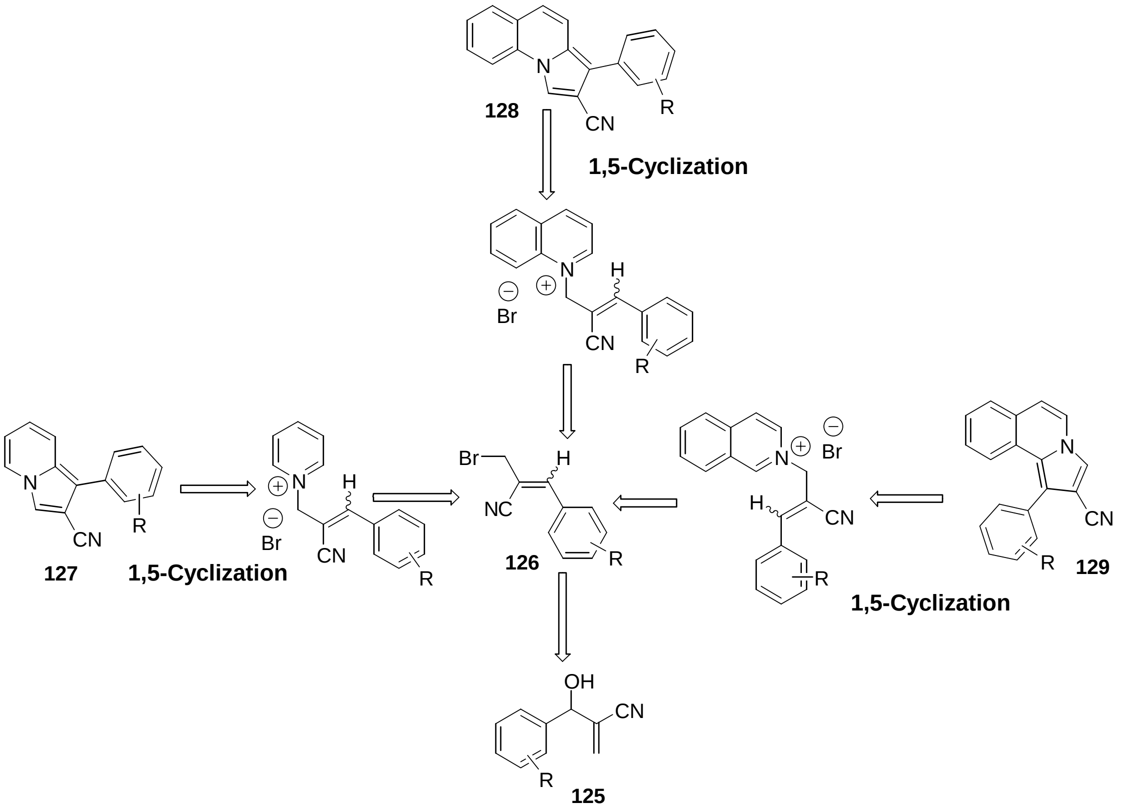
Subsequently Pohjala reported[229]similar methodology for obtaining dihydroindolizines and indolizine derivatives in high yields (eq 50). However in some cases he obtained mixtures of dihydroindolizine and indolizine derivatives.



eq. 50

We were indeed fascinated by these wonderful publications. We were particularly pleased to note that the allyl bromides used by Pohjala were nothing but the present day version of Baylis-Hillman bromides (they were not known at that time with this name). It subsequently occurred to us that this strategy will constitute a basic ground for the preparation of several indolizine and benzofused indolizine [pyrrolo(1,2-a)quinoline and pyrrolo(1,2-a)isoquinoline] frameworks using the Baylis-Hillman bromides. Accordingly we have planned the synthesis of these molecules according to the reterosynthetic strategy as shown in Scheme 76.

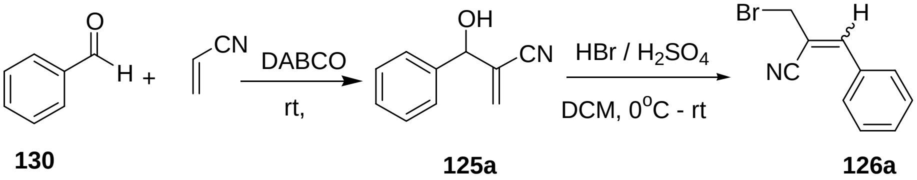
Scheme 76



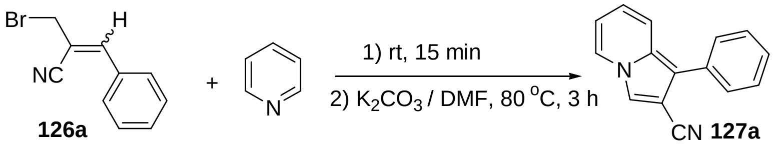
First we focused our attention towards the development of simple indolizine derivatives. Accordingly we have first directed our studies towards the transformation of 2-bromomethyl-3-phenylprop-2-enenitrile (**126a**) (as a mixture of *E* and *Z*-isomers) into indolizine [1-aza-8-cyano-7-phenylbicyclo(4.3.0)nona-2,4,6,8-tetraene] (eq. 47) *via* the treatment with pyridine. The Baylis-Hillman bromide (**126a**) was prepared from 3-hydroxy-3-phenyl-2-methylenepropanenitrile (**125a**), which in turn was prepared *via* the

Baylis-Hillman coupling reaction between benzaldehyde (**130a**) and acrylonitrile under the catalytic influence of DABCO (Scheme 77).

Scheme 77

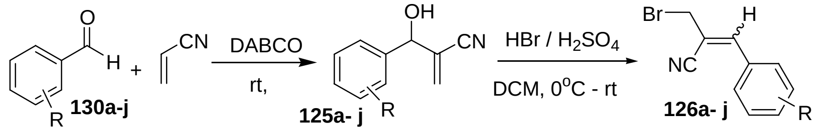


Next we have performed the reaction between 2-bromomethyl-3-phenylprop-2-enenitrile (**126a**) (as a mixture of *E* and *Z*-isomers) and pyridine under variety of conditions. The best results in this direction were obtained when 2-(bromomethyl)-3-phenylprop-2-enenitrile (**126a**), was treated with pyridine for 15 minutes at room temperature (for salt formation), followed by heating at 80 °C in the presence of potassium carbonate for 3 h, thus providing the desired 1-aza-8-cyano-7-phenylbicyclo(4.3.0)nona-2,4,6,8-tetraene (**127a**) in 52 % isolated yield after purification through column chromatography (eq 51 and Table 11)**.** The structure of this compound was established by IR, ^{1}H NMR (Spectrum 23), ^{13}C NMR (Spectrum 24), LCMS, and elemental analysis. We have also obtained single crystals for the compound (**127a)** and further confirmed the structure by single crystal X-ray data (see Figure 18 for ORTEP diagram).



eq. 51

Table 10. Synthesis of Baylis-Hillman bromides:



Aldehyde	R	B-H alcohol^a	Yield (%)^b	B-H bromide^{c,d}	Yield (%)^e
130a	H	**125a**	73	**126a**	75
130b	4-Me	**125b**	71	**126b**	80
130c	4-Et	**125c**	65	**126c**	76
130d	4-^{i}Pr	**125d**	55	**126d**	71
130e	4-N0$_2$	**125e**	44	**126e**	72
130f	2-Me	**125f**	61	**126f**	70
130g	2-Cl	**125g**	56	**126g**	62
130h	2-Br	**125h**	50	**126h**	60
130i	2,4(Cl)$_2$	**125i**	68	**126i**	45
130j	3-Cl	**125j**	37	**126j**	47

a) All reactions were carried out on 30 mmol scale of arylaldehydes (**130a-j**) with acrylonitrile (50 mmol) in the influence of DABCO (30 mol%).

b) Yields of pure alcohols based on aldehydes

c) All reactions were carried out on 20 mmol scale of Baylis-Hillman adducts (**125a-j**) with HBr (50 mmol) in the presence of H$_2$SO$_4$ (20 mol%).

d) All the compounds (**126a-j**) were fully characterized by spectral data (IR, ^{1}H & ^{13}C NMR)

e) Isolated yields of the pure products (**126a-j**) based on the Baylis-Hillman adducts (**125a-j**).

Encouraged by these results, we have focused our attention to understand the generality of this strategy. We have therefore prepared a representative class of the Baylis-Hillman bromides according to the (Table 10). These bromides were conveniently transformed into the desired 1-aza-8-cyano-7-arylbicyclo(4.3.0)nona-2, 4,6,8-tetraenes (**127a-j**) in 47-63% yields (Table-11). The structure of these compounds were established by IR, ^{1}H & ^{13}C NMR [Spectrum 25 & 26 for compound **127b** ^{1}H & ^{13}C NMR respectively, Spectrum 27 & 28 for compound **127f** ^{1}H & ^{13}C NMR respectively, Spectrum 29 & 30 for compound **127g** ^{1}H & ^{13}C NMR respectively, Spectrum 31 (for compound **127h**), Spectrum 32 (for compound **127j**)], LCMS, and elemental analysis.

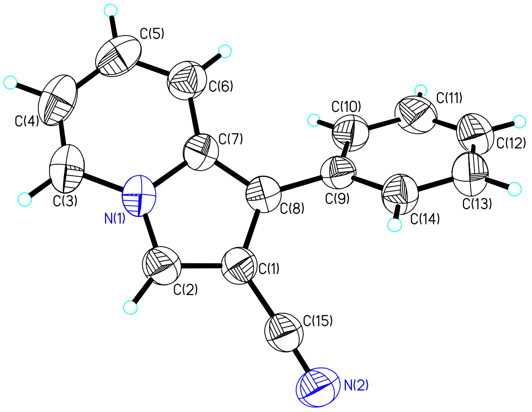
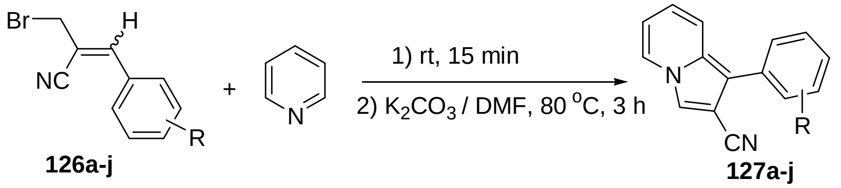


Figure 18. ORTEP diagram of compound **127a**

Table 11. **Synthesis of Indolizine derivatives**[a]



126a-j

127a-j

B-H bromide	**R**	**Product**[b]	**Yield** (%)[c]	**m.p°C**
126a	H	**127a**[d]	52	128-130
126b	4-Me	**127b**	54	132-134
126c	4-Et	**127c**	59	142-144
126d	4-^{i}Pr	**127d**	55	146-148
126e	4-NO_2	**127e**	47	170-172
126f	2-Me	**127f**	60	138-140
126g	2-Cl	**127g**	58	132-134
126h	2-Br	**127h**	54	136-138
126i	2,4 $(Cl)_2$	**127i**	63	136-138
126j	3-Cl	**127j**	49	144-146

a) All reactions were carried out on 1 mmol scale of Baylis-Hillman bromide (**126a-j**) with K_2CO_3 (5 mmol), pyridine (3 mL) in DMF (3 mL) at 80°C for 3 h.

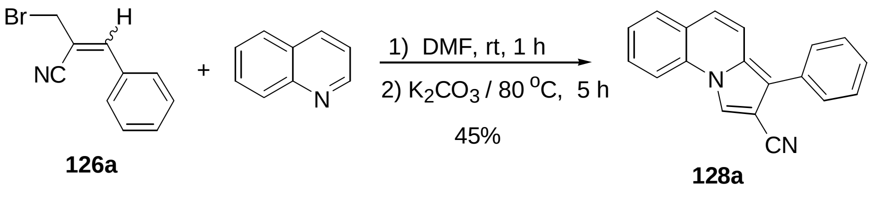
b) All the compounds **(127a-j)** were obtained as colorless solids and fully characterized by IR, ^{1}H & ^{13}C NMR, LCMS, and elemental analysis.

c) Isolated yields of the pure products and are based on the B.H.bromides.

d) Structures of this molecule (**127a**) was also established from the single-crystal X-ray data.

Towards the development of simple synthesis of Pyrrolo(1,2-a)quinoline derivatives:

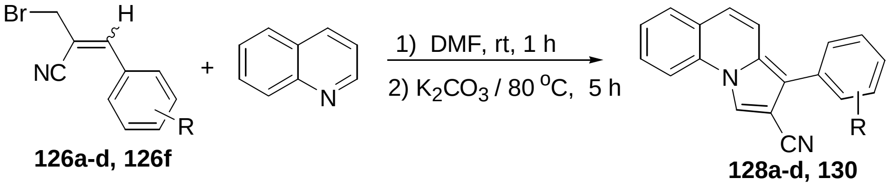
After developing a simple one-pot methodology for the synthesis of indolizine framework we have directed our attention towards the synthesis of benzofused indolizine [pyrrolo(1,2-a)quinoline] derivatives, *i.e.,* [1-aza-12-cyano-11-aryltricyclo(8.3.0.$0^{2,7}$)-trideca-2,4,6,8,10,12-hexaenes]. It appeared to us that this can in principle be achieved *via* the treatment of the Baylis-Hillamn bromides with quinoline. In this case also we have first selected 2-(bromomethyl)-3-phenylprop-2-enenitrile (**126a**) as a substance for reaction with quinoline. The best results in this strategy were obtained when the Baylis-Hillman bromide (**126a)**, was treated with quinoline in DMF for 1 h at room temperature followed by heating at 80 °C for 5 h in the presence of K_2CO_3, thus providing 1-aza-12-cyano-11-phenyltricyclo[8.3.0.$0^{2,7}$]trideca-2,4,6,8,10,12-hexaene (eq 52) in 45% isolated yield. We have confirmed the structure of (**128a**) by IR, ^{1}H NMR [Spectrum 33 (for compound **128a**)], ^{13}C NMR [Spectrum 34 (for compound **128a**)], LCMS, and elemental analysis. We have also established the structure by single crystal X-ray data (see Figure 19 for ORTEP diagram).



eq. 52

In order to understand the generality of this reaction strategy we have subjected various Baylis-Hillman bromides (**126b-d,** and **126f**) to the treatment with quinoline under similar conditions to provide 1-aza-12-cyano-11-aryltricyclo[8.3.0.0^{2,7}]trideca-2,4,6,8,10,12-hexaenes pyrrolo(1,2-a)quinoline derivatives] (**128b-d,** and **130**) in 47-51% isolated yields (Table 12). We have confirmed the structure of these compounds (**128b-d,** and **130**) by IR, ^{1}H NMR ,^{13}C NMR [Spectrum 35 (for compound **130**)], LCMS, and elemental analysis.

Table 12. Synthesis of pyrrolo(1,2-a)quinoline derivatives[a]



B-H bromide	R	Product[b]	Yield (%)[c]	m.p°C
126a	H	**128a**[d]	45	160-162
126b	4-Me	**128b**	45	156-158
126c	4-Et	**128c**	47	138-140
126d	4-^{i}Pr	**128d**	51	148-150
126f	2-Me	**130**[e]	47	168-170

a) All reactions were carried out on 1 mmol scale of the Baylis-Hillman bromides (**126a-d,** and **126f**) with quinoline (2 mmol) in DMF (3 mL).

b) All the compounds (**128a-d,** and **130**) were obtained as colorless solids and fully characterized by IR, ^{1}H & ^{13}C NMR, LCMS, and.elemental analysis.

c) Isolated yields of the pure products and are based on the B-H bromides.

d) Structure of this molecule (**128a**) was also established by the single crystal X-ray data.

e) This numbering has given for the sake of convenience and clarity.

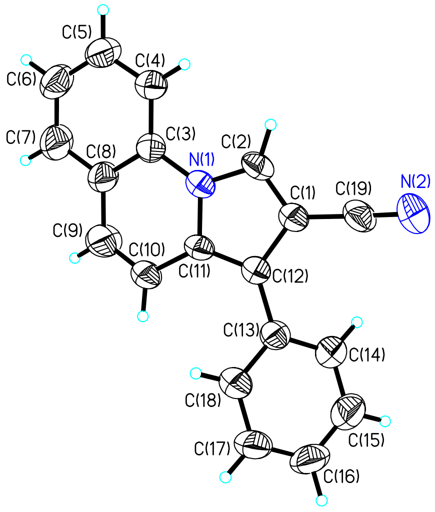


Figure 19. ORTEP diagram of compound **128a**

Simple synthesis of pyrrolo(1,2-a)isoquinoline derivatives:

Next we have focused our attention towards the synthesis of benzofused indolizine [pyrrolo(1,2-a)isoquinoline deriveatives] *via* the treatment of the Baylis-Hillman bromides with isoquinoline. We have first selected the allyl bromide (**126a**) as substrate for reaction with isoquinoline. The best results were obtained when the allyl bromide was treated with isoquinolne in DMF for 1 h at room temperature followed by heating at 80 ^{o}C for 5 h in the presence of K_2CO_3, thus providing the required benzofused indolizine [1-aza-12-cyano-11-phenyltricyclo(8.3.0.0^{4,9})trideca-2,4,6,8,10,12-hexaenes] (**129a**) in 68 % isolated yields (Table 13). The structure of this compound was established by IR, ^{1}H NMR (Spectrum 36), ^{13}C NMR (Spectrum 37), LCMS, and elemental analysis. We have also further confirmed the structure of this molecule (**129a**) by X-ray single crystal data (see Figure 20 for ORTEP diagram).

To understand the generality of this reaction strategy we have subjected a representative class of allyl bromides (**126b-d**, and **126g**)to the reaction with isoquinoline uunder similar reaction conditions in 52-63 % isolated yields (Table 13). We have confirmed the structure of these compounds (**129b-d** and **130**) by IR, ^{1}H NMR, ^{13}C NMR [Spectrum 38 (for compound **129c**), Spectrum 39 (for compound **129d**), Spectrum 40 (for compound **131**)], LCMS, and elemental analysis.

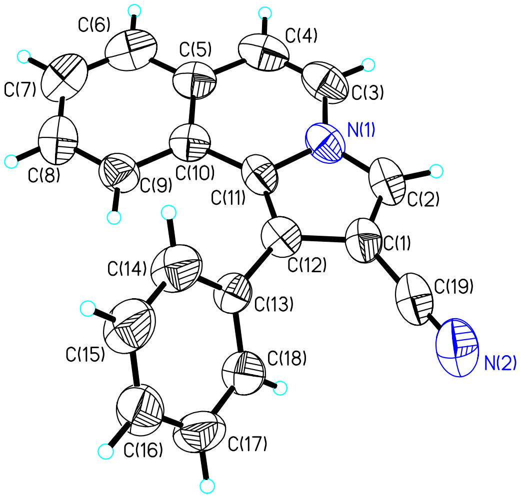
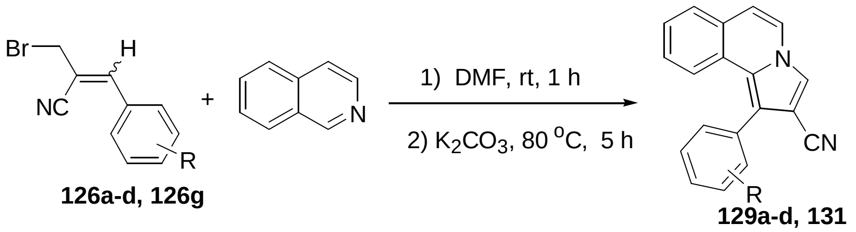


Figure 20. ORTEP diagram of compound **129a**

Table 13. Synthesis of pyrrolo(1,2-a)quinoline derivatives[a]



126a-d, 126g

129a-d, 131

B-H bromide	R	Product[b]	Yield (%)[c]	m.p^{o}C
126a	H	**129a**[d]	68	142-144
126b	4-Me	**129b**	63	160-162
126c	4-Et	**129c**	60	164-166
126d	4-^{i}Pr	**129d**	63	172-174
126g	2-Cl	**131**[e]	52	164-166

a) All reactions were carried out on 1 mmol scale of the Baylis-Hillman bromides (**126a-d, 126g**) with isoquinoline (2 mmol) in DMF (3 mL).

b) All the compounds (**129a-d, 131**) were obtained as colorless solids and fully characterized by (IR, ^{1}H & ^{13}C NMR, LCMS), and.elemental analysis.

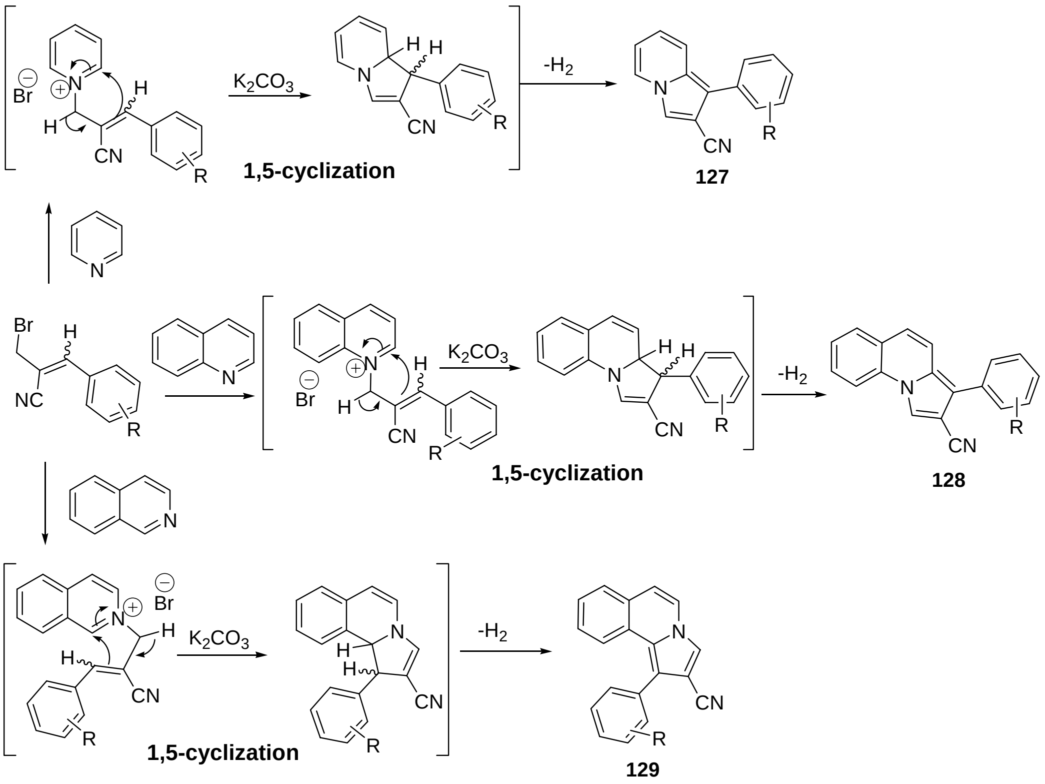
c) Isolated yields of the pure products and are based on the B-H bromides.

d) Structure of this molecule (**129a**) was also established from the single crystal X-ray data.

e) This numbering has given for the sake of convenience and clarity.

A plausible mechanism (based on 1,5-cylization pathway) for the preparation of indolizine and benzofused indolizine derivatives is provided in the Scheme 78. It is interesting to note that the dihydroindolizine (benzofused dihydro indolizine) derivatives formed *in situ* were oxidized (underwent dehydrogenation) during the course of the reaction to result in the formation of indolizine (benzofused indolizine) frameworks. Although the yields are not very high, this methodology still is very useful as it provides pyrrole containing heterocyclic compounds in one-pot operation.

Scheme 78:



In conclusion, we have successfully developed a convenient, facile and one-pot procedure for the synthesis of indolizine and benzofused indolizine [pyrrolo(1,2-a)quinoline and pyrrolo(1,2-a)isoquinoline] frameworks from the Baylis-Hillman bromides, thus demonstrating the applications of Baylis-Hillman bromides as valuable synthons in synthetic organic and medicinal chemistry.

Table 14: Crystal data collection and structure refinement for the compound **127a**

Empirical formula	: $C_{15}\ H_{10}\ N_2$
Formula weight	: 218.25
Temperature	: 298 K
Wavelength	: 0.71073 Å
Crystal system	: Orthorhombic
Space group	: Pbca (*International Table #14*)
Unit cell dimensions	: a = 10.1962(10) Å; α = 90 deg.
	b = 7.5079(7) Å; β = 90 deg.
	c = 29.504(3) Å; γ = 90 deg.
Volume	: 2258.6(4) $Å^3$
Z, Calculated density	: 8, 1.284 g / cm^3
Absorption coefficient	: 0.077 mm^{-1}
F(000)	: 912
Crystal size	: 0.48 x 0.28 x 0.20 mm
Theta range for data collection	: 2.43 to 25.95 deg.
Limiting indices	: $-10 \leq h \leq 12$, $-9 \leq k \leq 9$, $-36 \leq l \leq 32$
Reflections collected / unique	: 11455 / 2213 [R(int) = 0.0533]
Completeness to theta = 25.95	: 99.9 %
Absorption correction	: Multi-scan method (SADABS)
Max. and min. transmission	: 0.9847 and 0.9639
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 2213 / 0 / 154
Goodness-of-fit on F^2	: 1.221
Final R indices [I>2 sigma(I)]	: R1 = 0.0669, wR2 = 0.1416
R indices (all data)	: R1 = 0.0847, wR2 = 0.1511
Largest diff. peak and hole	: 0.188 and -0.262 e. $Å^{-3}$

Table 15. Crystal data collection and structure refinement for the compound **128a**

Empirical formula	: $C_{19} H_{12} N_2$
Formula weight	: 268.31
Temperature	: 298 K
Wavelength	: 0.71073 Å
Crystal system	: Triclinic
Space group	: P -1(*International Table #14*)
Unit cell dimensions	: a = 10.629(6) Å; α = 93.357(9) deg.
	b = 11.135(6) Å; β = 95.964(9) deg.
	c = 11.702(6) Å; γ = 94.709(9) deg.
Volume	: 1369.6(13) $Å^3$
Z, Calculated density	: 2, 1.301 g / cm^3
Absorption coefficient	: 0.077 mm^{-1}
F(000)	: 560
Crystal size	: 0.32 x 0.21 x 0.18 mm
Theta range for data collection	: 1.75 to 25.00 deg.
Limiting indices	: $-12 \le h \le 12$, $-13 \le k \le 13$, $-13 \le l \le 13$
Reflections collected / unique	: 12327 / 4815 [R(int) = 0.1178]
Completeness to theta = 25.00	: 99.5 %
Absorption correction	: Multi-scan method (SADABS)
Max. and min. transmission	: 0.9862 and 0.9756
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 4815 / 0 / 379
Goodness-of-fit on F^2	: 1.143
Final R indices [I>2 sigma(I)]	: R1 = 0.0725, wR2 = 0.1433
R indices (all data)	: R1 = 0.0975, wR2 = 0.1540
Largest diff. peak and hole	: 0.243 and -0.178 e. $Å^{-3}$

Table 16. Crystal data collection and structure refinement for the compound **129a**

Empirical formula	$C_{19}H_{12}N_2$
Formula weight	268.31
Temperature	298 K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P 21/c (*International Table #14*)
Unit cell dimensions	a = 14.079(3) Å; α = 90 deg.
	b = 16.431(4) Å; β = 91.820(4) deg.
	c = 12.208(3) Å; γ = 90 deg.
Volume	2822.6(11) $Å^3$
Z, Calculated density	8, 1.263 g / cm^3
Absorption coefficient	0.075 mm^{-1}
F(000)	1120
Crystal size	0.38 x 0.28 x 0.20 mm
Theta range for data collection	1.91 to 26.04 deg.
Limiting indices	$-17 \le h \le 17$, $-20 \le k \le 20$, $-15 \le l \le 15$
Reflections collected / unique	28580 / 5512 [R(int) = 0.1730]
Completeness to theta = 26.04	98.9 %
Absorption correction	Multi-scan method (SADABS)
Max. and min. transmission	0.9851 and 0.9720
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5512 / 0 / 379
Goodness-of-fit on F^2	0.970
Final R indices [I>2 sigma(I)]	R1 = 0.0830, wR2 = 0.1283
R indices (all data)	R1 = 0.2299, wR2 = 0.1714
Largest diff. peak and hole	0.168 and -0.160 e. $Å^{-3}$

CONCLUSIONS

We made significant progress and achieved considerable success in our objectives on the applications of Baylis-Hillman adducts as mentioned in the beginning of this section. We have successfully transformed 3-ethoxycarbonyl-3-hydroxy-3-aryl-2-methylene-propanenitrile (**100a-i**), and 3-ethoxycarbonyl-3-hydroxy-3-aryl-2-methylenepropanoate (**102a-c**) (Baylis-Hillman adducts), into disubstituted maleimde (**101a-i**), and disubstituted maleic anhydride derivatives (**103a-c**) respectively in a facile, one-pot methodology *via* Freidel-Crafts reaction with benzene in the presence of methatnesulfonic acid. We have developed a simple methodology for synthesis of functionalized 6, 6-dimethyl-3-aryl-6*H*-benzofuran-2-one derivatives (**113a-g**) and 3-phenyl-3*H*-benzofuran-2-one (**143**) from the Baylis-Hillman adducts *i.e.,* 2-hydroxy-2-aryl-2-(5,5-dimethylcyclohex-2-en-1-on-2-yl)ethanoate (**112a-g**), and 2-hydroxy-2-phenyl-2-cyclohex-2-en-1-on-2-yl)-ethanoate (**114**) respectively in an operationally simple procedure. We have also transformed the Baylis-Hillman bromides, 2-bromomethyl-3-arylprop-2-enenitrile (as a mixture of *E* and *Z*-isomers) (**126a-j**) into indolizine derivatives [1-aza-8-cyano-7-arylbicyclo-(4.3.0)nona-2,4,6,8-tetraene] (**127a-j**) *via* the treatment of pyridine in the presence of potassium carbonate. We have also developed a simple one-pot methodology for the synthesis of benzofused indolizine [pyrrolo(1,2-a)quinoline] derivatives, *i.e.,*. [1-aza-12-cyano-11-aryltricyclo-(8.3.0.$0^{2,7}$)-trideca-2,4,6,8,10,12-hexa-enes] (**128a-d, 130**), and [pyrrolo(1,2-a)isoquino-line] derivatives, *i.e.,* [1-aza-12-cy-ano-11-aryltricyclo(8.3.0.$0^{4,9}$)trideca-2,4,6,-8,10,12-hexaenes] (**129a-d, 131**) from the Baylis-Hillman bromides *via* the treatment with quinoline and isoquinoline respectively. Our studies clearly indicates importance of the Baylis-Hillman alcohols (adducts), and the Baylis-Hillamn bromides as versatile substrates for synthesis of various heterocyclic molecules.

EXPERIMENTAL

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

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

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

Nuclear Magnetic Resonance Spectra:

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

(2) standard abbre*via*tion for multiplicity, that is, s = singlet, d = doublet, t = triplet, q = quartet, sept = septet, m = multiplet, dd = doublet of doublet, br = broad, (3) number of hydrogens integrated for the signal, (4) coupling constant *J* in Hertz.

Mass Spectral Analysis: Shimadzu LCMS 2010A mass spectrometer.

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

X-ray Crystallography:

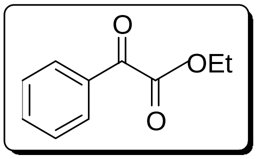
The X-ray diffraction measurements were carried out at 293 K on a Bruker SMART APEX CCD area detector system equipped with a graphite monochromator and a Mo-K_α fine-focus sealed tube (λ = 0.71073 A^o) operated at 1500 W power (50 kV, 30 mA). The detector was placed at a distance of 4.995 cm from the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

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

Ethyl phenylglyoxylate (99a):

This compound was prepared according to the literature procedure.[230]

To a stirred solution of diethyl oxalate (250 mmol, 36.5g, 33.85 mL) in THF (100 mL) was added a solution of phenylmagnesium bromide (100 mmol) [prepared from bromo-benzene (100 mmol, 15.70 g, 10.5 mL) and magnesium turnings (100 mmol, 2.4 g)] in THF (100 mL) slowly at -10 °C over a period of 1 h. The reaction mixture was quenched immediately with 2N HCl solution to a pH of 4.0 and extracted with ether (3 × 100 mL). The combined organic layer was dried over anhydrous sodium sulfate. Solvent was evaporated, the excess diethyl oxalate was distilled off and the residue was purified by column chromatography to provide the α-keto ester in 7.35 g (41%) to provide **99a**.



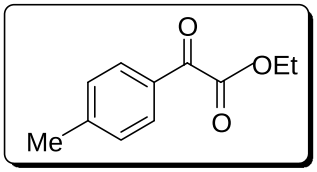
IR (Neat): ν 1738, 1689 cm^{-1}

^{1}H NMR (400 MHz): δ 1.42 (t, 3H, *J* = 7.2 Hz), 4.45 (q, 2H, *J* = 7.2 Hz), 7.55-7.71 (m, 3H), 8.01 (d, 2H, *J* = 7.2 Hz).

^{13}C NMR (50 MHz): δ 14.10, 62.32, 128.88, 130.00, 132.47, 134.90, 163.86, 186.45

Ethyl (4-methylphenyl)glyoxylate (99b):

This molecule was prepared *via* the treatment of 4-methylphenylmagnesium bromide with diethyl oxalate in THF, following the similar procedure described for the molecule **99a**, as a colorless liquid.



Reaction time: 1 h

Yield: 65%

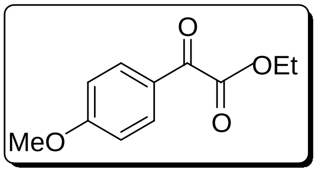
IR (Neat): ν 1738, 1682 cm^{-1}

^{1}H NMR (400 MHz): δ 1.42 (t, 3H, *J* = 6.8 Hz), 2.44 (s, 3H), 4.44 (q, 2H, *J* = 6.8 Hz), 7.31 (d, 2H, *J* = 8.8 Hz), 7.90 (d, 2H, *J* = 8.8 Hz).

^{13}C NMR (50 MHz): δ 14.11, 21.89, 62.23, 129.62, 130.15, 131.29, 146.25, 164.05, 186.12.

Ethyl (4-methoxyphenyl)glyoxylate (99c):

This molecule was obtained as a colorless liquid *via* the treatment of 4-methoxyphenylmagnesium bromide with diethyl oxalate in THF, following the similar procedure described for the molecule **99a**.



Reaction time: 1 h

Yield: 41%

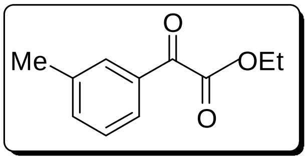
IR (Neat): ν 1720, 1608 cm^{-1}

^{1}H NMR (400 MHz): δ 1.41 (t, 3H, *J* = 7.2 Hz), 3.89 (s, 3H), 4.45 (q, 2H, *J* = 7.2 Hz), 6.98 (d, 2H, *J* = 8.8 Hz), 7.99 (d, 2H, *J* = 8.8 Hz).

^{13}C NMR (50 MHz): δ 13.84, 55.38, 61.90, 114.05, 125.17, 132.24, 164.04, 164.85, 184.76.

Ethyl (3-methylphenyl)glyoxylate (99d):

This compound was obtained as a colorless liquid *via* the reaction between 3-methyl phenylmagnesium bromide and diethyl oxalate in THF, following the similar procedure described for the molecule **99a**.



Reaction time: 1 h

Yield: 65%

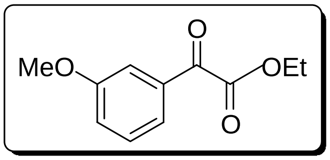
IR (Neat): ν 1738, 1687 cm^{-1}

^{1}H NMR (400 MHz): δ 1.42 (t, 3H, *J* = 7.2 Hz), 2.41 (s, 3H), 4.44 (q, 2H, *J* = 7.2 Hz), 7.18-7.50 (m, 2H), 7.70-7.82 (m, 2H).

^{13}C NMR (50 MHz): δ 13.98, 21.09, 62.10, 127.19, 128.67, 130.10, 132.38, 135.63, 138.73, 163.94, 186.59.

Ethyl (3-methoxyphenyl)glyoxylate (99e):

This molecule was obtained as a colorless liquid *via* the treatment of 3-methoxyphenylmagnesium bromide with diethyl oxalate in THF, following the similar procedure described for the molecule **99a**.



Reaction time: 1 h

Yield: 60%

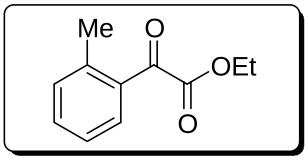
IR (Neat): ν 1736, 1689 cm^{-1}

^{1}H NMR (400 MHz): δ 1.42 (t, 3H, *J* = 7.2 Hz), 3.86 (s, 3H), 4.45 (q, 2H, *J* = 7.2 Hz), 7.20 (dd, 1H, *J* = 2.4 Hz & 8.0 Hz), 7.38-7.48 (m, 1H), 7.53 (s, 1H), 7.57 (d, 1H, *J* = 7.6 Hz).

^{13}C NMR (50 MHz): δ 14.08, 55.47, 62.30, 113.30, 121.76, 123.04, 129.90, 133.69, 159.94, 163.85, 186.31.

Ethyl (2-methylphenyl)glyoxylate (99f):

This molecule was obtained as a colorless liquid *via* the reaction between 2-methyl phenylmagnesium bromide and diethyl oxalate in THF, following the similar procedure described for the molecule **99a**.



Reaction time: 1 h

Yield: 47 %

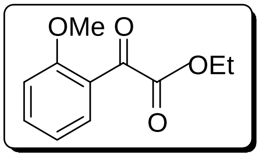
IR (Neat): ν 1738, 1682, 1601 cm^{-1}

^{1}H NMR (400 MHz): δ 1.40 (t, 3H, J = 6.8 Hz), 2.60 (s, 3H), 4.42 (q, 2H, J = 6.8 Hz), 7.07-7.36 (m, 3H), 7.44-7.52 (m, 1H), 7.69 (d, 1H, J = 8.0 Hz).

^{13}C NMR (50 MHz): δ 14.13, 21.47, 62.29, 125.96, 131.33, 132.29, 132.40, 133.70, 141.35, 164.68, 188.84.

Ethyl (2-methoxyphenyl)glyoxylate (99g):

This α-keto-ester was prepared *via* the treatment of 2-methoxyphenylmagnesium bromide with diethyl oxalate in THF, following the similar procedure described for the molecule **99a**, as a colorless liquid.



Reaction time: 1 h

Yield: 42 %

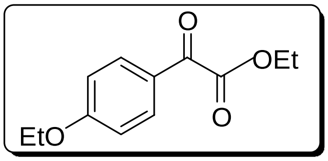
IR (Neat): ν 1741, 1672 cm^{-1}

^{1}H NMR (400 MHz): δ 1.39 (t, 3H, *J* = 6.8 Hz), 3.87 (s, 3H), 4.38 (q, 2H, *J* = 6.8 Hz), 6.98 (d, 1H, *J* = 8.8 Hz), 7.06-7.15 (m, 1H), 7.51-7.60 (m, 1H), 7.88 (d, 1H, *J* = 7.8 Hz).

^{13}C NMR (100 MHz): δ 14.16, 56.03, 61.80, 112.07, 112.33, 122.84, 130.78, 136.35, 160.32, 165.34, 186.65.

Ethyl (4-ethoxyphenyl)glyoxylate (99h):

This α- keto ester was prepared *via* the treatment of 4-ethoxyphenylmagnesium bromide with diethyl oxalate in THF, following the similar procedure described for the molecule **99a**, as a colorless liquid.



Reaction time: 1 h

Yield: 30%

IR (Neat): ν 1736, 1678 cm^{-1}

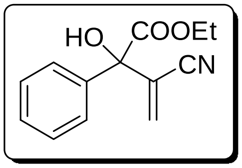
^{1}H NMR (400 MHz): δ 1.41-1.45 (m, 6H,), 4.14 (q, 2H, *J* = 7.2 Hz), 4.43 (q, 2H, *J* = 7.2 Hz), 6.95 (d, 2H, *J* = 8.8 Hz), 7.99 (d, 2H, *J* = 8.8 Hz).

^{13}C NMR (100 MHz): δ 14.12, 14.58, 62.13, 64.04, 114.67, 125.34, 132.57, 164.25, 164.49, 184.89.

3-Ethoxycarbonyl-3-hydroxy-3-phenyl-2-methylenepropanenitrile (100a):

This compound was prepared following the literature procedure.[231]

A mixture of ethyl phenylglyoxylate (**99a**) (20 mmol, 3.56 g), acrylonitrile (40 mmol, 2.12 g, 2.6 mL) and DABCO (30 mol %, 6.72 g) was kept at room temperature for 5 days. The reaction mixture was diluted with water (10 mL) and extracted with ether (3 x 15 mL). The combined organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and the residue, thus obtained, was purified by column chromatography (silica gel, 5% EtOAc in hexanes) to furnish the title compound in 58 % (2.68 g), as a colorless liquid.



IR (Neat): ν 3479, 2229, 1734, 1622 cm^{-1}

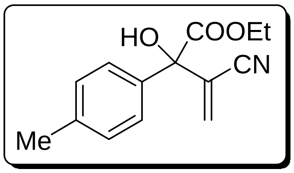
^{1}H NMR (400 MHz): δ 1.38 (t, 3H, *J* = 7.2 Hz), 4.17 (s, 1H), 4.39-4.44 (m, 2H), 6.15 (s, 1H), 6.19 (s, 1H), 7.34-7.45 (m, 3H), 7.50-7.58 (m, 2H).

^{13}C NMR (100 MHz): δ 13.88, 63.83, 78.62, 116.83, 125.32, 126.31, 128.59, 129.03, 132.81, 137.59, 171.58.

3-Ethoxycarbonyl-3-hydroxy-3-(4-methylphenyl)-2-methylenepropanenitrile (100b):

This product was obtained as a colorless liquid *via* the reaction between ethyl (4-methylphenyl)glyoxylate (**99b**) and acrylonitrile under the catalytic influence of DABCO, following the similar procedure described for the molecule **100a**.

Reaction Time: 5 d



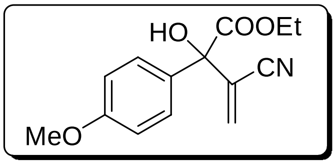
Yield: 71%

IR (Neat): ν 3477, 2229, 1738, 1614 cm^{-1}

^{1}H NMR (400 MHz): δ 1.37 (t, 3H, *J* = 7.2 Hz), 2.35 (s, 3H), 4.14 (s, 1H), 4.30-4.49 (m, 2H), 6.14 (s, 1H), 6.17 (s, 1H), 7.21 (d, 2H, *J* = 8.0 Hz), 7.40 (d, 2H, *J* = 8.0 Hz).

^{13}C NMR (100 MHz): δ 14.01, 21.15, 63.91, 78.55, 117.02, 125.41, 126.30, 129.42, 132.88, 134.69, 139.11, 171.87.

3-Ethoxycarbonyl-3-hydroxy-3-(4-methoxyphenyl)-2-methylenepropanenitrile (100c): This product was obtained as a colorless liquid *via* the reaction between ethyl (4-methoxyphenyl)glyoxylate (**99c**) and acrylonitrile under the influence of DABCO (cat) following the similar procedure described for the molecule **100a**.



Reaction Time: 5 d

Yield: 42%

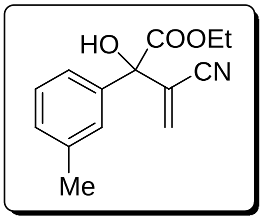
IR (Neat): ν 3501, 2229, 1736 cm^{-1}

^{1}H NMR (400 MHz): δ 1.38 (t, 3H, *J* = 7.2 Hz), 3.81 (s, 3H), 4.12 (s, 1H), 4.25-4.45 (m, 2H), 6.15 (s, 1H), 6.18 (s, 1H), 6.91 (d, 2H, *J* = 8.8 Hz), 7.43 (d, 2H, *J* = 8.8 Hz).

^{13}C NMR (100 MHz): δ 14.00, 55.34, 63.85, 78.38, 114.04, 117.02, 125.59, 127.77, 129.64, 132.72, 160.10, 171.87.

3-Ethoxycarbonyl-3-hydroxy-3-(3-methylphenyl)-2-methylenepropanenitrile (100d):

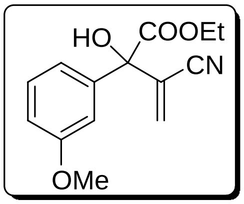
This tertiary alcohol was obtained as a colorless liquid *via* the Baylis-Hillman reaction between ethyl (3-methylphenyl)glyoxylate (**99d**) and acrylonitrile under the influence of DABCO as a catalyst following the similar procedure described for the molecule **100a**.



Reaction Time:	5 d
Yield:	47%
IR (Neat):	ν 3477, 2229, 1738, 1606 cm^{-1}
^{1}H NMR (400 MHz):	δ 1.38 (t, 3H, *J* = 7.2 Hz), 2.37 (s, 3H), 4.12 (s, 1H), 4.36-4.52 (m, 2H), 6.15 (s, 1H), 6.19 (s, 1H), 7.19 (d, 1H, *J* = 6.8 Hz), 7.16-7.30 (m, 2H), 7.32 (s, 1H).
^{13}C NMR (100 MHz):	δ 13.91, 21.47, 63.78, 78.67, 116.90. 123.43, 125.37, 126.87, 128.50, 129.81, 132.79, 137.57, 138.42, 171.67.

3-Ethoxycarbonyl-3-hydroxy-3-(3-methoxyphenyl)-2-methylenepropanenitrile (100e):

This adduct was obtained as a colorless liquid *via* the reaction between ethyl (3-methoxy phenyl)glyoxylate (**99e**) and acrylonitrile under the catalytic influence of DABCO, following the similar procedure described for the molecule **100a**.



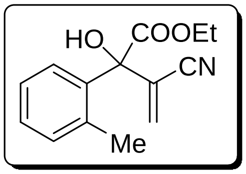
Reaction Time:	5 d
Yield:	62%
IR (Neat):	ν 3441, 2229, 1739 cm^{-1}

^{1}H NMR (400 MHz): δ 1.38 (t, 3H, *J* = 7.2 Hz), 3.81 (s, 3H), 4.18 (s, 1H), 4.35-4.50 (m, 2H), 6.14 (s, 1H), 6.18 (s, 1H), 6.90 (dd, 1H, *J* = 1.6 Hz & 7.0 Hz), 7.06-7.13 (m, 2H), 7.28-7.35 (m, 1H).

^{13}C NMR (100 MHz): δ 14.02, 55.35, 64.02, 78.53, 112.25, 114.61, 116.93, 118.66, 125.20, 129.73, 133.04, 139.02, 159.83, 171.61.

3-Ethoxycarbonyl-3-hydroxy-3-(2-methylphenyl)-2-methylenepropanenitrile (100f):

This adduct was obtained as a colorless liquid *via* the reaction between ethyl (2-methylphenyl)glyoxylate (**99f**) and acrylonitrile using DABCO as a catalyst following the similar procedure described for the molecule **100a**.



Reaction Time: 5 d

Yield: 44%

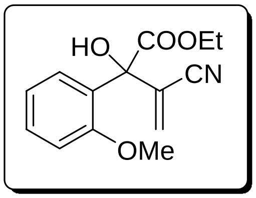
IR (Neat): ν 3423, 2235, 1743, 1608 cm^{-1}

^{1}H NMR (400 MHz): δ 1.36 (t, 3H, *J* = 7.2 Hz), 2.34 (s, 3H), 4.07 (s, 1H), 4.35-4.49 (m, 2H), 6.32 (s, 1H), 6.36 (s, 1H), 7.16-7.34 (m, 4H).

^{13}C NMR (100 MHz): δ 13.95, 20.40, 63.98, 80.09, 116.79, 125.07, 125.96, 127.62, 129.32, 132.67, 133.65, 135.86, 137.65, 172.77.

3-Ethoxycarbonyl-3-hydroxy-3-(2-methoxyphenyl)-2-methylenepropanenitrile (100g):

This Baylis-Hillman alcohol was obtained as a colorless liquid *via* the reaction between ethyl(2-methoxyphenyl)glyoxylate (**99g**) and acrylonitrile under the catalytic influence of DABCO, following the similar procedure described for the molecule **100a**.



Reaction Time: 5 d

Yield: 61%

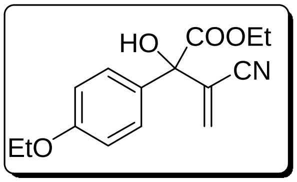
IR (Neat): ν 3468, 2229, 1739, 1601 cm^{-1}

^{1}H NMR (400 MHz): δ 1.31 (t, 3H, *J* = 7.2 Hz), 3.81 (s, 3H), 4.23-4.48 (m, 3H), 6.38 (s, 1H), 6.58 (s, 1H), 6.95 (d, 1H, *J* = 8.0 Hz), 7.00-7.09 (m, 1H), 7.28-7.42 (m, 2H).

^{13}C NMR (100 MHz): δ 13.95, 55.51, 63.20, 77.10, 111.66, 116.88, 120.99, 123.79, 127.10, 128.35, 130.73, 134.33, 156.73, 172.27.

3-Ethoxycarbonyl-3-hydroxy-3-(4-ethoxyphenyl)-2-methylenepropanenitrile (100h):

This compound was obtained as a colorless liquid *via* the reaction between ethyl (4-ethoxyphenyl)glyoxylate (**99h**) and acrylonitrile under the influence of DABCO (cat.) following the similar procedure described for the molecule **100a**.



Reaction Time: 5 d

Yield: 50%

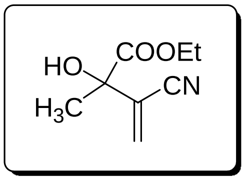
IR (Neat): ν 3474, 2229, 1738, 1610 cm^{-1}

^{1}H NMR (400 MHz): δ 1.30-1.48 (m, 6H), 4.04 (q, 2H, *J* = 7.2 Hz), 4.09 (s, 1H), 4.31-4.49 (m, 2H), 6.14 (s, 1H), 6.17 (s, 1H), 6.90 (d, 2H, *J* = 8.8 Hz), 7.43 (d, 2H, *J* = 8.8 Hz).

^{13}C NMR (100 MHz): δ 14.00, 14.78, 63.58, 63.83, 78.40, 114.57, 117.00, 125.68, 127.74, 129.47, 132.62, 159.52, 171.89.

3-Ethoxycarbonyl-3-hydroxy-2-methylenebutanenitrile (100i):

This molecule was obtained as a colorless liquid *via* the Baylis-Hillman coupling of acrylonitrile with ethyl pyruvate under the influence of DABCO as a catalyst following the similar procedure described for the molecule **100a**.



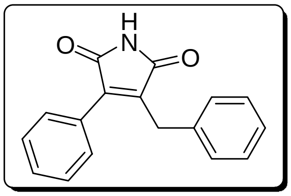
Reaction Time:	5 d
Yield:	30%
IR (Neat):	ν 3466, 2229, 1738, 1624 cm^{-1}
^{1}H NMR (400 MHz):	δ 1.35 (t, 3H, *J* = 7.2 Hz), 1.66 (s, 3H), 3.88 (bs, 1H), 4.25-4.40 (m, 2H), 6.10 (s, 1H), 6.28 (s, 1H).
^{13}C NMR (100 MHz):	δ 13.96, 24.74, 63.47, 74.02, 116.62, 125.68, 131.52, 173.13.

3-Benzyl-4-phenyl-1*H*-pyrrole-2, 5-dione (101a):

To a stirred solution of 3-ethoxycarbonyl-3-hydroxy-3-phenyl-2-methylenepropan-enitrile (**100a**) (1 mmol, 0.231 g) in benzene (6 mL) was added methanesulfonic acid (3 mmol, 0.288 g, 0.2 mL) at room temperature and heated under reflux for 4 h. Then the reaction mixture was allowed to cool to room temperature and diluted with water (10 mL). Aqueous $NaHCO_3$ solution was added slowly to neutralize the acid and extracted with ether (3 x 15 mL). The combined organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and the residue, thus obtained, was purified by column chromatography (silica gel, 5% EtOAc in hexanes) to furnish the compound **101a** as a colorless solid in 79 % isolated yield.

Mp: 118-120 °C

IR (KBr): ν 3335, 1776, 1699 cm^{-1}



^{1}H NMR (400 MHz): δ 3.93 (s, 2H), 7.16-7.32 (m, 5H), 7.42-7.57 (m, 5H), 7.81 (bs, 1H).

^{13}C NMR (100 MHz): δ 29.76, 126.92, 128.42, 128.49, 128.74, 128.91, 129.47, 130.07, 136.99, 139.31, 139.56, 171.02, 171.61.

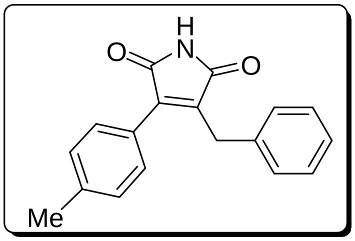
LCMS (*m/z*): 262 $(M-H)^+$

Anal. Calcd. for $C_{17}H_{13}NO_2$: C, 77.55; H, 4.98; N, 5.32.

Found: C, 77.56; H, 4.97; N, 5.25.

3-Benzyl-4-(4-methylphenyl)-1*H*-pyrrole-2, 5-dione (101b):

This compound was obtained as a colorless solid *via* the reaction between 3-ethoxycarbonyl-3-hydroxy-3-(4-methylphenyl)-2-methylenepropanenitrile (**100b**) and benzene under the influence of methanesulfonic acid, following the similar procedure described for the molecule **101a**.



Reaction Time: 4 h

Yield: 70%

Mp: 150-152°C

IR (KBr): ν 3223, 1774, 1716 cm^{-1}

^{1}H NMR (400 MHz): δ 2.38 (s, 3H), 3.93 (s, 2H), 7.16-7.33 (m, 7H), 7.44 (d, 2H, *J* = 8.4 Hz), 7.86 (bs, 1H).

^{13}C NMR (100 MHz): δ 21.52, 29.77, 125.61, 126.87, 128.48, 128.89, 129.44, 129.50,137.16, 138.42, 139.58, 140.46, 171.15, 171.73.

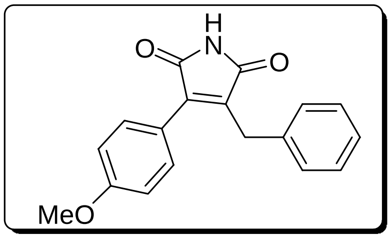
LCMS (*m/z*): 276 (M-H)$^{+}$

Anal. Calcd. for $C_{18}H_{15}NO_2$: C, 77.96; H, 5.45; N, 5.05.

Found: C, 77.92; H, 5.46; N, 5.13.

3-Benzyl-4-(4-methoxyphenyl)-1*H*-pyrrole-2, 5-dione (101c):

The reaction of 3-ethoxycarbonyl-3-hydroxy-3-(4-methoxyphenyl)-2-methyleneprop-anenitrile (**100c**) with benzene under the influence of methanesulfonic acid, following the similar procedure described for the molecule **101a**, provided the title compound as a colorless solid.



Reaction Time: 4 h

Yield: 63%

Mp: 160-162°C

IR (KBr): ν 3192, 1768, 1709 cm^{-1}

^{1}H NMR (400 MHz): δ 3.84 (s, 3H), 3.94 (s, 2H), 6.95 (d, 2H, *J* = 8.8 Hz), 7.17-7.36 (m, 5H), 7.53 (d, 2H, *J* = 8.8 Hz), 7.73 (bs, 1H).

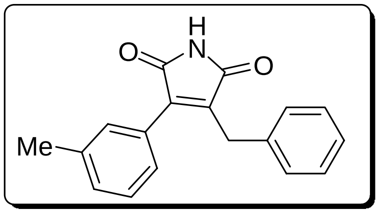
^{13}C NMR (100 MHz): δ 29.82, 55.44, 114.35, 121.01, 126.91, 128.43, 128.96, 131.23,137.08, 137.23, 139.18, 161.15, 171.09, 171.60.

LCMS (*m/z*): 292 $(M-H)^+$

Anal. Calcd. for $C_{18}H_{15}NO_3$: C, 73.71; H, 5.15; N, 4.78.
Found: C, 73.82; H, 5.13; N, 4.84.

3-Benzyl-4-(3-methylphenyl)-1*H*-pyrrole-2, 5-dione (101d):

This product was obtained as a colorless solid *via* the reaction between 3-ethoxycarbonyl-3-hydroxy-3-(3-methlyphenyl)-2-methylenepropanenitrile (**100d**) and benzene under the influence of methanesulfonic acid, following the similar procedure described for the molecule **101a**.



Reaction Time: 4 h

Yield: 76%

Mp: 70-72 °C

IR (KBr): ν 3375, 1768, 1707 cm^{-1}

^{1}H NMR (400 MHz): δ 2.37 (s, 3H), 3.92 (s, 2H), 7.16-7.36 (m, 9H), 7.78 (bs, 1H).

^{13}C NMR (100 MHz): δ 21.46, 29.82, 126.56, 126.88, 128.34, 128.56, 128.62, 128.87, 130.08, 130.88, 137.18, 138.44, 139.21, 139.77, 171.07, 171.69.

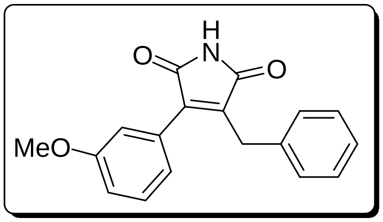
LCMS (*m/z*): 278 $(M+H)^+$

Anal. Calcd. for $C_{18}H_{15}NO_2$: C, 77.96; H, 5.45; N, 5.05.

Found: C, 77.91; H, 5.48; N, 4.99.

3-Benzyl-4-(3-methoxyphenyl)-1*H*-pyrrole-2, 5-dione (101e):

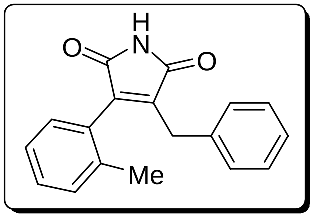
This product was obtained as a colorless solid *via* the treatment of 3-ethoxycarbonyl-3-hydroxy-3-(3-methoxyphenyl)-2-methylenepropanenitrile (**100e**) with benzene under the influence of methanesulfonic acid, following the similar procedure described for the molecule **101a**.



Reaction Time:	4 h
Yield:	55%
Mp:	103-105 °C
IR (KBr):	ν 3288, 1772, 1712 cm^{-1}
^{1}H NMR (400 MHz):	δ 3.75 (s, 3H), 3.94 (s, 2H), 6.97-7.03 (m, 2H), 7.09-7.14 (m, 1H), 7.18-7.32 (m, 5H), 7.34-7.39 (m, 1H), 7.44 (bs, 1H).
^{13}C NMR (100 MHz):	δ 29.76, 55.32, 114.71, 116.16, 121.90, 126.91, 128.49, 128.91, 129.62, 129.82, 137.06, 139.45, 139.48, 159.67, 170.88, 171.55.
LCMS (*m/z*):	294 (M+H)$^+$
Anal. Calcd. for $C_{18}H_{15}NO_3$:	C, 73.71; H, 5.15; N, 4.78.
Found:	C, 73.80; H, 5.13; N, 4.71.

3-Benzyl-4-(2-methylphenyl)-1*H*-pyrrole-2, 5-dione (101f):

This molecule was obtained as a colorless solid *via* the reaction between 3-ethoxycarbonyl-3-hydroxy-3-(2-methylphenyl)-2-methylenepropanenitrile (**100f**) and benzene under the influence of methanesulfonic acid, following the similar procedure described for the molecule **101a**.



Reaction Time: 4 h

Yield: 65%
Mp: 96-98^{o}C

IR (KBr): ν 3285, 1774, 1712 cm^{-1}

^{1}H NMR (400 MHz): δ 2.06 (s, 3H), 3.58 (s, 1H)*, 3.65 (s, 1H) *, 6.87-7.36 (m, 9H), 7.59 (bs, 1H).

^{13}C NMR (100 MHz): δ 20.05, 29.90, 125.94, 126.82, 128.14, 128.67, 128.85, 129.36, 129.75, 130.56, 136.55, 136.87, 141.87, 142.25, 170.64, 171.48.

These peaks look like unresolved ABq. but appear as two close singlets.

We have also recoeded ^{1}H and ^{13}C NMR spectra at 5^{o}C and 40^{o}C with a view to understand the conformation stability of the molecule at different temperatures

^{1}H NMR at 5^{o}C (400 MHz): δ 2.07 (s, 3H), 3.56 & 3.68 (ABq, 2H, *J* = 14.0 Hz), 6.90-7.34 (m, 9H), 7.83 (bs, 1H).

^{13}C NMR at 5^{o}C (100 MHz)**:** δ 20.16, 29.92, 126.03, 126.88, 127.95, 128.73, 128.83, 129.35, 129.87, 130.63, 136.47, 136.83, 141.77, 142.22, 170.47, 171.28.

^{1}H NMR at 40^{o}C (400 MHz): δ 2.04 (s, 3H), 3.61 (bs, 2H), 6.90-7.31 (m, 9H), 7.41 (bs, 1H).

^{13}C NMR at 40°C (100 MHz): δ 20.04, 29.98, 125.96, 126.86, 128.26, 128.70, 128.90, 129.41, 129.78, 130.59, 136.62, 136.93, 142.01, 142.35, 170.43, 171.30.

At 5°C in ^{1}H NMR spectrum of **(101f)** benzylic protons appear as ABq at δ 3.56 & 3.68 (ABq, 2H, *J* = 14.2 Hz). At room temperature they appear as two singlets at δ 3.58 (s, 1H), 3.65 (s, 1H), while at 40 °C they appear as broad singlet at δ 3.68 (bs, 2H). However ^{13}C NMR is almost the same at these temperatures. From these spectral studies it is quite clear that there is conformational rigidity at 5°C, while at room temperature and at 40°C there is conformational flexibility.

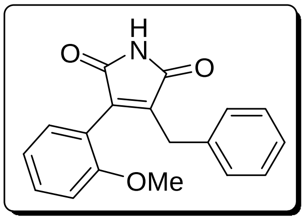
LCMS (*m/z*): 278 $(M+H)^+$

Anal. Calcd. for $C_{18}H_{15}NO_2$: C, 77.96; H, 5.45; N, 5.05.

Found: C, 78.05; H, 5.42; N, 5.08.

3-Benzyl-4-(2-methoxyphenyl)-1*H*-pyrrole-2, 5-dione (101g):

The reaction of 3-ethoxycarbonyl-3-hydroxy-3-(2-methoxyphenyl)-2-methylene-propanenitrile (**100g**) with benzene under the influence of methanesulfonic acid, following the similar procedure described for the molecule **101a** provided the title compound as a colorless solid.



Reaction Time: 4 h

Yield: 57%

Mp: 98-100°C

IR (KBr): ν 3296, 1774, 1712 cm^{-1}

^{1}H NMR (400 MHz): δ 3.74 (s, 3H), 3.75 (s, 2H), 6.95 (d, 1H, *J* = 8.4 Hz), 6.99-7.24 (m, 7H), 7.36-7.44 (m, 1H), 7.56 (bs, 1H).

^{13}C NMR (100 MHz): δ 30.51, 55.49, 111.29, 117.51, 120.55, 126.53, 128.46, 128.74, 130.88, 131.28, 136.96, 138.41, 141.88, 157.24, 170.82, 171.60.

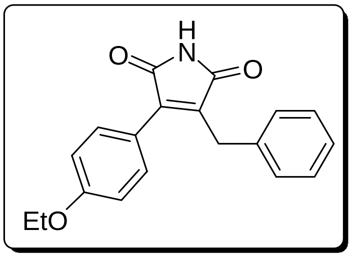
LCMS (*m/z*): 294 (M+H)$^{+}$

Anal. Calcd. for $C_{18}H_{15}NO_3$: C, 73.71; H, 5.15; N, 4.78.

Found: C, 73.63; H, 5.16; N, 4.69.

3-Benzyl-4-(4-ethoxyphenyl)-1*H*-pyrrole-2, 5-dione (101h):

Th reaction between 3-ethoxycarbonyl-3-hydroxy-3-(4-ethoxyphenyl)-2-methylenepropanenitrile (**100h**) and benzene under the influence of methanesulfonic acid, following the similar procedure described for the molecule **101a** furnished the title compound as a colorless solid.



Reaction Time: 4 h

Yield: 54%

Mp: 176-178°C

IR (KBr): ν 3269, 1772, 1714 cm^{-1}

^{1}H NMR (400 MHz): δ 1.43 (t, 3H, *J* = 6.8 Hz), 3.94 (s, 2H), 4.08 (q, 2H, *J* = 6.8 Hz), 6.94 (d, 2H, *J* = 8.0 Hz), 7.15-7.33 (m, 5H), 7.35 (bs, 1H), 7.53 (d, 2H, *J* = 8.0 Hz).

^{13}C NMR (100 MHz): δ 14.79, 29.84, 63.70, 114.84, 120.83, 126.90, 128.43, 128.95, 131.23, 136.96, 137.26, 139.24, 160.58, 171.00, 171.49.

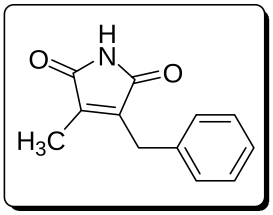
LCMS (*m/z*): 306 $(M-H)^+$

Anal. Calcd. for $C_{19}H_{17}NO_3$: C, 74.25; H, 5.58; N, 4.56.

Found: C, 74.27; H, 5.52; N, 4.49.

3-Benzyl-4-methyl-1*H*-pyrrole-2, 5-dione (101i):

This compound was obtained as a colorless solid *via* the reaction between 3-ethoxycarbonyl-3-hydroxy-2-methylenebutanenitrile (**100i**) and benzene under the influence of methanesulfonic acid, following the similar procedure described for the molecule **101a**.



Reaction Time: 4 h

Yield: 66%

Mp: 78-80°C

IR (KBr): ν 3314, 1774, 1705 cm^{-1}

^{1}H NMR (400 MHz): δ 1.95 (s, 3H), 3.71 (s, 2H), 7.20-7.34 (m, 5H), 7.49 (bs, 1H).

^{13}C NMR (100 MHz): δ 8.88, 29.58, 126.96, 128.80, 128.93, 136.75, 138.97, 140.38, 171.55, 171.87.

LCMS (*m/z*): 200 $(M-H)^+$

Anal. Calcd. for $C_{12}H_{11}NO_2$: C, 71.63; H, 5.51; N, 6.96.

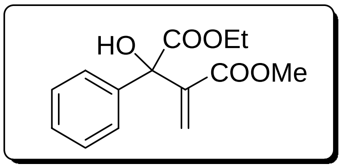
Found: C, 71.57; H, 5.52; N, 7.01.

Methyl 3-ethoxycarbonyl-3-hydroxy-3-phenyl-2-methylenepropanoate (102a):

This compound was prepared following the literature procedure.[231]

A mixture of ethyl phenylglyoxylate (**99a**) (20 mmol, 3.56 g), methyl acrylate (40 mmol, 3.44 g, 3.5 mL) and DABCO (30 mol%, 6.72 g) was kept at room temperature for 10 days. The reaction mixture was diluted with water (10 mL) and extracted with ether (3 x 15 mL). The combined organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and the residue, thus obtained, was purified by column chromatography (silica gel, 5% EtOAc in hexanes) to furnish the title compound **102a** in 60 % (3.2 g) as a colorless liquid

IR (Neat): ν 3499, 1730, 1693, 1631 cm^{-1}

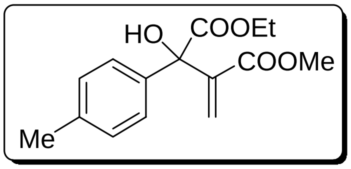


^{1}H NMR (400 MHz): δ 1.27 (t, 3H, *J* = 7.2 Hz), 3.70 (s, 3H), 4.28 (q, 2H, *J* = 7.2 Hz), 4.35 (s, 1H), 5.36 (s, 1H), 6.36 (s, 1H), 7.30-7.40 (m, 3H), 7.60-7.67 (m, 2H).

^{13}C NMR (100 MHz): δ 13.95, 52.17, 62.47, 78.70, 126.79, 128.13, 128.30, 129.05, 37.83, 142.94, 166.78, 173.27.

Methyl 3-ethoxycarbonyl-3-hydroxy-3-(4-methylphenyl)-2-methylenepropanoate (102b):

This allyl alcohol was obtained as a colorless liquid *via* the reaction between ethyl (4-methylphenyl)glyoxylate (**99b**) and methyl acrylate under the catalytic influence of DABCO, following the similar procedure described for the molecule **102a**.



Reaction Time: 12 d

Yield: 57%

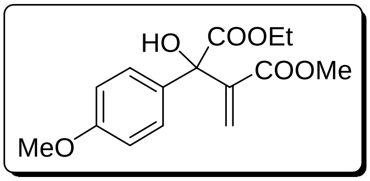
IR (Neat): ν 3497, 1732, 1631 Cm^{-1}

^{1}H NMR (400 MHz): δ 1.28 (t, 3H, *J* = 6.8 Hz), 2.35 (s, 3H), 3.80 (s, 3H), 4.28 (q, 2H, *J* = 6.8 Hz), 5.40 (s, 1H), 6.30 (s, 1H), 7.18 (d, 2H, *J* = 8.4 Hz), 7.50 (d, 2H, *J* = 8.4 Hz).

^{13}C NMR (100 MHz): δ 13.86, 20.89, 52.01, 62.27, 78.50, 126.60, 128.71, 134.83, 137.88, 142.95, 166.70, 173.27.

Methyl 3-ethoxycarbonyl-3-hydroxy-3-(4-methoxyphenyl)-2-methylenepropanoate (102c):

This adduct was obtained as a colorless liquid *via* the reaction between ethyl (4-methoxy phenyl)glyoxylate (**99c**) and methyl acrylate under the influence of DABCO as a catalyst following the similar procedure described for the molecule **102a**.



Reaction Time: 10 d

Yield: 47%

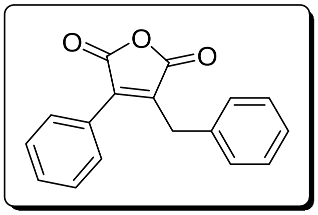
IR (Neat): υ 3495, 1734, 1631, 1610 cm^{-1}

^{1}H NMR (400 MHz): δ 1.28 (t, 3H, *J* = 7.2 Hz), 3.80 (s, 3H), 3.82 (s, 3H),4.29 (q, 2H, *J* = 7.2 Hz), 5.41 (s, 1H), 6.36 (s, 1H), 6.90 (d, 2H, *J* = 8.6 Hz), 7.53 (d, 2H, *J* = 8.6 Hz).

^{13}C NMR (100 MHz): δ 14.00, 52.18, 55.26, 62.44, 78.45, 113.53, 128.08, 129.01, 129.81, 143.15, 159.57, 166.90, 173.47.

3-Benzyl-4-phenylfuran-2, 5-dione (103a):

To a stirred solution of methyl 3-ethoxycarbonyl-3-hydroxy-3-phenyl-2-methylene propanoate (**102a**) (1 mmol, 0.264 g) in benzene (6 mL) was added methanesulfonic acid (3 mmol, 0.288 g, 0.2 mL) at room temperature and heated under reflux for 4 h. Then the reaction mixture was allowed to cool to room temperature and diluted with water (10 mL). Aqueous $NaHCO_3$ solution was added slowly to neutralize the acid and extracted with ether (3 x 15 mL). The combined organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and the residue, thus obtained, was purified by column chromatography (silicagel, 5% EtOAc in hexanes) to furnish the compound **103a** as a colorless solid in 52 % (0.137 g) yield.



Reaction Time: 4 h

Mp: 58-60 ^{o}C

IR (KBr): ν 1763, 1651 cm^{-1}

^{1}H NMR (400 MHz): δ 4.02 (s, 2H), 7.18 (d, 2H, *J* = 6.8 Hz), 7.22-7.35 (m, 3H), 7.45-7.54 (m, 3H), 7.56-7.64 (m, 2H).

^{13}C NMR (100 MHz): δ 30.45, 127.12, 127.33, 128.43, 128.99, 129.05, 129.36, 131.16, 135.45, 140.64, 141.06, 164.83, 165.81.

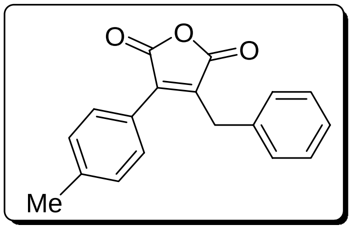
LCMS (*m/z*): 263 $(M-H)^+$

Anal. Calcd. for $C_{17}H_{12}O_3$: C, 77.26; H, 4.58.

Found: C, 77.30; H, 4.56.

3-Benzyl-4-(4-methylphenyl)furan-2, 5-dione (103b):

This compound was obtained as a colorless solid *via* the reaction between 3-ethoxycarbonyl-3-hydroxy-3-(4-methylphenyl)-2-methylenepropanoate (**102b**) and benzene under the influence of methanesulfonic acid, following the similar procedure described for the molecule **103a**.



Reaction Time: 4 h

Yield: 45%

Mp: 76-78°C

IR (KBr): ν 1768, 1653 cm^{-1}

^{1}H NMR (400 MHz): δ 2.41 (s, 3H), 4.01 (s, 2H), 7.19 (d, 2H, *J* = 8.0 Hz), 7.22-7.34 (m, 5H), 7.52 (d, 2H, *J* = 8.0 Hz).

^{13}C NMR (100 MHz): δ 21.60, 30.54, 124.43, 127.36, 128.45, 129.12, 129.42, 129.83, 135.66, 139.57, 141.11, 141.98, 165.07, 166.07.

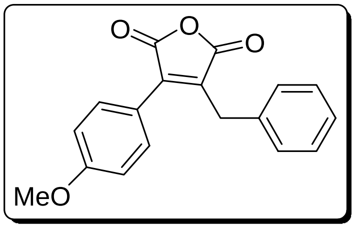
LCMS (*m/z*): 277 $(M-H)^+$

Anal. Calcd. for $C_{18}H_{14}O_3$: C, 77.68; H, 5.07.

Found: C, 77.81; H, 5.11.

3-Benzyl-4-(4-methoxyphenyl)furan-2, 5-dione (103c):

The reaction of 3-ethoxycarbonyl-3-hydroxy-3-(4-methoxyphenyl)-2-methylenepropanoate (**102c**) with benzene under the influence of methanesulfonic acid, following the similar procedure described for the molecule **103a** furnished the title compound as a colorless solid.

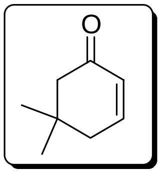


Reaction Time:	4 h
Yield:	40 %
Mp:	110-112°C
IR (KBr):	ν 1761, 1648 cm^{-1}
^{1}H NMR (400 MHz):	δ 3.86 (s, 3H), 4.03 (s, 2H), 7.00 (d, 2H, *J* = 8.8 Hz), 7.17-7.38 (m, 5H), 7.64 (d, 2H, *J* = 8.8 Hz).
^{13}C NMR (100 MHz):	δ 30.61, 55.54, 114.69, 119.83, 127.39, 128.38, 129.18, 131.44, 135.77, 137.78, 140.65, 162.10, 165.36, 166.30.
LCMS (*m/z*):	295 $(M+H)^+$
Anal. Calcd. for $C_{18}H_{14}O_4$:	C, 73.46; H, 4.79.
Found:	C, 73.39; H, 4.74.

5, 5-Dimethylcyclohex-2-enone (111a):

This molecule was prepared according to the known literature procedure.[232]

A mixture of 5,5-dimethyl-1,3-cyclohexanedione (dimedone) (137.5 mmol, 19.2 g), *p*-toluenesulfonic acid, (0.5 g) absolute ethanol (17.5 mL) in benzene (150 mL) was heated under reflux with conitinuous removal of water. After 24 h the mixture was fractionally distilled to provide the enol ether which crystalized on keeping in the freezer. This crystalline solid was dissolved in dry ether (150 mL) and lithium aluminum hydride (50 mmol, 1.9 g) was added carefully with stirring over a period of 1 h at room temperature. Reaction mixture was poured into water carefully and diluted with aqueous H_2SO_4. Organic layer was separated and the aqueous layer was extracted with ether (3 × 50 mL). Combined organic layer was dried over anhydrous Na_2SO_4. Solvent was removed and the residue thus obtained, was purified by column chromatography 52% (9.2 g) yield, as a colorless liquid.



IR (Neat): ν 1680, 1620 cm^{-1}

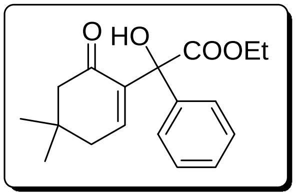
^{1}H NMR: δ 1.04 (s, 6H), 2.22-2.24 (m, 4H), 5.90-6.10 (m, 1H,), 6.79-6.93 (m,1H)

^{13}C NMR: δ 28.41, 33.96, 40.03, 51.89, 129.10, 148.38, 199.95

Ethyl 2-hydroxy-2-phenyl-2-(5,5-dimethylcyclohex-2-en-1-on-2-yl)ethanoate (112a):

This compound was prepared following the literature procedure.[105]

To a stirred solution of ethyl phenylglyoxylate (**99a**) (10 mmol, 1.78 g, 1.6 mL) and 5,5-dimethylcyclohex-2-en-1-one (**111a**) (30 mmol, 3.72 g) in CH_2Cl_2 (3 mL), was added titanium tetrachloride (10 mmol, 5 mL of 2M solution in CH_2Cl_2) at 0 °C. After stirring at room temperature for 6 h, the reaction mixture was quenched with water (5 mL) and extracted with ether (3 × 10 mL). The combined organic layer was dried over anhydrous sodium sulfate. Solvent was evaporated and the residue, thus obtained, was purified by column chromatography (silica gel, 10% EtOAc in hexanes) to furnish the pure compound **112a** in 61% (1.86 g) isolated yield, as a colorless liquid.



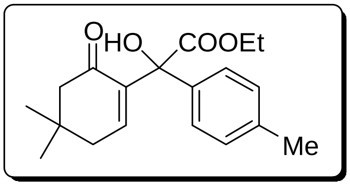
IR (Neat): ν 3460, 1747, 1672 cm^{-1}

^{1}H NMR (400 MHz): δ 1.03 (s, 3H), 1.07 (s, 3H), 1.25 (t, 3H, *J* = 7.2 Hz), 2.15-2.24 (m, 2H), 2.32 & 2.39(ABq, 2H, *J* = 16.4 Hz), 4.24 (q, 2H, *J* = 7.2 Hz), 4.34 (s, 1H), 6.27 (t, 1H, *J* = 4.0 Hz), 7.32-7.41 (m, 3H), 7.59 (d, 2H, *J* = 7.2 Hz).

^{13}C NMR (50 MHz): δ 14.04, 27.47, 28.69, 34.03, 39.90, 51.99, 62.22, 78.12, 126.79, 128.19, 137.90, 141.46, 147.08, 173.72, 199.65.

Ethyl 2-hydroxy-2-(4-methylphenyl)-2-(5,5-dimethylcyclohex-2-en-1-on-2-yl)ethanoate (112b):

This adduct was obtained as a colorless liquid *via* the reaction between ethyl(4-methylphenyl)glyoxylate (**99b**) and 5, 5-dimethylcyclohex-2-en-1-one under the influence of titanium tetrachloride, following the similar procedure described for the molecule **112a**.



Reacton time: 6 h

Yield: 32%

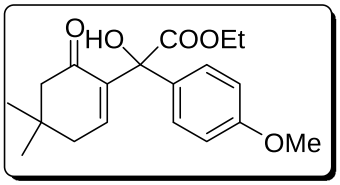
IR (Neat): ν 3503, 1728, 1672 cm^{-1}

^{1}H NMR (400 MHz): δ 1.03 (s, 3H), 1.07 (s, 3H), 1.25 (t, 3H, *J* = 7.2 Hz), 2.10-2.42 (m, 7H), 4.24 (q, 2H, *J* = 7.2 Hz), 4.30 (s, 1H), 6.21-6.34 (m, 1H), 7.18 (d, 2H, *J* = 7.6 Hz), 7.46 (d, 2H, *J* = 7.6 Hz).

^{13}C NMR (50 MHz): δ 14.02, 21.06, 27.44, 28.67, 34.02, 39.85, 51.97, 62.13, 77.98, 126.64, 128.88, 134.84, 137.83, 141.45, 147.03, 173.81, 199.70.

Ethyl 2-hydroxy-2-(4-methoxyphenyl)-2-(5,5-dimethylcyclohex-2-en-1-on-2-yl)ethanoate (112c):

This compound was isolated as a colorless viscous liquid *via* the $TiCl_4$ mediated Baylis-Hillman reaction between ethyl (4-methoxyphenyl)glyoxylate (**99c**) and 5,5-dimethyl-cyclohex-2-enone, following the similar procedure described for the molecule **112a**.



Reaction time: 6 h

Yield: 36%

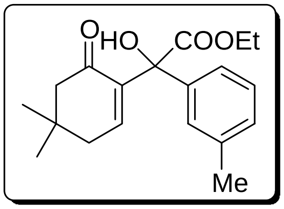
IR (Neat): ν 3503, 1736, 1666 cm^{-1}

^{1}H NMR (400 MHz): δ 1.03 (s, 3H), 1.07 (s, 3H), 1.25 (t, 3H, *J* = 8.0 Hz), 2.18-2.41 (m, 4H), 3.82 (s, 3H), 4.25 (q, 2H, *J* = 8.0 Hz), 4.30 (s, 1H), 6.31 (t, 1H, *J* = 4.0 Hz), 6.90 (d, 2H, *J* = 8.8 Hz), 7.49 (d, 2H, *J* = 8.8 Hz).

^{13}C NMR (50 MHz): δ 14.10, 27.51, 28.73, 34.09, 39.93, 52.04, 55.34, 62.18, 113.60, 128.06, 129.85, 141.64, 147.03, 159.47, 173.91, 199.79.

Ethyl 2-hydroxy-2-(3-methylphenyl)-2-(5,5-dimethylcyclohex-2-en-1-on-2-yl)ethanoate (112d):

This molecule was prepared *via* the coupling of ethyl(3-methylphenyl)glyoxylate (**99d**) with 5,5-dimethylcyclohex-2-en-1-one under the influence of $TiCl_4$, following the similar procedure described for the molecule **112a** as a colorless viscous liquid.



Reaction time: 6 h

Yield: 27%

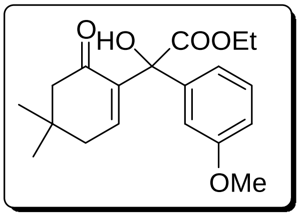
IR (Neat): ν 3506, 1732, 1678 cm^{-1}

^{1}H NMR (400 MHz): δ 1.03 (m, 3H), 1.08 (s, 3H), 1.25 (t, 3H, *J* = 7.2 Hz), 2.12-2.46 (m, 7H), 4.24 (q, 2H, *J* = 7.2 Hz), 4.34 (s, 1H), 6.28 (t, 1H, *J* = 4.4 Hz), 7.13 (d, 1H, *J* =7.2 Hz), 7.21-7.27 (m, 1H), 7.34 (d, 1H, *J* = 8.0Hz), 7.43 (s, 1H).

^{13}C NMR (50 MHz): δ 13.99, 21.59, 27.51, 28.57, 33.99, 39.82, 51.95, 62.08, 78.11, 123.83, 127.22, 127.96, 128.81, 137.66, 137.88, 141.38, 147.03, 173.68, 199.74.

Ethyl 2-hydroxy-2-(3-methoxyphenyl)-2-(5,5-dimethylcyclohex-2-en-1-on-2-yl)ethanoate (112e):

This Baylis-Hillman alcohol was prepared as a colorless viscous liquid *via* the coupling of ethyl (3-methoxyphenyl)glyoxylate (**99e**) with 5,5-dimethylcyclohex-2-en-1-one under the influence of TiCl$_4$, following the similar procedure described for the molecule **112a.**



Reaction time: 6 h

Yield: 48%

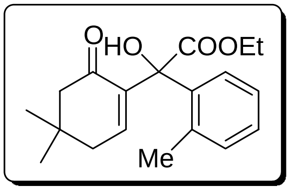
IR (Neat): ν 3470, 1734, 1674 cm^{-1}

^{1}H NMR (400 MHz): δ 1.04 (s, 3H), 1.07 (s, 3H), 1.26 (t, 3H, *J* = 6.8 Hz), 2.17-2.41 (m, 4H), 3.81 (s, 3H), 4.25 (q, 2H, *J* =6.8 Hz), 4.34 (bs, 1H), 6.31 (t, 1H, *J* = 4.0 Hz), 6.86 (d, 1H, *J* = 8.0 Hz), 7.13 (d, 1H, *J* = 7.6 Hz), 7.20 (s, 1H), 7.26-7.30 (m, 1H).

^{13}C NMR (100 MHz): δ 14.09, 27.48, 28.74, 34.09, 39.90, 52.00, 55.32, 62.31, 78.07, 112.50, 113.76, 119.18, 129.16, 139.51, 141.25, 147.29, 159.63, 173.66, 199.71.

Ethyl 2-hydroxy-2-(2-methylphenyl)-2-(5,5-dimethylcyclohex-2-en-1-on-2-yl)ethanoate (112f):

This Baylis-Hillman alcohol was prepared by the treatment of ethyl (2-methylphenyl)-glyoxylate (**99f**) with 5,5-dimethylcyclohex-2-en-1-one in the presence of TiCl$_4$, following the similar procedure described for the molecule **112a**, as a colorless viscous liquid.



Reaction time: 6 h

Yield: 54%

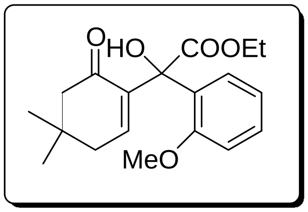
IR (Neat): ν 3487, 1739, 1672 cm^{-1}

^{1}H NMR (400 MHz): δ 1.07 (s, 6H), 1.28 (t, 3H, J = 7.2 Hz), 2.20-2.45 (m, 7H), 4.28-4.34 (m, 2H), 4.85 (s, 1H), 6.22 (t, 1H, J = 4.2 Hz), 7.15-7.28 (m, 4H).

^{13}C NMR (100 MHz): δ 14.09, 22.10, 27.67, 28.59, 34.28, 40.07, 52.30, 62.12, 81.76, 125.67, 127.20, 128.30, 132.62, 136.11, 138.17, 138.31, 147.38, 173.72, 201.16.

Ethyl 2-hydroxy-2-(2-methoxyphenyl)-2-(5,5-dimethylcyclohex-2-en-1-on-2-yl)ethanoate (112g):

The compound was obtained by the reaction between ethyl (2-methoxyphenyl)-glyoxylate (**99g**) and 5,5-dimethylcyclohex-2-enone in the presence of TiCl$_4$, following the similar procedure described for the molecule **112a**, as a colorless viscous liquid.



Reaction time: 6 h

Yield: 37%

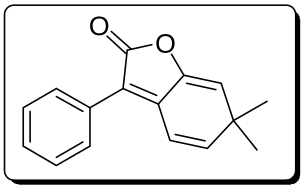
IR (Neat): ν 3312, 1730, 1645 cm^{-1}

^{1}H NMR (400 MHz): δ 1.02 (s, 3H), 1.11 (s, 3H), 1.23 (t, 3H, J = 7.6 Hz), 2.10-2.52 (m, 4H), 3.74 (s, 3H), 4.10-4.35 (m, 2H), 5.95 (s, 1H), 6.25 (t, 1H, *J* = 4.0 Hz), 6.90 (d, 2H, *J* = 8.0 Hz), 7.03 (t, 1H, *J* = 7.6 Hz), 7.33 (t, 1H, *J* = 7.6Hz), 7.58 (d, 1H, *J* = 7.6 Hz).

^{13}C NMR (100 MHz): δ 14.10, 27.96, 28.41, 34.11, 40.19, 52.47, 55.52, 61.50, 79.13, 111.16, 121.31, 128.03, 128.34, 129.55, 137.14, 146.89, 156.41, 172.95, 202.22.

7-Oxa-9-phenyl-4, 4-dimethylbicyclo(4.3.0)nona 1(9), 2, 5-trien-8-one (113a):

To a stirred solution of ethyl 2-hydroxy-2-phenyl-2-(5,5-dimethylcyclohex-2-en-1-one-2-yl)ethanoate (**112a**) (0.5 mmol, 0.151 g) in THF (2 mL) was added methanesulfonic acid (2.5 mmol, 0.240 g, 0.16 mL) at room temperature, and heated under reflux for 8 h. Then the reaction mixture was allowed to cool to room temperature and diluted with water and extracted with ether (5 x 10 mL). The combined organic layer was dried over anhydrous Na$_2$SO$_4$. Solvent was evaporated and the residue, thus obtained, was purified by column chromatography (silica gel, 5% EtOAc in hexanes) to furnish the title compound **113a** in 82 % (0.098 g) yield.



Mp: 78-80 °C

IR (KBr): υ 1759, 1618 cm^{-1}

^{1}H NMR (400 MHz): δ 1.30 (s, 6H), 5.88 (s, 1H), 6.41 (dd, 1H, *J* = 2.0 Hz & *J* = 9.6 Hz), 6.87 (d, 1H, *J* = 8.8 Hz), 7.33-7.40 (m, 1H), 7.42-7.50 (m, 2H), 7.67 (d, 2H, *J* = 7.2 Hz).

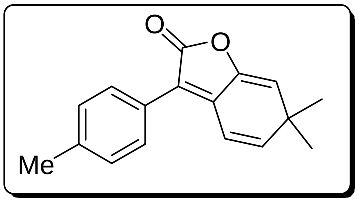
^{13}C NMR (100 MHz): δ 27.89, 39.82, 115.77, 117.06, 117.68, 128.49, 128.56, 128.69, 130.19, 140.26, 146.63, 150.77, 170.08.

LCMS (*m/z*): 239 (M+H)$^+$

Anal. Calcd. for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92.

Found: C, 80.56; H, 5.91.

7-Oxa-9-(4-methylphenyl)-4,4-dimethylbicyclo(4.3.0)nona 1(9)-2,5-trien-8-one (113b):
The reaction of ethyl 2-hydroxy-2-(4-methylphenyl)-2-(5, 5-dimethylcyclohex-2-en-1-one-2-yl)ethanoate **(112b)** with methanesulfonic acid in THF, following the similar procedure described for the molecule **113a**, provided the title compound as a crystaline solid.



Reaction time: 8 h

Yield: 81%

Mp: 86-88 °C

IR (KBr): ν 1751, 1676, 1610 cm^{-1}

^{1}H NMR (400 MHz): δ1.29 (s, 6H), 2.38 (s, 3H), 5.84 (s, 1H), 6.37 (d, 1H, *J* = 9.6 Hz), 6.85 (d, 1H, *J* = 9.6 Hz), 7.24 (d, 2H, *J* = 7.6 Hz)*, 7.58 (d, 2H, *J* = 7.6 Hz).(* One of the doublet peak merging with CHCl$_3$ peak)

^{13}C NMR (100 MHz): δ21.44, 28.00, 39.77, 115.91, 117.13, 117.30, 127.32, 128.40, 129.45, 138.67, 139.66, 146.71, 150.33, 170.27.

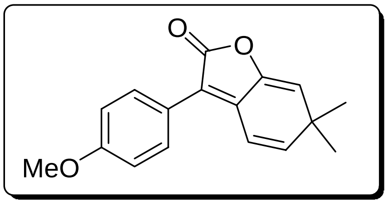
LCMS (*m/z*): 253 (M+H)$^+$

Anal. Calcd. for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39.

Found: C, 81.00; H, 6.32.

7-Oxa-9-(4-methoxyphenyl)-4,4-dimethylbicyclo(4.3.0)nona 1(9)-2,5-trien-8-one (113c):

The treatment of ethyl 2-hydroxy-2-(4-methoxyphenyl)-2-(5, 5-dimethylcyclohex-2-en-1-on-2-yl)ethanoate (**112c**) with methanesulfonic acid in THF, following the similar procedure described for the molecule **113a** provided the title compound as a colorless solid.



Reaction time: 8 h

Yield: 79%

Mp: 90-92 °C

IR (KBr): ν 1759, 1606 cm^{-1}

^{1}H NMR (400 MHz): δ 1.29 (s, 6H), 3.84 (s, 3H), 5.83 (d, 1H, J = 2.0 Hz), 6.36 (dd, 1H, J = 2.0 Hz & J = 9.6 Hz), 6.84 (d, 1H, J = 9.6 Hz), 6.97 (d, 2H, J = 8.8 Hz), 7.65 (d, 2H, J = 8.8 Hz).

^{13}C NMR (100 MHz): δ 28.09, 39.74, 55.42, 114.28, 115.92, 116.85, 117.00, 122.77, 129.89, 138.86, 146.76, 150.01, 159.91, 170.45.

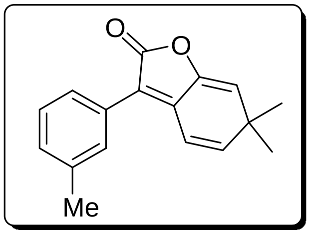
LCMS (*m/z*): 269 $(M+H)^+$, 287 $(M+H_2O+H)^+$

Anal. Calcd. for $C_{17}H_{16}O_3$: C, 76.10; H, 6.01.

Found: C, 76.26; H, 5.99.

7-Oxa-9-(3-methylphenyl)-4,4-dimethylbicyclo(4.3.0)nona1(9)-2,5-trien-8-one (113d):

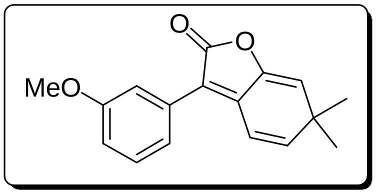
This compound was obtained as a colorless solid *via* the reaction between ethyl 2-hydroxy-2-(3-methylphenyl)-2-(5,5-dimethylcyclohex-2-en-1-on-2-yl)ethanoate (**112d**) and methanesulfonic acid in THF, following the similar procedure described for the molecule **113a**.



Reaction time:	8 h
Yield:	73%
Mp:	82-84 °C
IR (KBr):	ν 1759, 1616 cm^{-1}
^{1}H NMR (400 MHz):	δ 1.29 (s, 6H), 2.40 (s, 3H), 5.86 (s, 1H), 6.38 (d, 1H, *J* = 9.6 Hz), 6.85 (d, 1H, *J* = 9.6 Hz), 7.18 (d, 1H, *J* = 7.6 Hz), 7.28-7.36 (m, 1H), 7.45 (d, 1H, *J* = 7.6 Hz), 7.49 (s, 1H).
^{13}C NMR (100 MHz):	δ 21.55, 27.97, 39.82, 115.92, 117.31, 117.53, 125.68, 128.62, 129.12, 129.45, 130.11, 138.41, 140.20, 146.71, 150.56, 170.19.
LCMS (*m/z*):	253 (M+H)$^+$
Anal. Calcd. for $C_{17}H_{16}O_2$:	C, 80.93; H, 6.39.
Found:	C, 80.75; H, 6.34

7-Oxa-9-(3-methoxyphenyl)-4,4-dimethylbicyclo(4.3.0)nona 1(9)-2,5-trien-8-one (113e):

This lactone was obtained as a colorless solid *via* the reaction of ethyl 2-hydroxy-2-(3-methoxyphenyl)-2-(5,5-dimethylcyclohex-2-en-1-on-2-yl)ethanoate (**112e**) in THF with methanesulfonic acid, following the similar procedure described for the molecule **113a**.



Reaction time: 8 h

Yield: 76%

Mp: 84-86 °C

IR (KBr): ν 1765, 1680, 1620 cm^{-1}

^{1}H NMR (400 MHz): δ 1.30 (s, 6H), 3.84 (s, 3H), 5.88 (d, 1H, *J* = 1.2 Hz), 6.40 (dd, 1H, *J* = 1.2 Hz & *J* = 9.6 Hz), 6.87 (d, 1H, *J* = 9.6 Hz), 6.89-6.96 (m, 1H), 7.23-7.28 (m, 2H), 7.31-7.38 (m, 1H).

^{13}C NMR (100 MHz): δ 27.90, 39.84, 55.38, 113.89, 114.50, 115.85, 116.95, 117.78, 120.98, 129.72, 131.44, 140.42, 146.62, 150.85, 159.80, 170.00.

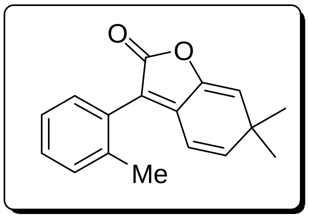
LCMS (*m/z*): 269 (M+H)$^+$

Anal. Calcd. for $C_{17}H_{16}O_3$: C, 76.10; H, 6.01.

Found: C, 76.00; H, 6.05.

7-Oxa-9-(2-methylphenyl)-4,4-dimethylbicyclo(4.3.0)nona 1(9)-2,5-trien-8-one (113f):

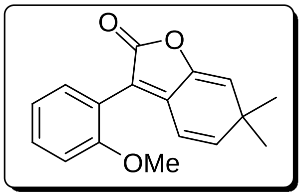
This 2-furanone derivative was obtained as a colorless solid *via* the reaction of ethyl 2-hydroxy-2-(2-methylphenyl)-2-(5, 5-dimethylcyclohex-2-en-1-on-2-yl) ethanoate (**112f**) in with methanesulfonic acid in THF following the similar procedure described for the molecule **113a**.



Reaction time:	8 h
Yield:	83.5%
Mp:	108-110 °C
IR (KBr):	ν 1730, 1631 cm^{-1}
^{1}H NMR (400 MHz):	δ 1.30 (s, 6H), 2.29 (s, 3H), 5.87 (d, 1H, *J* = 1.6 Hz), 6.34 (dd, 1H, *J* = 1.6 Hz & *J* = 9.6 Hz), 6.44 (d, 1H, *J* = 9.6 Hz), 7.16-7.35 (m, 4H).
^{13}C NMR (100 MHz):	δ 20.15, 27.87, 39.97, 115.82, 117.55, 118.83, 125.76, 128.91, 128.97, 130.24, 130.69, 137.47, 142.42, 146.82, 150.47, 169.89.
LCMS (*m/z*):	253 (M+H)$^{+}$
Anal. Calcd. for $C_{17}H_{16}O_2$:	C, 80.93; H, 6.39.
Found:	C, 80.80; H, 6.36.

7-Oxa-9-(2-methoxyphenyl)-4,4-dimethylbicyclo(4.3.0)nona 1(9)-2,5-trien-8-one (113g):

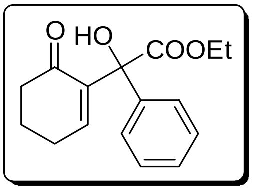
This compound was obtained as a colorless solid *via* the treatment of ethyl 2-hydroxy-2-(2-methoxyphenyl)-2-(5,5-dimethylcyclohex-2-en-1-on-2-yl)ethanoate (**112g**) in THF with methanesulfonic acid, following the similar procedure described for the molecule **113a**.



Reaction time:	8 h
Yield:	62.5%
Mp:	102-104 ^{o}C
IR (KBr):	ν 1766, 1631 cm^{-1}
^{1}H NMR (400 MHz):	δ 1.29 (s, 6H), 3.84 (s, 3H), 5.84 (d, 1H, *J* = 2.0 Hz), 6.29 (dd, 1H, *J* = 2.0 Hz & *J* = 9.6 Hz), 6.53 (d, 1H, *J* = 9.6 Hz), 6.97 (d, 1H, *J* = 8.8 Hz), 7.00-7.08 (m, 1H), 7.32 -7.40 (m, 1H), 7.40-7.45 (m, 1H).
^{13}C NMR (100 MHz):	δ 27.85, 39.59, 55.51, 111.37, 115.03, 117.07, 118.87, 120.59,130.15, 131.09, 142.01, 146.88, 149.09, 157.24, 170.07.
LCMS (*m/z*):	269 (M+H)$^{+}$
Anal. Calcd. for $C_{17}H_{16}O_3$:	C, 76.10; H, 6.01.
Found:	C, 76.24; H, 6.06.

Methyl 2-hydroxy-2-phenyl-2-(cyclohex-2-en-1-on-2-yl)ethanoate (114):

A solution of ethyl phenylglyoxylate (**99a**) (20 mmol, 3.56 g, 3.17 mL), cyclohex-2-en-1-one (40 mmol, 3.84g) in methanolic trimethylamine (25% w/w) (20 mmol, 1.182g, 1.55 mL) was kept at room temperature for one day. Low boiling liquids were removed under reduced pressure and the crude compound thus obtained, was purified by silica gel column chromatography (10% EtOAc in hexanes) to furnish the required molecule in 36% (1.96 g) isolated yield, as a colorless liquid.



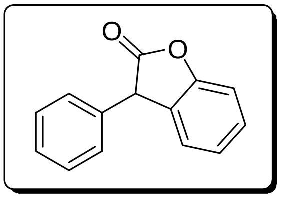
IR (Neat): ν 3449, 1743, 1664 cm^{-1}

^{1}H NMR (400 MHz): δ 1.25 (t, 3H, *J* = 7.2 Hz), 1.93-2.07 (m, 2H), 2.22-2.58 (m, 4H), 4.12-4.34 (m, 2H), 6.40 (t, 1H, *J* = 4.0 Hz), 7.28-7.46 (m, 3H), 7.56-7.60 (m, 2H).

^{13}C NMR (100 MHz): δ 13.91, 22.26, 25.71, 38.26, 62.10, 78.15, 126.70, 128.03, 128.08, 137.74, 142.24, 149.19, 173.54, 199.35.

3-Phenyl-3*H*-benzofuran-2-one (115):

This furanone derivative was obtained as a colorless solid *via* the reaction of methyl 2-hydroxy-2-phenyl-2-(cyclohex-2-en-1-on-2-yl)ethanoate (**114**) with methanesulfonic acid, in THF under the influence of following the similar procedure described for the molecule **113a**.



Reaction time: 8 h

Yield: 59%

Mp: 106-108 °C

IR (KBr): ν 1797, 1608 cm^{-1}

^{1}H NMR (400 MHz): δ 4.79 (s, 1H), 7.04-7.17 (m, 5H), 7.24-7.34 (m, 4H).

^{13}C NMR (100 MHz): δ 49.76, 110.90, 124.53, 125.40, 127.15, 128.25, 128.30, 129.18, 129.42, 135.19, 154.02, 175.08.

LCMS (*m/z*): 209 (M-H)$^-$

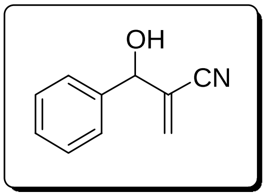
Anal. Calcd. for $C_{14}H_{10}O_2$: C, 79.98; H, 4.79.

Found: C, 79.96; H, 4.73

3-Hydroxy-2-methylene-3-phenylpropanenitrile (125a):

This was prepared according to the known procedure.[18]

A solution of benzaldehyde (**130a**) (50 mmol, 5.306 g) and DABCO (15 mol%, 7.5 mmol, 0.841g). in acrylonitrile (75 mmol, 3.975 g), was kept at room temperature for 2 days. Then the reaction mixture was diluted with ether (50 mL) and washed successively with 2N HCl, aqueous $NaHCO_3$ solution and water. The organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and the residue was purified by column chromatogarphy to furnish the pure title compound as a colorless liquid.



Reaction time: 2 d

Yield: 73 %

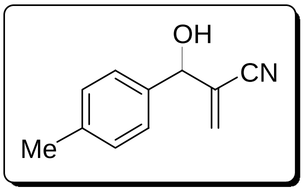
IR (Neat): ν 3441, 2229, 1622 cm^{-1}

^{1}H NMR (400 MHz): δ 3.21 (bs, 1H), 5.18 (s, 1H), 5.94 (d, 1H, J = 1.2 Hz), 6.01 (d, 1H, J = 1.2 Hz), 7.28-7.42 (m, 5H).

^{13}C NMR (100 MHz): δ 73.97, 116.98, 126.16, 126.51, 128.85, 130.04, 139.15.

3-Hydroxy-2-methylene-3-(4-methylphenyl)propanenitrile (125b):

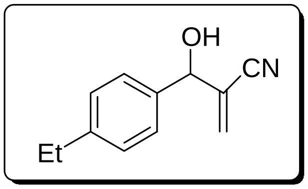
This molecule was obtained as a colorless viscous liquid *via* the Baylis-Hillman reaction between 4-methylbenzaldehyde (**130b**) and acrylonitrile under the catalytic influence of DABCO following a similar procedure described for the molecule **125a**.



Reaction time:	4 d
Yield:	71%
IR (Neat):	ν 3441, 2229, 1616 cm^{-1}
^{1}H NMR (400 MHz):	δ 2.33 (s, 3H), 3.08 (bs, 1H), 5.16 (s, 1H), 5.95 (s, 1H), 6.03 (s, 1H), 7.12-7.30 (m, 4H).
^{13}C NMR (100 MHz):	δ 21.15, 73.88, 117.07, 126.35, 126.49, 129.56, 129.70, 136.29, 138.75.

3-Hydroxy-2-methylene-3-(4-ethylphenyl) propanenitrile (125c):

The Baylis-Hillman reaction between 4-ethylbenzaldehyde (**130c**) and acrylonitrile under the influence of DABCO as a catalyst following a similar procedure described for the molecule **125a** provided the title compound as a colorless liquid.



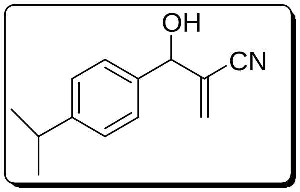
Reaction time:	4 d
Yield:	65 %
IR (Neat):	ν 3443, 2229, 1614 cm^{-1}

^{1}H NMR (400 MHz): δ 1.22 (t, 3H, *J* = 7.6 Hz), 2.63 (q, 2H, *J* = 7.6 Hz), 5.20 (s, 1H), 5.97 (d, 1H, *J* = 1.2 Hz), 6.06 (d, 1H, *J* = 1.2 Hz), 7.20 (d, 2H, *J* = 8.0 Hz), 7.26 (d, 2H, *J* = 8.0Hz).

^{13}C NMR (100 MHz): δ 15.45, 28.58, 74.02, 117.09, 126.35, 126.59, 128.44, 129.68, 136.52, 145.17.

3-Hydroxy-2-methylene-3-(4-isopropylphenyl)propanenitrile (125d):

The Baylis-Hillman adduct was obtained as a colorless viscous liquid *via* the reaction between 4-isopropylbenzaldehyde (**130d**) and acrylonitrile under the influence of DABCO (cat) following a similar procedure described for the molecule **125a**.



Reaction time: 2 d

Yield: 55 %

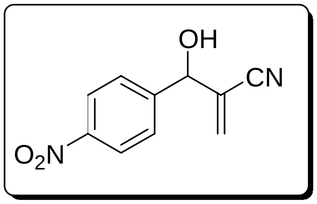
IR (Neat): ν 3466, 2229, 1614 cm^{-1}

^{1}H NMR (400 MHz): δ 1.22 (d, 6H, *J* = 6.8 Hz), 2.82-2.98 (m, 1H), 5.16 (s, 1H), 5.93 (s, 1H), 6.01 (s, 1H), 7.16-7.30 (m, 4H).

^{13}C NMR (100 MHz): δ 23.84, 33.79, 73.84, 117.09, 126.30, 126.53, 126.89, 129.72, 136.57, 149.59.

3-Hydroxy-2-methylene-3-(4-nitrophenyl)propanenitrile (125e):

This was obtained as a yellow solid *via* the reaction of 4-nitrobenzaldehyde with acrylonitrile under the catalytic influence of DABCO following a similar procedure described for the molecule **125a**.



Reaction time: 2 d

Yield: 44%

Mp: 60-62 °C

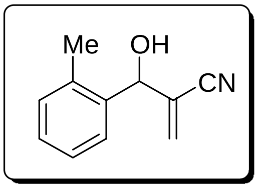
IR (KBr): ν 3479, 2229, 1601 cm^{-1}

^{1}H NMR (400 MHz): δ 3.33 (bs, 1H), 5.45 (s, 1H), 6.09 (s, 1H), 6.18 (s, 1H), 7.59 (d, 2H, J = 8.6 Hz), 8.22 (d, 2H, J = 8.6 Hz).

^{13}C NMR (100 MHz): δ 73.22, 116.36, 124.03, 125.38, 127.40, 131.25, 146.19, 147.99.

3-Hydroxy-2-methylene-3-(2-methylphenyl)propanenitrile (125f):

This alcohol was obtained as a colorless viscous liquid *via* the reaction between 2-methylbenzaldehyde (**130f**) and acrylonitrile under the influence of DABCO as catalyst following a similar procedure described for the molecule **125a**.



Reaction time: 4 d

Yield: 61%

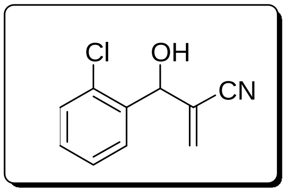
IR (Neat): ν 3447, 2229, 1622 cm^{-1}

^{1}H NMR (400 MHz): δ 2.31 (s, 3H), 2.90 (bs, 1H), 5.45 (s, 1H), 5.96 (s, 1H), 6.00 (s, 1H), 7.13-7.18 (m, 1H), 7.20-7.27 (m, 2H), 7.36-7.42 (m, 1H).

^{13}C NMR (100 MHz): δ 19.06, 70.69, 117.17, 125.49, 126.37, 126.66, 128.79, 130.30, 130.88, 135.68, 137.00.

3-Hydroxy-2-methylene-3-(2-chlorophenyl)propanenitrile (125g):

This Baylis-Hillman alcohol was obtained as a colorless viscous liquid *via* the coupling between 2-chlorobenzaldehyde (**130g**) and acrylonitrile under the influence of DABCO as a catalyst following a similar procedure described for the molecule **125a**.



Reaction time: 5d

Yield: 56%

Mp: 50-52 °C

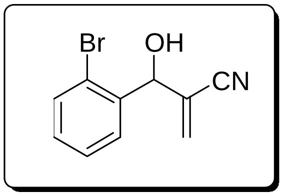
IR (Neat): ν 3458, 2229, 1626 cm^{-1}

^{1}H NMR (400 MHz): δ 3.18 (d, 1H, *J* = 3.0 Hz), 5.71 (s, 1H), 6.02 (s, 2H), 7.23-7.42 (m, 3H), 7.58(d, 1H, *J* = 7.6 Hz).

^{13}C NMR (100 MHz): δ 70.40, 116.71, 124.58, 127.55, 127.96, 129.72, 129.98, 131.47, 132.56, 136.48.

3-Hydroxy-2-methylene-3-(2-bromophenyl)propanenitrile (125h):

This molecule was obtained as a colorless solid *via* the reaction between 2-bromo benzaldehyde (**130h**) and acrylonitrile under the influence of DABCO (cat) following a similar procedure described for the molecule **125a**.



Reaction time: 4 d

Yield: 50%

Mp: 42-44 °C

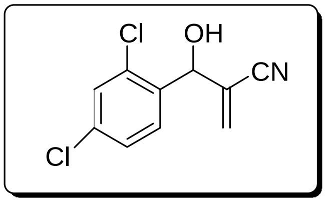
IR (KBr): ν 3398, 2237 cm^{-1}

^{1}H NMR (400 MHz): δ 2.87 (bs, 1H), 5.71 (s, 1H), 6.06 (s, 2H), 7.10-7.24 (m, 1H), 7.28-7.48 (m, 1H), 7.51-7.64 (m, 2H).

^{13}C NMR (100 MHz): δ 72.60, 116.75, 122.73, 124.56, 128.32, 130.32, 131.72, 133.03, 138.05.

3-Hydroxy-2-methylene-3-(2, 4-dichlorophenyl)propanenitrile (125i):

This product was obtained as a colorless viscous liquid *via* the reaction between 2, 4-di chlorobenzaldehyde (**130i**) and acrylonitrile under the catalytic influence of DABCO following a similar procedure described for the molecule **125a**.



Reaction time: 5 d

Yield: 68%

Mp: 64-66 °C

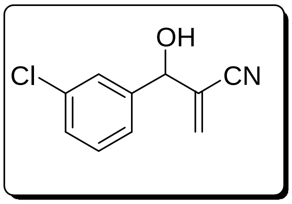
IR (KBr): ν 3497, 2235, 16116 cm^{-1}

^{1}H NMR (100 MHz): δ 3.51 (d, 1H, J = 4.2 Hz), 5.63 (d, 1H, J = 4.2 Hz), 6.02 (s, 2H), 7.30 (dd, 1H, J = 2.0 Hz & 8.8 Hz), 7.37 (d, 1H, J = 2.0 Hz), 7.51 (d, 1H, J = 8.8 Hz).

^{13}C NMR (100 MHz): δ 69.84, 116.47, 124.15, 127.82, 128.85, 129.39, 131.84, 133.05, 135.10, 135.13.

3-Hydroxy-2-methylene-3-(3-chlorophenyl)propanenitrile (125j):

The reaction of 3-chlorobenzaldehyde (**130j**) with acrylonitrile under the influence of DABCO as a catalyst following a similar procedure described for the molecule **125a** provided the title compound as a colorless liquid.



Reaction time: 6 d

Yield: 37 %

IR (Neat): ν 3456, 2231, 1606 cm^{-1}

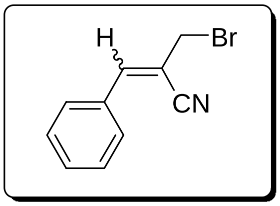
^1H NMR (400 MHz): δ 3.36 (bs, 1H), 5.21 (s, 1H), 6.00 (s, 1H), 6.06 (d, 1H, *J* = 1.2 Hz), 7.20-7.40 (m, 4H).

^{13}C NMR (100 MHz): δ 73.31, 116.72, 124.70, 125.67, 126.59, 128.95, 130.16, 130.70, 134.70, 141.14.

2-(Bromomethyl)-3-phenylprop-2-enenitrile (126a):

This molecule was prepared according to the literaure procedure.[233]

To a stirred solution of 3-hydroxy-2-methylene-3-phenylpropanenitrile (**125a**) (10 mmol, 1.59 g) in CH_2Cl_2 (20 mL) was added dropwise aqueous HBr (48%, 25 mmol, 2.023 g) followed by conc. H_2SO_4 (10 mmol, 0.98 g) at 0 °C. After stirring 12 h at room temperature, the reaction mixture was carefully poured into ice-cold water and extracted with ether (3 x 20 mL). The combined organic layer was washed with water, dried over anhydrous Na_2SO_4 and concentrated. The crude product was purified by column chromatography (silicagel, 2% ethylacetate in hexanes) to afford (**126a**) as a colorless solid in 75% yield as *E:Z* mixtures in the ratio of 90:10 (as evidenced by the integration of allylic methylene protons singlets at δ 4.20 and 4.18).



Reaction time: 12 h

Mp: 48-50 °C

IR (KBr): ν 2216, 1616 cm^{-1}

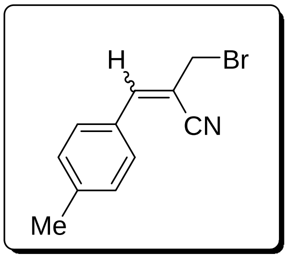
^{1}H NMR (400 MHz): δ 4.18 & 4.20 (s, 2H), 7.20 & 7.32 (2s, 1H), 7.40-7.50 & 7.74-7.81 (2 m, 5H).

^{13}C NMR (100 MHz): δ 26.67, 32.77, 107.91, 117.07, 129.02, 129.17, 129.20, 130.45, 131.35, 132.35, 132.89, 146.50, 147.20 (The underlined chemical shift values are due to minor *Z*-isomer)

2-(Bromomethyl)-3-(4-methylphenyl)prop-2-enenitrile (126b):

This compound was prepared as a colorless solid *via* the treatment of 3-hydroxy-2-methylene-3-(4-methylphenyl)propanenitrile (**125b**) with aqueous HBr (48%) in the presence of conc. H_2SO_4 following the similar procedure described for the molecule **126a**

E:Z ratio: 84:16 (as evidenced by the isomeric peaks of allylic methylene corbons at δ 33.67, 26.97).



Reaction time: 12 h

Yield: 80%

Mp: 54-56 ^{o}C

IR: ν 2212, 1604 cm^{-1}

^{1}H NMR (400 MHz): δ 2.39 (s, 3H), 4.20 (s, 2H), [7.16 (s), 7.24 (d, J = 8.0 Hz), 7.25-7.36 (m), 7.69 (d, *J* = 8.0 Hz)] 4H.

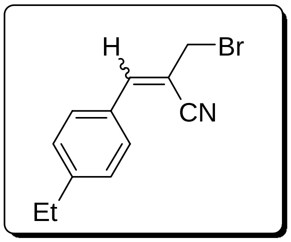
^{13}C NMR (100 MHz): δ 21.65, 26.97, 33.07, 106.69, 117.34, 118.98, 129.34, 129.40, 129.80, 129.96, 142.20, 146.61, 147.37.

(The underlined chemical shift values are due to minor *Z*-isomer)

2-(Bromomethyl)-3-(4-ethyphenyl)prop-2-enenitrile (126c):

This bromide was prepared as a colorless solid *via* the treatment of 3-hydroxy-2-methylene-3-(4-ethylphenyl)propanenitrile (**125c**) with aqueous HBr (48 %) in the presence of conc. H_2SO_4 following the similar procedure described for the molecule **126a**.

E:Z ratio: 75:25 (as evidenced by the isomeric peaks of allylic methylene corbons at δ 33.10, 27.01).



Reaction time: 12 h

Yield: 76%

IR (KBr): ν 2218, 1606 cm^{-1}

^{1}H NMR (400 MHz): δ 1.24 (t, 3H, *J* = 7.6 Hz), 2.68 (q, 2H, *J* = 7.6 Hz), 4.21 (s, 2H), 7.10-7.79 (m, 5H).

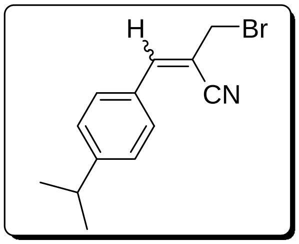
^{13}C NMR (100 MHz): δ 15.15, 15.19, 27.01, 28.78, 28.86, 33.10, 106.64, 110.75, 117.32, 118.94, 128.54, 128.71, 129.38, 129.48, 129.90, 130.12, 146.57, 147.33, 148.33.

(The underlined chemical shift values are due to minor *Z*-isomer)

2-(Bromomethyl)-3-(4-isopropylphenyl)prop-2-enenitrile (126d):

This Baylis-Hillman bromide was prepared as a colorless solid by the treatment of 3-hydroxy-2-methylene-3-(4-isopropylphenyl)propanenitrile (**125d**) with aqueous HBr (48 %) in the presence of conc. H_2SO_4 following the similar procedure described for the molecule **126a**.

E Z ratio: 85:15 (as evidenced by the isomeric peaks of allylic methylene corbons at δ 33.10, 27.04).



Reaction time: 12 h

Yield: 71%

IR (KBr): ν 2218, 1606 cm^{-1}

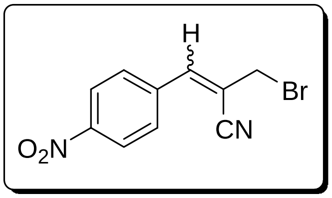
^{1}H NMR (400 MHz): δ 1.25 (d, 6H, *J* = 6.8 Hz), 2.89-3.00 (m, 1H), 4.20 (s, 2H), 7.12-7.74 (m, 5H).

^{13}C NMR (100 MHz): δ 23.68, 27.04, 31.69, 33.10, 34.19, 106.74, 110.83, 117.36, 125.21, 127.19, 127.36, 129.28, 129.47, 129.58, 130.08, 130.32, 146.60, 147.35, 151.97, 152.96.

(The underlined chemical shift values are due to minor *Z*-isomer).

2-(Bromomethyl)-3-(4-nitrophenyl)prop-2-enenitrile (126e):

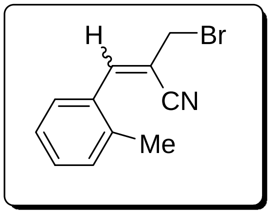
It was prepared as a colorless solid by the treatment of 3-hydroxy-2-methylene-3-(4-nitrophenyl)propanenitrile (**125e**) with aqueous HBr (48 %) in the presence of conc. H_2SO_4 following the similar procedure described for the molecule **126a**.



E: Z ratio:	92:8 (as eveidenced by the isomeric methylene singlets at δ 4.24, 4.13).
Reaction time:	12 h
Yield:	71%
Mp:	70-72 ^{o}C
IR (KBr):	ν 2222, 1595 cm^{-1}
^{1}H NMR (400 MHz):	δ 4.13 & 4.24 (s, 2H), 7.31 & 7.40 (2s, 1H), 7.63 & 7.94 (2d, 2H, *J* = 8.8 Hz), 8.30 & 8.34 (d, 2H, *J* = 8.8 Hz).
^{13}C NMR (100 MHz):	δ 25.48, 31.47, 112.66, 116.15, 124.20, 129.98, 138.22, 143.44, 144.21, 148.82. (The underlined chemical shift values are due to minor *Z*-isomer)

2-(Bromomethyl)-3-(2-methylphenyl)prop-2-enenitrile (126f):

It was prepared as a colorless solid *via* the treatment of 3-hydroxy-2-methylene-3-(2-methylphenyl)propanenitrile (**125f**) with aqueous HBr (48 %) in the presence of conc. H_2SO_4 following the similar procedure described for the molecule **126a**.



E: Z ratio:	70:30 (as eveidenced by the isomeric methylene singlets at δ 4.26, 4.09).
Reaction time:	12 h
Yield:	70%

Mp: 46-48 °C

IR (KBr): ν 2222, 1612 cm^{-1}

^{1}H NMR (400 MHz): δ <u>2.29</u> & 2.34 (2s, 3H), <u>4.09</u> & 4.26 (2s, 2H), 7.20-7.86 (m, 5H)

^{13}C NMR (100 MHz): δ 19.78, <u>19.87</u>, <u>26.44</u>, 32.22, 110.21, <u>112.92</u>, 116.87, <u>118.47</u>, <u>126.35</u>, 126.54, 127.98, <u>130.34</u>, 130.64, <u>130.83</u>, 130.94, <u>131.69</u>, 137.46, 145.27, <u>146.54.</u>

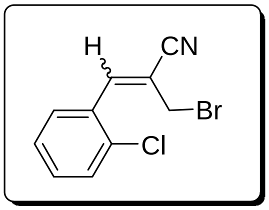
(The underlined chemical shift values are due to minor *Z*-isomer)

2-(Bromomethyl)-3-(2-chlorophenyl)prop-2-enenitrile (126g):

Treatment of 3-hydroxy-2-methylene-3-(2-chlorophenyl)propanenitrile (**125g**) with aqueous HBr (48 %) in the presence of conc. H_2SO_4 following the similar procedure described for the molecule (**126a**) furnished the title compound as a colorless solid.

E: Z ratio: 40:60 (as evidenced by the integration of allylic methylene protons singlets at δ <u>4.24</u>, 4.08).

Reaction time: 12 h



Yield: 62%

Mp: 44-46 °C

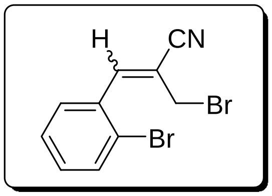
IR (KBr): ν 2214, 1618 cm^{-1}

^{1}H NMR (400 MHz): δ 4.08 & <u>4.24</u> (2s, 2H), 7.30-8.10 (m, 5H)

^{13}C NMR (100 MHz):	δ 26.16, 31.84, 111.30, 113.92, 116.36, 117.95, 127.22, 127.31, 129.23, 129.42, 129.95, 130.22, 130.74, 131.02, 131.51, 132.03, 134.26, 134.58, 142.65, 143.89. (The underlined chemical shift values are due to minor *E*-isomer).

2-(Bromomethyl)-3-(2-bromophenyl)prop-2-enenitrile (126h):

It was prepared as a colorless solid by the treatment of 3-hydroxy-2-methylene-3-(2-bromophenyl)propanenitrile (**125h**) with aqueous HBr (48%) in the presence of conc. H_2SO_4 following the similar procedure described for the molecule **126a**.

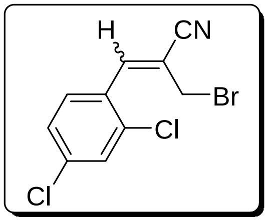


E: Z ratio:	2:98 (as evidenced by the integration of allylic methylene protons singlets at δ 4.18, 4.06).
Reaction time:	12 h
Yield:	60%
Mp:	48-50 °C
IR (KBr):	ν 2222, 1612 cm^{-1}
^{1}H NMR (400 MHz):	δ 4.06 & 4.18 (s, 2H), 7.25-7.55 (m, 4H), 7.67(d, 1H, *J* = 8.0 Hz).
^{13}C NMR (100 MHz):	δ 26.12, 113.79, 117.94, 124.13, 127.85, 129.54, 131.61, 132.94, 133.47, 146.06. (The underlined chemical shift values are due to minor *E*-isomer).

2-(Bromomethyl)-3-(2,4-dichlorophenyl)prop-2-enenitrile (126i):

It was prepared as a colorless solid by the treatment of 3-hydroxy-2-methylene-3-(2, 4-di chlorophenyl)propanenitrile (**125i**) with aqueous HBr (48%) in the presence of conc. H_2SO_4 following the similar procedure described for the molecule **126a**.

E: Z ratio: 29:71 (as evidenced by the integration of allylic methylene protons singlets at δ 4.21, 4.04).



Reaction time: 12 h

Yield: 45%

IR (KBr): ν 2224, 1620 cm^{-1}

^{1}H NMR (400 MHz): δ 4.04 & 4.21 (2s, 2H), [7.30-7.53 (m), 7.98 (d, *J* = 7.6 Hz] 4H.

^{13}C NMR (100 MHz): δ 25.92, 31.65, 111.66, 114.26, 116.00, 117.57, 127.53, 127.55, 129.11, 129.33, 129.65, 129.72, 129.95, 130.06, 134.89, 135.11, 136.75, 137.16, 141.07, 142.39.

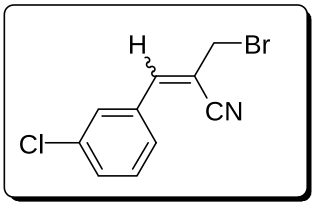
(The underlined chemical shift values are due to minor *E*-isomer).

2-(Bromomethyl)-3-(3-chlorophenyl)prop-2-enenitrile (126j):

This Baylis-Hillman bromide prepared as a colorless solid by the treatment of 3-hydroxy-2-methylene-3-(3-chlorophenyl)propanenitrile (**125j**) with HBr (48%) in the presence of conc. H_2SO_4 following the similar procedure described for the molecule **126a**.

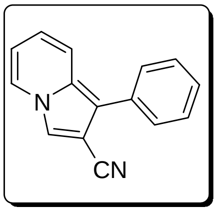
E:Z ratio: 63:37 (as evidenced by the integration of allylic methylene

	protons singlets at δ 4.20, 4.14).
Reaction time:	12 h
Yield:	47%
IR (KBr):	ν 2222, 1620 cm^{-1}
^{1}H NMR (400 MHz):	δ 4.14 & 4.20 (2s, 2H), 7.13-7.75 (m, 5H)
^{13}C NMR (100 MHz):	δ 26.03, 32.14, 109.79, 113.51, 116.56, 118.21, 127.01, 127.07, 128.98, 129.20, 130.35, 130.45, 130.51, 131.24, 134.05, 134, 23,135.05, 135.25, 144.70, 145.43. (The underlined chemical shift values are due to minor *Z*-isomer).



1-Aza-8-cyano-7-phenylbicyclo[4.3.0]nona-2,4,6,8-tetraene (127a):

To 2-(bromomethyl)-3-phenylprop-2-enenitrile (**126a**) (mixture of *E* and *Z* isomers) (1 mmol, 0.222 g) pyridine (3 mL) was added and stirred for 15 minutes [formation of pyridinium salt was observed as shown by TLC] at room temperature. The reaction mixture was diluted with dimethylformamide (DMF) (3 mL) and potassium carbonate (5 mmol, 0.690 g) was added. The reaction mixture was then heated at 80 °C for 3 h and was allowed to cool to room temperature. Saturated aqueous NaCl solution (5 mL) was added and extracted with dichloromethane (5 x 10 mL). The combined organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and the residue, thus obtained, was purified by column chromatography (silica gel, 5% EtOAc in hexanes) to furnish the compound **127a** as colorless solid in 52 % isolated yield.



Mp: 128-130 °C

IR (KBr): ν 2222 cm^{-1}

^{1}H NMR (400 MHz): δ 6.60-6.70 (m, 1H), 6.77-6.86 (m, 1H), 7.32-7.40 (m, 1H), 7.46-7.53 (m, 2H), 7.56-7.68 (m, 3H), 7.74 (s, 1H), 7.88 (d, 1H, *J* = 7.2 Hz).

^{13}C NMR (100 MHz): δ 96.94, 113.60, 116.22, 117.46, 118.16, 118.92, 120.05, 125.31, 127.15, 128.67, 129.00, 129.68, 132.56.

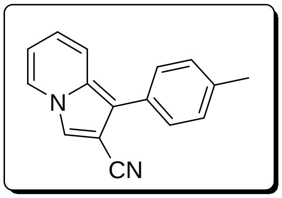
LCMS (*m/z*): 219 (M+H)$^+$

Anal. Calcd. for $C_{15}H_{10}N_2$: C, 82.55; H, 4.62; N, 12.84.

Found: C, 82.51, H, 4.65; N, 12.70.

1-Aza-8-cyano-7-(4-methylphenyl)bicyclo[4.3.0]nona-2,4,6,8-tetraene (127b):

Treatment of 2-(bromomethyl)-3-(4-methylphenyl)prop-2-enenitrile (**126b**) with pyridine in the presence of K_2CO_3 in DMF, following the similar procedure described for the molecule **127a** provided the title compound as a colorless solid.



Reaction Time: 3 h

Yield: 54 %

Mp: 132-134 °C

IR (KBr): ν 2224 cm^{-1}

^{1}H NMR (400 MHz): δ 2.41 (s, 3H), 6.60-6.68 (m, 1H), 6.75-6.84 (m, 1H), 7.29 (d, 2H, *J* = 7.6 Hz), 7.50 (d, 2H, *J* = 7.6 Hz), 7.58 (d, 1H, *J* = 9.2 Hz), 7.72 (s, 1H), 7.86 (d, 1H, *J* = 6.8 Hz).

^{13}C NMR (100 MHz): δ 21.30, 97.02, 113.57, 116.32, 117.68, 117.97, 119.13, 119.76, 125.27, 127.62, 128.61, 129.63, 129.76, 137.01;

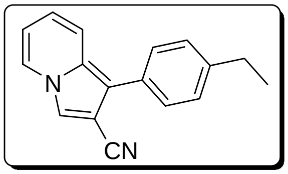
LCMS (*m/z*): 233 $(M+H)^{+}$

Anal. Calcd. for $C_{16}H_{12}N_2$: C, 82.73; H, 5.21; N, 12.06.

Found: C, 82.82; H, 5.25; N, 12.21.

1-Aza-8-cyano-7-(4-ethylphenyl)bicyclo[4.3.0]nona-2,4,6,8-tetraene (127c):

This indalozine derivative was obtained as a colorless solid *via* the treatment of 2(bromomethyl)-3-(4-ethylphenyl)prop-2-enenitrile (**126c**) with pyridine in the presence of K_2CO_3 in DMF, following the similar procedure described for the molecule (**127a**).



Reaction Time: 3 h

Yield: 59%

Mp: 142-144^{o}C

IR (KBr): ν 2224 cm^{-1}

^{1}H NMR (400 MHz): ^{1}H NMR (400 MHz): δ 1.29 (t, 3H, *J* = 7.6 Hz), 2.71 (q, 2H, *J* = 7.6 Hz), 6.60-6.70 (m, 1H), 6.75-6.84 (m, 1H), 7.31 (d, 2H, *J* = 7.6 Hz), 7.52 (d, 2H, *J* = 7.6 Hz), 7.59 (d, 1H, *J* = 9.2 Hz), 7.72 (s, 1H), 7.86 (d, 1H, *J* = 6.8 Hz).

^{13}C NMR (100 MHz): δ 15.57, 28.67, 96.89, 113.54, 116.36, 117.62, 117.99, 119.10, 119.74, 125.25, 128.54, 128.61, 129.57, 129.83, 143.26.

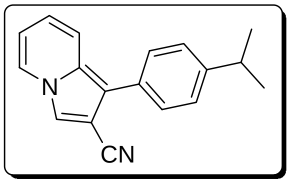
LCMS (*m/z*): 247(M+H)$^+$

Anal. Calcd. for $C_{17}H_{14}N_2$: C, 82.90; H, 5.73; N, 11.37.

Found: C, 82.83; H, 5.70; N, 11.28.

1-Aza-8-cyano-7-(4-isopropylphenyl)bicyclo[4.3.0]nona-2,4,6,8-tetraene (127d)

This compound was obtained as a colorless solid *via* the reaction between 2-(bromomethyl)-3-(4-isopropylphenyl)prop-2-enenitrile (**126d**) and pyridine in the presence of K_2CO_3 in DMF, following the similar procedure described for the molecule **127a**.



Reaction Time: 3 h

Yield: 55%

Mp: 146-148^{o}C

IR (KBr): ν 2227 cm^{-1}

^{1}H NMR (400 MHz): δ 1.30 (d, 6H, *J* = 6.8 Hz), 2.97 (sept, 1H, *J* = 6.8 Hz), 6.61-6.68 (m, 1H), 6.77-6.84 (m, 1H), 7.34 (d, 2H, *J* = 8.0 Hz), 7.53 (d, 2H, *J* = 8.0 Hz), 7.61 (d, 1H, *J* = 9.2 Hz), 7.73 (s, 1H), 7.87 (d, 1H, *J* = 6.8 Hz).

^{13}C NMR (100 MHz): δ 24.02, 33.95, 96.89, 113.55, 116.40, 117.64, 118.00, 119.15, 119.73, 125.25, 127.11, 128.59, 129.59, 129.97, 147.85.

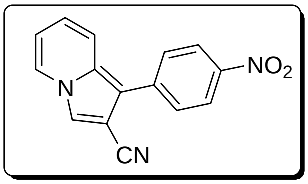
LCMS (*m/z*): 261 (M+H)$^+$

Anal. Calcd. for $C_{18}H_{16}N_2$: C, 83.04; H, 6.19; N, 10.76.

Found: 83.16; H, 6.20; N, 10.81.

1-Aza-8-cyano-7-(4-nitrophenyl)bicyclo[4.3.0]nona-2,4,6,8-tetraene (127e)

This product was obtained as a colorless solid *via* the treatment of 2-(bromomethyl)-3-(4-nitrophenyl)prop-2-enenitrile (**126e**) with pyridine in the presence of K_2CO_3 in DMF, following the similar procedure described for the molecule **127a**.



Reaction Time: 3 h

Yield: 47 %

Mp: 170-172^{o}C

IR (KBr): ν 2220, 1678 cm^{-1}

^{1}H NMR (400 MHz): δ 6.80-6.86 (m, 1H), 7.00-7.09 (m, 1H), 7.69 (d, 1H, *J* = 9.2 Hz), 7.83 (d, 2H, *J* = 8.8 Hz), 8.29 (s, 1H), 8.34 (d, 3H, *J* = 8.8 Hz).

^{13}C NMR (100 MHz): δ 94.64, 111.86, 112.37, 114.12, 116.16, 119.36, 120.91, 122.66, 125.25, 127.12, 128.67, 138.13, 144.25.

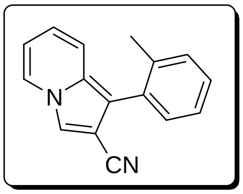
LCMS (*m/z*): 264 (M+H)$^+$

Anal. Calcd. for $C_{15}H_9N_3O_2$: C, 68.44; H, 3.45; N, 15.96.

Found: C, 68.65; H, 3.40; N, 15.90.

1-Aza-8-cyano-7-(2-methylphenyl)bicyclo[4.3.0]nona-2,4,6,8-tetraene (127f):

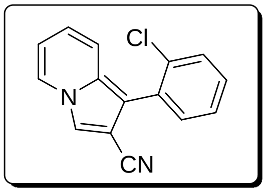
This product was obtained as a colorless solid *via* the reaction between 2-(bromomethyl)-3-(2-methylphenyl)prop-2-enenitrile (**126f**) and pyridine in the presence of K_2CO_3 in DMF, following the similar procedure described for the molecule **127a**.



Reaction Time:	3 h
Yield:	60%
Mp:	138-140^{o}C
IR (KBr):	ν 2227 cm^{-1}
^{1}H NMR (400 MHz):	δ 2.24 (s, 3H), 6.58-6.67 (m, 1H), 6.71-6.78 (m, 1H), 7.13 (d, 1H, *J* = 8.8 Hz), 7.20-7.40 (m, 4H), 7.74 (s, 1H), 7.87 (d, 1H, *J* = 7.2 Hz).
^{13}C NMR (100 MHz):	δ 20.08, 98.37, 113.31, 116.10, 117.28, 119.13, 119.36, 125.13, 125.82, 128.06, 130.06, 130.55, 131.32, 131.36, 137.58.
LCMS (*m/z*):	233 (M+H)$^{+}$
Anal. Calcd. for $C_{16}H_{12}N_2$:	C, 82.73; H, 5.21; N, 12.06.
Found:	C, 82.63; H, 5.14; N, 12.09.

1-Aza-8-cyano-7-(2-chlorophenyl)bicyclo[4.3.0]nona-2,4,6,8-tetraene (127g):

This compound was obtained as a colorless solid *via* the treatment of 2-(bromomethyl)-3-(2-chlorophenyl)prop-2-enenitrile(**126g**) with pyridine in the presence of K_2CO_3 in DMF, following the similar procedure described for the molecule **127a**.



Reaction Time: 3 h

Yield: 58%

Mp: 132-134°C

IR (KBr): ν 2224 cm^{-1}

^{1}H NMR (400 MHz): δ 6.65-6.72 (m, 1H), 6.78-6.87 (m, 1H), 7.24 (d, 1H, J = 10.0 Hz)*, 7.32-7.40 (m, 2H), 7.43-7.48 (m, 1H), 7.53-7.56 (m, 1H), 7.77 (s, 1H), 7.91 (d, 1H, J = 7.2 Hz).

^{13}C NMR (100 MHz): δ 98.56, 113.48, 114.47, 115.73, 117.76, 119.41, 119.96, 125.25, 126.94, 129.25, 130.19, 130.32, 131.09, 132.75, 134.25.

LCMS (*m/z*): 253 (M+H)$^+$, 255 (M+2+H)$^+$;

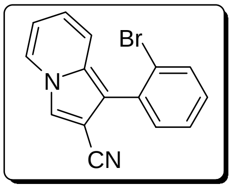
Anal. Calcd. for $C_{15}H_9ClN_2$: C, 71.29; H, 3.59; N, 11.09.

Found: C, 71.37; H, 3.64; N, 11.00.

*One of the peaks of the doublet mixes with $CHCl_3$ peak

1-Aza-8-cyano-7-(2-bromophenyl)bicyclo[4.3.0]nona-2,4,6,8-tetraene (127h):

Treatment of 2-(bromomethyl)-3-(2-bromophenyl)prop-2-enenitrile (**126h**) with pyridine in the presence of K_2CO_3 in DMF, following the similar procedure described for the molecule **127a**. Provided the title compound as a colorless solid.



Reaction Time: 3 h

Yield: 54%

Mp: 136-138°C

IR (KBr): ν 2226 cm^{-1}

^{1}H NMR (400 MHz): δ 6.65-6.72 (m, 1H), 6.79-6.86 (m, 1H), 7.21 (d, 1H, J = 9.2 Hz), 7.25-7.33 (m, 1H), 7.38-7.46 (m, 2H), 7.73 (d, 1H, J = 8.0 Hz), 7.76 (s, 1H), 7.91 (d, 1H, J = 6.8 Hz).

^{13}C NMR (100 MHz): δ 98.50, 113.46, 115.69, 116.31, 117.54, 119.39, 119.90, 124.73, 125.22, 127.48, 129.52, 130.15, 132.88, 133.13, 133.35.

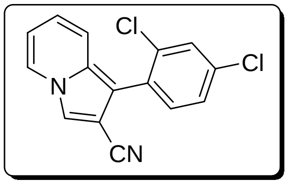
LCMS (*m/z*): 297 (M+H)$^{+}$, 299 (M+2+H)$^{+}$

Anal. Calcd. for $C_{15}H_9BrN_2$: C, 60.63; H, 3.05; N, 9.03.

Found: C, 60.52; H, 3.03; N, 9.32.

1-Aza-8-cyano-7-(2,4-dichlorophenyl)bicyclo[4.3.0]nona-2,4,6,8-tetraene (127i):

This product was obtained as a colorless solid *via* the treatment of 2-(bromomethyl)-3-(2, 4-dichlorophenyl)prop-2-enenitrile (**126i**) with pyridine in the presence of K_2CO_3 in DMF, following the similar procedure described for the molecule **127a**.



Reaction Time: 3 h

Yield: 63%

Mp: 139-141°C

IR (KBr): ν 2224 cm^{-1}

^{1}H NMR (400 MHz): δ 6.68-6.74 (m, 1H), 6.82-6.88 (m, 1H), 7.20 (d, 1H, J = 9.2 Hz), 7.32-7.40 (m, 2H), 7.56 (d, 1H, J = 1.6 Hz), 7.77 (s, 1H), 7.91 (d, 1H, J = 6.8 Hz).

^{13}C NMR (100 MHz): δ 98.56, 113.21, 113.61, 115.50, 117.94, 119.17, 120.35, 125.35, 127.36, 129.74, 130.07, 130.38, 133.42, 134.50, 135.00.

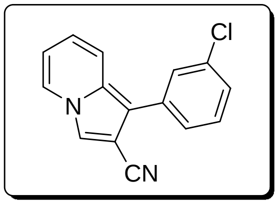
LCMS (*m/z*): 287 $(M+H)^+$, 289 $(M+2+H)^+$, 291 $(M+4+H)^+$

Anal. Calcd. for $C_{15}H_8Cl_2N_2$: C, 62.74; H, 2.81; N, 9.76.

Found: C, 62.78; H, 2.85; N, 9.67.

1-Aza-8-cyano-7-(3-chlorophenyl)bicyclo[4.3.0]nona-2,4,6,8-tetraene (127j):

Treatment of 2-(bromomethyl)-3-(3-chlorophenyl)prop-2-enenitrile (**126j**) with pyridine in the presence of K_2CO_3 in DMF, following the similar procedure described for the molecule **127a** provided the title compound as a colorless solid.



Reaction Time: 3 h

Yield: 49%

Mp 144-146°C

IR (KBr): ν 2224 cm^{-1}

^{1}H NMR (400 MHz): δ 6.65-6.72 (m, 1H), 6.84-6.92 (m, 1H), 7.32 (d, 1H, J = 8.4 Hz), 7.38-7.45 (m, 1H), 7.50 (d, 1H, J = 7.6 Hz), 7.55-7.64 (m, 2H), 7.75 (s, 1H), 7.90 (d, 1H, J = 7.2 Hz).

^{13}C NMR (100 MHz): δ 97.00, 113.81, 115.78, 115.84, 118.45, 118.57, 120.72, 125.44, 126.90, 127.20, 128.46, 129.90, 130.30, 134.37, 134.78.

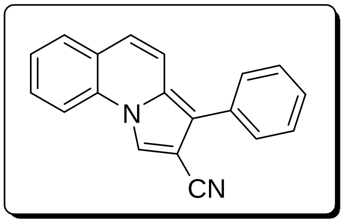
LCMS (*m/z*): 253 $(M+H)^+$, 255 $(M+2+H)^+$

Anal. Calcd. for $C_{15}H_9ClN_2$: C, 71.29; H, 3.59; N, 11.09.

Found: C, 71.43; H, 3.54; N, 11.14.

1-Aza-12-cyano-11-phenyltricyclo[$8.3.0.0^{2,7}$]trideca-2,4,6,8,10,12-hexaene (128a):

To a stirred solution of 2-(bromomethyl)-3-phenylprop-2-enenitrile (**126a**) (1 mmol, 0.222 g) in DMF (3 mL) was added quinoline (2 mmol, 0.258 g) at room temperature. After stirring 1 h, [salt formation was observed as evidenced by TLC] potassium carbonate (5 mmol, 0.690 g) was added and heated for 5 h at 80 °C. The reaction mixture was allowed to cool to room temperature and diluted with saturated aqueous NaCl solution (5 mL) and extracted with dichloromethane (5 x 10 mL). The combined organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and the residue, thus obtained, was purified by column chromatography (silica gel, 8 % EtOAc in hexanes) to furnish the compound **128a** as colorless solid.



Yield: 45% (0.120 g);

Mp: 160-162°C

IR (KBr): ν 2226 cm^{-1}

^{1}H NMR (400 MHz): δ 7.11 (d, 1H, J = 9.6 Hz), 7.34-7.68 (m, 9H), 7.85 (d, 1H, J = 8.4 Hz), 8.26 (s, 1H).

^{13}C NMR (100 MHz): δ 96.68, 114.43, 116.19, 117.35, 118.04, 120.39, 122.03, 124.52, 125.64, 127.50, 128.10, 128.84, 128.92, 129.00, 129.05, 132.28, 132.38.

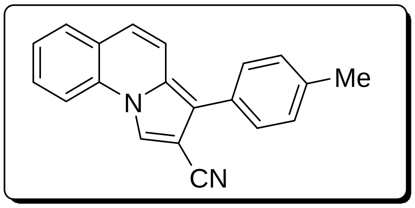
LCMS (*m/z*): 269 $(M+H)^+$

Anal. Calcd. for $C_{19}H_{12}N_2$: C, 85.05; H, 4.51; N, 10.44.

Found: C, 85.11; H, 4.54; N, 10.57.

1-Aza-12-cyano-11-(4-methylphenyl)tricyclo[8.3.0.0^{2,7}]trideca-2,4,6,8,10,12-hexaene (128b):

This molecule was obtained as a colorless solid *via* the treatment of 2-(bromomethyl)-3-(4-methylphenyl)prop-2-enenitrile (**126b**) with quinoline in the presence of K_2CO_3 in DMF, following the similar procedure described for the molecule **128a**.



Reaction Time: 6 h

Yield: 48%

Mp: 156-158 °C

IR (KBr): ν 2226 cm^{-1}

^{1}H NMR (400 MHz): δ 2.42 (s, 3H), 7.10 (d, 1H, *J* = 9.2 Hz), 7.31 (d, 2H, *J* = 7.6 Hz), 7.38-7.49 (m, 2H), 7.50 (d, 2H, *J* = 7.6 Hz), 7.54-7.60 (m, 1H), 7.65 (d, 1H, *J* = 7.6 Hz), 7.85 (d, 1H, *J* = 8.4 Hz), 8.25 (s, 1H).

^{13}C NMR (100 MHz): δ 21.33, 96.69, 114.43, 116.29, 117.52, 117.90, 120.53, 121.78, 124.58, 125.61, 128.00, 128.80, 129.00, 129.34, 129.78, 132.45, 137.35.

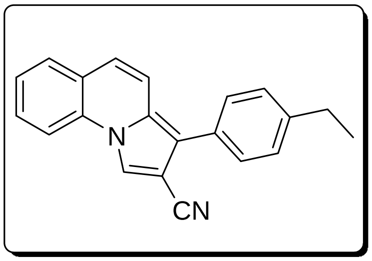
LCMS (*m/z*): 283 (M+H)$^+$

Anal. Calcd. for $C_{20}H_{14}N_2$: C, 85.08; H, 5.00; N, 9.92.

Found: C, 84.90; H, 5.04; N, 10.03.

1-Aza-12-cyano-11-(4-ethylphenyl)tricyclo[8.3.0.0^{2,7}]trideca-2,4,6,8,10,12-hexaene (128c):

This compound was obtained as a colorless solid *via* the reaction between 2-(bromomethyl)-3-(4-ethylphenyl)prop-2-enenitrile (**126c**) and quinoline in the presence of K_2CO_3 in DMF, following the similar procedure described for the molecule **128a**.



Reaction Time: 6 h

Yield: 47%

Mp: 138-140°C

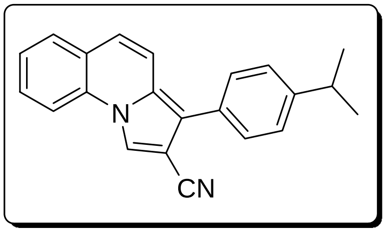
IR (KBr): ν 2226 cm^{-1}

^{1}H NMR (400 MHz): δ 1.29 (t, 3H, *J* = 7.6 Hz), 2.72 (q, 2H, *J* = 7.6 Hz), 7.09 (d, 1H, *J* = 9.2 Hz), 7.33 (d, 2H, *J* = 8.0 Hz), 7.39-7.48 (m, 2H), 7.52-7.60 (m, 3H), 7.64 (d, 1H, *J* = 7.6 Hz), 7.85 (d, 1H, *J* = 8.4 Hz), 8.25 (s, 1H).

^{13}C NMR (100 MHz):	δ 15.57, 28.72, 96.68, 114.42, 116.32, 117.56, 117.91, 120.55, 121.76, 124.58, 125.60, 128.00, 128.58, 128.78, 128.86, 128.99, 129.57, 132.44, 143.65.
LCMS (*m/z*):	297 $(M+H)^+$
Anal. Calcd. for $C_{21}H_{16}N_2$:	C, 85.11; H, 5.44; N, 9.45.
Found:	C, 85.02; H, 5.42; N, 9.40.

1-Aza-12-cyano-11-(4-isopropylphenyl)tricyclo[8.3.0.0^{2,7}]trideca-2,4,6,8,10,12-hexaene (128d):

Treatment of 2-(bromomethyl)-3-(4-isopropylphenyl)prop-2-enenitrile (**126d**) with quinoline in the presence of K_2CO_3 in DMF, following the similar procedure described for the molecule **128a** furnished the title compound as a colorless solid.



Reaction Time:	6 h
Yield:	51%
Mp:	148-150°C
IR (KBr):	ν 2220 cm^{-1}
^{1}H NMR (400 MHz):	δ 1.31 (d, 6H, *J* = 6.8 Hz), 2.98 (sept, 1H, *J* = 6.8 Hz), 7.10 (d, 1H, *J* = 9.6 Hz), 7.36 (d, 2H, *J* = 8.00 Hz), 7.40-7.50 (m, 2H), 7.54-7.60 (m, 3H), 7.66 (d, 1H, *J* = 7.6 Hz), 7.86 (d, 1H, *J* = 8.4 Hz), 8.26 (s, 1H).
^{13}C NMR (100 MHz):	δ 24.05, 34.03, 96.71, 114.46, 116.37, 117.66, 117.94, 120.60, 121.76, 124.63, 125.63, 127.18, 128.05, 128.81, 128.86, 129.02, 129.72, 132.49, 148.25.

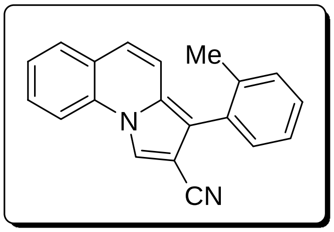
LCMS (*m/z*): 311 $(M+H)^+$

Anal. Calcd. for $C_{20}H_{18}N_2$: C, 85.13; H, 5.85; N, 9.03.

Found: C, 85.28; H, 5.91; N, 8.99.

1-Aza-12-cyano-11-(2-methylphenyl)tricyclo[8.3.0.0^{2,7}]trideca-2,4,6,8,10,12-hexaene (130):

This product was obtained as a colorless solid *via* the treatment of 2-(bromomethyl)-3-(2-methylphenyl)prop-2-enenitrile (**126f**) with quinoline in the presence of K_2CO_3 in DMF, following the similar procedure described for the molecule **128a**.



Reaction Time: 6 h

Yield: 50%

Mp: 168-170°C

IR (KBr): ν 2226 cm^{-1}

^{1}H NMR (400 MHz): δ 2.27 (s, 3H), 7.02-7.12 (m, 2H), 7.28-7.38 (m, 4H), 7.41-7.45 (m, 1H), 7.56-7.64 (m, 1H), 7.66-7.70 (m, 1H), 7.90 (d, 1H, *J* = 8.0 Hz), 8.30 (s, 1H).

^{13}C NMR (100 MHz): δ 20.16, 98.12, 114.45, 116.09, 117.30, 117.65, 120.23, 121.52, 124.52, 125.59, 125.92, 128.35, 128.64, 128.81, 129.10, 130.64, 131.21, 131.34, 132.46, 137.68.

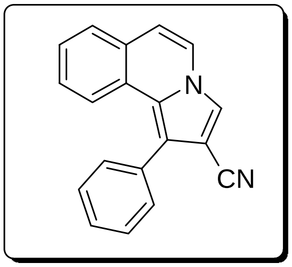
LCMS (*m/z*): 283 $(M+H)^+$

Anal. Calcd. for $C_{20}H_{14}N_2$: C, 85.08; H, 5.00; N, 9.92.

Found: C, 85.00; H, 4.95; N, 9.98.

1-Aza-12-cyano-11-phenyltricyclo[8.3.0.0^{4,9}]trideca-2,4,6,8,10,12-hexaene (129a):

To a stirred solution of 2-(bromomethyl)-3-phenylprop-2-enenitrile (1 mmol, 0.222 g) (**126a**) in DMF (3 mL) was added isoquinoline (2 mmol, 0.258 g) at room temperature. After stirring 1 h, [salt formation was observed as evidenced by TLC] potassium carbonate (5 mmol, 0.690 g) was added and heated for 5 h at 80 °C. The reaction mixture was allowed to cool to room temperature and diluted with saturated aqueous NaCl solution (5 mL) and extracted with dichloromethane (5 x 10 mL). The combined organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and the residue, thus obtained, was purified by column chromatography (silica gel, 8 % EtOAc in hexanes) to furnish the title compound (**129a)** as colorless solid.



Yield: 68% (0.182 g);

Mp: 142-144 °C

IR (KBr): ν 2220 cm^{-1}

^{1}H NMR (400 MHz): δ 6.87 (d, 1H, *J* = 7.6 Hz), 7.19-7.28 (m, 1H), 7.32-7.40 (m, 1H), 7.46-7.59 (m, 6H), 7.60 (d, 1H, *J* = 7.6 Hz), 7.70 (s, 1H), 7.73 (d, 1H, *J* = 8.0 Hz).

^{13}C NMR (100 MHz): δ 98.28, 114.52, 115.82, 120.21, 121.47, 122.93, 123.72, 125.59, 126.08, 127.04, 127.41, 127.67, 127.96, 128.27, 129.04, 130.36, 133.79.

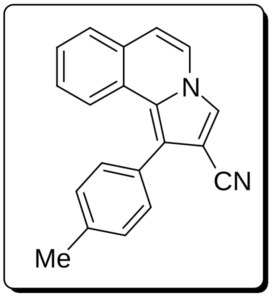
LCMS (*m/z*): 269 (M+H)$^+$

Anal. Calcd. for $C_{19}H_{12}N_2$: C, 85.05; H, 4.51; N, 10.44.

Found: C, 85.20; H, 4.54; N, 10.36.

1-Aza-12-cyano-11-(4-methylphenyl)tricyclo[8.3.0.$0^{4,9}$]trideca-2,4,6,8,10,12-hexaene (129b):

This compound was obtained as a colorless solid *via* the treatment of 2-(bromomethyl)-3-(4-methylphenyl)prop-2-enenitrile (**126b**) with isoquinoline in the presence of K_2CO_3 in DMF, following the similar procedure described for the molecule **129a**.



Reaction Time: 6 h

Yield: 63%

Mp: 160-162°C

IR (KBr): ν 2226 cm^{-1}

^1H NMR (400 MHz): δ 2.45 (s, 3H), 6.84 (d, 1H, *J* = 7.2 Hz), 7.18-7.28 (m, 1H), 7.30-7.38 (m, 3H), 7.41 (d, 2H, *J* = 8.0 Hz), 7.52 (d, 1H, *J* = 7.6 Hz), 7.64 (d, 1H, *J* = 7.6 Hz), 7.68 (s, 1H), 7.78 (d, 1H, *J* = 8.4 Hz).

^{13}C NMR (100 MHz): δ 21.46, 98.31, 114.42, 115.94, 120.08, 121.55, 122.92, 123.73, 125.49, 126.18, 127.34, 127.61, 127.89, 129.75, 130.13, 130.68, 137.98.

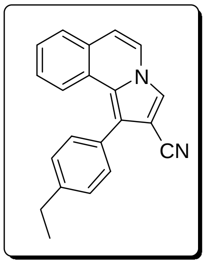
LCMS (*m/z*): 283 $(M+H)^+$

Anal. Calcd. for $C_{20}H_{14}N_2$: C, 85.08; H, 5.00; N, 9.92.

Found: C, 85.15; H, 5.06; N, 10.02.

1-Aza-12-cyano-11-(4-ethylphenyl)tricyclo[8.3.0.$0^{4,9}$]trideca-2,4,6,8,10,12-hexaene (129c):

This product was obtained as a colorless solid *via* the reaction between 2-(bromomethyl)-3-(4-ethylphenyl)prop-2-enenitrile (**126c**) and isoquinoline in the presence of K_2CO_3 in DMF, following the similar procedure described for the molecule **129a**.



Reaction Time: 6 h

Yield: 60%

Mp: 164-166°C

IR (KBr): ν 2220 cm^{-1}

^{1}H NMR (400 MHz): δ 1.34 (t, 3H, *J* = 7.6 Hz), 2.76 (q, 2H, *J* = 7.6 Hz), 6.87 (d, 1H, *J* = 7.2 Hz), 7.20-7.38 (m, 4H), 7.45 (d, 2H, *J* = 8.0 Hz), 7.53 (d, 1H, *J* = 7.6 Hz), 7.67 (d, 1H, *J* = 7.2 Hz), 7.70 (s, 1H), 7.79 (d, 1H, *J* = 8.0 Hz).

^{13}C NMR (100 MHz): δ 15.36, 28.74, 98.25, 114.39, 115.97, 120.13, 121.54, 122.90, 123.71, 125.47, 126.15, 126.91, 127.32, 127.59, 127.87, 128.47, 130.14, 130.85, 144.17.

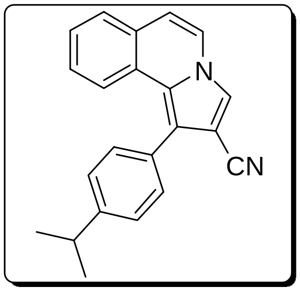
LCMS (*m/z*): 297 $(M+H)^+$

Anal. Calcd. for $C_{21}H_{16}N_2$: C, 85.11; H, 5.44; N, 9.45.

Found: C, 84. 91; H, 5.49; N, 9.42.

1-Aza-12-cyano-11-(4-isopropylphenyl)tricyclo[8.3.0.$0^{4,9}$]trideca-2,4,6,8,10,12-hexaene (129d):

Treatment of 2-(bromomethyl)-3-(4-isopropylphenyl)prop-2-enenitrile (**126d**) with isoquinoline in the presence of K_2CO_3 in DMF, following the similar procedure described for the molecule **129a** furnished the title compound as a colorless solid.



Reaction Time: 6 h

Yield: 63%

Mp: 172-174°C

IR (KBr): ν 2222 cm^{-1}

^{1}H NMR (400 MHz): δ 1.33 (d, 6H, J = 6.8 Hz), 2.98 (sept, 1H, J = 6.8 Hz), 6.82 (d, 1H, J = 7.2 Hz), 7.16-7.25 (m, 1H), 7.30-7.38 (m, 3H), 7.43 (d, 2H, J = 8.0 Hz), 7.50 (d, 1H, J = 7.6 Hz), 7.61 (d, 1H, J = 7.2 Hz), 7.65 (s, 1H), 7.79 (d, 1H, J = 8.0 Hz).

^{13}C NMR (100 MHz): δ 24.00, 33.98, 98.20, 114.37, 116.00, 120.16, 121.52, 122.90, 123.70, 125.44, 126.14, 126.89, 127.02, 127.31, 127.58, 127.85, 130.10, 130.90, 148.75.

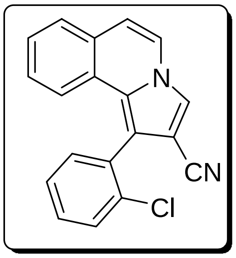
LCMS (m/z): 311 $(M+H)^+$

Anal. Calcd. for $C_{20}H_{14}N_2$: C, 85.13; H, 5.85; N, 9.03.

Found: C, 85.00; H, 5.81; N, 9.07.

1-Aza-12-cyano-11-(2-chlorophenyl)tricyclo[8.3.0.0^{4,9}]trideca-2,4,6,8,10,12-hexaene (131):

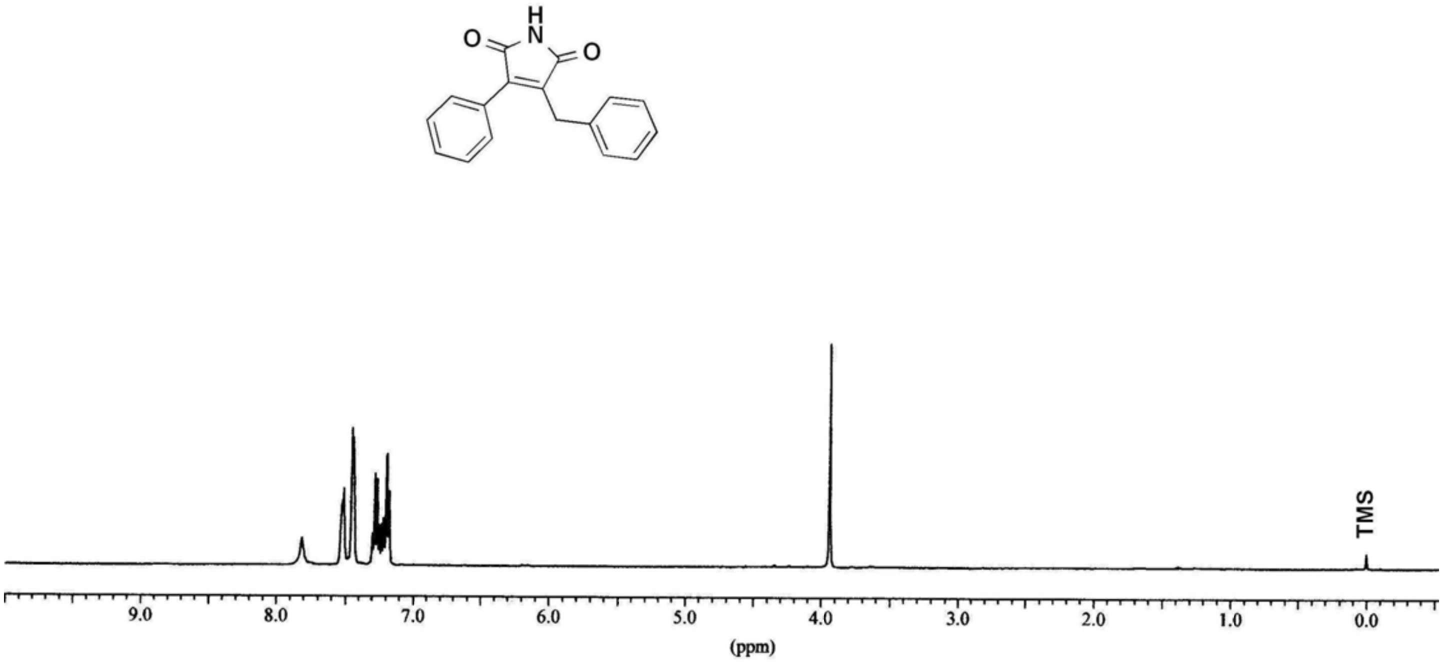
This product was obtained as a colorless solid *via* the treatment of 2-(bromomethyl)-3-(2-chlorophenyl)prop-2-enenitrile (**126g**) with isoquinoline in the presence of K_2CO_3 in DMF, following the similar procedure described for the molecule **129a**.



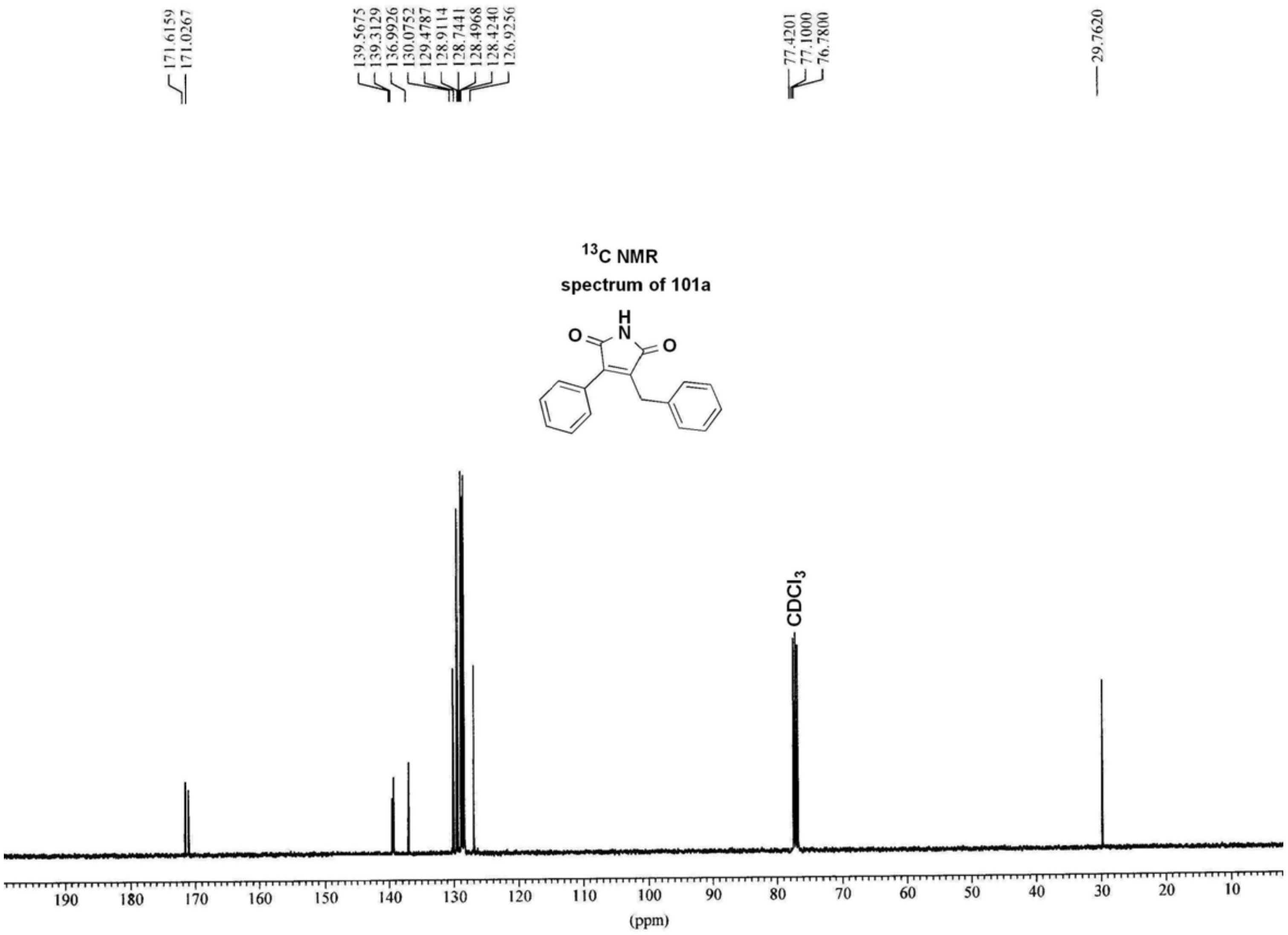
Reaction Time:	6 h
Yield:	52%
Mp:	168-169 °C
IR (KBr):	ν 2227 cm^{-1}
^{1}H NMR (400 MHz):	δ 6.89 (d, 1H, *J* = 7.2 Hz), 7.20-7.26 (m, 1H), 7.32-7.50 (m, 5H), 7.53-7.63 (m, 2H), 7.68 (d, 1H, *J* = 7.2 Hz), 7.73 (s, 1H).
^{13}C NMR (100 MHz):	δ 98.25, 114.59, 115.41, 117.66, 120.18, 122.77, 123.70, 125.89, 126.37, 127.17, 127.28, 127.39, 127.63, 128.25, 130.07, 130.16, 132.69, 132.75, 135.21.
LCMS (*m/z*):	303 (M+H)$^+$, 305 (M+2+H)$^+$;
Anal. Calcd. for $C_{19}H_{11}N_2Cl$:	C, 75.38; H, 3.66; N, 9.25.
Found:	C, 75.53; H, 3.64; N, 9.34.

Spectrum 1

^{1}H NMR spectrum of 101a



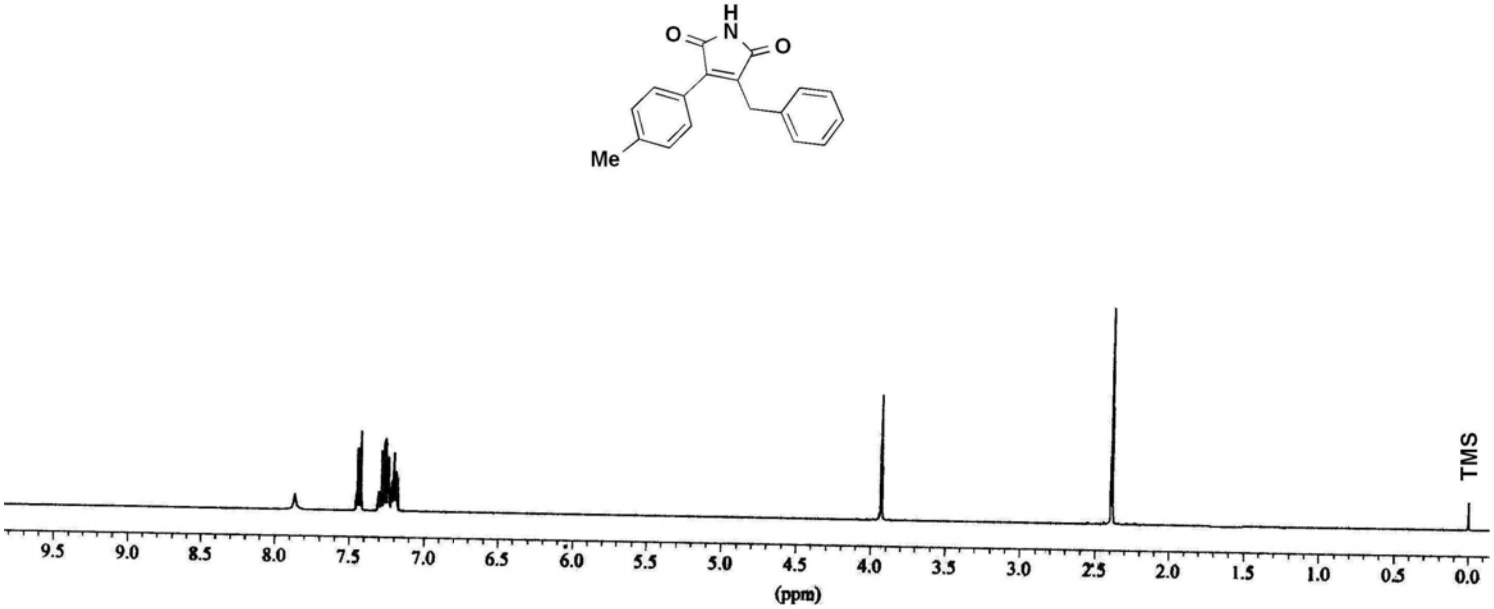
Spectrum 2



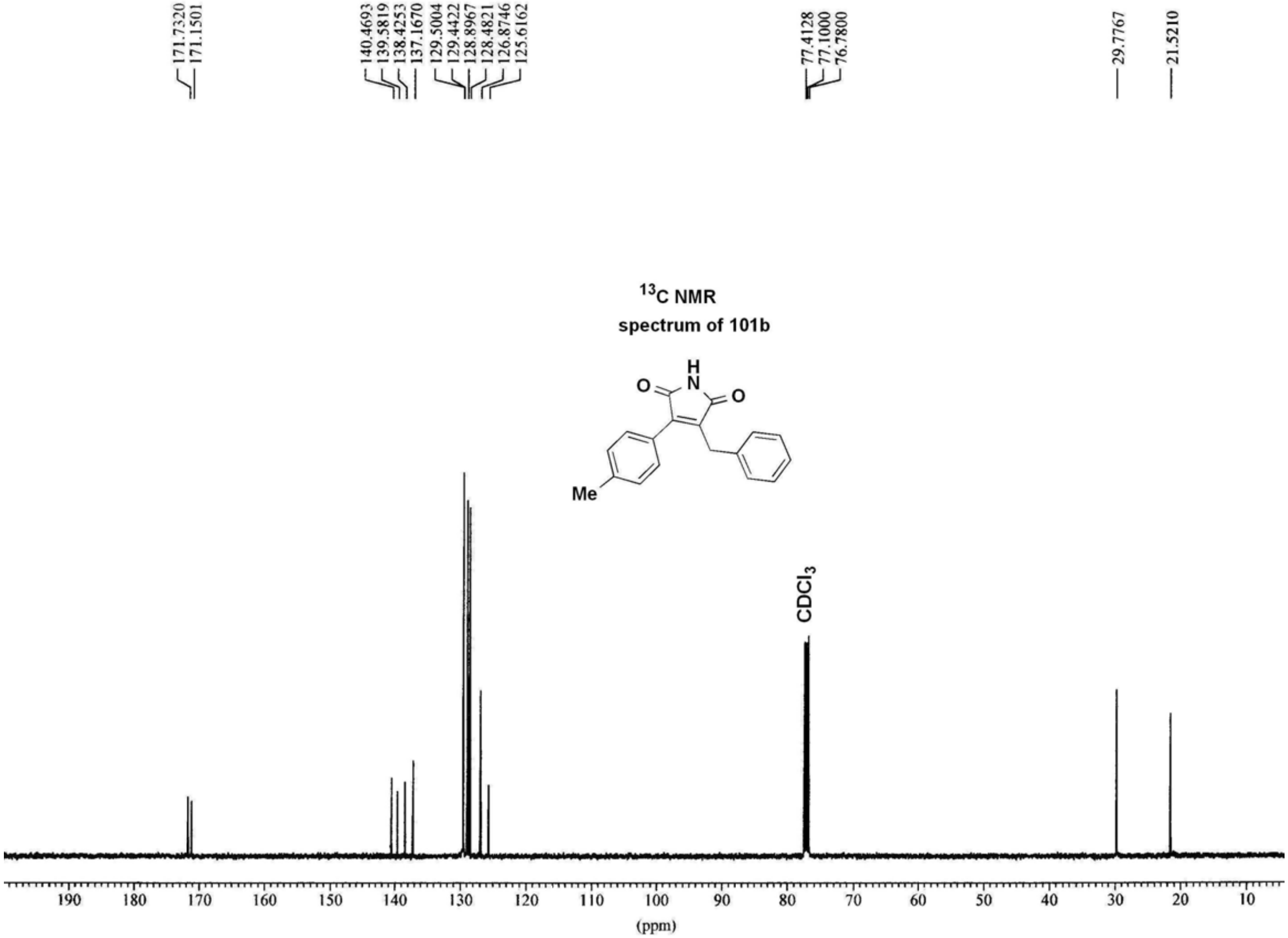
^{13}C NMR spectrum of 101a

Spectrum 3

^{1}H NMR spectrum of 101b



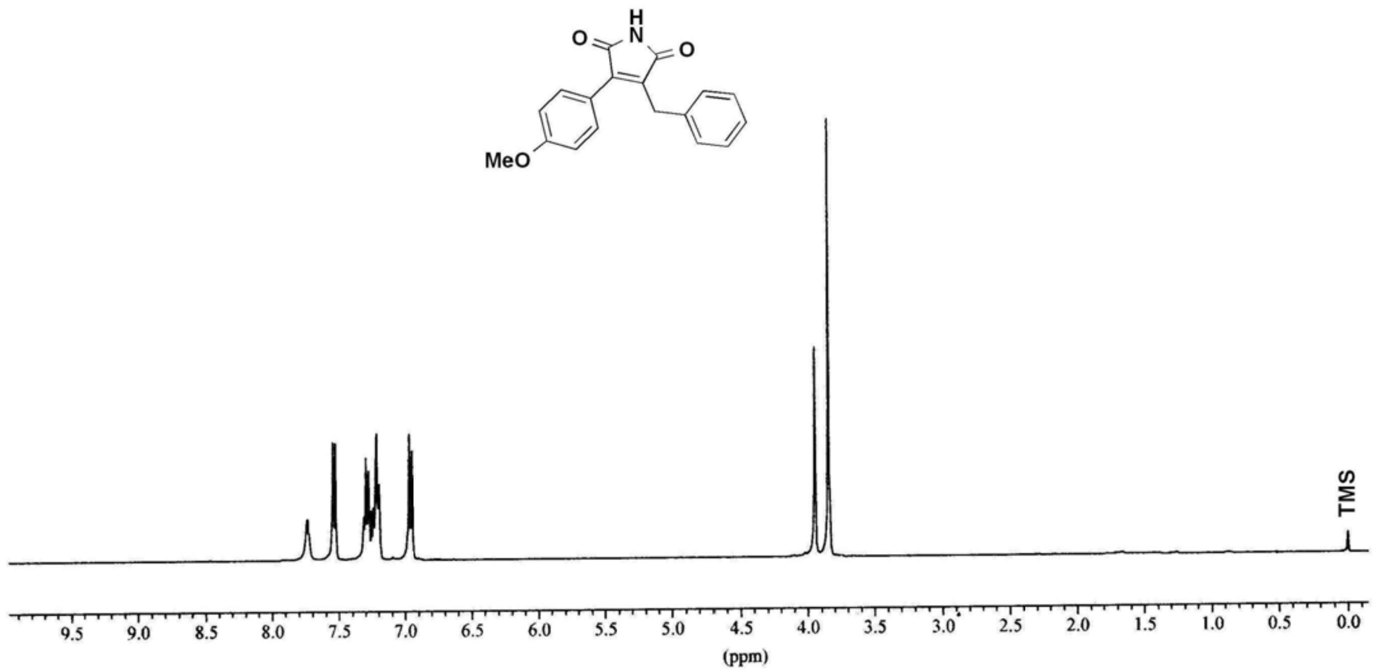
Spectrum 4



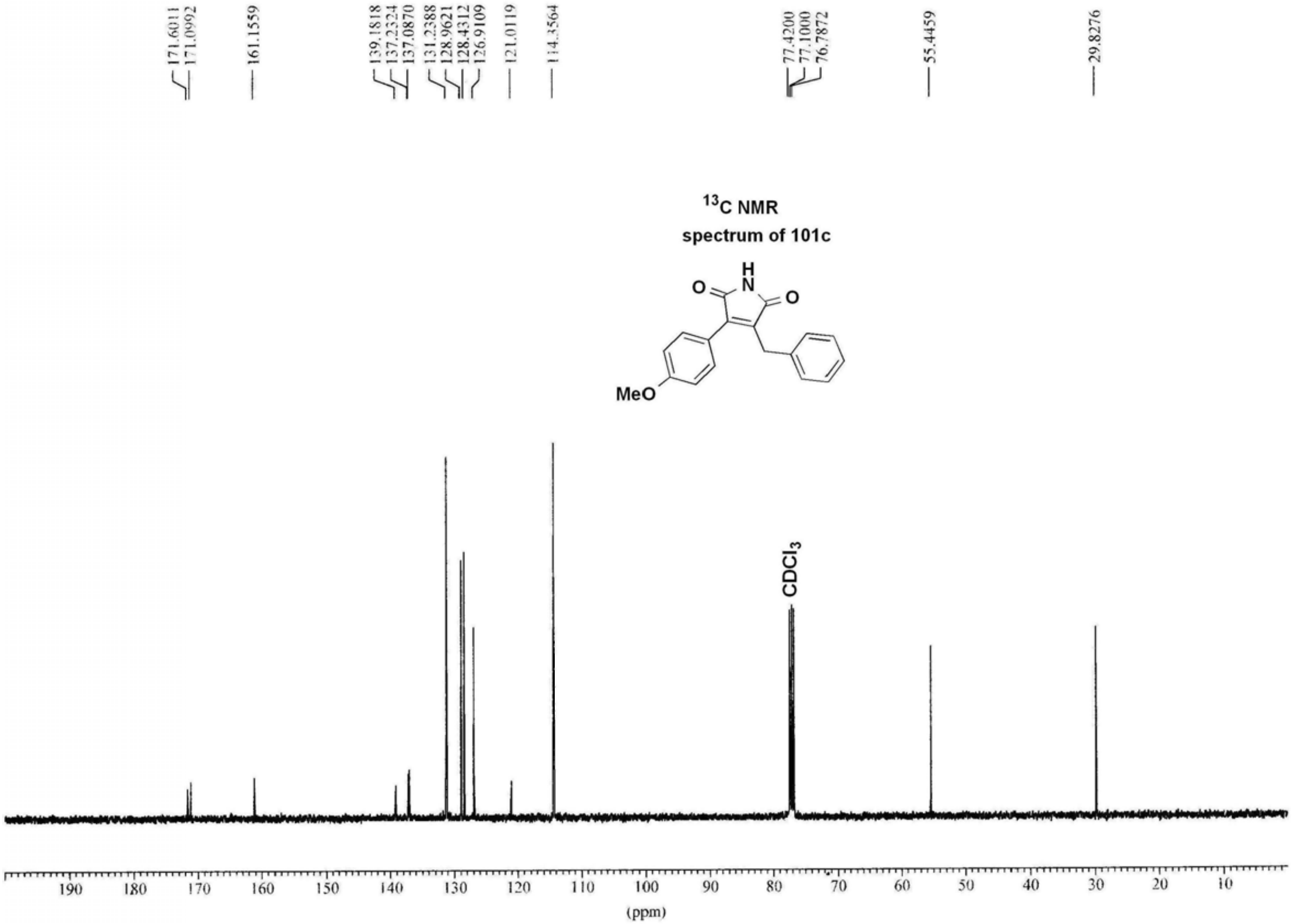
^{13}C NMR spectrum of 101b

Spectrum 5

^{1}H NMR spectrum of 101c



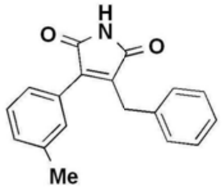
Spectrum 6

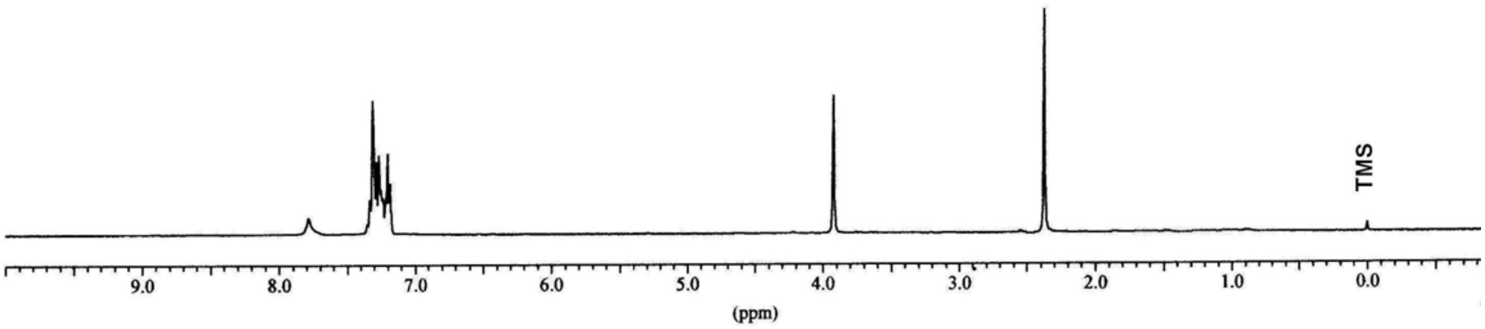


^{13}C NMR spectrum of 101c

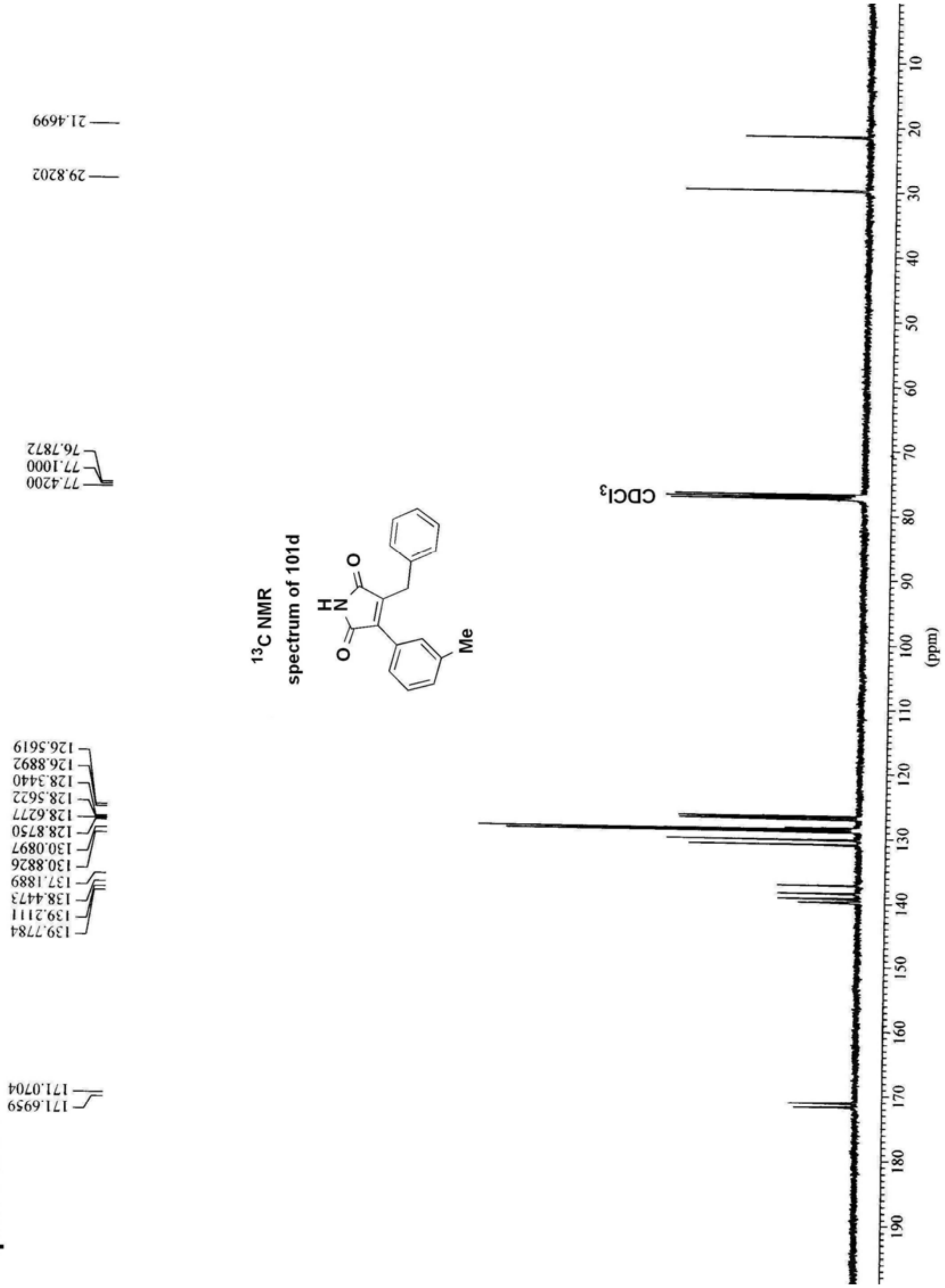
Spectrum 7

^{1}H NMR spectrum of 101d

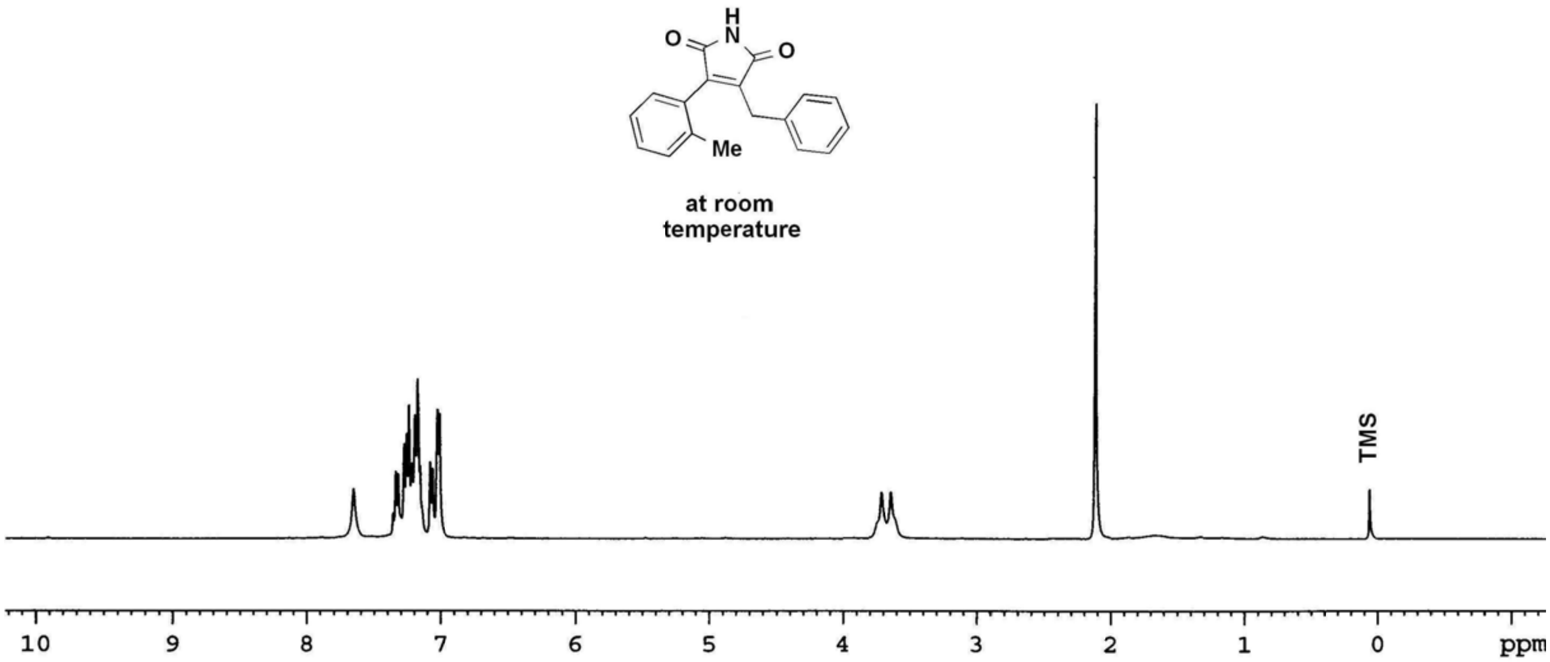




Spectrum 8

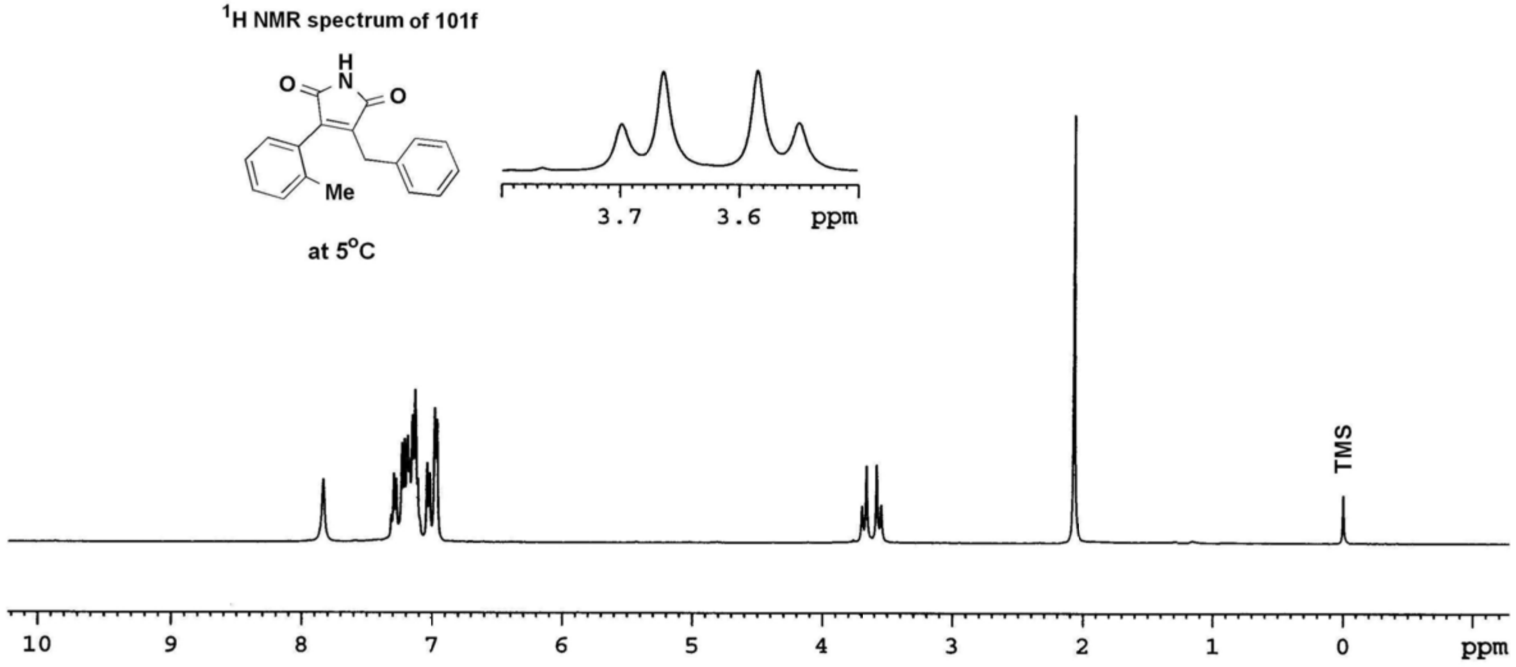

^{13}C NMR
spectrum of 101d
H
N
O
O
Me
CDCl$_3$
21.4699
29.8202
76.7872
77.1000
77.4200
126.5619
126.8892
128.3440
128.5622
128.6277
128.8750
130.0897
130.8826
137.1889
138.4473
139.2111
139.7784
171.0704
171.6959
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
(ppm)

Spectrum 9



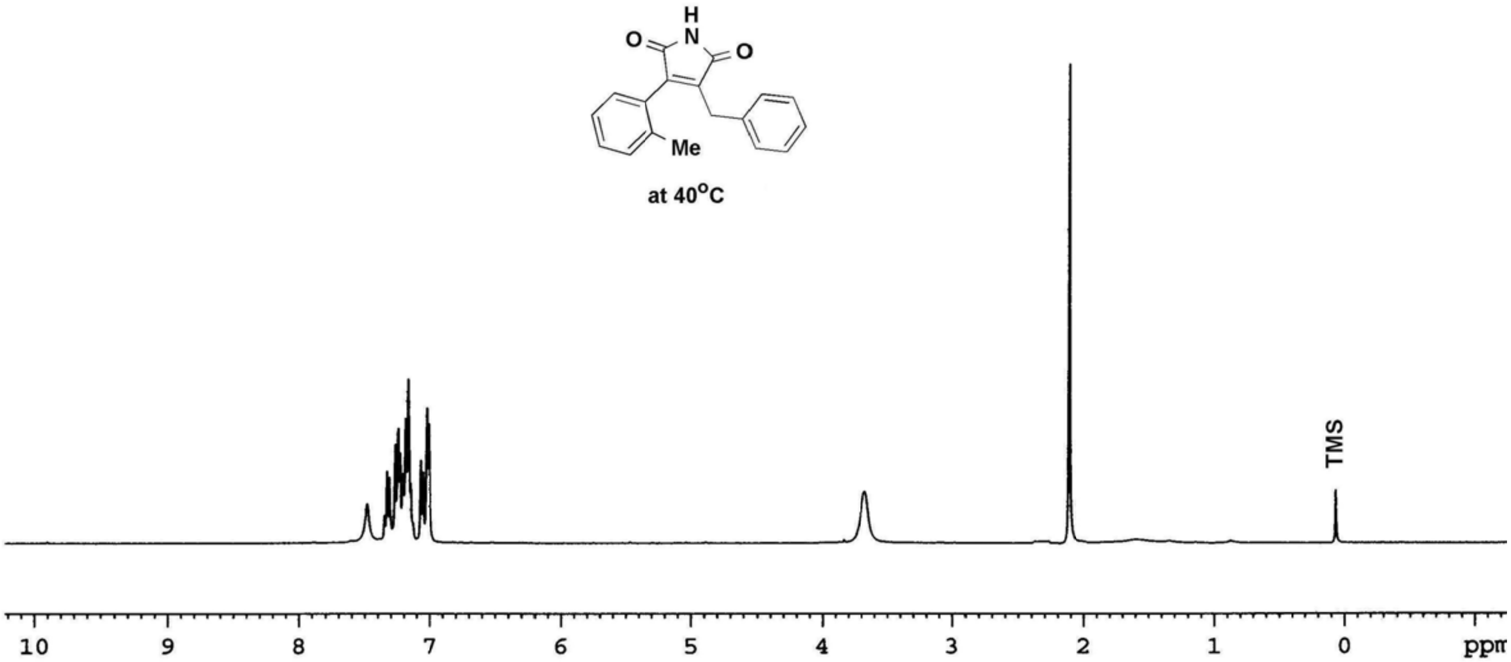
^{1}H NMR spectrum of 101f

Spectrum 10

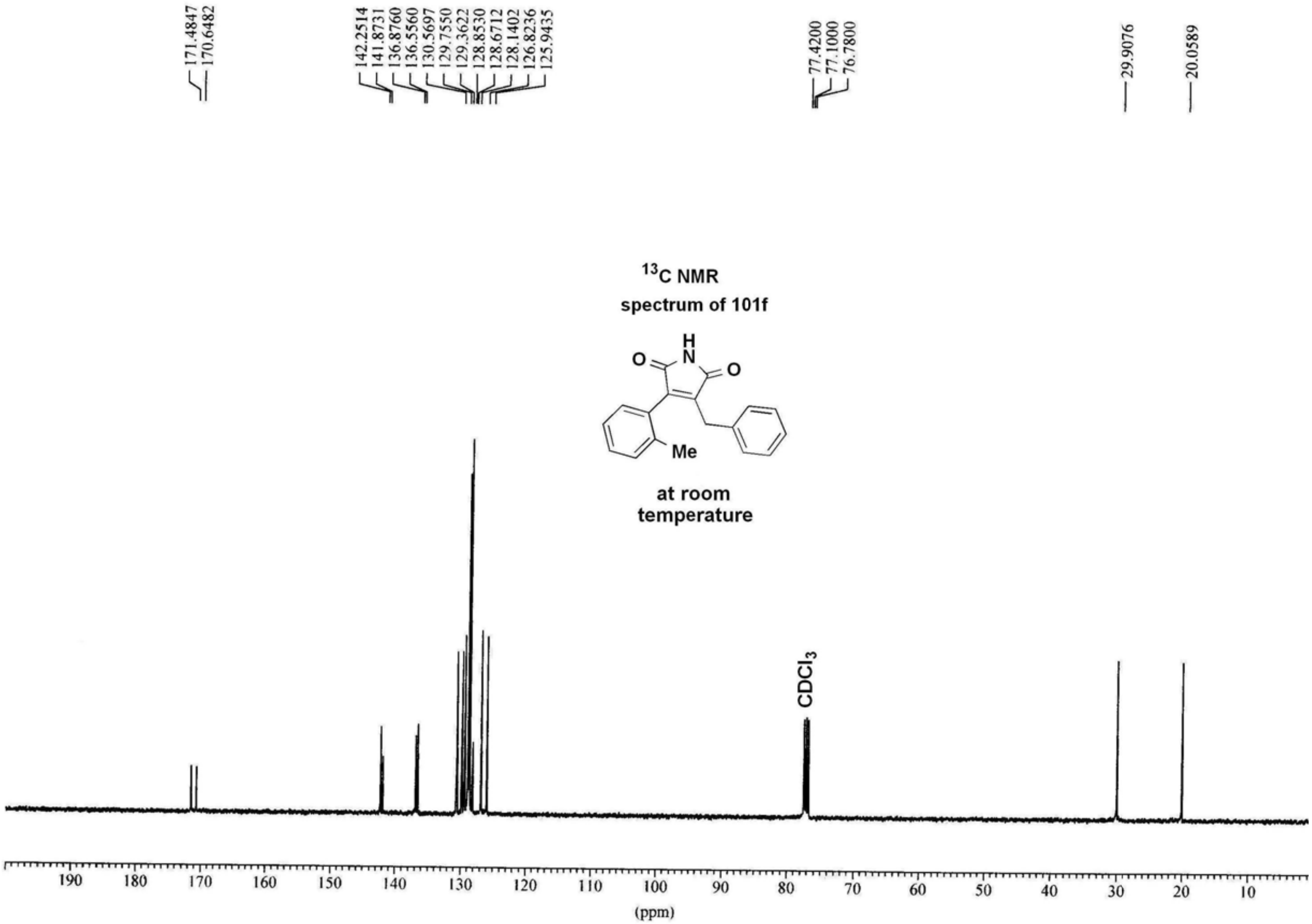

^{1}H NMR spectrum of 101f
H
N
O
O
Me
at 5^{o}C
3.7
3.6
ppm
TMS
10
9
8
7
6
5
4
3
2
1
0
ppm

Spectrum11

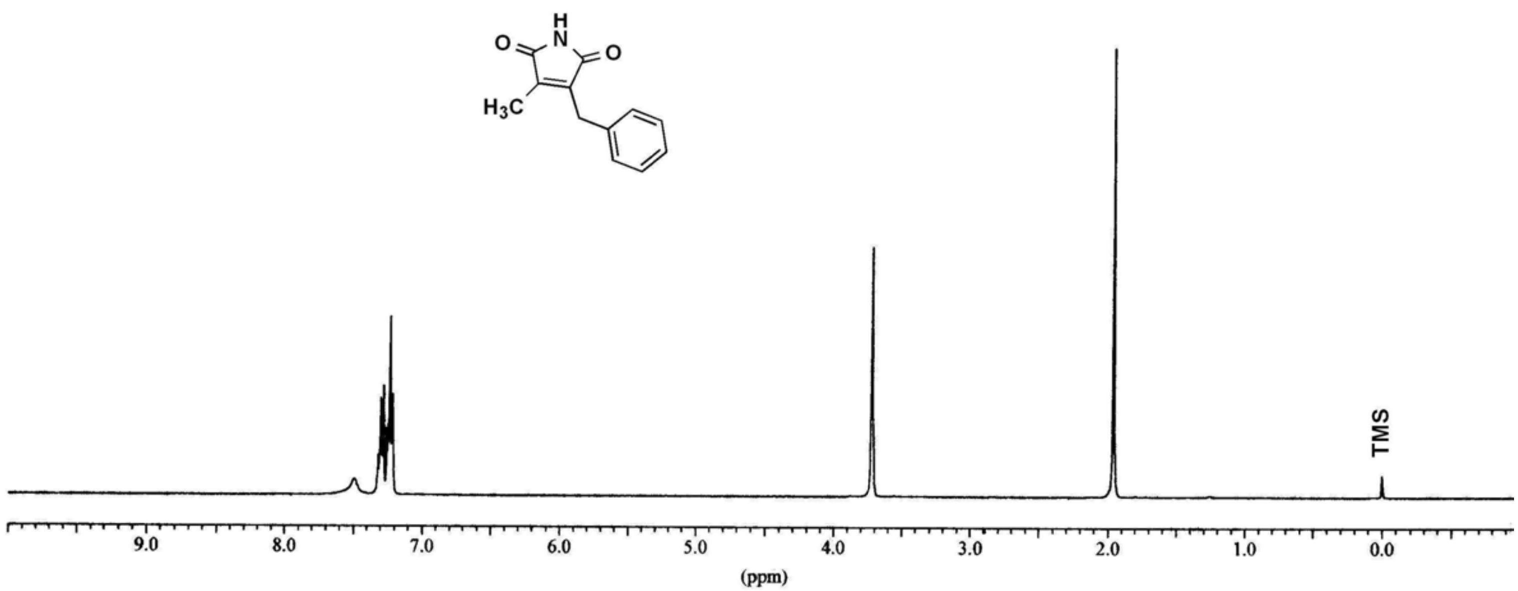
^{1}H NMR spectrum of 101f



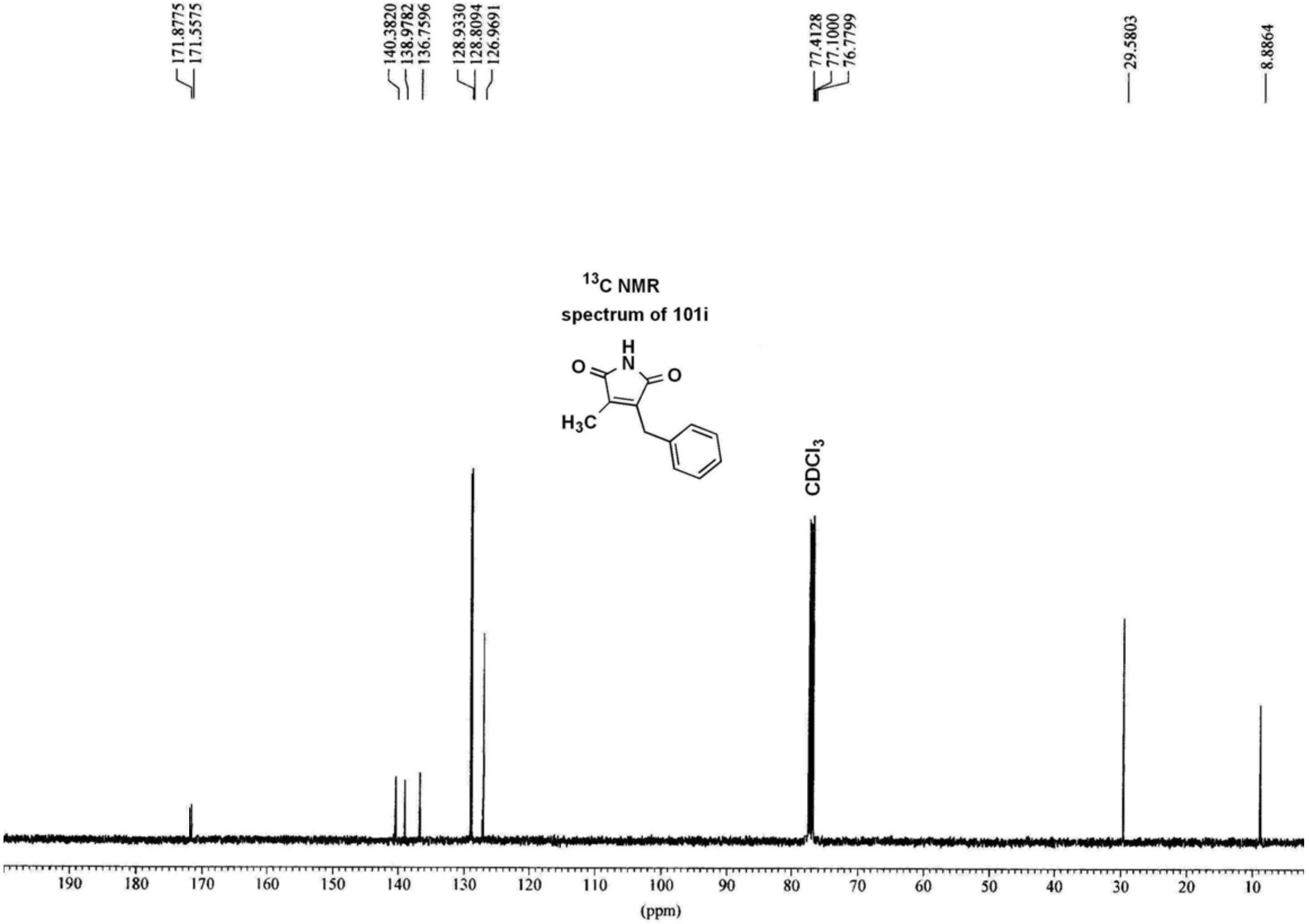
Spectrum 12


171.4847
170.6482
142.2514
141.8731
136.8760
136.5560
130.5697
129.7550
129.3622
128.8530
128.6712
128.1402
126.8236
125.9435
77.4200
77.1000
76.7800
29.9076
20.0589
^{13}C NMR
spectrum of 101f
H
N
O
O
Me
at room
temperature
CDCl$_3$
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
(ppm)

Spectrum 13

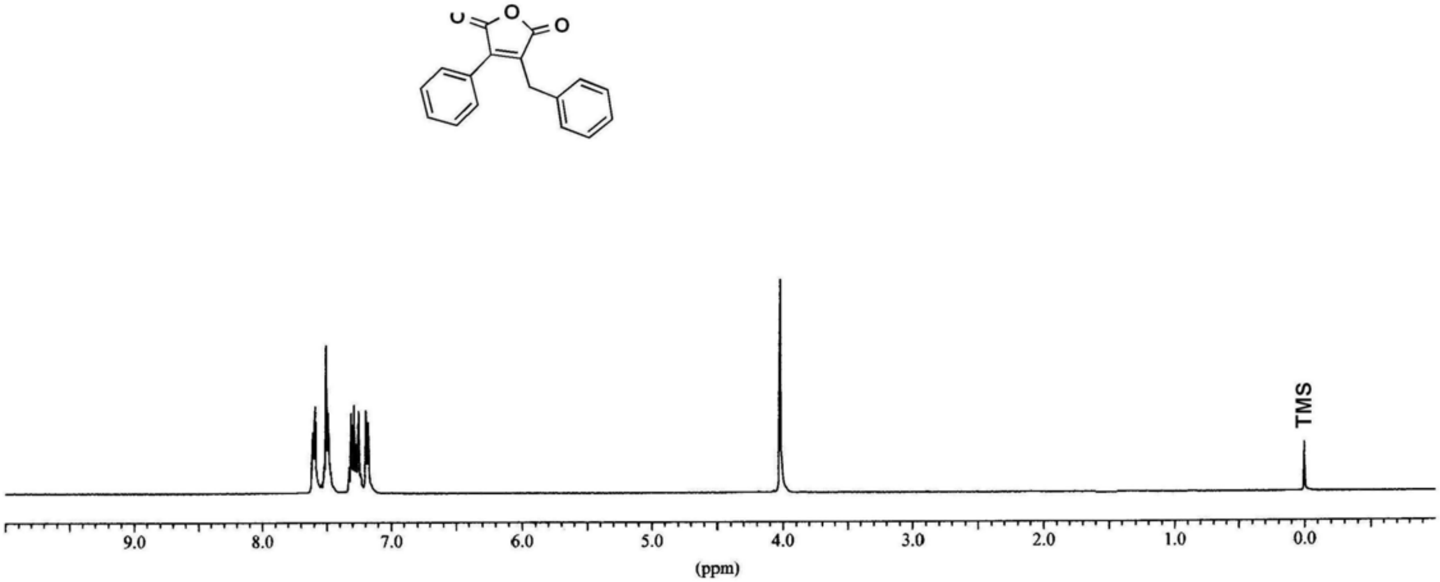

^{1}H NMR spectrum of 101i

Spectrum 14

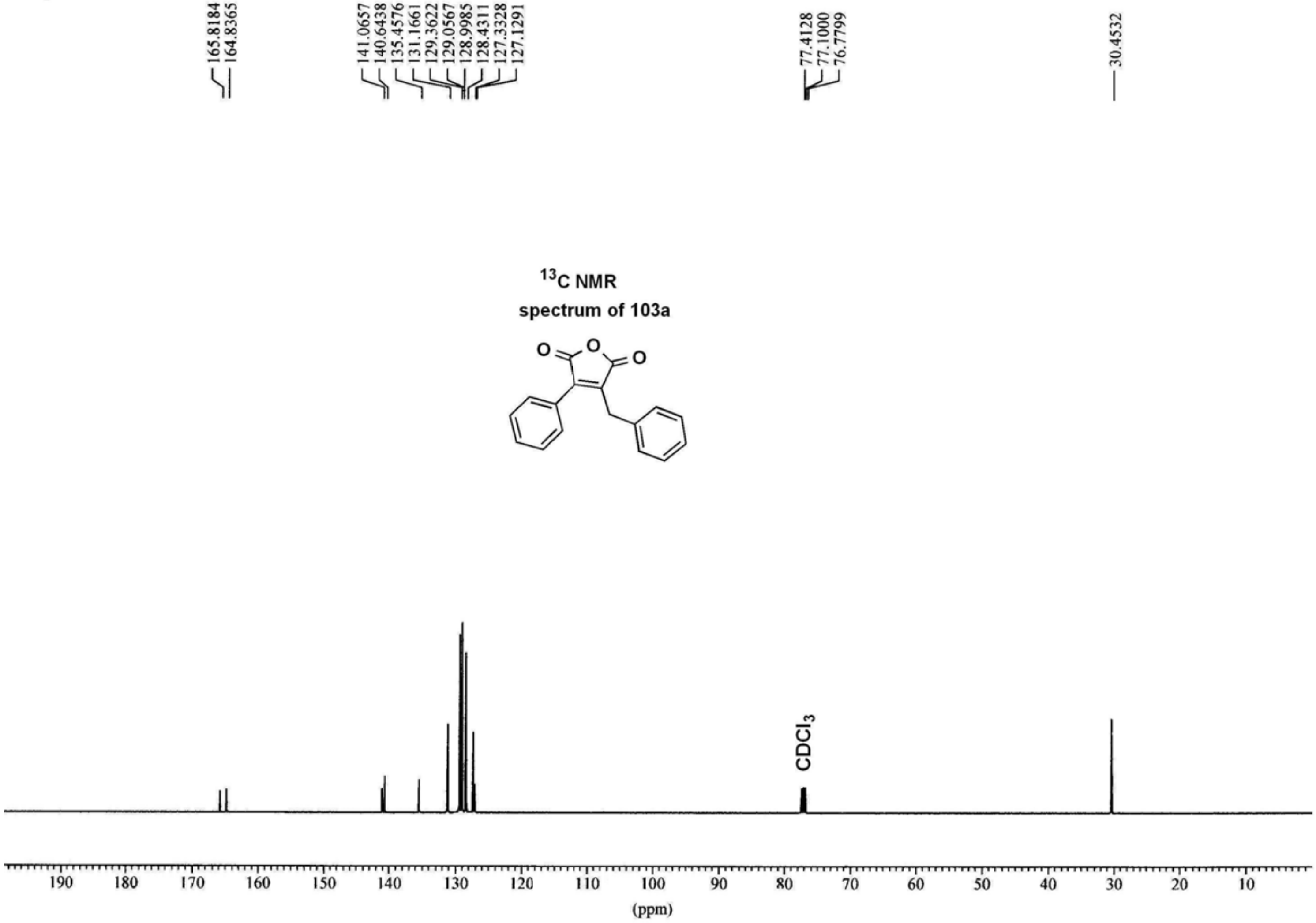

171.8775
171.5575
140.3820
138.9782
136.7596
128.9330
128.8094
126.9691
77.4128
77.1000
76.7799
29.5803
8.8864
^{13}C NMR
spectrum of 101i
H
N
O
O
H_3C
$CDCl_3$
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
(ppm)

Spectrum 15

^{1}H NMR spectrum of **103a**



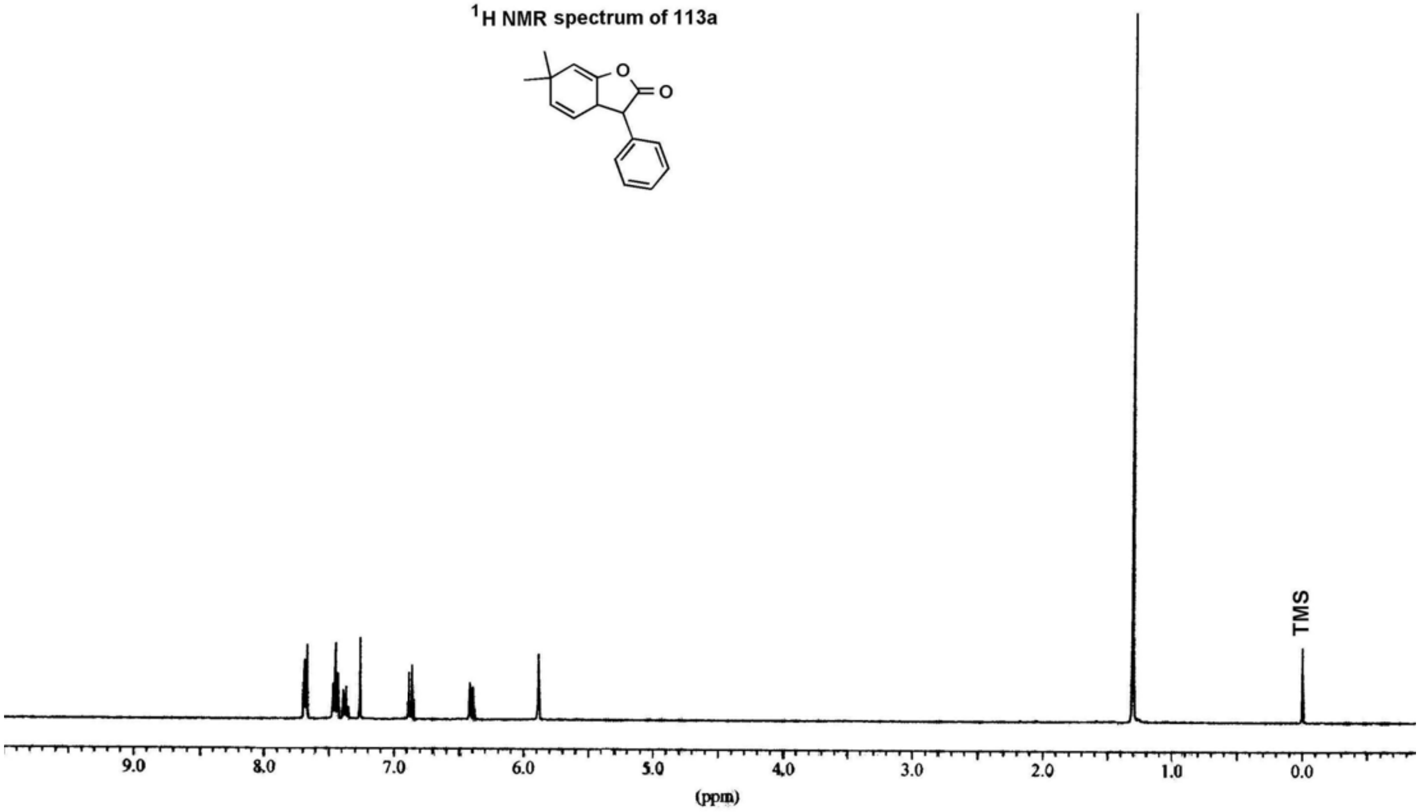
Spectrum16



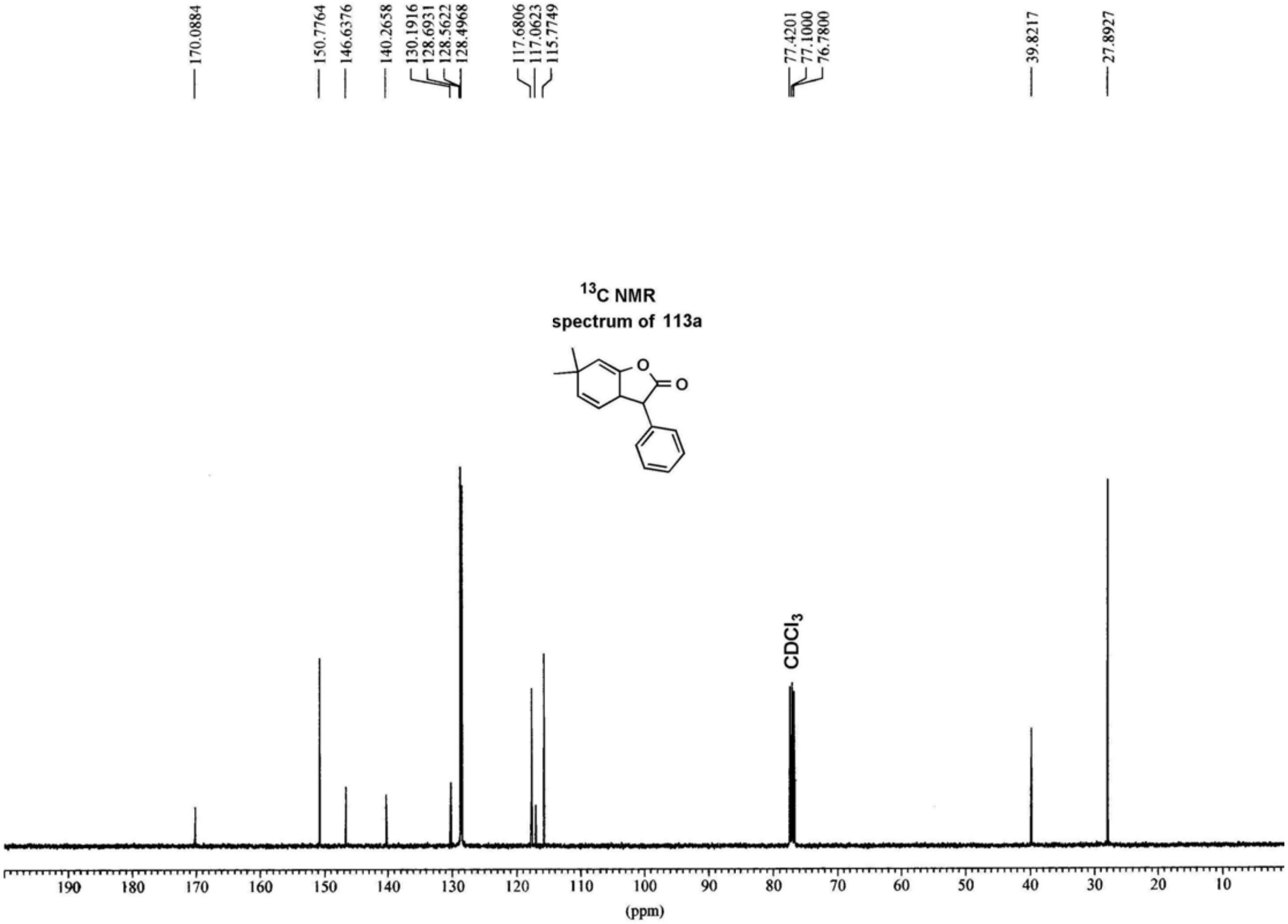
^{13}C NMR spectrum of 103a

Spectrum 17

^{1}H NMR spectrum of 113a

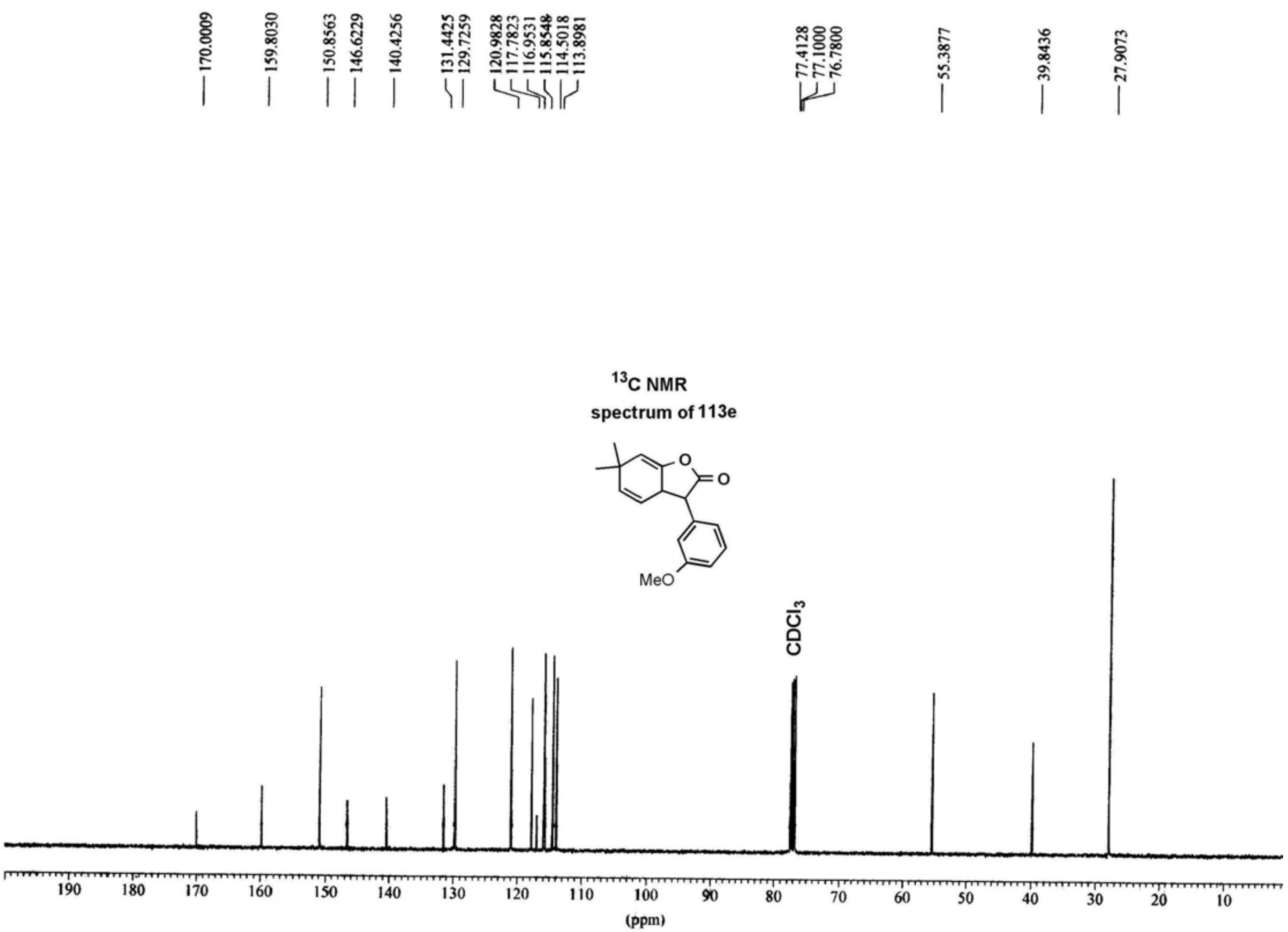


Spectrum 18



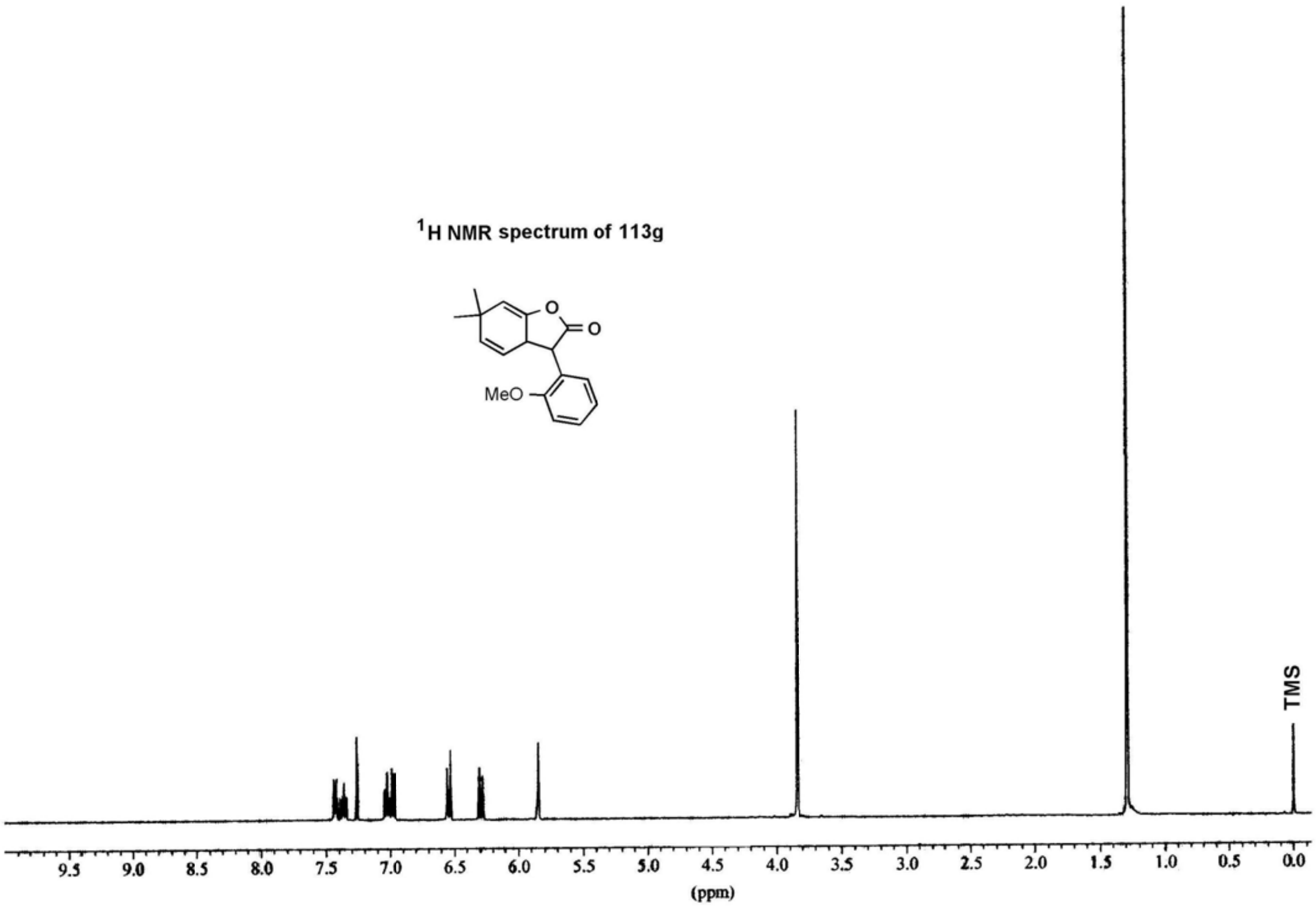
^{13}C NMR spectrum of 113a

Spectrum 19



^{13}C NMR spectrum of 113e

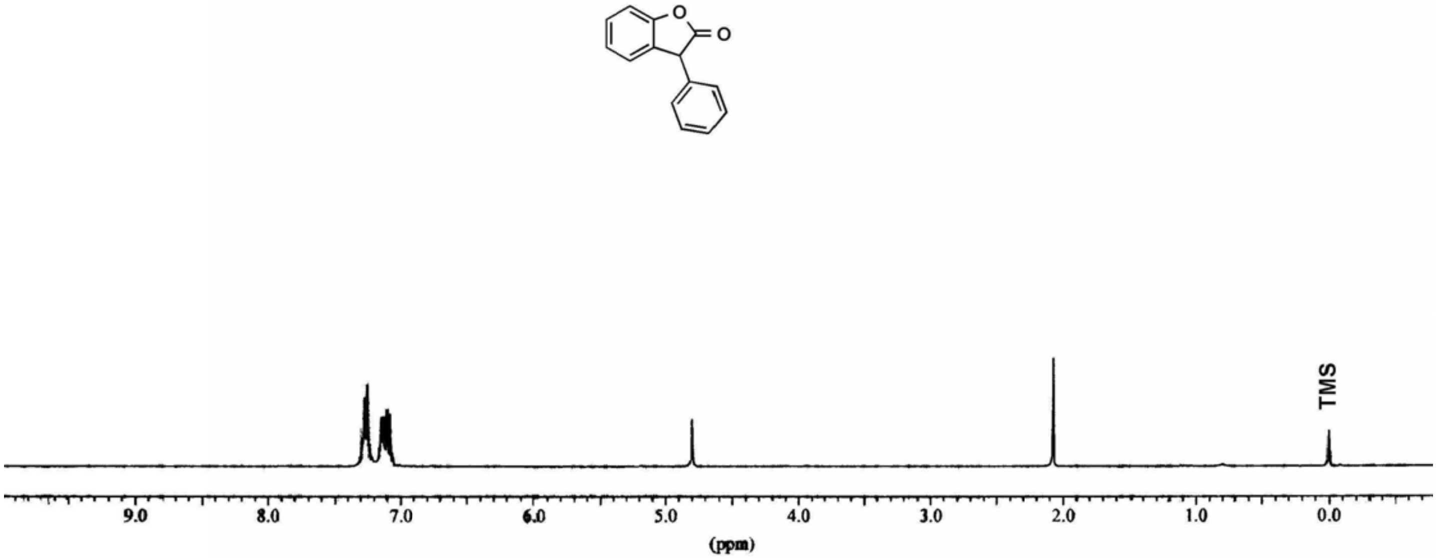
Spectrum 20



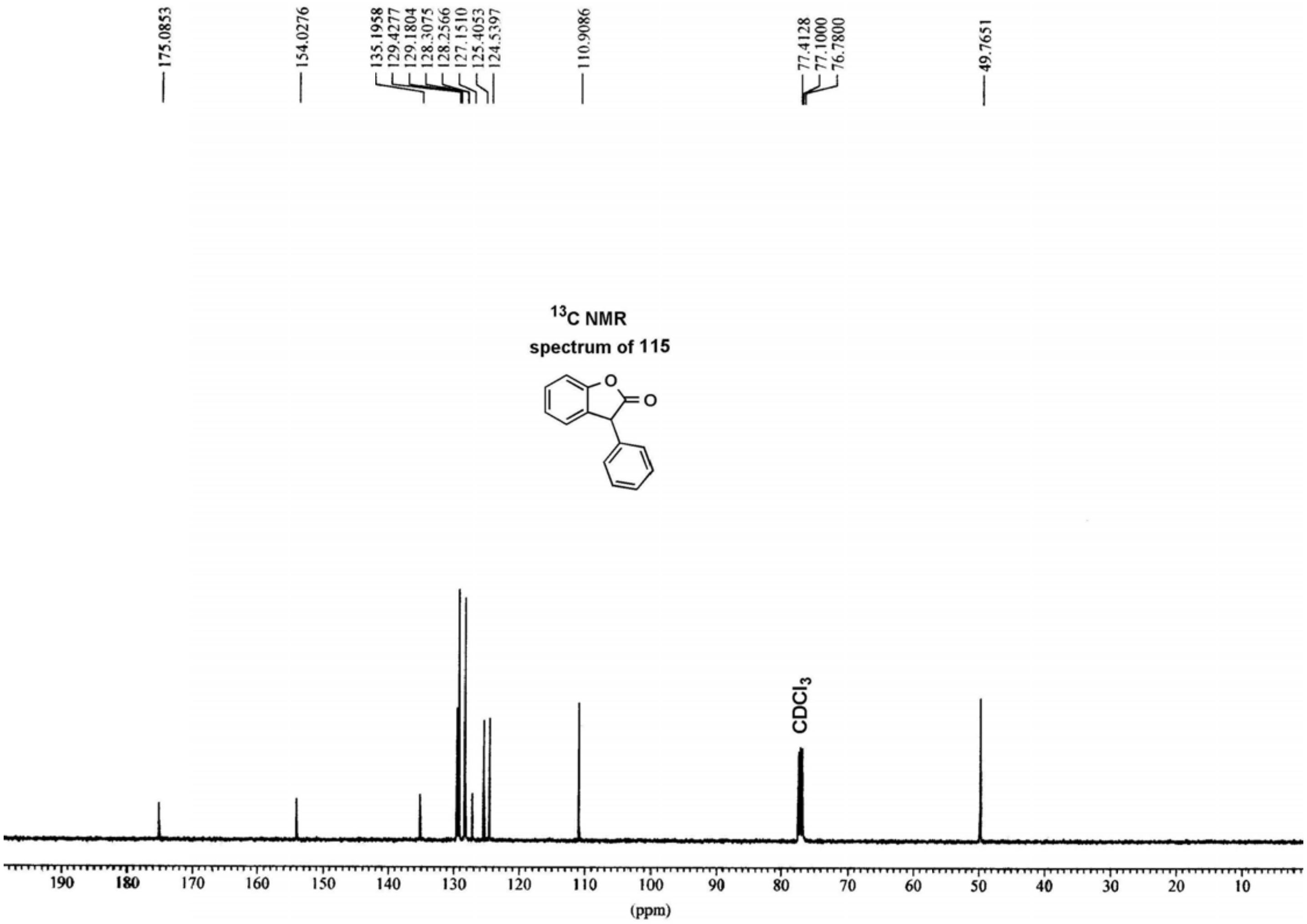
^{1}H NMR spectrum of 113g

Spectrum 21

^{1}H NMR spectrum of 115

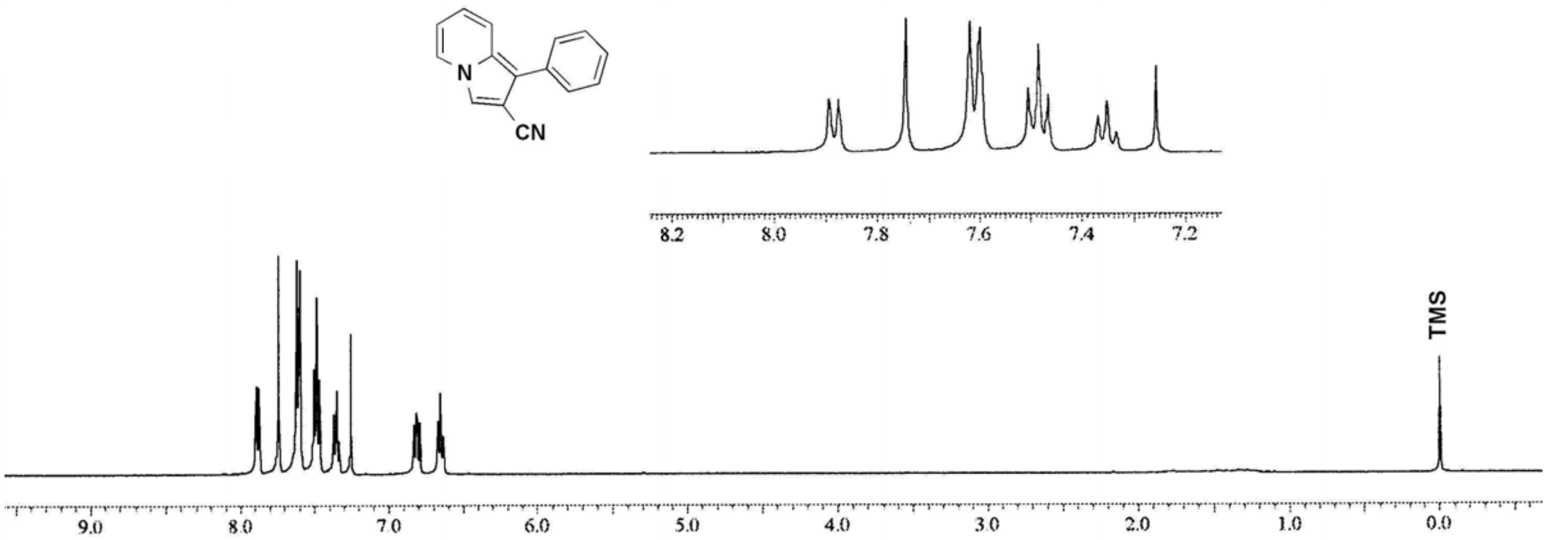


Spectrum 22



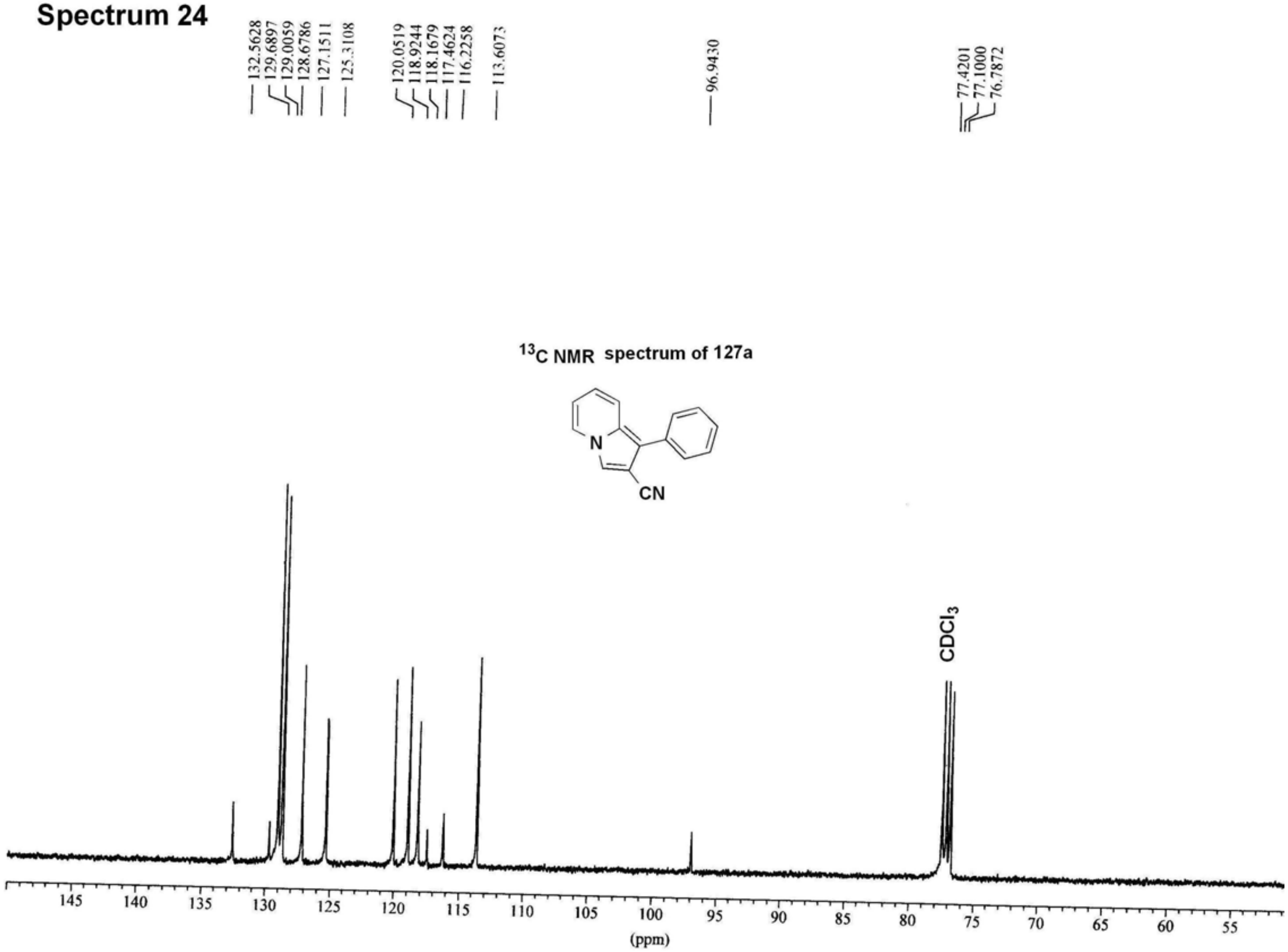
^{13}C NMR spectrum of 115

Spectrum 23



^{1}H NMR spectrum of 127a

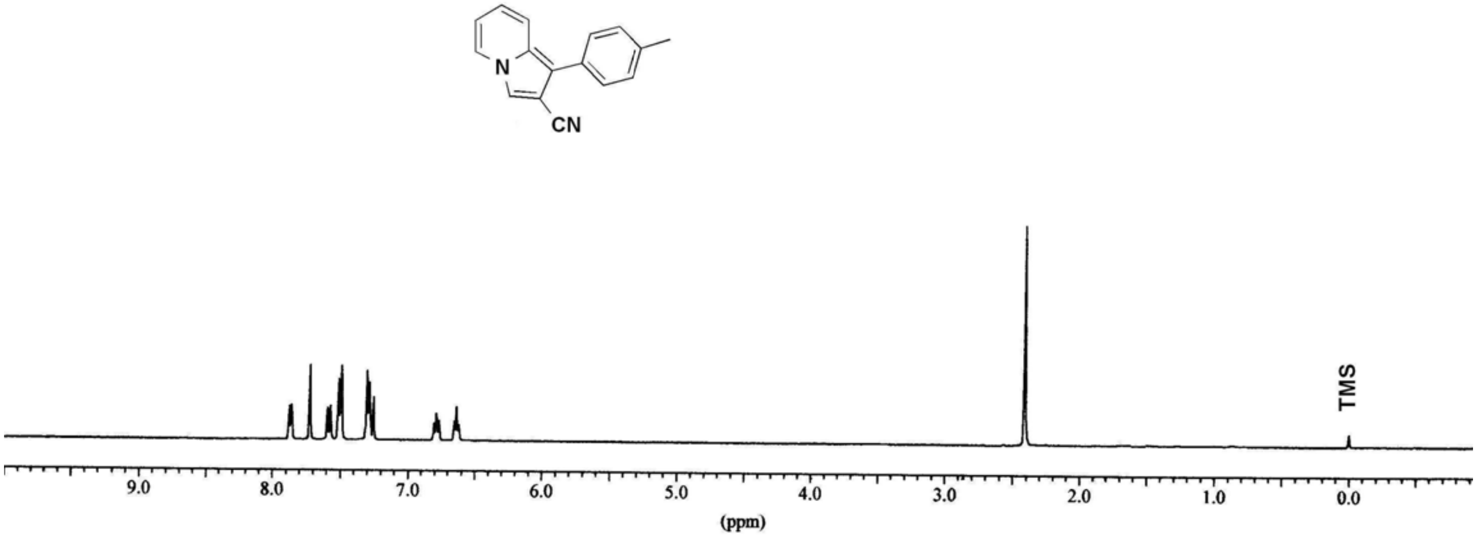
Spectrum 24



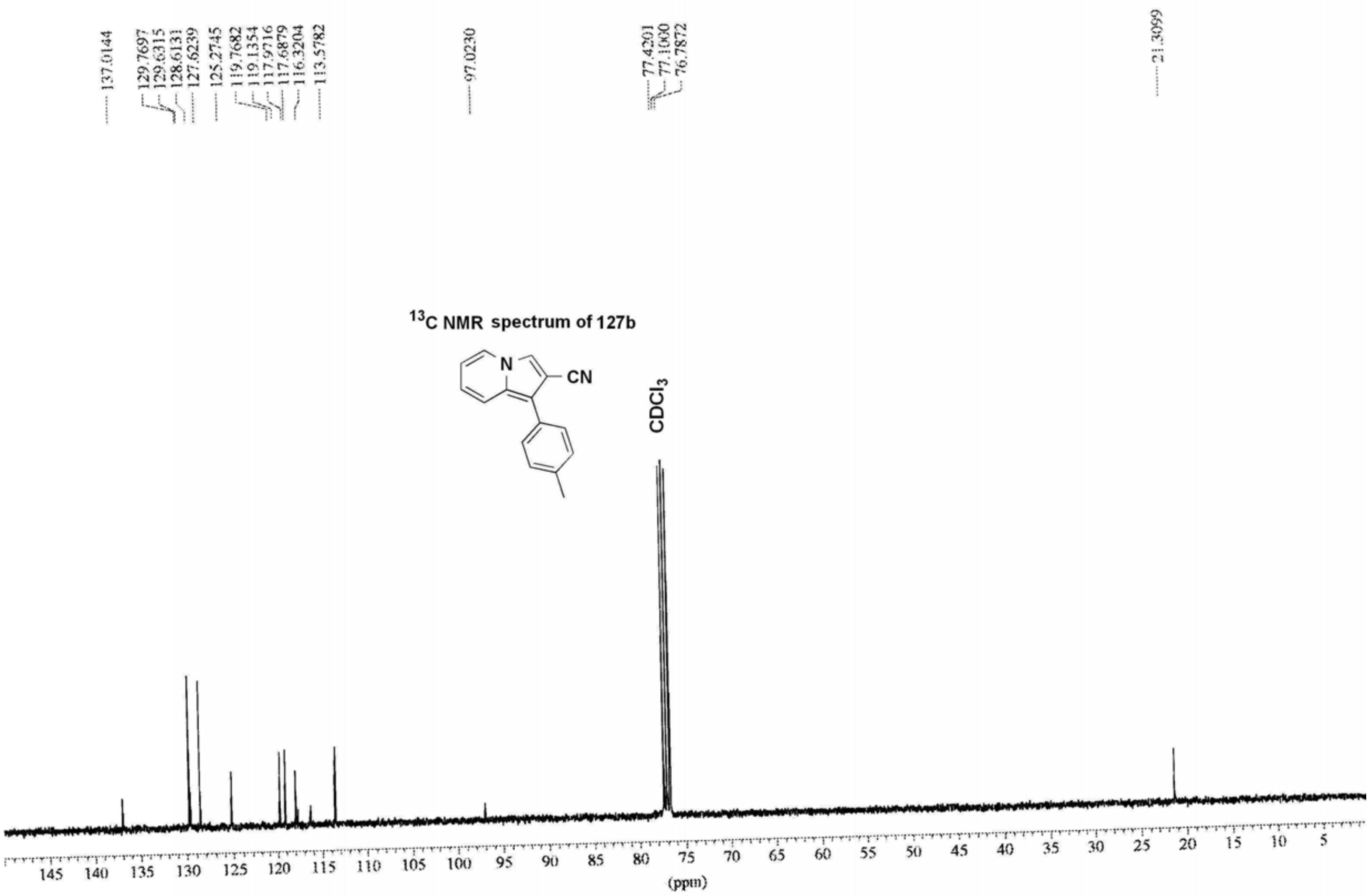
^{13}C NMR spectrum of 127a

Spectrum 25

^{1}H NMR spectrum of 127b



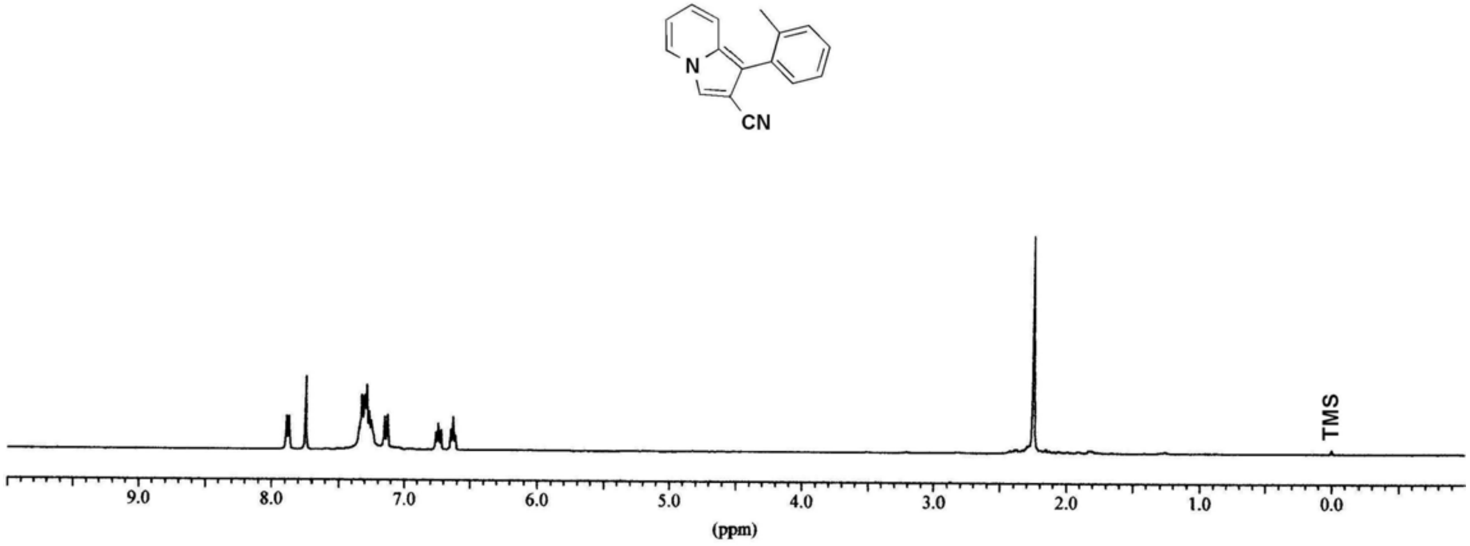
Spectrum 26



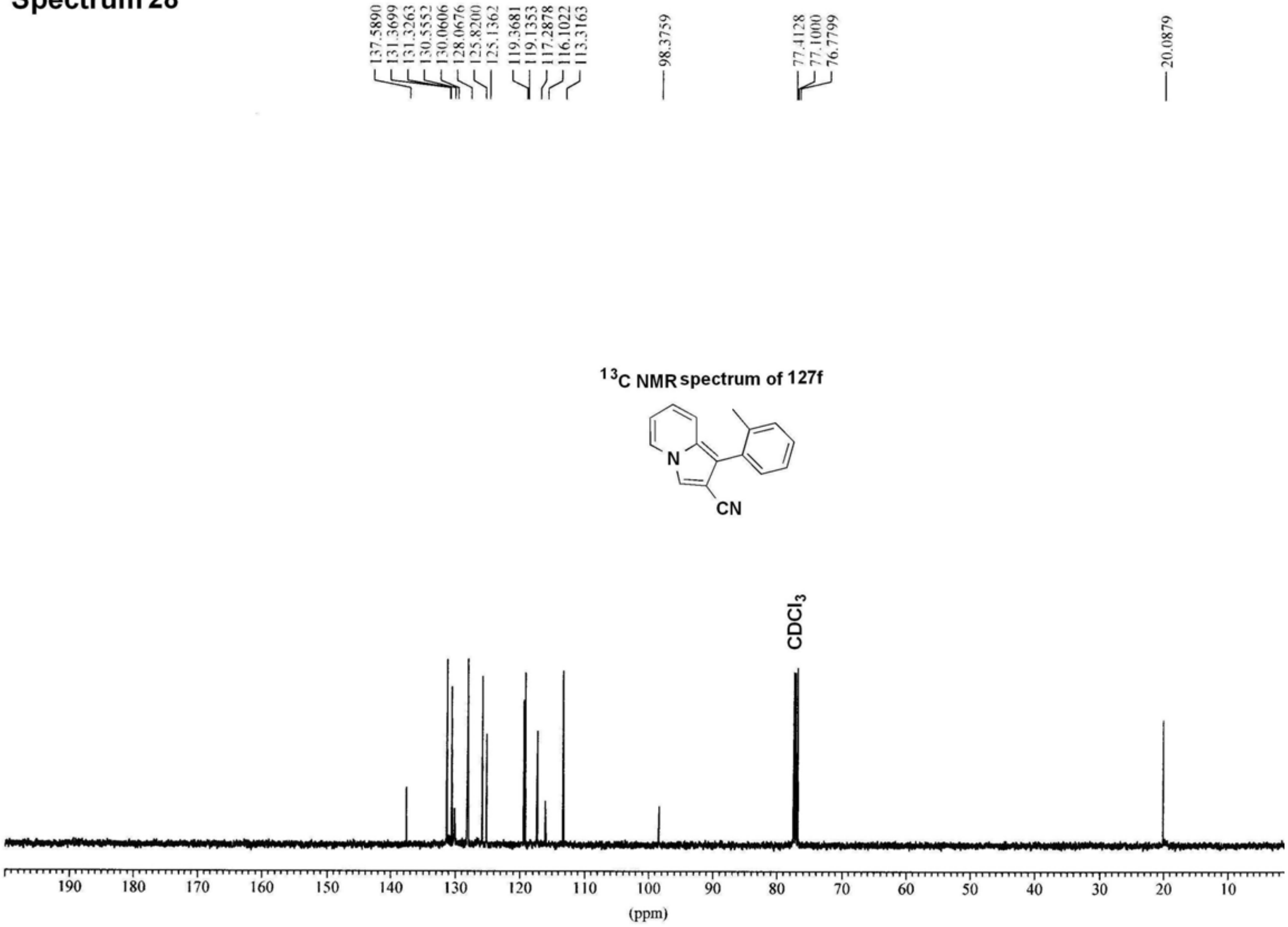
^{13}C NMR spectrum of 127b

Spectrum 27

^{1}H NMR spectrum of 127f



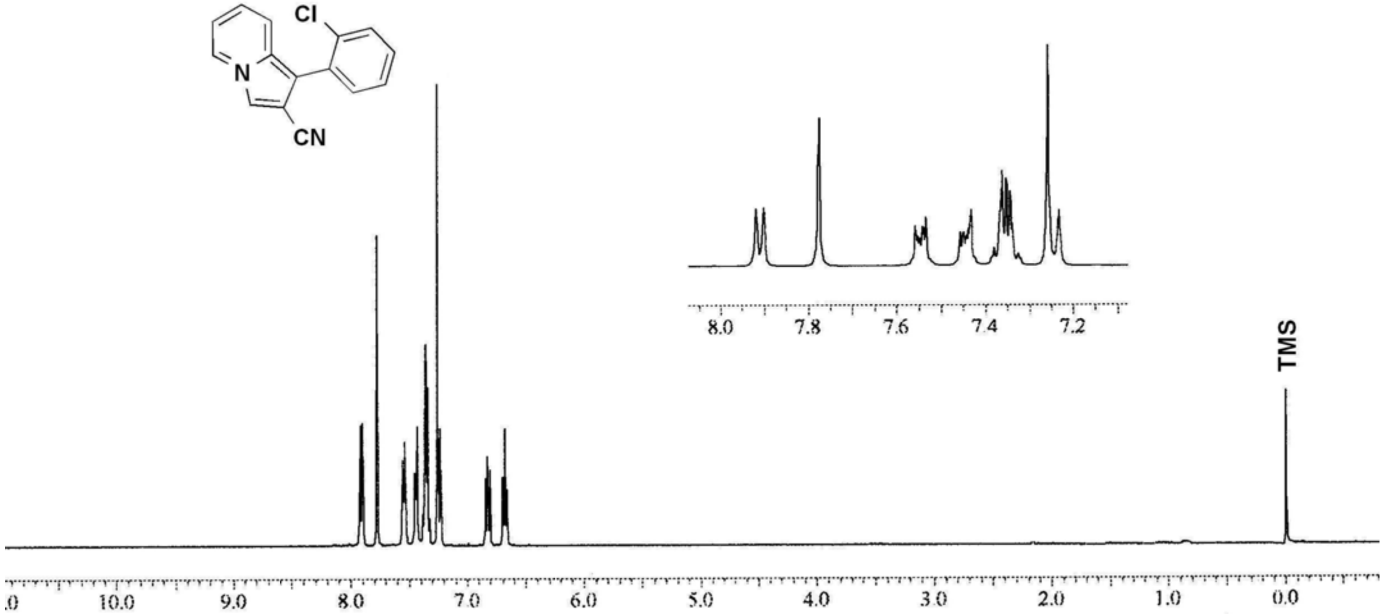
Spectrum 28



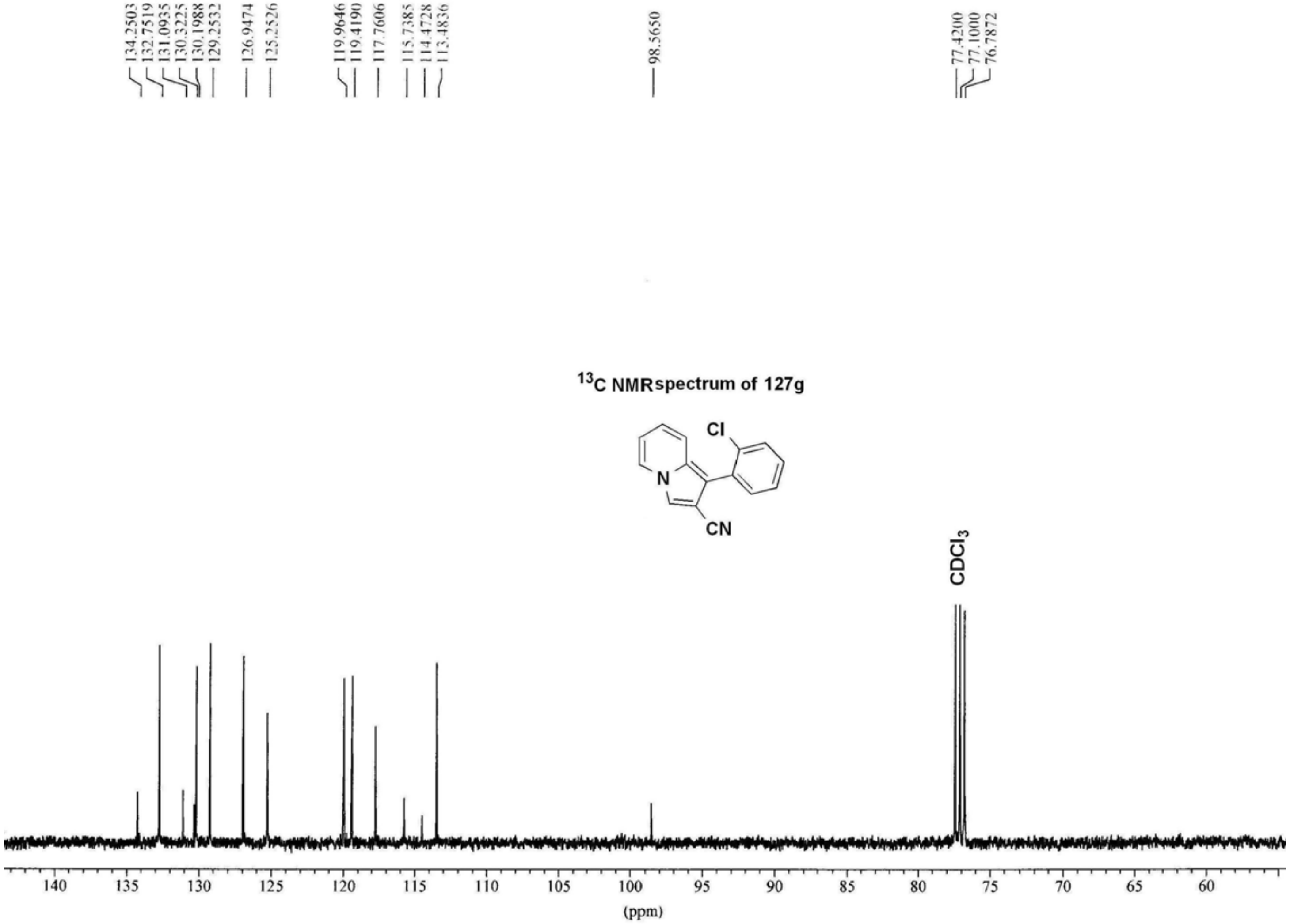
^{13}C NMR spectrum of 127f

Spectrum 29

^{1}H NMR spectrum of 127g

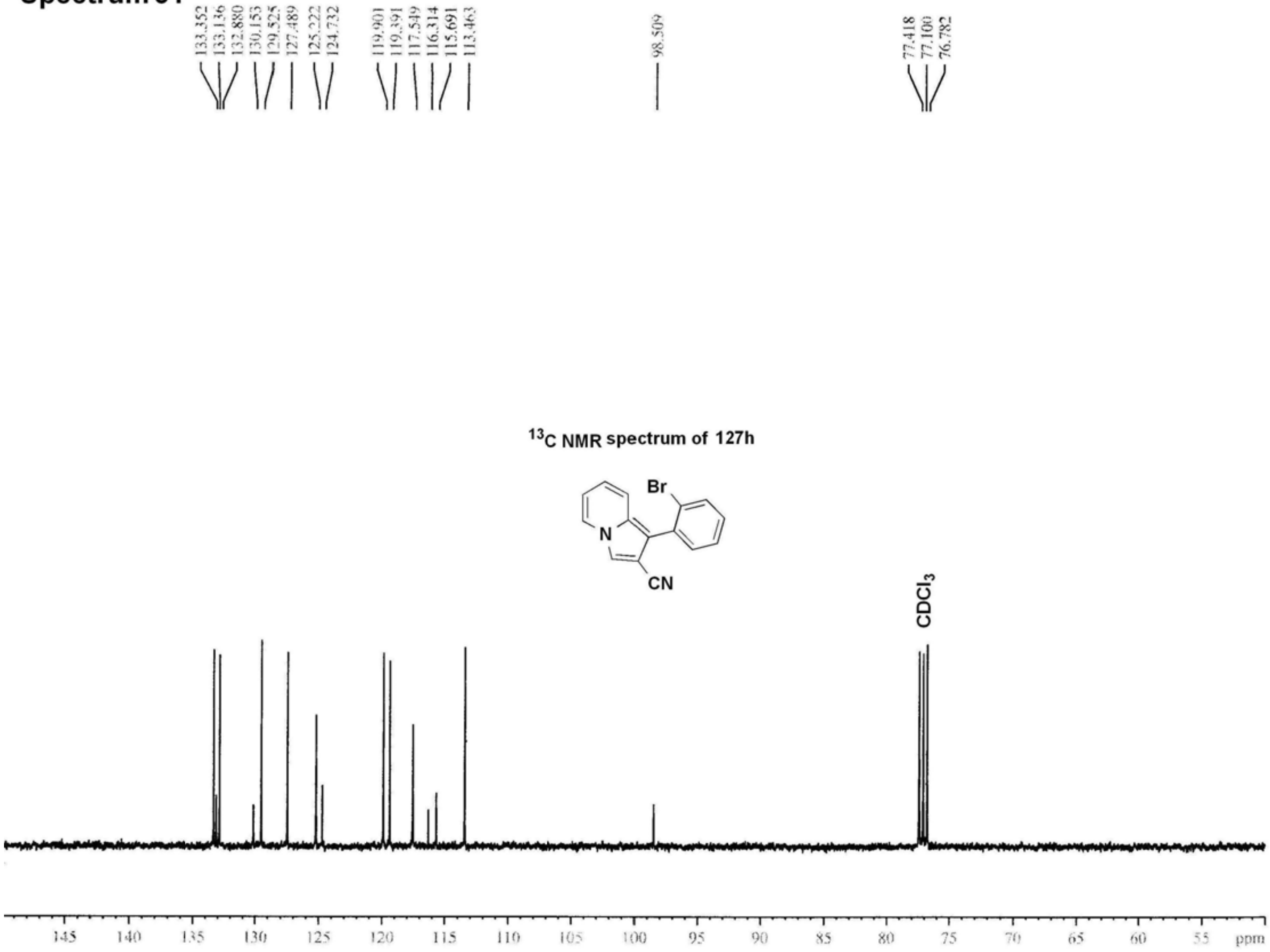


Spectrum 30



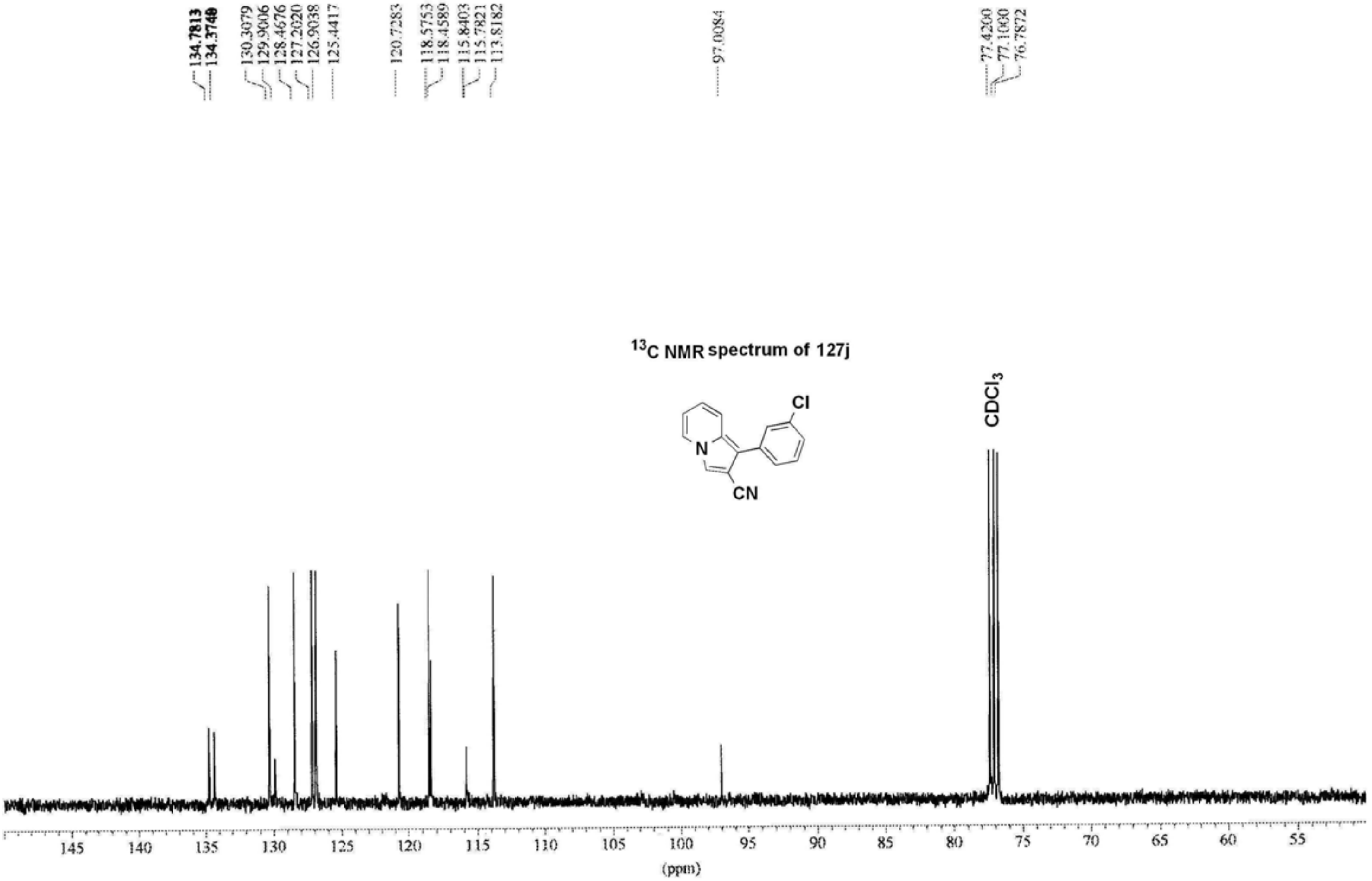
^{13}C NMR spectrum of 127g

Spectrum 31



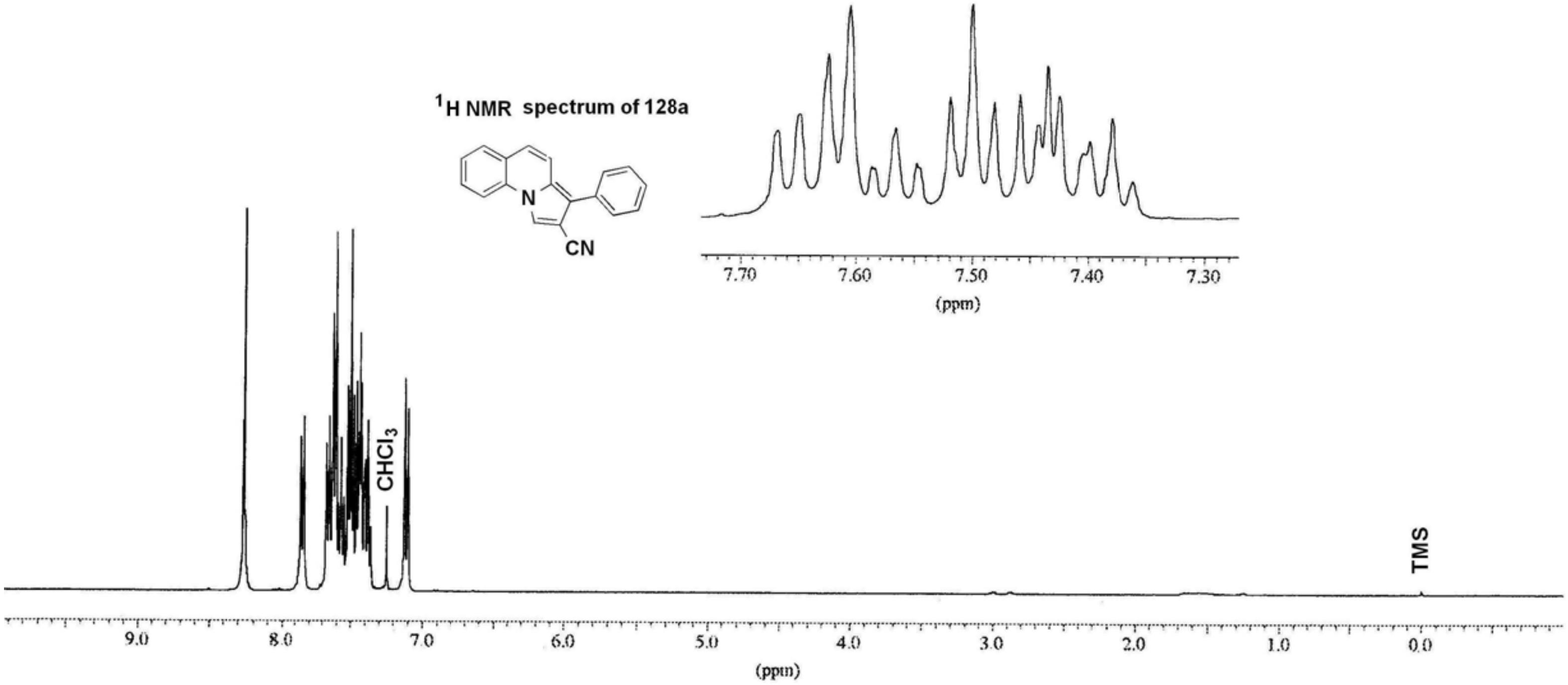
^{13}C NMR spectrum of 127h

Spectrum 32



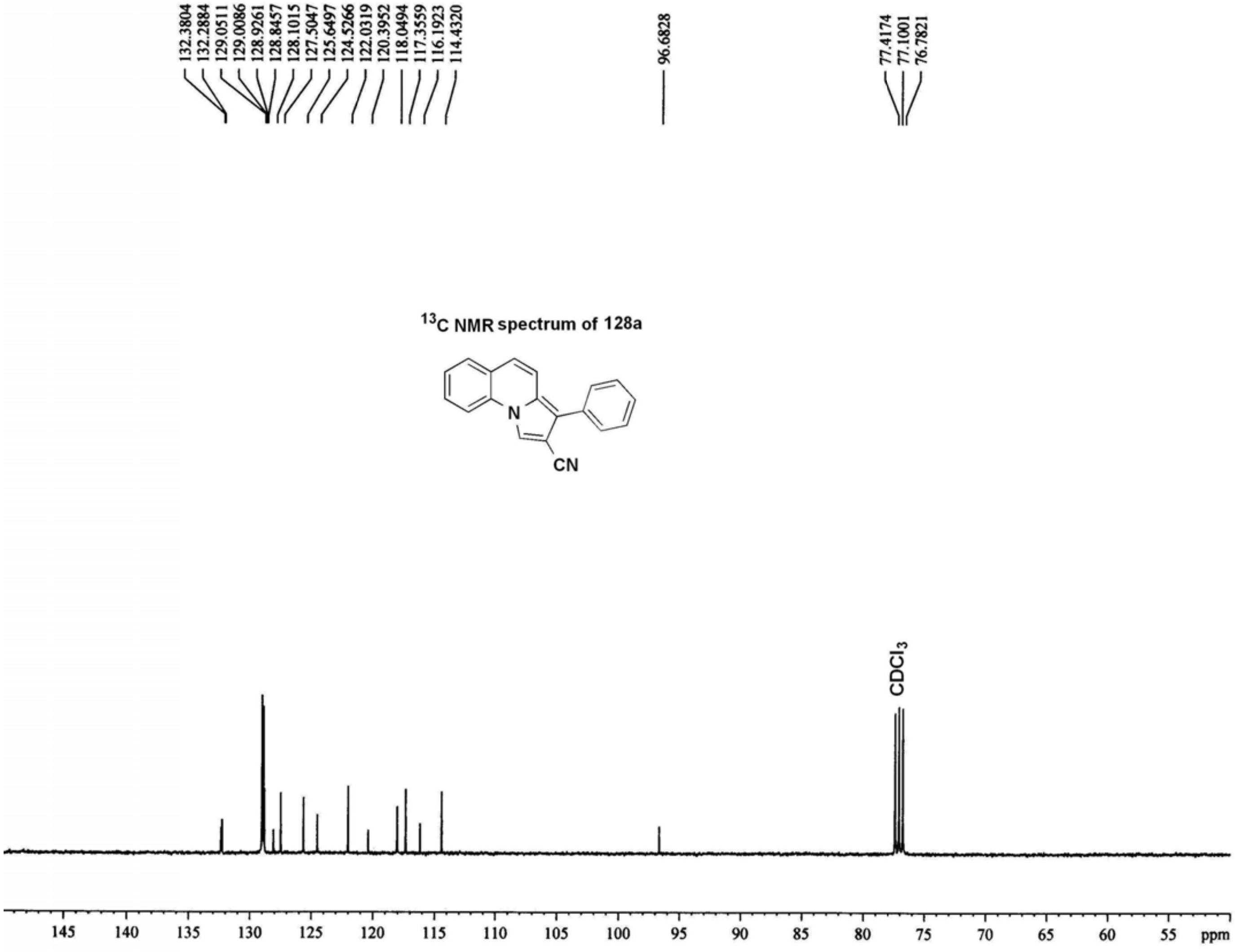
^{13}C NMR spectrum of 127j

Spectrum 33



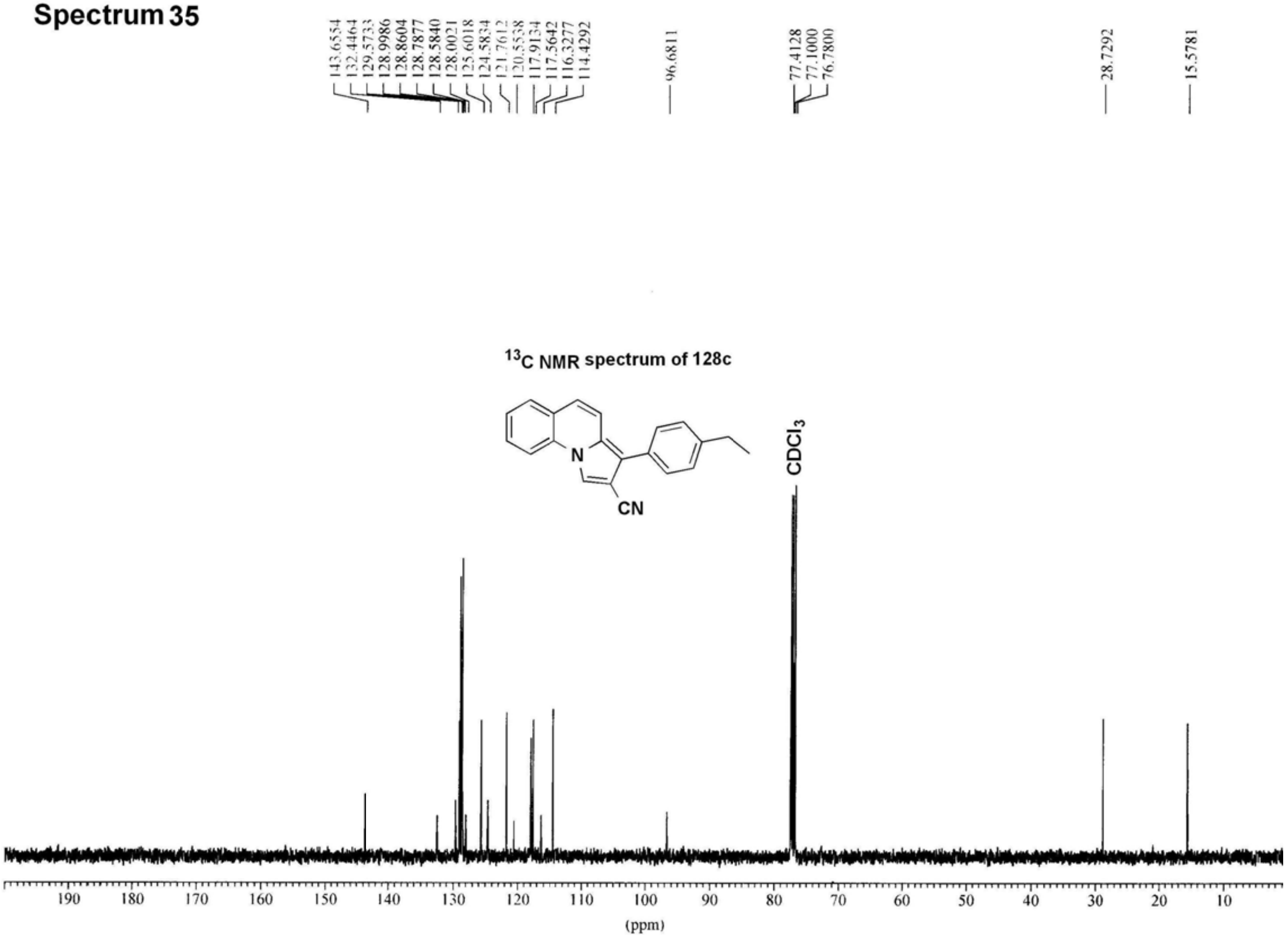
^{1}H NMR spectrum of 128a

Spectrum 34



^{13}C NMR spectrum of 128a

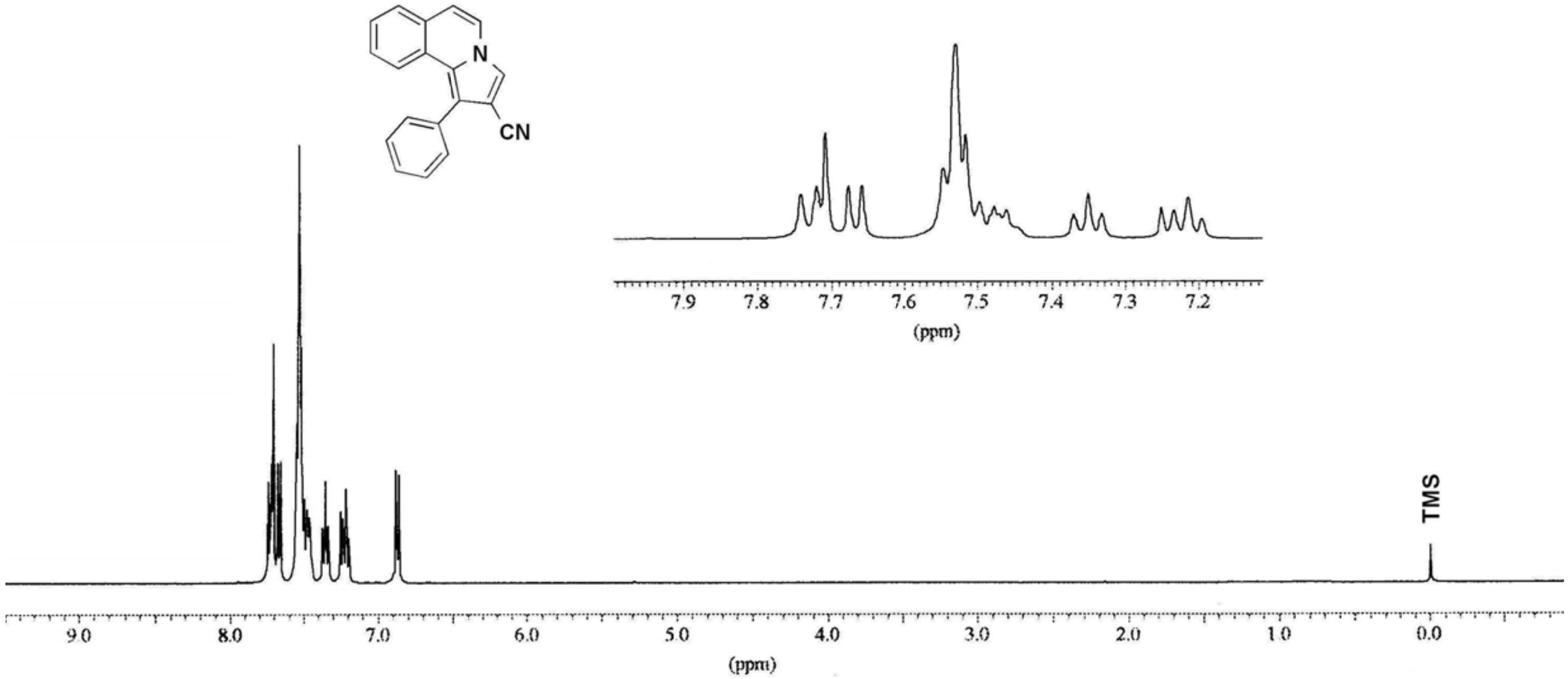
Spectrum 35

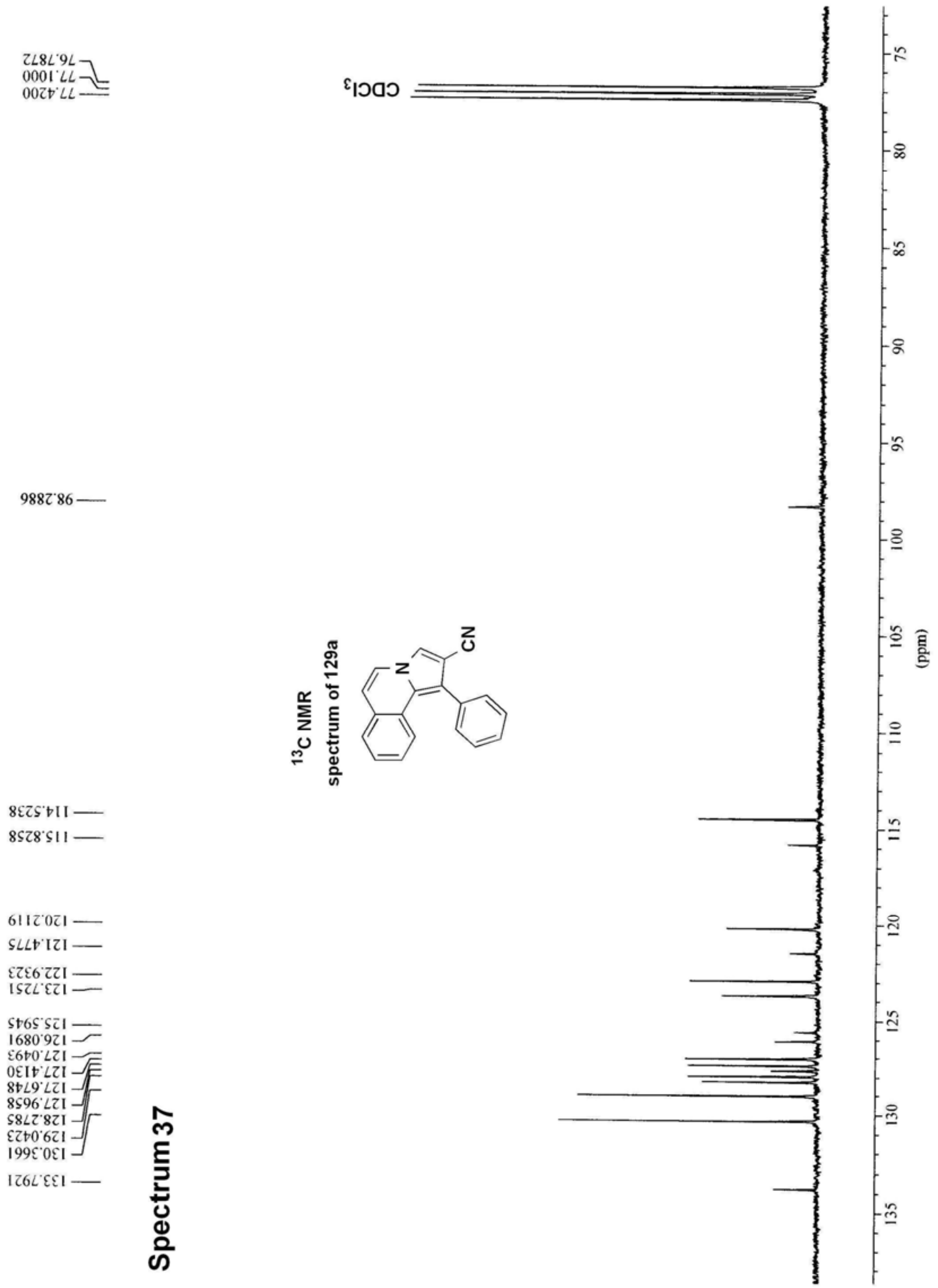


^{13}C NMR spectrum of 128c

Spectrum36

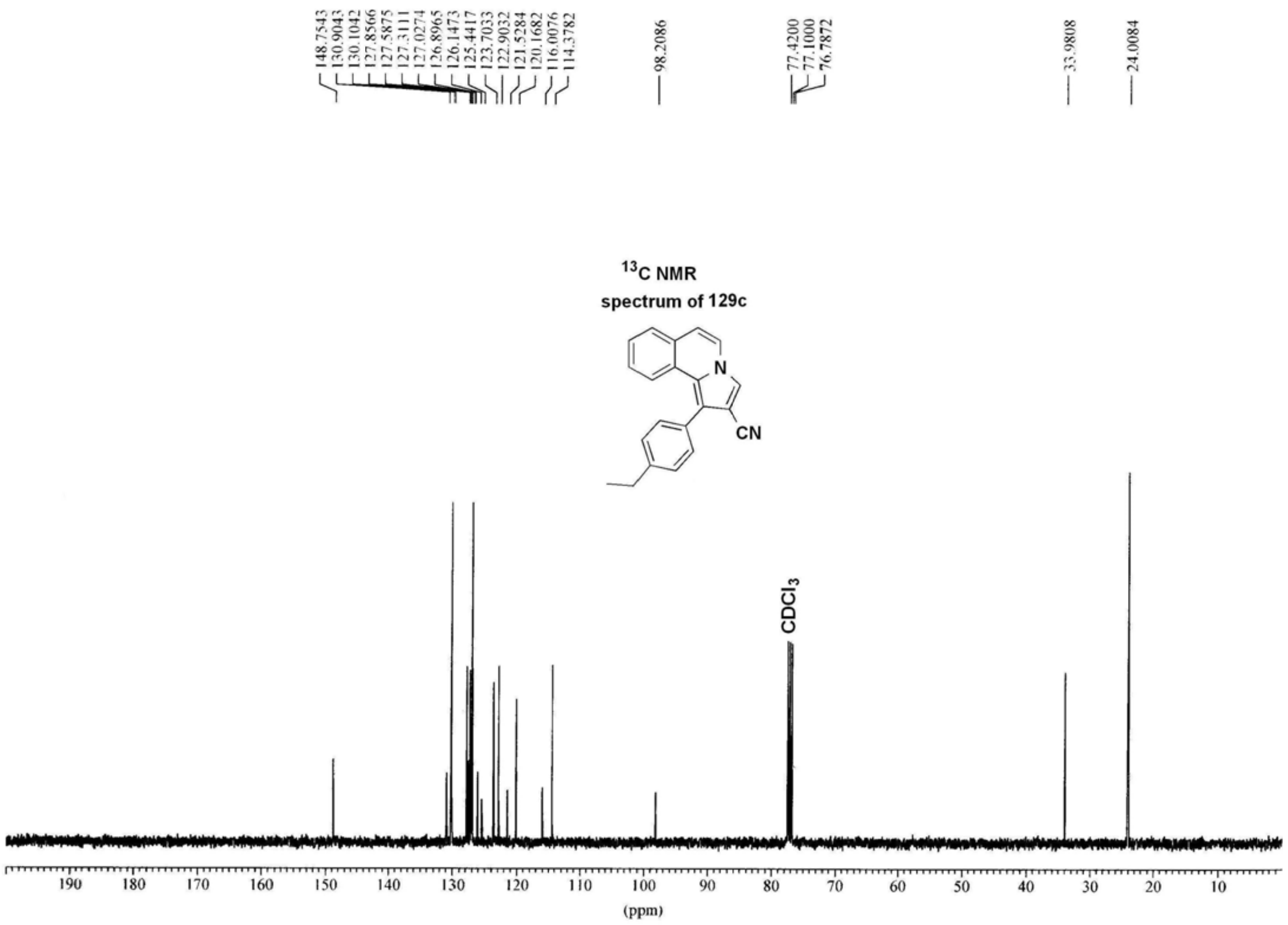
^{1}H NMR spectrum of 129a




76.7872
77.1000
77.4200
98.2886
114.5238
115.8258
120.2119
121.4775
122.9323
123.7251
125.5945
126.0891
127.0493
127.4130
127.6748
127.9658
128.2785
129.0423
130.3661
133.7921
$CDCl_3$
^{13}C NMR
spectrum of 129a
N
CN
75
80
85
90
95
100
105
110
115
120
125
130
135
(ppm)

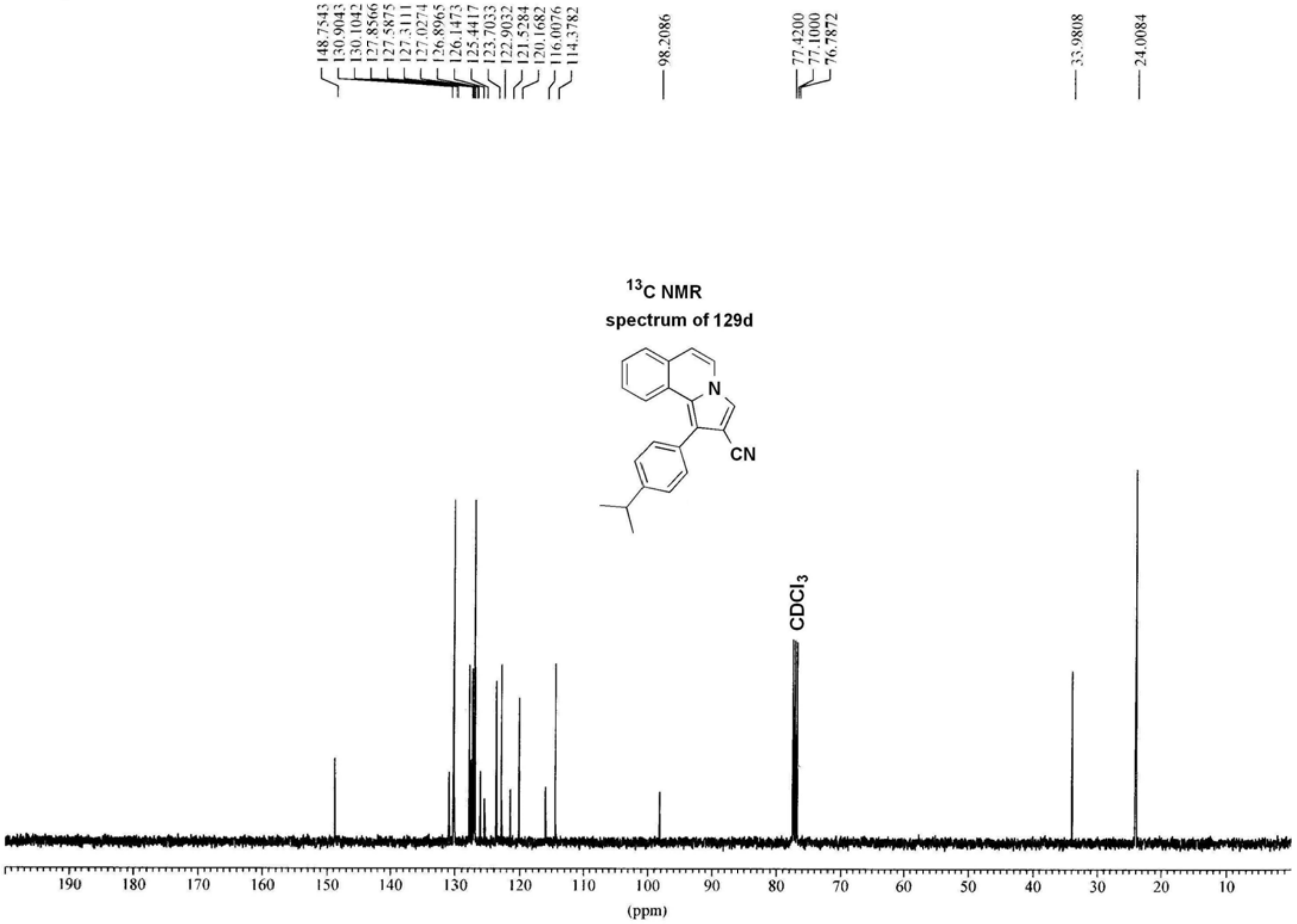
Spectrum 37

Spectrum 38

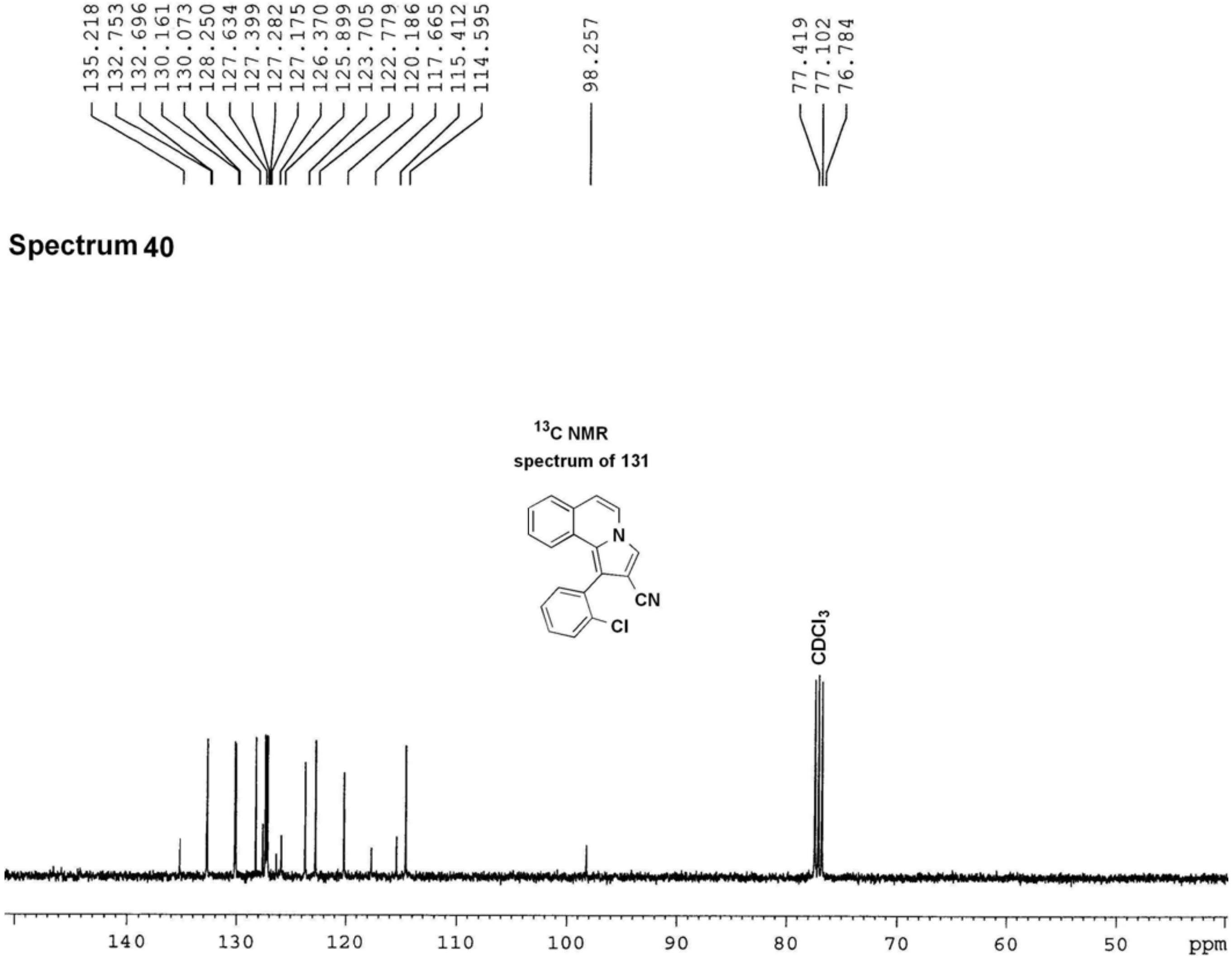


^{13}C NMR spectrum of 129c

Spectrum 39



^{13}C NMR spectrum of 129d



Spectrum 40

135.218
132.753
132.696
130.161
130.073
128.250
127.634
127.399
127.282
127.175
126.370
125.899
123.705
122.779
120.186
117.665
115.412
114.595
98.257
77.419
77.102
76.784
^{13}C NMR
spectrum of 131
N
CN
Cl
CDCl$_3$
140
130
120
110
100
90
80
70
60
50
ppm

APPENDIX

(X-RAY CRYSTALLOGRAPHIC DATA)

Table I: Atomic coordinates (x10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for **101a.** U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

atom	x	y	z	U(eq)
C(1)	3714(1)	2021(2)	1218(1)	53(1)
C(2)	4646(1)	1521(2)	1125(1)	45(1)
C(3)	4678(1)	-245(2)	907(1)	45(1)
C(4)	3758(1)	-979(2)	862(1)	54(1)
C(5)	5347(1)	2952(2)	1240(1)	55(1)
C(6)	5734(1)	2847(2)	1781(1)	49(1)
C(7)	6384(1)	4115(2)	1919(1)	77(1)
C(8)	6763(1)	4014(3)	2409(1)	94(1)
C(9)	6500(1)	2677(3)	2757(1)	79(1)
C(10)	5862(1)	1455(3)	2629(1)	82(1)
C(11)	5474(1)	1526(2)	2146(1)	69(1)
C(12)	5428(1)	-1366(2)	719(1)	49(1)
C(13)	6217(1)	-1359(2)	985(1)	61(1)
C(14)	6917(1)	-2375(3)	793(1)	75(1)
C(15)	6853(1)	-3400(2)	339(1)	77(1)
C(16)	6079(1)	-3443(2)	76(1)	70(1)
C(17)	5369(1)	-2446(2)	265(1)	59(1)
N(1)	3231(1)	468(2)	1051(1)	61(1)
O(1)	3433(1)	3518(2)	1396(1)	72(1)
O(2)	3513(1)	-2530(2)	698(1)	78(1)

Table II: Atomic coordinates (x10^4) and equivalent isotropic displace-ment parameters (A^2 x 10^3) for **101e.** U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

atom	x	y	z	U(eq)
C(1)	778(1)	2910(3)	5197(1)	48(1)
C(2)	1360(1)	4983(3)	5183(1)	45(1)

C(3)	1397(1)	5693(3)	4416(1)	45(1)
C(4)	791(1)	4189(3)	3907(1)	52(1)
C(5)	1729(1)	6032(3)	5949(1)	51(1)
C(6)	2941(1)	3103(4)	5981(1)	74(1)
C(7)	3714(2)	2298(4)	6305(2)	98(1)
C(8)	4132(2)	3508(6)	6917(2)	95(1)
C(9)	3780(2)	5490(5)	7208(1)	95(1)
C(10)	3010(1)	6285(4)	6885(1)	73(1)
C(11)	2580(1)	5097(3)	6270(1)	49(1)
C(12)	1903(1)	7576(3)	4071(1)	47(1)
C(13)	2717(1)	8057(3)	4392(1)	55(1)
C(14)	3204(1)	9829(4)	4070(1)	59(1)
C(15)	2884(1)	11107(4)	3424(1)	66(1)
C(16)	2082(1)	10626(3)	3099(1)	64(1)
C(17)	1589(1)	8882(3)	3412(1)	57(1)
C(18)	4484(1)	12090(4)	4164(2)	110(1)
N(1)	451(1)	2564(3)	4425(1)	54(1)
O(1)	605(1)	1723(2)	5779(1)	61(1)
O(2)	606(1)	4317(2)	197(1)	66(1)
O(3)	3994(1)	10135(3)	4431(1)	84(1)

Table III: Atomic coordinates (x10^4) and equivalent isotropic displac-ement parameters (A^2 x 10^3) for **101i.** U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

atom	**x**	**y**	**z**	**U(eq)**
C(1)	10384(3)	10295(2)	2096(1)	46(1)
C(2)	8402(3)	9530(2)	1698(1)	43(1)
C(3)	6935(3)	10748(2)	1520(1)	45(1)
C(4)	7870(3)	12350(2)	1803(1)	49(1)
C(5)	8358(3)	7704(2)	1549(1)	55(1)
C(6)	9761(3)	282(2)	1037(1)	45(1)
C(7)	11570(3)	6213(2)	1154(1)	58(1)
C(8)	12840(3)	5834(2)	691(1)	70(1)
C(9)	12322(3)	6511(3)	101(1)	71(1)
C(10)	10531(3)	7573(2)	-23(1)	68(1)
C(11)	9268(3)	7954(2)	445(1)	57(1)
C(12)	4735(3)	10711(3)	1108(1)	69(1)
N(1)	9933(3)	11977(2)	2138(1)	54(1)

O(1)	12083(2)	9607(2)	2333(1)	63(1)
O(2)	7020(2)	13720(2)	1754(1)	71(1)

Table IV: Atomic coordinates (x10^4) and equivalent isotropic displace-ment parameters (A^2 x 10^3) for **103a.** U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

atom	**x**	**y**	**z**	**U(eq)**
C(1)	-164(6)	3483(3)	318(2)	87(1)
C(2)	1673(5)	4039(2)	699(1)	61(1)
C(3)	2287(5)	3254(2)	1130(1)	61(1)
C(4)	836(7)	2157(3)	1040(2)	86(1)
C(5)	2623(5)	5241(2)	544(1)	72(1)
C(6)	1204(5)	6303(2)	767(1)	63(1)
C(7)	1956(6)	7450(2)	614(1)	78(1)
C(8)	722(8)	8446(3)	803(2)	90(1)
C(9)	-1285(7)	8323(3)	1139(2)	93(1)
C(10)	-2063(6)	7201(3)	1299(2)	94(1)
C(11)	-793(6)	6199(2)	1116(2)	80(1)
C(12)	4022(5)	3361(2)	1622(1)	69(1)
C(13)	4268(7)	4423(3)	1945(1)	91(1)
C(14)	5929(8)	4537(5)	2398(2)	130(2)
C(15)	7374(9)	3598(6)	2543(2)	146(2)
C(16)	7186(8)	2549(5)	2230(2)	128(2)
C(17)	5519(7)	2410(3)	1770(2)	98(1)
O(1)	-663(4)	2355(2)	549(1)	104(1)
O(2)	-1149(5)	3863(2)	-119(1)	130(1)
O(3)	772(5)	1242(2)	1317(1)	119(1)

Table V: Atomic coordinates (x10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for **113a.** U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

atom	**x**	**y**	**z**	**U(eq)**
C(1)	1848(2)	10526(2)	9380(2)	59(1)
C(2)	1611(2)	9421(1)	9444(2)	52(1)
C(3)	2551(2)	8725(2)	10415(2)	55(1)
C(4)	2113(2)	7927(2)	11078(2)	66(1)

C(5)	2991(3)	7267(2)	11971(3)	83(1)
C(6)	4310(3)	7379(2)	12211(3)	92(1)
C(7)	4751(2)	8159(2)	11545(3)	87(1)
C(8)	3883(2)	8826(2)	10666(2)	70(1)
C(9)	433(2)	9236(1)	8451(2)	51(1)
C(10)	-104(2)	10182(1)	7751(2)	52(1)
C(11)	-1197(2)	10274(2)	6677(2)	63(1)
C(12)	-2011(2)	9359(2)	6057(2)	63(1)
C(13)	-1447(2)	8408(2)	6847(3)	67(1)
C(14)	-333(2)	8335(1)	7927(2)	64(1)
C(15)	-2051(3)	9227(3)	4465(3)	111(1)
C(16)	-3406(2)	9512(2)	6112(3)	91(1)
O(1)	2762(2)	11043(1)	10011(2)	82(1)
O(2)	764(1)	10955(1)	8362(2)	63(1)

Table VI: Atomic coordinates (x10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for **127a.** U(eq) is defined as one third of the trace of the orthogonalized Uijtensor.

atom	**x**	**y**	**z**	**U(eq)**
C(1)	92(2)	803(3)	4296(1)	45(1)
C(2)	1135(2)	1179(3)	4576(1)	52(1)
C(3)	3531(2)	973(3)	4483(1)	61(1)
C(4)	4491(2)	539(3)	4199(1)	68(1)
C(5)	4216(2)	-113(3)	3761(1)	67(1)
C(6)	2966(2)	-295(3)	3620(1)	55(1)
C(7)	1918(2)	189(3)	3907(1)	44(1)
C(8)	564(2)	177(2)	3872(1)	42(1)
C(9)	-226(2)	-342(3)	3478(1)	42(1)
C(10)	131(2)	130(3)	3041(1)	54(1)
C(11)	-618(3)	-360(4)	2673(1)	68(1)
C(12)	-1746(2)	-1325(4)	2737(1)	67(1)
C(13)	-2120(2)	-1806(3)	3165(1)	62(1)
C(14)	-1372(2)	-1321(3)	3533(1)	49(1)
C(15)	-1239(2)	1148(3)	4418(1)	51(1)
N(1)	2243(2)	807(2)	4343(1)	48(1)
N(2)	-2285(2)	1457(3)	4525(1)	68(1)

Table VII: Atomic coordinates (x10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for **128a.** U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

atom	**x**	**y**	**z**	**U(eq)**
C(1)	1493(2)	6968(2)	306(2)	44(1)
C(2)	1984(2)	6113(3)	-345(2)	47(1)
C(3)	4098(2)	5873(2)	-1044(2)	2(1)
C(4)	3786(3)	4734(3)	-1580(2)	51(1)
C(5)	4654(3)	4212(3)	-2193(2)	60(1)
C(6)	5817(3)	4799(3)	-2270(3)	68(1)
C(7)	6135(3)	5915(3)	-1722(3)	71(1)
C(8)	5276(3)	6485(3)	-1102(2)	55(1)
C(9)	5587(3)	7668(3)	-512(3)	81(1)
C(10)	4805(2)	8133(3)	174(2)	51(1)
C(11)	3545(2)	7552(2)	209(2)	41(1)
C(12)	2488(2)	7892(2)	682(2)	41(1)
C(13)	2393(2)	8993(2)	1402(2)	44(1)
C(14)	1350(3)	9656(3)	1263(3)	58(1)
C(15)	1275(3)	10683(3)	1931(3)	74(1)
C(16)	2250(3)	11092(3)	2770(3)	75(1)
C(17)	3288(3)	10456(3)	2918(3)	68(1)
C(18)	3366(3)	9418(3)	2261(2)	57(1)
C(19)	195(3)	6931(3)	522(2)	54(1)
C(20)	3312(2)	6382(2)	5726(2)	42(1)
C(21)	2838(2)	5192(2)	5534(2)	45(1)
C(22)	923(2)	3989(2)	6033(2)	39(1)
C(23)	1243(3)	2903(3)	5602(2)	52(1)
C(24)	435(3)	1886(3)	5657(3)	58(1)
C(25)	-682(3)	1952(3)	6145(2)	56(1)
C(26)	-1000(2)	3032(3)	6573(2)	54(1)
C(27)	-205(2)	4091(3)	6534(2)	43(1)
C(28)	-499(2)	5240(3)	6988(2)	52(1)
C(29)	304(2)	6233(3)	6967(2)	47(1)
C(30)	1467(2)	6172(2)	6491(2)	38(1)
C(31)	2457(2)	7016(2)	6333(2)	41(1)
C(32)	2593(2)	8301(2)	6708(2)	39(1)
C(33)	2229(2)	8708(3)	7763(2)	49(1)
C(34)	2350(3)	9914(3)	8112(3)	59(1)
C(35)	2825(3)	10743(3)	7419(3)	62(1)
C(36)	3212(3)	10372(3)	6383(3)	60(1)
C(37)	3095(2)	9159(3)	6026(2)	50(1)

C(38)	4499(3)	6832(3)	5388(2)	51(1)
N(1)	3230(2)	6457(2)	-421(2)	42(1)
N(2)	-848(2)	6890(3)	666(2)	79(1)
N(3)	1726(2)	5065(2)	5998(2)	39(1)
N(4)	5452(2)	7178(2)	5115(2)	72(1)

Table VIII: Atomic coordinates (x10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for **129a.** U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	x	y	z	U(eq)
C(1)	4836(3)	800(3)	8305(3)	53(1)
C(2)	5299(3)	92(3)	8066(4)	57(1)
C(3)	5169(3)	-909(3)	6590(4)	64(1)
C(4)	4717(3)	-1130(3)	5676(4)	66(1)
C(5)	3918(3)	-675(3)	5239(3)	52(1)
C(6)	3419(4)	-926(3)	4290(4)	73(1)
C(7)	2639(4)	-522(3)	3893(4)	79(2)
C(8)	2330(3)	155(3)	4458(4)	67(1)
C(9)	2807(3)	433(2)	5374(3)	54(1)
C(10)	3619(3)	40(2)	5777(3)	47(1)
C(11)	4164(3)	311(2)	6745(3)	45(1)
C(12)	4122(3)	956(2)	7472(3)	45(1)
C(13)	3511(3)	1691(2)	7445(3)	43(1)
C(14)	3451(3)	2202(3)	6539(3)	66(1)
C(15)	2906(4)	2891(3)	6556(4)	80(2)
C(16)	2404(3)	3093(3)	7466(4)	73(1)
C(17)	2473(3)	2603(3)	8387(4)	71(1)
C(18)	3029(3)	1908(2)	8370(3)	54(1)
C(19)	5037(3)	1299(3)	9238(4)	57(1)
C(20)	7463(3)	744(2)	1557(3)	44(1)
C(21)	6889(3)	1347(2)	1934(3)	49(1)
C(22)	7035(3)	2336(2)	3443(4)	57(1)
C(23)	7564(3)	2595(2)	4287(4)	61(1)
C(24)	8442(3)	2202(2)	4603(3)	49(1)
C(25)	8967(4)	2441(3)	5545(4)	71(1)
C(26)	9777(4)	2052(3)	5873(4)	83(2)
C(27)	10085(3)	1390(3)	5271(4)	78(2)
C(28)	9597(3)	1144(2)	4340(3)	59(1)
C(29)	8777(3)	1544(2)	3987(3)	45(1)

C(30)	8224(3)	1304(2)	3021(3)	42(1)
C(31)	8313(3)	710(2)	2208(3)	41(1)
C(32)	9140(3)	198(2)	1964(3)	41(1)
C(33)	10010(3)	547(3)	1753(3)	60(1)
C(34)	10763(3)	78(3)	1433(4)	74(1)
C(35)	10662(4)	-740(3)	1308(4)	78(2)
C(36)	9795(4)	-1103(3)	1510(4)	76(1)
C(37)	9042(3)	-640(3)	1846(3)	59(1)
C(38)	7244(3)	253(2)	610(3)	46(1)
N(1)	4898(2)	-204(2)	7127(3)	51(1)
N(2)	5209(3)	1700(2)	9990(3)	78(1)
N(3)	7345(2)	1693(2)	2813(3)	47(1)
N(4)	7076(2)	-135(2)	-151(3)	63(1)

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