# TOWARDS DEVELOPMENT OF NOVEL METHODOLOGIES FOR SYNTHESIS OF HETEROCYCLES USING THE BAYLIS-HILLMAN ADDUCTS

A THESIS SUBMITTED FOR THE DEGREE OF

**DOCTOR OF PHILOSOPHY**

BY

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**JULY 2004**

*To My*
*Beloved Parents*

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# 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**

**JULY, 2004**

**T. SATYANARAYANA**

# CERTIFICATE

Certified that the work embodied in this thesis entitled "**Towards development of novel methodologies for synthesis of heterocycles using the Baylis-Hillman adducts**" has been carried out by **Mr. T. Satyanarayana**, under my supervision and the same has not been submitted elsewhere for a degree.

D Basavaiah July 21, 2004

**Professor D. BASAVAIAH**

**(THESIS SUPERVISOR)**

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**SATYAM**

# ABBREVIATIONS

| | |
|---|---|
| Ac | acetyl |
| AIBN | azobisisobutyronitrile |
| aq. | aqueous |
| BINAP | 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl |
| bmim | 1-butyl-3-methyl-1*H*-imidazolium |
| *Nt*-Boc | *N*-butoxycarbonyl |
| Bp | boiling point |
| Bu | *n*-butyl |
| Bz | benzyl |
| *i*-Bu or Bu$^i$ | *iso* butyl |
| *s*-Bu or Bu$^s$ | *secondary*-butyl |
| *t*-Bu or Bu$^t$ | *tertiary* butyl |
| BINOL | 1,1′-bi-2-naphthol |
| cat. | Catalyst |
| cod | 1,5-cyclooctadiene |
| mCPBA | *meta*-chloroperbenzoic acid |
| CSA | 10-camphorsulfonic acid |
| DABCO | 1,4-diazabicyclo(2.2.2)octane |
| DBU | 1,8- diazabicyclo(5.4.0)undec-7-ene |
| *de* | diastereomeric excess |
| DEAD | diethyl azodicarboxylate |
| dec. | decompose |
| DMAP | 4-(dimethylamino)pyridine |
| DMSO | dimethyl sulfoxide |
| DMF | N,N-dimethylformamide |
| *ee* | enantiomeric excess |
| Et | ethyl |

| | |
|---|---|
| emim | 1-ethyl-3-methyl-1*H*-imidazolium |
| equiv. or eq. | equivalents |
| $Eu(fod)_3$ | Europium tris[6,6,7,7,8,8,8,-heptafluoro-2,2-dimethyl-3,5-octanedionate] |
| EWG | electron withdrawing group |
| Hex | hexyl |
| c-Hex | cyclohexyl |
| 3-HQD | 3-hydroxyquinuclidine |
| LAH | lithium aluminum hydride |
| KDP | ketodicyclopentadiene |
| Me | methyl |
| Mp | melting point |
| MEMCl | (2-methoxyethoxy)methyl chloride |
| MS | molecular sieves |
| MsCl | mesyl chloride |
| MVK | methyl vinyl ketone |
| NBS | N-bromosuccinimide |
| PAP | polymer bound 4-(*N*-benzyl-*N*-methylamino)pyridine |
| Ph | phenyl |
| PPTS | pyridinium *p*-toluenesulfonate |
| Pr | *n*-propyl |
| *i*-Pr or $Pr^i$ | *iso*-propyl |
| rt | room temperature |
| THF | tetrahydrofuran |
| TFA | trifluoroacetic acid |
| TFAA | trifluoroacetic anhydride |
| TMEDA | tetramethylethylenediamine |
| TMSOTf | trimethylsilyl trifluoromethanesulfonate |
| TsOH or *p*-TSA | *para*-toluenesulfonic acid |

# ABSTRACT

Synthetic organic chemistry continues to plays a key role in several exciting and useful discoveries in chemistry, biology and medicine. Construction of C-C bonds is one of the most fundamental reactions in organic synthesis. Although the present day synthetic organic chemistry is well equipped to deal with most of the aspects of organic synthesis once considered to be difficult, the ever changing requirements in drug discovery and biomedical applications demand the continuous evolution of novel and sophisticated synthetic tools involving most important concepts like atom economy, selectivity (chemo-, regio- and stereo-) and organo-catalytic processes. Baylis-Hillman reaction, one such novel emerging C-C bond forming reaction possessing most of these requirements (atom economy, selectivity and organo-catalytic process), provides a unique class of multifunctional molecules having enormous synthetic potential.

This thesis deals with the studies towards development of novel methodologies for synthesis of heterocycles and stereoselective transformations using the Baylis-Hillman adducts and consists of three chapters, that is, 1. Introduction 2. Objectives, Results & Discussion and 3. Experimental. The first chapter, *i.e.*, Introduction presents a brief literature survey on the recent developments in the Baylis–Hillman reaction and also on applications of the Baylis–Hillman adducts in the organic synthesis.

The second chapter deals with the objectives, results and discussion. With a view to expand the scope of the Baylis-Hillman adducts as valuable source for various organic transformations and also for synthesis of heterocyclic molecules, we have undertaken major research program with the following objectives.

1) To develop a novel and facile methodology for the synthesis of functionalized [4.4.3] and [4.4.4]propellano-bislactones using acetates of the Baylis-Hillman adducts.
2) To develop a facile methodology for one-pot conversion of the acetates of Baylis-Hillman adducts into substituted fused pyrimidones in aqueous medium.
3) To develop a novel methodology for tandem construction of C-N and C-C bonds leading to facile one-pot transformation of the Baylis-Hillman adducts into 2-benzazepines.
4) To understand the influence of substituents on the stereochemical outcome in the Johnson-Claisen rearrangement of Baylis-Hillman adducts.
5) To develop a novel one-pot multi-reaction strategy for facile transformation of the Baylis-Hillman adducts into substituted (1*H*)-quinolin-2-ones and substituted quinolines.

**A novel and facile synthesis of functionalized [4.4.3] and [4.4.4]propellano-bislactones using acetates of the Baylis-Hillman adducts**

Carbocyclic and heterocyclic propellanes occupy a special place in synthetic organic chemistry because of their aesthetically appealing structural architecture and enormous

synthetic potential due to their high strain energy. Also, several natural products and biologically active molecules were found to possess this fascinating structural feature. Similarly, polycyclic polylactone framework is an important structural feature present in various biologically active natural products. Also, polylactone framework with α-*exo* alkene functionality is present in many biologically active molecules.

We have successfully developed a novel synthetic methodology for convenient transformation of the Baylis-Hillman adducts into functionalized [4.4.3] and [4.4.4]propellano-bislactones (**130a-g, 134**) in very high yields (Schemes 50-52, Eq. 30 and Table 1,2).

**One-pot facile conversion of the acetates of Baylis-Hillman adducts into substituted fused pyrimidones in aqueous media**

The pyrimidine framework is an important structural moiety present in various biologically active molecules including DNA and RNA. Also, fused pyrimidine derivatives possess important and interesting physiological properties. Hence, the development of simple methodology for the synthesis of pyrimidine derivatives represents an attractive area in organic synthesis. We have developed a facile and environment-friendly methodology for one-pot transformation of Baylis-Hillman adducts into substituted fused pyrimidone derivatives (**156a-i**) *via* the treatment with 2-aminopyridine in aqueous media (Eqs. 34-36 and Table 5).

**A novel, tandem construction of C-N and C-C bonds: facile and one-pot transformation of the Baylis-Hillman adducts into 2-benzazepines**

2-Benzazepine moiety is present in many pharmaceutically active naturally occurring molecules and several synthetic 2-benzazepines have been found to exhibit important physiological properties. We have developed a novel reaction involving tandem construction of C-N and C-C bonds *via* the simultaneous Ritter and Houben–Hoesch reactions on Baylis-Hillman adducts, derived from alkoxy substituted benzaldehydes and alkyl acrylates, leading to a convenient, one-pot synthesis of 2-benzazepine derivatives (**184-194**) (Eq. 47,48,50 and Table 7). During these studies, we have found that Baylis-Hillman adducts, derived from benzaldehyde / alkyl substituted benzaldehydes and alkyl acrylates, provided, stereoselectively, alkyl (2*E*)-2-alkanoylaminomethyl-3-arylprop-2-enoate (**177a-c, 179-181**) when treated with alkyl nitriles in the presence of $CH_3SO_3H$ (Scheme 65, Eqs. 39-41 and Table 6).We have also found that Baylis-Hillman adducts derived from acrylonitrile provided, stereoselectively, the (2*Z*)-2-acetylaminomethyl-3-arylprop-2-enenitrile (**183a-c**) under similar conditions (Eqs. 43,44 and Table 7).

**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 the transition state**

Our research group has examined the Johnson-Claisen rearrangement of methyl 3-hydroxy-2-methylenealkanoates, the Baylis-Hillman adducts obtained *via* the reaction of

representative aromatic and aliphatic aldehydes with methyl acrylate. During these studies, our research group noticed an interesting unprecedented stereochemical reversal from alkyl to aryl substituents. However, our research group did not examine the Johnson-Claisen rearrangement of Baylis-Hillman adducts derived from *ortho* substituted benzaldehydes. With a view to understand the effect of *ortho* substitution on the aromatic ring of Baylis-Hillman adducts, we have prepared various Baylis-Hillman adducts (**126g, 126n-s, 126w-y, 178f-i, 233a,b**), derived from 2-substituted benzaldehydes, and examined the Johnson-Claisen rearrangement of these products (**126g, 126n-s, 126w-y, 178f-i, 233a,b**) with various orthoalkanoates (Schemes 73-81, Eqs. 53,56,57,59 and Tables 11-14). We have also examined the Johnson-Claisen rearrangement of the Baylis-Hillman adducts (**126t-v, 126f**), derived from *meta* chloro / *meta* bromo / *para* chloro / *para* bromo benzaldydes (Eq. 56 and Table 12). These results have revealed a novel substituent dependant stereochemical control in the Johnson-Claisen rearrangement of Baylis-Hillman adducts. These stereochemical selectivities are explained by the possible transition state models involving an interesting competition between [1,3] and [1,2] interactions.

**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**

(1*H*)-Quinolin-2-one and quinoline are important structural features present in several natural products Also, several synthetic molecules possessing these important structural

framework are found to exhibit some interesting pharmacological properties. We have developed a facile and convenient methodology for the transformation of the Baylis-Hillman adducts into ethyl 3-(2-oxo-1,2-dihydro-3-quinolinyl)propanoates (**257-263**) [substituted (1*H*)-quinolin-2-ones] (Eqs. 62-64, Scheme 94 and Table 15) and ethyl 3-(2-methyl-3-quinolinyl)propanoates (**264-265**) [substituted quinolines] (Eqs. 65,67 and Table 17) *via* a novel one-pot multi-reaction strategy involving Johnson-Claisen rearrangement, reduction and cyclization.

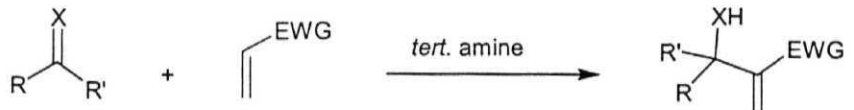
The third chapter deals with the detailed experimental procedures, IR, $^{1}$H NMR, $^{13}$C NMR, mass spectral data, microanalyses and physical constants (Mp, Bp).

# INTRODUCTION

Synthetic organic chemistry continues to plays a key role in several exciting and useful discoveries in chemistry, biology and medicine.[1-8] Construction of C-C bonds is one of the most fundamental reactions in organic synthesis.[9-16] Important and successfully explored C-C bond forming reactions include aldol reaction,[17,18] Reformatsky reaction,[19] Claisen rearrangements,[20] Friedel-Crafts reaction,[21,22] Grignard reaction,[23] Diels-Alder reaction,[24,25] Wittig reaction,[26] Heck reaction,[27] Suzuki coupling,[28] Grubb's ring closing metathesis[29,30] *etc.*, whose applications in developing various stereoselective transformations leading to the synthesis of natural products, carbocycles, heterocycles, and medicinally important compounds have been well documented.

Although the present day synthetic organic chemistry is well equipped to deal with most of the aspects of organic synthesis once considered to be difficult, the ever changing requirements in drug discovery and biomedical applications demand the continuous evolution of novel and sophisticated synthetic tools involving most important concepts like atom economy, selectivity (chemo-, regio- and stereo-) and organo-catalytic proceses.[14-16,31] Baylis-Hillman reaction is one such novel emerging C-C bond forming reaction possessing most of these requirements (atom economy, selectivity and organo-catalytic process). The origin of this reaction dates back to a German patent filed in 1972 by A. B. Baylis and M. E. D. Hillman.[32] This is essentially a three component atom economy reaction involving the coupling of α-position of an

activated alkene with an electrophile under the catalytic influence of a tertiary amine leading to the formation of densely functionalized molecules (Eq. 1).[32-37] DABCO (**1**) is the most commonly employed tertiary amine catalyst in this novel coupling reaction.



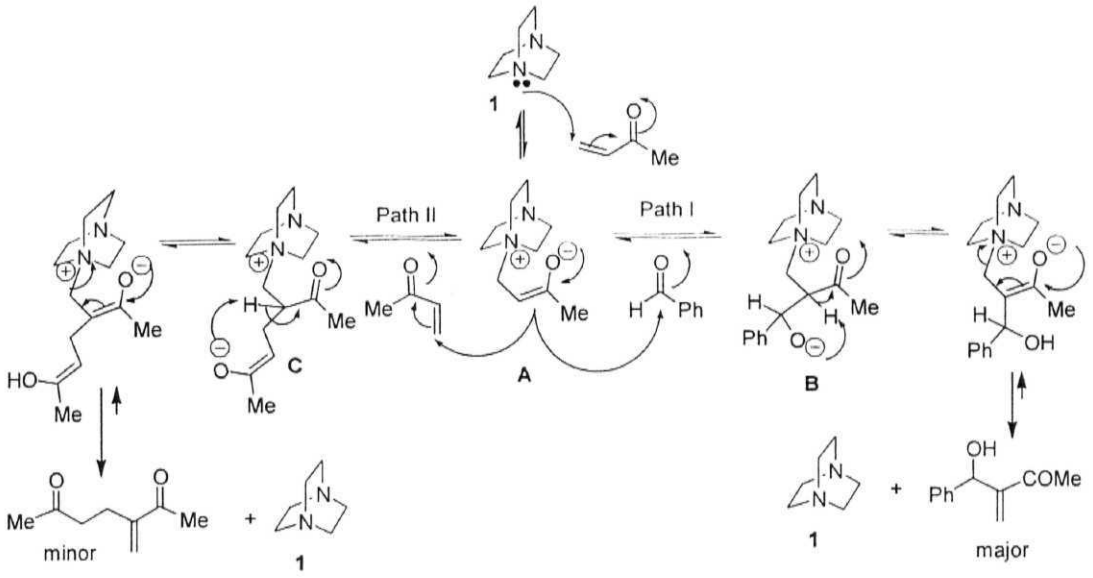

Eq. 1

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

## MECHANISM:

The most generally accepted mechanism[38-40] of the amine-catalyzed reaction is depicted pictorially in the Scheme 1 taking the reaction between methyl vinyl ketone (as an activated olefin) and benzaldehyde (as an electrophile) under the catalytic influence of DABCO (**1**) (as a catalyst), as a model case. This reaction is believed to proceed through the Michael initiated addition-elimination sequence. The first step in this catalytic cycle involves the Michael type nucleophilic addition of the tertiary amine to the activated alkene (methyl vinyl ketone) to produce a zwitterionic enolate **A**, which makes a nucleophilic attack onto the aldehyde (benzaldehyde) in aldol fashion to generate zwitterion **B**. Subsequent proton migration followed by the release of catalyst leads to the formation of highly functionalized molecules which are familiarly known as Baylis-Hillman adducts (Path I). In the case of reactive activated alkenes (such as alkyl vinyl ketones), Michael type dimers are formed as side products because these activated alkenes them selves act as electrophiles (Scheme 1; Path II).

**Scheme 1**



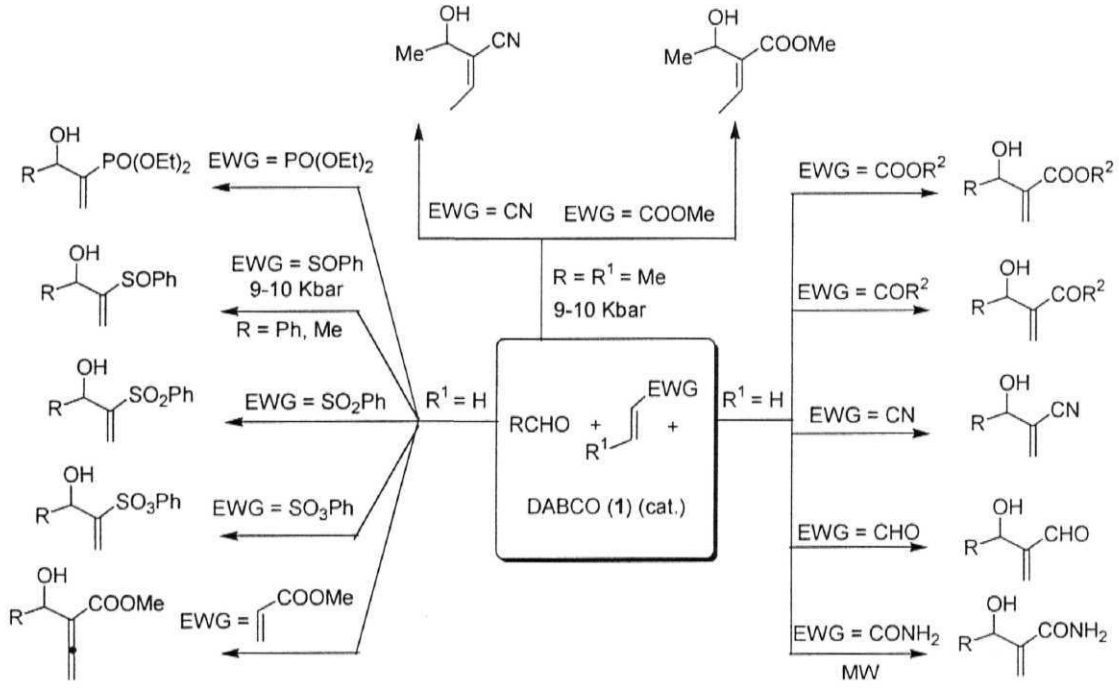

During the last fifteen years, the Baylis-Hillman reaction has seen a tremendous progress with respective to all the three essential components, *i.e.,* activated alkene, electrophile and catalyst as evidenced by large number of research publications and four major reviews.[33-35,37] Also, applications of the Baylis-Hillman adducts in various organic transformations have been well documented in the literature.[33-37] Since there is a vast literature available on various aspects of this fascinating reaction, it will not be possible to present all the information in this section. However, few recent, relevant and important developments, both in the reaction development and in the applications of the Baylis-Hillman adducts, are either presented or cited in this section.

## ACTIVATED ALKENES:

In addition to the most commonly used activated alkenes [alkyl vinyl ketones,[41-43] alkyl (aryl) acrylates,[40,44,45] and acrylonitrile[42,46]] variety of other activated alkenes such as

vinyl sulphones,[47] acrylamides,[48] allenic esters,[49,50] vinyl sulphonates,[51] vinyl phosphonates[52] and acrolien[53,54] have also been effectively employed in the Baylis-Hillman coupling with a number of carbon electrophiles to provide the desired densely functionalized molecules (Scheme 2). However, the activated alkenes having β-substituents such as crotononitrile,[55,56] crotonic acid esters[55] and less reactive alkenes like phenyl vinyl sulfoxide[57] require high pressure to participate in this reaction (Scheme 2).

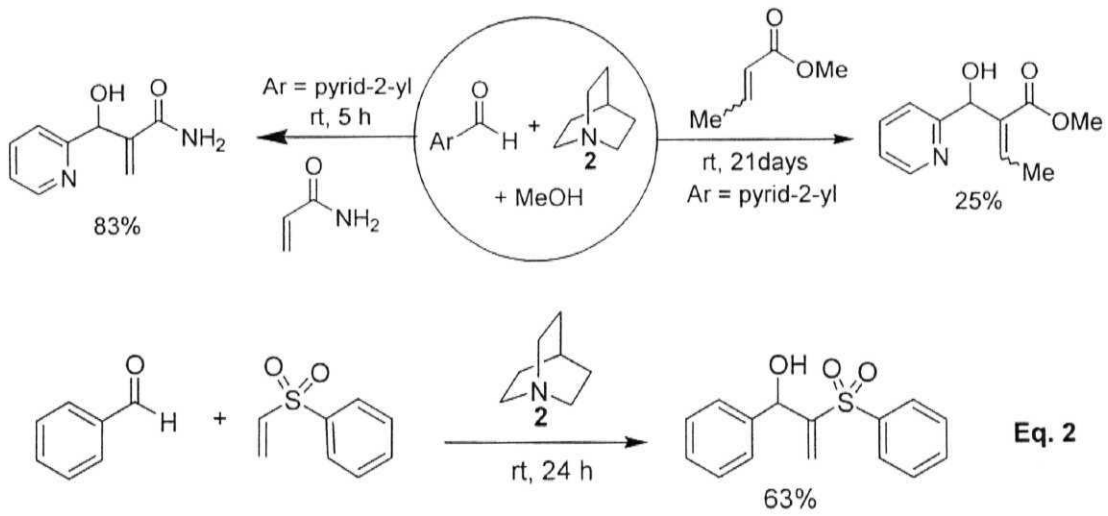
**Scheme 2**



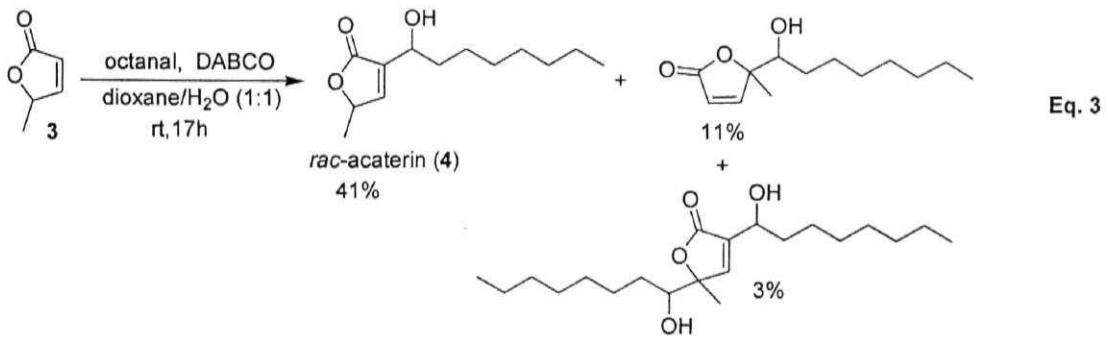

Recently, Aggarwal and co-workers[58] have used various less reactive activated olefins such as acrylamides, and β-substituted α,β-unsaturated esters for coupling with various aldehydes using quinuclidine (**2**) as a catalyst in methanol. Representative examples are

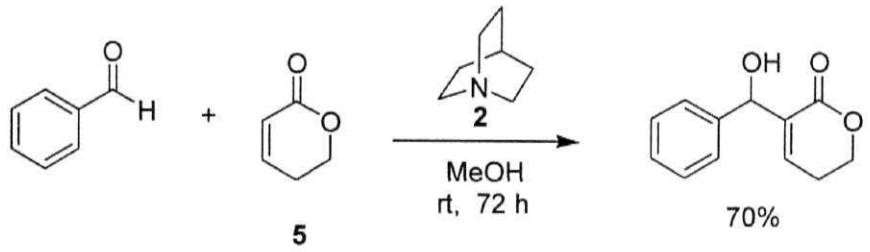
described in the Scheme 3. They have also used vinyl sulfones as an activated alkene for coupling with benzaldehyde under these conditions (Eq. 2).

**Scheme 3**




Cyclic activated alkenes such as δ-butyrolactone (**3**) (Eq. 3)[59] and 5,6-dihydro-(2*H*)-pyran-2-one (**5**) (Eq. 4)[58] were successfully employed in the Baylis-Hillman reaction. In fact, racemic acaterin (**4**) (a natural product) has been prepared in one step *via* the coupling of δ-butyrolactone (**3**) with octanal under the catalytic influence of DABCO (Eq. 3).[59]

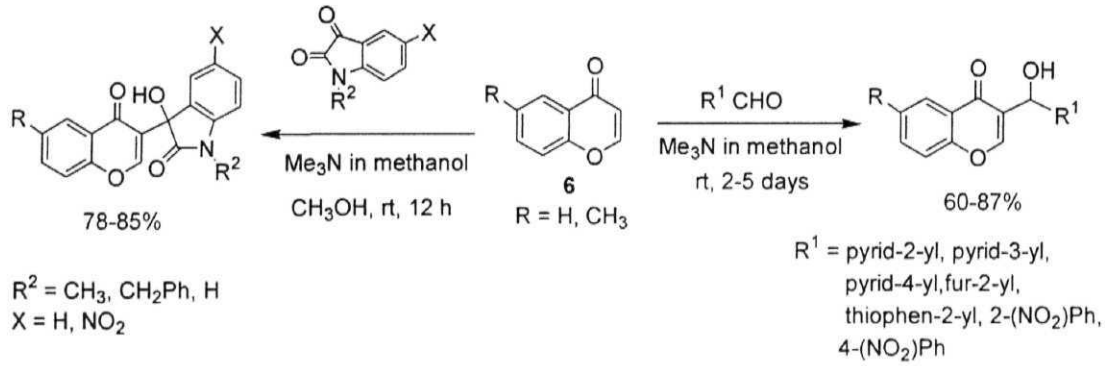





Eq. 4

Very recently, our research group,[60] for the first time, used 1-benzopyran-4(4*H*)-one derivatives (**6**) as activated alkenes in the Baylis-Hillman reaction with various electrophiles such as heteroaromatic aldehydes, nitrobezaldehydes and isatin derivatives under the influence of methanolic trimethylamine to provide the respective Baylis-Hillman adducts in good yields (Scheme 4).

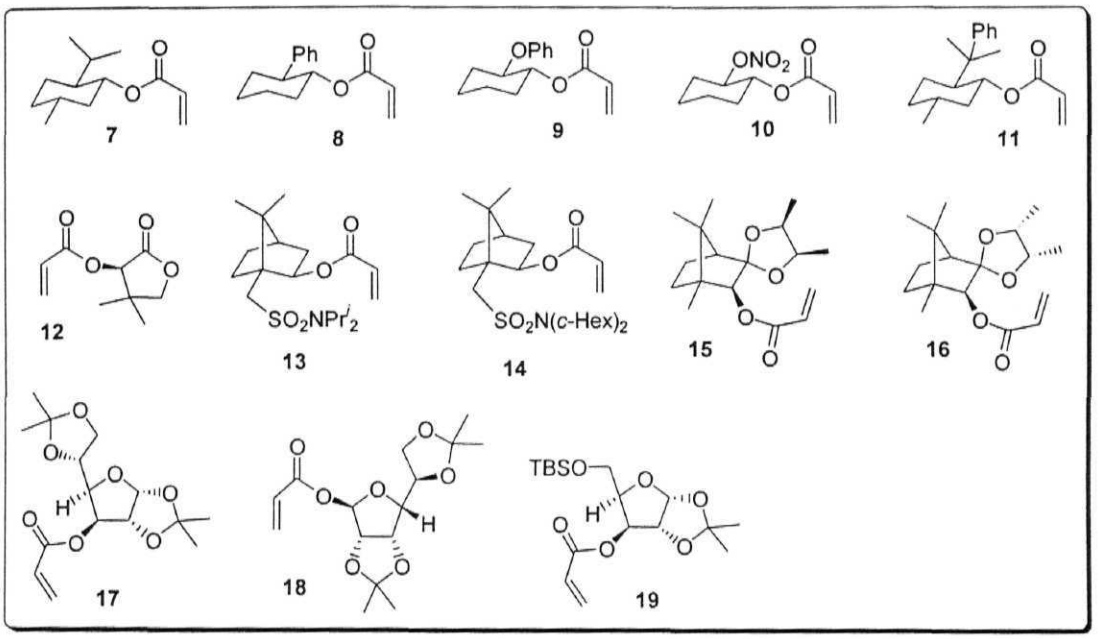
**Scheme 4**




## CHIRAL ACTIVATED ALKENES:

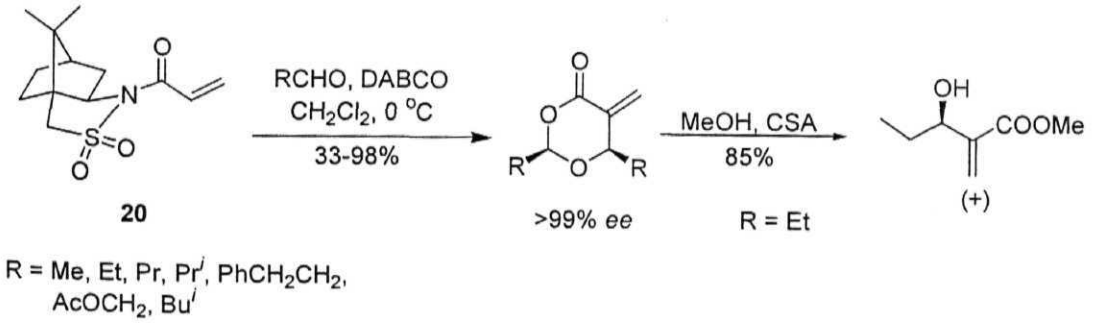
A variety of chiral acrylate esters (**7-19**) derived from various chiral auxiliaries such as cyclohexanol derivatives (**7-11**), (*R*)-(+)-pentolactone (**12**), camphor (**13-16**), [33-37,61-71] and sugar derivatives (**17-19**)[72] (Figure 1) have been employed in the Baylis-Hillman reaction as chiral activated alkenes to provide the resulting adducts in low to moderate diastereoselectivities.

**Figure 1**

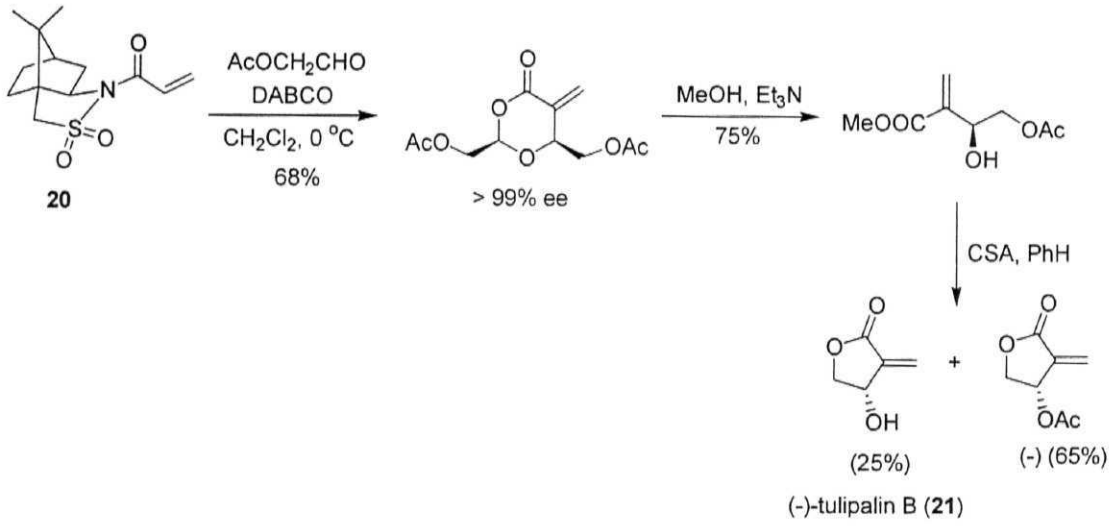



Leahy and co-workers[73,74] have successfully employed enantiopure acrylamide **20**, derived from camphorsulphonic acid, for asymmetric Baylis-Hillman reaction (Scheme 5) and subsequently applied this strategy to the synthesis of (-)-tulipalin B (**21**), a biologically important natural product (Scheme 6).[74]

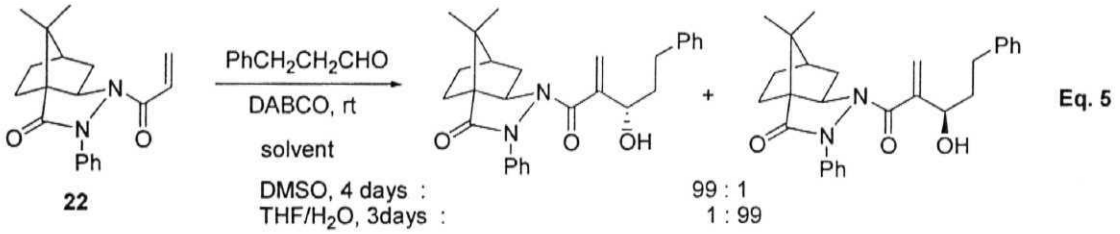
**Scheme 5**



**Scheme 6**




Quite recently, Yang and Chen[75] have used optically pure acryloylhydrazide **22** for Baylis-Hillman coupling with various aldehydes 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/$H_2O$. One representative example is described in Eq. 5.



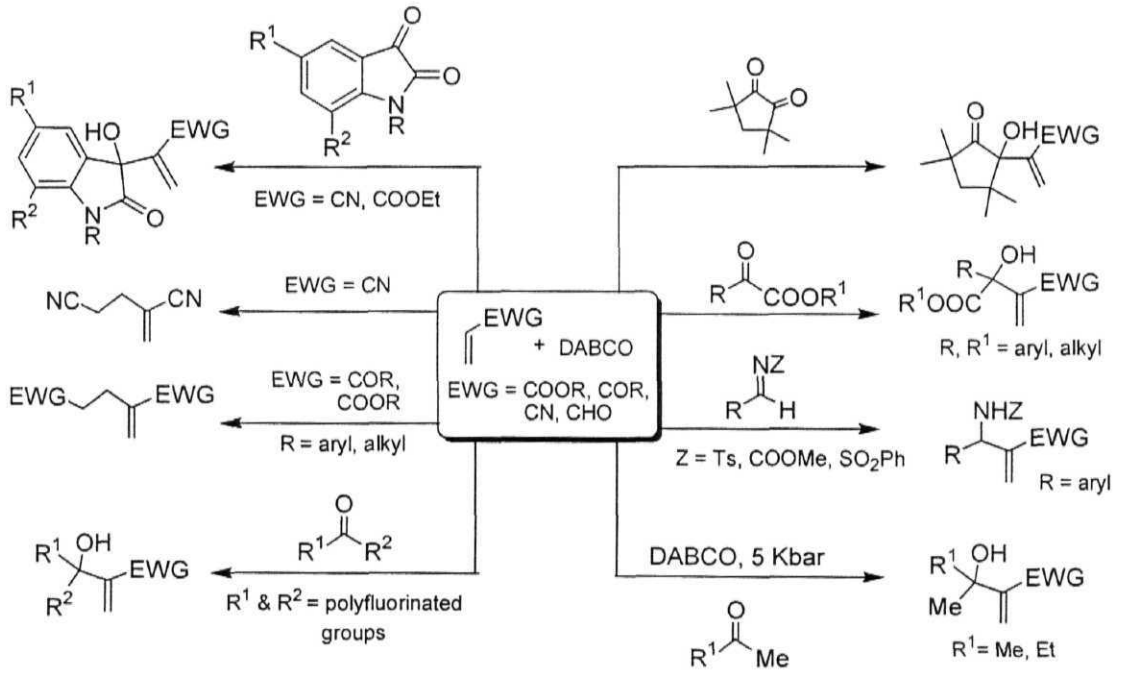

Eq. 5

**ELECTROPHILES:**

Aldehydes (aliphatic, aromatic, hetero-aromatic) are the most commonly used electrophiles in this reaction and in fact are considered as the primary source of electrophiles for Baylis-Hillman coupling.[33-37] In addition to these, other electrophiles

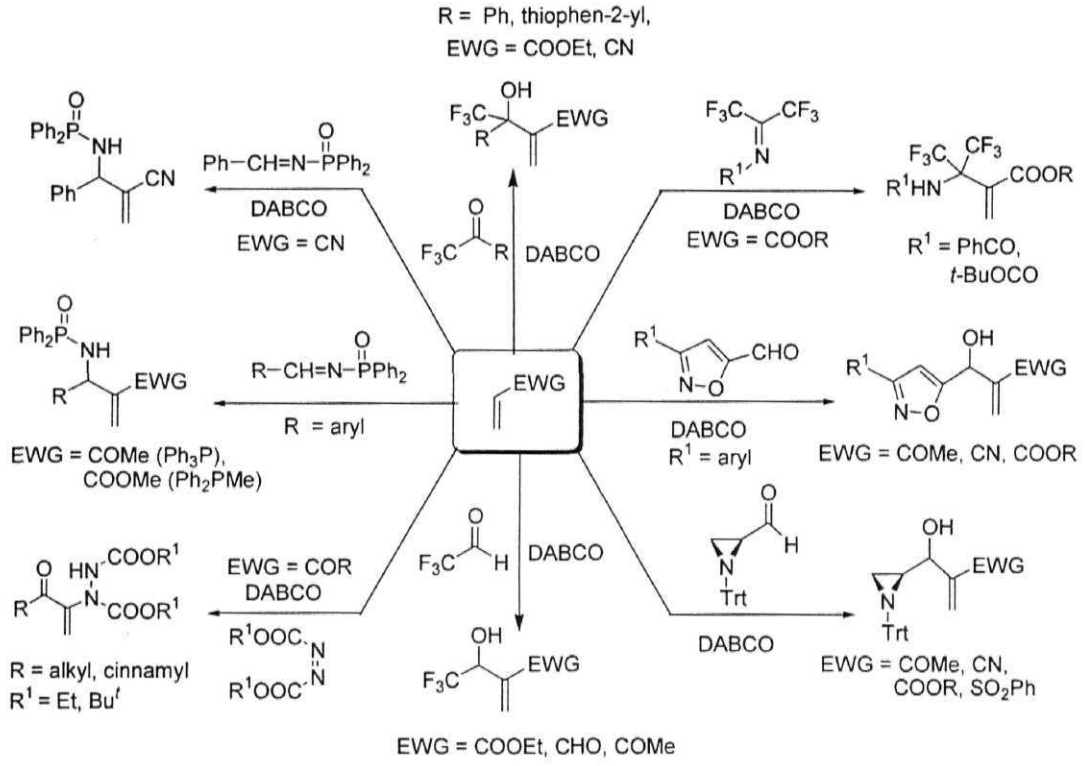
such as α-keto esters,[76-78] non-enolizable 1,2-diketones,[54] aldimine derivatives,[79-81] fluoro ketones,[82] activated alkenes[83-86] and isatin derivatives[87] have also been successfully employed in this reaction (Scheme 7). However, simple ketones, such as acetone and 2-butanone, which are usually less reactive, were also brought into the scope of Baylis-Hillman reaction under high pressure conditions[53,55] (Scheme 7).

**Scheme 7**



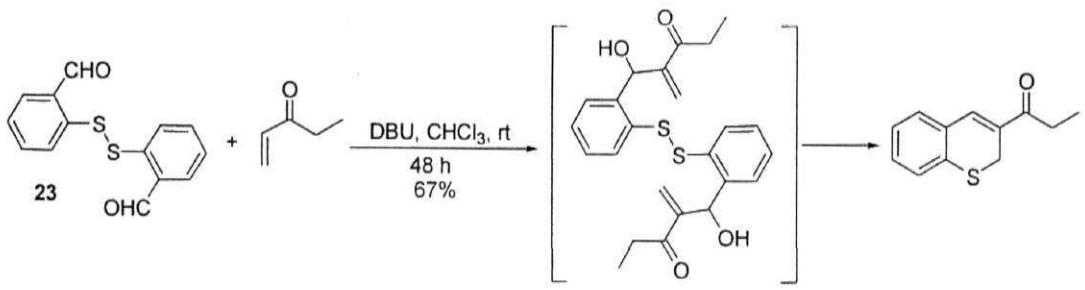

Recently, fluoro imines,[88] azodicarboxylates,[89] *N*-tritylaziridine-2-(*S*)-carboxaldehyde,[90] 5-isoxazolecarboxaldehydes,[91] fluorinated aldehydes,[92] fluorinated ketones,[93] and *N*-arylidenediphenylphosphinamides[94] have been successfully employed as electrophiles in Baylis-Hillman reaction (Scheme 8).

**Scheme 8**

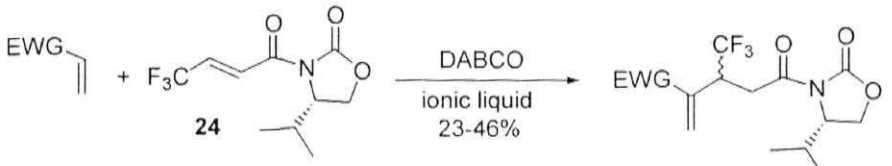



Kaye and Nocanda successfully employed 2,2′-dithiobenzaldehyde (**23**) as an electrophile for Baylis-Hillman coupling with activated alkenes under the influence of DBU, to provide benzothiopyran derivatives. One representative example is presented in the Scheme 9.[95]

**Scheme 9**



3-Trifluoromethylprop-2-enamide (**24**) was successfully used as electrophile in the Baylis-Hillman reaction with activated alkenes by Kitazume and coworkers[96] under the influence of DABCO in ionic liquids (Eq. 6).



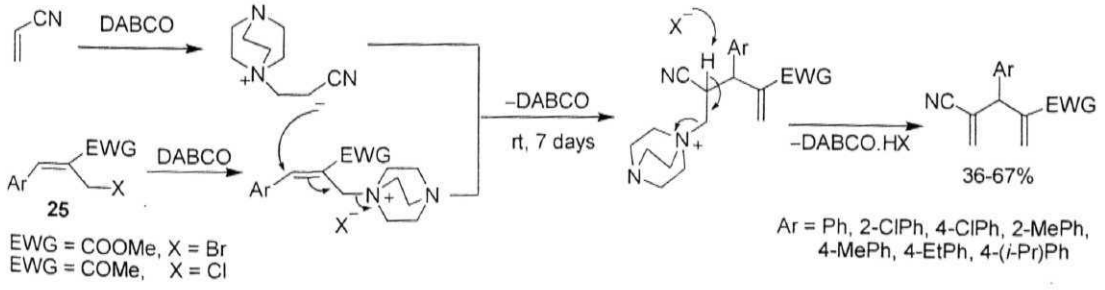

**Eq. 6**

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

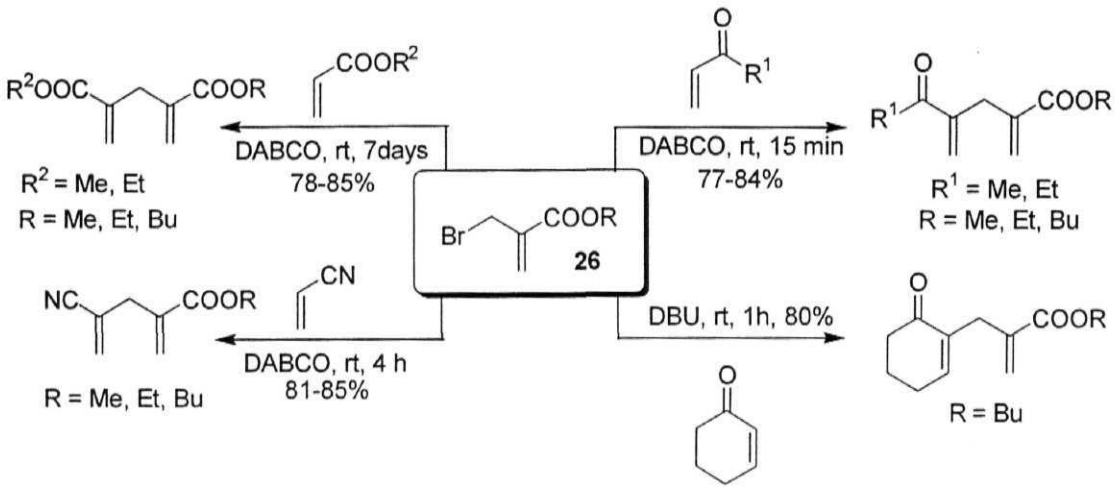
*dr* = 50:50 to 55:45

Our research group[97,98] has elegantly demonstrated, for the first time, that allyl halides (**25**) (allyl bromides/allyl chlorides), derived from the corresponding Baylis-Hillman adducts (which in turn were prepared from methyl acrylate and MVK respectively) act as electrophiles in the Baylis-Hillman coupling with acrylonitrile under the influence of DABCO thus leading to the formation of 3-substituted functionalized 1,4-pentadienes following reaction sequence as described in Scheme 10. Subsequently, our research group also developed a simple synthesis of a variety of 2,4-functionalized 1,4-pentadienes *via* the Baylis-Hillman reaction of the allyl bromides (**26**), derived from alkyl 3-hydroxy-2-methylenepropanoates, as electrophiles, with alkyl acrylates, alkyl vinyl ketones and acrylonitrile (Scheme 11).[98]

**Scheme 10**

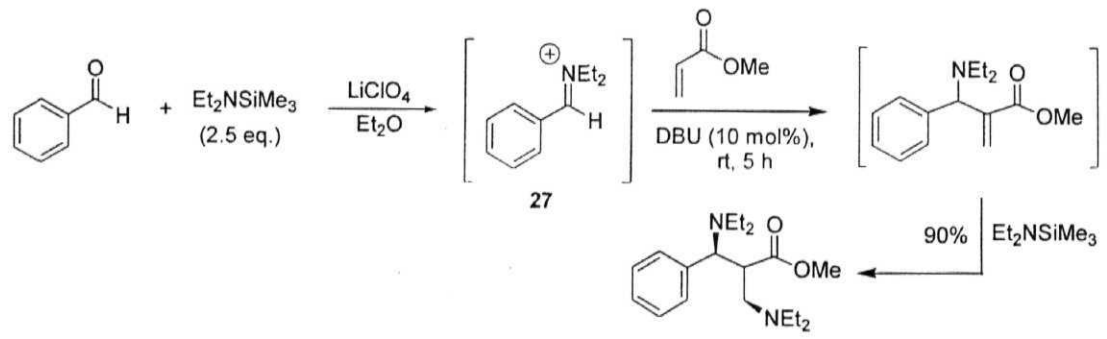


**Scheme 11**




Azizi and Saidi[99] have successfully utilized *in situ* generated iminium salts (**27**), obtained *via* the treatment of aldehydes with (trimethylsilyl)dialkylamines, as electrophiles in the Baylis–Hillman reaction with methyl acrylate in the presence of DBU as the catalyst. The Baylis-Hillman adducts, thus formed, in situ, further react with (trimethylsilyl)dialkylamines to produce the 1,3-diamine derivatives as final products. A selective example is presented in the Scheme 12.

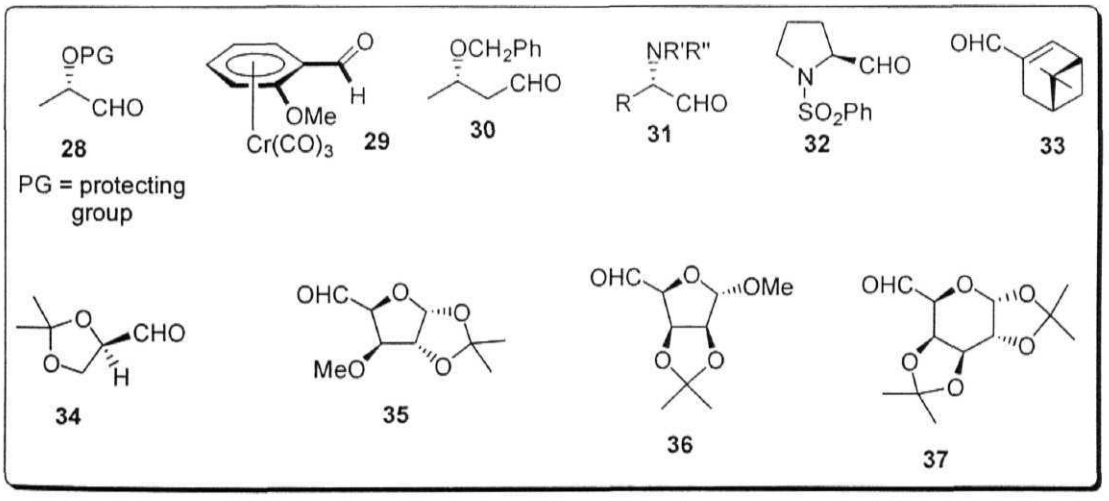
**Scheme 12**



## CHIRAL ELECTROPHILES:

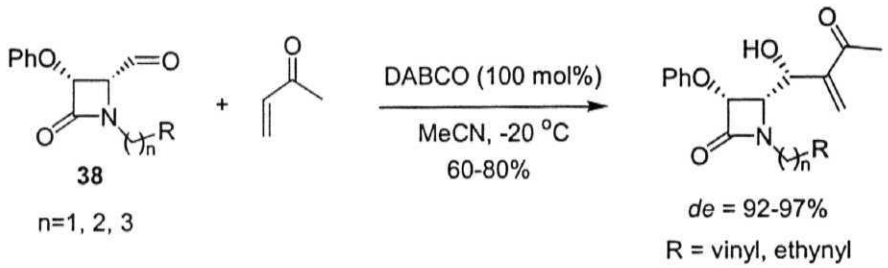
Applications of various enantiopure electrophiles such as (*S*)-*O*-protected lactaldehyde (**28**),[100] enantiopure *ortho* substituted benzaldehyde tricarbonylchromium complex (**29**),[101,102] (*S*)-3-benzyloxybutyraldehyde (**30**),[103] α-dialkylamino and α-(*N*-acylamino)aldehydes (**31**),[104,105] *N*-phenylsulfonyl-(*L*)-prolinal (**32**),[105] (*R*)-myrtenal (**33**),[66] isopropylidene (*R*)-glyceraldehyde (**34**)[66] and various sugar derived chiral aldehydes (**35-37**)[106] *etc.*, (Figure 2) have been studied in Baylis-Hillman reaction. The resulting products were obtained in low to good diastereoselectivities.

**Figure 2**

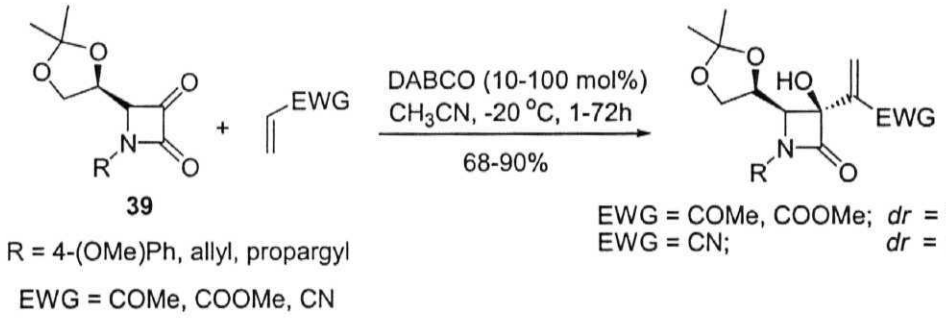



Recently, Alcaide and co-workers[107] have examined the application of enantiopure 1-alkenyl(alkynyl)-4-oxoazetidine-2-carbaldehydes (**38**) as chiral electrophiles in the Baylis-Hillman reaction with MVK which provided resulting adducts with very high diastereoselectivities (Eq. 7). Subsequently, they have also successfully employed optically pure 3-oxo-2-azetidinones (**39**) for coupling with activated alkenes under the

influence of DABCO to provide the resulting Baylis-Hillman adducts in high diastereoselectivities (Eq. 8).[108]




Eq. 7

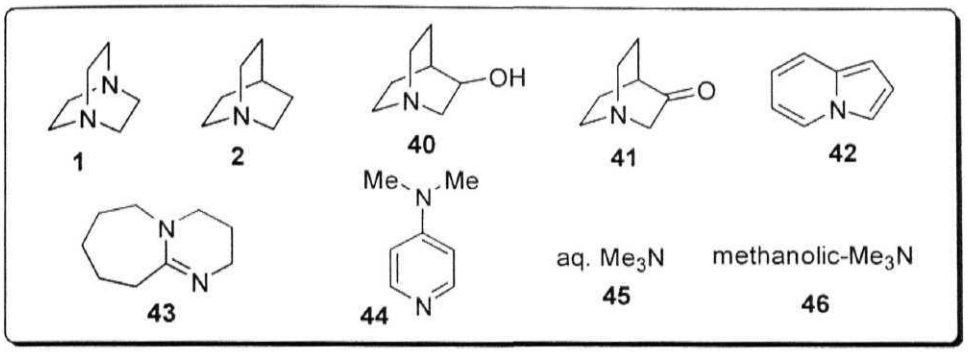



Eq. 8

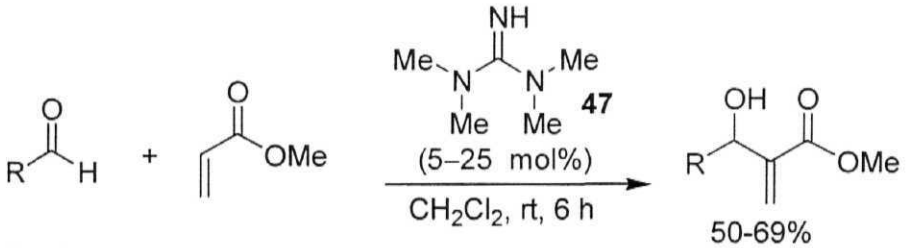
## AMINE CATALYZED BAYLIS-HILLMAN REACTIONS:

Although, DABCO (**1**) has been used as the catalyst of choice in this reaction, various other tertiary amine catalysts such as quinuclidine (**2**), 3-hydroxyquinuclide (3-HQD) (**40**), 3-quinuclidinone (**41**) and indolizine (**42**) have also been employed to perform the Baylis-Hillman reaction (Figure 3).[32-37] Recently, DBU (**43**),[109] DMAP (**44**),[110,111] aq. $Me_3N$ (**45**),[112] methanolic-$Me_3N$ (**46**)[113] (Figure 3) were also found to promote Baylis-Hillman reaction.

**Figure 3**

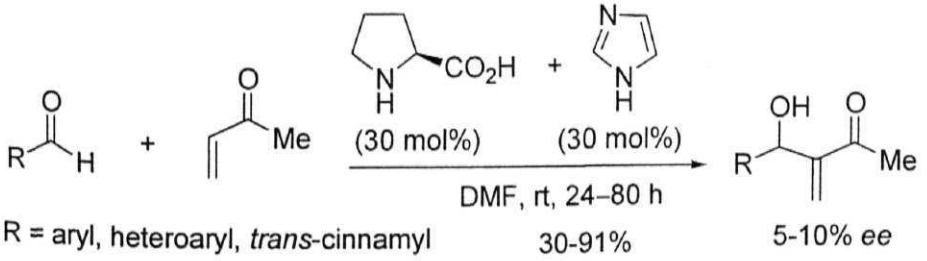



Leadbeater *et. al.* have, for the first time, used tetramethylguanidine (TMG) (**47**) as a novel catalyst to perform the coupling of various aldehydes with methyl acrylate to provide the Baylis-Hillman adducts in good yields (Eq. 9).[114]




**Eq. 9**

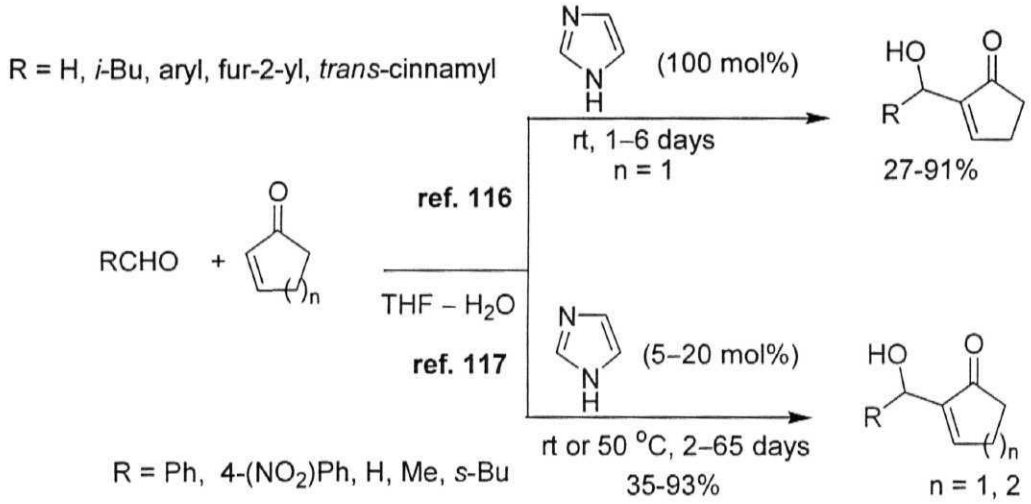
Shi and co-workers[115] have observed that imidazole catalyzes Baylis–Hillman reaction of various aldehydes with MVK in the presence of proline. Although the yields of the reaction were satisfactory, the enantioselectivities were found to be very low (Eq. 10).



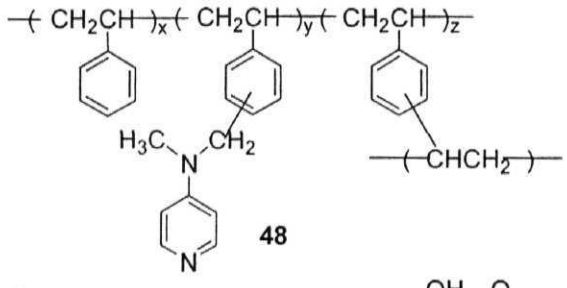

**Eq. 10**

Very recently, Cheng and co-workers[116] and later Gatri and El Gaied[117] have employed imidazole as the catalyst for performing the Baylis–Hillman coupling of cycloalkenones with various aldehydes (Scheme 13).

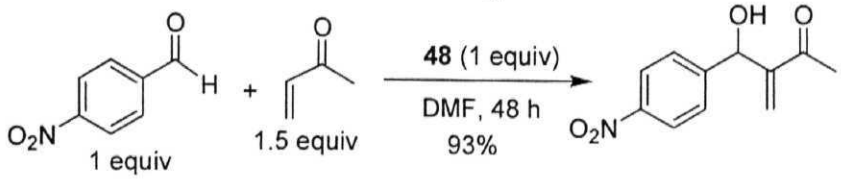
**Scheme 13**




Very recently, Corma and co-workers[118] have used 4-(N-benzyl-N-methylamino)pyridine bound to an insoluble polystyrene scaffold (PAP) (**48**) as suitable and reusable heterogeneous catalyst for the Baylis–Hillman coupling of aromatic aldehydes with unsaturated ketones (Eq. 11).

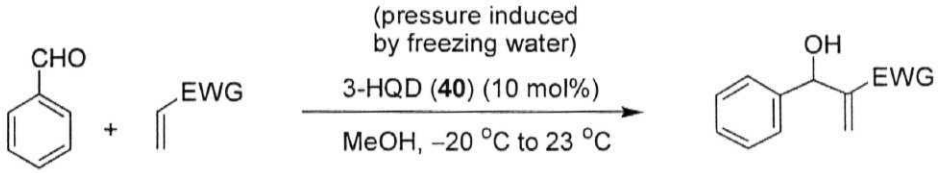


**48**




**Eq. 11**

Hayashi and co-workers[119] have observed remarkable rate acceleration in the Baylis–Hillman coupling of benzaldehyde with various activated olefins in the presence of 3-HQD (**40**) under high pressure induced by freezing water in a sealed autoclave. Representative examples are described in Eq. 12.

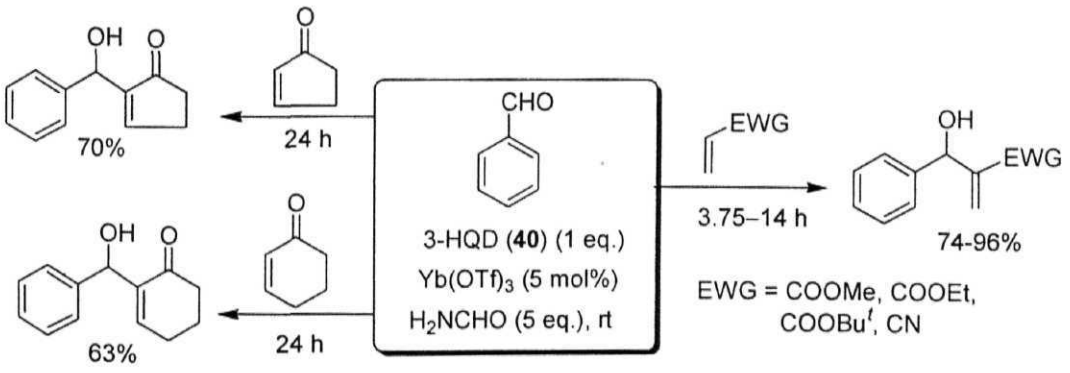



**Eq. 12**

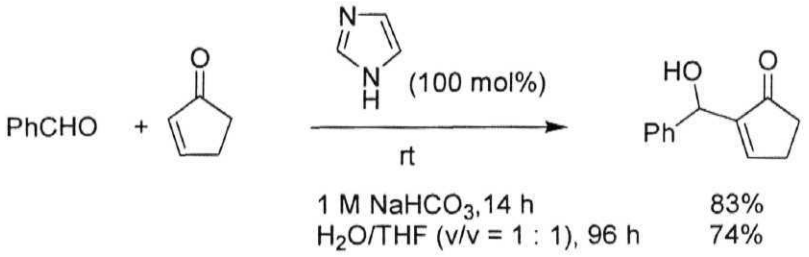
| EWG | Pressure (MPa) | Time (h) | Yield (%) |
|---|---|---|---|
| COOMe | 0.1 | 24 | 40 |
| | 200 | 24 | 78 |
| $COOBu^t$ | 0.1 | 52 | 52 |
| | 200 | 52 | 71 |

Recently, Aggarwal and co-workers[120] have examined the application of protic solvents such as water, formamide in accelerating the Baylis–Hillman reaction and demonstrated the importance of hydrogen bonding for faster reaction. They found that the presence of 5 equivalents of formamide gave better results. Further acceleration was observed when they add catalytic amount of metal salts such as $Yb(OTf)_3$. Representative examples are presented in Scheme 14.

**Scheme 14**



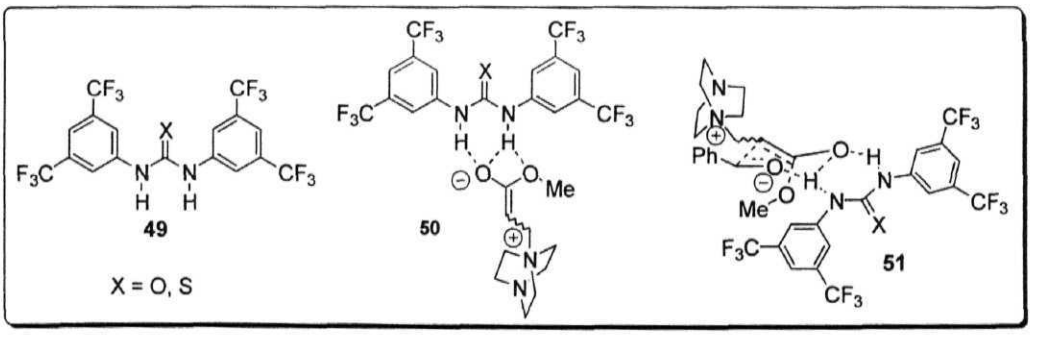
Recently, Cheng and co-workers[121] have observed that the presence of basic water solution along with imidazole as catalyst significantly accelerated the Baylis-Hillman reaction of cyclic enones with various aldehydes. They attributed the enhanced reactivities in alkaline solutions to the apparent enhanced basicity of imidazoles. Bicarbonate solution was found to be the optimal reaction medium in this case. A representative example is presented in the Eq. 13.

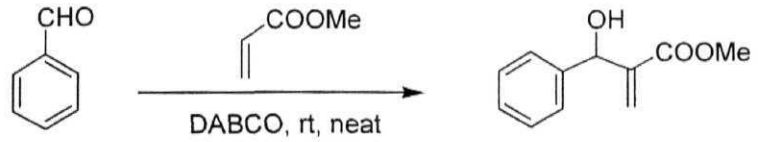



**Eq. 13**

Maher and Connon[122] found that catalytic amounts of bis-aryl (thio)ureas (**49**) (Figure 4) accelerate the DABCO-promoted Baylis–Hillman reaction between aromatic aldehydes and methyl acrylate in the absence of solvent (Eq. 14). Enhancements in the reaction rates were attributed to the possible double H-bonding of the urea with zwitterionic intermediate (**50**, **51**) (Figure 4). Representative example is presented in Eq. 14.

**Figure 4**





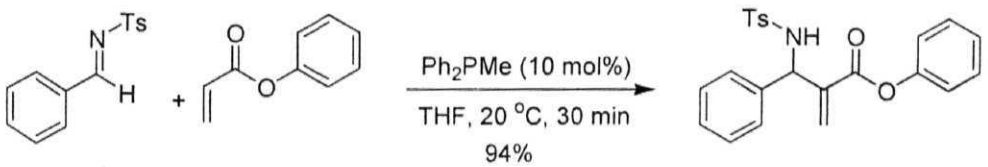

Eq. 14

| | time | yield |
|---|---|---|
| with **49** (X = O) (20 mol%) | 20 h | 88% |
| without **49** | 20 h | 32% |

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

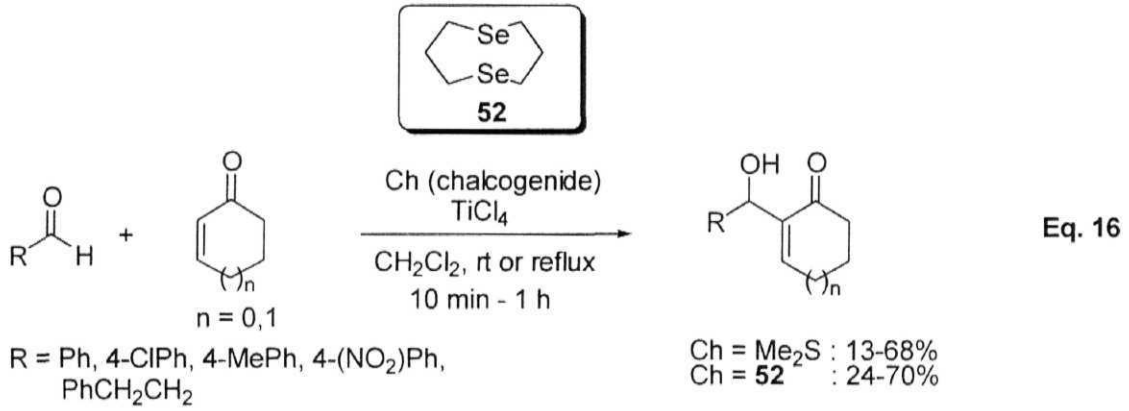
Several non-amine catalysts such as trialkyl phosphines,[123-125] triaryl phosphines,[126] and metal complexes like $RhH(PPh_3)_4$,[127,128] $RuH_2(PPh_3)_4$,[128,129] have been found to promote coupling of activated alkenes with aldehydes to provide the desired adducts. Recently, $R_2S$–$TiCl_4$,[37,130-133] $R_2S$–$BF_3$,[37,134-136] $TiCl_4$-$NR_4X$ (X = halide),[37,137,138] $TiCl_4$-$NR_3$,[139] $TiCl_4$[140] and $Et_2AlI$[141,142] were also successfully employed as catalysts/catalytic systems in Baylis-Hillman-type coupling. Some of the recent developments in this direction are discussed in the following.

Recently, Shi and Xu[143] have examined the application of $Ph_2PMe$ as catalyst to promote the Baylis-Hillman coupling between various activated alkenes and imines. Best results were obtained when the coupling was carried between aryl acrylates and imines. One representative example is presented in the Eq. 15.



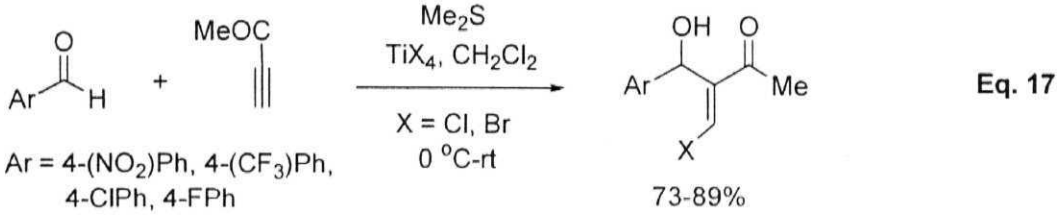

Eq. 15

Kataoka *et al.*[130,131] have developed an interesting Baylis-Hillman coupling of vinyl ketones with various aldehydes catalyzed by sulfides or selinides ($Me_2S$, PhSMe) in the presence of $TiCl_4$ as a Lewis acid. Selinide **52** and $Me_2S$ were proved to be the best catalysts for this reaction (Eq. 16).



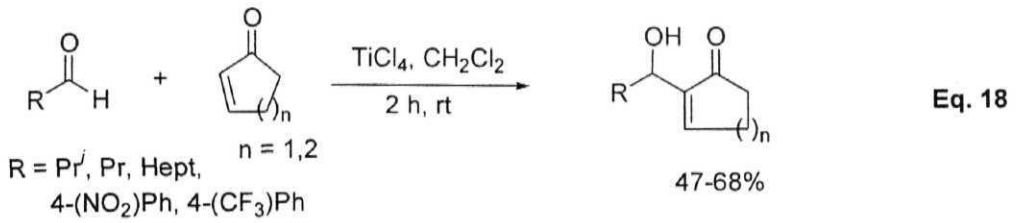

**Eq. 16**

Kataoka has further extended chalcogeno-Baylis-Hillman reaction to activated alkynes. Thus, the reaction between activated alkynes with aldehydes under the influence of $Me_2S$ in the presence of $TiX_4$ provided an interesting α-halomethylene aldols *i.e.*, β-halo Baylis-Hillman adducts (Eq. 17).[144]




**Eq. 17**

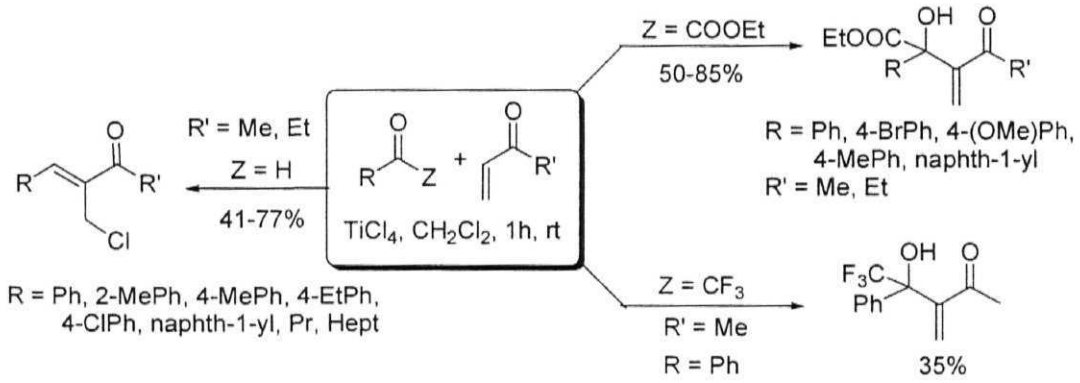
Li and co-workers[140] have reported an interesting $TiCl_4$-mediated coupling of cycloalkenones with various aldehydes (without the direct use of Lewis base) to provide the Baylis-Hillman adducts (Eq. 18).




**Eq. 18**

Our research group[145] has recently described $TiCl_4$-promoted Baylis-Hillman coupling of α-keto esters and trifluoromethyl phenyl ketone with alkyl vinyl ketones to provide the desired adducts in moderate to good yields (Scheme 15). Similar reaction with aldehydes provided (*Z*)-allyl chlorides (Scheme 15).

**Scheme 15**

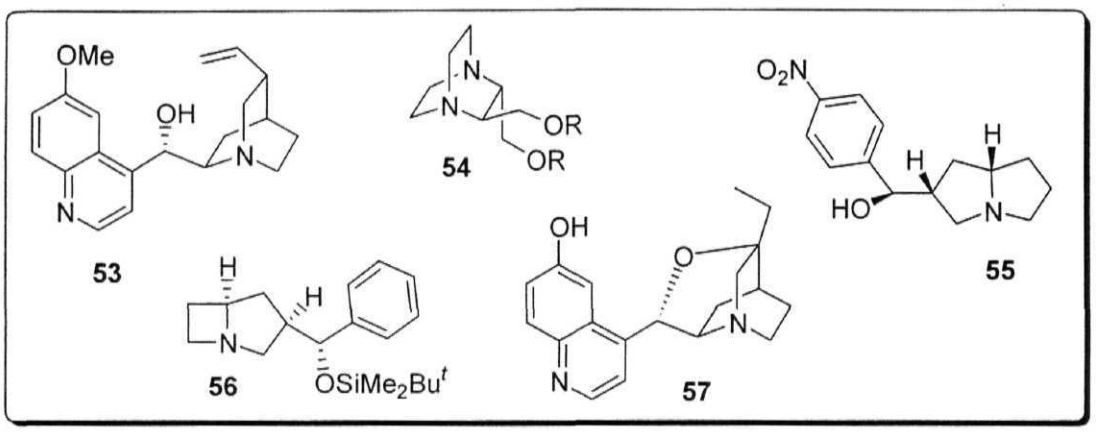



## CHIRAL CATALYSTS:

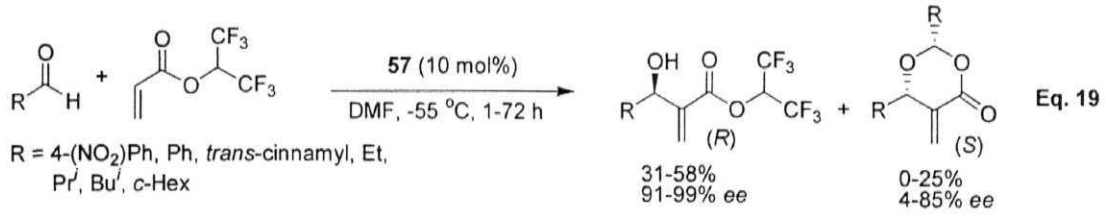
Attempts were also directed towards the application of chiral tertiary amines in achieving asymmetric version of Baylis-Hillman reaction.[33-37] Quinidine **53**,[33,146] the first catalyst examined in this direction, provided poor enantioselectivities (maximum upto 20% *ee*). Later on, various other chiral tertiary amines such as chiral DABCO (**54**),[147,148] enantiopure pyrrolizidine (**55**)[149] and chiral bicyclic azetidine (**56**),[150] (Figure 5) have also been employed in this reaction which provided lower to moderate

enantioselectivities.

**Figure 5**

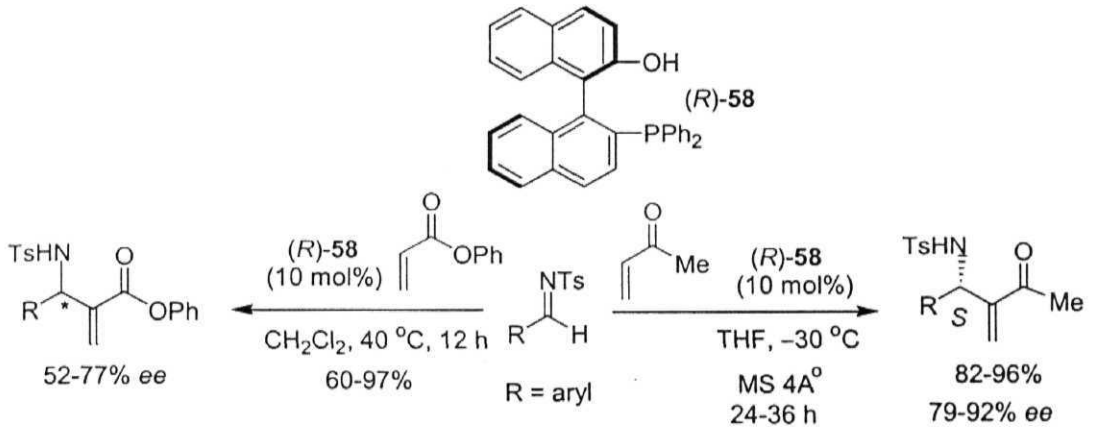



Hatakeyama and coworkers[151-154] have successfully employed tertiary amine **57** (Figure 5) derived from cinchona alkaloids as a catalyst for Baylis-Hillman coupling. Thus, the reaction between 1,1,1,3,3,3-hexafluoroisopropyl acrylate and various aldehydes under the catalytic influence of **57** provided the desired adducts in upto 99% enantiomeric purity (Eq. 19).

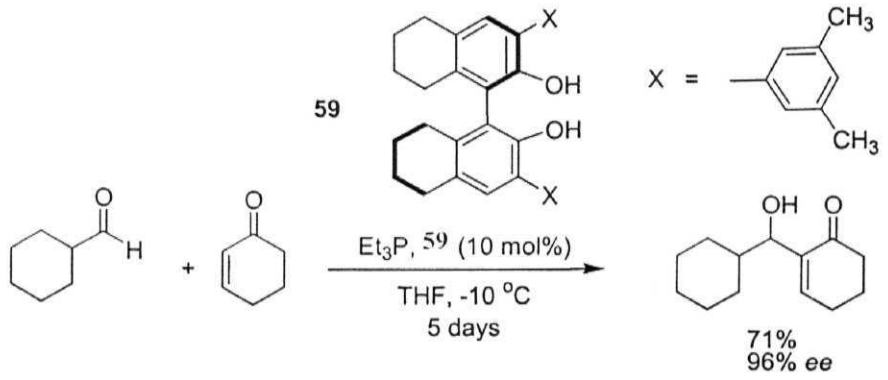



Recently, Shi and Chen[155] have described an interesting asymmetric Baylis–Hillman reaction employing (*R*)-2′-diphenylphosphinyl-[1,1′]binaphthalenyl-2-ol [(*R*)-**58**] as a chiral phosphine catalyst. Thus, the coupling of *N*-sulfonated imines with methyl vinyl ketone and phenyl acrylate in presence of (*R*)-**58** provided the corresponding Baylis–Hillman adducts in high enantioselectivities (Scheme 16).

**Scheme 16**

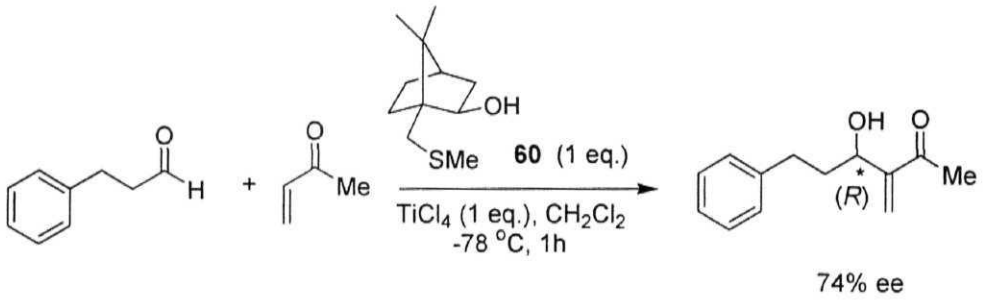



Recently, Schaus and McDougal[156] reported a highly enantioselective Baylis-Hillman coupling of cyclohexenone with various aliphatic aldehydes under the influence of $Et_3P$ in presence of various chiral tetrahydro-BINOL-derived Brønsted acids (**59**). One of the best results is described in the Eq. 20.




**Eq. 20**

Kataoka and co-workers[157] have reported an interesting asymmetric chalcogeno-Baylis-Hillman reaction with enantiopure hydroxy chalcogenides as catalysts. One representative reaction between hydrocinnamaldehyde and MVK in the presence of 10-methylthioisoborneol (**60**) is presented in Eq. 21

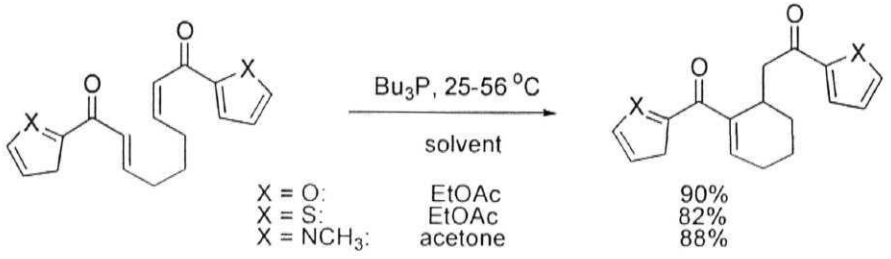



Eq. 21

## INTRAMOLECULAR BAYLIS-HILLMAN REACTIONS:

Though the Baylis-Hillman reaction has seen a tremendous development with respective to all the three essential components *i.e.*, activated alkene, electrophile and catalyst, intramolecular version of Baylis-Hillman reaction, yet another interesting aspect of this reaction, has not been studied systematically.[33-35,37] Some of the recent and interesting developments in this direction are presented in the following.

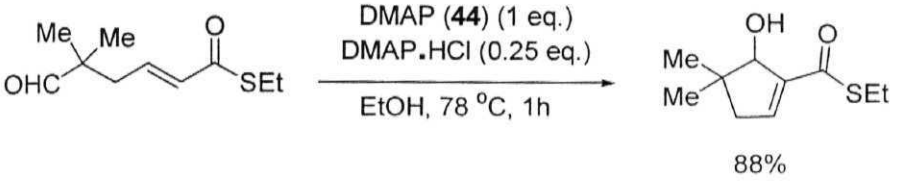
Krische and co-workers reported an interesting intramolecular coupling of various bis-enones, under the influence of $Bu_3P$, to provide the cyclic compounds. Representative examples are presented in Eq. 22.[158]




Eq. 22

Recently, Keck and Welch[159] examined intramolecular Baylis-Hillman reaction of α, β-unsaturated esters / thioesters containing aldehyde group using DMAP (**44**) and

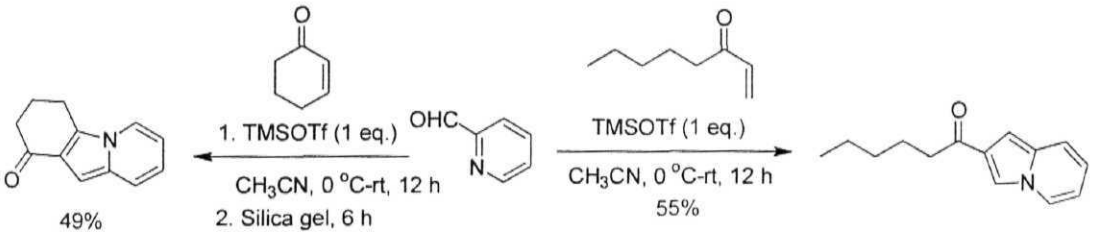
DMAP·HCl in EtOH (at 78 °C for 1h) or $Me_3P$ in $CH_2Cl_2$ (at room temperature for 15h) as catalyst. Representative example is described in the Eq. 23.



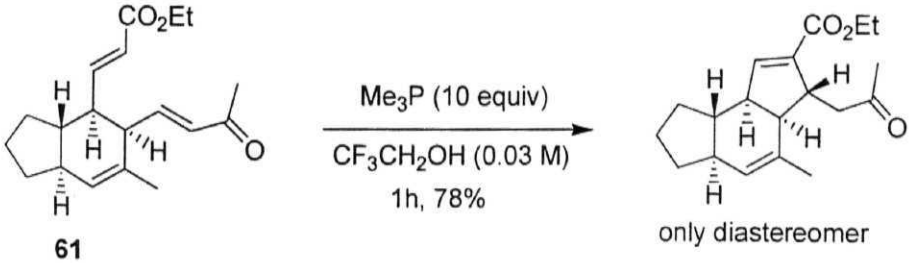

**Eq. 23**

Our research group, for the first time, described an electrophile induced intramolecular Baylis–Hillman reaction between activated alkenes and pyridine-2-carboxldehyde under the influence of trimethylsilyl trifluoromethanesulfonate (TMSOTf), leading to a novel synthesis of indolizine derivatives in one-pot operation. Representative examples are presented in the Scheme 17.[160]

**Scheme 17**




Very recently, Methot and Roush[161] have reported an interesting intramolecular Baylis-Hillman reaction of **61** under the influence of $Me_3P$ (Eq. 24).




**Eq. 24**

## APPLICATIONS OF THE BAYLIS-HILLMAN ADDUCTS:

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 very close proximity which make them valuable substrates for various organic reactions like Friedel-Crafts reaction, isomerization, Heck reaction, Johnson-Claisen rearrangement, hydrogenation, hydride addition, photochemical reactions and *etc.*[33-35,37] These adducts have been elegantly employed as valuable synthons in the synthesis of various trisubstituted olefins and several important heterocycles, carbocycles, natural products and biologically active molecules.[33-35,37] Some of the important and recent developments in the application of these adducts are presented in this section so as to provide a glimpse of the importance of Baylis-Hillman adducts.

Our research group has developed 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 Baylis-Hillman adducts, obtained respectively from methyl acrylate and acrylonitrile, with LAH:EtOH (Scheme 18). Subsequently, this methodology has been successfully applied for the synthesis of (*E*)-nuciferol (**62**), a biologically active terpene and **63**, a precursor for (*Z*)-nuciferol (Figure 6).[162]

**Scheme 18**

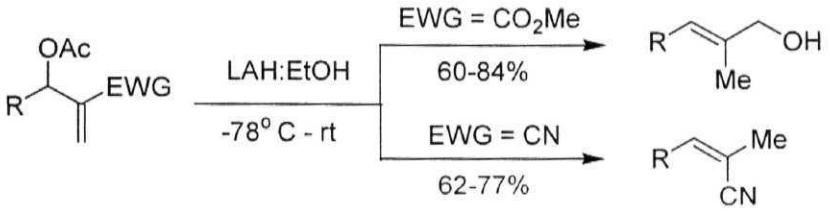
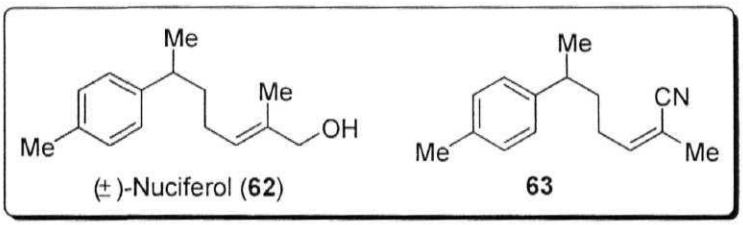
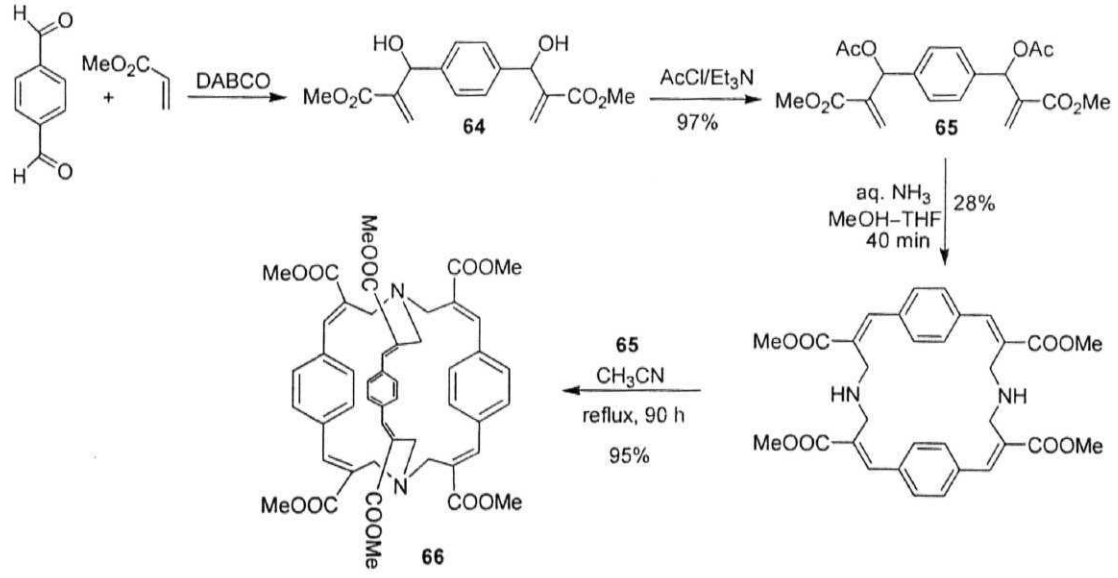



**Figure 6**




The diacetate (**65**) obtained from the Baylis–Hillman adduct (**64**) (which in turn, was prepared from terephthaldehyde and methyl acrylate) has been transformed into a novel cryptand-type molecule (**66**) by Bauchat and Foucaud following the reaction sequence as described in Scheme 19.[163]

**Scheme 19**



Our research group[164] has described a simple and convenient synthesis of (*E*)-α-methylcinnamic acids (**67**) *via* the nucleophilic addition of hydride ion from $NaBH_4$ to the acetates of the Baylis–Hillman adducts, followed by hydrolysis and crystallization (Scheme 20). This methodology has been successfully applied for the synthesis (*E*)-*p*-(myristyloxy)-α-methylcinnamic acid (**68a**), a hypolipidemic active agent [which is also a precursor for another active hypolipidemic agent LK-903 (**69a**)] and [*E*]-*p*-(carbomethoxy)-α-methylcinnamic acid (**68b**) which is valuable synthon for orally active serine protease inhibitor (**69b**) (Figure 7).[164]

**Scheme 20**

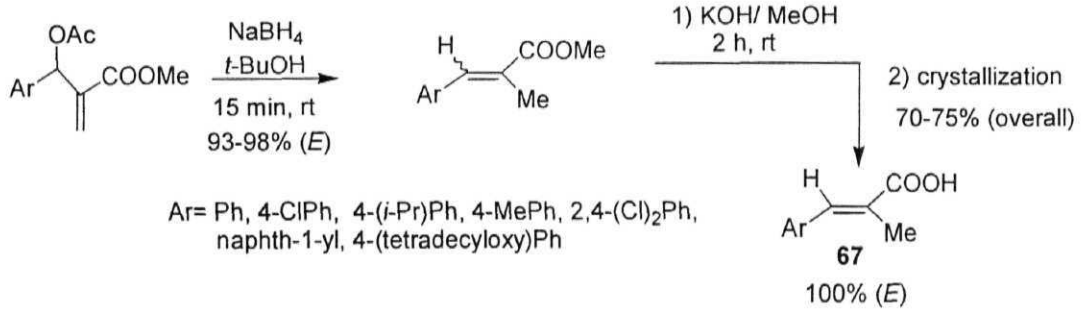
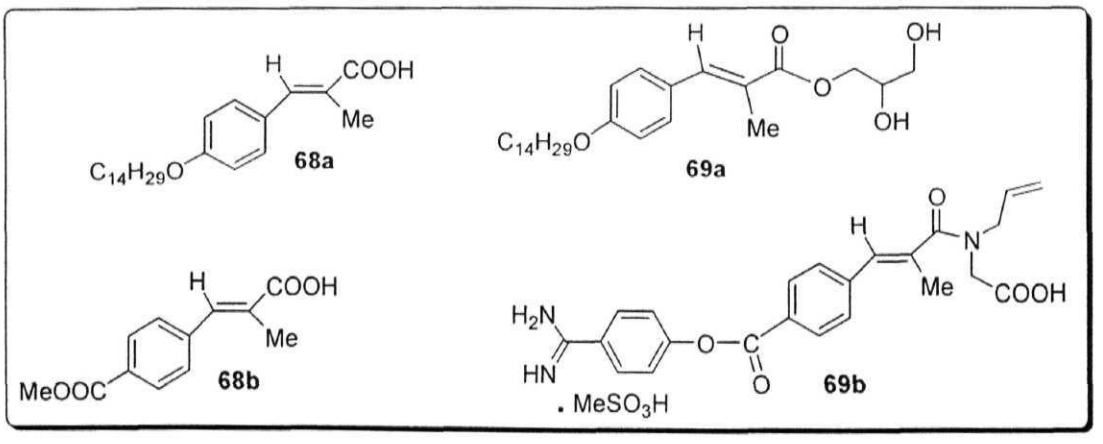
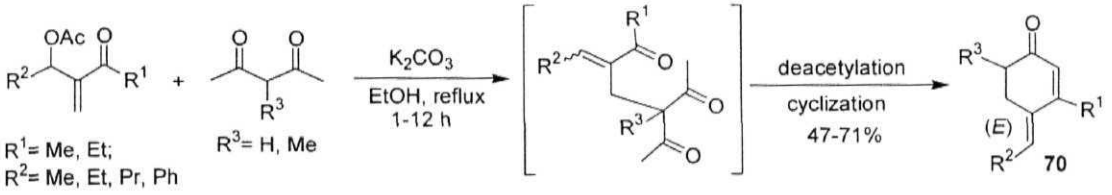



**Figure 7**



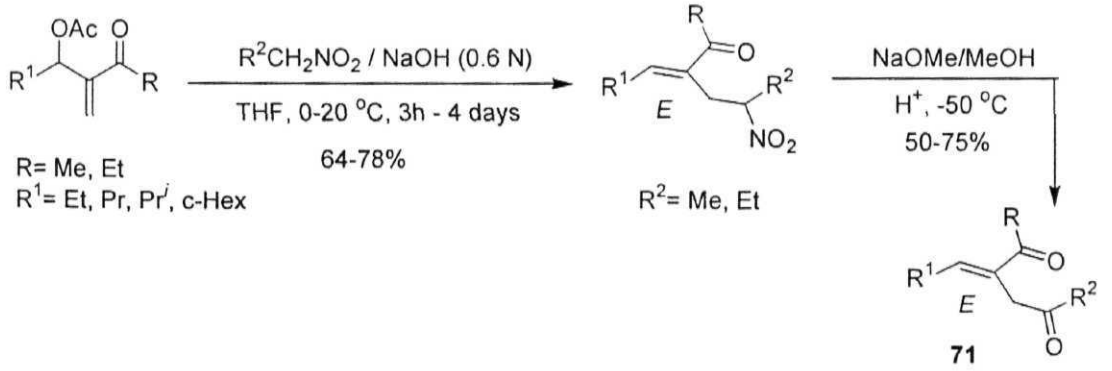
Chamakh and Amri[165] have reported a facile one pot synthesis of (*E*)-4-alkylidene-2-cyclohexen-1-ones (**70**) from acetates of the Baylis-Hillman adducts *via* a treatment with aliphatic 1,3-diketones (Scheme 21).

**Scheme 21**

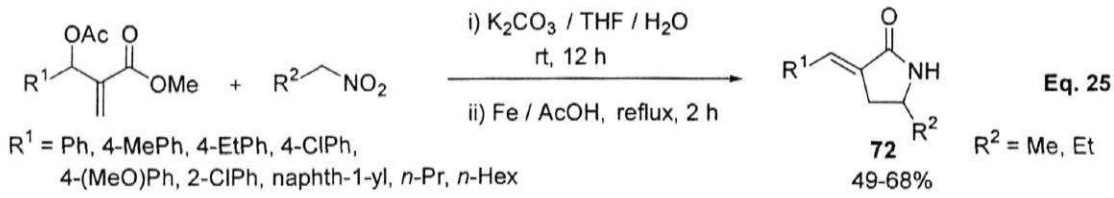



Amri and co-workers[166,167] have also successfully described the synthesis of 1,4-diketones (**71**) from the acetates of the Baylis-Hillman adducts following a reaction sequence as described in Schemes 22.

**Scheme 22**

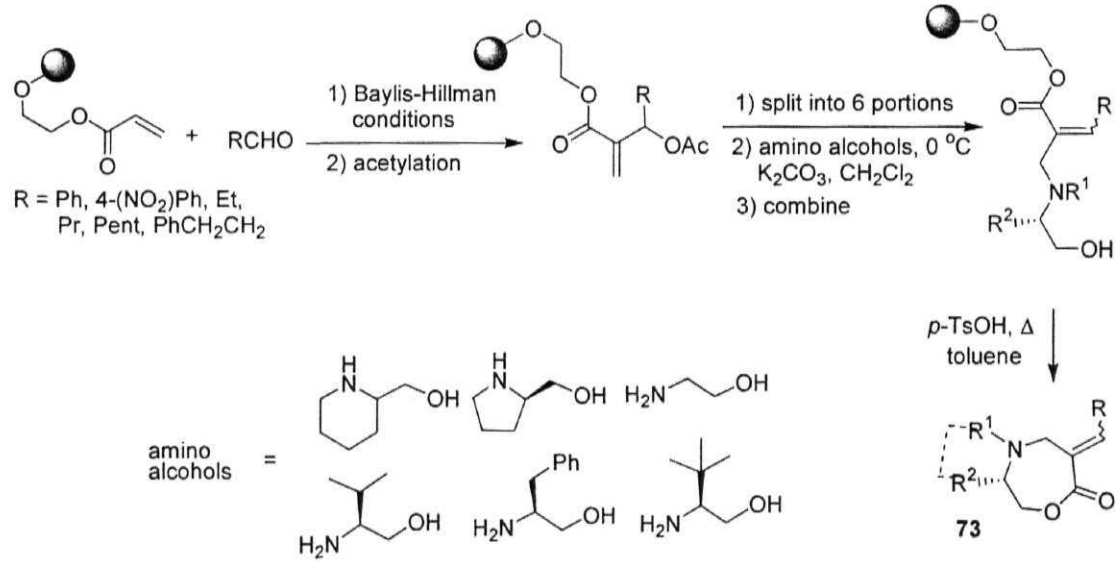



Very recently, our research group has reported a convenient one-pot synthesis of (*E*)-5-alkyl-3-arylidenepyrrolidin-2-ones (**72**), γ-lactam derivatives *via* the treatment of acetates of Baylis-Hillman adducts with nitroalkanes in the presence of a base, followed by reductive cyclization, using Fe / AcOH (Eq. 25).[168]



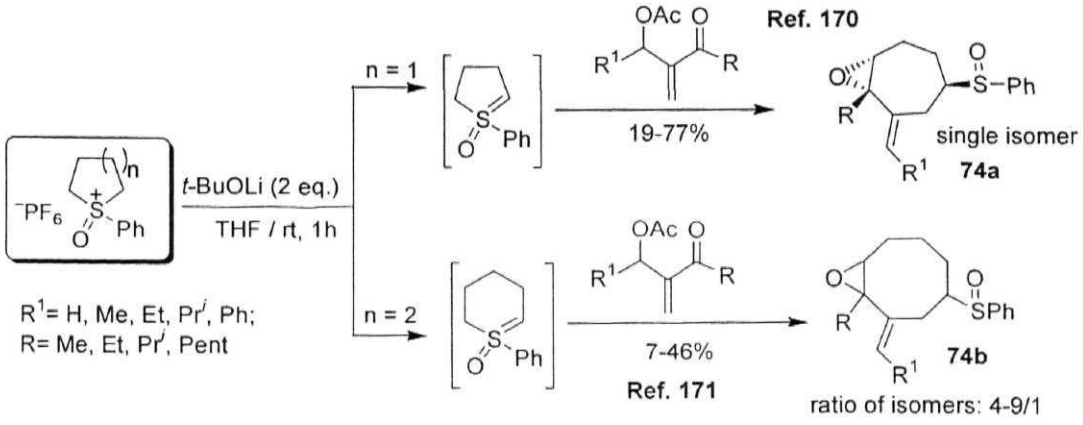

Reiser and co-workers[169,170] have reported a facile combinatorial liquid phase synthesis of [1,4]oxazepine-7-ones (**73**) (which can serve as important building blocks), employing the Baylis-Hillman adducts (Scheme 23).

**Scheme 23**



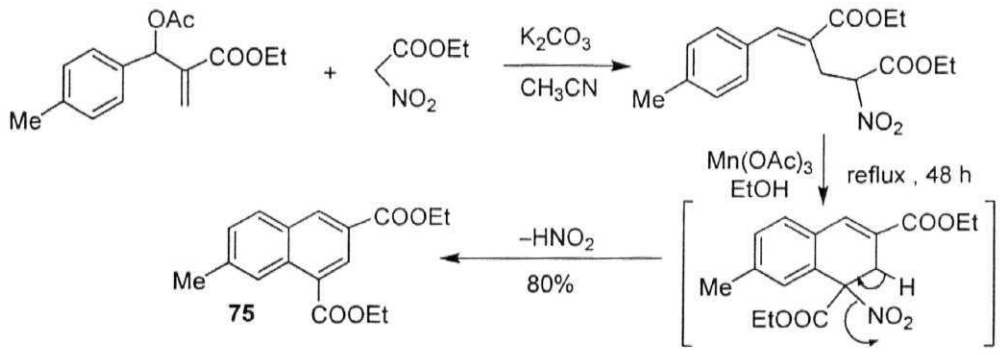

Fujimoto and co-workers[171,172] have subjected the acetates of Baylis-Hillman adducts to tandem Michael-intramolecular Corey-Chaykovsky reaction with five membered cyclic oxosulfonium ylide in the presence of base to provide cycloheptene oxide derivatives, **74a**, as a single stereoisomer. They also observed that a six membered oxosulfonium ylide under similar conditions resulted in the formation of cyclooctane oxide derivatives, **74b**, as mixture of stereoisomers in moderate yields (Scheme 24).

**Scheme 24**




Kim and co-workers[173] have reported an interesting methodology for the synthesis of 1,3-disubstituted naphthalenes (**75**) from the acetates of Baylis-Hillman adducts according to Scheme 25 (One representative example is presented).

**Scheme 25**




Our research group[174] has described a facile transformation of the allyl bromides derived from Baylis–Hillman adducts into 3-arylidene(alkylidene)chroman-4-ones, following the reaction sequence as described in Scheme 26. This methodology was successfully employed in synthesis of important natural products, bonducellin methyl ether (**76**) and antifungal agent (**77**) (Figure 8).[174]

**Scheme 26**

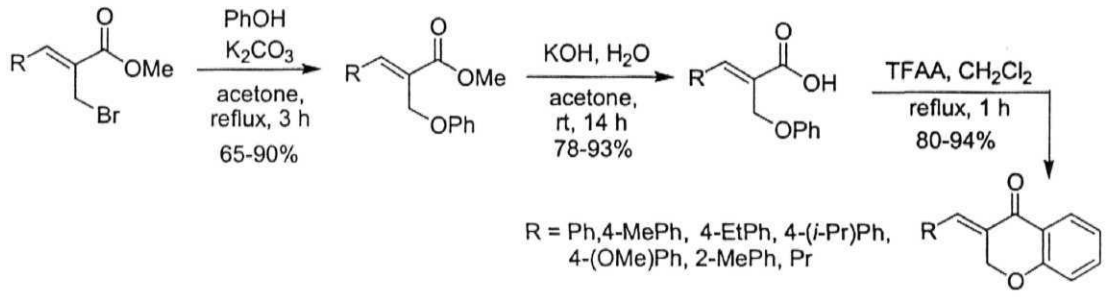
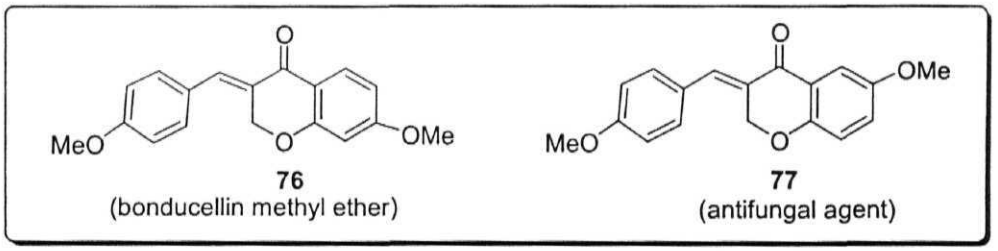
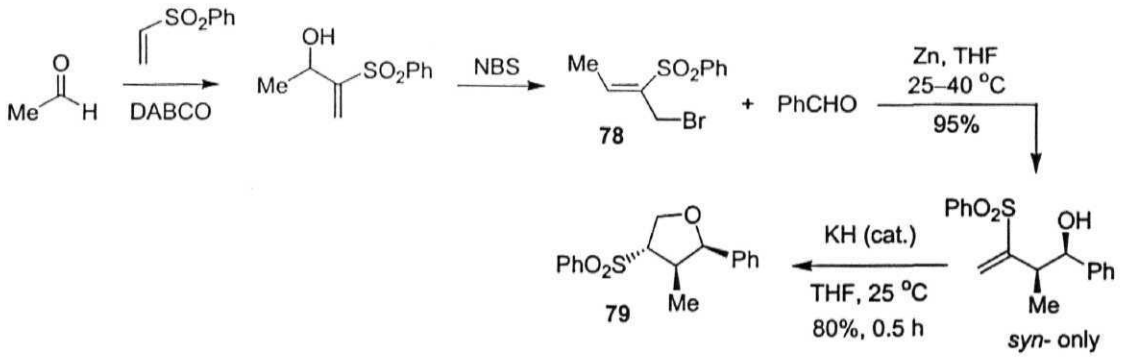



**Figure 8**

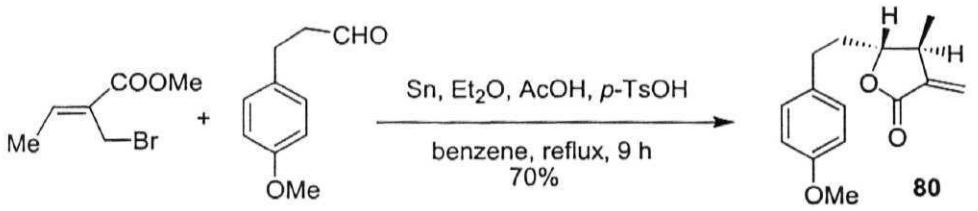



(2*Z*)-1-Bromo-2-(phenylsulphonyl)but-2-ene (**78**), obtained from the corresponding Baylis–Hillman adduct, was successfully employed in the diastereoselective allylation of aldehydes in the presence of zinc or chromium (II) to provide *syn*-homoallyl alcohols which were subsequently transformed into diastereopure 2,3,4-trisubstituted tetrahydrofurans (**79**). One representative example is presented in Scheme 27.[175]

**Scheme 27**



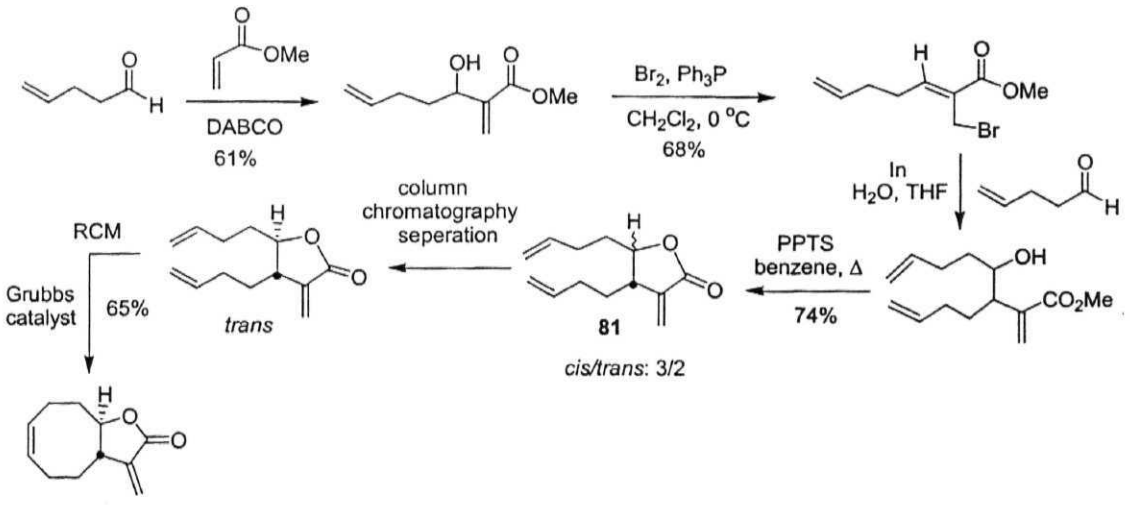
Bermejo *et. al.*,[176] have synthesized a biological active compound **80**, possessing apoptosis-inducing ability in HL-60 cells, using the methyl 2-bromomethylbut-2-enoate, derived from the corresponding Baylis-Hillman adduct, according to Eq. 26.




**Eq. 26**

Paquette and Mendez-Andino[177] have described an interesting synthesis of *cis*- or *trans*-lactones (**81**) starting from the Baylis-Hillman adducts following the reaction sequence as shown in the Scheme 28. These lactones were further transformed into larger rings using ring closing metathesis (RCM) (Scheme 28).

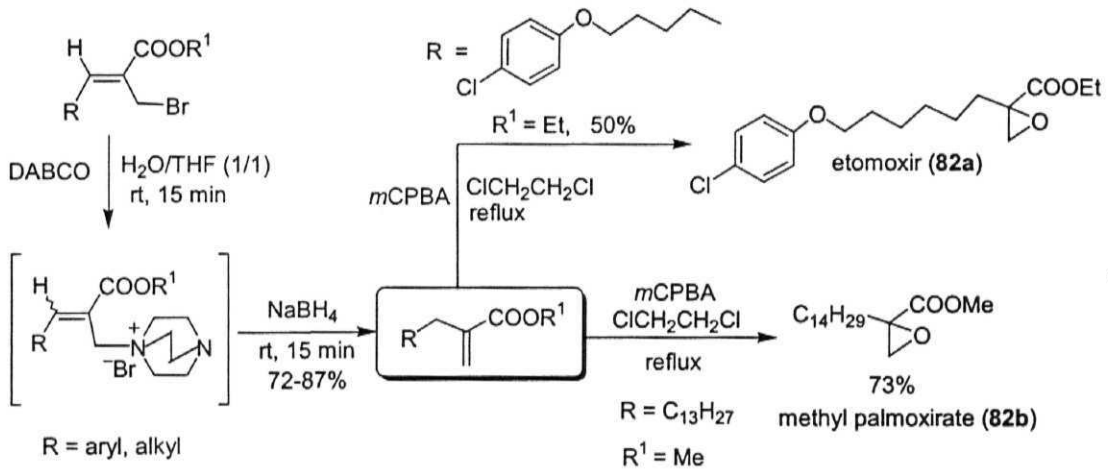
**Scheme 28**



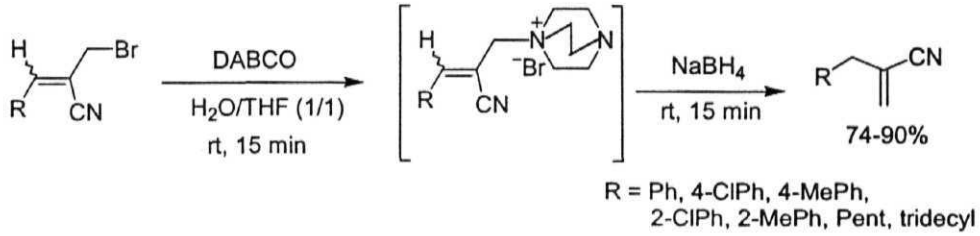

Our research group[178] has developed a convenient synthesis of 2-methylenealkanoates *via* the treatment of DABCO salt of the allyl bromide (derived from Baylis-Hillman

alcohol *i.e.*, 3-hydroxy-2-methylenealkanoates) with $NaBH_4$ in aqueous media (Scheme 30). This methodology has been successfully applied for the synthesis of two hypoglycemic agents, etomoxir (**82a**) and methyl palmoxirate (**82b**) (Scheme 29). Similar treatment of allyl bromides, derived from 3-hydroxy-2-methylenealkanenitriles, with DABCO followed by reaction with $NaBH_4$ in aqueous media provided 2-methylenealkanenitriles (Scheme 30).[178]

**Scheme 29**

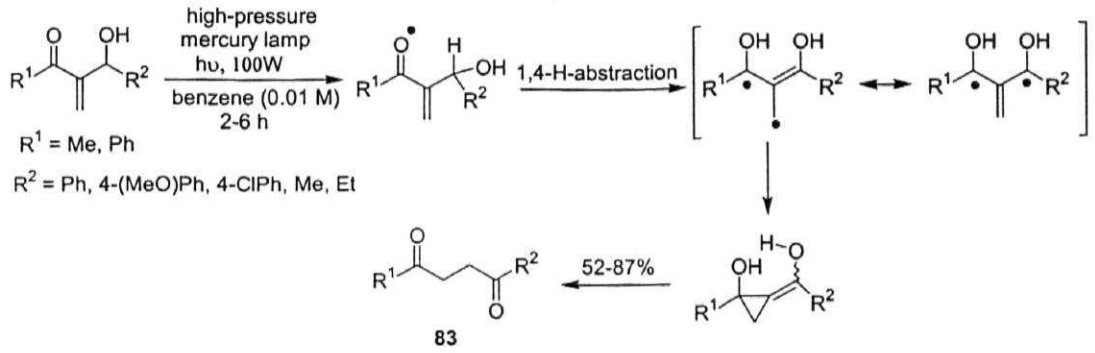



**Scheme 30**

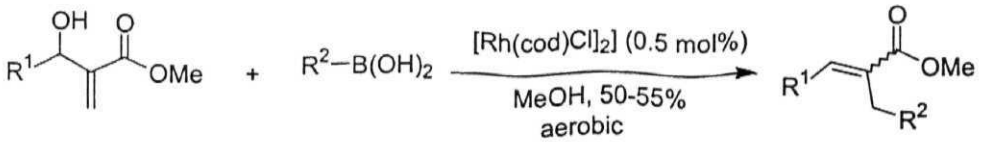



Mikami and co-workers[179] have reported an elegant transformation of the Baylis-Hillman adducts, derived from alkyl vinyl ketones, into 1,4-dicarbonyl compounds (**83**) under photochemical conditions as described in Scheme 31.

**Scheme 31**




Genet and co-workers[180] have reported an interesting synthesis of trisubstituted alkenes *via* the reaction of Baylis-Hillman adducts with arylboronic acids in the presence of rhodium catalyst $[Rh(cod)Cl]_2$ (Eq. 27).




**Eq. 27**

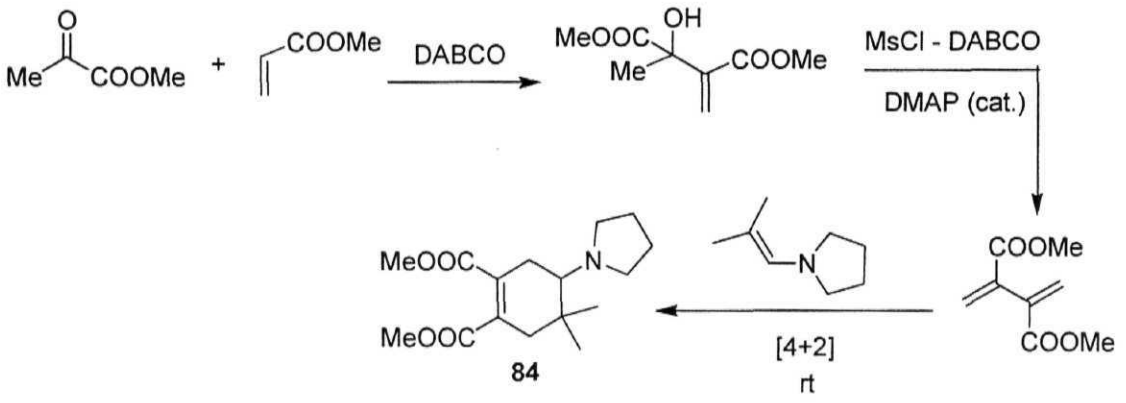
*E* / *Z* : 90-99 / 10-1

$R^1$ = Me, *i*-Bu, nonyl, c-hex,
4-$NO_2$Ph, 4-ClPh, naphth-1-yl

$R^1$ = Ph, 4-$CF_3$Ph, 4-(MeO)Ph, 3-$CF_3$Ph,
2-MePh, 4-MePh, naphth-1-yl,
naphth-2-yl

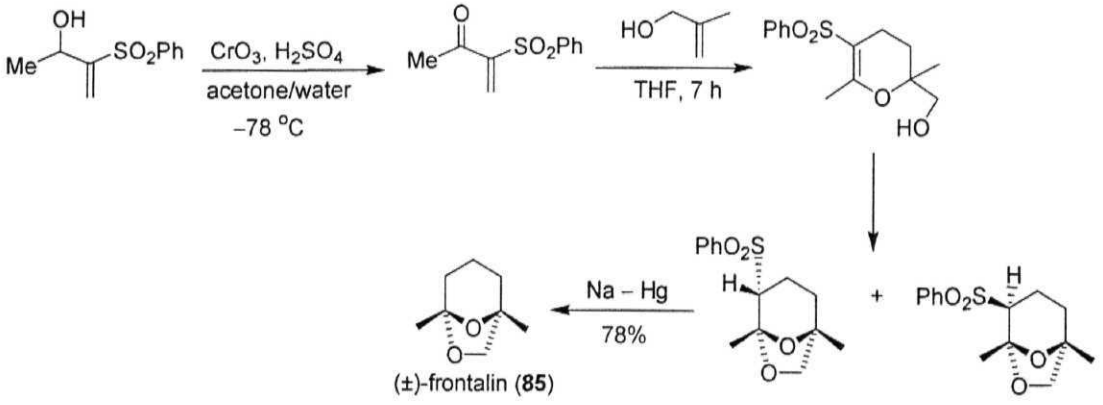
Grundke and Hoffman have reported an interesting synthesis of 2,3-dimethoxy-carbonyl-1,3-butadiene from the Baylis-Hillman adduct derived from methyl acrylate and methyl pyruvate. This diene was subjected to Diels-Alder cycloaddition with pyrrolidinoisobutene to provide adduct **84** (Scheme 32).[78]

**Scheme 32**



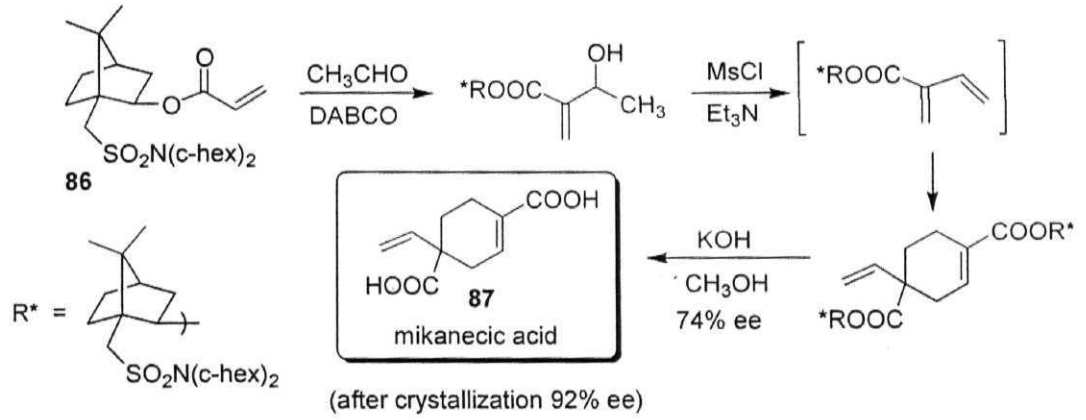

Racemic frontalin (**85**), an interesting biologically active molecule, was elegantly synthesized by Weichert and Hoffmann starting from the Baylis–Hillman adduct, phenyl 2-hydroxy-1-methylenepropylsulphonate following the reaction sequence as described in the Scheme 33.[181]

**Scheme 33**



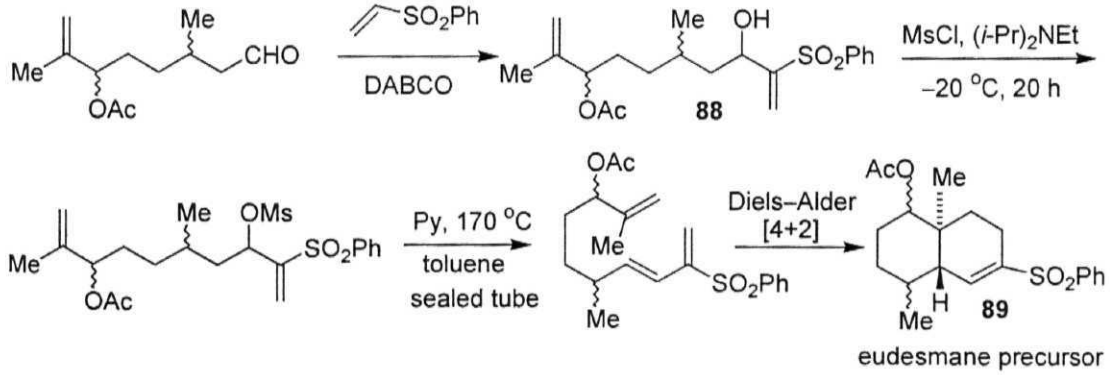

Our research group[182] has demonstrated a facile enantioselective synthesis of mikanecic acid (**87**), a terpene dicarboxylic acid, from the Baylis–Hillman adduct derived from the chiral acrylate **86** following the reaction sequence as described in Scheme 34.

**Scheme 34**



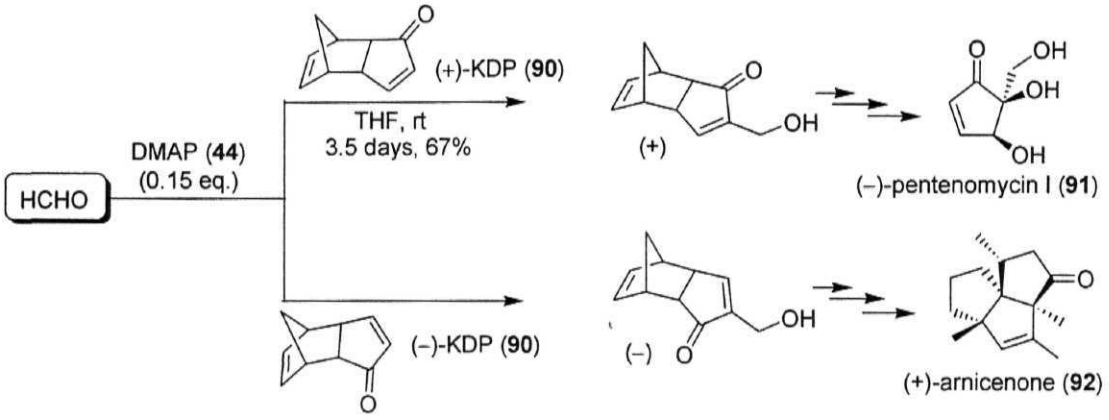

Weichert and Hoffmann[183] have reported an interesting synthesis of the eudesmane (an important natural product) precursor (**89**) using the Baylis–Hillman adduct (**88**) according to Scheme 35.

**Scheme 35**



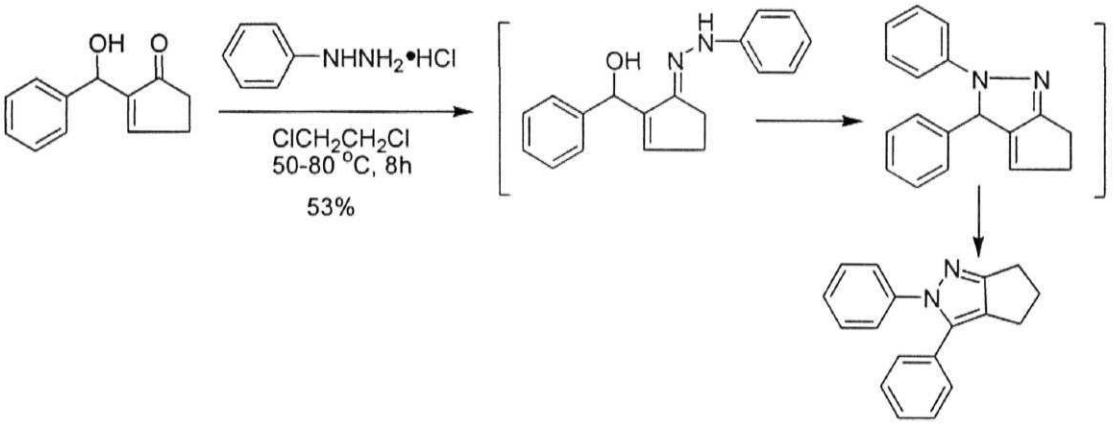

Ogasawara and co-workers[184,185] have reported an elegant synthesis of cyclopentanoid antibiotic (–)-pentenomycin I (**91**) and angular triquinane sesquiterpene (+)-arnicenone (**92**) isolated from *Arnica* plants, using the Baylis–Hillman adducts obtained by the coupling of chiral bicyclic enones (+)- & (–)-**90** with formalin under the influence of DMAP (Scheme 36).

**Scheme 36**



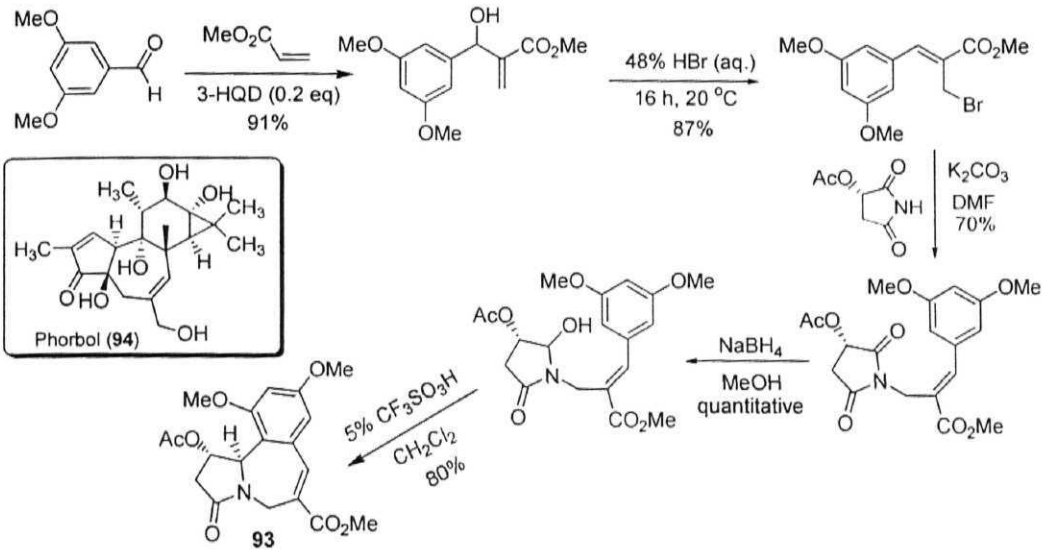

Kim and co-workers[186] have reported a facile synthesis of tetrasubsituted pyrazoles *via* the treatment of Baylis-Hillman adducts derived from cyclic / acyclic enones with phenylhydrazine hydrochloride in moderate to high yields. One representative example is presented in the Scheme 37.

**Scheme 37**



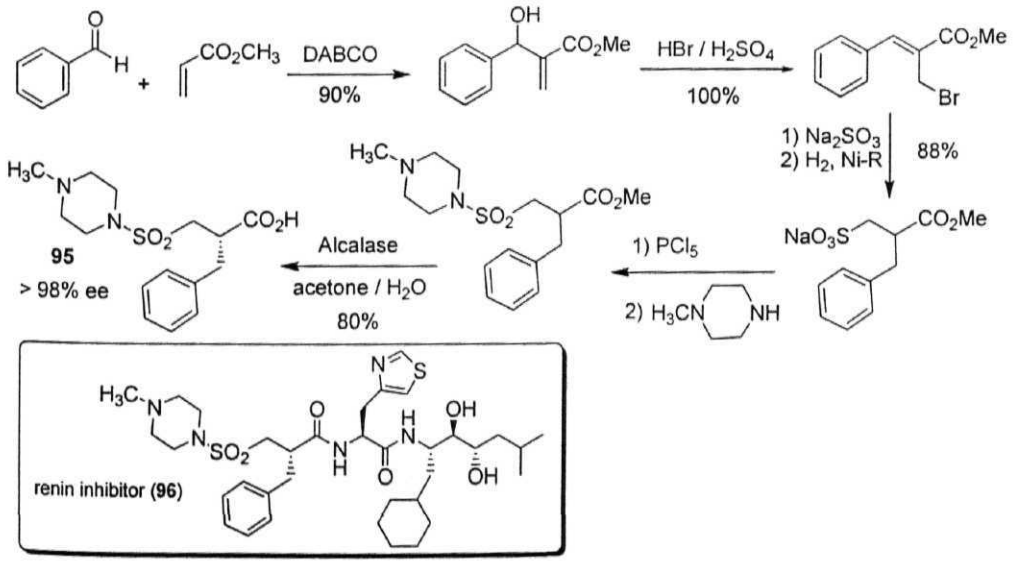

Marson and co-workers[187] have reported an interesting synthesis of aza analogues (**93**) of the phorbol (**94**) and related 5-6-7 tricylic fused frameworks starting from the Baylis-Hillman adducts. One representative example is presented in the Scheme 38.

**Scheme 38**



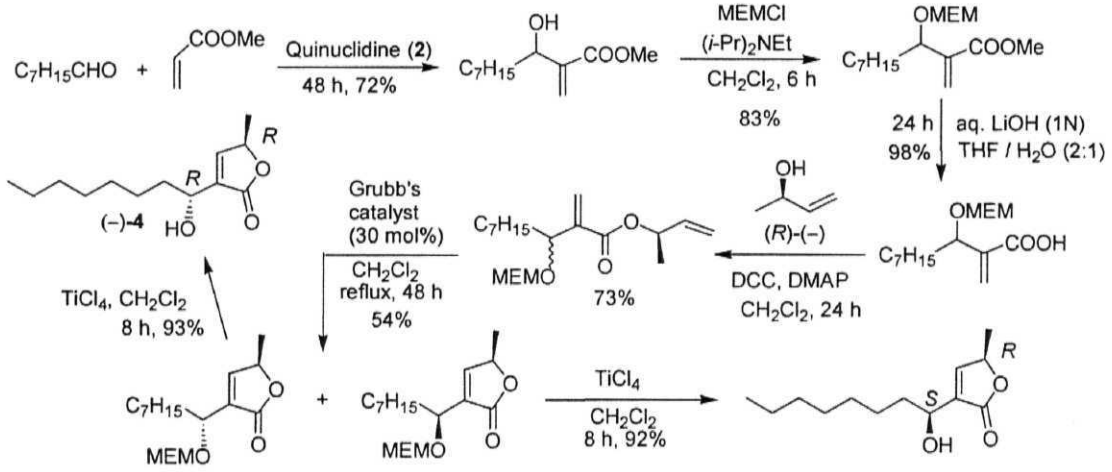

Mazdiyasni and co-workers[188] have reported a simple synthesis of optically pure β-sulfonamidopropionic acids (**95**), which is an useful synthon for the preparation of P-3 site modified renin inhibitors (**96**) following the reaction sequence as described in the Scheme 39.

**Scheme 39**



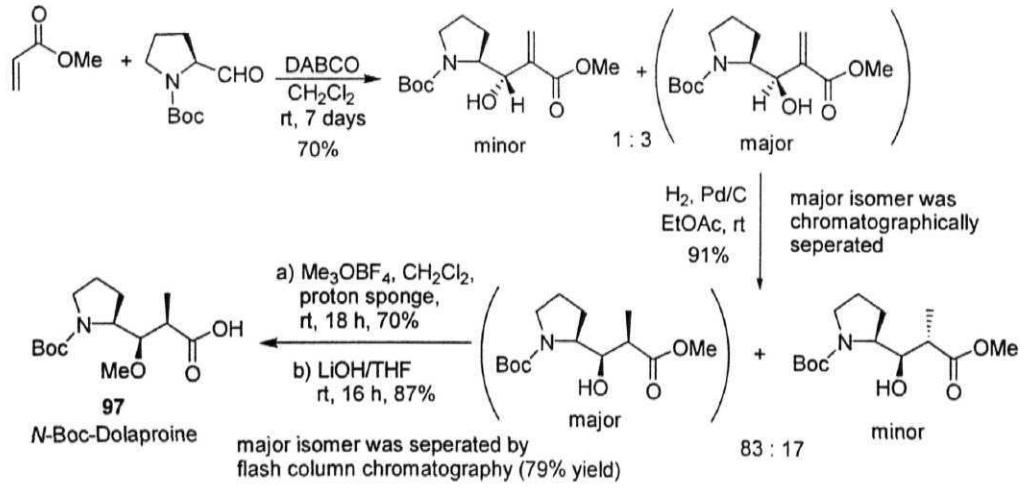
Recently, (−)-acaterin [(−)-**4**], a biologically important natural product, was synthesized by Singh and co-workers utilizing the Baylis-Hillman adduct derived from octanal and methyl acrylate following the reaction sequence presented in Scheme 40. [189]

**Scheme 40**




Very recently, Almeida and Coelho synthesized *N*-Boc-dolaproine (**97**), an amino acid residue of the antineoplastic pentapeptide, Dolastatin-10, using Baylis–Hillman reaction as the key step according to reaction sequence described in the Scheme 41.[190]

**Scheme 41**



# OBJECTİVES, RESULTS AND DISCUSSION

From the preceding chapter it is quite clear that the Baylis–Hillman reaction is one of the useful carbon-carbon bond forming reactions providing an unique class of multifunctional molecules having enormous synthetic potential.[33-37] These multifunctional molecules, usually known as Baylis-Hillman adducts, have been elegantly employed in a variety of stereoselective transformation methodologies and in the synthesis of several important heterocycles, carbocycles, natural products and biologically active molecules.[33-35,37] During the last nineteen years, our research group has been working on various aspects of this fascinating reaction with the main goal of developing this reaction into a valuable source for various stereoselective organic transformations and has in fact contributed significantly to this effect.[33-35,37] With a view to further expand the scope of this fascinating reaction in synthetic organic chemistry, we have undertaken the research project with the following objectives:

## OBJECTIVES

1) To develop a novel and facile methodology for the synthesis of functionalized [4.4.3] and [4.4.4]propellano-bislactones using acetates of the Baylis-Hillman adducts.

2) To develop a facile methodology for one-pot conversion of the acetates of Baylis-Hillman adducts into substituted fused pyrimidones in aqueous media.

3) To develop a novel methodology for tandem construction of C-N and C-C bonds leading to facile one-pot transformation of the Baylis-Hillman adducts into 2-benzazepines.
4) To understand the influence of substituents on the stereochemical outcome in the Johnson-Claisen rearrangement of Baylis-Hillman adducts.
5) To develop a novel one-pot multi-reaction strategy for facile transformation of the Baylis-Hillman adducts into substituted (1*H*)-quinolin-2-ones and substituted quinolines.

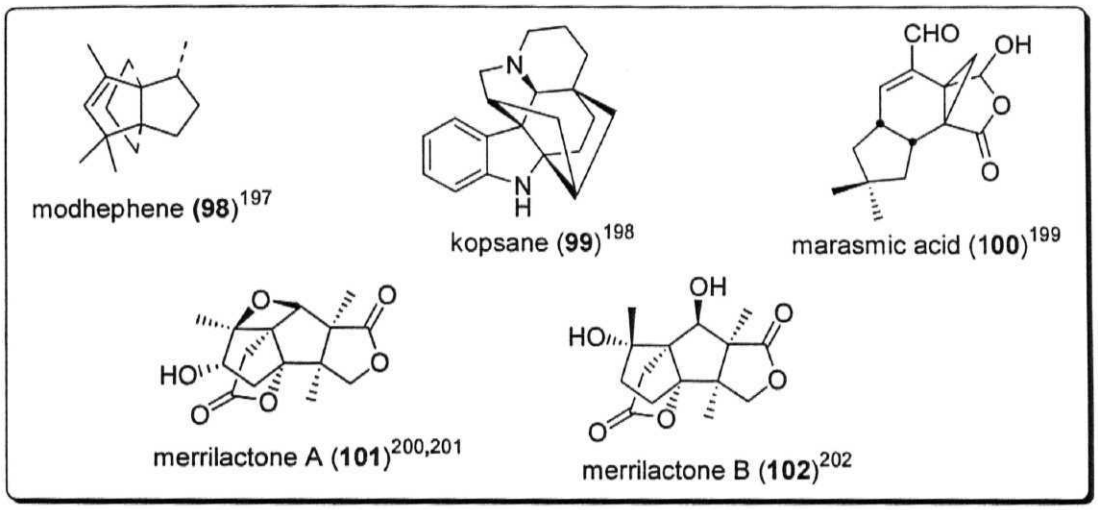
## RESULTS AND DISCUSSION

### A novel and facile synthesis of functionalized [4.4.3] and [4.4.4]propellano-bislactones using acetates of the Baylis-Hillman adducts:

Carbocyclic and heterocyclic propellanes, the tricyclic compounds conjoined in a carbon-carbon single bond, occupy a special place in synthetic organic chemistry because of their aesthetically appealing structural architecture and enormous synthetic potential due to their high strain energy.[191-196] Also, several natural products and biologically active molecules such as modhephene (**98**),[197] kopsane (**99**),[198] marasmic acid (**100**),[199] merrilactone A (**101**)[200,201] and merrilactone B (**102**)[202] (Figure 9) *etc.*, were found to possess this fascinating structural feature. Due to the biological importance of propellanes and also due to their fascinating structural organization, development of novel methodologies for the facile synthesis of these fascinating

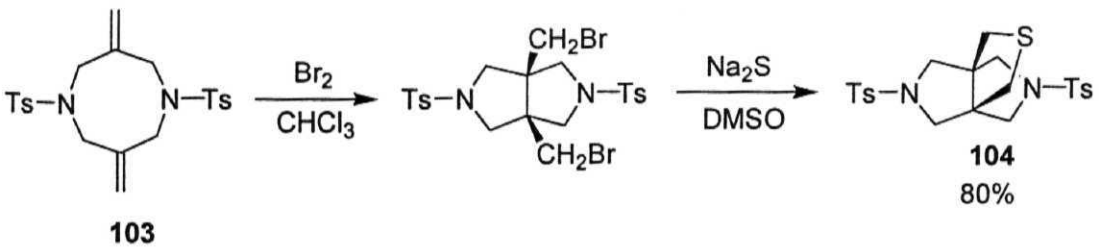
structural scaffolds is a challenging endeavor in organic synthesis. Some of the important methods for the synthesis of propellanes are presented in the following Schemes 42-45.

**Figure 9**




Dave and co-workers[203] have reported a facile synthesis of 3,7,10-heterocyclic [3.3.3]propellane (**104**) *via* an unusual transannular reaction of 3,7-bismethylene-1,5-diazacyclooctane (**103**) as described in the Scheme 42.

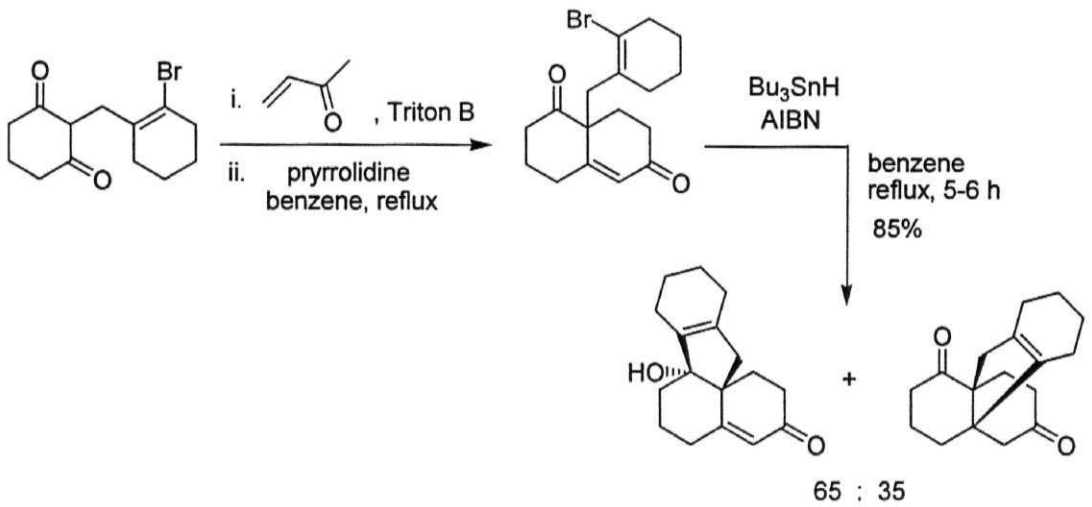
**Scheme 42**




Rajamannar and Balasubramanian have employed an intramolecular radical addition to enone olefin for the synthesis of [4.4.4]propellane ring systems. However, they also

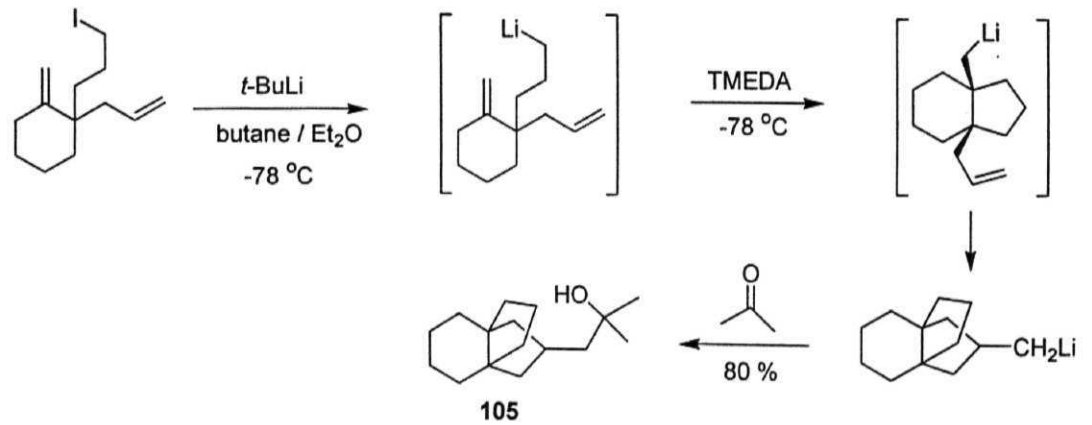
noticed the formation of angularly fused carbocycles due to competitive intramolecular radical addition to ketone functionality. One representative example is presented in Scheme 43.[204]

**Scheme 43**



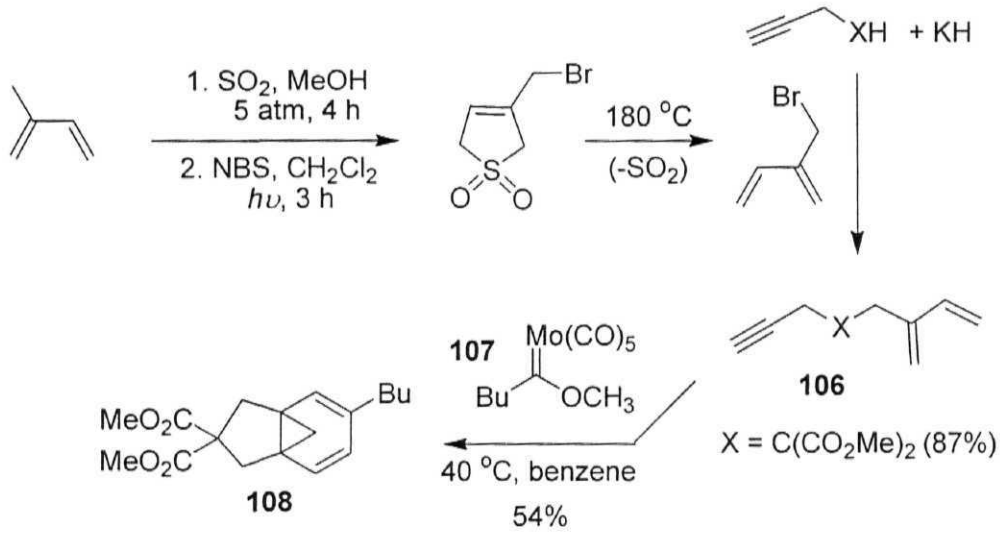

Bailey and Rossi have reported an interesting synthesis of [4.3.3]propellanes (**105**) *via* the strategy involving tandem anion cyclization. One representative example is described in the Scheme 44.[205]

**Scheme 44**



Recently, Harvey and co-workers[206] have reported that treatment of 6-methylene-7-octen-1-yne derivatives (**106**) (which was obtained starting from 2-bromomethylbut-1,3-diene) with molybdenum Fischer carbene complex (**107**) provided the [4.3.1]propellanes (**108**). A representative example is given in the Scheme 45.

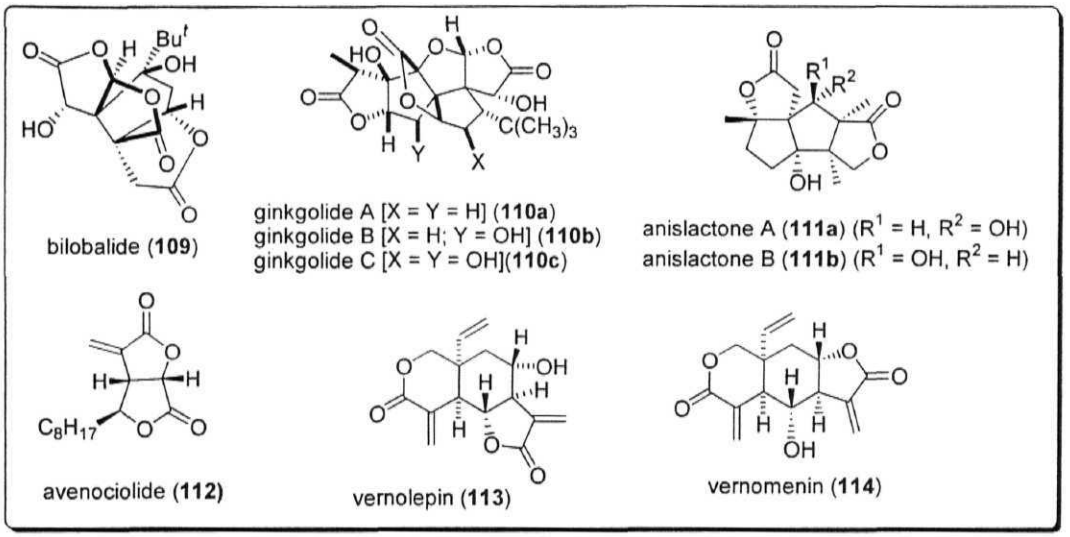
**Scheme 45**




Polycyclic polylactone framework is an important structural feature present in various biologically active natural products such as **100-102**, bilobalide (**109**),[207,208] ginkgolide A (**110a**),[208,209] ginkgolide B (**110b**),[208,209] ginkgolide C (**110c**),[208,209] anislactone A (**111a**)[202] and anislactone B (**111b**)[202] (Figure 10). Also, polylactone frame work with α-*exo* alkene functionality is present in many biologically active molecules such as avenociolide (**112**),[210] vernolepin (**113**),[211] and vernomenin (**114**)[211] (Figure 10). Because of the biological importance of the molecules containing polylactone framework, development of simple methodologies for the synthesis of polylactone framework represents an interesting synthetic endeavor in organic chemistry. Organic

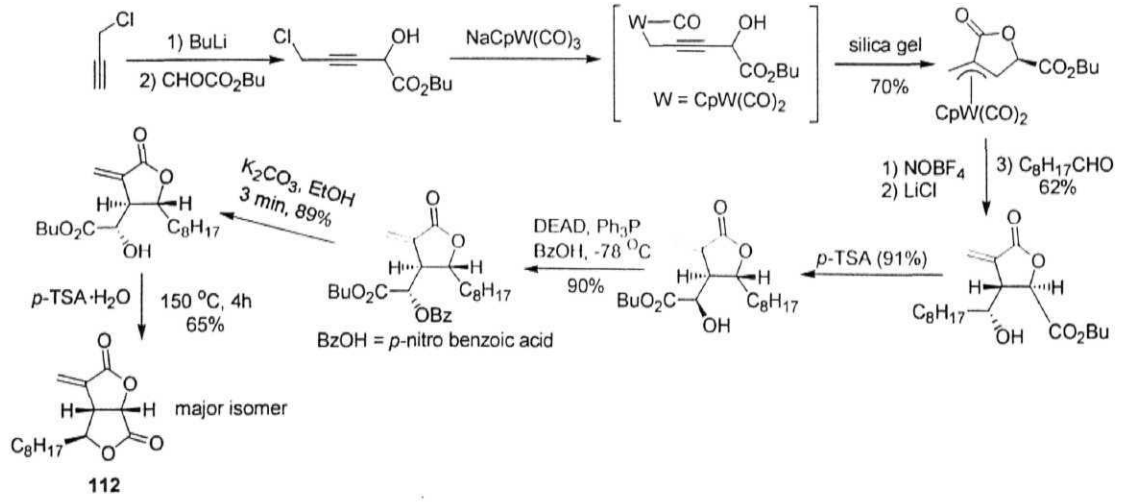
chemists, therefore, have directed their efforts in this direction and some recent relevant methodologies are presented in the Schemes 46, 47 and Eqs. 27, 28.

**Figure 10**



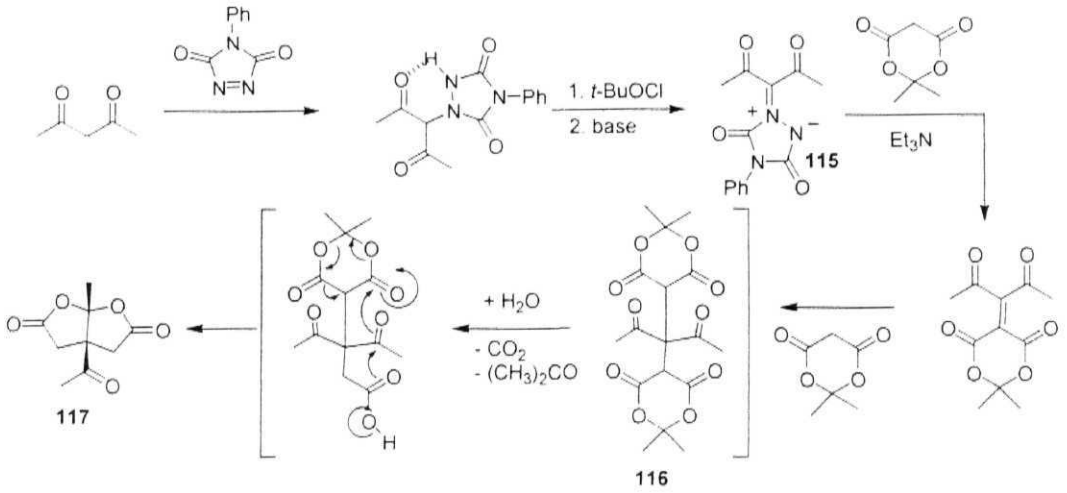

Liu and co-workers[210] have reported the total synthesis of naturally occurring bicyclic-bislactone [avenociolide, (**112**)] following the reaction sequence described in Scheme 46.

**Scheme 46**

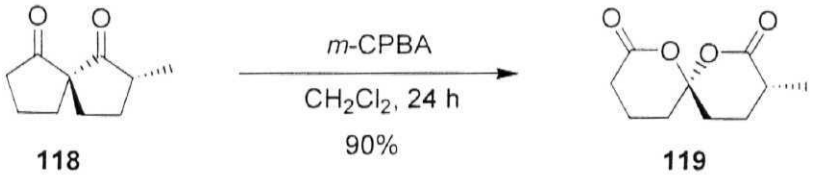


Wilson and co-workers[212] have reported an interesting synthesis of bislactones (**117**) from the bis(Meldrum's acid) coupling product (**116**), derived from urazolyl acetyl acetone (**115**) and Meldrum's acid, following a reaction sequence as described in Scheme 47.

**Scheme 47**

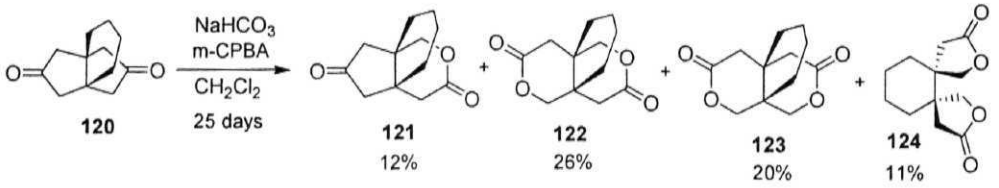



Interesting spiro bicyclic-bislactones (**119**) were prepared by Cossy *et.al. via* Baeyer-Villiger oxidation of spiro cyclic diketones (**118**). A representative example is presented in Eq. 28.[213]




**Eq. 28**

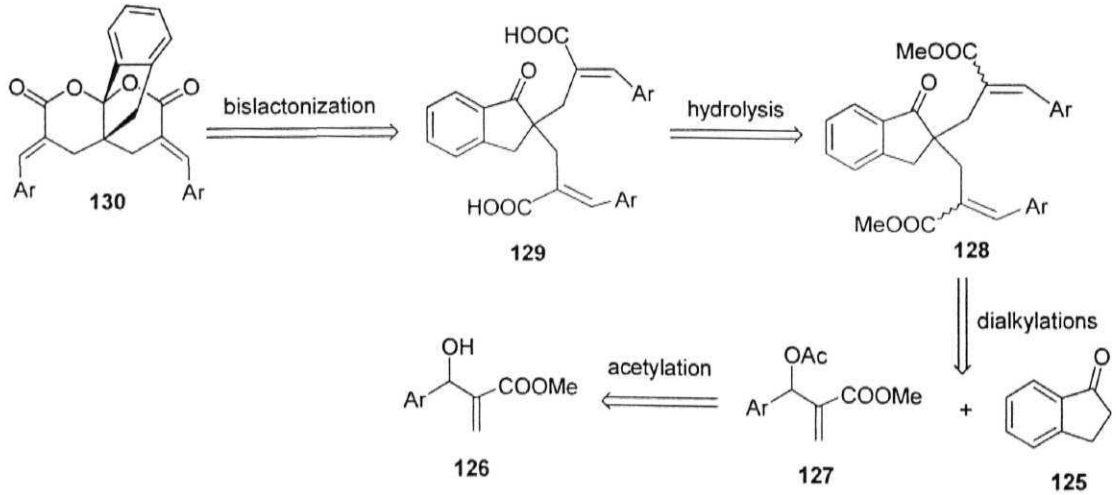
Ashkenazi and co-workers[214] reported that a mixture of propellano-lactone (**121**) and propellano-bislactones (**122**, **123**) were formed along with dispiro-bislactone **124**, when [4.3.3]propellane-8,11-dione (**120**) was subjected to Baeyer-Villiger oxidation (Eq. 29).




Eq. 29

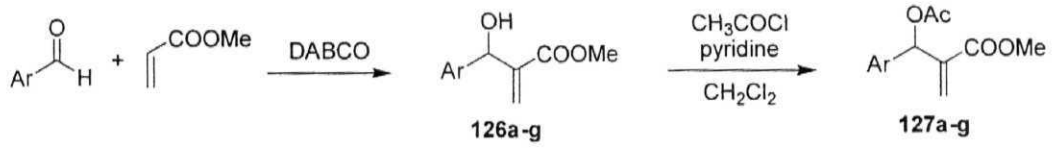
The beautiful structural architecture of propellanes and important biological properties of polylactones have attracted our attention. We envisioned that combination of these two important features *i.e.*, propellane scaffold with polylactone framework will be of importance. Therefore, we have undertaken a research program on the application of Baylis-Hillman adducts for the synthesis of functionalized propellano-bislactones. Thus, we have envisaged that the bisalkylation at 2-position of 1-indanone (**125**) with methyl 3-acetoxy-3-aryl-2-methylenepropanoates (**127**) [the acetates of Baylis-Hillman adducts (**126**)] followed by hydrolysis of resulting biscinnamic ester (**128**) would lead to the formation of 2,2-bis[(2*E*)-3-aryl-2-carboxyprop-2-en-1-yl]indan-1-ones (**129**). Subsequent lactonization under appropriate conditions might provide the desired propellano-bislactones (**130**). The possible retrosynthetic route is given in Scheme 48.

**Scheme 48**



Accordingly, we have first planned synthesis of 11,16-di[(*E*)-benzylidene]-13,14-dioxatetracyclo[7.4.4.0.$^{1,9}$0$^{2,7}$]heptadeca-2,4,6-triene-12,15-dione (**130a**) *i.e.* 2,10-dioxa[4.4.3]propellane-3,9-dione. Thus, the required acetate, methyl 3-acetoxy-2-methylene-3-phenylpropanoate (**127a**), was prepared from corresponding Baylis-Hillman adduct (**126a**) according to Scheme 49.

**Scheme 49**




**126a-g**

Ar = Ph (**126a**), 4-MePh (**126b**), 4-EtPh (**126c**), 4-(*i*-Pr)Ph (**126d**), 4-(OMe)Ph (**126e**), 4-ClPh (**126f**), 2-ClPh (**126g**)

**127a-g**

Ar = Ph (**127a**), 4-MePh (**127b**), 4-EtPh (**127c**), 4-(*i*-Pr)Ph (**127d**), 4-(OMe)Ph (**127e**), 4-ClPh (**127f**), 2-ClPh (**127g**)

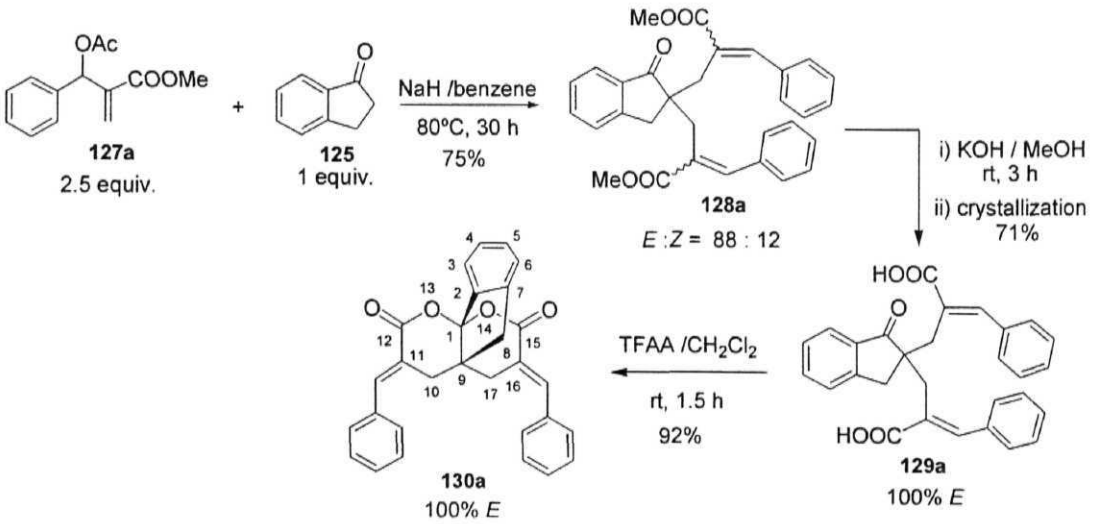
The allyl acetate, **127a**, was treated with 1-indanone (**125**) for bisalkylation at 2-position under various conditions. The best results were achieved when the bisalkylation of 1-indanone (**125**) (2 mmol) was carried out with methyl 3-acetoxy-2-methylene-3-phenylpropanoate (**127a**) (5 mmol) in the presence of NaH (10 mmol) (excess) in benzene as solvent at reflux, thus providing the desired biscinnamic ester (**128a**) in 75% yield with high (*E*)-stereoselectivity[Π] after column chromatography (silica gel, 15% EtOAc in hexanes) (Scheme 50). The structure of the biscinnamic ester was in agreement with IR, $^{1}$H NMR, $^{13}$C NMR spectral data. This compound was cont-aminated with (*Z*)-isomer (≈ 12%) and other unidentified impurities (≈ 5%).[Π]

---

[Π] In the $^{1}$H NMR spectra of trisubstituted alkenes (with ester group at α- position), the β-vinylic proton *cis* to the ester group appears downfield while the β-vinylic proton *trans* to ester group appears upfield.[215-218] $^{1}$H NMR spectra of the biscinnamic ester (**128a**) indicated the presence of ≈ 12% minor (*Z*)-isomer. The *E*/*Z* selectivity was determined by the integration ratio of isomeric β-vinylic protons [In the $^{1}$H NMR spectra of **128a**, β-vinylic proton *cis* to ester group (*E*-isomer) appeared as singlet at δ 7.59 while the same proton *trans* to ester group (*Z*-isomer) appeared as singlet at δ 6.58].

However, subsequent hydrolysis of this biscinnamic ester **(128a)** as such, with KOH / MeOH, followed by crystallization from a mixture of EtOAc and hexanes (1:2), furnished the desired biscinnamic acid (**129a**) with 100% chemical purity and exclusive (*E*)-stereochemistry[Ψ] in 71% yield (Scheme 50). The structure was established by IR, $^{1}$H NMR (Spectrum 1), $^{13}$C NMR (Spectrum 2) spectral data. Bislactonization of this biscinnamic acid (**129a**) was accomplished *via* the treatment with trifluoroacetic anhydride (TFAA) in $CH_2Cl_2$ at room temperature for 1.5 h to provide the desired 11,16-di[(*E*)-benzylidene]-13,14-dioxatetracyclo[7.4.4.0$^{1,9}$.0$^{2,7}$]heptadeca-2,4,6-triene-12,15-dione (**130a**) *i.e.*, 2,10-dioxa[4.4.3]propellane-3,9-dione (**130a**) in 92% yield as a crystalline solid (Scheme 50). Structure of the product (**130a**) was in full agreement

**Scheme 50**

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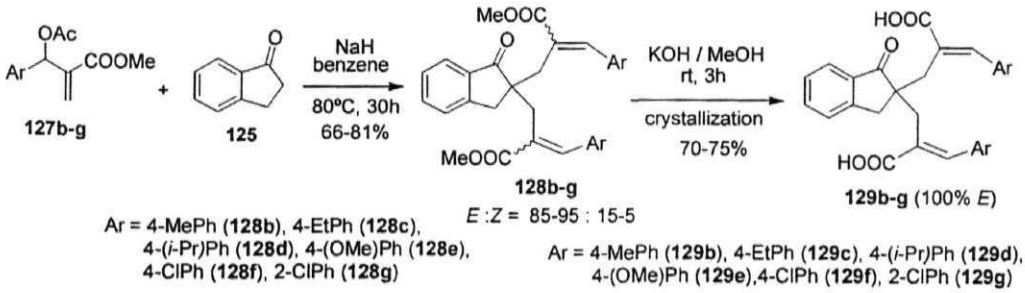
[Ψ] (E)-stereochemistry was assigned on the basis of the $^{1}$H NMR spectral analysis. $^{1}$H NMR spectrum of the biscinnamic acid (**129a**) (Spectrum 3) showed the singlet at δ 7.76 and there was no proton signal observed in the range δ 6.55-7.00 which clearly indicates 100% *E*-stereochemistry in the case of biscinnamic acid (**129a**). See foot note. '∏' in page no: 49

with the spectral data [IR, $^1$H NMR (Spectrum 3)**, $^{13}$C NMR (Spectrum 4), mass] and elemental analysis.

This result was indeed very encouraging. We have then prepared a representative class of Baylis-Hillman adducts (**126b-g**) *via* the coupling of various aldehydes with methyl acrylate in the presence of DABCO and transformed them into the corresponding allyl acetates (**127b-g**) by the treatment with acetyl chloride and pyridine in $CH_2Cl_2$ (Scheme 49). We have, then, successfully employed these allyl acetates (**127b-g**) for bisalkylation at 2-position of 1-indanone (**125**) which provided corresponding biscinnamic esters (**128b-g**) in 66-81% yield. Hydrolysis of biscinnamic esters (**128b-g**) followed by crystallization furnished the desired biscinnamic acids (**129b-g**) with exclusive (*E*)-stereochemistry in 70-75% yields (Scheme 51, Table 1). All the biscinnamic esters (**128b-g**) and biscinnamic acids (**129b-g**) were characterized by IR, $^1$H NMR (Spectrum 5, for molecule **128e**), $^{13}$C NMR (Spectrum 6, for molecule **128e**) spectral data. (*E*)-stereochemistry in the case of biscinnamic esters (**128b-g**) and bisci-

**Scheme 51**




** *It looks that both the allylic $CH_2$ protons (four protons) (at C-10 & C-17) appear as AB part of ABX system (doublet of AB quartet i. e. two dd) and the down field doublet (of this system) is merged with singlet at $\delta$ 3.02 of benzylic $CH_2$ protons (at C-8). This is confirmed by the very clear appearance of AB quartet for the allylic $CH_2$ protons (four protons) (at C-10 & C-17) when the $^1$H NMR spectrum was recorded in the presence of shift reagent Eu(fod)$_3$ (Spectrum 3).*

nnamic acids (**129b-g**) were assigned on the basis of chemical shift value (δ) of olefinic proton in $^1$H NMR spectra.†

**Table.1: Synthesis of biscinnamic esters (128a-g) and biscinnamic acids (129a-g) (127[a]→128[b]→129):**

| Allyl acetate | Ar | Product[c] | Yield[d] (%) | Product[e] | Yield[f] ( % ) | Mp (°C) |
|---|---|---|---|---|---|---|
| **127a** | Ph | **128a** | 75 | **129a** | 71 | 161 |
| **127b** | 4-MePh | **128b** | 74 | **129b** | 70 | 215 |
| **127c** | 4-EtPh | **128c** | 70 | **129c** | 75 | 163–164 |
| **127d** | 4-(*i*-Pr)Ph | **128d** | 77 | **129d** | 72 | 169–171 |
| **127e** | 4-(MeO)Ph | **128e** | 81 | **129e** | 72 | 191 |
| **127f** | 4-ClPh | **128f** | 66 | **129f** | 73 | 234–236 |
| **127g** | 2-ClPh | **128g** | 74 | **129g** | 70 | 213 |

a) All the reactions were carried out on 2 mmol scale of 1-indanone (**125**) with 5 mmol of the allyl acetate (**127a-g**) in the presence of excess NaH (10 mM) in benzene at reflux for 30 h in $N_2$ atm.

b) Hydrolysis was carried out on 1 mmol scale of biscinnamic ester (**128a-g**) with KOH / MeOH (1 g in 4 mL) at room temperature for 3 h.

c) All the biscinnamic esters (**128a-g**) were obtained as colorless viscous liquids. $^1$H NMR and $^{13}$C NMR spectral data of compounds **128a-g** indicated the presence of minor *Z*-isomer (≈ 5-15%) and unidentified impurity (≈ 5%).

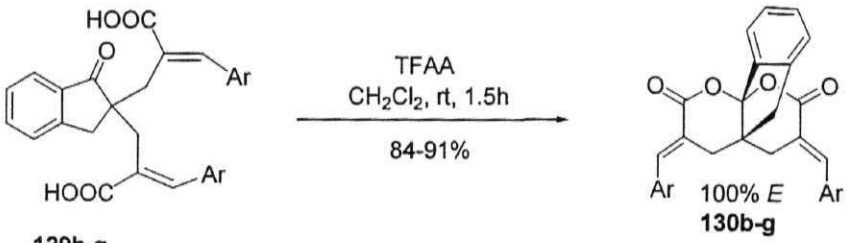
d) Yields of the biscinnamates (**128a-g**) [with impurities as mentioned in the above (c) footnote] after column chromatography (silica gel, 15% ethyl acetate in hexanes).

e) All the the biscinnamic acids (**129a-g**) were obtained as colorless solids in chemically pure form with 100% (*E*)-stereochemistry and gave satisfactory IR, $^1$H NMR, and $^{13}$C NMR spectral data.

f) Yields of the pure biscinnamic acids (**129a-g**) after crystallization from mixtures of EtOAc and hexanes.

† In the $^1$H NMR spectra of trisubstituted alkenes (with ester group at α- position), the β-vinylic proton *cis* to the ester group appears downfield while the β-vinylic proton *trans* to ester group appears upfield.[215-218] $^1$H NMR spectra of the biscinnamic esters (**128b-g**) indicated the presence of 5-15% minor (*Z*)-isomer. The *E*/*Z* selectivity was determined by the integration ratio of isomeric β-vinylic protons [the β-vinylic proton *cis* to ester group (*E*-isomer) appeared at δ 7.76-7.82 while the same proton *trans* to ester group (*Z*-isomer) appeared at δ 6.55-6.94]. Similarly, $^1$H NMR spectra of the biscinnamic acids (**129b-g**) indicated the presence of peaks in the range of δ 7.50-7.77 and there were no proton signal observed at δ 6.55-7.00 which clearly indicates 100% *E*-stereochemistry in the case of biscinnamic acids (**129b-g**).

The desired propellano-bislactones (**130b-g**) were obtained in 84-91% yields *via* bislactonization of biscinnamic acids (**129b-g**) by the treatment with trifluoroacetic anhydride (TFAA) in $CH_2Cl_2$ at room temperature for 1.5 h (Eq. 30, Table 2). All the propellano-bislactones (**130b-g**) were characterized by IR, $^1H$ NMR (Spectrum 7, for the compound **130e**), $^{13}C$ NMR (Spectrum 8, for the compound **130e**), mass spectral data, and elemental analyses. Also, to ensure the formation of propellano-bislactones, we have obtained the single crystal in the case of **130d** and established the structure by X-ray crystallography data (Fig. X1, Table 3).




**129b-g**

**130b-g**

**Eq. 30**

Ar = 4-MePh (**130b**), 4-EtPh (**130c**), 4-(*i*-Pr)Ph (**130d**), 4-(OMe)Ph (**130e**), 4-ClPh (**130f**), 2-ClPh (**130g**)

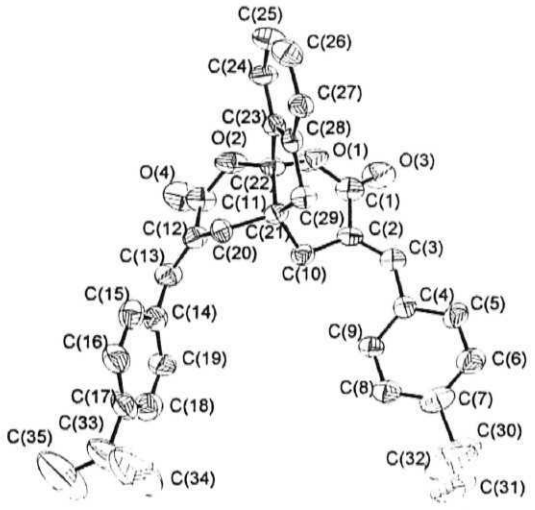



**Fig. X1**
**ORTEP diagram of the compound 130d**
(*Hydrogen atoms were omitted for clarity*)

**Table.2: Synthesis of propellano-bislactones (129→130)** [a]:

| Diacid | Ar | Product[b] | Yield[c] (%) | Mp (°C) |
|---|---|---|---|---|
| **129a** | Ph | **130a**[d] | 92 | 200–201 |
| **129b** | 4-MePh | **130b**[d] | 91 | 229–230 |
| **129c** | 4-EtPh | **130c**[d] | 84 | 164–165 |
| **129d** | 4-(*i*-Pr)Ph | **130d**[d,e] | 89 | 192–193 |
| **129e** | 4-(MeO)Ph | **130e**[d] | 85 | 179–180 |
| **129f** | 4-ClPh | **130f** | 90 | 250–251 |
| **129g** | 2-ClPh | **130g**[d] | 86 | 157–158 |

a) Bislactonization was carried out on 0.5 mmol scale of biscinnamic acid (**129a-g**) with TFAA (1 mmol) in $CH_2Cl_2$ (5 mL) at room temperature for 1.5 h in $N_2$ atm.

b) All the bislactones (**130a-g**) were obtained as colorless crystalline solids and gave the satisfactory IR, $^1H$ NMR, $^{13}C$ NMR spectral data, and elemental analyses.

c) Yields of the pure bislactones (**130a-g**) after crystallization from mixtures of EtOAc and hexanes.

d) Compounds **130a-e** and **130g** were also characterized by mass spectral data.

e) Structure of this compound (**130d**) was further confirmed by single crystal X-ray data (Fig. X1, Table 3).

**Table 3 : Crystal data and structure refinement for 130d**

| | |
|---|---|
| Identification code | : **130d** |
| Empirical formula | : $C_{35}H_{34}O_4$ |
| Formula weight | : 518.62 |
| Temperature | : 293(2) K |
| Wavelength | : 0.71073 Å |
| Crystal system, space group | : $P2_1/n$ (International Table No = 14) |
| Unit cell dimensions | : a = 16.377(2) Å; $\alpha$ = 90 deg. |
| | : b = 10.404(3) Å; $\beta$ = 94.106(11) deg. |
| | : c = 16.595(2) Å; $\gamma$ = 90 deg. |
| Volume | : 2820.4(9) $Å^3$ |
| Z, Calculated density | : 4, 1.221 $Mg/m^3$ |
| Absorption coefficient | : 0.079 $mm^{-1}$ |
| F(000) | : 1104 |
| Crystal size | : 0.7 x 0.6 x 0.6 mm |
| Theta range for data collection | : 1.69 to 24.98 deg. |
| Limiting indices | : $0 \le h \le 19$, $0 \le k \le 12$, $-19 \le l \le 19$ |
| Reflections collected / unique | : 4966 / 4966 [R(int) = 0.0000] |
| Completeness to theta = 24.98 | : 99.9 % |
| Absorption correction | : None |
| Refinement method | : Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | : 4966 / 0 / 357 |
| Goodness-of-fit on $F^2$ | : 0.986 |
| Final R indices [I>2sigma(I)] | : R1 = 0.0600, wR2 = 0.1262 |
| R indices (all data) | : R1 = 0.1353, wR2 = 0.1657 |
| Extinction coefficient | : 0.0053(6) |
| Largest diff. peak and hole | : 0.359 and -0.219 e. $Å^{-3}$ |

With a view to understand the generality of the reaction, we have also extended this strategy for the synthesis of [4.4.4]propellane **134** starting from 1-tetralone. Thus, the treatment of 1-tetralone (**131**)$^{\partial}$ (2 mmol) with methyl 3-acetoxy-2-methylene-3-phenylpropanoate (**127a**) (5 mmol) in the presence of NaH (10 mmol) (excess) in benzene at reflux provided the desired biscinnamic ester (**132**)$^{\partial}$ in 59% yield with high (*E*)-stereoselectivity$^{\nabla}$ after column chromatography (silica gel, 15% EtOAc in hexanes) (Scheme 52). This compound (**132**)$^{\partial}$ is contaminated with minor (*Z*)-isomer (≈ 18%) and other unidentified impurities (≈ 5-7%).$^{\nabla}$ Subsequent hydrolysis of this biscinnamic ester **(132)** with KOH/MeOH furnished the desired biscinnamic acid **(133)**$^{\partial}$ with major (*E*)-stereochemistry$^{\nabla}$ in 81% yield (Scheme 52). (*Z*)-Isomer (≈ 15%) and other unidentified impurities (≈ 5%) were also present along with major (*E*)-isomer.$^{\nabla}$ Structure of products **132** and **133** were in agreement with the spectral data (IR, $^{1}$H NMR, $^{13}$C NMR). Bislactonization of this biscinnamic acid (**133**) *via* treatment with triflouroacetic anhydride (TFAA) in $CH_2Cl_2$ at room temperature for 1.5 h provided the desired 12,17-di[(*E*)-benzylidene]-14,15-dioxatetracyclo[8.4.4.$0^{1,10}$.$0^{2,7}$]octadeca-2,4,6-triene-13,16-dione (**134**)$^{\partial}$ *i.e.*, 2,10-dioxa-[4.4.4]propellane-3,9-dione (**134**) in 68%

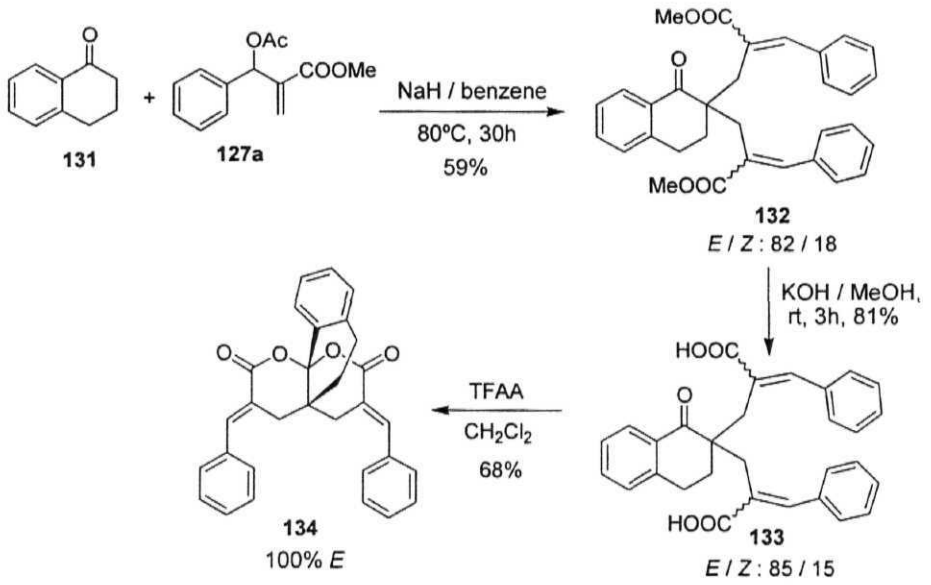
---

$\nabla$ It is well documented in the literature that $^{1}$H NMR spectra of trisubstituted alkenes (with ester group at α-position), the β-vinylic proton *cis* to the ester group appears downfield while the β-vinylic proton *trans* to ester group appears upfield.[215-218] $^{1}$H NMR spectra of the biscinnamic ester (**132**) indicated the presence of 18% minor (*Z*)-isomer. Similarly, $^{1}$H NMR spectra of biscinnamic acid (**133**) indicated the presence of 15% (*Z*)-isomer as impurity. The *E*/*Z* ratios were calculated from the integration ratio of isomeric β-vinylic protons [In the case of **132**, the β-vinylic proton *cis* to ester group (*E*-isomer) appeared at δ 7.58 while the same proton *trans* to ester group (*Z*-isomer) appeared at δ 6.44 and in the case of **133**, the β-vinylic proton *cis* to ester group (*E*-isomer) appeared at δ 7.79 while the same proton *trans* to ester group (*Z*-isomer) appeared at δ 6.59].

$\partial$ For continuity and better understanding, tetralone and tetralone-derived diester, diacid & propellane have been numbered as **131**, **132**, **133** and **134**.

yield (Scheme 52). Structure of product (**134**) was confirmed by IR, $^{1}H$ NMR (Spectrum 9), $^{13}C$ NMR (Spectrum 10), mass spectral data, and elemental analysis. Structure of **134** was further established using X-ray crystallography data (Fig. X2 and Table 4).

**Scheme 52**



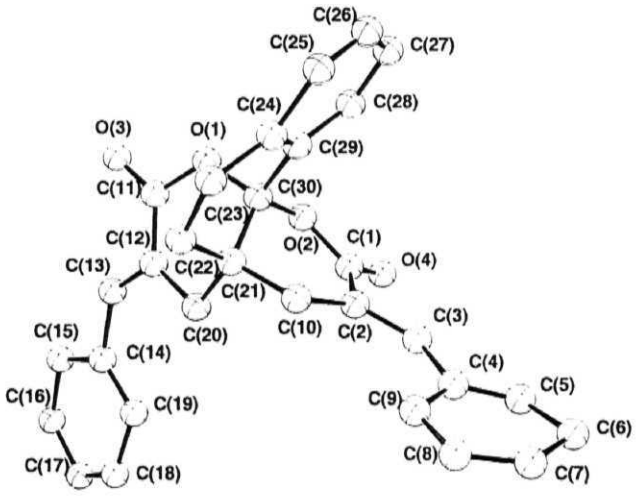



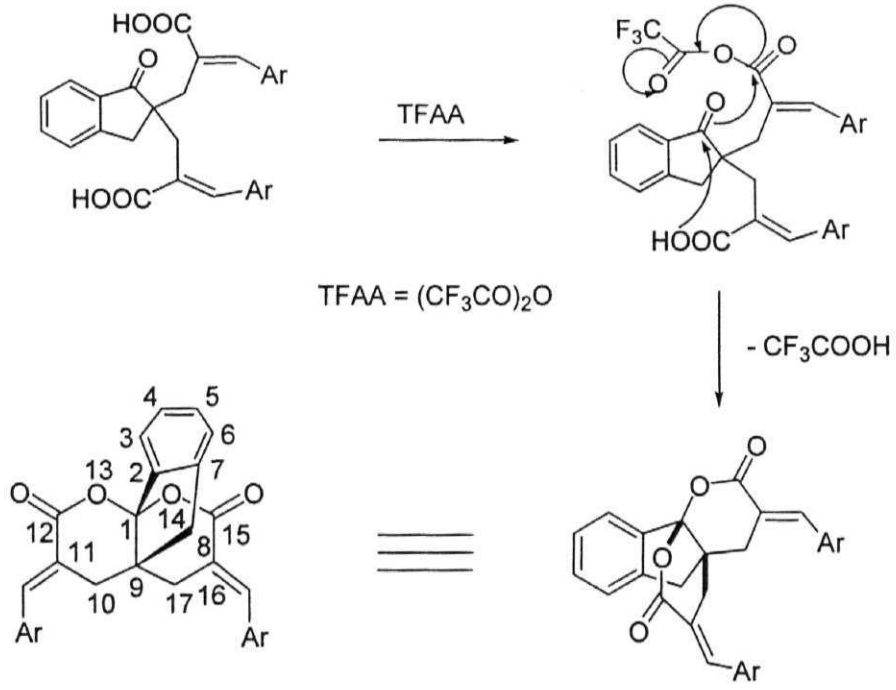

**Fig. X2**
**ORTEP diagram of the compound 134**
(*Hydrogen atoms were omitted for clarity*)

**Table 4. Crystal data and structure refinement for 134**

| | |
|---|---|
| Identification code | : **134** |
| Empirical formula | : $C_{30}H_{24}O_4$ |
| Formula weight | : 448.49 |
| Temperature | : 293(2) K |
| Wavelength | : 0.71073 Å |
| Crystal system, space group | : $P2_1/c$ (International Table No = 14) |
| Unit cell dimensions | : a = 8.9137(10) Å; $\alpha$ = 90 deg. |
| | : b = 11.806(4) Å; $\beta$ = 93.556(9) deg. |
| | : c = 21.405(3) Å; $\gamma$ = 90 deg. |
| Volume | : 2248.3(8) $Å^3$ |
| Z, Calculated density | : 4, 1.325 $Mg/m^3$ |
| Absorption coefficient | : 0.087 $mm^{-1}$ |
| F(000) | : 944 |
| Crystal size | : 0.96 x 0.36 x 0.28 mm |
| Theta range for data collection | : 1.91 to 24.97 deg. |
| Limiting indices | : $0 \le h \le 10$, $0 \le k \le 14$, $-25 \le l \le 25$ |
| Reflections collected / unique | : 3944 / 3944 [R(int) = 0.0000] |
| Completeness to theta = 24.97 | : 100.0 % |
| Absorption correction | : None |
| Refinement method | : Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | : 3944 / 0 / 308 |
| Goodness-of-fit on $F^2$ | : 1.107 |
| Final R indices [I>2sigma(I)] | : R1 = 0.0579, wR2 = 0.1528 |
| R indices (all data) | : R1 = 0.1187, wR2 = 0.2012 |
| Extinction coefficient | : 0.010(2) |
| Largest diff. peak and hole | : 0.455 and -0.247 e. $Å^{-3}$ |

A plausible mechanism for the formation of propellano-bislactone from the diacid is presented in the Scheme 53.

**Scheme 53**

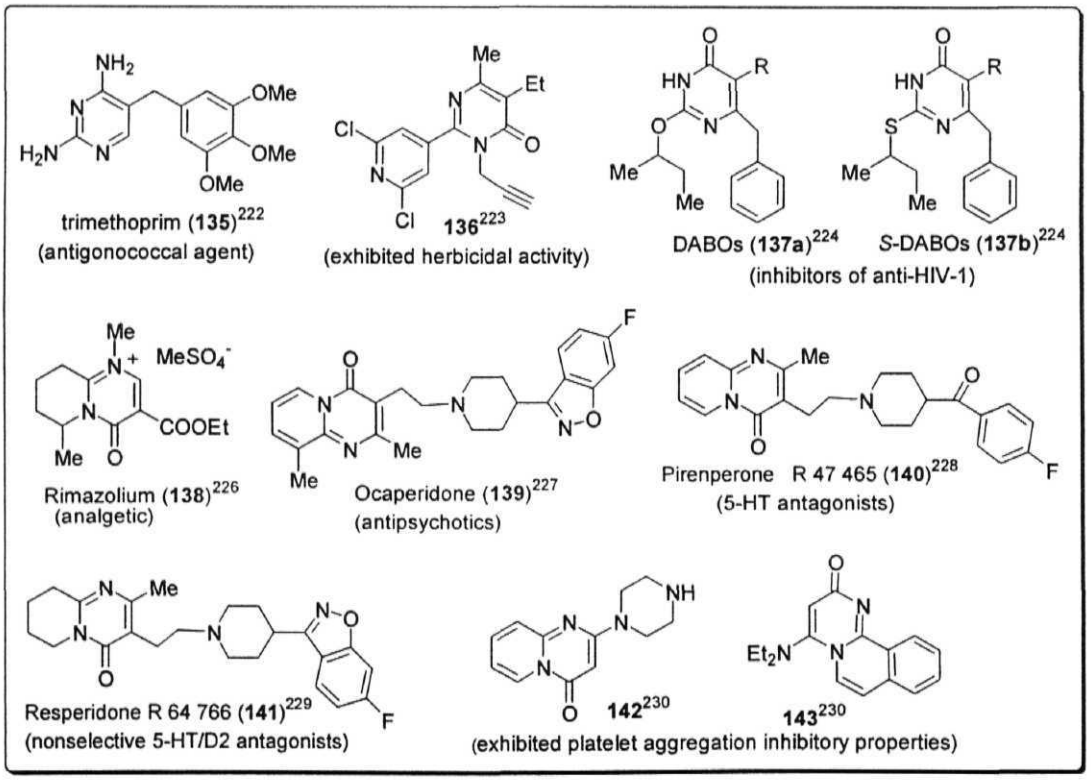



Thus, we have successfully developed a novel synthetic methodology for the convenient transformation of acetates of the Baylis-Hillman adducts into functionalized [4.4.3] and [4.4.4]propellano-bislactones (**130a-g**, **134**) in very high yield. These results clearly demonstrate the importance of Baylis-Hillman acetates in synthetic organic chemistry.

## One-pot facile conversion of the acetates of Baylis-Hillman adducts into substituted fused pyrimidones in aqueous media:

The pyrimidine framework[219-221] is an important structural moiety present in various biologically active molecules such as trimethoprim (**135**)[222] (antigonococcal agent), **136**[223] (herbicidal activity) and DABOs (**137a**)[224] & *S*-DABOs (**137b**)[224] (inhibitors of anti-HIV-1) (Figure 11) including DNA and RNA. Also, in recent years, there has been increasing interest in fused pyrimidine molecules[221,225] because of their useful and important physiological properties[225] such as analgetic (**138**),[225,226] antipsychotics (**139**),[225,227] nonselective 5-HT/D2 antagonists (**140**, **141**),[225,228,229] and platelet aggrega-

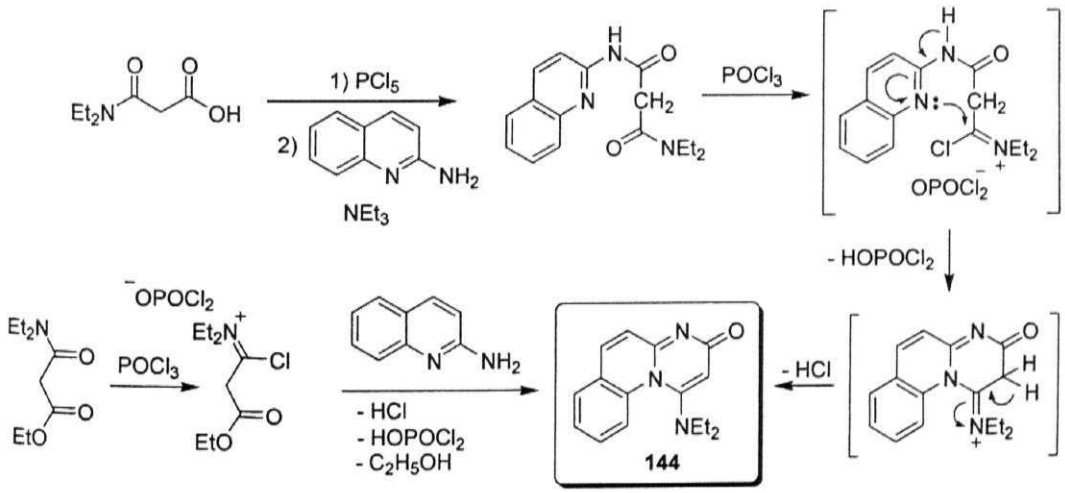
**Figure 11**



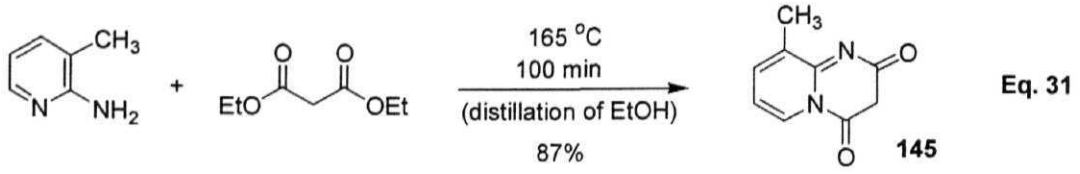
tion inhibitory properties (**142**, **143**).[230] Therefore development of simple and convenient methodologies for the synthesis of such molecules represents an attractive and interesting area of research in synthetic organic and medicinal chemistry.[221-230] Some recent and relevant literature methods for the synthesis of pyrimidine derivatives are described in the following.

Roma and co-workers[231] have recently synthesized fused pyrimidone derivatives (**144**) *via* the reaction of aminoquinoline with acid chlorides (derived by the treatment of *N,N*-dialkylmalonomic acid with $PCl_5$) or with imine chloride derived from ethyl malonamide. One representative example for each method is presented in Scheme 54.[231]

**Scheme 54**



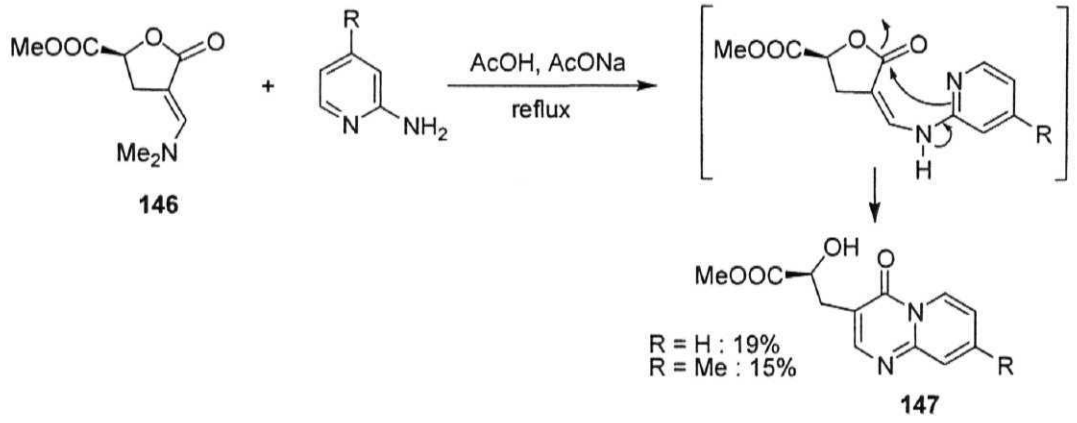

Yale has reported the synthesis of fused pyrimidone (**145**) *via* the reaction of 2-amino-3-picoline with excess diethyl malonate (Eq. 31).[232]




Eq. 31

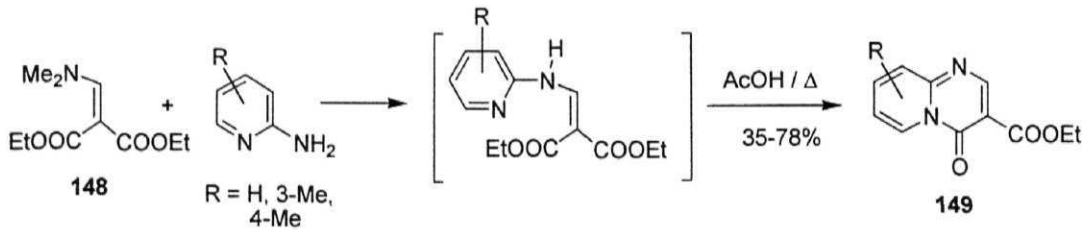
Stanovnik and co-workers[233] have reported an interesting one-step transformation of (S)-3-[(dimethylamino)methylene]-5-(methoxycarbonyl)tetrahydrofuran-2-one (**146**) into fused pyrimidones (**147**) by the treatment with various 2-aminopyridines. However, the yields of products were very low (Scheme 55).

**Scheme 55**

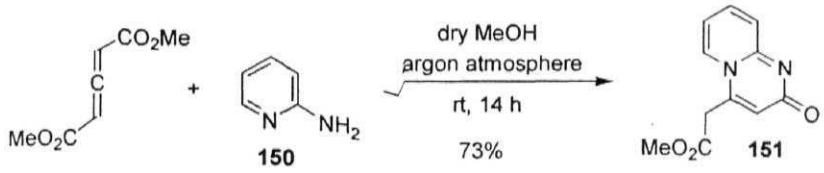



Stanovnik and co-workers[234] have also employed diethyl N,N-dimethylaminomethylenemalonate (**148**) for the synthesis of fused pyrimidones (**149**) in moderate to good yields *via* the reaction with 2-aminopyridines (Scheme 56).

**Scheme 56**



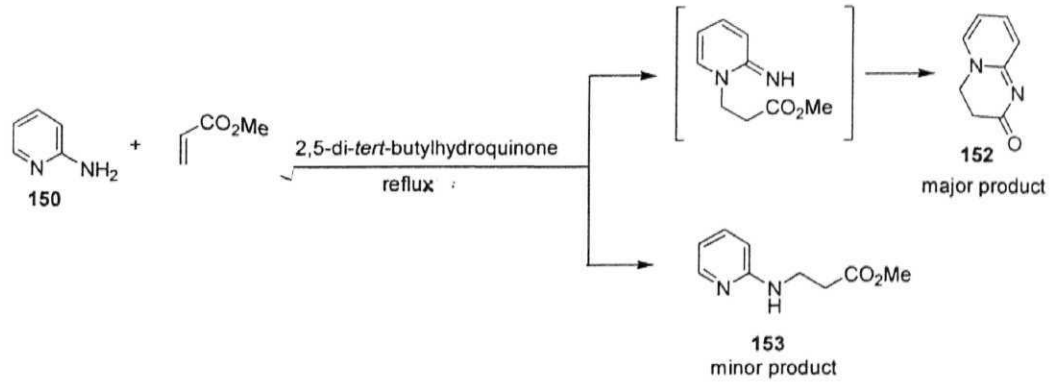
Scheinmann and co-workers have described the synthesis of fused pyrimidine derivative (**151**) *via* the reaction of dimethyl allene-1,3-dicarboxylate with 2-aminopyridine (**150**) (Eq. 32).[235]



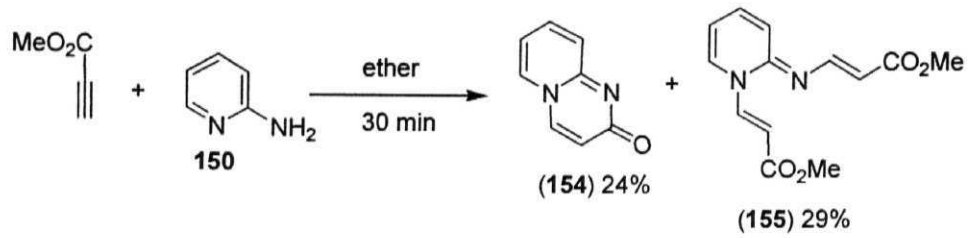

Eq. 32

It was interesting to note that as early as 1956, Lappin[236] reported that reaction of 2-aminopyridine (**150**) with alkyl acrylates provided 1,5-diazabicyclo(4.4.0)deca-5,7,9-trien-4-one (fused pyrimidone) (**152**) *via* the Michael attack of ring nitrogen onto the acrylate (Scheme 57). Also, they noticed the formation of *N*-(pyridin-2-yl)-β-alanine (**153**) *via* the Michael attack of an amino group onto the acrylate (Scheme 57).

**Scheme 57**

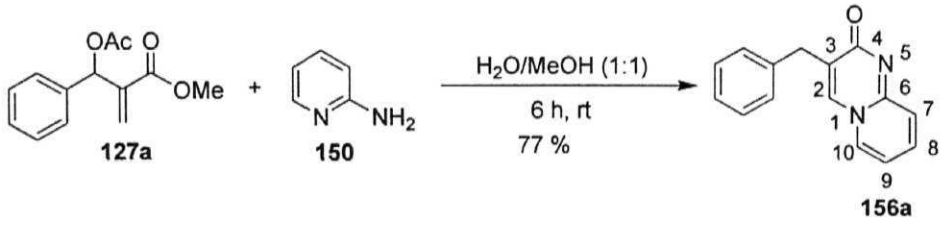



Subsequently Lappin[237] also reported that reaction of 2-aminopyridine (**150**) with methyl propiolate provided fused pyrimidone derivative (**154**) in 24% yield. In this reaction, di-Michael addition product (**155**) was also isolated (Eq. 33).




Eq. 33

It occurred to us that the reaction of 2-aminopyridine (**150**) with the acetates of Baylis-Hillman adducts (**127**) would provide desired substituted fused pyrimidine derivatives (**156**) in a one-pot operation. In this direction we first carried out the reaction of methyl 3-acetoxy-2-methylene-3-phenylpropanoate (**127a**) with 2-aminopyridine (**150**) under various conditions. The best results were obtained when the allyl acetate **127a** was treated with 2-aminopyridine (**150**) in $H_2O$ / MeOH (1:1) at room temperature for 6 hours thus providing the desired fused pyimidone (**156a**) *i.e.,* 3-benzyl-1,5-diazabicyclo(4.4.0)deca-2,5,7,9-tetraen-4-one (**156a**) in 77 % yield after the usual workup, column chromatography and followed by crystallization (Eq. 34, Table 5). Structure of product (**156a**) was in full agreement with IR, $^1$H NMR (Spectrum 11), $^{13}$C NMR (Spectrum 12), mass spectral data, and elemental analysis.[θ]



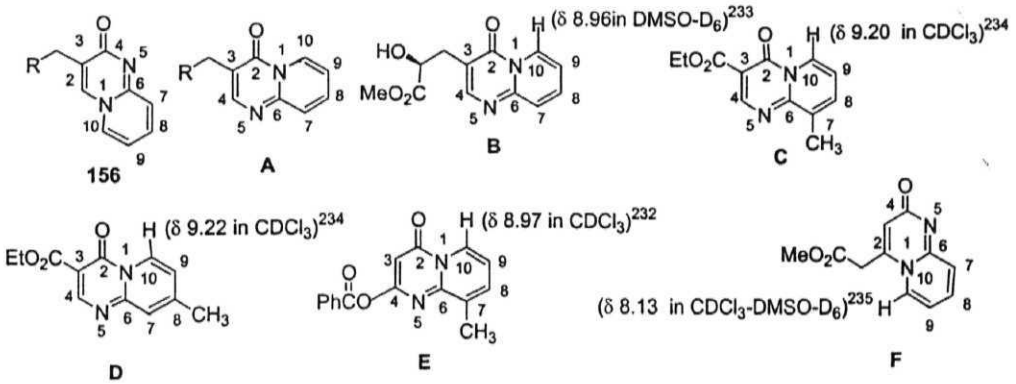

Eq. 34

This was indeed an encouraging result in the sense that the reaction was carried in aqueous media. We have then extended this strategy to a representative methyl 3-acetoxy-2-methylene-3-arylpropanoates **127b-h**. Thus the treatment of these allyl

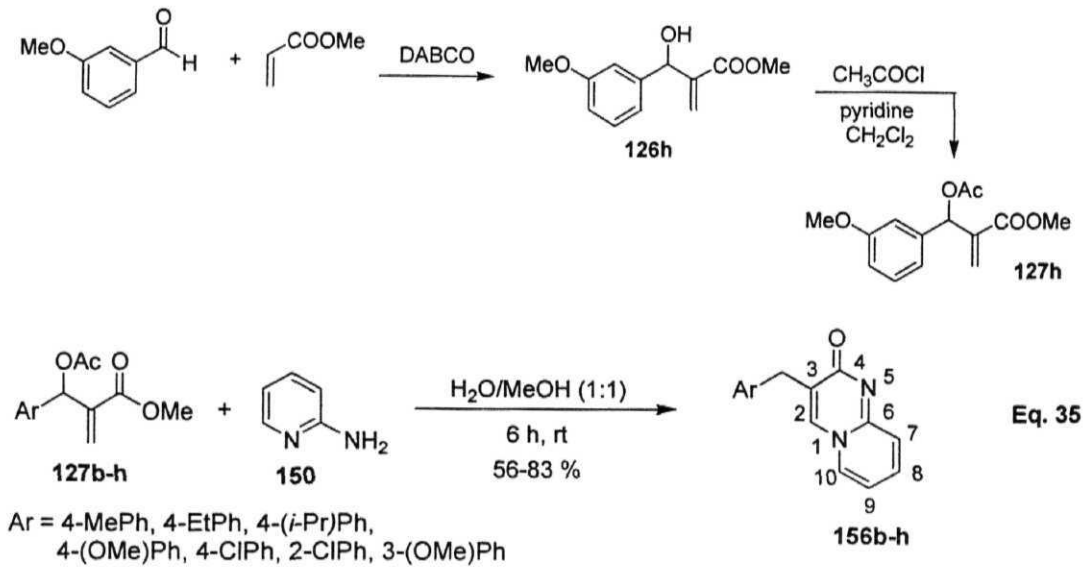
acetates (**127b-h**) with 2-aminopyridine (**150**) in the aqueous media provided the desired substituted fused pyrimidones (**156b-h**) in 56-83% yield (Eq. 35 and Table 5). Structures of the products (**156b-h**)[θ] were characterized by IR, $^1$H NMR, $^{13}$C NMR (Spectrum 13 for molecule **156b**) spectral data and elemental analyses. The required allyl acetate **127h** was prepared from corresponding Baylis-Hillman adduct **126h**, derived from 3-methoxybenzaldehyde and methyl acrylate, according to Scheme 58.

---

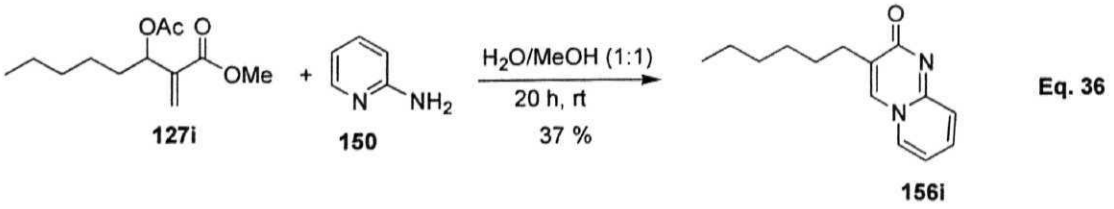
θ Actually we considered the possibility of the formation of two products *i.e.* **156** and **A**. Molecules with similar skeletons to **A** are known in literature (for example **B**, **C**, **D**, **E**).[232-234] It is observed in the $^1$H NMR spectra (in $CDCl_3$ or DMSO-$D_6$) that the H-10 proton of compounds **B**, **C**, **D**, **E** appears at ≈ δ 8.96-9.22 (see below). In the $^1$H NMR spectra (28.5% $CD_3OD$ in $CDCl_3$) of our molecules, **156a-i**, the H-10 proton appears as a doublet at ≈ δ 7.73-7.91 and no peak was observed at ≈ δ 8.00-9.30. [Also in the $^1$H NMR spectra (in $CDCl_3$) of the crude products (**156a-h**) no peak was observed at ≈ δ 8.00-9.30. However, in the case of **156i**, the $^1$H NMR spectrum (in $CDCl_3$) of the crude product showed some peaks at δ 8.00-8.30. In fact, we have also isolated as unidentified more polar compound in ≈ 20% yield and in its $^1$H NMR spectrum (in $CDCl_3$) no peak was observed at ≈ δ 8.50-9.30]. To confirm the structures, we have also recorded the $^1$H NMR spectrum of **156a** (R = Phenyl) in DMSO-$D_6$ and it was noticed that the H-10 proton appeared as doublet at δ 8.17 and no peak was observed at ≈ δ 8.30-9.30. Therefore we have assigned the structure **156** for all these fused pyrimidones. It is also worth mentioning here that the H-10 proton in the compound **F** (in $CDCl_3$-DMSO-$D_6$) appears at δ 8.13 (ref. No. 235). Our assignment is in close agreement with that of **F**.



**Scheme 58**




With a view to understand the generality of the methodology, we have also subjected methyl 3-acetoxy-2-methylene-3-octanoate (**127i**) to the reaction with 2-aminopyridine (**150**). The desired product, 3-hexyl-1,5-diazabicyclo(4.4.0)deca-2,5,7,9-tetraen-4-one (**156i**) was obtained in 37% yield (Eq. 36, Table 5) after silica gel column chromatography. Structure of the product (**156i**) was in full agreement with the spectral data [IR, $^{1}$H NMR, $^{13}$C NMR (Spectrum 14)] and elemental analysis. However, in this case, the reaction was not clean. We have noticed that ≈ 25% of starting material was intact as evidenced by $^{1}$H NMR spectral analysis of the crude product. We have also isolated ≈ 20% unidentified more polar product.



The required starting material (**127i**) was obtained *via* the acetylation of Baylis-Hillman alcohol (**126i**) derived from hexanal and methyl acrylate (Scheme 59). A plausible mechanism for the formation of 3-substituted-1,5-diazabicyclo(4.4.0)deca-2,5,7,9-tetraen-4-ones (**156**) is shown in Scheme 60.

**Table 5: Synthesis of substituted fused pyrimidones (156a-i)** [a]

| Acetates | R | Time (h) | Product[b,c] | Yield[d] (%) | m.p (°C) |
|---|---|---|---|---|---|
| **127a** | Phenyl | 6 | **156a**[e] | 77 | 218-220 (dec.) |
| **127b** | *p*-Methylphenyl | 6 | **156b**[e] | 74 | 230-233 (dec.) |
| **127c** | *p*-Ethylphenyl | 6 | **156c** | 83 | 210-212 |
| **127d** | *p*-(*iso*-Propyl)phenyl | 6 | **156d** | 75 | 214-216 (dec.) |
| **127e** | *p*-Methoxyphenyl | 6 | **156e** | 56 | 219-222 (dec.) |
| **127f** | *p*-Chlorophenyl | 6 | **156f** | 74 | 212-214 (dec.) |
| **127g** | *o*-Chlorophenyl | 6 | **156g** | 79 | 186-188 (dec.) |
| **127h** | *m*-Methoxyphenyl | 6 | **156h** | 58 | 207-208 |
| **127i** | *n*-Pentyl | 20 | **156i**[e,f] | 37 | 100 |

a) All the reactions were carried out on 1 mmol scale of the acetates of Baylis-Hillman adducts **127a-i** with 1 mmol of 2-aminopyridine (**150**) in $H_2O$ / MeOH (1:1, 10mL) at room temperature.

b) All the fused pyrimidones **156a-i** were obtained as colorless solids and gave satisfactory IR, $^1H$, $^{13}C$ NMR spectral data and elemental analyses.

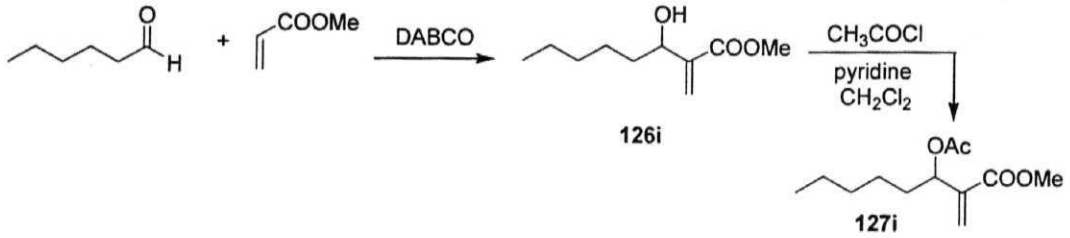
c) $^1H$ NMR spectra of the crude products indicated the presence of ≈ 2-5% starting materials in the case of **156a-h**.

d) Yields of the pure fused pyrimidones (**156a-i**) obtained after column chromatography (silica gel, 15 % MeOH in EtOAc) followed by crystallization (EtOAc).

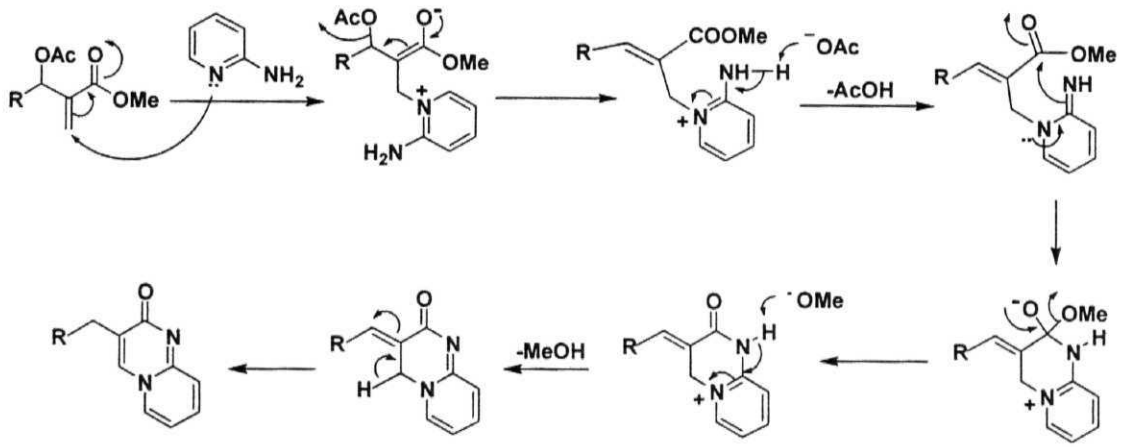
e) These compounds were also characterized by mass spectral data.

f) The $^1H$ NMR spectrum of the crude product indicated the presence of ≈ 25% of starting material. We have also isolated an unidentified more polar compound in ≈ 20% yield.

**Scheme 59**




**Scheme 60**

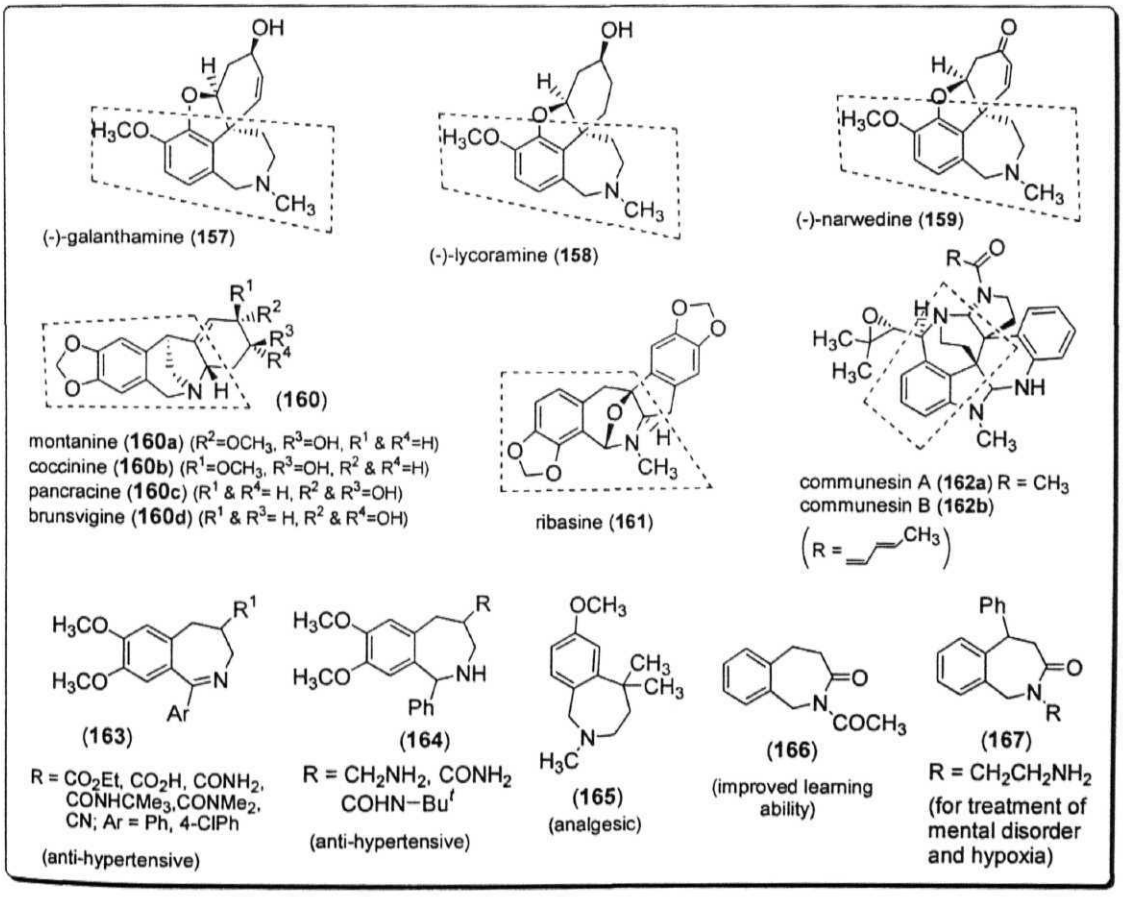



Thus, this methodology describes a simple and facile transformation of Baylis-Hillman acetates, particularly, methyl 3-acetoxy-2-methylene-3-arylpropanoates (**127a-h**), into a useful and important class of fused pyrimidones (**156a-h**) in an environment-friendly aqueous media. Also these results clearly demonstrate the efficacy of Baylis-Hillman adducts in synthesis of heterocycles.

## A novel, tandem construction of C-N and C-C bonds: facile and one-pot transformation of the Baylis-Hillman adducts into 2-benzazepines

2-Benzazepine moiety is present in many pharmaceutically active naturally occurring molecules such as galanthamine (**157**)[238] (one of the most effective current drug for Alzheimer's disease), lycoramine (**158**),[238] narwedine (**159**),[238] montanine (**160a**),[239,240] coccinine (**160b**),[239,240] pancracine (**160c**),[239,240] brunsvigine (**160d**),[239,240] ribasine (**161**),[241] communesin A (**162a**),[242] communesin B (**162b**)[242] *etc.*, (Figure 12) and in fact, several synthetic 2-benzazepines[243-248] (**163-167**, Figure 12) have also been found

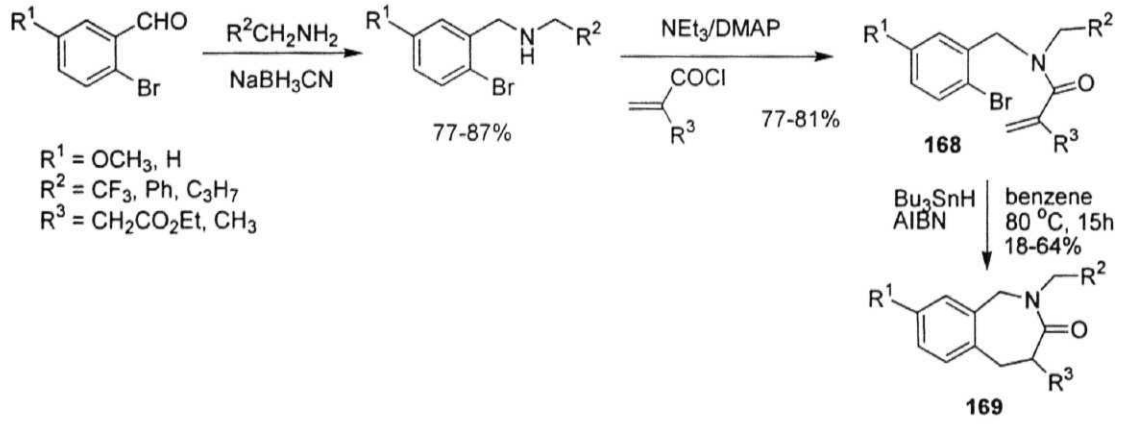
**Figure 12**



to exhibit hypotensive, analgesic, antiarrhythmic activity and also found useful for treatment of mental disorder and hypoxia. Therefore, development of simple and convenient procedures for synthesis of 2-benzazepine derivatives has been and continues to be a challenging endeavor in synthetic organic chemistry.[249-262] Several synthetic strategies have been reported for synthesis of 2-benzazepine systems and some of the recent and important methods for the construction of 2-benzazepines are discussed in the following.

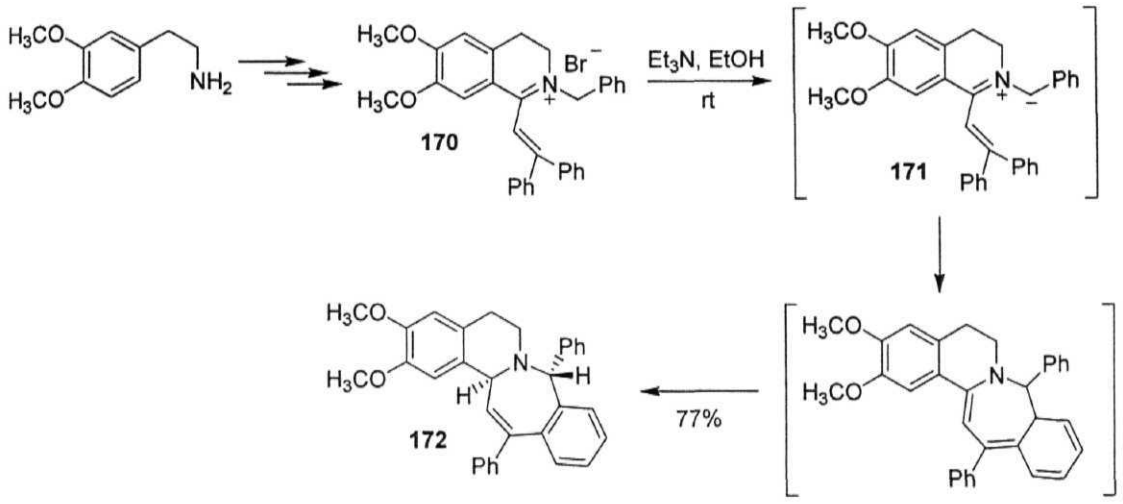
Recently, Kamimura and co-workers[249] have reported an interesting synthesis of 2-benzazepines (**169**) involving a 7-endo radical cyclization of N-(*o*-bromobenzyl)acrylamides (**168**) as the key step (Scheme 61).

**Scheme 61**



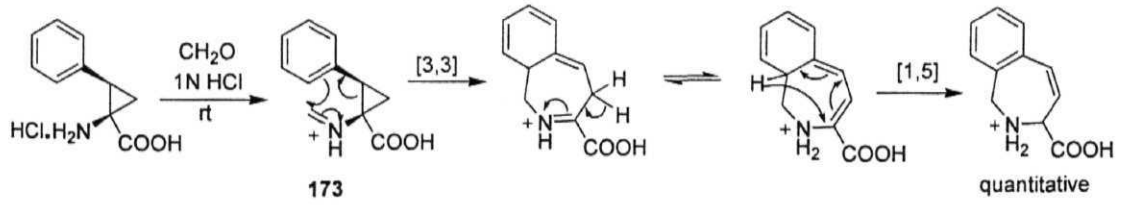

Nyerges *et al.* have developed an interesting synthesis of fused 2-benzazepine (**172**) from isoquinolinium salt (**170**) according to Scheme 62. The key step involved in this reaction is 1,7-electrocyclization of azomethine ylide (**171**). One representative example is presented in Scheme 62.[250]

**Scheme 62**

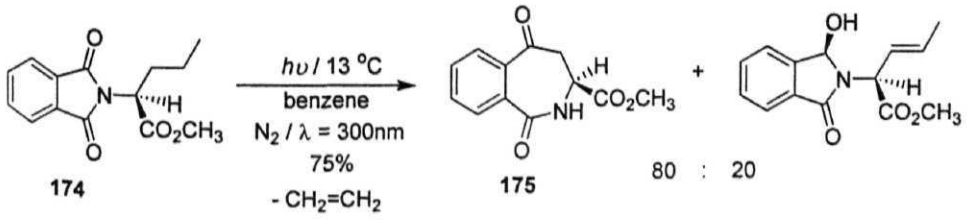



Tourwe and co-workers[251] have reported an unprecedented sigmatropic rearrangement of **173**, derived from *cis*-2,3-methanophenylalanine hydrochloride, leading to a 2-benzazepine derivative as described in Scheme 63.

**Scheme 63**



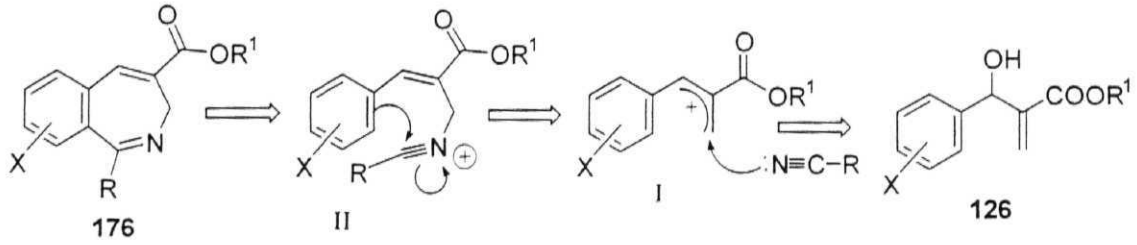

A novel photochemical reaction of *N*-phthaloyl α-aminoacid esters **174** leading to the synthesis of dihydrobenzazepinedione **175** has been reported by Griesbeck and Mauder (Eq. 37).[252]




**Eq. 37**

Due to the importance of 2-benzazepine derivatives, we have undertaken a research project with the main aim of developing novel methodology for the synthesis of these molecules (*i.e.*, 2-benzazepines) from the Baylis-Hillman adducts. We have envisioned that 2-benzazepine derivatives (**176**) can in principle be obtained from the Baylis-Hillman adducts (**126**) *via* the construction of C-N bond through the Ritter reaction[253-255] followed by simultaneous construction of C-C bond through the Houben-Hoesch reaction[256-262] as there would be a nitrilium ion intermediate **II** (Scheme 64).

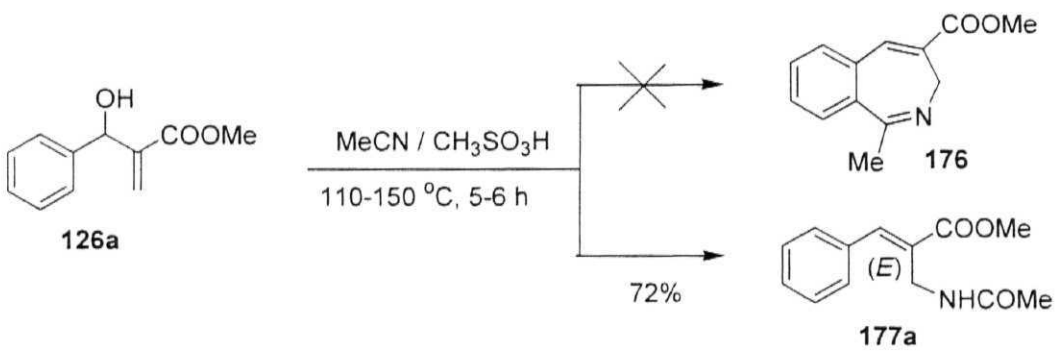
**Scheme 64: Schematic representation of synthetic strategy for 2-benzazepine derivatives**




Accordingly, we have first selected methyl 3-hydroxy-2-methylene-3-phenylpropanoate (**126a**) as substrate for performing the Ritter and the Houben-Hoesch reactions with acetonitrile in the presence of methanesulfonic acid at various conditions. However, this reaction did not proceed to the formation of the desired 2-benzazepine derivative (**176**) but stopped at the stage of allyl amide only (**177a**) (Scheme 65). The best result, in this direction, was obtained when methyl 3-hydroxy-2-methylene-3-phenylpropanoate (**126a**) (1 mmol) in acetonitrile (5 mL) was treated with methanesulfonic acid (3 mL) at 110 $^{0}$C for 5 hours, thus providing the resulting product, methyl (2*E*)-2-acetylaminomethyl-3-phenylprop-2-enoate (**177a**), in 72% yield with (*E*)-stereochemistry[vii]

(after silica gel column chromatography). Structure of the molecule was established by IR, $^1$H NMR (Spectrum 15), $^{13}$C NMR (Spectrum 16), mass spectral data and elemental analysis. Stereochemical assignment was based on chemical shift value (δ) of β-vinylic proton in $^1$H NMR.[ψ]

**Scheme 65**

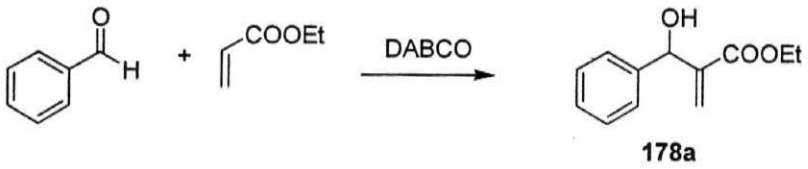



We have then prepared representative (*E*)-allyl amides (**177b**, **177c** and **179***) *via* treatment of various Baylis-Hillman adducts [**126b**, **126c** and **178a*** (obtained *via* the reaction of benzaldehyde with ethyl acrylate according to the Eq. 38)] with acetonitrile in the presence of methanesulfonic acid (Eq. 39, Table 6). Structures of all the products (**177b**, **177c** and **179**) were determined by IR, $^1$H NMR, $^{13}$C NMR spectral data and elemental analyses. (*E*)-Stereochemistry in all the cases was established by $^1$H NMR spectral analysis.[ψ]

---

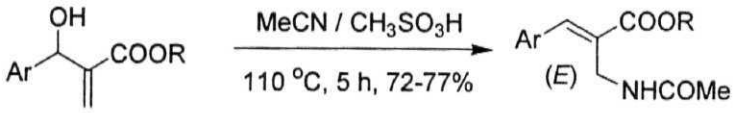
[ψ] In the $^1$H NMR spectra of trisubstituted alkenes (with ester group at α-position) the β-vinylic proton *cis* to the ester group appears downfield while the β-vinylic proton *trans* to ester group appears upfield.[215-218] $^1$H NMR spectra of the crude samples of **177a-c**, **179-181** indicated the presence of 5-12% minor (*Z*)-isomer. The *E*/*Z* selectivity was determined by the integration ratio of isomeric β-vinylic protons [the β-vinylic proton *cis* to ester group (*E*-isomer) appeared at δ 7.77-7.82 while the same proton *trans* to ester group (*Z*-isomer) appeared at δ 6.35-7.03].

* For better understanding and continuity, the Baylis-Hillman alcohol derived from benzaldehyde and ethyl acrylate is numbered as **178a** and the corresponding allyl amide is numbered as **179**.




**178a**

**Eq. 38**



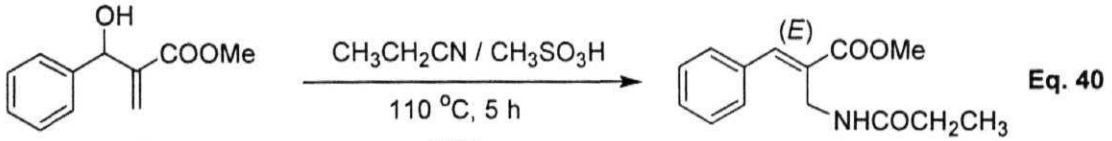

**Eq. 39**

**126b** (Ar = 4-MePh, R = Me),
**126c** (Ar = 4-EtPh, R = Me),
**178a** (Ar = Ph, R = Et)

**177b, 177c, 179**

**177b** (Ar = 4-MePh, R = Me),
**177c** (Ar = 4-EtPh, R = Me),
**179** (Ar = Ph, R = Et)

With a view to understand the application of other nitriles in the Ritter reaction of Baylis-Hillman adducts, we also employed propionitrile in this reaction. Thus, the reaction of methyl 3-hydroxy-2-methylene-3-phenylpropanoate (**126a**) with propionitrile in the presence of methanesulfonic acid provided the expected methyl (2*E*)-3-phenyl-2-propanoylaminomethylprop-2-enoate (**180**)[λ] in 83% yield (Eq. 40, Table 6). Structure of the product was in full agreement with the spectral data (IR, $^1$H NMR, $^{13}$C NMR) and elemental analysis. (*E*)-Stereochemistry was established by $^1$H NMR spectral analysis.[ψ]




**126a**

**180**

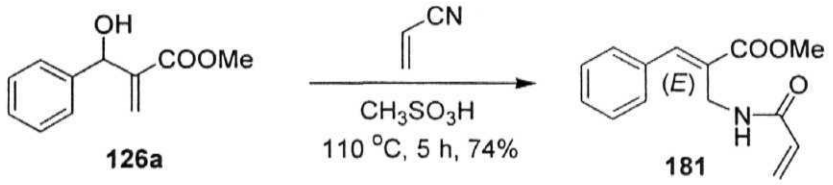
**Eq. 40**

We have also used acrylonitrile for Ritter reaction with Baylis-Hillman alcohol (**126a**). Thus, the reaction of methyl 3-hydroxy-2-methylene-3-phenylpropanoate (**126a**) with acrylonitrile in the presence of methanesulfonic acid provided the expected methyl

---

λ For better understanding and continuity, the allyl amide derived from **126a** and propionitrile is numbered as **180** and allyl amide derived from **126a** and acrylonitrile is numbered as **181**.

(2*E*)-2-acryloylaminomethyl-3-phenylprop-2-enoate (**181**)[λ] in 74% yield (Eq. 41, Table 6).[ψ] Structure of product was in full agreement with the spectral data (IR, $^1$H NMR, $^{13}$C NMR) and elemental analysis.




Eq. 41

**Table 6: Stereoselective transformation of Baylis-Hillman adducts (126a-c, 178a) into (*E*)-allyl amides (177a-c, 179-181) under Ritter conditions.[a,b]**

| Alcohol | Alkanonitrile | Product[c] | Yield[d] (%) | Mp (°C) |
|---|---|---|---|---|
| **126a** | acetonitrile | **177a**[e] | 72 | 112-114 |
| **126b** | acetonitrile | **177b** | 75 | 115-116 |
| **126c** | acetonitrile | **177c** | 72 | 78-80 |
| **178a** | acetonitrile | **179** | 77 | 66 |
| **126a** | propionitrile | **180** | 83 | 93-94 |
| **126a** | acrylonitrile | **181** | 74 | 90 |

a) All the reactions were carried out on 1 mmol scale of the Baylis-Hillman alcohols (**126a-c**, **178a**) in alkanonitriles (5mL) in the presence of methanesulphonic acid at 110 °C for 5 hours.

b) All the allyl amides (**177a-c, 179-181**) were obtained as colorless solids and gave satisfactory IR, $^1$H NMR, $^{13}$C NMR spectral data and elemental analyses.

c) $^1$H NMR spectra of the crude products indicated the presence of ≈ 5-10% minor *Z*-isomer along with major *E*-isomer.

d) Yields of the pure allyl amides (**177a-c, 179-181**) obtained after column chromatography (silica gel, 30 % EtOAc in hexanes).

e) This compound was also characterized by mass spectral data.

With a view to understand stereochemical directive effects of cyano group, we have examined the reaction of 3-hydroxy-2-methylene-3-phenylpropanenitrile (**182a**),[⊗] which was prepared *via* the treatment of benzaldehyde with acrylonitrile in the presence of DABCO (Eq. 42), with the acetonitrile under similar conditions. The resulting product, (2*Z*)-2-acetylaminomethyl-3-phenylprop-2-enenitrile (**183a**),[⊗] was obtained in 82% isolated yield with exclusively (*Z*)-selectivity[ξ] (Eq. 43, Table 6). Structure of the molecule was established by IR, $^{1}$H NMR (Spectrum 17), $^{13}$C NMR (Spectrum 18), mass spectral data and elemental analysis. Stereochemical assignment was based on chemical shift values (δ) of allylic methylene carbon in $^{13}$C NMR spectrum.[ξ]


**Eq. 42**

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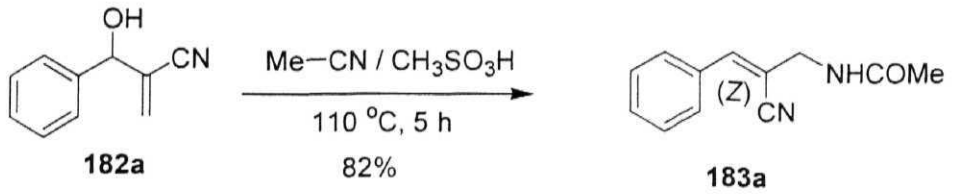
⊗ For better understanding and continuity, the Baylis-Hillman alcohols derived from acrylonitrile and aldehydes are numbered as **182a-c** and the corresponding allyl amides are numbered as **183a-c**.

ξ $^{1}$H NMR spectra of the crude products of **183a-c** showed at least 95% (*Z*)-selectivity [in the case of **183a**, $^{1}$H NMR spectrum of the crude sample showed the isomeric allylic protons doublet at δ 4.14 (*Z*-isomer) & δ 4.29 (E-isomer) in the ratio of 96/4].
The (*Z*)-stereochemistry of compounds **183a-c** was assigned on the basis of $^{13}$C NMR chemical shift values of allylic methylene carbons (δ 43.42, 43.38 and 43.28) in comparison with that of allylic methylene carbons of **177a-c**, **179-181** (having *E*-stereochemistry) (δ 36.61-36.79) [In the $^{13}$C NMR spectra of trisubstituted alkenes, allylic carbon *cis* to aryl group appears upfield while same carbon *trans* to aryl group appears downfield.[263-265] We and others[264-269] observed that the allylic methylene carbons of **G** and **H** derived from (m)ethyl 3-hydroxy(or acetoxy)-3-aryl-2-methylenepropanoates and 3-hydroxy(or acetoxy)-3-aryl-2-methylenepropanenitriles have similar $^{13}$C NMR chemical shifts while allylic methylene carbons of **I** and **J** derived from (m)ethyl 3-hydroxy(or acetoxy)-3-aryl-2-methylenepropanoates and 3-hydroxy(or acetoxy)-3-aryl-2-methylene-propanenitriles have similar $^{13}$C NMR chemical shifts].



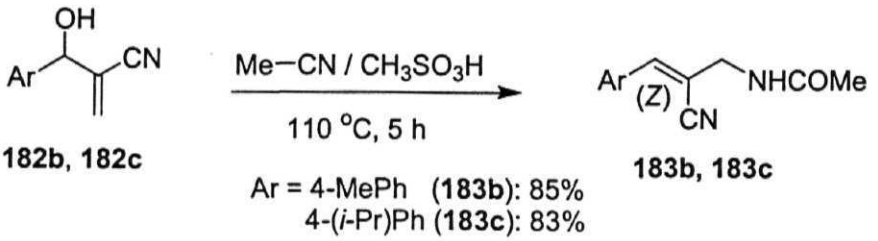

**182a** **183a** **Eq. 43**

We have then prepared representative class of Baylis-Hillman adducts (**182b**, **182c**) (Eq. 42) and successfully transformed into corresponding (*Z*)-allyl amides (**183b**, **183c**) *via* the treatment with acetonitrile in the presence of methanesulfonic acid (Eq. 44, Table 7). The structures of these products (**183b**, **183c**) (obtained after silica gel column chromatography) were in full agreement with IR, $^{1}$H NMR, $^{13}$C NMR spectral data and elemental analyses. Stereochemical assignments were based on chemical shift values (δ) of allylic methylene carbon in $^{13}$C NMR spectrum.[5]

**Table 7: Stereoselective transformation of Baylis-Hillman adducts (182a-c) into (*Z*)-allyl amides (183a-c) under Ritter conditions[a,b]**

| Alcohol (**182a-c**) | Ar | Product[c] (**183a-c**) | Yield[d] (%) | Mp (°C) |
|---|---|---|---|---|
| **182a** | Ph | **183a** | 82 | 98-100 |
| **182b** | 4-MePh | **183b** | 85 | 108-110 |
| **182c** | 4-(*i*-Pr)Ph | **183c** | 83 | 76-78 |

a) All the reactions were carried out on 1 mmol scale of the Baylis-Hillman alcohols (**182a-c**) in acetonitriles (5mL) in the presence of methanesulphonic acid at 110 °C for 5 hours.
b) All the allyl amides (**183a-c**) were obtained as colorless solids and gave satisfactory IR, $^{1}$H NMR, $^{13}$C NMR spectral data and elemental analyses.
c) $^{1}$H NMR spectrum of the crude products did not show the indication of any (*E*)-isomer.
d) Yields of the pure allyl amides (**183a-c**) obtained after column chromatography (silica gel, 30 % EtOAc in hexanes).

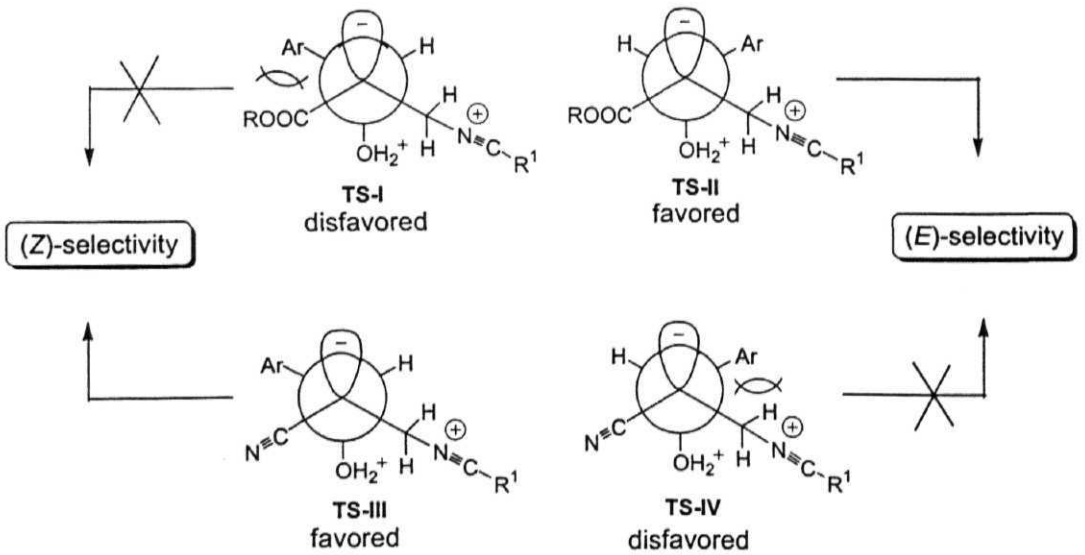



**182b, 182c** **183b, 183c** **Eq. 44**

## Transition state models for explaining the stereoselectivity:

These stereochemical directive effects of ester and cyano group are in consistent with our earlier reports in various stereoselective transformations of the Baylis-Hillman adducts.[264,266,268] (*E*)-Stereoselectivity in the case of ester group and (*Z*)-stereoselectivity in case of cyano group can possibly be explained based on the transition state models **TS-1** & **TS-II** and **TS-III** & **TS-IV** (Scheme 66). In the case of methyl 3-hydroxy-2-methylene-3-arylpropanoates (**126a-c, 178a**), ester group has a greater steric effect than the nitroliummethyl ($CH_2N^+{\equiv}C{-}R^1$) group thus favoring transition state model **TS-II** over **TS-I** (Scheme 66). While in the case of 3-hydroxy-2-

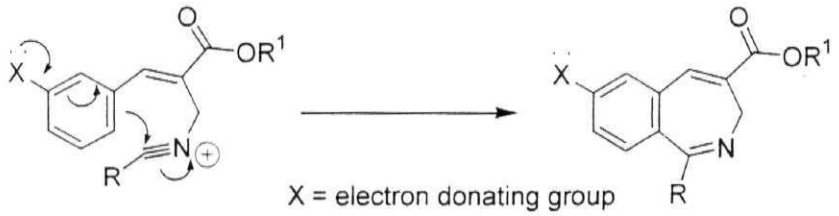
**Scheme 66**



methylene-3-arylpropanenitrile (**182a-c**), cyano group offers very less steric effect than the nitroliummethyl ($CH_2N^+\equiv C-R^1$) group thus favoring transition state model **TS-III** over **TS-IV** leading to (*Z*)-stereoselectivity (Scheme 66).

## Synthesis of 2-benzazepines :

At this stage it occurred to us that the presence of electron donating group(s) on the aromatic ring might help in the construction of C-C bond (*via* the Houben-Hoesch reaction) after construction of C-N bond (*via* the Ritter reaction) thus leading to the formation of 2-benzazepine derivatives in the case of Baylis-Hillman adducts derived from alkyl acrylates (Eq. 45).

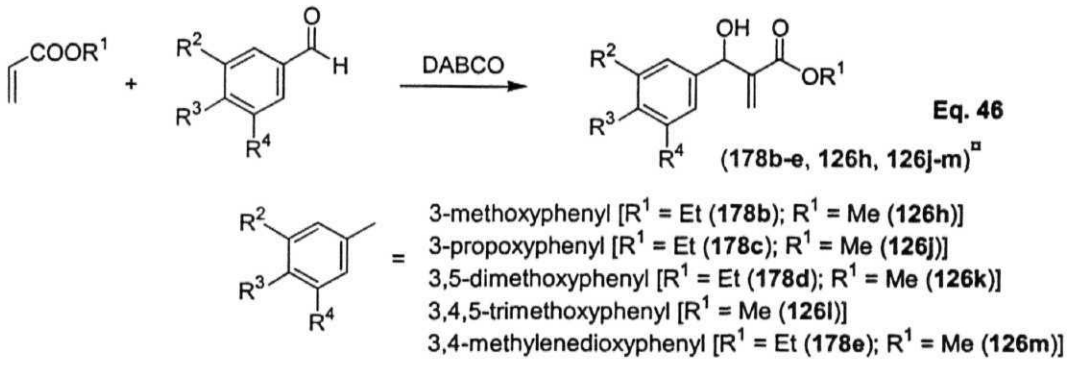


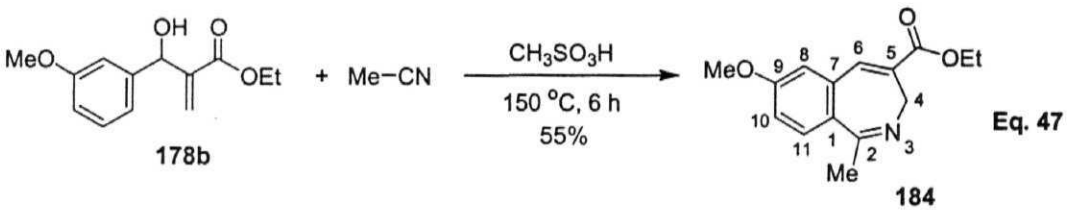

**Eq. 45**

Accordingly, we have first treated ethyl 3-hydroxy-3-(3-methoxyphenyl)-2-methylene-propanoate (**178b**),[¤] the Baylis-Hillman adduct obtained from ethyl acrylate and 3-methoxybenzaldehyde (Eq. 46), with acetonitrile in the presence of methanesulfonic acid under various conditions. We were indeed pleased to isolate the expected 3-aza-5-ethoxycarbonyl-9-methoxy-2-methylbicyclo[5.4.0]undeca-1(7),2,5,8,10-pentaene (**184**) in 55% yield, when **178b** (2 mmol) in acetonitrile (5 mL) was treated with methanesulf-

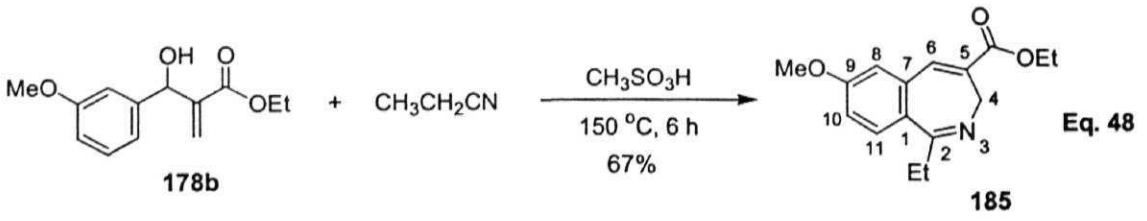
¤ For better understanding and continuity, we have numbered the Baylis-Hillman alcohols derived from ethyl acrylate and 3-methoxybenzaldehyde, 3-propoxybenzaldehyde, 3,5-dimethoxy-benzaldehyde, piperanal as **178b**, **178c**, **178d**, **178e** (*i.e.*, as **178** series) respectively. Similarly, Baylis-Hillman alcohols derived from methyl acrylate and 3-methoxybenzaldehyde, 3-propoxybenzaldehyde, 3,5-dimethoxybenzaldehyde, 3,4,5-trimethoxybenzaldehyde, piperanal as **126h**, **126j**, **126k**, **126l**, **126m** (*i.e.*, as **126** series).

onic acid (3 mL) at 150 °C for 6 hours (Eq. 47, Table 8). Structure of the molecule (**184**) was established by IR, $^{1}$H NMR (Spectrum 19), $^{13}$C NMR (Spectrum 20), mass spectral data and elemental analysis.



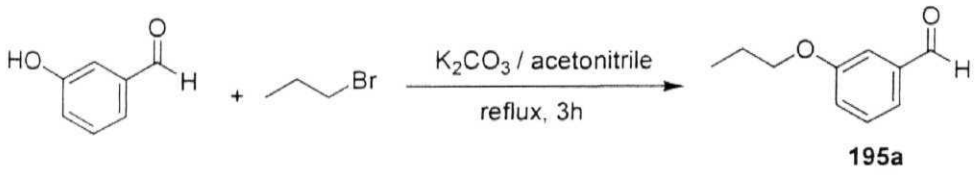




With a view to understand the generality of this strategy, we have examined the reaction between ethyl 3-hydroxy-3-(3-methoxyphenyl)-2-methylenepropanoate (**178b**) with propionitrile in the presence of methanesulfonic acid (Eq. 48). The reaction worked equally well, thus, providing the desired 3-aza-2-ethyl-5-ethoxycarbonyl-9-methoxybicyclo[5.4.0]undeca-1(7),2,5,8,10-pentaene (**185**) in 67% yield (Eq. 48, Table




¤ For easy understanding and continuity, we have numbered all the 2-benzazepine molecules, derived from both **178b-e** and **126h, j-m**, continuously from **184** to **194**.

8). Structure of the molecule (**185**) was in full agreement with spectral data [IR, $^1$H NMR (Spectrum 21), $^{13}$C NMR (Spectrum 22), mass] and elemental analysis. We have then extended this strategy to representative Baylis-Hillman adducts (**178c-e, 126h, 126j-m**) prepared *via* the coupling of various alkoxybenzaldehydes and methyl (or ethyl) acrylates in the presence of DABCO (Eq. 46). The required 3-propoxybenzaldehyde (**195a**)[χ] was prepared from 3-hydroxybenzaldehyde according to the Eq. 49. The desired 2-benzazepine derivatives (**186-194**) were obtained in moderate to good yields *via* the reaction of Baylis-Hillman adducts (**178c-e, 126h, 126j-m**) with aceto- and propionitriles in the presence of methanesulfonic acid (Eq. 50, Table 8). Structures of all products (**186-194**)[$] were in full agreement with IR, $^1$H NMR (Spectrum 23, for molecule **192**), $^{13}$C NMR (Spectrum 24, for molecule **192**) spectral data and elemental analyses. Structures of compounds **192** and **194** were also established by single crystal X-ray crystallographic data (**192** : Fig. X3, Table 9; **194** : Fig. X4, Table 10).




**195a**

**Eq. 49**

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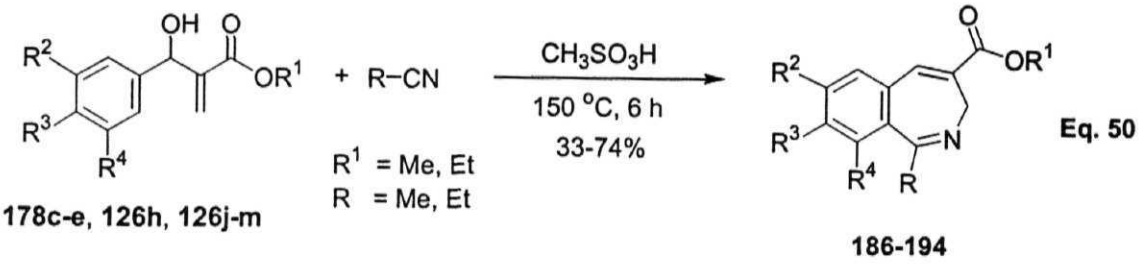
[$] It is interesting to note that in the case of compounds **189-192** (having methoxy group at 11 position), one of the ring-allylic methylene protons in $^1$H NMR spectrum appears as a doublet at δ 2.84-2.97 while the other proton appears as a doublet at δ 4.70-4.88. We have in fact confirmed this assignment in one case (compound **192**) by hydrogen-carbon (hetero) COSY NMR experiment (Spectrum 25) and also by single crystal X-ray data (Fig. X3). In the case of all the remaining 2-benzazepine derivatives **184-188, 193, 194** (without the methoxy group at 11-position) both the ring allylic methylene protons appear as a singlet at δ 3.84-3.92.

[χ] 3-Propoxybenzaldehyde is given number **195a** so as to maintain the continuity and easy understanding.




**178c-e, 126h, 126j-m**

**186-194**

**Eq. 50**

R = Et; $R^1$ = Me; $R^2$ = OMe; $R^3$ = $R^4$ = H (**186**)
R = Et; $R^1$ = Et; $R^2$ = OPr; $R^3$ = $R^4$ = H (**187**)
R = Et; $R^1$ = Me; $R^2$ = OPr; $R^3$ = $R^4$ = H (**188**)
R = Me; $R^1$ = Et; $R^2$ = OMe; $R^4$ = OMe, $R^3$ = H (**189**)
R = Et; $R^1$ = Et; $R^2$ = OMe; $R^4$ = OMe, $R^3$ = H (**190**)
R = Me $R^1$ = Me; $R^2$ = OMe; $R^4$ = OMe, $R^3$ = H (**191**)
R = Et; $R^1$ = Me; $R^2$ = $R^4$ = $R^3$ = OMe (**192**)
$R^1$ = Et; R = Et; $R^2$ & $R^3$ = $OCH_2O$; $R^4$ = H (**193**)
$R^1$ = Me; R = Et; $R^2$ & $R^3$ = $OCH_2O$; $R^4$ = H (**194**)

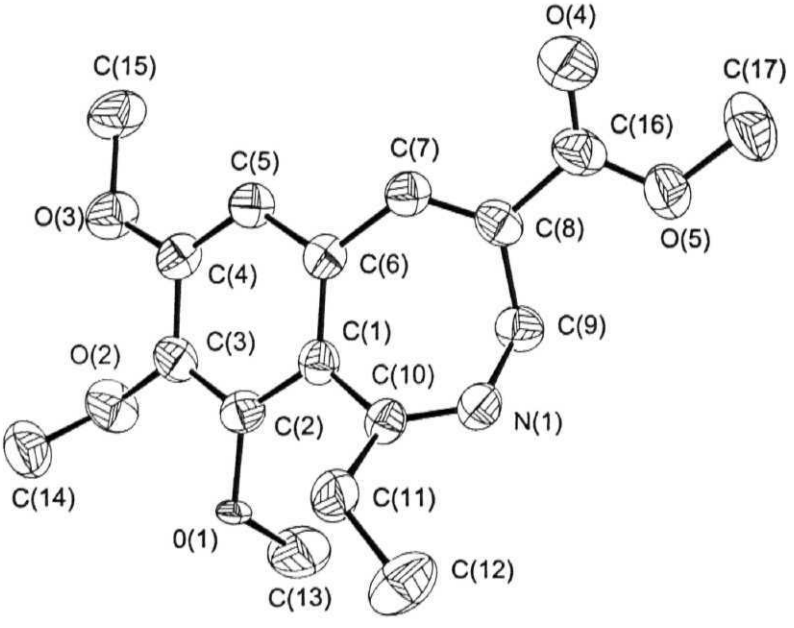
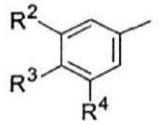



**Fig. X3**

**ORTEP diagram of the compound 192**

(*Hydrogen atoms were omitted for clarity*)

**Table 8: Synthesis of 2-benzazepines (184-194)[a,b]**

| Alcohol |  | $R^1$ (of $COOR^1$) | R (of R-CN) | Product | Yield[c] (%) | Mp (°C) |
|---|---|---|---|---|---|---|
| **178b** | 3-(MeO)Ph | Et | Me | **184** | 55 | 86-88 |
| **178b** | 3-(MeO)Ph | Et | Et | **185**[d] | 67 | 89-90 |
| **126h** | 3-(MeO)Ph | Me | Et | **186**[d] | 44 | - |
| **178c** | 3-(PrO)Ph | Et | Et | **187**[d] | 58 | - |
| **126j** | 3-(PrO)Ph | Me | Et | **188** | 65 | - |
| **178d** | 3,5-$(MeO)_2$Ph | Et | Me | **189**[d] | 70 | - |
| **178d** | 3,5-$(MeO)_2$Ph | Et | Et | **190**[d] | 74 | - |
| **126k** | 3,5-$(MeO)_2$Ph | Me | Me | **191**[d] | 72 | 108 |
| **126l** | 3,4,5-$(OMe)_3$Ph | Me | Et | **192**[e] | 33 | 140-141 |
| **178e** | 3,4-$(OCH_2O)$Ph | Et | Et | **193**[d] | 48 | 78-79 |
| **126m** | 3,4-$(OCH_2O)$Ph | Me | Et | **194**[e] | 46 | 126-127 |

a) All the reactions were carried out on 2 mmol scale of Baylis-Hillman alcohols (**178b-e, 126h, j-m)** in alkane nitriles (5mL) in the presence of the methanesulphonic acid at 150 °C for 6 hours.

b) All the pure 2-benzazepines (**184, 185, 191-194**) were obtained as solids and gave satisfactory IR, $^1$H NMR, $^{13}$C NMR spectral data and elemental analyses.

c) All the pure 2-benzazepines (**186-190**) were obtained as viscous liquids and gave satisfactory IR, $^1$H NMR, $^{13}$C NMR spectral data and elemental analyses.

c) Yields of the pure 2-benzazepines (**184-194**) obtained after column chromatography (30 % EtOAc in hexanes).

d) These molecules were also characterized by mass spectral data.

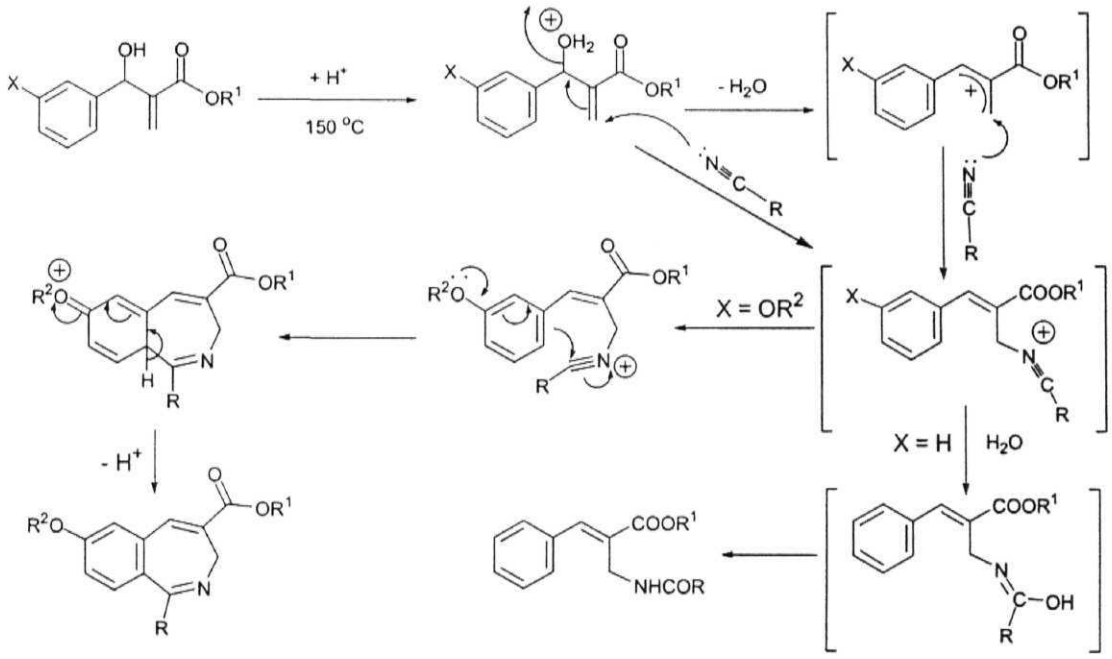
e) Structures of the compounds **192** and **194** were further confirmed by single crystal X-ray data (Fig. X3 and Fig. X4).

**Table 9. Crystal data and structure refinement for 192.**

| | |
|---|---|
| Identification code | : **192** |
| Empirical formula | : $C_{17}H_{21}NO_5$ |
| Formula weight | : 319.35 |
| Temperature | : 293(2) K |
| Wavelength | : 0.71073 Å |
| Crystal system | : Monoclinic |
| space group | : P21/a:b3 (International Table No.14) |
| Unit cell dimensions | : a = 10.669(6) Å; $\alpha$ = 90 deg. |
| | : b = 13.041(8) Å; $\beta$ = 93.18(5) deg. |
| | : c = 12.062(9) Å; $\gamma$ = 90 deg. |
| Volume | : 1675.6(18) $Å^3$ |
| Z, Calculated density | : 4, 1.266 $Mg/m^3$ |
| Absorption coefficient | : 0.093 $mm^{-1}$ |
| F(000) | : 680 |
| Crystal size | : 0.5 x 0.48 x 0.24 mm |
| Theta range for data collection | : 1.69 to 28.74 deg. |
| Limiting indices | : $0 \le h \le 13$, $0 \le k \le 16$, $-15 \le l \le 15$ |
| Reflections collected / unique | : 3791 / 3791 [R(int) = 0.0000] |
| Completeness to theta = 28.74 | : 87.2 % |
| Refinement method | : Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | : 3791 / 0 / 209 |
| Goodness-of-fit on $F^2$ | : 0.854 |
| Final R indices [I>2sigma(I)] | : R1 = 0.0569, wR2 = 0.1845 |
| R indices (all data) | : R1 = 0.1198, wR2 = 0.2709 |
| Extinction coefficient | : 0.010(4) |
| Largest diff. peak and hole | : 0.310 and -0.225 e. $Å^{-3}$ |

A plausible mechanism for the formation of 2-benzazepines as well as for allyl amides is presented in the Scheme 67.

**Scheme 67:**



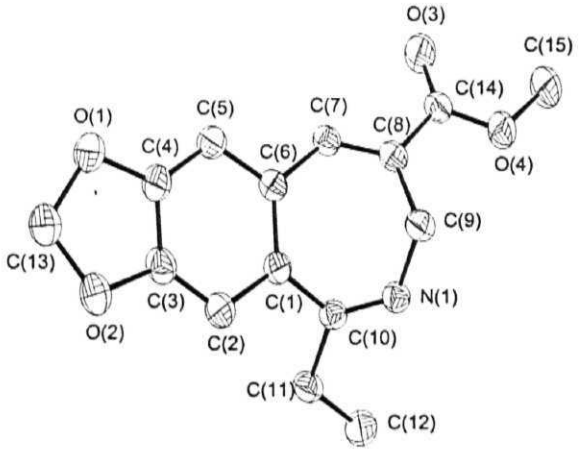




**Fig. X4**
**ORTEP diagram of the compound 194**
(*Hydrogen atoms were omitted for clarity*)

**Table 10. Crystal data and structure refinement for 194**

| | |
|---|---|
| Identification code | : **194** |
| Empirical formula | : $C_{15}H_{15}NO_4$ |
| Formula weight | : 273.28 |
| Temperature | : 293(2) K |
| Wavelength | : 0.71073 Å |
| Crystal system | : Monoclinic |
| Space group | : P21/a:b3 (International Table No. 14) |
| Unit cell dimensions | : a = 8.096(5) Å; $\alpha$ = 90 deg. |
| | : b = 16.436(8) Å $\beta$ = 98.73(5) deg. |
| | : c = 10.159(8) Å $\gamma$ = 90 deg. |
| Volume | : 1336.1(15) $Å^3$ |
| Z, Calculated density | : 4, 1.359 $Mg/m^3$ |
| Absorption coefficient | : 0.099 $mm^{-1}$ |
| F(000) | : 576 |
| Crystal size | : 0.47 x 0.42 x 0.40 mm |
| Theta range for data collection | : 2.03 to 29.96 deg. |
| Limiting indices | : $0 \le h \le 11$, $0 \le k \le 23$, $-14 \le l \le 14$ |
| Reflections collected / unique | : 3881 / 3881 [R(int) = 0.0000] |
| Completeness to theta = 29.96 | : 100.0 % |
| Max. and min. transmission | : 0.9521 and 0.9293 |
| Refinement method | : Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | : 3881 / 0 / 182 |
| Goodness-of-fit on $F^2$ | : 1.026 |
| Final R indices [I>2sigma(I)] | : R1 = 0.0441, wR2 = 0.1081 |
| R indices (all data) | : R1 = 0.0795, wR2 = 0.1254 |
| Extinction coefficient | : 0.037(3) |
| Largest diff. peak and hole | : 0.254 and -0.168 e. $Å^{-3}$ |

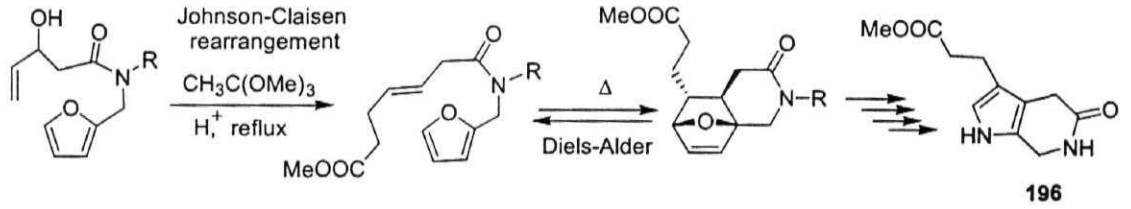
Thus, we have developed a novel reaction involving tandem construction of C-N and C-C bonds *via* the simultaneous Ritter and Houben-Hoesch reactions on Baylis-Hillman adducts, derived from alkoxy substituted benzaldehydes and alkyl acrylates, leading to a convenient, one-pot synthesis of 2-benzazepine derivatives. We have successfully described stereoselective transformation of the Baylis-Hillman adducts, derived from benzaldehyde / alkyl substituted benzaldehydes and alkyl acrylates into (*E*)-allyl amides. We have also described transformation of Baylis-Hillman adducts, derived from benzaldehyde / alkyl substituted benzaldehydes and acrylonitrile, into (*Z*)-allyl amides, thus demonstrating the efficacy of the Baylis-Hillman adducts as an important source for exploration of new reactions and stereoselective transformation methodologies.

## 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 the transition state:

Control of the stereochemistry is an essential requirement for any useful synthetic reaction. Claisen rearrangement, with its variety of variants, represents one such useful synthetic reaction whose stereochemical applications have been well documented in the literature.[20,270-274] Johnson-Claisen rearrangement,[20,270-274,275] an important variant of Claisen rearrangement involves the reaction of allylic alcohols with orthoesters in the presence of catalytic amount of acid to provide the γ,δ-unsaturated esters. This reaction has been successfully employed in synthesis of various natural products and biologically active compounds.[20,270-274] Some interesting, recent and relevant applications have been described in the following.

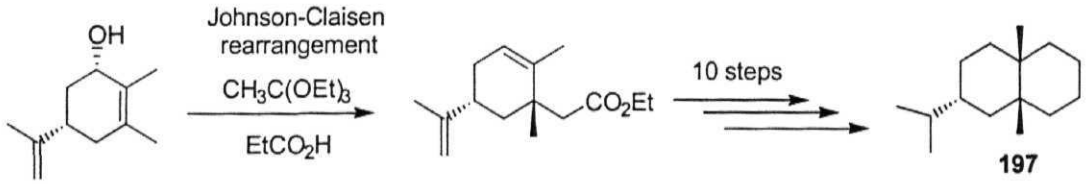
Jacobi and Li[276] have reported the synthesis of porphobilinogen lactam methyl ester (**196**) which involved tandem Johnson-Claisen rearrangement and Diels-Alder reaction as key steps (Scheme 68).

**Scheme 68**:



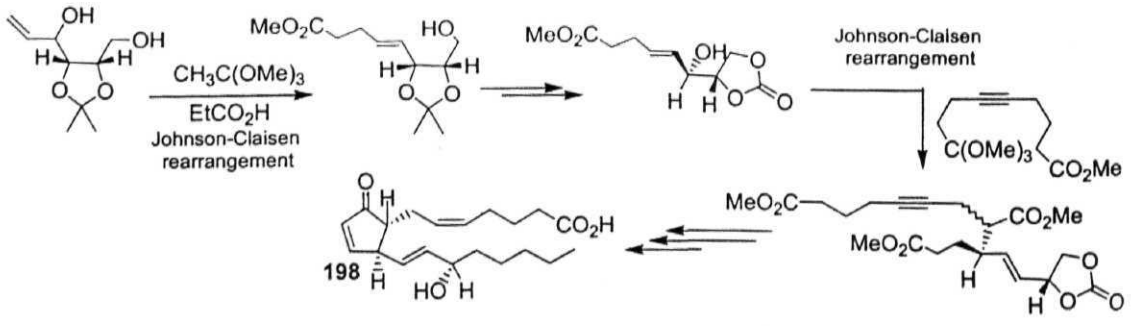

Srikrishna and co-workers have successfully employed Johnson-Claisen rearrangement as key step in the synthesis of (+)-valerane (**197**) (Scheme 69).[277]

**Scheme 69**



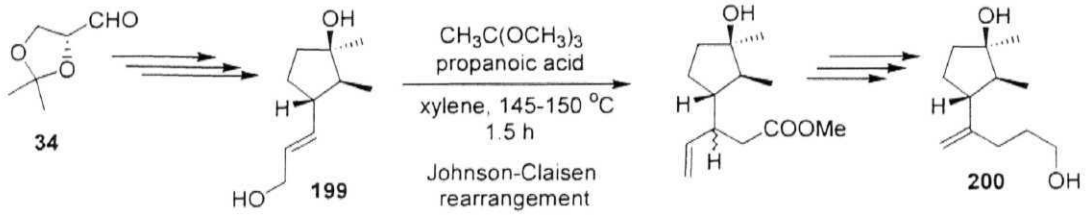

Stork and Raucher[278] have employed Johnson-Claisen rearrangement twice as the key step, once for creating *trans* geometry and second time for transferring chirality, in chiral synthesis of (*S*)-prostaglandin $A_2$ (**198**) (Scheme 70).

**Scheme 70**

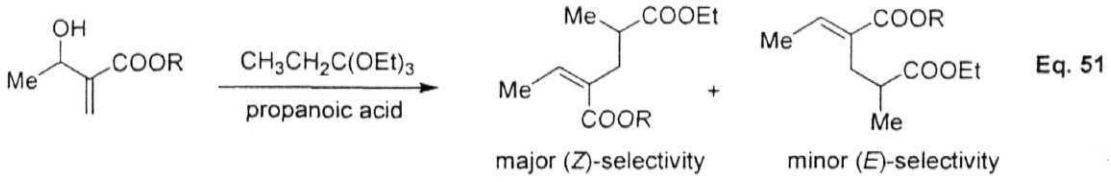


Suzuki and co-workers have described the synthesis of (-)-chokol A (**200**) employing the Johnson-Claisen rearrangement of the allylic alcohol (**199**) as the key step. The allylic alcohol (**199**), in turn, was synthesized from (*R*)-2,3-*O*-isopropylideneglyceraldehyde (**34**) (Scheme 71).[279]

**Scheme 71**



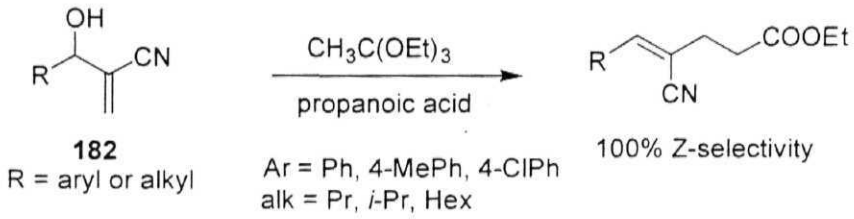

Baylis-Hillman reaction provides an interesting class of functionalized allyl alcohols which can in principle be used as valuable substrates for Johnson-Claisen rearrangement. Drewes and co-workers have reported Johnson-Claisen rearrangement of various alkyl 3-hydroxy-2-methylenebutanoates, derived from acetaldehyde and alkyl acrylates, with triethyl orthopropanoate producing isomeric mixture of corresponding products with (*Z*)-isomer predominating. However, they did not report the *Z* / *E* ratios (Eq. 51).[280]




Eq. 51

Our research group described an interesting Johnson-Claisen rearrangement of 3-hydroxy-2-methylenealkanenitriles obtained *via* the reaction of various aldehydes with acrylonitrile, providing a general and simple synthesis of (4*Z*)-4-cyanoalk-4-enoates

(Eq. 52).[281] Exclusive (*Z*)-selectivity was explained on the basis of severe classical [1,3]-interactions in the transition state **TS-V** (Figure 13).[281]

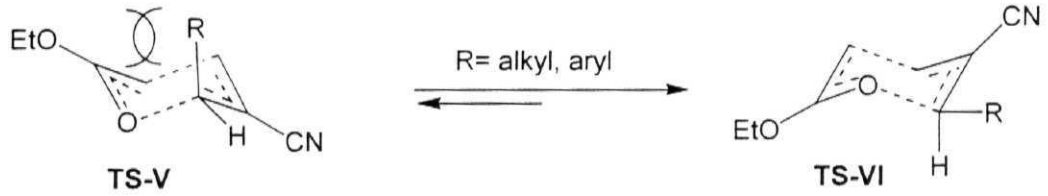



**182**
R = aryl or alkyl

Ar = Ph, 4-MePh, 4-ClPh
alk = Pr, *i*-Pr, Hex

100% Z-selectivity

**Figure 13**




**TS-V** **TS-VI**

Our research group has also examined the Johnson-Claisen rearrangement of methyl 3-hydroxy-2-methylenealkanoates, the Baylis-Hillman adducts obtained *via* the reaction of various aldehydes with methyl acrylate, with triethyl orthoacetate (Scheme 72).[216] During these studies, our research group noticed an interesting unprecedented stereochemical reversal from alkyl to aryl substituents.[216] Thus, methyl 3-hydroxy-3-aryl-2-methylenepropanoates (the Baylis-Hillman adducts derived from aromatic aldehydes) provided the resulting Johnson-Claisen products *i.e.*, ethyl 4-methoxycarbonyl-5-(aryl)pent-4-enoates, with high (*E*)-selectivity, while methyl 3-hydroxy-2-methylenealkanoates (the Baylis-Hillman adduct derived from aliphatic aldehydes) provided the resulting Johnson-Claisen products *i.e.*, ethyl 4-methoxycarbonyl-4-alkenoates, in high (*Z*)-selectivity (Scheme 72). The reversal of stereoselectivity from alkyl to aryl substituent is attributed to the competition between

usual [1,3]-interactions (in **TS-VII**) and unusual [1,2]-interactions in the transition state **TS-IX** (Figure 14).[216]

**Scheme 72**

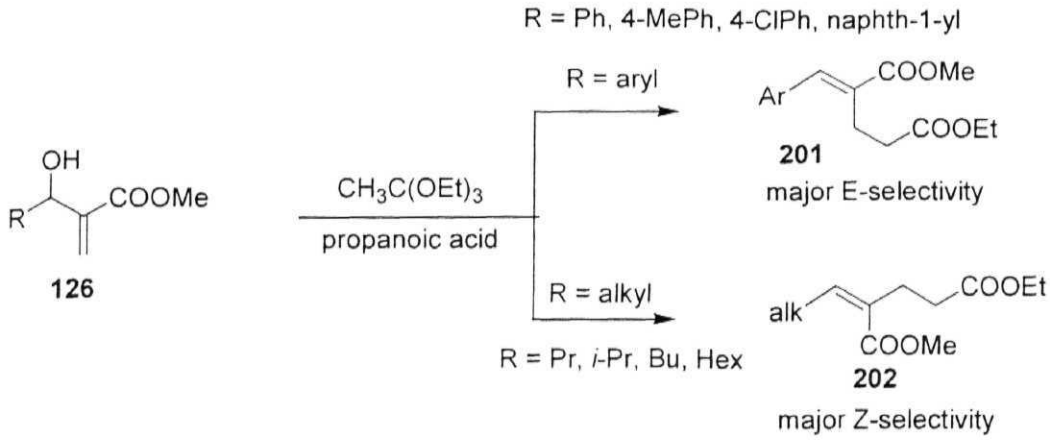
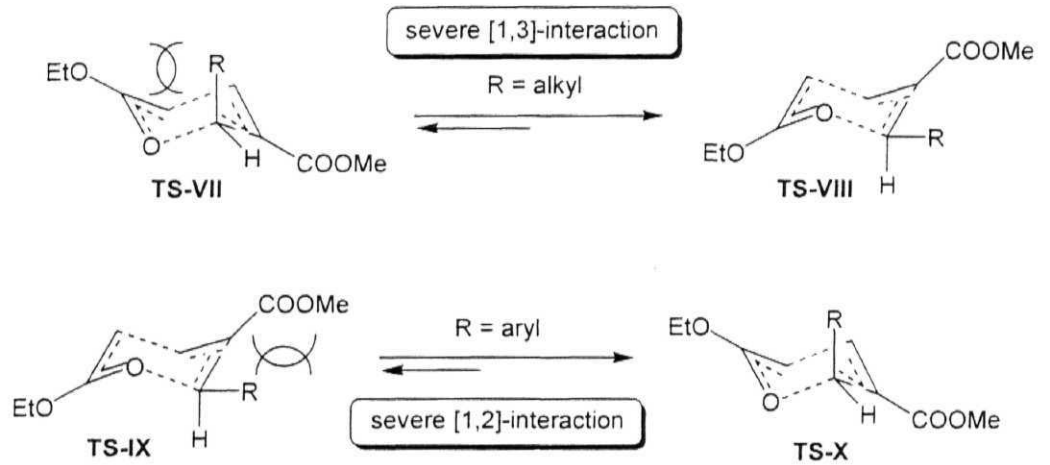
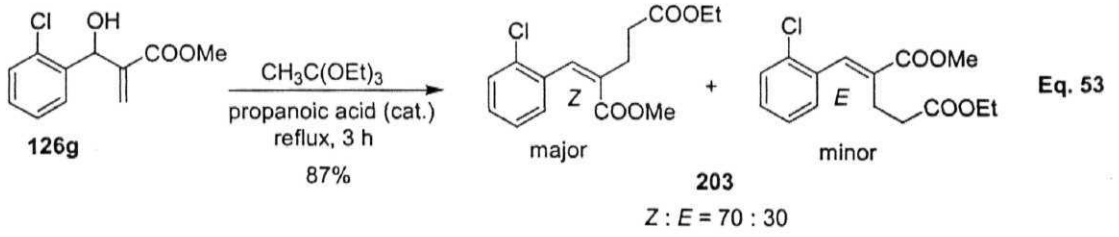



**Figure 14**




However, our research group did not examine the Johnson-Claisen rearrangement of Baylis-Hillman adducts derived from *ortho* substituted benzaldehydes. With a view to understand the effect of *ortho* substitution on the aromatic ring of Baylis-Hillman adducts derived from 2-substituted benzaldehydes and alkyl acrylates, we have first

selected methyl 3-(2-chlorophenyl)-3-hydroxy-2-methylenepropanoate (**126g**), the Baylis-Hillman alcohol derived from 2-chlorobenzaldehyde as a substrate for the Johnson-Claisen rearrangement (Eq. 53). Thus, the reaction of methyl 3-(2-chlorophenyl)-3-hydroxy-2-methylenepropanoate (**126g**) with triethyl orthoacetate in the presence of catalytic amount of propanoic acid at reflux temperature for 3 hours provided the resulting product, ethyl 5-(2-chlorophenyl)-4-methoxycarbonylpent-4-enoate (**203**), with high *Z*-selectivity (*Z* / *E* : 70 / 30) as evidenced by the $^1$H NMR spectral analysis of the crude as well pure product.♣ Silica gel column chromatography of crude product provided the pure product (**203**) in 87% yield as mixture of *Z*- and *E*-isomers with (*Z*)-isomer predominating (Eq. 53, Table 11). Structure of the product (**203**, isomer mixture) was in full agreement with IR, $^1$H NMR (Spectrum 26), $^{13}$C NMR (Spectrum 27) spectral data and elemental analysis.




Eq. 53

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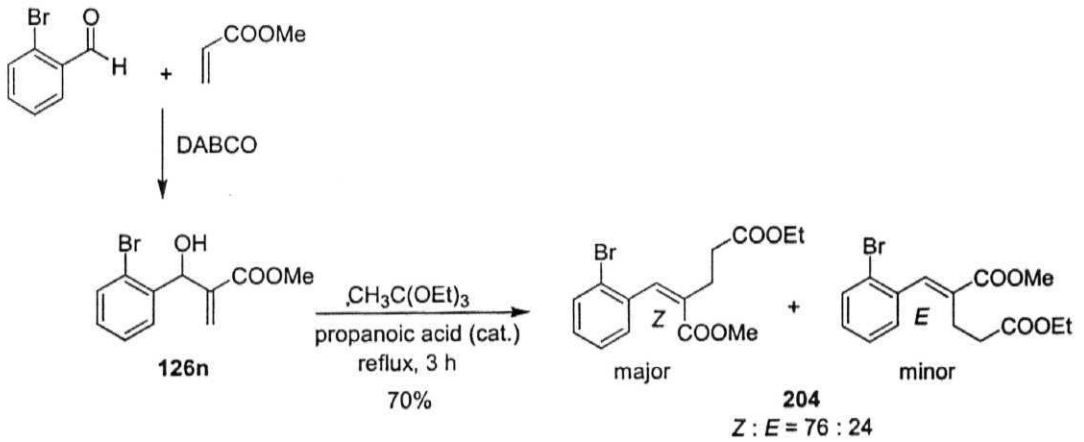
♣ Stereochemical assignments (*Z*- and *E*-stereochemistry) and stereochemical yields (*Z* / *E*) were made on the basis of chemical shift values and integration values of the isomeric β-vinylic proton signals in $^1$H NMR spectra of the crude products. It is well documented in the literature that in the $^1$H NMR spectra of trisubstituted alkenes (with ester group at α-position), the β-vinylic proton *cis* to the ester group appears downfield while the β-vinylic proton *trans* to ester group appears upfield.[215-218] $^1$H NMR spectra of the crude as well as purified sample of **203** indicated the presence of 30% minor (*E*)-isomer. The *E*/*Z* selectivity was determined by the integration ratio of isomeric β-vinylic proton [the β-vinylic proton *cis* to ester group (*E*-isomer) appeared at δ 7.77 with low intensity (30%) while the same proton *trans* to ester group (*Z*-isomer) appears at δ 6.89 with high intensity (70%)]

This was, indeed, a pleasant surprise as this result was opposite to that observed for Baylis-Hillman adducts derived from non *ortho* substituted benzaldehydes[216] (Scheme 72). Then we have examined Johnson-Claisen rearrangement of methyl 3-(2-bromophenyl)-3-hydroxy-2-methylenepropanoate (**126n**), Baylis-Hillman adduct derived from *ortho* bromobenzaldehyde and methyl acrylate (Scheme 73), with triethyl orthoacetate. The resulting product (**204**) was also obtained with high *Z*-selectivity (*Z* / *E* : 76 / 24) as evidenced by $^1$H NMR spectral analysis$^{\pi}$ of the crude as well pure product (Scheme 73, Table 11). Structure of this product (**204**) was in full agreement with spectral data (IR, $^1$H NMR, $^{13}$C NMR) and elemental analysis.

**Scheme 73**




Similar Johnson-Claisen rearrangement of methyl 3-hydroxy-2-methylene-3-(2-nitrophenyl)propanoate (**126o**), the Baylis-Hillman adduct derived from *ortho* nitrobenzald-

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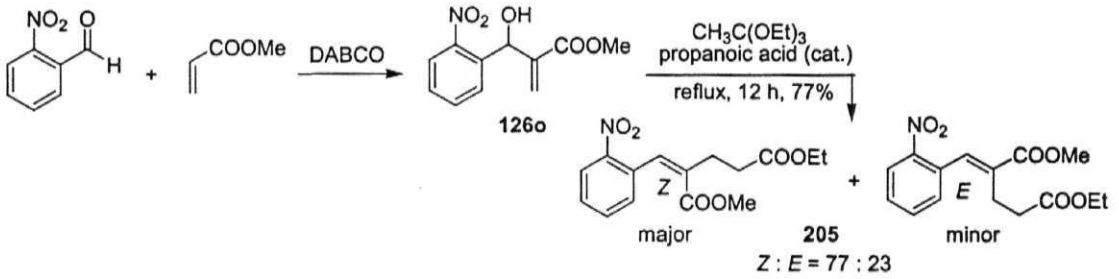
π The *E*/*Z* selectivity was determined by the integration ratio of isomeric β-vinylic protons[215-218] [the β-vinylic proton *cis* to ester group (*E*-isomer) appeared at δ 7.71with low intensity while the same proton *trans* to ester group (*Z*-isomer) appeared at δ 6.84 with high intensity]. Also, see the foot note '♣' in page 92.

ehyde and methyl acrylate (Scheme 74), with triethyl orthoacetate, also provided the resulting product (**205**) with high *Z*-selectivity (*Z* / *E* : 77 / 23) (Scheme 74, Table 11), as evidenced by $^1$H NMR spectral analysis$^{\Upsilon}$ of the crude as well as pure product. Structure of this product (**205**) [obtained as mixture of *Z*- and *E*-isomers (after silica gel column chromatography) with (*Z*)-isomer predominating], was in full agreement with IR, $^1$H NMR (Spectrum 28), $^{13}$C NMR (Spectrum 29) spectral data and elemental analysis.

**Scheme 74**




With a view to understanding the generality of the reaction, we have examined Johnson-Claisen rearrangement of Baylis-Hillman adducts (**126g, 126n-q, 178f-h**),® derived from various alkyl acrylates and *ortho* chloro, *ortho* bromo and *ortho* nitro benzaldehydes (Scheme 75), with various orthoesters (triethyl orthoacetate, triethyl orthopropanoate and trimethyl orthoacetate) (Scheme 75). In all the cases, the resulting products (**206- 218**)§ were obtained with high *Z*-selectivity (*Z* / *E* : 64-89 / 36-11)

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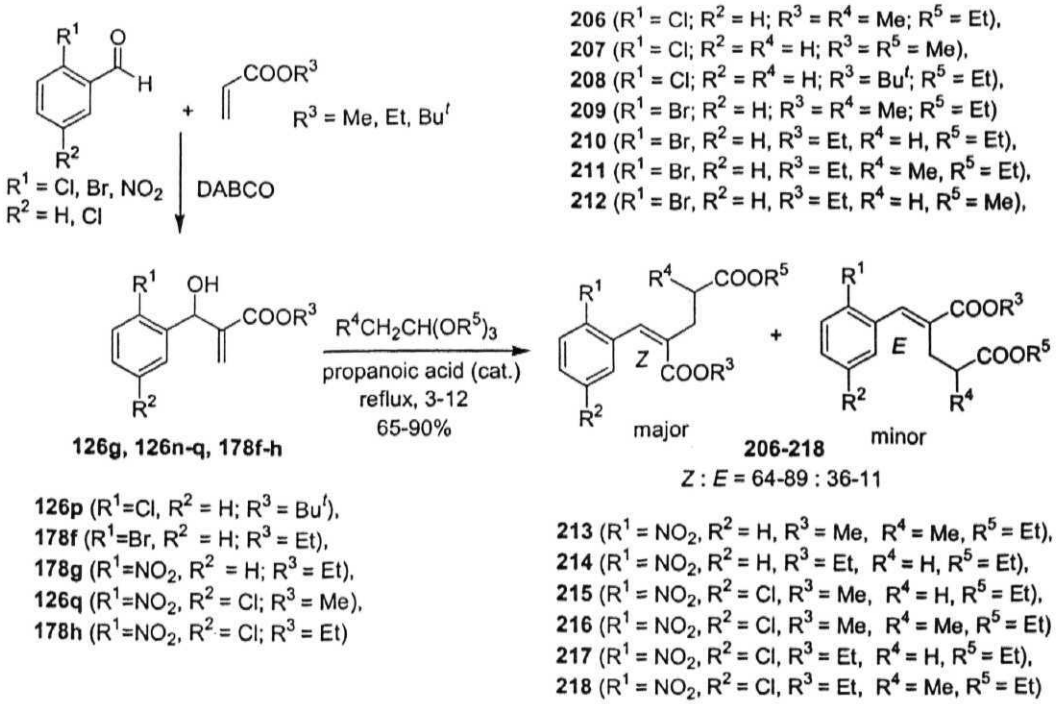
Υ The *E*/*Z* selectivity was determined by the integration ratio of isomeric β-vinylic protons[215-218] [the β-vinylic proton *cis* to ester group (*E*-isomer) appeared at δ 7.97 with low intensity while the same proton *trans* to ester group (*Z*-isomer) appeared at δ 7.21 with high intensity]. Also see the foot note '♣' in page 92.

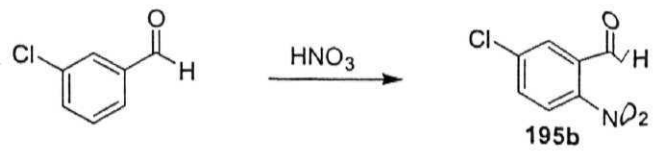
® For continuity and easy understanding, the Baylis-Hillman adducts derived from various 2-substituted benzaldehydes and methyl acrylate / *t*-butyl acrylate were numbered as **126** series (*i.e.*, **126g, 126n-q**) and Baylis-Hillman adducts derived from various 2-substituted benzaldehydes and ethyl acrylate have been numbered **178** series (*i.e.*, **178f-h**). Also, see the foot note '¤' in page no: 79.

as evidenced by $^1$H NMR spectral analysis$^{\varnothing}$ of the crude as well as pure products (**206-218**)$^{\S}$ (Scheme 75, Table 11). Structures of all the products (**206-218**) were in full agreement with IR, $^1$H NMR, $^{13}$C NMR spectral data and elemental analyses.

**Scheme 75**




The required 5-chloro-2-nitrobenzaldehyde (**195b**) was prepared from 3-chlorobenzaldehyde according to the literature procedure (Eq. 54).[282]




**Eq. 54**

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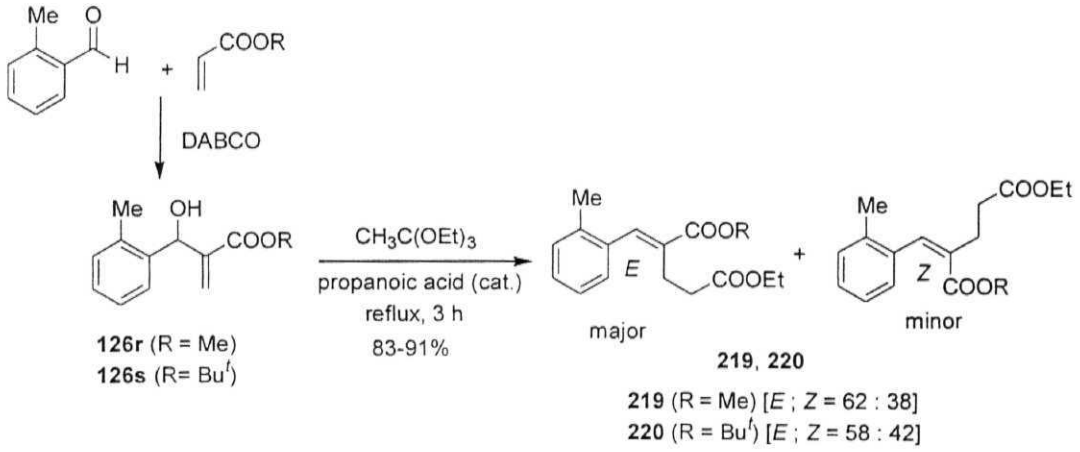
§ For continuity and easy understanding, the Johnson-Claisen rearrangement products of the Baylis-Hillman alcohols, derived from alkyl acrylates (**126g, 126n-q** and **178f-h**), have been given continuous numbers from **203** to **218.**

$^{\varnothing}$ In the $^1$H NMR spectra of the crude as well pure products, the β-vinylic proton *cis* to ester group (*E*-isomer) appeared at δ 7.66-7.96 with low intensity while the same proton *trans* to ester group (*Z*-isomer) appeared at δ 6.94-7.03 with high intensity]. In each case, the *E*/*Z* selectivity was determined by the integration ratio of these isomeric β-vinylic singlets.[215-218]

With a view to understand the effect of 2-methyl group, we prepared the Baylis-Hillman alcohols (**126r**, **126s**) from 2-methylbenzaladehyde and alkyl acrylates (Scheme 76) and subjected these alcohols to Johnson-Claisen rearrangement with triethyl orthoacetate. We had an interesting observation. The resulting products (**219**, **220**) were obtained with major *E*-selectivity (in the case of **219**; *Z* / *E* : 38 / 62 and in the case of **220**; *Z* / *E* : 42 / 58) (Scheme 76, Table 12) as evidenced by $^{1}$H NMR spectral analysis[Σ] of the crude as well as pure products. Structures of pure products (**219**, **220**) (obtained after silica gel column chromatography) were in full agreement with IR, $^{1}$H NMR (Spectrum 30), $^{13}$C NMR (Spectrum 31) spectral data.

**Scheme 76**

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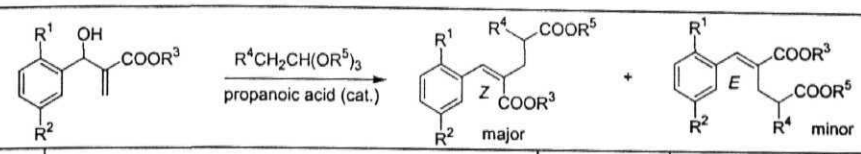
Σ In the case of **219**, the β-vinylic proton *cis* to ester group (*E*-isomer) appeared at δ 7.78 with high intensity while the same proton *trans* to ester group (*Z*-isomer) appeared at δ 6.88 with low intensity. Similarly, in the case of **220**, the β-vinylic proton *cis* to ester group (*E*-isomer) appeared at δ 7.68 with high intensity while the same proton *trans* to ester group (*Z*-isomer) appeared at δ 6.78 with low intensity. The *E*/*Z* selectivities were determined by the integration ratio of these isomeric β-vinylic proton singlets observed in the $^{1}$H NMR spectrum of the crude as well as column purified samples.[215-218] Also, see the foot note ζ, in page 52.

**Table 11: Stereochemical studies in the Johnson-Claisen rearrangement of Baylis-Hillman adducts derived from 2-substituted benzaldehydes.[a]**




| Alcohol | $R^1$, $R^2$, $R^3$, $R^4$, $R^5$ | Product[b] | $Z:E$[c] | Yield[d] % |
|---|---|---|---|---|
| **126g** | $R^1$ = Cl; $R^2$ = $R^4$ = H; $R^3$ = Me; $R^5$ = Et | **203**[e] | 70 : 30 | 87 |
| **126n** | $R^1$ = Br; $R^2$ = $R^4$ = H; $R^3$ = Me; $R^5$ = Et | **204**[e] | 76 : 24 | 70 |
| **126o** | $R^1$ = $NO_2$; $R^2$ = $R^4$ = H; $R^3$ = Me; $R^5$ = Et | **205**[e] | 77 : 23 | 77 |
| **126g** | $R^1$ = Cl; $R^2$ = H; $R^3$ = $R^4$ = Me; $R^5$ = Et | **206** | 69 : 31 | 85 |
| **126g** | $R^1$ = Cl; $R^2$ = $R^4$ = H; $R^3$ = $R^5$ = Me | **207** | 70 : 30 | 83 |
| **126p** | $R^1$ = Cl; $R^2$ = $R^4$ = H; $R^3$ = Bu$^t$; $R^5$ = Et | **208**[e] | 80 : 20 | 86 |
| **126n** | $R^1$ = Br; $R^2$ = H; $R^3$ = $R^4$ = Me; $R^5$ = Et | **209** | 73 : 27 | 90 |
| **178f** | $R^1$ = Br, $R^2$ = H, $R^3$ = Et, $R^4$ = H, $R^5$ = Et | **210**[e] | 79 : 21 | 83 |
| **178f** | $R^1$ = Br, $R^2$ = H, $R^3$ = Et, $R^4$ = Me, $R_5$ = Et | **211** | 77 : 23 | 80 |
| **178f** | $R^1$ = Br, $R^2$ = H, $R^3$ = Et, $R^4$ = H, $R^5$ = Me | **212**[e] | 78 : 22 | 65 |
| **126o** | $R^1$ = $NO_2$, $R^2$ = H, $R^3$ = Me, $R^4$ = Me, $R^5$ = Et | **213**[e] | 80 : 20 | 75 |
| **178g** | $R^1$ = $NO_2$, $R^2$ = H, $R^3$ = Et, $R^4$ = H, $R^5$ = Et | **214**[e] | 84 : 16 | 80 |
| **126q** | $R^1$ = $NO_2$, $R^2$ = Cl, $R^3$ = Me, $R_4$ = H, $R^5$ = Et | **215**[e] | 86 : 14 | 72 |
| **126q** | $R^1$ = $NO_2$, $R^2$ = Cl, $R^3$ = Me, $R^4$ = Me, $R^5$ = Et | **216**[e] | 82 : 18 | 73 |
| **178h** | $R^1$ = $NO_2$, $R^2$ = Cl, $R^3$ = Et, $R^4$ = H, $R^5$ = Et | **217**[e] | 85 : 15 | 71 |
| **178h** | $R^1$ = $NO_2$, $R^2$ = Cl, $R^3$ = Et, $R^4$ = Me, $R^5$ = Et | **218**[e] | 85 : 15 | 71 |

a) All the reactions were carried out on 2 mmol scale of the alcohol (**126g, 126n-q, 178f-h**) with 2 mL of orthoesters in presence of catalytic amount of propanoic acid (5-6 drops) at reflux temperature for 3-12 h.

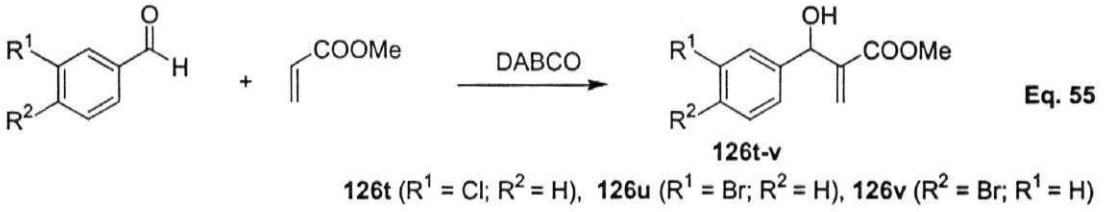
b) In the case of (**203-218**) products were obtained as colorless liquids and are characterized by IR, $^1$H NMR, $^{13}$C NMR spectroscopy.

c) Stereochemical assignments and the *Z*/*E* ratios were based on the chemical shift values and integration ratios of isomeric olefin proton signals in $^1$H NMR of the crude products as well as pure products (**203-218**).

d) Yields are of the pure products (**203-218**) obtained as a mixture of (*Z*)- and (*E*)-isomers after silica gel column chromatography (5-6% EtOAc in hexanes).

e) These compounds were also characterized by elemental analyses.

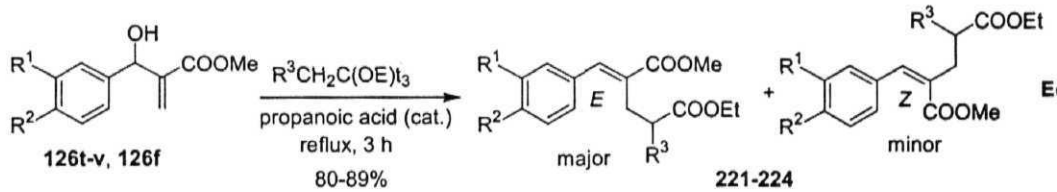
With a view to understand the effect of *meta* chloro / *meta* bromo / *para* chloro / *para* bromo substitution, we have examined Johnson-Claisen rearrangement of the Baylis-Hillman alcohols (**126t-v**©, **126f**) obtained from *meta* chloro / *meta* bromo / *para* chloro / *para* bromo benzaldydes and methyl acryalate (Eq. 55). The resulting products (**221-224**) were obtained with high (*E*)-selectivity (*Z* / *E* : 32-39 / 61-68) (Eq 56, Table 12) which was evident from $^1$H NMR spectral analyses$^{\in}$ of the crude as well as pure products. Structures of these products (**221-224**) were in full agreement with IR, $^1$H NMR (Spectrum 32, for molecule **222**), $^{13}$C NMR (Spectrum 33, for molecule **222**) spectral data.




**126t-v**

**126t** ($R^1$ = Cl; $R^2$ = H), **126u** ($R^1$ = Br; $R^2$ = H), **126v** ($R^2$ = Br; $R^1$ = H)

**Eq. 55**




**126t-v, 126f**

**221-224**

*E* ; *Z* = 61-68 : 32-39

**221** ($R^1$ = Cl; $R^2$ = H; $R^3$ = Me), **222** ($R^1$ = Br; $R^2$ = H; $R^3$ = H),
**223** ($R^1$ = H; $R^2$ = Cl; $R^3$ = H), **224** ($R^1$ = H; $R^2$ = Br; $R^3$ = H)

**Eq. 56**

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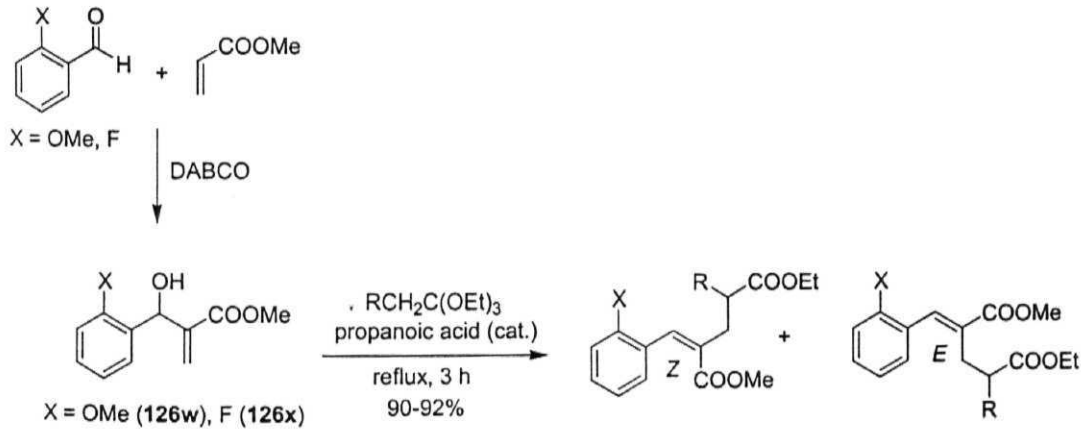
$\in$ *E* / *Z* selectivity was determined by the integration ratio of isomeric β-vinylic proton signals (singlets) observed in the $^1$H NMR spectrum of the crude as well as column purified sample. [the β-vinylic proton *cis* to ester group (*E*-isomer) appeared at δ 7.66-7.64 with high intensity while the same proton *trans* to ester group (*Z*-isomer) appeared at δ 6.64-6.69 with low intensity]. It is well documented in the literature that in the $^1$H NMR spectra of trisubstituted alkenes (with ester group at α-position), the β-vinylic proton *cis* to the ester group appears downfield while the β-vinylic proton *trans* to ester group appears upfield.[215-218]

© For continuity and easy understanding, the Baylis-Hillman adducts derived from *meta* chloro / *meta* bromo / *para* bromo benzaldydes and methyl acryalate were numbered as **126t, 126u** and **126v** respectively.

With a view to understand the effect of 2-methoxy and 2-fluoro groups, we have also examined the Johnson-Claisen rearrangement of the Baylis-Hillman alcohols obtained from 2-methoxybenzaldehyde (**126w**) and 2-flourobenzaldehyde (**126x**) (Scheme 77) with triethyl orthoacetate. The resulting products (**225**, **226**) were obtained with major (*Z*)-selectivity [**225**, *Z* / *E* : 55 / 45 (2-OMe) and **226**, *Z* / *E* : 54 / 46 (2-F)] (Scheme 77) as evidenced by $^{1}$H NMR spectral analysis$^{\Omega}$ of the crude as well as pure products. Structures of these products (**225**, **226**) (obtained as isomeric mixture) were in full agreement with $^{1}$H NMR, $^{13}$C NMR, IR spectral data.

**Scheme 77**

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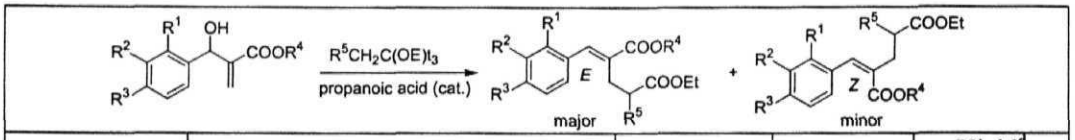
Ω In both the cases (**225**, **226**), the β-vinylic proton *cis* to ester group (*E*-isomer) appeared at δ 7.69 with high intensity while the same proton *trans* to ester group (*Z*-isomer) appeared at δ 6.78 with low intensity]. The *E*/*Z* selectivities were determined by the integration ratio of these isomeric β-vinylic proton peaks observed in the $^{1}$H NMR spectrum of the crude as well as column purified sample.[215-218]

**Table 12: Stereochemical studies in the Johnson-Claisen rearrangement of Baylis-Hillman adducts derived from 2-Me / 3-Cl / 3-Br / 4-Cl / 4-Br substituted benzaldehydes.[a]**



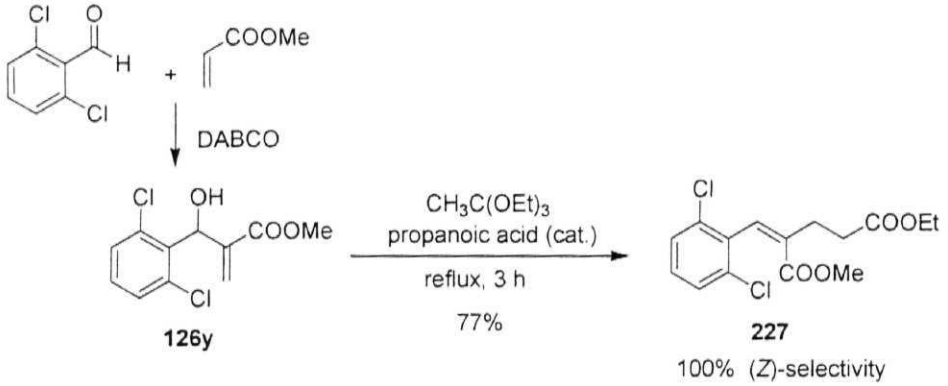

| Alcohol | $R^1$, $R^2$, $R^3$, $R^4$, $R^5$ | Product[b] | $Z : E$[c] | Yield[d] % |
|---|---|---|---|---|
| **126r** | $R^1$ = Me; $R^2$ = $R^3$ = $R^5$ = H; $R^4$ = Me | **219** | 38 : 62 | 91 |
| **126s** | $R^1$ = Me; $R^2$ = $R^3$ = $R^5$ = H; $R^4$ = Bu$^t$ | **220**[e] | 42 : 58 | 83 |
| **126t** | $R^1$ = H; $R^2$ = Cl; $R^3$ = H; $R^4$ = $R^5$ = Me | **221** | 39 : 61 | 80 |
| **126u** | $R^1$ = H; $R^2$ = Br; $R^3$ = $R^5$ = H; $R^4$ = Me | **222** | 32 : 68 | 87 |
| **126f** | $R^1$ = $R^2$ = H; $R^3$ = Cl; $R^4$ = Me; $R^5$ = H | **223** | 35 : 65 | 89 |
| **126v** | $R^1$ = $R^2$ = H; $R^3$ = Br; $R^4$ = Me; $R^5$ = H | **224** | 38 : 62 | 82 |

a) All the reactions were carried out on 2 mmol scale of the alcohol (**126r-v, 126f**) with 2 mL of orthoalkanoate in presence of catalytic amount of propanoic acid (5-6 drops) at reflux temperature for 3 h.
b) All the products (**219-224**) were obtained as colorless liquids and are characterized by IR, $^1$H NMR, $^{13}$C NMR spectroscopy.
c) Stereochemical assignment and the *Z*/*E* ratios were based on the chemical shift values and integration ratios of isomeric olefin proton signals in $^1$H NMR of the crude as well as pure products (**219-224**) (See foot note '∈' in page no: 98).
d) Yields are of the pure product (**219-224**) obtained as a mixture of (*Z*)- and (*E*)-isomers after silica gel column chromatography (5-6% EtOAc in hexanes)
e) This molecule was also characterized by elemental analysis.

With a view to examine the effect of 2,6-dichloro substitution (both in *ortho* position), we have prepared methyl 3-(2,6-dichlorophenyl)-3-hydroxy-2-methylenepropanoate (**126y**), Baylis-Hillman alcohol *via* the reaction between 2,6-dichlorobenzaldehyde and methyl acrylate (Scheme 78). We have then carried out the Johnson-Claisen rearrangement of **126y** with triethyl orthoacetate at reflux temperature for 3 hours in the presence of catalytic amount of propanoic acid. The resulting product (**227**) was obtained with exclusively *Z*-selectivity (*Z* / *E* : 100 / 0) (Scheme 78, Table 13) as

evidenced by $^{1}H$ NMR spectral analysis$^{\Theta}$ of the crude as well as pure product. Structure of pure (*Z*)-product (**227**) was in full agreement with IR, $^{1}H$ NMR (Spectrum 34), $^{13}C$ NMR (Spectrum 35) spectral data and elemental analysis.

**Scheme 78**




This was indeed an encouraging result. We have then subjected this alcohol (**126y**)$^{\blacktriangledown}$ to Johnson-Claisen rearrangement with other orthoesters *i.e.*, triethyl orthopropanoate and trimethyl orthoacetate. In both the cases, the resulting products (**228**, **229**)$^{\copyright}$ were obtained with exclusively *Z*-stereochemistry as evidenced by $^{1}H$ NMR spectral analysis$^{\Theta}$ of the crude as well as pure products (Eq. 57, Table 13). Structures of the pure

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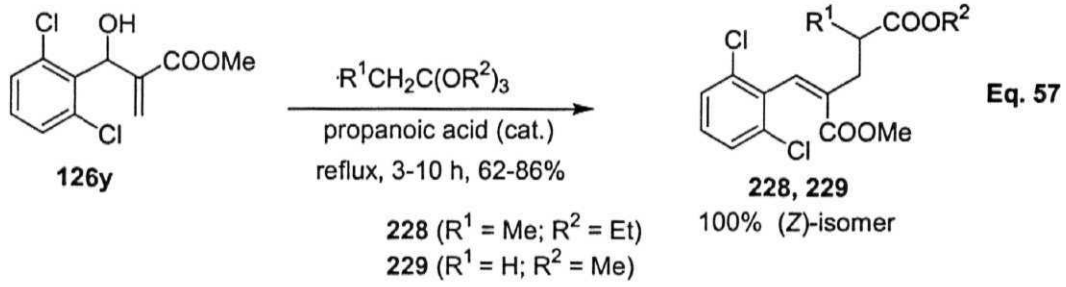
$^{\Theta}$ (*Z*)-Stereochemistry was assigned on the basis of chemical shift value (δ) of the β-vinylic proton signals in $^{1}H$ NMR spectra of the crude as well as pure products. It is well documented in the literature that in the $^{1}H$ NMR spectra of trisubstituted alkenes (with ester group at α-position), the β-vinylic proton *cis* to the ester group appears downfield while the β-vinylic proton *trans* to ester group appears upfield.[215-218] The 100% (*Z*)-selectivity was determined by the absence of *E*-olefinic proton signal in $^{1}H$ NMR spectrum of crude as well as pure product. [in the $^{1}H$ NMR spectrum of the crude as well as column purified sample, the β-vinylic proton signal appeared at δ 6.70-6.72 (*i.e.*, *Z*-olefinic proton) and there was no peak observed in the range δ 7.60-8.00 (*i.e.*, *E*-olefinic proton)].

$^{\blacktriangledown}$ For continuity and easy understanding, the Baylis-Hillman adducts derived from 2,6-dichlorobenzaldehyde and methyl acrylate was numbered as **126y** and Baylis-Hillman adducts derived from 2,6-dichlorobenzaldehyde and ethyl acrylate was numbered as **178i**

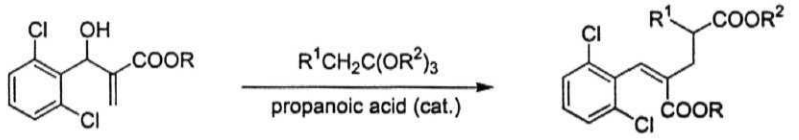
$^{\copyright}$ For continuity and easy understanding, the Johnson-Claisen rearrangement products of the Baylis-Hillman alcohols, derived from **126y**, and **178i** with various orthoesters, have been given continuous numbers from **227** to **232**.

products (**228, 229**)© (obtained after silica gel column chromatography) were in full agreement with all spectral data (IR, $^1$H NMR, $^{13}$C NMR) and elemental analyses.




Eq. 57

**Table 13: Substituent directed stereoselective synthesis of alkyl (4*Z*)-4-alkoxycarbonyl-5-(2,6-dichlorophenyl)pent-4-enoate (227-232).**[a]




| Alcohol | R, R$^1$, R$^2$ | Product[b] | *Z* : *E* | Yield[c] % |
|---|---|---|---|---|
| **126y** | R = Me; R$^1$ = H; R$^2$ = Et | **227** | 100 : 0 | 77 |
| **126y** | R = Me; R$^1$ = Me; R$^2$ = Et | **228** | 100 : 0 | 86 |
| **126y** | R = Me; R$^1$ = H; R$^2$ = Me | **229** | 100 : 0 | 62 |
| **178i** | R = Me; R$^1$ = H; R$^2$ = Et | **230** | 100 : 0 | 77 |
| **178i** | R = Me; R$^1$ = Me; R$^2$ = Et | **231** | 100 : 0 | 80 |
| **178i** | R = Me; R$^1$ = H; R$^2$ = Me | **232** | 100 : 0 | 74 |

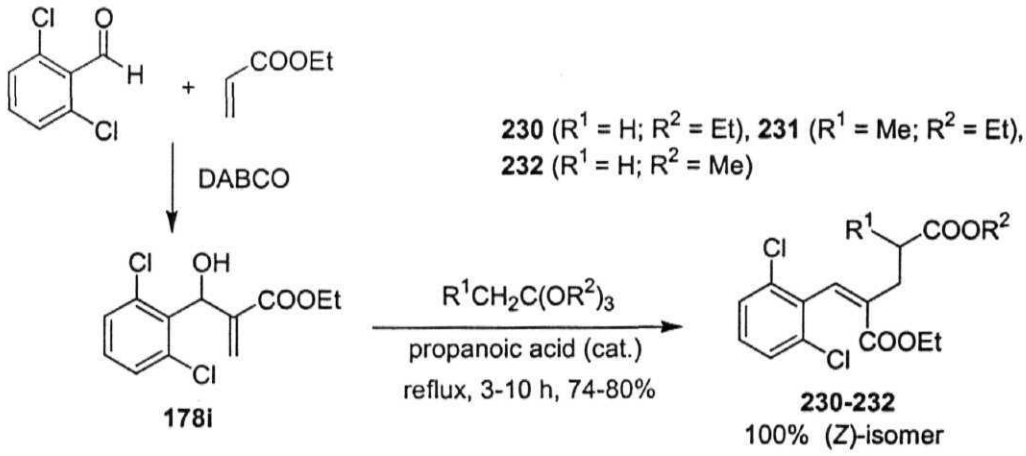
a) All the reactions were carried out on 2 mmol scale of the alcohols (**126y, 178i**) with 2 mL of orthoesters in presence of catalytic amount of propanoic acid (5-6 drops) at reflux temperature for 3-10 h.

b) All the products (**227-232**) were obtained as colorless liquids with 100% (*Z*)-stereochemisrty and gave satisfactory IR, $^1$H NMR, $^{13}$C NMR spectral data and elemental analyses.

c) Yields are of pure (*Z*)-products (**227-232**) obtained after silica gel column chromatography (5-6% EtOAc in hexanes).

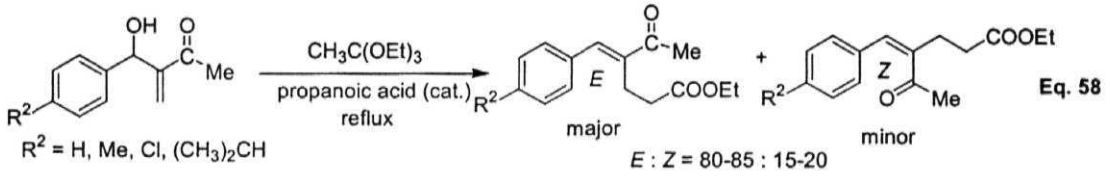
With a view to understand the influence of ester group, we have also prepared ethyl 3-(2,6-dichlorophenyl)-3-hydroxy-2-methylenepropanoate (**178i**)▼ from 2,6-dichlorobenzaldehyde and ethyl acrylate (catalyzed by DABCO in silica gel solid phase medium) (Scheme 79). Then we have examined the Johnson-Claisen rearrangement of this alcohol (**178i**) with various orthoesters *i.e.,* triethyl orthoacetate, triethyl orthopropanoate and trimethyl orthoacetate. In all the cases, the resulting products (**230-232**) were obtained with exclusively *Z*-stereochemistry as evidenced by $^1$H NMR spectral analysis# of the crude as well as pure products (Scheme 79, Table 13). Structures of these molecules (**230-232**) were in full agreement with the spectral data (IR, $^1$H NMR, $^{13}$C NMR) and elemental analyses.

**Scheme 79**



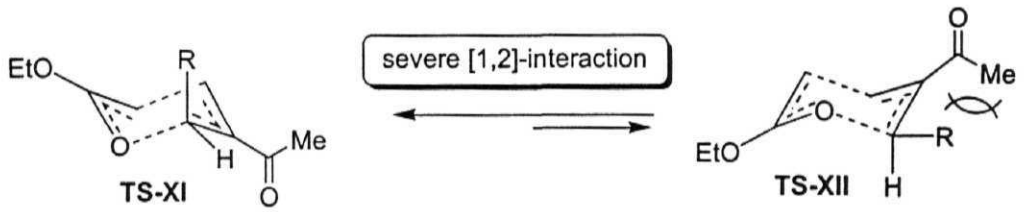

# It is well documented in the literature that in the $^1$H NMR spectra of trisubstituted alkenes (with ester group at α-position), the β-vinylic proton *cis* to the ester group appears downfield while the β-vinylic proton *trans* to ester group appears upfield.[215-218] 100% (*Z*)-Selectivity was determined by the absence of *E*-olefinic proton signal in $^1$H NMR spectrum of crude as well as pure product [in the $^1$H NMR spectrum of the crude as well as column purified sample, the β-vinylic proton signal appeared at δ 6.70-6.72 (*i.e.*, *Z*-olefinic proton) and there was no peak observed in the range of δ 7.60-8.00 (*i.e.*, *E*-olefinic proton)].

Fascinated by these results, and also to understand mechanistic details of the Johnson-Claisen rearrangement, our attention was directed towards the Baylis-Hillman adducts obtained from methyl vinyl ketones. Earlier work in our laboratory[283] revealed that Johnson-Claisen rearrangement of Baylis-Hillman adducts, derived from methyl vinyl ketone and variety of benzaldehydes (without *ortho*-substitution on aryl ring), with triethyl orthoacetate provided the resulting products with high *E*-selelctivity (Eq. 58).




The (*E*)-selectivity was explained by the possible transition state models **XI** and **XII** involving severe [1,2]-interactions (Figure 15)

**Figure 15**

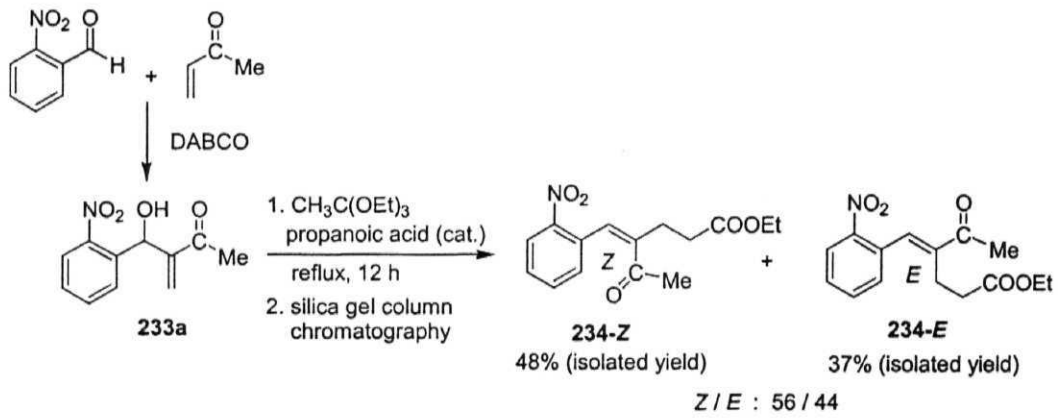



R = Ph, 4-ClPh, 4-(*i*-Pr)Ph, 4-MePh

Since our research group did not earlier examine the Johnson-Claisen rearrangement of the Baylis-Hillman adducts derived from 2-chloro / 2-nitrobenzaldehydes and methyl vinyl ketone, we have now undertaken the work in this direction. Thus, we have examined the Johnson-Claisen rearrangement of 4-hydroxy-3-methylene-4-(2-nitrophenyl)butan-2-one (**233a**), derived from 2-nitrobenzaldehyde and methyl vinyl ketone (Scheme 80), with triethyl orthoacetate. The resulting product (**234**) was

obtained with high (*Z*)-stereoselectivity (Z / E : 56 / 44) as evidenced by $^1$H NMR spectral analysis[Ψ] of crude (Scheme. 80, Table 14). Careful column chromatography of the crude product provided the pure *Z*- isomer in 48% isolated yield and *E*-isomer in 37% isolated yield. Structures of both the isomers were in full agreement with all the spectral data [IR $^1$H NMR (Spectrum 36, for **234-*Z*** and Spectrum 38, for **234-*E***) and $^{13}$C NMR (Spectrum 37, for **234-*Z*** and Spectrum 39, for **234-*E***)] and elemental analysis.

**Scheme 80**




With a view to examine the effect of 2,6-dichloro substitution (both *ortho*) in this case, we have subjected 4-(2,6-dichlorophenyl)-4-hydroxy-3-methylenebutan-2-one (**233b**), the Baylis-Hillman alcohol obtained *via* the reaction of 2,6-dichlorobenzaldehyde with methyl vinyl ketone (Scheme 81), to Johnson-Claisen rearrngement with triethyl ortho-

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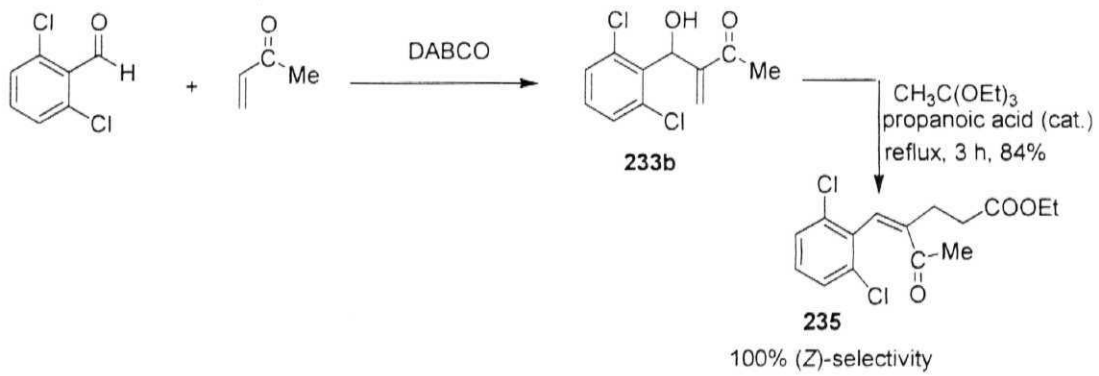
Ψ The *E/Z* selectivity was determined by the integration ratio of isomeric β-vinylic protons observed in $^1$H NMR spectrum of the crude product [the β-vinylic proton *cis* to acetyl (*E*-isomer) appeared at δ 7.84 with lower intensity while the same proton *trans* to acetyl group (*Z*-isomer) appeared at δ 7.08 with high intensity]. It is well documented in the literature that in the $^1$H NMR spectra of trisubstituted alkenes (with carbonyl group at α-position), the β-vinylic proton *cis* to the carbonyl group appears downfield while the β-vinylic proton *trans* to carbonyl group appears upfield.[284, 285]

acetate. The resulting Johnson-Claisen product, ethyl (4*Z*)-4-acetyl-5-(2,6-dichlorophenyl)pent-4-enoate (**235**), was obtained in 84% isolated yield with exclusively (*Z*)-stereochemistry as evidenced by $^1$H NMR spectral analysis of crude as well as pure product[Γ] (Scheme 81, Table 14). Structure of product (**235**) was in full agreement with the spectral data [IR, $^1$H NMR (Spectrum 40), $^{13}$C NMR (Spectrum 41)] and elemental analyses.

**Scheme 81**




We have then subjected this alcohol (**233b**) to Johnson- Claisen rearrngement with trimethyl orthoacetate and triethyl orthopropanoate. The resulting products in these cases were obtained with exclusively (*Z*)-stereochemistry as evidenced by $^1$H NMR spectral analysis[Γ] of crude as well as pure products (Eq. 59, Table 14). Structures of products (**236**, **237**) were in agreement with IR, $^1$H NMR, $^{13}$C NMR spectral data and elemental analyses.

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Γ This 100% (*Z*)-selectivity was determined by the absence of *E*-olefinic proton signal in $^1$H NMR spectrum of crude as well as pure product. It is well documented in the literature that in the $^1$H NMR spectra of trisubstituted alkenes (with carbonyl group at α-position), the β-vinylic proton *cis* to the carbonyl group appears downfield while the β-vinylic proton *trans* to carbonyl group appears upfield.[284, 285] [In the $^1$H NMR spectrum of the crude as well as column purified sample, the β-vinylic proton signal appeared at δ 6.72 (*i.e. Z*-olefinic proton) and there was no peak observed in the range δ 7.60-8.00 (*i.e., E*-olefinic proton)].

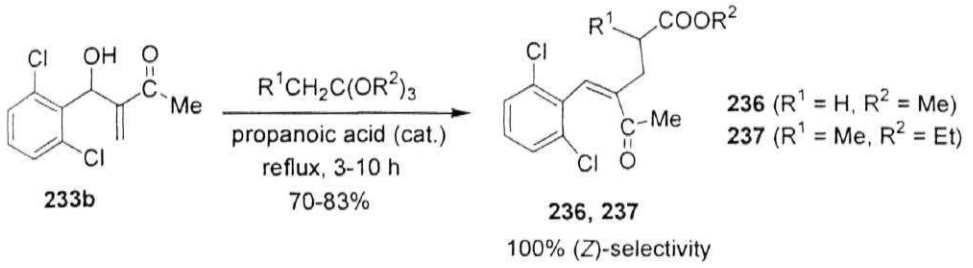



**Table 14: Substitution controlled stereoselective synthesis of alkyl 4-acetyl-5-arylpent-4-enoate (234-237) with major (*Z*)-selectivity** [a]

| Alcohols | Orthoesters | Product[b] | *Z* : *E*[c] | Yield % |
|---|---|---|---|---|
| **233a** | $CH_3C(OEt)_3$ | **234**[d] | 56 : 44 | 85[e] |
| **233b** | $CH_3C(OEt)_3$ | **235**[f] | 100 : 0 | 84 |
| **233b** | $CH_3C(OMe)_3$ | **236**[f] | 100 : 0 | 70 |
| **233b** | $CH_3CH_2C(OEt)_3$ | **237**[f] | 100 : 0 | 83 |

a) All the reactions were carried out on 1 mmol scale of the Baylis-Hillman alcohols (**233a**, **233b**) with 1 mL of orthoesters in presence of catalytic amount of propanoic acid (3 drops) at reflux temperature for 3-12 h.

b) All the pure products were obtained as colorless liquids and gave satisfactory $^1$H NMR, $^{13}$C NMR, IR spectral data.

c) Stereochemical assignments and yields were based on differences in chemical shifts and integration ratios of isomeric olefinic proton signals observed in $^1$H NMR spectra of the crude as well as pure products. (See the foot note 'Γ' in page no: 106).

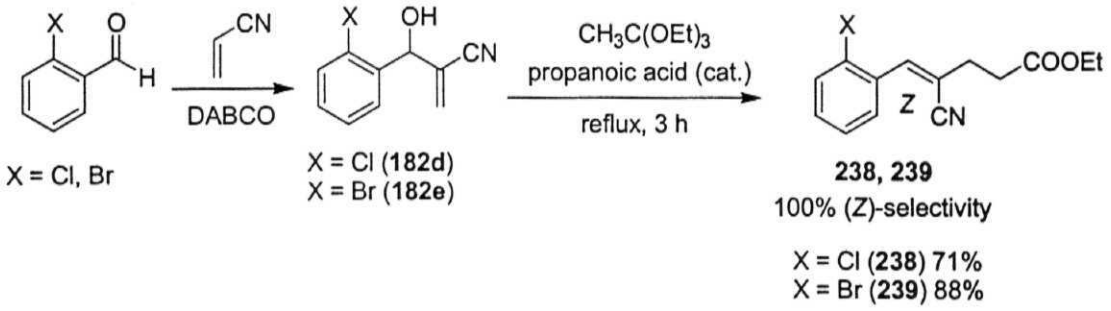
d) Pure (*Z*)-isomer (**234-*Z***) and (*E*)-isomer (**234-*E***) were isolated after a careful silica gel column chromatography (3-5% EtOAc in hexanes).

e) Combined yield of the isolated pure (*Z*)-isomer (**234-*Z***) (48%) and (*E*)-isomer (**234-*E***) (37%).

f) These molecules were also characterized by elemental analyses

With a view to understand the effect of *ortho* substitution on the aromatic ring of Baylis-Hillman adducts, derived from 2-substituted benzaldehydes and acrylonitrile, we have examined the Johnson-Claisen rearrangement of Baylis-Hillman alcohol (**182d, 182e**) derived from 2-chloro / 2-bromo benzaldehydes and acrylonitrile (Scheme 82) with triethyl orthoacetate. The resulting products (**238, 239**) were obtained with exclusively *Z*-selectivity as evidenced by the $^{1}$H NMR spectral analysis$^{\Lambda}$ (Scheme 82) which is in consistent with our earlier reports.[281] These results, thus, demonstrate that *ortho* substitution on aryl group of Baylis-Hillman adducts derived from acrylonitrile (**182d, 182e**) has no effect on stereoselectivity in the Johnson-Claisen rearrangement. Structures of the products (**238, 239**) were in full agreement with IR, $^{1}$H NMR and $^{13}$C NMR spectral data.

**Scheme 82**




X = Cl, Br

X = Cl (**182d**)
X = Br (**182e**)

**238, 239**
100% (*Z*)-selectivity

X = Cl (**238**) 71%
X = Br (**239**) 88%

---

$^{\Lambda}$ In the $^{13}$C NMR spectra of trisubstituted alkenes, allylic carbon *cis* to aryl group appears upfield while same carbon *trans* to aryl group appears downfield.[263-265] The (*Z*)-stereochemistry of compounds **238** and **239** was assigned on the basis of $^{13}$C NMR chemical shift values of allylic methylene carbons (δ 31.08 and 30.73) in comparison with that of allylic methylene carbons of **203** and **204** [δ 29.99 and 29.93 (*Z*-isomer) & 23.03 and 23.09 (of *E*-isomer)][263-269]. Also, see the note '**ξ**' in page no: 36 for detailed explanation. The $^{1}$H NMR spectrum of crude as well as pure products did not show any indication of the presence of (*E*)-isomer.

## Brief summary of the all results in Johnson-Claisen rearrangement of the Baylis-Hillman alcohols:

All the results are summarized in the following five points and are also presented pictorially in Scheme 83.

1) Johnson-Claisen rearrangement of the Baylis-Hillman alcohols (**126g, 126n-q, 178f-h, 233a**) derived from *ortho* chloro, *ortho* bromo and *ortho* nitro benzaldehyedes provide the resulting products (**203-218, 234**) with high (*Z*)-selectivity (Eq. 51, Schemes 73-75, 80; Table 11).

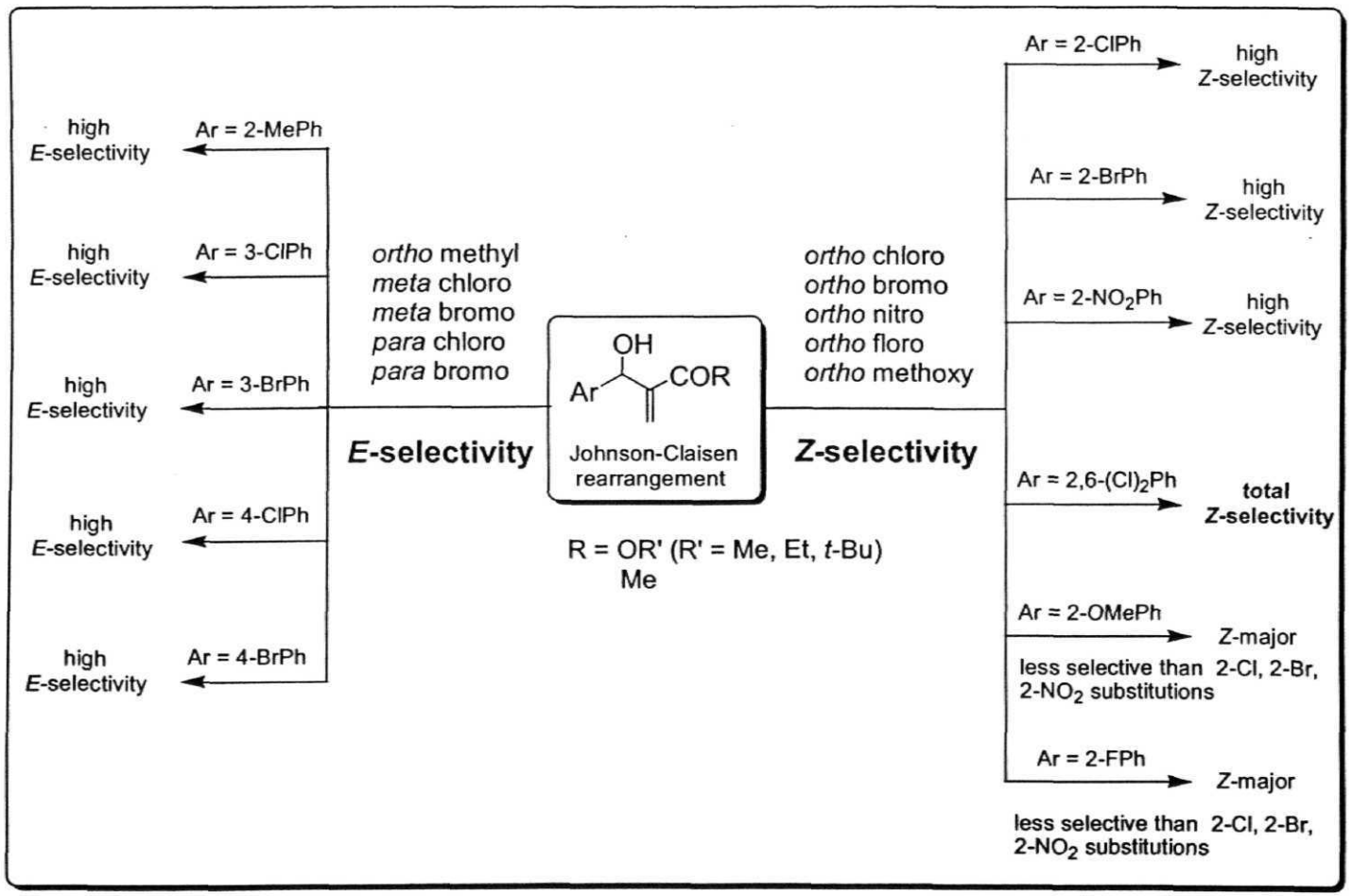
2) Johnson-Claisen rearrangement of the Baylis-Hillman alcohols (**126y, 178i, 233b**) derived from, 2,6-dichlorbenzaldehyede provide the resulting products (**227-232, 235-237**) with total (*Z*)-selectivity (Eq. 57, Scheme 78, 79; Table 13, 14).

3) Johnson-Claisen rearrangement of the Baylis-Hillman alcohols (**126r, 126s**) derived from, *ortho*-methylbenzaldehyede provide the resulting products (**219, 220**) with high (*E*)-selectivity (Scheme 76, Table 12).

4) Johnson-Claisen rearrangement of the Baylis-Hillman alcohols (**126t-v, 126f**) derived from *meta* chloro / *meta* bromo / *para* chloro / *para* bromo benzaldydes provide the resulting products (**221-224**) with high (*E*)-selectivity (Eq. 56, Table 12).

5) Johnson-Claisen rearrangement of the Baylis-Hillman alcohols (**126w, 126x**) derived from, *ortho*-methoxybenzaldehyede and *ortho*-flourobenzaldehyede provide the resulting products (**225, 226**) with reduced (*Z*)-selectivity (Scheme 77).

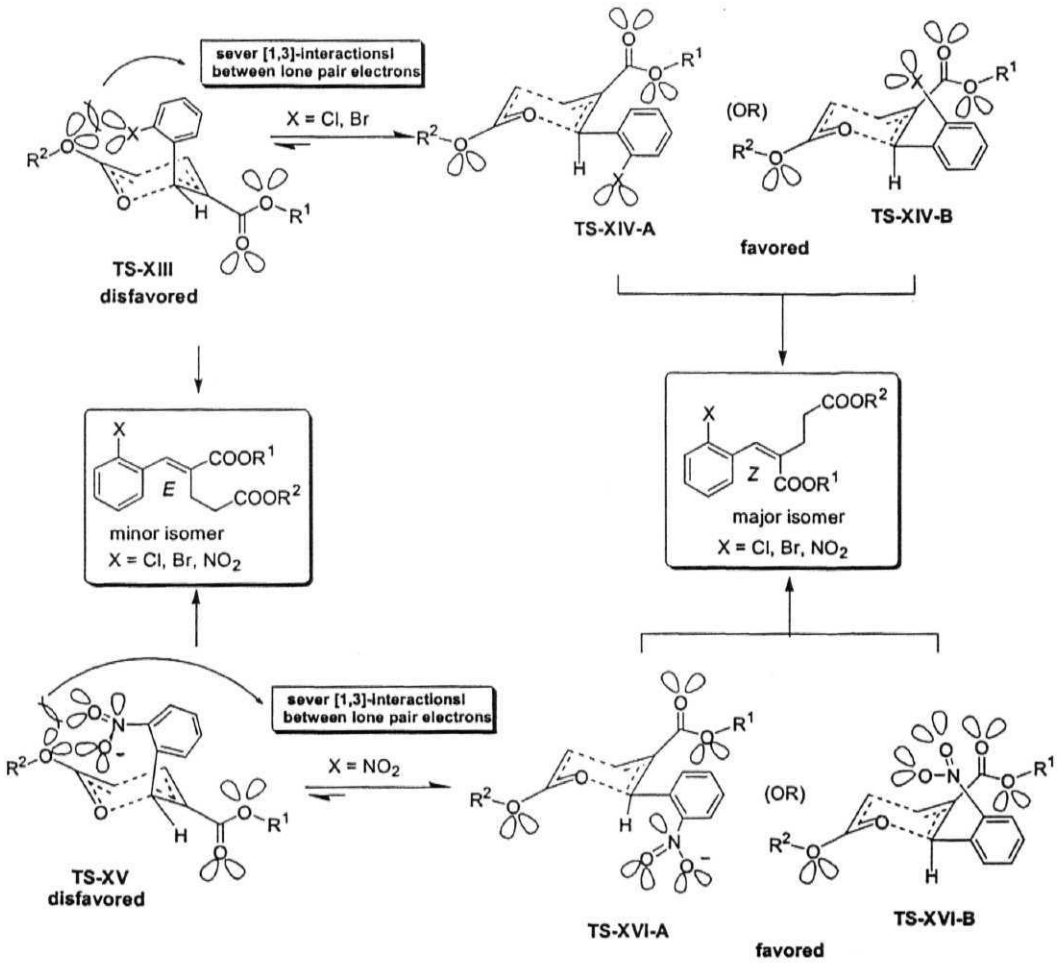
**Scheme 83**


high
E-selectivity
Ar = 2-MePh
high
E-selectivity
Ar = 3-ClPh
high
E-selectivity
Ar = 3-BrPh
high
E-selectivity
Ar = 4-ClPh
high
E-selectivity
Ar = 4-BrPh
ortho methyl
meta chloro
meta bromo
para chloro
para bromo
E-selectivity
OH
Ar
COR
Johnson-Claisen
rearrangement
R = OR' (R' = Me, Et, t-Bu)
Me
ortho chloro
ortho bromo
ortho nitro
ortho floro
ortho methoxy
Z-selectivity
Ar = 2-ClPh
high
Z-selectivity
Ar = 2-BrPh
high
Z-selectivity
Ar = 2-NO2Ph
high
Z-selectivity
Ar = 2,6-(Cl)2Ph
total
Z-selectivity
Ar = 2-OMePh
Z-major
less selective than 2-Cl, 2-Br,
2-NO2 substitutions
Ar = 2-FPh
Z-major
less selective than 2-Cl, 2-Br,
2-NO2 substitutions

## Transition state models for explaining the stereochemical results:

All the above results can be possibly explained using transition state models **TS-XIII** and **TS-XIV** for *ortho* chloro / *ortho* bromo (Scheme 84), **TS-XV** and **TS-XVI** for *ortho* nitro, **TS-XVII**, **TS-XVIII** for *ortho* dichloro (Figure 16) **TS-XIX**, **TS-XX** for *ortho* methyl (Figure 17) and **TS-XXI**, **TS-XXII** for *meta* chloro / *meta* bromo (Figure 18) substituted Baylis-Hillman adducts.

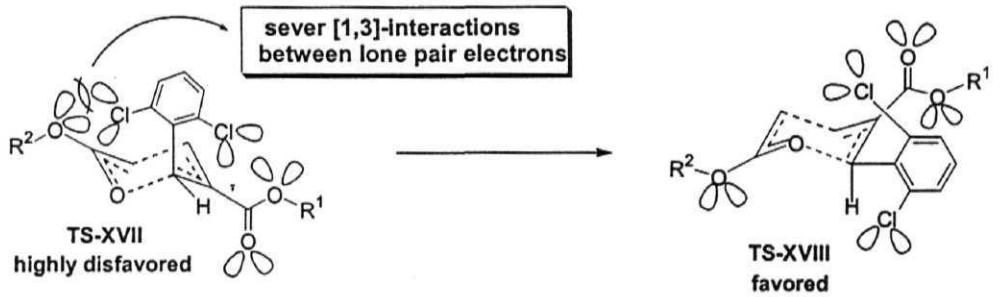
**Scheme 84: Severe [1,3]-interaction due to electronic repulsions**




1) High (*Z*)-selectivity in the case of Baylis-Hillman adducts (**126g, 126n-q, 126y, 178f-i, 233a, 233b**) derived from 2-chloro / 2-bromo / 2-nitro benzaldehyedes might be attributed to severe [1,3]-interaction due to electronic repulsions

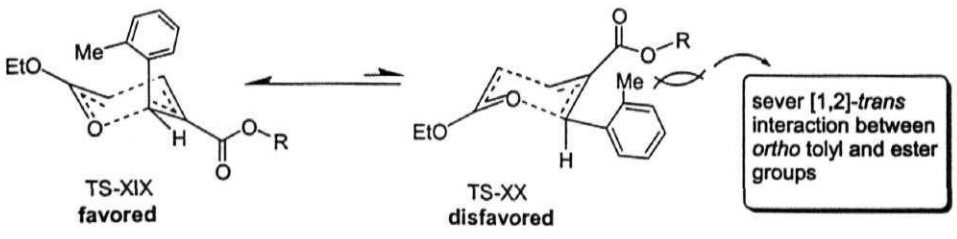
between lone pairs of electrons present on 'O' of ethoxy group and lone pairs of electrons present on Cl / Br / $NO_2$ (substituted at *ortho* position of aryl ring) as depicted in **TS-XIII** (for Cl, Br) and **TS-XV** (for $NO_2$) (Scheme. 84) {*i.e.* [1,3]-interaction in **TS-XIII** probably dominates the [1,2]-interaction in **TS-X1V-A / TS-X1V-B** and [1,3]-interaction in **TS-XV** probably dominates the [1,2]-interaction in **TS-XVI-A / TS-XVI-B** }. In the case of Baylis-Hillman adducts derived from 2,6-dichlorobenzaldehyede (**126y, 178i, 233b**) [1,3]-interaction (**TS-XVII**) totally dominates the [1,2]-interaction (**TS-XVIII**) (due to two *ortho* chloro groups, free rotation around single bond also gives the same [1.3]-electronic repulsions in **TS-XVII**) to provide exclusively (*Z*)-selectivity (Figure 16).

**Figure 16: Severe [1,3]-interaction due to electronic repulsions**



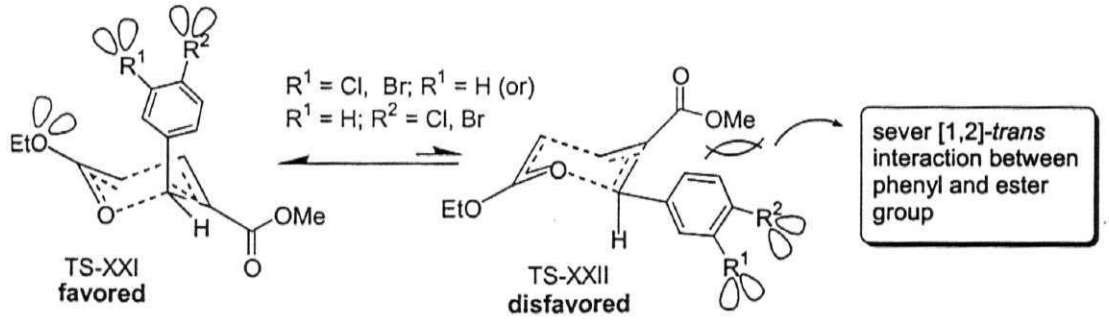

2) (*E*)-Selectivity in the case of Baylis-Hillman adducts (**126r, 126s**) derived from 2-methylbenzaldehyede might be attributed to dominant [1,2]-interaction due to steric repulsions between aryl and ester groups as depicted in the **TS-XX** (Figure 17) {*i.e.* [1,2]-interaction (**TS-XX**) probably dominates [1,3]-interaction (**TS-XIX**)}.

**Figure 17: Severe [1,2]-interaction due to steric repulsions between aryl and ester groups**



3) Similarly, high (*E*)-selectivity in the case of Baylis-Hillman adducts (**126t-v, 126f**) derived from *meta* chloro / *meta* bromo / *para* chloro / *para* bromo benzaldydes might be attributed to the dominance of [1,2]-interaction due to steric repulsions between aryl and ester groups over [1,3]-interactions as depicted in **TS-XXII** (Figure 16). In this case, lone pair of electrons present on Cl / Br / (substituted at *meta* or *para* position of aryl ring) are far from lone pairs of electrons present on 'O' of ethoxy group, thus resulting in less degree of [1,3] electronic repulsions as shown in **TS-XXI**. Thus, **TS-XXI** is favored over **TS-XXII** (Figure 18) as [1,2]-interaction probably dominates the [1,3]-interaction leading to (*E*)-selectivity.

**Figure 18: Severe [1,2]-interaction due to steric repulsions between aryl and ester groups**



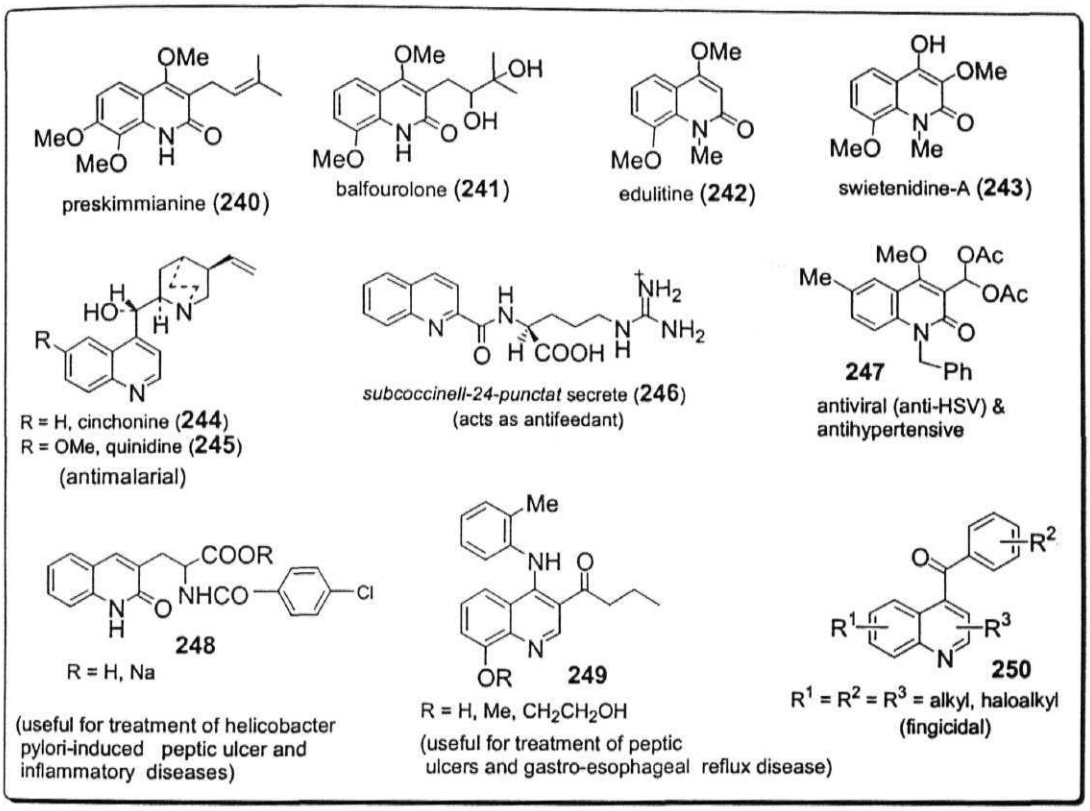

4) Lower levels of (*Z*)-selectivity in the case of Baylis-Hillman adducts (**126w, 126x**) derived from 2-methoxybenzaldehyde and 2-flourobenzaldehyde might be attributed to reduced [1,3]-interaction (caused due to electronic repulsions between lone pair of electrons) because of the increased distance between lone pair electrons of 'O' of ethoxy group and lone pair electrons of F / O (of OMe) as sizes of oxygen and fluorine atoms are smaller than bulky Cl, Br and $NO_2$. This may be also evident, to some extent, from increasing trend of (*Z*)-selectivity in the order of F (*Z* / *E* : 54 / 46 for **226**), O (of OMe) (*Z* / *E* : 55 / 45 for **225**), Cl (*Z* / *E* : 70 / 30 for **203**), Br (*Z* / *E* : 76 / 24 for **204**) and $NO_2$ (*Z* / *E* : 77 / 23 for **205**).

In conclusion, we have revealed a novel substituent dependant stereochemical control in Johnson-Claisen rearrangement of Baylis-Hillman adducts involving an interesting competition between [1,3]- and [1,2]-interactions in the transition states, thus demonstrating the importance of Baylis-Hillman alcohols as possible probes in understanding the stereochemical path way and mechanism of the Johnson-Claisen rearrangement. These studies also helped in developing a simple synthesis of alkyl (4*Z*)-4-alkoxycarbonyl-5-(2,6-dichlorophenyl)pent-4-enoates (**227-232**) and alkyl (4*Z*)-4-acetyl-5-(2,6-dichlorophenyl)pent-4-enoates (**234-237**) in 100% Z-selectivity.

## 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:

(1*H*)-Quinolin-2-one and quinoline are important structural features present in several natural products[286-288] such as preskimmianine (**240**),[289] balfourolone (**241**),[290] edulitine (**242**),[291] swietenidine-A (**243**),[292] cinchonine (**244**), quinidine (**245**) and *subcoccinell-24-punctat* secrete (**246**)[293] (Figure 19). Also, several other synthetic molecules possessing these structural frameworks are found to exhibit some interesting pharmacological activities: For example, **247** acts as antiviral (anti-HSV) & antihypertensive,[294] **248** is useful for treatment of *Helicobacter pylori*-induced peptic ulcer & inflammatory diseases,[294] **249** is useful for treatment of peptic ulcers and gastro-esophageal reflux disease[296] and **250** showed fungicidal activity[297] (Figure 19).

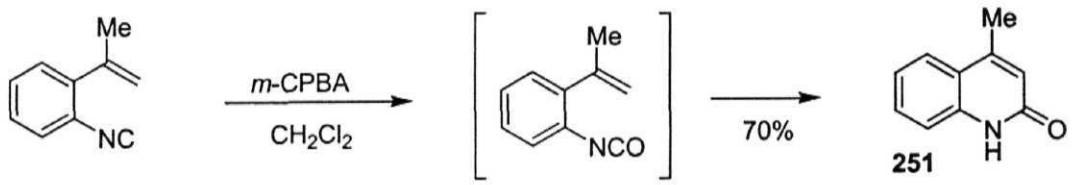
**Figure 19**




Due to biological and medicinal importance of (1*H*)-quinolin-2-one and quinoline derivatives, development of convenient and simple methodologies for the synthesis of (1*H*)-quinolin-2-one and quinoline derivatives represents an interesting and attractive endeavor in organic synthesis. Some of the recent and interesting synthetic strategies are presented in the following.

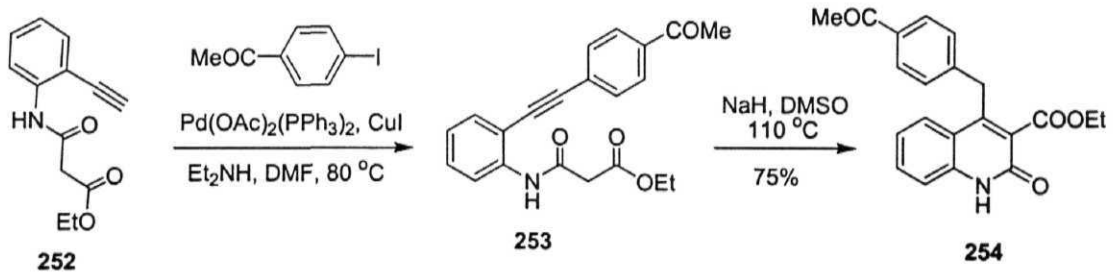
Kobayashi and co-workers[298] have reported a facile synthesis of (1*H*)-quinolin-2-ones (**251**) through the electrocyclic reaction of *o*-isocyanostyrenes generated *in situ via* the reaction with *m*-CPBA. One representative example is presented in Scheme 85.

**Scheme 85**

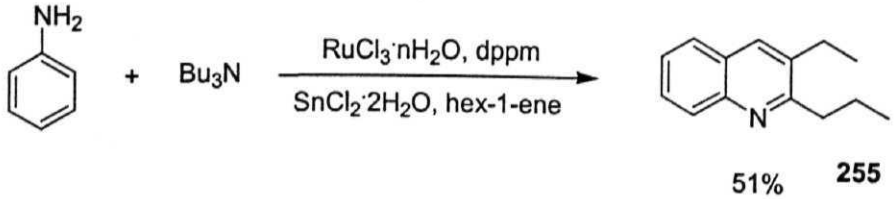



Arcadi and co-workers[299] have reported an interesting synthesis of 3,4-disubstituted (1*H*)-quinolin-2-ones (**254**) *via* cyclization of **253**, obtained by arylation of *N*-(*o*-ethynylphenyl)malonanilide (**252**) with aryl or vinyl halides in the presence of palladium catalyst under basic condition. A representative example is described in Scheme 86.

**Scheme 86**

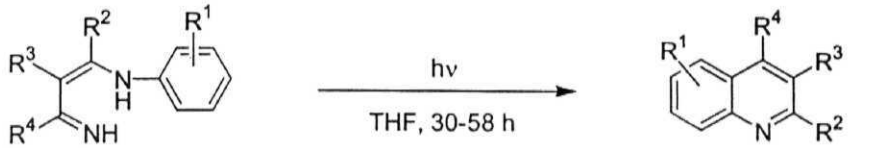



Shim and co-workers[300] have synthesized quinolines (**255**) *via* $RuCl_3 \cdot H_2O$-catalyzed amine exchange reaction between anilines and various trialkyl amines in presence of bis(diphenylphosphino)methane together with $SnCl_2 \cdot 2H_2O$ and hex-1-ene as hydrogen acceptors. One representative example is presented in Eq. 60.




**Eq. 60**

Campos and co-workers described an interesting synthesis of substituted quinolines through the photochemical reaction of 3-amino-2-alkenimines in moderate to good yields Eq. 61.[301]



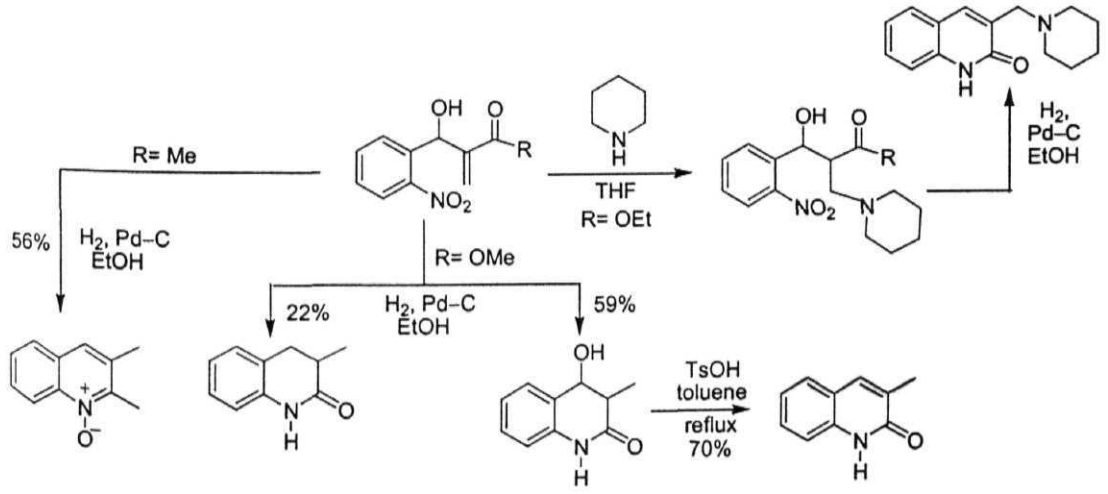

32-95%

**Eq. 61**

$R^1$ = H, 2-Me, 3-Me, 4-Me; $R^2$ = Ph, 4-ClPh
$R^3$ = Me, Et, allyl, propargyl, benzyl
$R^4$ = Ph, 4-MePh, 4-ClPh, cyclohexyl

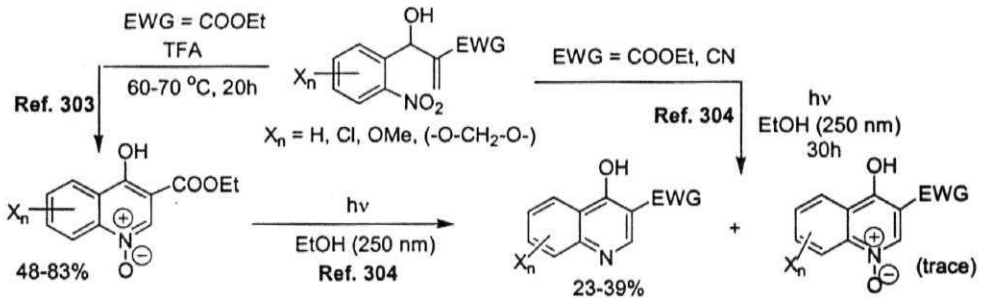
The Baylis-Hillman adducts have also been conveniently transformed into quinoline derivatives. Kaye and co-workers[302] have described an interesting transformation of the Baylis-Hillman adducts, derived from 2-nitrobenzaldehyde and acrylates / alkyl vinyl ketones, into quinoline derivatives under hydrogenation conditions as described in the Scheme 87.

**Scheme 87**



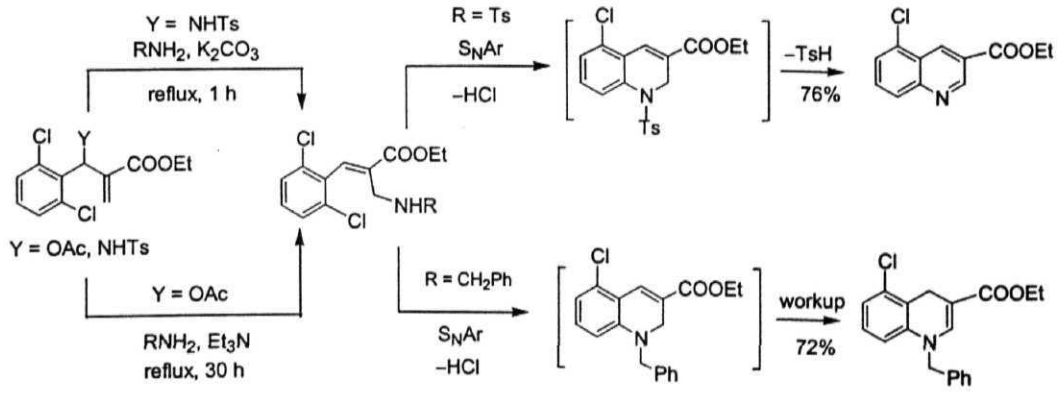
Kim and co-workers[303] have reported an elegant synthesis of 3-ethoxycarbonyl-4-hydroxyquinoline *N*-oxides from the Baylis-Hillman adduct, obtained from 2-nitrobenzaldehydes and ethyl acrylate, *via* the treatment with TFA at 60-70 °C. Subsequently, they have developed a photochemical synthesis of 4-hydroxyquinolines using the Baylis-Hillman adducts (Scheme 88).[304]

**Scheme 88**



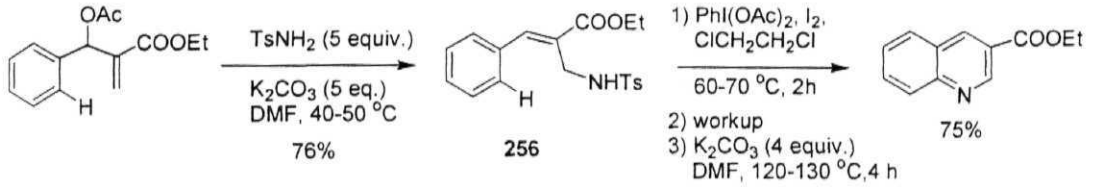

Kim and co-workers have later developed a convenient synthesis of quinoline derivatives from the acetates of Baylis-Hillman adducts, derived from *o*-halobenzaldehydes and ethyl acrylate, and the Baylis-Hillman adducts, derived from *o*-halobenzaldehyde *N*-tosylimines and ethyl acrylate, following reaction sequence as described in Scheme 89.[305-307]

**Scheme 89**



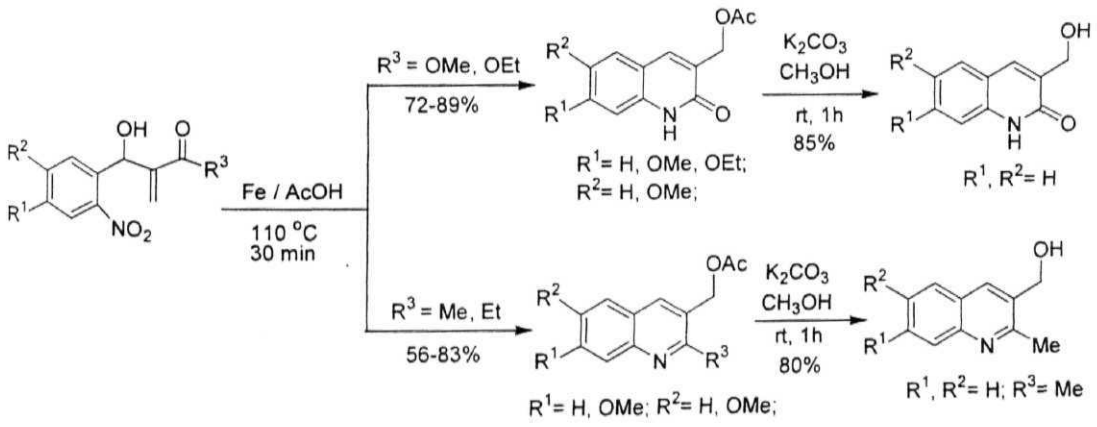
Later, Kim *et al.*[308] have also employed an alternate method for the synthesis of quinoline derivatives *via* the oxidative cyclization of allyl amine derivatives (**256**) (obtained from the Baylis-Hillman acetates) using $PhI(OAc)_2$ in moderate to good yields (Scheme 90).

**Scheme 90**




Our research group has successfully transformed the Baylis-Hillman alcohols derived from *o*-nitrobenzaldehydes and alkyl acrylates into functionalized (1*H*)-quinolin-2-ones *via* the reductive cyclization using Fe/AcOH as reagent (Scheme 91). Our research group has also developed a simple methodology for synthesis of quinolines from the Baylis-Hillman adducts, obtained from *o*-nitrobenzaldehydes and methyl vinyl ketone, *via* the reductive cyclization using Fe/AcOH as described in Scheme 91.[309]

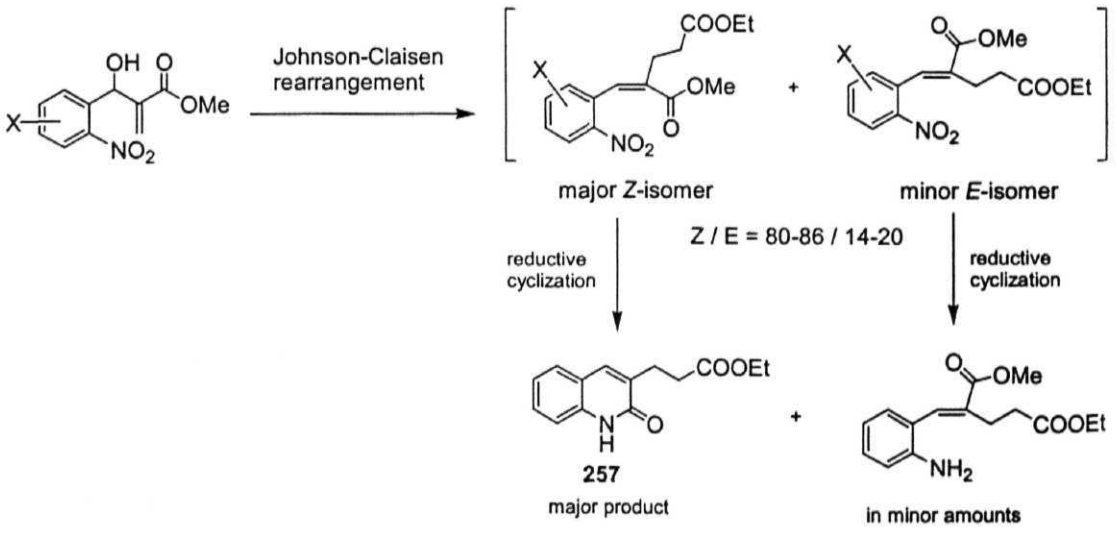
**Scheme 91**



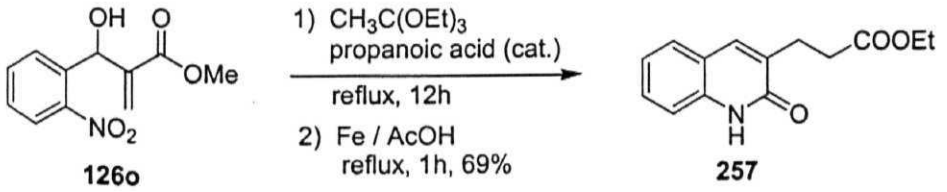
Although there are several methods developed for the synthesis of these quinolinones and quinolines, due to their importance and wide spread applications, development of facile and useful synthetic route for substituted (1*H*)-quinolin-2-one and quinolines with variety of functionality and substitution pattern still continues to be an interesting endeavor in the synthetic organic chemistry.

Our results on the Johnson-Claisen rearrangement of the Baylis-Hillman adducts derived from 2-nitrobenzaldehydes and alkyl acrylates, providing the resulting product with high (Z)-stereoselectivity (*Z* / *E* = 80-86 / 14-20), led us to envision that reductive cyclization of this major (Z)-isomer under appropriate conditions might provide the substituted (1*H*)-quinolin-2-ones (Scheme 92). We have also envisioned that the resulting substituted quinolinones can be easily separated from reduced (E)-isomer. We have also envisaged that Johnson-Claisen rearrangement and reductive cyclization can be carried out in one-pot, to provide the desired quinolinone derivatives, thus leading

**Scheme 92: Strategy for multi-step one-pot synthesis of quinolines**



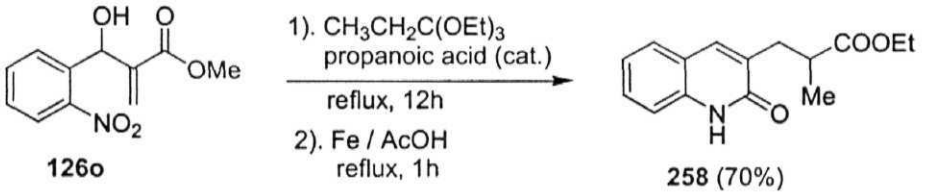
to the development of simple methodology for multi-step one-pot synthesis of quinolines (Scheme 92). In this direction, we have first selected methyl 3-hydroxy-2-methylene-3-(2-nitrophenyl)propanoate (**126o**), Baylis-Hillman alcohol obtained *via* the reaction between 2-nitrobenzaldehyde and methyl acrylate, for examining the multi-step one-pot reaction sequence to provide the desired quinoline derivatives. Best result in this direction was obtained when **126o** (1 mmol) was treated with triethyl orthoacetate (1 mL) in the presence of catalytic amount of propanoic acid (2-3 drops) at reflux temperature (146 °C) for 12 hours followed by the treatment of the resulting product (obtained after removal of excess triethyl orthoacetate under reduced pressure) with Fe (6 equiv) / AcOH (5 mL) at reflux temperature (110 °C) for 1 hour thus providing the expected ethyl 3-(1,2-dihydro-2-oxo-3-quinolinyl)propanoate (**257**) in 69% yield (Eq. 62, Table 15) after usual work-up and followed by column chromatography (30% EtOAc in hexane mixtures). Structure of the product was in full agreement with IR, $^{1}$H NMR (Spectrum 42), $^{13}$C NMR (Spectrum 43) spectral data and elemental analysis.




**Eq. 62**

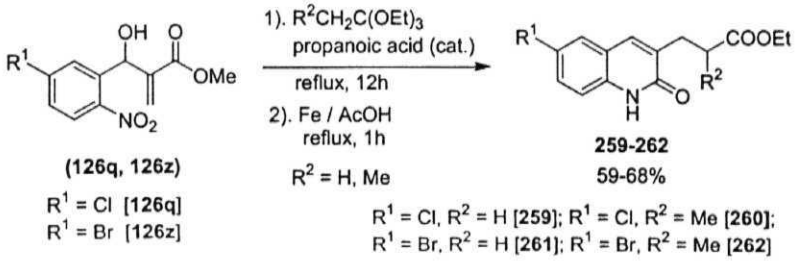
With a view to understand the application of other orthoesters in this multi-step one-pot strategy, we have examined the reaction of **126o** with triethyl orthopropanoate. Thus, the Johnson-Claisen rearrangement of methyl 3-hydroxy-2-methylene-3-(2-nitro-

phenyl)propanoate (**126o**) with triethyl orthopropanoate followed by reductive cyclization of the resulting product with Fe/AcOH for 1 hour at reflux temperature, provided the expected ethyl 3-(1,2-dihydro-2-oxo-3-quinolinyl)-2-methylpropanoate (**258**)[⊗] in 70% yield (Eq. 63, Table 15). Structure of the product was in full agreement with IR, $^{1}$H NMR (Spectrum 44), $^{13}$C NMR (Spectrum 45) spectral data and elemental analysis.




**Eq. 63**

With a view to provide the generality of the reaction, we successfully transformed a representative class of Baylis-Hillman adducts (**126q**, **126z**), derived from 2-nitrobenzaldehydes with methyl acrylate, into (1*H*)-quinolin-2-ones (**259-262**)[⊗] in 59-68% yield *via* Johnson-Claisen rearrangement followed by reductive cyclization in one-pot operation (Eq. 64, Table 15). Structures of all the products (**259-262**) were in full agreement with IR, $^{1}$H NMR, $^{13}$C NMR spectral data and elemental analyses.




**Eq. 64**

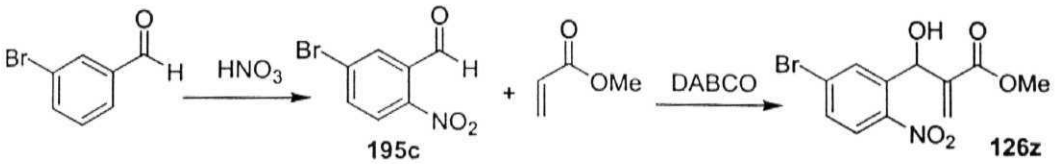
The required 5-bromo-2-nitrobenzaldehyde (**195c**) was prepared from 3-brombenzaldehyde according to the literature procedure[282] (Schemes 93) and the corresponding

---

⊗ For continuity and easy understanding, all the (1*H*)-quinolin-2-ones were given continuous numbers *i.e.*, **257-263**

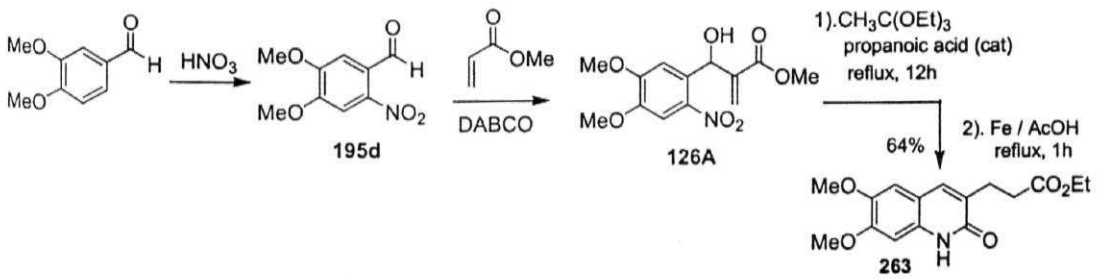
Baylis-Hillman adduct (**126z**) was obtained *via* the treatment this aldehyde (**195c**) with methyl acrylate in the presence of DABCO (Schemes 93).

**Scheme 93**




We have also prepared methyl 3-(4,5-dimethoxy-2-nitrophenyl)-3-hydroxy-2-methyl-enepropanoate (**126A**)[¥] from 4,5-dimethoxy-2-nitrobenzaldehyde (**195d**) (which in turn was prepared according to the literature procedure)[310] (Schemes 94) and subsequently transformed into the desired ethyl 3-(1,2-dihydro-7,8-dimethoxy-2-oxo-3-quinolinyl)propanoate (**263**)[⊗,¥] *via* Johnson-Claisen rearrangement followed by reductive cyclization in one-pot operation (Scheme 94, Table 15). Structure of this product was in full agreement with IR, $^{1}H$ NMR, $^{13}C$ NMR, mass spectral data and elemental analysis. Structure of this product was also rigorously established by single crystal X-Ray crystallography data analysis (Fig. X5, Table 16).

**Scheme 94**




¥ Since the numbering of Baylis-Hillman alcohols of **126** series is completed with **126z** (*i.e.*, numbering from **126a** to **126z** is over) for better understanding and continuity, the Baylis-Hillman alcohol derived from the aldehyde **195d** and methyl acrylate is numbered as **126A** (Also, see the foot note '®' in page no: 94). And, for continuity, the (1*H*)-quinolin-2-one derived from this alcohol (*i.e.*, **126A**) is given **263.**

**Table 15: Synthesis of (1*H*)-quinolin-2-ones (257-263)[a]**

| Alcohol | Orthoester | Product[b] | Yield[c] (%) | m. p. (°C) |
|---|---|---|---|---|
| **126o** | $CH_3C(OEt)_3$ | **257**[d] | 69 | 128-130 |
| **126o** | $CH_3CH_2C(OEt)_3$ | **258** | 70 | 126-128 |
| **126q** | $CH_3C(OEt)_3$ | **259** | 62 | 152-154 |
| **126q** | $CH_3CH_2C(OEt)_3$ | **260** | 68 | 158-160 |
| **126z** | $CH_3C(OEt)_3$ | **261** | 59 | 168-170 |
| **126z** | $CH_3CH_2C(OEt)_3$ | **262** | 62 | 128-130 |
| **126A** | $CH_3C(OEt)_3$ | **263**[d,e] | 64 | 154-156 |

a) All the reactions were carried out on 1 mmol scale of Baylis-Hillman adducts (**126o, 126q, 126z, 126A**) with orthoesters (1 mL) in the presence of propanoic acid (3 drops) followed by the treatment of the resulting products (after removal of the excess orthoester) with Fe (5 equiv) and acetic acid (5 mL).

b) All the pure products (**257-263**) were obtained as colorless solid and gave satisfactory $^1H$ NMR, $^{13}C$ NMR, IR spectral data and elemental analyses.

c) Yields are of the pure compounds (**257-263**) obtained after column chromatography (20-30% EtOAc in hexanes).

d) These compounds were also characterized by mass spectroscopy

e) Structure of this compound was also established by single crystal X-Ray crystallography data (Figure X5, Table 16).

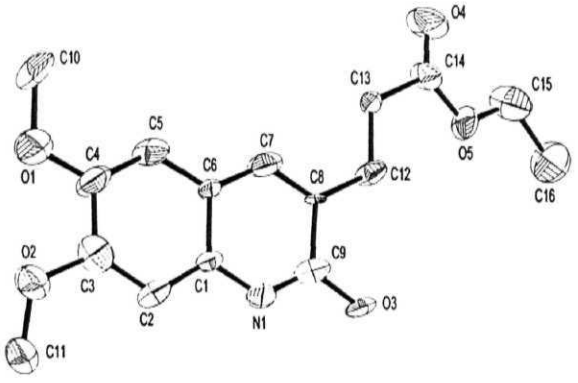



**Figure X5**
**ORTEP diagram of the compound 263**
(*Hydrogen atoms were omitted for clarity*)

From these results (i.e., 59-70% yield of quinolin-2-ones **257-263**) it is quite clear that only Z-isomers, which are formed as major product after Johnson-Claisen rearrangement in these reactions, are undergoing reductive cyclization to provide the desired quinolin-2-ones. While the (*E*)-isomers, which are formed as minor product, after the Johnson-Claisen rearrangement in the reaction, might get converted into aniline derivatives after the treatment with treatment with Fe / AcOH (Scheme 95) which probably get separated from the desired quinoline derivatives while work/purification steps. In fact, in one case (**126o**), we have isolated this aniline derivative, though in less yields, and the structure was in agreement with $^1$H NMR spectrum (however with impurity). A plausible mechanism for the formation (1*H*)-quinolin-2-ones (**257-263**) is presented in the Scheme 95.

**Scheme 95**

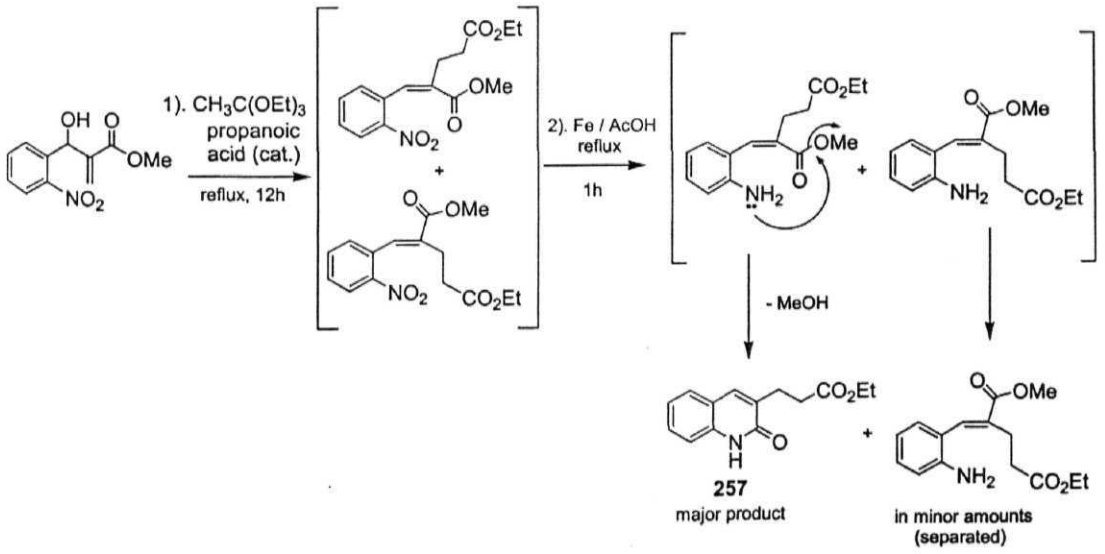
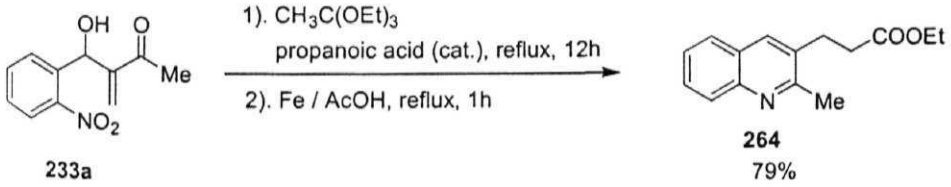


**Table 16: Crystal data and structure refinement for 263**

| | |
|---|---|
| Identification code | : **263** |
| Empirical formula | : $C_{16}H_{19}NO_5$ |
| Formula weight | : 305.32 |
| Temperature | : 293(2) K |
| Wavelength | : 0.71073 Å |
| Crystal system, space group | : Triclinic, P-1 (International Table No: 2) |
| Unit cell dimensions | : a = 7.617(2) Å; $\alpha$ = 86.957(14) deg. |
| | : b = 9.2624(12) Å; $\beta$ = 84.340(18) deg. |
| | : c = 11.942(2) Å; $\gamma$ = 69.774(17) deg. |
| Volume | : 786.6(3) $Å^3$ |
| Z, Calculated density | : 2, 1.289 $Mg/m^3$ |
| Absorption coefficient | : 0.096 $mm^{-1}$ |
| F(000) | : 324 |
| Crystal size | : 0.48 x 0.34 x 0.16 mm |
| Theta range for data collection | : 1.71 to 27.46 deg. |
| Limiting indices | : $0 \leq h \leq 9$, $-10 \leq k \leq 12$, $-15 \leq l \leq 15$ |
| Reflections collected / unique | : 3590 / 3590 [R(int) = 0.0000] |
| Completeness to theta = 27.46 | : 100.0 % |
| Absorption correction | : None |
| Max. and min. transmission | : 0.9848 and 0.9553 |
| Refinement method | : Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | : 3590 / 3 / 398 |
| Goodness-of-fit on $F^2$ | : 0.981 |
| Final R indices [I>2sigma(I)] | : R1 = 0.0751, wR2 = 0.1839 |
| R indices (all data) | : R1 = 0.2055, wR2 = 0.2689 |
| Largest diff. peak and hole | : 0.898 and -0.249 e. $Å^{-3}$ |

Since the Johnson-Claisen rearrangement of 4-hydroxy-3-methylene-4-(2-nitrophenyl)butan-2-one (**233a**) derived from 2-nitrobenzaldehyde and methyl vinyl ketone provides the resulting product with substantial (major) (Z)-selectivity, it occurred to us that reductive cyclization of this mixture might provide, under appropriate conditions, the desired quinoline derivative in reasonable yields. Accordingly, we have treated 4-hydroxy-3-methylene-4-(2-nitrophenyl)butan-2-one (**233a**) (1 mmol), with triethyl orthoacetate in the presence of catalytic amount of propanoic acid (2-3 drops) at reflux temperature (146 °C) for 12 hours. Subsequent reductive cyclization of the residue (obtained after removal of excess triethyl orthoacetate) with Fe (6 equiv) / AcOH (5 mL) at reflux temperature (110 °C) for 1 hour provided the desired product (**264**) in very high yields (79%) after purification through silica gel column chromatography (Eq. 65, Table 17). Structure of the product (**264**) was in full agreement with all spectral data [IR, $^{1}$H NMR (Spectrum 46), $^{13}$C NMR (Spectrum 47)] and elemental analysis.

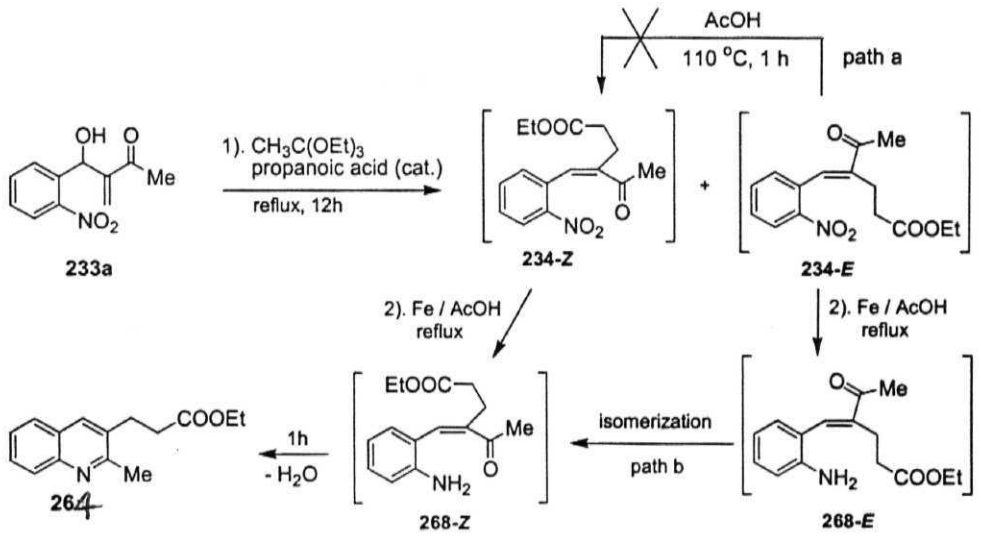



**233a** **264** 79% **Eq. 65**

This result was a pleasant surprise. The very high yield (i.e., 79% yield of the quinoline derivative **264**), despite the presence of ~ 45% of (*E*)-isomer (**234-*E***) in the reaction mixture [Johnson-Claisen rearrangement of 4-hydroxy-3-methylene-4-(2-nitrophenyl)-butan-2-one (**233a**) with triethyl orthoacetate provides the resulting products **234-*E*** and **234-*Z*** in 45 / 55 ratio (Scheme 80)] clearly suggests that (*E*)-isomer (**234-*E***), formed

in the reaction mixture after Johnson-Claisen rearrangement of **233a** might be isomerizing to corresponding (*Z*)-isomer (**234-*Z***) under the reductive cyclization condition (Fe/AcOH). Isomerization of (*E*)-isomer to corresponding (*Z*)-isomer can, in principle, happen in two possible ways *i.e.,* 1). AcOH may cause the isomerization of (*E*)-product (**234-*E***) to corresponding to (*Z*)-product (**234-*Z***) [*i. e.* **234-*E*** to **234-*Z*** as depicted in Scheme 96, *path a*] (OR) 2). Isomerization from *E*-isomer to *Z*-isomer might be occurring after reduction under these conditions (Fe/AcOH) [*i.e.* **268-*E*** to **268-*Z*** as depicted in Scheme 96, *path b*] there by providing high yields of the quinoline derivative **264** (Scheme 96).

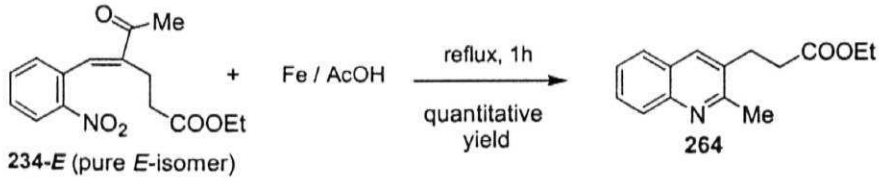
**Scheme 96**




To understand the pathway of the isomerization process, we have first treated the pure *E*-isomer, ethyl (4*E*)-4-acetyl-5-(2-nitrophenyl)pent-4-enoate (**234-*E***) (Please see the page no: 105 for isolation of pure *E* / *Z*-isomers) with AcOH at 110 °C for 1 hour. $^1$H NMR spectral data of the resulting crude product (as well as purified product) clearly

indicated that *E*-isomer was intact as evidenced from the absence of any isomeric Z-olefinic singlet. Thus, this experiment clearly rules out the possibility of isomerization of *E*-isomer into the corresponding *Z*-isomer [*i. e.* **234-*E*** to **234-*Z***, *path a*] under the influence of AcOH.

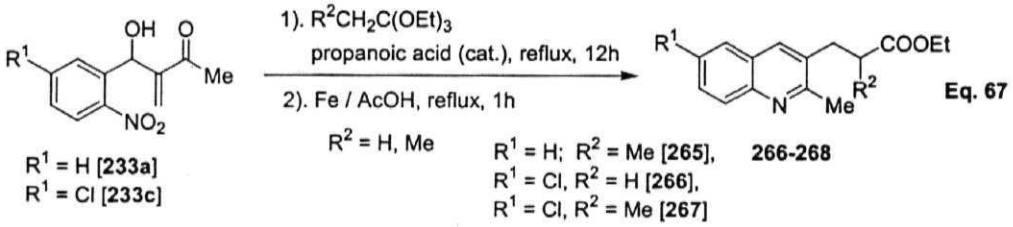
To examine the possibility of isomerization of *E*-isomer into the corresponding *Z*-isomer after reduction, we have carried out the reaction of *E*-isomer with Fe (6 equiv) / AcOH (5 mL) (Eq. 66) at reflux temperature for 1 hour. We were indeed pleased to isolate the pure ethyl 3-(2-methyl-3-quinolinyl)propanoate (**264**) in 85% yield. The spectral data (IR, $^{1}H$ & $^{13}C$ NMR) of this molecule (**264**) was in complete agreement with that of molecule **264** that was obtained *via* the one-pot procedure (Eq. 65). This result clearly demonstrates that *E*-isomer isomerizes into the corresponding *Z*-isomer during reductive cyclization conditions (Fe / AcOH).




**Eq. 66**

Encouraged by this result and to establish the generality of this one-pot multi reaction strategy (Johnson-Claisen rearrangement/reduction/isomerization and cyclization) for the synthesis of quinoline derivatives, we have then successfully transformed the Baylis-Hillman adducts **233a** and **233c,** derived from 2-nitrobenzaldehyde and 5-chloro-2-nitrobenzaldehyde (**195b**), into desired quinolines (**265-267**) *via* the Johnson-Claisen rearrangement with various orthoesters (triethyl orthoacetate and triethyl orthopropanoate) and subsequent reductive cyclization with Fe/AcOH. The resulting

products (**265-267**) were obtained in high yields (73-83%) (Eq. 67, Table 17). Structures of the products were in full agreement with the spectral data (IR, $^1$H NMR, $^{13}$C NMR) and elemental analyses. The required Baylis-Hillman adduct, 4-(5-chloro-2-nitrophenyl)-4-hydroxy-3-methylenebutan-2-one (**233c**), was prepared according to Eq. 68.



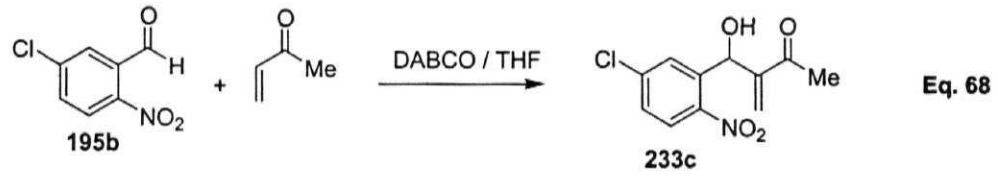




**Table 17: Synthesis of quinolines (264-267)**[a]

| Alcohol | Orthoesters | Product[b] | Yield[c] (%) |
|---|---|---|---|
| **233a** | $CH_3C(OEt)_3$ | **264** | 79 |
| **233a** | $CH_3CH_2C(OEt)_3$ | **265** | 83 |
| **233c** | $CH_3C(OEt)_3$ | **266** | 73 |
| **233c** | $CH_3CH_2C(OEt)_3$ | **267** | 76 |

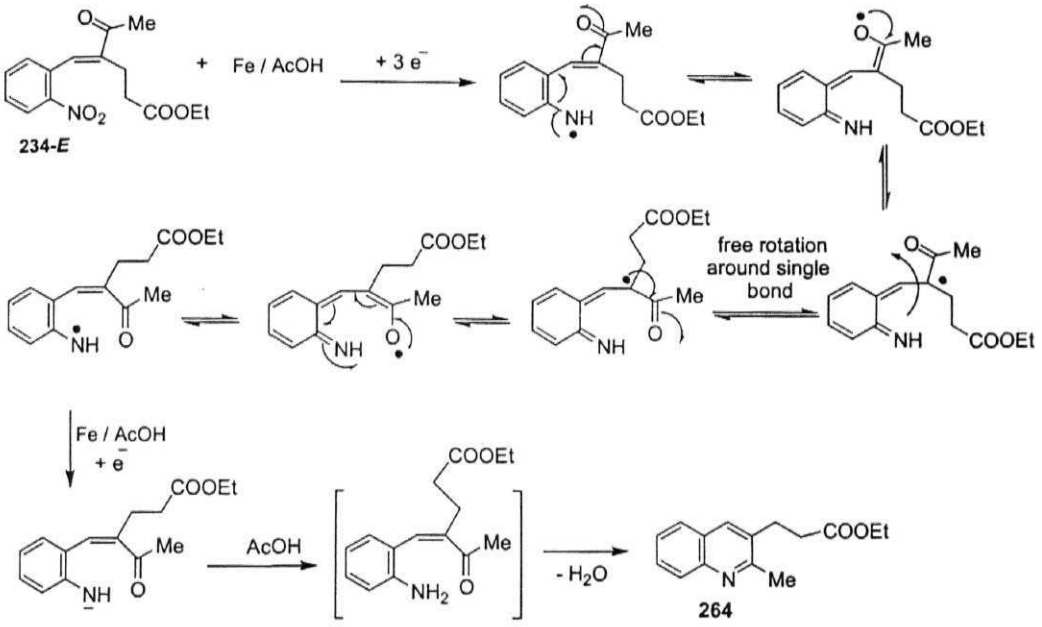
a) All the reactions were carried out on 1 mmol scale of Baylis-Hillman adducts (**233a, 233c**) with orthoesters (1 mL) in the presence of propanoic acid (2-3 drops) followed by the treatment with Fe (6 equiv.) and acetic acid (5 mL) (after removal of the excess orthoester).

b) All the pure products were obtained viscous liquids (**264-267**) and gave satisfactory $^1$H NMR, $^{13}$C NMR, IR, mass spectral data and elemental analyses.

c) Yields are of the pure compounds (**264-267**) obtained after column chromatography (20-30% EtOAc in hexanes).

The plausible mechanism for isomerization / cyclization of *E*-isomer under reductive cyclization conditions is presented in the Scheme 97.[æ]

**Scheme 97**




We have thus developed a facile and convenient methodology for the transformation of the Baylis-Hillman adducts into ethyl 3-(2-oxo-2,3-dihydro-3-quinolinyl)propanoates (**257-263**) [substituted (1*H*)-quinolin-2-ones] and ethyl 3-(2-methyl-3-quinolinyl)propanoates (**264-267**) [substituted quinolines] *via* a novel one-pot multi-reaction strategy involving Johnson-Claisen rearrangement, reduction (and also isomerization in the case of **264-267**) and cyclization.

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æ It is very well known in the literature that reduction of '$NO_2$' to '$NH_2$', using Fe / AcOH, proceeds *via* the radical mechanism. See the reference 10 and references cited therein for the complete mechanistic details of '$NO_2$' reduction using this reagent system.

## CONCLUSIONS:

All the objectives mentioned in the beginning of the chapter have been achieved with considerable success. We have developed a novel methodology for the synthesis of functionalized [4.4.3] and [4.4.4]propellano-bislactones (**130a-g, 134**) starting from the acetates of the Baylis-Hillman adducts in three steps. Also, we have conveniently transformed the acetates of Baylis-Hillman adducts into useful and important class of fused pyrimidones (**156a-i**) in aqueous media in one-pot operation.

We have developed a novel reaction for synthesis of 2-benzazepine derivatives (**184-194**) involving tandem construction of C-N and C-C bonds *via* the simultaneous Ritter and Houben-Hoesch reactions on Baylis-Hillman adducts derived from alkoxy substituted benzaldehydes and alkyl acrylates. We have also successfully transformed the Baylis-Hillman adducts, derived from benzaldehyde / alkyl substituted benzaldehydes and alkyl acrylates, into alkyl (2*E*)-2-acetylaminomethyl-3-arylprop-2-enoate (**177a-c, 179-181**) and Baylis-Hillman adducts, derived from benzaldehyde / alkyl substituted benzaldehydes and acrylonitrile, into (2*Z*)-2-acetylaminomethyl-3-arylprop-2-enenitrile (**183a-c**).

Also, we have investigated the substitution effects on stereochemical direction in Johnson-Claisen rearrangement of the Baylis-Hillman adducts derived from *ortho* substituted benzaldehydes and revealed a novel substituent dependant stereochemical control in Johnson-Claisen rearrangement of the Baylis-Hillman adducts involving an interesting competition between [1,3]- and [1,2]-interactions in the transition states. We

have sucessfully used these results in developing a simple stereoselective synthesis of (*Z*)-trisubstituted alkenes (**203-232, 234-239**) .

We have further developed a facile and convenient one-pot multi-reaction strategy for the transformation of the Baylis-Hillman adducts, derived from various 2-nitrobenzaldehydes and methyl acrylates, into substituted (1*H*)-quinolin-2-ones (*i.e.,* substituted carbostyril derivatives) (**257-263**) and for transformation of the Baylis-Hillman adducts, derived from various 2-nitrobenzaldehydes and MVK into substituted quinolines (**264-267**) involving Johnson-Claisen rearrangement, reduction/isomerization and cyclization.

We believe that these studies further demonstrate the efficacy of Baylis-Hillman adducts in synthesis of important heterocycles and also the importance of Baylis-Hillman adducts in the development of interesting stereoselective transformation methodologies.

# 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.

**Elemental Analysis:** Elemental analyses were performed on a Perkin–Elmer 240C- and Thermo Finnigan Flash EA 1112-CHN analyzer.

**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 (200 MHz/400 MHz) spectra for all the samples were measured in chloroform-d, unless otherwise mentioned, with TMS ($\delta$ = 0 ppm) as internal standard. $^{13}C$ NMR (50 MHz/100 MHz) spectra for all the samples were measured in chloroform-d, unless otherwise mentioned, with its middle peak of the triplet ($\delta$ = 77.10 ppm) as internal standard. Spectral assignments are as follows: (1) chemical shifts on the $\delta$ scale, (2) standard abbreviation for multiplicity, that is, s = singlet, d = doublet, t = triplet, q = quartet, sept = septet, m = multiplet, dd = doublet of doublet, td = triplet of doublet, dt = doublet of triplet, b = broad, d of ABq = doublet of

AB quartet, (3) number of hydrogens integrated for the signal, (4) coupling constant *J* in Hertz.

**Mass Spectral Analysis:** Mass spectra were recorded either on VG7070H mass spectrometer using EI technique or on Auto spec mass spectrometer using LSIMS technique (EI) or on shimadzu LCMS 2010A mass spectrometer.

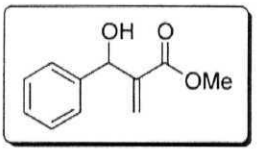
**X-ray Crystallography:**

The X- ray diffraction measurements were carried out at 293 K on an automated Enraf-Nonious MACH 3 diffractometer using graphite monochromated, Mo-Kα ($\lambda$ = 0.71073 $A^0$ ) radiation with CAD4 software. The single crystal was fixed to a capillary head by an appropriate fixing material. Primary unit cell constants were determined with a set of 25 narrow frame scans. Intensity data were collected by the ω scan mode. Stability of the crystal during the measurements was monitored measuring the intensity of the standard reflections after every one and half hour intervals. No appreciable variation of the crystal was detected. The data were reduced using XTAL program. No absorption correction was applied. The structure was resolved by direct methods and refined by full-matrix least-squares using the SHELXS-86 and SHELXL-93 program packages respectively.

**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).

**Methyl 3-hydroxy-2-methylene-3-phenylpropanoate (126a):**

A mixture of benzaldehyde (100 mmol, 10.612 g), methyl acrylate (150 mmol, 12.912 g) and DABCO (15 mol%, 15 mmol, 1.682 g) was kept at room temperature for 7 days. The reaction mixture was diluted with ether (50 mL) and washed successively with 2N HCl, aqueous $NaHCO_3$ solution and water. Organic layer was dried over anhydrous $Na_2SO_4$. Solvent was evaporated and the residue thus obtained was purified by distillation under reduced pressure to provide the pure product (**126a**) as colorless liquid in 78% (15 g).




Bp : 135-137 °C / 4.9mm

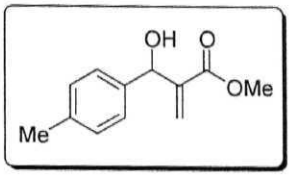
IR (neat) : ν 3452, 1720, 1630 $cm^{-1}$

$^1H$ NMR : δ 3.04 (b, 1H), 3.72 (s, 3H), 5.56 (s, 1H), 5.83 (s, 1H), 5.93 (s, 1H), 7.18-7.52 (m, 5H).

$^{13}C$ NMR : δ 51.62, 72.55, 125.45, 126.56, 127.55, 128.16, 141.38, 142.21, 166.55.

**Methyl 3-hydroxy-2-methylene-3-(4-methylphenyl)propanoate (126b):**

This molecule was obtained as a colorless solid *via* the reaction between 4-methylbenzaldehyde and methyl acrylate catalyzed by DABCO following a similar procedure described for the molecule **126a**.




Reaction time : 8 days

Yield : 70%

Mp : 44-46 °C

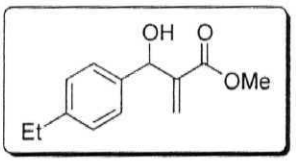
IR (KBr) : ν 3501, 1712, 1620 $cm^{-1}$

$^1H$ NMR : δ 2.34 (s, 3H), 3.45 (b, 1H), 3.66 (s, 3H), 5.50 (s, 1H), 5.89 (s, 1H), 6.31 (s, 1H), 7.13 (d, 2H, $J$ = 8.0 Hz), 7.24 (d, 2H, $J$ = 8.0 Hz).

$^{13}C$ NMR : δ 20.91, 51.61, 72.51, 125.24, 126.51, 128.89, 137.20, 138.44, 142.24, 166.55.

**Methyl 3-(4-ethylphenyl)-3-hydroxy-2-methylenepropanoate (126c):**

This compound was prepared *via* the Baylis-Hillman reaction of 4-ethylbenzaldehyde with methyl acrylate under the catalytic influence of DABCO, as a colorless viscous liquid, following a similar procedure described for the molecule **126a**.




Reaction time : 8 days

Yield : 72%

Bp : 148-152 °C / 4.3 mm

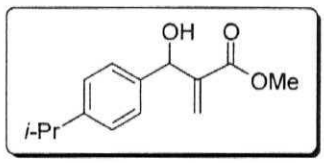
IR (neat) : ν 3433, 1722, 1630, $cm^{-1}$

$^1H$ NMR : δ 1.24 (t, 3H, $J$ = 7.2 Hz), 2.64 (q, 2H, $J$ = 7.2 Hz), 3.15 (b, 1H), 3.68 (s, 3H), 5.52 (s, 1H), 5.58 (s, 1H), 6.31 (s, 1H), 7.16 (d, 2H, $J$ = 8.0 Hz), 7.27 (d, 2H, $J$ = 8.0 Hz).

$^{13}$C NMR : δ 15.44, 28.53, 51.82, 72.82, 125.54, 126.71, 127.69, 138.79, 142.37, 143.80, 166.78.

**Methyl 3-hydroxy-3-(4-isopropylphenyl)-2-methylenepropanoate (126d):**

This molecule was obtained as a colorless viscous liquid *via* the treatment of 4-isopropylbenzaldehyde with methyl acrylate in the presence of DABCO following a similar procedure described for the molecule **126a**.




Reaction time : 8 days

Yield : 70%

Bp : 163-165 °C / 3.6 mm

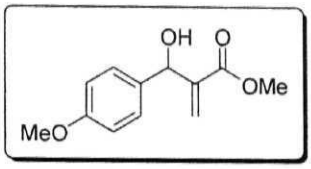
IR (neat) : ν 3435, 1720, 1631 cm$^{-1}$

$^{1}$H NMR : δ 1.24 (d, 6H, $J$ = 6.8 Hz), 2.79-3.00 (m, 2H), 3.73 (s, 3H), 3.55 (d, 1H, $J$ = 4.8 Hz), 5.86 (s, 1H), 6.34 (s, 1H), 7.20 (d, 2H, $J$ = 7.8 Hz), 7.30 (d, 2H, $J$ = 7.8 Hz).

$^{13}$C NMR : δ 23.68, 33.53, 51.48, 72.20, 125.00, 126.12, 126.56, 138.78, 142.25, 148.00, 166.46.

**Methyl 3-hydroxy-2-methylene-3-(4-methoxyphenyl)propanoate (126e):**

This compound was prepared *via* the Baylis-Hillman reaction of 4-methoxybenzaldehyde with methyl acrylate under the influence of DABCO, as a colorless solid following a similar procedure described for the molecule **126a**.




Reaction time : 10 days

Yield : 71%

Mp : 60-62 °C

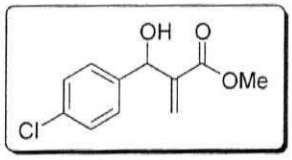
IR (KBr) : ν 3344, 1714, 1620 $cm^{-1}$

$^1H$ NMR : δ 2.76 (b, 1H), 3.70 (s, 3H), 3.79 (s, 3H), 5.51 (s, 1H), 5.51 (s, 1H), 5.86 (s, 1H), 6.86 (d, 2H, $J$ = 8.8 Hz), 7.28 (d, 2H, $J$ = 8.8 Hz).

$^{13}C$ NMR : δ 51.75, 55.12, 72.36, 113.72, 125.20, 127.89, 133.57, 142.30, 159.11, 166.65.

**Methyl 3-(4-chlorophenyl)-3-hydroxy-2-methylenepropanoate (126f):**

This molecule was obtained as a colorless solid *via* the DABCO catalyzed Baylis-Hillman reaction of 4-chlorobenzaldehyde with methyl acrylate following a similar procedure described for the molecule **126a**.




Reaction time : 7 days

Yield : 76%

Mp : 46-48 °C

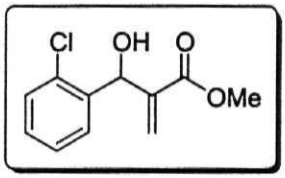
IR (KBr) : ν 3339, 1722, 1635 $cm^{-1}$

$^1H$ NMR : δ 2.99 (b, 1H), 3.71 (s, 3H), 5.51 (s, 1H), 5.81 (s, 1H), 6.33 (s, 1H), 7.30 (s, 4H).

$^{13}C$ NMR : δ 51.88, 72.02, 125.84, 128.19, 128.47, 133.44, 140.15, 142.02, 166.51.

**Methyl 3-(2-chlorophenyl)-3-hydroxy-2-methylenepropanoate (126g):**

This compound was prepared *via* the DABCO catalyzed Baylis-Hillman reaction between 2-chlorobenzaldehyde and methyl acrylate, following a similar procedure described for the molecule **126a**. Column chromatography (5% EtOAc in hexanes, silica gel) of the resulting crude product provided the pure alcohol **126g** as a colorless viscous liquid.




Reaction time : 8 days

Yield : 73%

IR (neat) : ν 3441, 1722, 1631 $cm^{-1}$

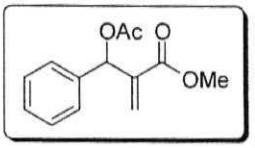
$^1H$ NMR : δ 3.77 (b, 1H & s, 3H), 5.18 (s, 1H), 5.98 (s, 1H), 6.33 (s, 1H), 7.12-7.40 (m, 4H).

$^{13}C$ NMR : δ 51.49, 68.88, 126.69, 126.95, 128.18, 128.92, 129.40, 132.84, 138.65, 141.08, 166.85.

**Methyl 3-acetoxy-2-methylene-3-phenylpropanoate (127a):**

To a stirred solution of methyl 3-hydroxy-2-methylene-3-phenylpropanoate (**126a**) (25 mmol, 4.80 g), pyridine (50 mmol, 3.95 g) in dry dichloromethane (25 mL) at °C was added acetyl chloride (50 mmol, 3.92 g). After stirring at room temperature for 2 hours, the reaction mixture was diluted with ether (50 mL) and washed successively with 2N HCl solution water and saturated aqueous $Na_2HCO_3$ solution. Organic layer was dried over anhydrous $Na_2SO_4$. Solvent was removed and the crude product, thus obtained,

was purified by column chromatography (3% EtOAc in hexanes, silica gel) to afford the pure methyl 3-acetoxy-2-methylene-3-phenylpropanoate (**127a**) as colorless liquid in 83% (4.855 g) yield.




IR (neat) : ν 1743, 1726, 1633 $cm^{-1}$

$^1H$ NMR : δ 2.07 (s, 3H), 3.67 (s, 3H), 5.86 (s, 1H), 6.39 (s, 1H), 6.69 (s, 1H), 7.22-7.48 (m, 5H).

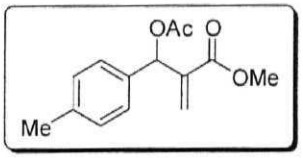
$^{13}C$ NMR : δ 20.94, 51.86, 73.11, 125.68, 127.63, 128.35, 128.43, 137.90, 139.83, 165.36, 169.26.

**Methyl 3-acetoxy-2-methylene-3-(4-methylphenyl)propanoate (127b):**

This molecule was obtained as a colorless viscous liquid *via* the treatment of 3-hydroxy-2-methylene-3-(4-methylphenyl)propanoate (**126b**) with acetyl chloride, in the presence of pyridine, following a similar procedure described for the molecule **127a**.

Reaction time : 2 hours

Yield : 82%



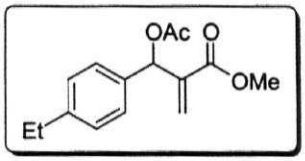

IR (neat) : ν 1745, 1725, 1633 $cm^{-1}$

$^1H$ NMR : δ 2.08 (s, 3H), 2.33 (s, 3H), 3.70 (s, 3H), 5.85 (s, 1H), 6.38 (s, 1H), 6.65 (s, 1H), 7.14 (d, 2H, $J$ = 7.8 Hz), 7.26 (d, 2H, $J$ = 7.8 Hz).

$^{13}$C NMR : δ 21.07, 51.86, 73.00, 125.36, 127.62, 129.12, 134.83, 138.17, 139.78, 165.40, 169.33.

**Methyl 3-acetoxy-3-(4-ethylphenyl)-2-methylenepropanoate (127c):**

This compound was prepared *via* the reaction of methyl 3-(4-ethylphenyl)-3-hydroxy-2-methylenepropanoate (**126c**) with acetyl chloride in the presence of pyridine, as a colorless viscous liquid, following a similar procedure described for the molecule **127a**.




Reaction time : 2 hours

Yield : 80%

IR (neat) : ν 1735, 1724, 1633 cm$^{-1}$

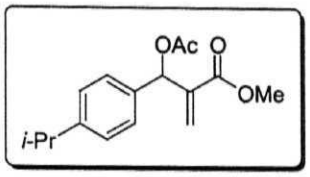
$^{1}$H NMR : δ 1.22 (t, 3H, $J$ = 7.7 Hz), 2.08 (s, 3H), 2.66 (q, 2H, $J$ = 7.7 Hz), 3.70 (s, 3H), 5.85 (s, 1H), 6.37 (s, 1H), 6.65 (s, 1H), 7.16 (d, 2H, $J$ = 7.9 Hz), 7.28 (d, 2H, $J$ = 7.9 Hz).

$^{13}$C NMR : δ 15.19, 20.86, 28.40, 51.72, 72.90, 125.23, 127.58, 127.81, 134.97, 139.78, 144.29, 165.28, 169.18.

**Methyl 3-acetoxy-3-(4-isopropylphenyl)-2-methylenepropanoate (127d):**

Treatment of methyl 3-hydroxy-3-(4-isopropylphenyl)-2-methylenepropanoate (**126d**) with acetyl chloride in the presence of pyridine, following a similar procedure described for the molecule **127a**, provided **127d** as a colorless viscous liquid.

Reaction time : 2 hours




Yield : 83%

IR (neat) : ν 1747, 1735, 1633 $cm^{-1}$

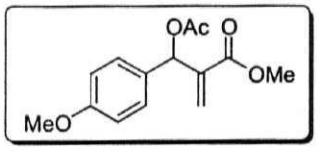
$^1H$ NMR : δ 1.23 (d, 6H, $J$ = 6.8 Hz), 2.09 (s, 3H), 2.88 (sept, 1H, $J$ = 6.8 Hz), 3.71 (s, 3H), 5.85 (s, 1H), 6.38 (s, 1H), 6.66 (s, 1H), 7.18 (d, 2H, $J$ = 7.0 Hz), 7.29(d, 2H, $J$ = 7.0 Hz).

$^{13}C$ NMR : δ 20.96, 23.79, 33.75, 51.81, 72.95, 125.32, 126.46, 127.60, 135.09, 139.67, 148.95, 165.38, 169.28.

**Methyl 3-acetoxy-3-(4-methoxyphenyl)-2-methylenepropanoate (127e):**

Treatment of methyl 3-hydroxy-3-(4-methoxyphenyl)-2-methylenepropanoate (**126e**) with acetyl chloride in the presence of pyridine, following a similar procedure described for the molecule **127a**, provided **127e** as a colorless solid.

Reaction time : 2 hours




Yield : 84%

Mp : 51-53 °C

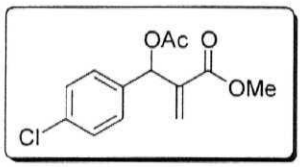
IR (KBr) : ν 1741, 1718, 1633 $cm^{-1}$

$^1H$ NMR : δ 2.09 (s, 3H), 3.70 (s, 3H), 3.79 (s, 3H), 5.87 (s, 1H), 6.37 (s, 1H), 6.64 (s, 1H), 6.86 (d, 2H, $J$ = 8.7 Hz), 7.30 (d, 2H, $J$ = 8.7 Hz).

$^{13}C$ NMR : δ 20.87, 51.72, 55.08, 72.77, 113.80, 124.91, 129.00, 129.86, 139.88, 159.62, 165.32, 169.19.

**Methyl 3-acetoxy-3-(4-chlorophenyl)-2-methylenepropanoate (127f):**

This compound was prepared *via* the reaction of methyl 3-(4-chlorophenyl)-3-hydroxy-2-methylenepropanoate (**126f**) with acetyl chloride in the presence of pyridine, as a colorless viscous liquid, following a similar procedure described for the molecule **127a**.




Reaction time : 2 hours

Yield : 85%

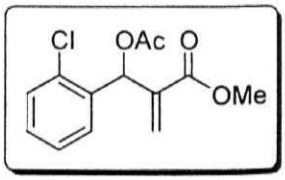
IR (neat) : ν 1745, 1720, 1633 $cm^{-1}$

$^1H$ NMR : δ 2.10 (s, 3H), 3.70 (s, 3H), 5.88 (s, 1H), 6.40 (s, 1H), 6.63 (s, 1H), 7.31 (s, 4H).

$^{13}C$ NMR : δ 20.93, 51.96, 72.42, 125.79, 128.64, 129.07, 134.24, 136.49, 139.35, 165.16, 169.18.

**Methyl 3-acetoxy-3-(2-chlorophenyl)-2-methylenepropanoate (127g):**

This molecule was obtained as a colorless viscous liquid *via* the treatment of methyl 3-(2-chlorophenyl)-3-hydroxy-2-methylenepropanoate (**126g**) with acetyl chloride in the presence of pyridine following a similar procedure described for the molecule **127a**.




Reaction time : 2 hours

Yield : 81%

IR (neat) : ν 1745, 1725, 1639 $cm^{-1}$

$^1$H NMR : δ 2.10 (s, 3H), 3.73 (s, 3H), 5.63 (s, 1H), 6.45 (s, 1H), 7.02 (s, 1H), 7.18-7.47 (m, 4H).

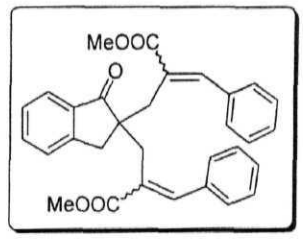
$^{13}$C NMR : δ 20.77, 52.03, 70.13, 126.87, 127.73, 128.44, 129.58, 129.86, 133.70, 135.44, 138.32, 165.32, 169.08.

**2,2-Bis[(2*E*)-2-methoxycarbonyl-(3-phenyl)prop-2-en-1-yl]indan-1-one (128a):**

To oil free NaH (10 mmol, 0.24 g) in dry benzene (15 mL), were added 1-indanone (**125**) (2 mmol, 0.264 g) and methyl 3-acetoxy-2-methylene-3-phenylpropanoate (**127a**) (5 mmol, 1.17 g) at room temperature and heated at 80°C for 30 hours under $N_2$ atmosphere. Then, the reaction mixture was allowed to come to room temperature and then cooled to 0°C. Excess NaH was quenched with very slow and careful addition of acetic acid (1 mL). Reaction mixture was diluted with water (15 mL) and extracted with ether (3 x 20 mL). Combined organic layer was dried over anhydrous $Na_2SO_4$. Solvent was evaporated and the crude product, thus obtained, was purified by column chromatography (10% ethyl acetate in hexanes) to provide 0.72 g (75%) of **128a** as viscous liquid. This compound is contaminated with (*Z*)-isomer (≈ 10-12%) and other unidentified impurities (≈ 5%) as evidenced by the spectral analysis.

IR (neat) : ν 1709, 1630 cm$^{-1}$

$^1$H NMR (major *E*-along with minor *Z*) : δ 2.82-3.62 (m, 12H), 6.58 (s) & 7.01-7.69 (m, 16H).




*Singlet at δ 6.58 (Z-olefinic proton) with low intensity indicates the presence of (Z)-*

*isomer (≈ 10-12%). $^1H$ NMR spectrum also indicated the presence other unidentified impurity (≈ 5%).*

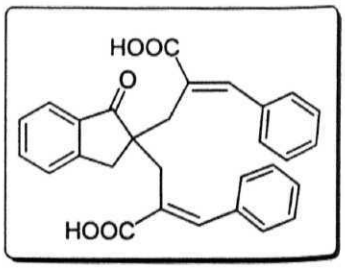
$^{13}C$ NMR (major isomer) : δ 33.58, 36.48, 51.62, 53.98, 123.66, 126.08, 127.20, 127.98, 128.45, 128.62, 129.16, 130.20, 134.60, 135.47, 141.84, 152.58, 168.73, 208.02.

*$^{13}C$ NMR spectrum also showed some minor peaks, which arise due the presence minor Z-isomer (≈ 7-8%) and unidentified impurity (≈ 5%).*

Since we are converting this diester (**128a**) to diacid (**129b**), no attempt was made to further purify this compound. This molecule, as such, was subjected to hydrolysis to provide the pure diacid (**129a**) as described below.

**2,2-Bis[(2*E*)-2-carboxy-3-phenylprop-2-en-1-yl]indan-1-one (129a):**

To a solution of 2,2-bis[(2*E*)-2-methoxycarbonyl-3-phenylprop-2-en-1-yl]indan-1-one (**128a**, obtained as above) (1 mmol, 0.48 g) in MeOH (2 mL), was added a solution of KOH (85% KOH pellets, 1 g) in MeOH (4 mL). After stirring for 3 hours at room temperature, MeOH was removed. Then the reaction mixture was diluted with water (15 mL) and washed with ether (2 x 20 mL) to remove any organic impurities. Aqueous layer was acidified with 2N HCl solution and extracted with ethyl acetate (3 x 20 mL). Combined organic layer was dried over anhydrous $Na_2SO_4$ and concentrated. The crude product thus obtained, was purified by crystallization [ethyl acetate/hexanes (1 : 2) to provide biscinnamic acid (**129a**) as crystalline solid (0.32 g, 71%) with exclusive (*E*)-stereochemistry.




Mp : 161 °C

IR (KBr) : ν 3350-2300, 1711, 1680, 1628 $cm^1$

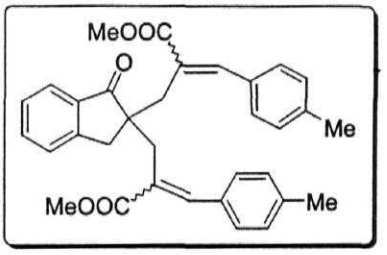
$^1$H NMR : δ 2.99 & 3.17 (ABq, 4H, $J$ = 14.2 Hz),* 3.13 (s, 2H),* 3.85 (b, 2H), 7.15-7.58 (m, 14H), 7.76 (s, 2H).

** One of the peaks of AB quartet is merged with singlet at δ 3.13.*

$^{13}$C NMR : δ 33.08, 37.28, 54.39, 124.29, 126.14, 127.40, 128.75, 128.98, 129.44, 134.87, 135.18, 136.03, 144.09, 153.09, 173.72, 208.96.

**2,2-Bis[(2*E*)-2-methoxycarbonyl-3-(4-methylphenyl)prop-2-en-1-yl]indan-1-one (128b):**

This molecule was obtained as a colorless viscous liquid *via* the reaction between 1-indanone (**125**) and methyl 3-acetoxy-3-(4-methylphenyl)-2-methylenepropanoate (**127b**) in the presence of NaH following the similar procedure described for the molecule **128a**.




Reaction time : 30 h

Yield : 74%

IR (neat) : ν 1724, 1709, 1625, 1607 cm$^{-1}$

$^1$H NMR (major *E*-along with minor *Z*) : δ 2.38 (s, 6H), 2.82-3.20 (m, 6H), 3.53 (s, 6H), 6.55 (s) & 6.95-7.72 (m, 14H).

*Singlet at δ 6.55 (Z-olefinic proton) with low intensity indicates the presence of (Z)-isomer (≈ 7-8%). $^1$H NMR spectrum also indicated the presence other unidentified impurity (≈ 5%).*

$^{13}$C NMR (major isomer) : δ 21.23, 33.65, 36.37, 51.47, 54.02, 123.55, 126.02, 127.06, 127.96,

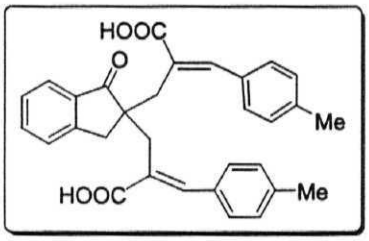
128.66, 129.30, 132.50, 134.46, 138.49, 141.86, 152.64, 168.81, 208.15.

*$^{13}C$ NMR spectrum also showed some minor peaks, which arise due the presence minor Z-isomer (≈ 7-8%) and unidentified impurity (≈ 5%).*

Since we are converting this diester (**128b**) to diacid (**129b**), no attempt was made to further purify this compound. This molecule was, as such, subjected to hydrolysis to provide the pure diacid (**129b**) as described below.

**2,2-Bis[(2*E*)-2-carboxy-3-(4-methylphenyl)prop-2-en-1-yl]indan-1-one (129b):**

Hydrolysis of the above mentioned molecule *i.e.,* 2,2-bis[(2*E*)-2-methoxycarbonyl-3-(4-methylphenyl)prop-2-en-1-yl]indan-1-one (**128b**) using KOH / MeOH, following the similar procedure described for the compound **129a**, provided the bisacid **129b** as a colorless solid.




Reaction time : 3 h

Yield : 70%

Mp : 215 °C

IR (KBr) : ν 3400-2350, 1710, 1678, 1603 $cm^{1}$

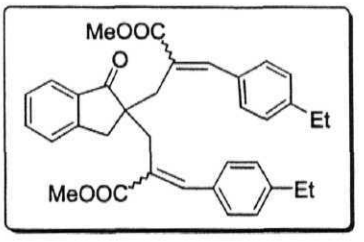
$^{1}H$ NMR (DMSO-$D_6$) : δ 2.33 (s, 6H), 2.78 & 2.98 (ABq, 4H, $J$ = 15.0 Hz),* 2.94 (s, 2H),* 7.09-7.64 (m, 14H), 12.32 (b, 2H).

** One of the peaks of AB quartet is mixed with singlet at δ 2.94.*

$^{13}C$ NMR (DMSO-$D_6$) : δ 21.09, 33.03, 36.00, 53.81, 123.62, 126.42, 127.41, 129.45, 129.95, 132.56, 134.78, 135.52, 138.38, 140.55, 152.39, 169.65, 207.36

**2,2-Bis[(2*E*)-3-(4-ethylphenyl)-2-methoxycarbonylprop-2-en-1-yl]indan-1-one (128c):**

This compound was prepared *via* the treatment of 1-indanone (**125**) with methyl 3-acetoxy-3-(4-ethylphenyl)-2-methylenepropanoate (**127c**) in the presence of NaH, as a colorless viscous liquid, following a similar procedure described for the molecule **128a**.




Reaction time : 30 h

Yield : 70%

IR (neat) : ν 1712, 1628, 1607 $cm^{-1}$

$^1$H NMR (major *E*-along with minor *Z*) : δ 1.19 & 1.27, (2t, 6H, *J* = 7.8 Hz), 2.61 & 2.68 (2q, 4H, *J* = 7.8 Hz), 2.80-3.21 (m, 6H), 3.54 & 3.56 (2s, 6H), 6.58 (s) & 7.01-7.68 (m, 14H).

*The underlined chemical shift values, with low intensity, arise due to minor Z-isomer, Singlet at δ 6.58 with very low intensity indicate the presence of ≈ 5-6% minor Z-isomer. $^1$H NMR spectrum also indicated the presence of other unidentified impurity (≈ 5%).*

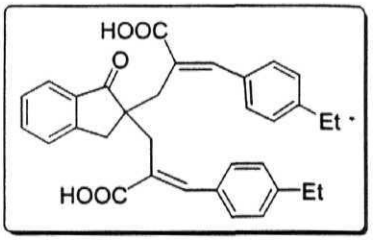
$^{13}$C NMR (major isomer) : δ 15.26, 28.67, 33.63, 36.33, 51.58, 54.05, 123.60, 126.08, 127.13, 128.13, 129.20, 129.51, 132.72, 134.57, 142.02, 144.91, 152.73, 168.91, 208.38.

*$^{13}$C NMR spectrum also showed some minor peaks, which arise due to the presence of minor Z-isomer (≈ 5-6%) and unidentified impurity (≈ 5%).*

Since we are converting this diester (**128b**) to diacid (**129b**), no attempt was made to further purify this compound. This molecule, as such, was subjected to hydrolysis to provide the pure diacid (**129b**) as described below.

**2,2-Bis[(2*E*)-2-carboxy-3-(4-ethylphenyl)prop-2-en-1-yl]indan-1-one (129c):**

This compound was obtained from 2,2-bis[(2*E*)-2-methoxycarbonyl-3-(4-ethylphenyl)-prop-2-en-1-yl]indan-1-one (**128c**) (above obtained product) *via* the treatment with KOH / MeOH, following similar procedure described for the compound **129a**, as a colorless solid.




Reaction time : 3 h

Yield : 75%

Mp : 163–164 °C

IR (KBr) : ν 3400-2300, 1716, 1678, 1604 $cm^{-1}$

$^1H$ NMR : δ 1.24 (t, 6H, *J* = 7.6 Hz), 2.68 (q, 4H, *J* = 7.6 Hz), 3.07 (s, 2H), 2.99 & 3.24 (ABq, 4H, *J* = 14.2 Hz), 7.08-7.61 (m, 12H), 7.75 (s, 2H), 8.35 (b, 2H).

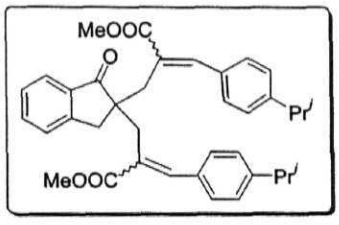
*In addition, the presence of singlet at δ 6.65 with very low intensity indicates the presence of minor Z-isomer (≈ 2%).*

$^{13}C$ NMR : δ 15.21, 28.72, 33.03, 36.80, 54.54, 124.18, 126.02, 127.26, 128.23, 128.32, 129.82, 132.49, 134.64, 136.07, 144.15, 145.53, 152.87, 174.02, 208.86.

**2,2-Bis[(2*E*)-3-(4-isopropylphenyl)-2-methoxycarbonylprop-2-en-1-yl]indan-1-one (128d):**

This molecule was obtained as a colorless viscous liquid *via* the dialkylation of 1-indanone (**125**) with methyl 3-acetoxy-3-(4-isopropylphenyl)-2-methylenepropanoate

(**127d**) in the presence of NaH following the similar procedure described for the molecule **128a**.




Reaction time: 30 h

Yield : 77%

IR (neat) : ν 1710, 1630, 1607 $cm^{-1}$

$^1H$ NMR (major *E*-along with minor *Z*) : δ 1.11-1.41 (m, 12H), 2.81-3.26 (m, 8H), 3.53 (s, 6H), 6.58 (s) & 7.05-7.68 (m, 14H)

*Singlet at δ 6.58 (Z-olefinic proton) with low intensity indicates the presence of ≈ 7-8% (Z)-isomer. $^1H$ NMR spectrum also indicated the presence of other unidentified impurity (≈ 5%).*

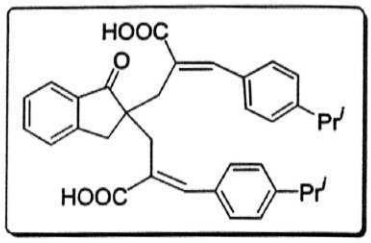
$^{13}C$ NMR (major isomer) : δ 23.81, 33.61, 33.96, 36.38, 51.58, 54.09, 123.64, 126.10, 126.72, 127.14, 129.20, 129.59, 132.87, 134.57, 136.09, 142.03, 149.59, 152.77, 168.96, 208.46.

*$^{13}C$ NMR spectrum also showed some minor peaks, which arise due to the presence of minor Z-isomer (≈ 10-12%) and unidentified impurity (≈ 5%).*

Since we are converting this diester (**128c**) to diacid (**129c**) no attempt was made to further purify this compound. This molecule was, as such, subjected to hydrolysis to provide the pure diacid (**129c**) as described below.

**2,2-Bis[(2*E*)-2-carboxy-3-(4-isopropylphenyl)prop-2-en-1-yl]indan-1-one (129d):**

This diacid was prepared *via* the hydrolysis of 2,2-bis[(2*E*)-2-methoxycarbonyl-3-(4-isopropylphenyl)prop-2-en-1-yl]indan-1-one (**128d**) (above mentioned diester) using KOH / MeOH, following the similar procedure described for the compound **129a**, as a colorless solid.




Reaction time : 3 h

Yield : 72%

Mp : 169-171 °C

IR (KBr) : ν 3350-2400, 1714, 1680, 1606 $cm^{-1}$

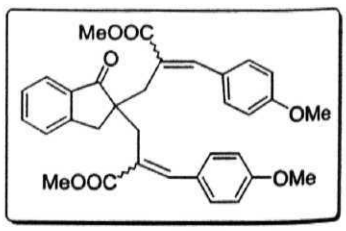
$^1H$ NMR : δ 1.27 (d, 12H, $J$ = 6.8 Hz), 2.82-3.40 (m, 8H), 4.62 (b, 2H), 7.15-7.65 (m, 12H), 7.77 (s, 2H).

*In addition, a doublet at δ 1.18 and a singlet at δ 6.62, with very low intensity, indicate the presence of ≈ 2% (Z)-isomer.*

$^{13}C$ NMR : δ 23.83, 33.03, 34.03, 36.84, 54.49, 124.21, 126.07, 126.85, 127.29, 128.25, 129.93, 132.56, 134.70, 136.04, 144.24, 150.24, 152.95, 174.14, 209.10.

**2,2-Bis[(2*E*)-2-methoxycarbonyl-3-(4-methoxyphenyl)prop-2-en-1-yl]indan-1one (128e):**

This molecule was obtained as a colorless viscous liquid *via* the dialkylation of 1-indanone (**125**) with methyl 3-acetoxy-3-(4-methoxyphenyl)-2-methylenepropanoate (**127e**) in the presence of NaH following the similar procedure described for the molecule **128a**.




Reaction time : 30 h

Yield : 81%

IR (neat) : ν 1715, 1603 $cm^{-1}$

$^1$H NMR (major *E*-along with minor *Z*) : δ 2.91-3.29 (m, 6H), 3.54 (s, 6H), 3.84 (s, 6H), 6.57 (s) & 6.75-7.71 (m, 14H),

*Singlet at δ 6.57 (Z-olefinic proton) with low intensity indicates the presence of ≈ 7-8% (Z)-isomer. $^1$H NMR spectrum also indicated the presence of other unidentified impurity (≈ 5%).*

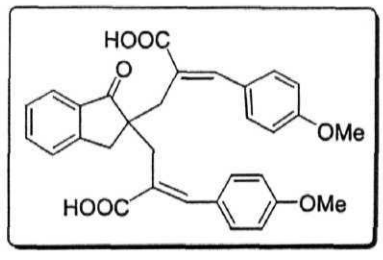
$^{13}$C NMR (major isomer) : δ 33.52, 36.38, 51.47, 54.03, 55.15, 114.04, 123.50, 126.02, 127.05, 127.66, 127.75, 131.15, 134.51, 135.98, 141.62, 152.71, 159.87, 168.93, 208.48.

*$^{13}$C NMR spectrum also showed some minor peaks, which arise due to the presence of minor Z-isomer (≈ 7-8%) and unidentified impurity (≈ 5%).*

Since we are converting this diester (**128d**) to diacid (**129d**), no attempt was made to further purify this compound. This molecule was, as such, subjected to hydrolysis to provide the pure diacid (**129d**) as described below.

**2,2-Bis[(2*E*)-2-carboxy-3-(4-methoxyphenyl)prop-2-en-1-yl]indan-1-one (129e):**

Treatment of 2,2-bis[(2*E*)-2-methoxycarbonyl-3-(4-methoxyphenyl)prop-2-en-1-yl]indan-1-one (**128e**) (above mentioned product) with KOH in methanol, following similar procedure described for **129a**, provided the diacid **129e** as a colorless solid.




Reaction time : 3 h

Yield : 72%

Mp : 191 °C

IR (KBr) : ν 3350-2350, 1711, 1678, 1602 cm$^{-1}$.

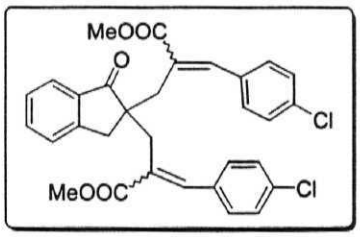
$^1$H NMR (DMSO-$D_6$) : δ 2.85 & 3.04 (ABq, 4H, *J* = 15.5 Hz), 2.98 (s, 2H) [merged with one

of the peaks of ABq], 3.80 (s, 6H), 6.95 (d, 4H, $J$ = 8.6 Hz), 7.25-7.65 (m, 10H), 12.25 (b, 2H).

$^{13}$C NMR (DMSO-$D_6$) : δ 33.01, 35.81, 53.84, 55.43, 114.34, 123.65, 126.48, 127.45, 127.65, 128.32, 131.45, 134.85, 135.66, 140.47, 152, 49, 159.77, 169.84, 207.69

**2,2-Bis[(2*E*)-3-(4-chorophenyl)-2-methoxycarbonylprop-2-en-1-yl]indan-1-one (128f):**

This molecule was obtained as a colorless viscous liquid *via* the reaction between 1-indanone (**125**) and methyl 3-acetoxy-3-(4-chlorophenyl)-2-methylenepropanoate (**127f**) in the presence of NaH following the similar procedure described for the molecule **128a**.




Reaction time : 30 h

Yield : 66%

IR (neat) : ν 1705, 1630 cm$^{-1}$.

$^{1}$H NMR (major *E*-along with minor *Z*) : δ 2.61-3.10 (m, 6H), 3.50 & 3.55 (2s, 6H), 6.53 (s) & 7.15-7.66 (m, 14H).

*The underlined chemical shift values are attributed to the minor Z-isomer. Singlet at δ 6.53 (Z-olefinic proton) with very low intensity clearly indicate presence of ≈ 7% minor Z-isomer. $^{1}$H NMR spectrum also indicated the presence of other unidentified impurity (≈ 5%).*

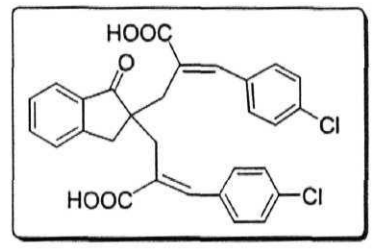
$^{13}$C NMR (major isomer) : δ 33.42, 36.73, 51. 64, 53.68, 123.57, 125.94, 127.23,128.74, 129.15, 130.34, 130.54, 133.64, 134.34, 134.63, 140.29, 152.20, 168.26, 207.60.

*$^{13}C$ NMR spectrum also showed some minor peaks, which arise due to the presence of minor Z-isomer (≈ 7%) and unidentified impurity (≈ 5%).*

Since we are converting this diester (**128e**) to diacid (**129e**), no attempt was made to further purify this compound. This molecule was, as such, subjected to hydrolysis to provide the pure diacid (**129e**) as described below.

**2,2-Bis[(2*E*)-2-carboxy-3-(4-chlorophenyl)prop-2-en-1-yl]indan-1-one (129f):**

This diacid was obtained *via* the treatment of 2,2-bis[(2*E*)-3-(4-chlorophenyl)2-methoxycarbonylprop-2-en-1-yl]indan-1-one (**128f**) (above mentioned diester) with KOH in MeOH, following the similar procedure described for the compound **129a**, as a colorless solid.




Reaction time : 3 h

Yield : 73%

Mp : 234-236 °C

IR (KBr) : ν 3350-2300, 1720, 1685, 1612 cm$^{-}$

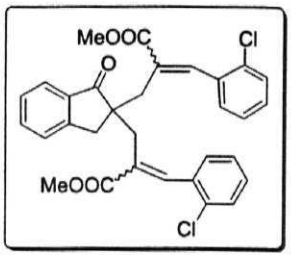
$^{1}H$ NMR (DMSO-$D_6$) : δ 2.94 (s, 2H), 2.75 & 2.85 (ABq, 4H, J = 13.8 Hz), 7.23-7.68 (m, 14H), 12.48 (b, 2H).

$^{13}C$ NMR (DMSO-$D_6$) : δ 32.99, 36.18, 53.64, 123.65, 126.47, 127.51, 128.81, 131.02, 131.57, 133.30, 134.36, 134.90, 135.54, 139.15, 152.10, 169.35, 207.01.

**2,2-Bis[(2*E*)-3-(2-chlorophenyl)-2-methoxycarbonylprop-2-en-1-yl]indan-1-one (128g):**

Treatment of 1-indanone (**125**) with methyl 3-acetoxy-3-(2-chlorophenyl)-2-methylen-

epropanoate (**127g**) in the presence of NaH, following the similar procedure described for the molecule **128a**, provided diester **128f** as a colorless viscous liquid.




Reaction time : 30 h

Yield : 74%

IR (neat) : ν 1716, 1634, 1608 $cm^{-1}$

$^1H$ NMR (major *E*-along with minor *Z*) : δ 2.69-3.65 (m, 12H), 6.58 (s) & 6.99-7.70 (m, 14H).

*Singlet at δ 6.58 (Z-olefinic proton) with very low intensity clearly indicates presence of ≈ 15% minor Z-isomer. $^1H$ NMR spectrum also indicated the presence of other unidentified impurity (≈ 5%).*

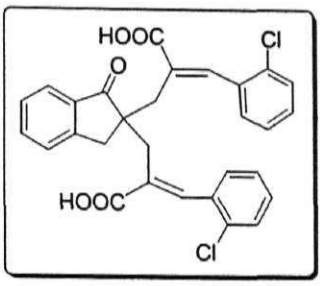
$^{13}C$ NMR (major isomer) : δ 33.30, 36.37, 51.73, 53.56, 123.57, 126.28, 126.80, 127.14, 128.93, 129.52 129.99, 131.75, 133.85, 134.07, 134.61, 135.97, 139.12, 152.4, 167.96, 207.60.

*$^{13}C$ NMR spectrum also showed some minor peaks, which arise due to the presence of minor Z-isomer (≈ 15%) and unidentified impurity (≈ 5%).*

Since we are converting this diester (**128f**) to diacid (**129f**), no attempt was made to further purify this compound. This molecule, as such, was subjected to hydrolysis to provide the pure diacid (**129f**) as described below.

**2,2-Bis[(2*E*)-2-carboxy-3-(2-chlorophenyl)prop-2-en-1-yl]indan-1-one (129g):**

Hydrolysis of 2,2-bis[(2*E*)-3-(2-chlorophenyl)2-methoxycarbonylprop-2-en-1-yl]indan-1-one (**128g**, above mentioned diester) using KOH in methanol, following the similar reaction procedure described for the compound **129a**, provided the diacid **129g** as a colorless solid.




Reaction time : 3 h

Yield : 70%

Mp : 213 °C

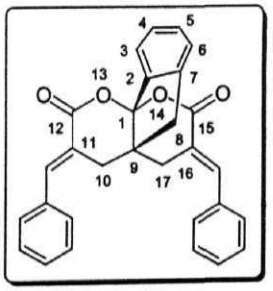
IR (KBr) : ν 3350-2400, 1714, 1686, 1614 $cm^{-1}$.

$^1H$ NMR (DMSO-$D_6$) : δ 2.58 & 2.70 (ABq, 4H, $J$ = 13.6Hz), 2.83 (s, 2H), 7.12-7.62 (m, 14H), 12.46 (b, 2H).

$^{13}C$ NMR (DMSO-$D_6$) : δ 32.73, 35.85, 53.38, 123.68, 126.47, 127.44, 129.58, 130.17, 132.71, 133.03, 134.07, 134.82, 135.67, 137.60, 152.17, 168.87, 206.72.

**11,16-Di [(*E*)-benzylidene]-13,14-dioxatetracyclo[7.4.4.$0^{1,9}$.$0^{2,7}$]heptadeca-2,4,6-triene-12,15-dione (130a):**

To a stirred solution of 2,2-bis[(2*E*)-2-carboxy-3-phenylprop-2-en-1-yl]indan-1-one (**129a**) (0.5 mmol, 0.226 g) in dry $CH_2Cl_2$ (5 mL) was added trifluoroacetic anhydride (TFAA) (1 mmol, 0.21 g). After stirring for 1.5 h at room temperature under $N_2$ atmosphere, the reaction mixture was diluted with water (10 mL) and extracted with $CH_2Cl_2$ (3 x 20 mL). The combined organic layer was dried over anhydrous $Na_2SO_4$. Solvent was evaporated and the crude solid, thus obtained was purified by crystallization [ethyl acetate: hexanes (2 : 3)] to provide 0.20 g (92%) of propellano-bislactone (**130a**).




Mp : 200–201 °C

IR (KBr) : ν 1740, 1623 $cm^{-1}$

$^1H$ NMR : δ 2.75 (dd, 2H, *J* = 1.8 Hz, and 15.8 Hz)*, 2.95 (d, *J* = 1.8 Hz) & 3.02 (s) [4H]*, 7.15-7.49 (m, 13H), 7.69-7.80 (m, 1H), 7.89 (s, 2H).

* *It looks that both the allylic $CH_2$ protons (four protons) (at C-10 & C-17) appear as AB part of ABX system (doublet of AB quartet i. e. two dd) and the down field doublet (of this system) is merged with singlet at δ 3.02 of benzylic $CH_2$ protons (at C-8). This is confirmed by the very clear appearance of AB quartet for the allylic $CH_2$ protons (four protons) (at C-10 & C-17) when the $^1H$ NMR spectrum was recorded in the presence of shift reagent Eu(fod)$_3$ (Spectrum 3).*

$^{13}C$ NMR : δ 33.22, 42.55, 43.14, 111.88, 122.75, 124.28, 125.50, 128.25, 128.76, 129.54, 129.83, 131.02, 134.22, 139.29, 139.64, 143.86, 164.07.

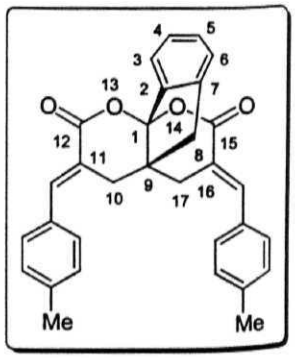
MS(m/z) : 434 ($M^+$)

Analysis calcd for $C_{29}H_{22}O_4$ : C, 80.17; H, 5.10

Found : C, 80.11; H, 5.14

**11,16-Di [(*E*)-*p*-methylbenzylidene]-13,14-dioxatetracyclo[7.4.4.$0^{1,9}$.$0^{2,7}$]heptadeca-2,4,6-triene-12,15-dione (130b):**

This compound was obtained as a colorless solid *via* the bislactonization of 2,2-bis[(2*E*)-2-carboxy-3-(4-methylphenyl)prop-2-en-1-yl]indan-1-one **(129b)** by the treatment with TFAA following similar procedure described for the molecule **130a**.




Reaction time : 1.5 h

Yield : 91%

Mp : 229-230 °C

IR (KBr) : ν 1742, 1623 $cm^{-1}$

$^1H$ NMR : δ 2.38 (s, 6H), 2.73 (dd, 2H, *J* = 1.6 and 15.7 Hz)*, 2.94 (s) & 3.01 (s) [4H]*, 7.08-7.45 (m, 11H), 7.68-7.75 (m, 1H), 7.86 (s, 2H).

* *It looks that the both allylic $CH_2$ protons (four protons) (at C-10 & C-17) appear as AB quartet and the down field peak of AB quartet is merged with singlet at δ 3.01 of benzylic $CH_2$ protons (at C-8). Also, first doublet (of AB quartet) appears as doublet of doublet due to allylic coupling (at δ 2.73).*

$^{13}C$ NMR : δ 21.46, 33.22, 42.41, 43.03, 111.72, 121.71, 124.18, 125.49, 128.16, 129.42, 129.97, 130.90, 131.43, 139.31, 139.76, 139.98, 143.97, 164.21.

MS(m/z) : 462 ($M^+$)

Analysis calcd for $C_{31}H_{26}O_4$ : C, 80.50; H, 5.67

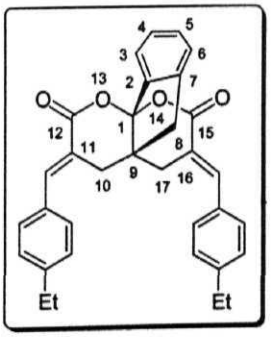
Found : C, 80.25; H, 5.70

**11,16-Di [(*E*)-*p*-ethylbenzylidene]-13,14-dioxatetracyclo[7.4.4.$0^{1,9}$.$0^{2,7}$]heptadeca-2,4,6-triene-12,15-dione (130c):**

Bislactonization of 2,2-bis[(2*E*)-2-carboxy-3-(4-ethylphenyl)prop-2-en-1-yl]indan-1-one (**129c**) *via* the treatment with TFAA, following similar procedure described for the molecule **130a**, provided the desired compound, **130c**, as colorless solid.

Reaction time : 1.5 h

Yield : 84%



Mp : 164-165 °C

IR (KBr) : ν 1736, 1628 $cm^{-1}$

$^1H$ NMR : δ 1.25 (t, 6H, *J* = 7.8 Hz), 2.61-3.10 (m, 10H), 7.11-7.48 (m, 11H), 7.68-7.76 (m, 1H), 7.89 (s, 2H).

$^{13}C$ NMR : δ 15.17, 28.72, 33.22, 42.40, 43.01, 111.74, 121.75, 124.12, 125.49, 128.20, 130.03, 130.87, 131.67, 139.34, 139.80, 143.93, 146.16, 164.16.

MS(m/z) : 490 ($M^+$)

Analysis calcd for $C_{33}H_{30}O_4$ : C, 80.79; H, 6.16

Found : C, 80.98; H, 6.12

**11,16-Di [(*E*)-*p*-isopropylbenzylidene]-13,14-dioxatetracyclo[7.4.4.$0^{1,9}$.$0^{2,7}$]hepta-deca-2,4,6-triene-12,15-dione (130d):**

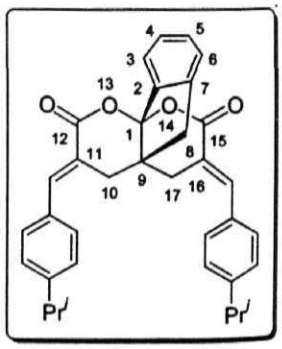
This propellano-bislactone was obtained *via* the treatment of 2,2-bis[(2*E*)-2-carboxy-3-(4-isopropylphenyl)prop-2-en-1-yl]indan-1-one (**129d**) with trifluoroacetic anhydride, as a colorless solid, following similar procedure described for the molecule **130a**.

Reaction time : 1.5 h

Yield : 89%

Mp : 192-193 °C

IR (KBr) : ν 1738, 1628 $cm^{-1}$



$^1$H NMR : δ 1.26 (d, 12H, $J$ = 6.8 Hz), 2.71-3.09 (m, 8H), 7.12-7.45 (m, 11H), 7.69-7.76 (m, 1H), 7.90 (s, 2H).

$^{13}$C NMR : δ 23.73, 33.18, 34.01, 42.32, 42.94, 111.74, 121.70, 124.12, 125.50, 126.81, 128.11, 130.08, 130.86, 131.82, 139.33, 139.83, 143.98, 150.75, 164.11.

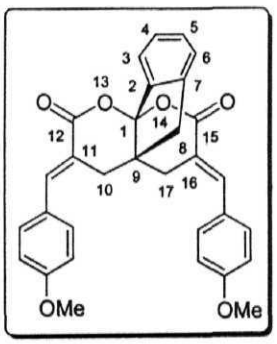
MS(m/z) : 518 ($M^+$)

Analysis calcd for $C_{35}H_{34}O_4$ : C, 81.05; H, 6. 61

Found : C, 80.72; H, 6.64

**11,16-Di [(*E*)-*p*-methoxybenzylidene]-13,14-dioxatetracyclo[7.4.4.0$^{1,9}$.0$^{2,7}$]heptadeca-2,4,6-triene-12,15-dione (130e):**

Treatment of 2,2-bis[(2*E*)-2-carboxy-3-(4-methoxyphenyl)prop-2-en-1-yl]indan-1-one (**129e**) with TFAA, following similar procedure described for the molecule **130a**, provided the propellane **130e**, as a colorless solid.




Reaction time : 1.5 h

Yield : 85%

Mp : 179-180 °C

IR (KBr) : ν 1714, 1620, cm$^{-1}$

$^1$H NMR : δ 2.76 (dd, 2H, 1.6 Hz & 15.8 Hz)*, 2.96 (s) & 3.02 (s) [4H]*, 3.84 (s, 6H), 6.89 (d, 4H, $J$ =8.6 Hz), 7.16-7.46 (m, 7H), 7.69-7.74 (m, 1H), 7.86 (s, 2H).

** It looks that the both allylic $CH_2$ protons (four protons) (at C-10 & C-17) appear as AB quartet. The first doublet (of AB quartet) appears as dd due to allylic coupling. The down field peak of (second part of AB quartet) is merged with the singlet at δ 3.02 of benzylic $CH_2$ protons (at C-8).*

$^{13}$C NMR : δ 33.23, 42.29, 42.78, 55.37, 111.51, 114.19, 120.07, 123.99, 125.51, 126.78, 128.04, 130.79, 131.89, 139.34, 139.91, 143.63, 160.72, 164.27

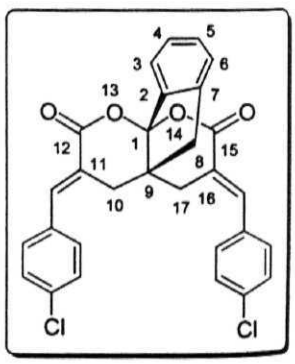
MS(m/z) : 494 ($M^+$)

Analysis calcd for $C_{31}H_{26}O_6$ : C, 75.29; H, 5.30

Found : C, 75.53; H, 5.33

**11,16-Di [(*E*)-*p*-chlorobenzylidene]-13,14-dioxatetracyclo[7.4.4.0$^{1,9}$.0$^{2,7}$]heptadeca-2,4,6-triene-12,15-dione (130f):**

This molecule was obtained as a colorless solid *via* the bislactonization of 2,2-bis[(2*E*)-2-carboxy-3-(4-chlorophenyl)prop-2-en-1-yl]indan-1-one (**129f**) by the treatment with TFAA following similar procedure described for the molecule **130a**.




Reaction time : 1.5 h

Yield : 90%

Mp : 250-251 °C

IR (KBr) : ν 1718, 1624 cm$^{-1}$.

$^1$H NMR : δ 2.71 (dd, 2H, $J$ = 2.2 Hz, 15.6 Hz), 2.92 (d, 2H, $J$ = 15.6 Hz), 3.06 (s, 2H), 7.10 (d, 4H, $J$ = 8.6 Hz), 7.22-7.49 (m, 7H), 7.72 (m, 1H), 7.76 (s, 2H)

*The underlined chemical shift values arise due to the allylic $CH_2$ protons (four protons) (at C-10 & C-17). It looks that these protons appear as AB quartet. The first doublet (of AB quartet) appears (at δ 2.71) as dd due to allylic coupling .*

$^{13}$C NMR : δ 33.46, 43.00, 43.43, 111.78, 123.43, 124.33, 125.40, 128.32, 129.05, 130.99, 132.47, 135.72, 139.16, 142.13, 163.69.

Analysis calcd for $C_{29}H_{20}O_4Cl_2$ : C, 69.20; H, 4.00

Found : C, 69.03; H, 3.97

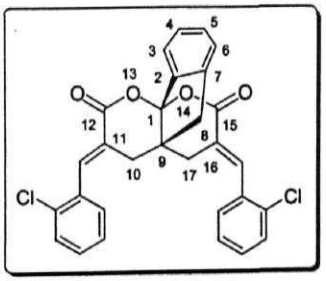
**11,16-Di [(*E*)-2-chlorobenzylidene]-13,14-dioxatetracyclo[7.4.4.0$^{1,9}$.0$^{2,7}$]heptadeca-2,4,6-triene-12,15-dione (130g):**

Bislactonization of 2,2-bis[(2*E*)-2-carboxy-3-(2-chlorophenyl)prop-2-en-1-yl]indan-1-one (**129g**) *via* the treatment with trifluoroacetic anhydride, following similar procedure described for the molecule **130a**, provided desired molecule (**130g**) as colorless solid.

Reaction time : 1.5 h

Yield : 86%

Mp : 157-158 °C



IR (KBr) : ν 1732, 1628 $cm^{-1}$

$^1H$ NMR : δ 2.60 & 2.79 (ABq, 4H, $J$ = 15.6 Hz), 2.92 (s, 2H), 7.01-7.51 (m, 11H), 7.67-7.76 (m, 1H), 8.03 (s, 2H).

$^{13}C$ NMR : δ 32.77, 41.58, 42.88, 112.46, 124.39, 125.02, 125.55, 126.76, 128.40, 130.05, 130.22, 130.54, 131.17, 133.01, 134.48, 138.92, 139.70, 141.38, 162.95.

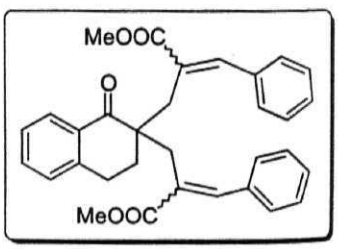
MS(m/z) : 502 $(M^+)$, 504 $(M+2)^+$, 506 $(M+4)^+$

Analysis calcd for $C_{29}H_{20}O_4Cl_2$ : C, 69.20; H, 4.00

Found : C, 69.41; H, 3.98

**2,2-Bis[(2*E*)-2-methoxycarbonyl-3-phenylprop-2-en-1-yl]tetral-1-one (132):**

This molecule was prepared *via* the dialkylation of 1-tetralone (**131**) with methyl 3-acetoxy-2-methylene-3-phenylpropanoate (**127a**) in the presence of NaH, as a colorless viscous liquid, following the similar procedure described for the molecule **128a**.




Reaction time : 30 h.

Yield : 59%

IR (neat) : ν 1714, 1680, 1630 $cm^{-1}$.

$^1H$ NMR (major *E*-along with minor *Z*) : δ 1.75 (t, 2H, $J$ = 6.8), 2.78-3.70 (m, 12H), 6.44 & 7.58 (2s, 2H) 7.08-7.47 (m, 13H), 7.77-7.91 (m, 1H).

*Singlet at δ 6.44 (Z-olefinic proton) with very low intensity clearly indicate presence of ≈ 15% minor Z-isomer. $^1H$ NMR spectrum also indicated the presence of other unidentified impurity (≈ 5%).*

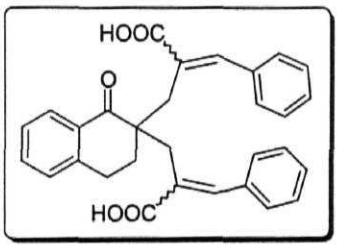
$^{13}$C NMR (major isomer) : δ 25.21, 30.81, 32.21, 41.10, 51.75, 126.42, 127.72, 127.92, 128.10, 128.51, 129.01, 130.76, 132.60, 132.79, 135.82, 141.48, 142.78, 169.35, 199.02.

*$^{13}$C NMR spectrum also showed some minor peaks, which arise due to the presence of minor Z-isomer (≈ 15%) and unidentified impurity (≈ 5%).*

Since we are converting this diester (**132**) to diacid (**133**), no attempt was made to further purify this compound. This molecule was, as such, subjected to hydrolysis to provide the pure diacid (**133**) as described below.

**2,2-Bis[(2*E*)-2-carboxy-3-phenylprop-2-en-1-yl]tetral-1-one (133):**

This molecule was obtained as a colorless solid on hydrolysis of 2,2-bis[(2*E*)-2-carboxy-3-phenylprop-2-en-1-yl]tetral-1-one (**132**) (above mentioned diester) using KOH following similar procedure described for the compound **129a**.




Reaction time : 3 h

Yield : 84%

Mp : 97-102 °C

IR (KBr) : ν 3500-2350, 1680, 1630 cm$^{-1}$.

$^{1}$H NMR (major *E*-along with minor *Z*) : δ 1.75-1.99 (m, 2H), 2.70–3.59 (m, 6H), 5.82 (b, 2H), 7.01–7.52 (m, 13H), 7.71-7.99 (m, 1H), 6.59 & 7.79 (2s, 2H).

*Singlet at δ 6.59 (Z-olefinic proton), with very low intensity, clearly indicates presence of ≈ 15% minor Z-isomer. $^{1}$H NMR spectrum also indicated the presence of other unidentified impurity (≈ 5%).*

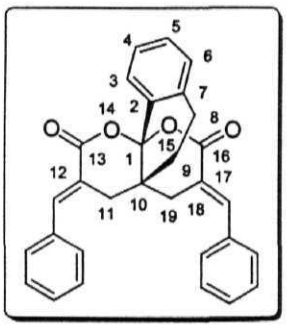
$^{13}$C NMR : δ 25.22, 30.72, 31.53, 51.07, 126.54, 128.11, 128.33, 128.56, 129.04, 129.18, 129.76, 132.66, 132.86, 135.56, 142.78, 143.93, 174.03, 199.97.

*$^{13}C$ NMR spectrum also showed some minor peaks which arise due to the presence of minor Z-isomer (≈ 15 and unidentified impurity (≈ 5%).*

Since we are converting this diacid (**133**) to corresponding propellane (**134**), no attempt was made to further purify this compound. This molecule, as such, was subjected to hydrolysis to provide the pure diacid (**134**) as described below.

**12,17-Di [(*E*)-benzylidene]-14,15-dioxatetracyclo[8.4.4.0$^{1,10}$.0$^{2,7}$]octadeca-2,4,6-triene-13,16-dione (134):**

This molecule was obtained as a colorless solid *via* the bislactonization of 2,2-bis[(2*E*)-2-carboxy-3-phenylprop-2-en-1-yl]tetral-1-one (above-mentioned diacid) by the treatment with trifluoroacetic anhydride following similar procedure described for the molecule **130a**.




Reaction time : 1.5 h

Yield : 68%

Mp : 204-205 °C

IR (KBr) : ν 1733, 1705, 1652 cm$^{-1}$

$^{1}H$ NMR : δ 2.04 (t, 2H, *J* = 6. 8 Hz), 2.78 & 2.93 (d of ABq, 4H, *J* = 16.8 Hz & 1.6 Hz), 3.09 (t, 2H, *J* = 6.8 Hz), 7.12-7.51 (m, 13H), 7.82-7.92 (m, 1H), 8.04 (s, 2H).

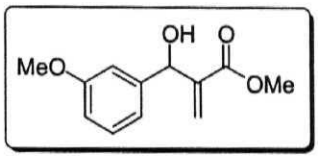
$^{13}C$ NMR : δ 24.13, 28.49, 32.68, 33.06, 103.82, 121.47, 126.49, 127.21, 128.74, 129.84, 130.08, 130.41, 133.54, 134.27, 134.55, 144.84, 163.73,

Analysis calcd for $C_{30}H_{24}O_4$ : C, 80.34; H, 5.39

Found : C, 80.07; H, 5.42.

**Methyl 3-hydroxy-3-(3-methoxyphenyl)-2-methylenepropanoate (126h):**

This molecule was obtained as a colorless viscous liquid *via* the reaction between 3-methoxybenzaldehyde and methyl acrylate catalyzed by DABCO following a similar procedure described for the molecule **126a**. The crude product was purified by column chromatography (10% EtOAc in hexanes, silica gel).




Reaction time : 12 days

Yield : 63%

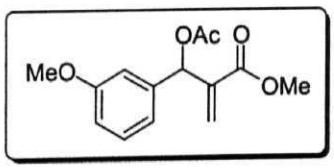
IR (neat) : ν 3474, 1720, 1621 $cm^{-1}$

$^{1}H$ NMR : δ 3.60 (s, 3H), 3.69 (s, 3H), 3.77 (b, 1H), 5.45 (s, 1H), 5.84 (s, 1H), 6.25 (s, 1H), 6.66-6.95 (m, 3H). 7.17 (t, H, $J$ = 7.92 Hz).

$^{13}C$ NMR : δ 51.71, 55.10, 72.57, 112.39, 113.29, 119.07, 125.56, 129.30, 142.40, 143.28, 159.69, 166.69.

**Methyl 3-acetoxy-3-(3-methoxyphenyl)-2-methylenepropanoate (127h):**

This molecule was obtained as a colorless viscous liquid *via* the treatment of methyl 3-hydroxy-3-(3-methoxyphenyl)-2-methylenepropanoate (**126h**) with acetyl chloride in presence of pyridine following a similar procedure described for the molecule **127a**.




Reaction time : 2 h

Yield : 82%

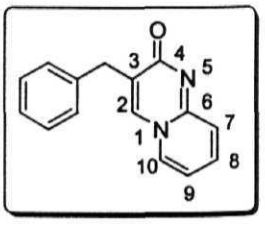
IR (neat) : ν 1745 1724, 1633 $cm^{-1}$

$^1$H NMR : δ 2.08 (s, 3H), 3.69 (s, 3H), 3.76 (s, 3H), 5.83 (s, 1H), 6.37 (s, 1H), 6.65 (s, 1H), 6.76-7.03 (m, 3H), 7.18-7.30 (m, 1H).

$^{13}$C NMR : δ 20.88, 51.83, 55.09, 72.85, 113.31, 113.65, 119.81, 125.82, 129.40, 139.31, 139.63, 159.59, 165.31, 169.22.

**3-Benzyl-1,5-diazabicyclo-(4.4.0)deca-2,5,7,9-tetraen-4-one (156a):**

To a stirred solution of methyl 3-acetoxy-2-methylene-3-phenypropanoate **(127a)** (1 mmol, 0.234 g) in $H_2O$ / MeOH (1:1, 10mL), was added, 2-aminopyridine **(150)** (1 mmol, 0.094 g) at room temperature. After stirring for 6 hours at room temperature, reaction mixture was saturated with NaCl and extracted with ethyl acetate (3 x 10 mL). 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, 15% MeOH in EtOAc) followed by crystallization (EtOAc) to furnish the pure compound **(156a)** in 77 % (0.182 g) yield.




Mp : 218-220 °C (dec.)

IR (KBr) : ν 1649, 1602 cm$^{-1}$

$^1$H NMR (28.5% $CD_3OD$ in $CDCl_3$) : δ 3.91 (s, 2H), 6.90-7.02 (m, 1H), 7.22-7.76 (m, 8H), 7.85 (d, 1H, J= 6.8Hz).

$^{13}$C NMR (28.5% $CD_3OD$ in $CDCl_3$) : δ 34.02, 113.53, 123.52, 126.73, 128.68, 129.24, 130.18, 132.72, 135.76, 135.85, 137.13, 151.02, 168.57.

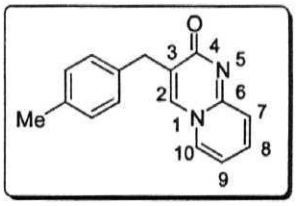
MS (m/z) : 236 ($M^+$)

Analysis calcd for $C_{15}H_{12}N_2O$ : C, 76.25; H, 5.12; N, 11.86.

Found : C, 76.18; H, 5.10; N, 11.91.

**3-(4-Methylbenzyl)-1,5-diazabicyclo(4.4.0)deca-2,5,7,9-tetraen-4-one (156b):**

This molecule was obtained as a colorless solid *via* the treatment of methyl 3-acetoxy-2-methylene-3-(4-methylphenyl)propanoate (**127b**) with 2-aminopyridine (**150**) following similar procedure as described for the molecule **156a**.




Reaction time : 6 h

Yield : 74%

Mp : 230-233 °C (dec.)

IR (KBr) : ν 1649, 1608 $cm^{-1}$

$^1H$ NMR (28.5% $CD_3OD$ in $CDCl_3$) : δ 2.35 (s, 3H), 3.86 (s, 2H), 6.88-7.02 (m, 1H), 7.17 (s, 4H), 7.34 (d, 1H, $J$ = 9.0 Hz), 7.51 (s, 1H), 7.61-7.72 (m 1H), 7.79 (d, 1H, $J$ = 6.6 Hz).

$^{13}C$ NMR (28.5% $CD_3OD$ in $CDCl_3$) : δ 20.53, 33.46, 113.78, 123.15, 129.04, 129.29, 130.28, 132.83, 133.64, 135.90, 136.14, 136.33, 150.86, 168.71.

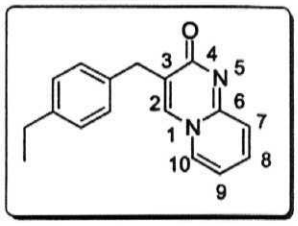
MS (m/z) : 250 ($M^+$)

Analysis calcd for $C_{16}H_{14}N_2O$ : C, 76.78; H, 5.64; N, 11.19

Found : C, 76.86; H, 5.68; N, 11.10.

**3-(4-Ethylbenzyl)-1,5-diazabicyclo(4.4.0)deca-2,5,7,9-tetraen-4-one (156c):**

This compound was prepared *via* the reaction between methyl 3-acetoxy-3-(4-ethylphenyl)-2-methylenepropanoate (**127c**) and 2-aminopyridine (**150**), as a colorless solid, following similar procedure as described for the molecule **156a**.




Reaction time : 6 h

Yield : 83%

Mp : 210-214 °C

IR (KBr) : ν 1649, 1593 $cm^{-1}$

$^1H$ NMR (28.5% $CD_3OD$ in $CDCl_3$) : δ 1.25 (t, 3H, $J$ = 7.6 Hz), 2.66 (q, 2H, $J$ = 7.6 Hz), 3.87 (d, 2H, $J$ = 1.2 Hz), 6.87-7.01 (m, 1H), 7.21 (s, 4H), 7.35 (d, 1H, $J$ = 9.0 Hz), 7.51 (s, 1H), 7.59-7.72 (m, 1H), 7.83 (d, 1H, $J$ = 6.8 Hz)

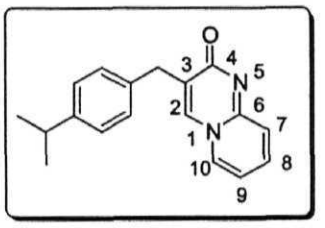
$^{13}C$ NMR (28.5% $CD_3OD$ in $CDCl_3$) : δ 15.07, 28.09, 33.42, 113.67, 123.04, 128.01, 129.00, 130.06, 132.84, 133.99, 135.89, 136.03, 142.63, 150.82, 168.63.

Analysis calcd for $C_{17}H_{16}N_2O$ : C, 77.25; H, 6.10; N, 10.60

Found : C, 77.36; H, 6.08; N, 10.55.

**3-(4-Isopropylbenzyl)-1,5-diazabicyclo(4.4.0)deca-2,5,7,9-tetraen-4-one (156d):**

Treatment of methyl 3-acetoxy-3-(4-isopropylphenyl)-2-methylenepropanoate (**127d**) with 2-aminopyridine (**150**), following similar procedure as described for the molecule **156a**, provided required fused pyrimidone (**156d**) as a colorless solid.



Reaction time : 6 h

Yield : 75%

Mp : 214-216 °C (dec.)

IR (KBr) : ν 1649, 1597 $cm^{-1}$

$^1H$ NMR (28.5% $CD_3OD$ in $CDCl_3$) : δ 1.24 (d, 6H, *J* = 6.8 Hz), 2.89 (sept, 1H, *J* = 6.8 Hz), 3.89 (s, 2H), 6.88-7.02 (m, 1H), 7.23 (s, 4H), 7.35 (d, 1H, *J* = 9.0 Hz), 7.56 (s, 1H), 7.61-7.72 (m, 1H), 7.81 (d, 1H, *J* = 6.8 Hz)

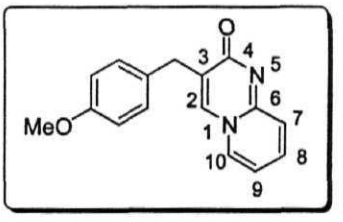
$^{13}C$ NMR ($CDCl_3$) : δ 24.04, 33.80, 33.95, 112.85, 124.46, 126.99, 129.54, 130.92, 132.40, 134.62, 135.07, 147.57, 151.04, 168.40.

Analysis calcd for $C_{18}H_{18}N_2O$ : C, 77.67, H, 6.52, N, 10.06.

Found : C, 77.72, H, 6.58, N, 10.12.

**3-(4-Methoxybenzyl)-1,5-diazabicyclo(4.4.0)deca-2,5,7,9-tetraen-4-one (156e):**

Treatment of methyl 3-acetoxy-3-(4-methoxyphenyl)-2-methylenepropanoate (**127e**) with 2-aminopyridine (**150**), following similar procedure as described for the molecule **156a**, provided the required fused pyrimidine derivative (**156e**) as a colorless solid.



Reaction time : 6 h

Yield : 56%

Mp : 214-217 °C (dec.)

IR (KBr) : ν 1655, 1610 $cm^{-1}$

$^1H$ NMR : δ 3.82 (s, 3H), 3.84 (s, 2H), 6.82-6.98 (m, 3H), 7.13-7.29 (m,

(28.5% $CD_3OD$ in $CDCl_3$) 2H), 7.34 (d, 1H, $J$ =9.0 Hz), 7.51 (s, 1H), 7.57-7.77 (m, 1H), 7.80 (d, 1H, $J$ = 6.6 Hz)

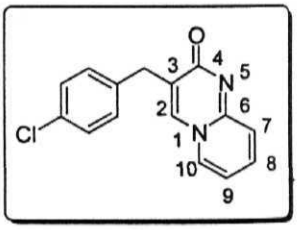
$^{13}C$ NMR (28.5% $CD_3OD$ in $CDCl_3$) : δ 33.05, 54.95, 113.65, 114.05, 123.19, 128.83, 130.17, 130.34, 132.81, 135.77, 135.99, 150.84, 158.33, 168.62.

Analysis calcd for $C_{16}H_{14}N_2O_2$ : C, 72.15; H, 5.30; N, 10.52

Found : C, 72.10; H, 5.33; N, 10.58.

**3-(4-Chlorobenzyl)-1,5-diazabicyclo(4.4.0)deca-2,5,7,9-tetraen-4-one (156f):**

This fused pyrimidine derivative was prepared *via* the reaction between 3-acetoxy-3-(4-chlorophenyl)-2-methylenepropanoate (**127f**) and 2-aminopyridine (**150**), as a colorless solid, following similar procedure as described for the molecule **156a**.




Reaction time : 6 h

Yield : 74%

Mp : 212-214 °C (dec.)

IR (KBr) : ν 1651, 1587cm$^{-1}$

$^{1}H$ NMR (28.5% $CD_3OD$ in $CDCl_3$) : δ 3.88 (s, 2H), 6.92-7.04 (m, 1H), 7.21-7.41 (m, 5H), 7.66 (d, 1H, $J$ = 7.6 Hz), 7.72 (s, 1H), 7.91 (d, 1H, $J$ = 6.8 Hz).

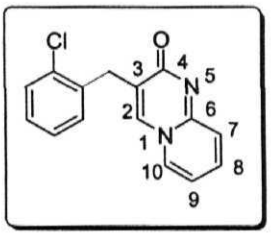
$^{13}C$ NMR (28.5% $CD_3OD$ in $CDCl_3$) : δ 33.28, 113.91, 123.09, 128.62, 129.30, 130.45, 132.50, 132.95, 135.65, 136.11, 136.34, 151.00, 168.40.

Analysis calcd for $C_{15}H_{11}ClN_2O$ : C, 66.55; H, 4.10; N, 10.35

Found : C, 66.65; H, 4.16; N; 10.45.

**3-(2-Chlorobenzyl)-1,5-diazabicyclo(4.4.0)deca-2,5,7,9-tetraen-4-one (156g):**

This molecule was obtained as a colorless solid *via* the treatment of methyl 3-acetoxy-3-(2-chlorophenyl)-2-methylenepropanoate (**127g**) with 2-aminopyridine (**150**) following similar procedure as described for the molecule **156a**.




Reaction time : 6 h

Yield : 79%

Mp : 186-188 °C (dec.)

IR (KBr) : ν 1655, 1595cm$^{-1}$

$^{1}$H NMR (28.5% $CD_3OD$ in $CDCl_3$) : δ 4.03 (s, 2H), 6.88-7.02 (m, 1H), 7.20-7.51 (m, 6H).7.60-7.71 (m, 1H), 7.87 (d, 1H, $J$ = 6.8 Hz)

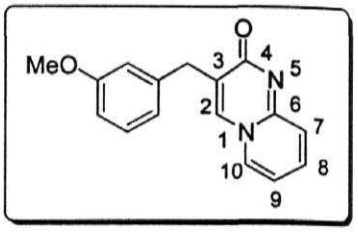
$^{13}$C NMR (28.5% $CD_3OD$ in $CDCl_3$) : δ 31.62, 113.75, 122.80, 126.89, 127.60, 128.25, 129.34, 131.27, 133.03, 133.90, 134.47, 135.84, 136.23, 150.75, 168.16.

Analysis calcd for $C_{15}H_{11}ClN_2O$ : C, 66.55; H, 4.10; N, 10.35

Found : C, 66.48; H, 4.12; N, 10.44.

**3-(3-Methoxybenzyl)-1,5-diazabicyclo(4.4.0)deca-2,5,7,9-tetraen-4-one (156h):**

This fused pyrimidine derivative was obtained as a colorless solid *via* the treatment of methyl 3-acetoxy-3-(3-methoxyphenyl)-2-methylenepropanoate (**127h**) with 2-aminopyridine (**150**) following similar procedure as described for the molecule **156a**.




Reaction time : 6 h

Yield : 58%

Mp : 207-208 °C

IR (KBr) : ν 1653, 1604 $cm^{-1}$

$^1H$ NMR (28.5% $CD_3OD$ in $CDCl_3$) : δ 3.80 (s, 3H), 3.87 (s, 2H), 6.78-7.05 (m, 4H), 7.21-7.30 (m, 1H) 7.34 (d, 1H, *J* = 8.8 Hz), 7.61 (s, 1H), 7.68 (d, 1H, *J* = 8.8 Hz), 7.85 (d, 1H, *J* = 6.8 Hz).

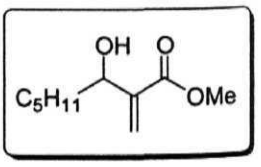
$^{13}C$ NMR (28.5% $CD_3OD$ in $CDCl_3$) : δ 33.96, 54.93, 112.12, 113.81, 114.98, 121.56, 123.28, 129.68, 129.92, 132.87, 135.99, 136.17, 138.53, 150.98, 159.86, 168.67.

Analysis calcd for $C_{16}H_{14}N_2O_2$ : C, 72.15; H, 5.30; N, 10.52.

Found : C, 72.25; H, 5.28; N, 10.62.

**Methyl 3-hydroxy-2-methyleneoctanoate (126i):**

This molecule was obtained as a colorless viscous liquid *via* the reaction between hexanal and methyl acrylate under the catalytic influence of DABCO following a similar procedure described for the molecule **126a**.




Reaction time : 6 days

Yield : 65%

Bp : 88-90 °C/1.4 mm

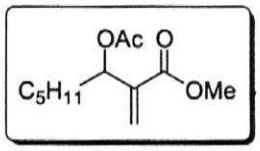
IR (neat) : ν 3429, 1720, 1630 $cm^{-1}$

$^1H$ NMR : δ 0.88 (t, 3H, *J* = 6.6 Hz), 1.20-1.78 (m, 8H), 2.16 (b, 1H), 3.78 (s, 3H), 4.38 (t, 1H, *J* = 6.37 Hz), 5.79 (s, 1H), 6.21 (s, 1H).

$^{13}$C NMR : δ 13.83, 22.43, 25.32, 31.53, 36.24, 51.62, 71.13, 124.48, 142.94, 166.99.

**Methyl 3-acetoxy-2-methyleneoctanoate (127i):**

This molecule was obtained as a colorless viscous liquid *via* the treatment of methyl 3-hydroxy-2-methyleneoctanoate (**126i**) with acetyl chloride in presence of pyridine following a similar procedure described for the molecule **127a**.




Reaction time : 2 h

Yield : 80%

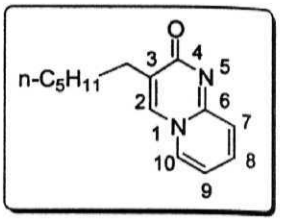
IR (neat) : ν 1745, 1735, 1633 cm$^{-1}$

$^{1}$H NMR : δ 0.86 (t, 3H, $J$ = 6.82 Hz), 1.12-1.48 (m, 6H), 1.52-1.87 (m, 2H), 2.06 (s, 3H), 3.76 (s, 3H), 5.53-5.68 (m, 1H), 5.74 (s, 1H), 6.26 (s, 1H).

$^{13}$C NMR : δ 13.71, 20.72, 22.27, 24.79, 31.25, 34.10, 51.61, 71.64, 124.58, 140.31, 165.50, 169.55.

**3-Hexyl-1,5-diazabicyclo(4.4.0)deca-2,5,7,9-tetraen-4-one (156i):**

Treatment of methyl 3-acetoxy-2-methyleneoctanoate (**127i**) with 2-aminopyridine (**150**), following similar procedure as described for the molecule **156a**, provided the required fused pyrimidine derivative (**156i**) as a colorless solid.




Reaction time : 6 h

Yield : 37%

Mp : 100 °C

IR (KBr) : ν 1657, 1599 $cm^{-1}$

$^1H$ NMR ($CDCl_3$) : δ 0.86 (t, 3H, *J* = 6.2 Hz), 1.16-1.75 (m, 8H), 2.56 (t, 2H, *J* = 6.0 Hz), 6.78-6.88 (m, 1H), 7.32 (d, 1H, *J* = 9.0 Hz), 7.46-7.58 (m, 1H), 7.69 (s, 1H), 7.73 (d, 1H, *J* = 6.8 Hz).

$^{13}C$ NMR ($CDCl_3$) : δ 14.11, 22.65, 27.50, 28.65, 29.22, 31.69, 112.92, 124.45, 130.93, 132.26, 133.96, 135.01, 151.12, 168.59.

MS (m/z) : 230 ($M^+$)

Analysis calcd for $C_{14}H_{18}N_2O$ : C, 73.01; H, 7.88; N, 12.16

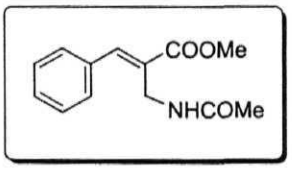
Found : C, 73.10; H, 7.85; N, 12.25.

**Methyl (2*E*)-2-acetylaminomethyl-3-phenylprop-2-enoate (177a):**

To a stirred solution of methyl 3-hydroxy-2-methylene-3-phenylpropanoate (**126a**) (1 mmol, 0.192 g) in acetonitrile (5 mL) was added methanesulfonic acid (3 mL) at 60 °C and immediately temperature was raised to 110 °C. After stirring for 5 h at 110 °C, reaction mixture was brought to room temperature and diluted with water. Aqueous $K_2CO_3$ solution was added slowly till the acid was neutralized 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, 30% EtOAc in hexanes) to furnish the pure compound (**177a**) in 72 % (0.166 g) yield.

*E* / *Z* : 90 / 10 [determined by the integration of isomeric olefinic proton singlets at δ 7.80 (*E*-isomer) & δ 7.10 (Z-isomer) in the $^1$H NMR spectrum of the crude sample. However, the pure *E*-isomer was obtained on column chromatography (30% EtOAc in hexanes)]




Mp : 112-114 °C

IR (KBr) : ν 3266, 1707, 1639 cm$^{-1}$

$^1$H NMR : δ 1.98 (s, 3H), 3.86 (s, 3H), 4.35 (d, 2H, *J* = 5.7 Hz), 6.09 (b, 1H), 7.30-7.60 (m, 5H), 7.80 (s, 1H).

$^{13}$C NMR : δ 23.06, 36.74, 52.07, 127.85, 128.60, 129.19, 129.53, 134.12, 142.39, 168.15, 169.61.

MS (m/z) : 233 ($M^+$)

Analysis calcd. for $C_{13}H_{15}NO_3$ : C, 66.94; H, 6.48; N, 6.00

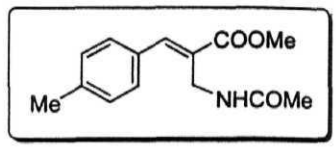
Found : C, 66.75; H, 6.51; N, 6.01

**Methyl (2*E*)-2-acetylaminomethyl-3-(4-methylphenyl)prop-2-enoate (177b):**

This molecule was obtained as a colorless solid *via* the reaction between methyl 3-hydroxy-3-(4-methylphenyl)-2-methylenepropanoate (**126b**) and acetonitrile in presence of methanesulfonic acid following similar procedure described for the molecule **177a**.

*E* / *Z* : 92 / 8 [determined by the integration of isomeric olefinic proton singlets at δ 7.77 (*E*-isomer) & δ 6.70 (Z-isomer) in the $^1$H NMR spectrum of the crude sample.

However, the pure *E*-isomer was obtained on column chromatography (30% EtOAc in hexanes)]




Reaction time : 5 h

Yield : 75%

Mp : 115-116 °C

IR (KBr) : ν 3254, 1712, 1639 $cm^{-1}$

$^1H$ NMR : δ 1.98 (s, 3H), 2.37 (s, 3H), 3.84 (s, 3H), 4.35 (d, 2H, $J$ = 5.8 Hz), 6.06 (b, 1H), 7.22 (d, 2H, $J$ = 8.2 Hz), 7.42 (d, 2H, $J$ = 8.2 Hz), 7.77 (s, 1H).

$^{13}C$ NMR : δ 21.15, 22.95, 36.69, 51.92, 126.77, 129.27, 129.59, 131.19, 139.43, 142.48, 168.19, 169.56.

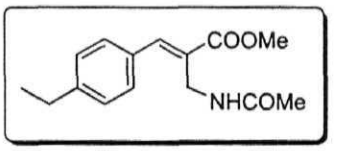
Analysis calcd. for $C_{14}H_{17}NO_3$ : C, 68.00; H, 6.93; N, 5.66.

Found : C, 67.86; H, 6.95; N, 5.69.

**Methyl (2*E*)-2-acetylaminomethyl-3-(4-ethylphenyl)prop-2-enoate (177c):**

This was prepared *via* the Ritter reaction of methyl 3-hydroxy-3-(4-ethylphenyl)-2-methylenepropanoate (**126c**) with acetonitrile in presence of methanesulfonic acid, following similar procedure described for the molecule **177a**, as a colorless solid.

*E* / *Z* : 87 / 13 [determined by the integration of isomeric olefinic proton singlets at δ 7.80 (E-isomer) & δ 6.94 (Z-isomer) in the $^1H$ NMR spectrum of the crude sample. However, the pure *E*-isomer was obtained on column chromatography (30% EtOAc in hexanes)]




Reaction time : 5 h

Yield : 72%

Mp : 78-80 °C

IR (KBr) : ν 3294, 1716, 1649, 1620 $cm^{-1}$

$^{1}H$ NMR : δ 1.24 (t, 3H, $J$ = 7.6 Hz), 1.98 (s, 3H), 2.66 (q, 2H, $J$ = 7.6 Hz), 3.84 (s, 3H), 4.36 (d, 2H, $J$ = 5.5 Hz), 6.10 (b, 1H), 7.24 (d, 2H, $J$ = 8.2 Hz), 7.46 (d, 2H, $J$ = 8.2 Hz), 7.78 (s, 1H).

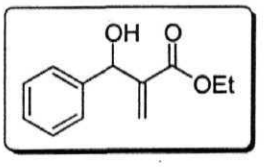
$^{13}C$ NMR : δ 15.09, 23.05, 28.58, 36.79, 52.01, 126.78, 128.14, 129.77, 131.45, 142.59, 145.80, 168.31, 169.63.

Analysis calcd. for $C_{15}H_{19}NO_3$ : C, 68.94; H, 7.33; N, 5.36

Found : C, 69. 11; H, 7.28; N, 5.34

**Ethyl 3-hydroxy-2-methylene-3-phenylpropanoate (178a):**

This molecule was obtained as a colorless viscous liquid *via* the Baylis-Hillman reaction between benzaldehyde and ethyl acrylate catalyzed by DABCO following a similar procedure described for the molecule **126a**.




Yield : 71%

Reaction time : 7 days

Bp : 122-124 °C/1.3 mm

IR (neat) : ν 3437, 1714, 1630 $cm^{-1}$

$^1$H NMR : δ 1.24 (t, 3H, $J$ = 7.0 Hz), 3.05 (b, 1H), 4.17 (q, 2H, $J$ = 7.0 Hz), 5.56 (s, 1H), 5.82 (s, 1H), 6.34 (s, 1H), 7.20-7.50 (m, 5H).

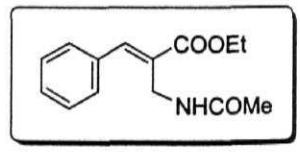
$^{13}$C NMR : δ 13.98, 60.84, 72.92, 125.43, 126.73, 127.69, 128.32, 141.62, 142.58, 166.31.

**Ethyl (2*E*)-2-acetylaminomethyl-3-phenylprop-2-enoate (179):**

Treatment of ethyl 3-hydroxy-3-phenyl-2-methylenepropanoate (**178a**) with acetonitrile in the presence of $CH_3SO_3H$ following similar procedure described for the molecule **177a** provided the desired amide, **179**, as a colorless solid.

*E* / *Z* : 92 / 8 [determined by the integration of isomeric olefinic proton singlets at δ 7.79 (*E*-isomer) & δ 7.00 (Z-isomer) in the $^1$H NMR spectrum of the crude sample. However, the pure *E*-isomer was obtained on column chromatography (30% EtOAc in hexanes)]

Reaction time : 5 h




Yield : 77%

Mp : 66 °C

IR (KBr) : ν 3294, 1709, 1649 cm$^{-1}$

$^1$H NMR : δ 1.37 (t, 3H, $J$ = 7.4 Hz), 1.98 (s, 3H), 4.23-4.43 (m, 4H), 6.08 (b, 1H), 7.30-7.61 (m, 5H), 7.79 (s, 1H).

$^{13}$C NMR : δ 14.10, 22.96, 36.67, 60.98, 128.10, 128.50, 129.04, 129.44, 134.13, 142.01, 167.60, 169.61.

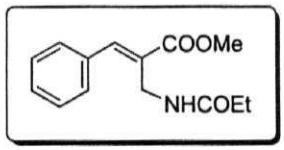
Analysis calcd. for $C_{14}H_{17}NO_3$ : C, 68.00; H, 6.93; N, 5.66.

Found : C, 68.23; H, 6.88; N, 5.70.

**Methyl (2*E*)-3-phenyl-2-propionoylaminomethylprop-2-enoate (180):**

The Ritter reaction of methyl 3-hydroxy-2-methylene-3-phenylpropanoate (**126a**) with propionitrile in the presence of methanesulfonic acid, following similar procedure described for the molecule **177a**, provide desired allyl amide, **180**, as a colorless solid.

*E* / *Z* : 92 / 8 [determined by the integration of isomeric olefinic proton singlets at δ 7.79 (*E*-isomer) & δ 6.35 (Z-isomer) in the $^1$H NMR spectrum of the crude sample. However, the pure *E*-isomer was obtained on column chromatography (30% EtOAc in hexanes)]




Reaction time : 5 h

Yield : 83%

Mp : 93-94 °C

IR (KBr) : ν 3294, 1714, 1639 cm$^{-1}$

$^1$H NMR : δ 1.15 (t, 3H, *J* = 7.6 Hz), 2.21 (q, 2H, *J* = 7.6 Hz), 3.85 (s, 3H), 4.37 (d, 2H, *J* = 5.7 Hz), 6.08 (b, 1H), 7.30- 7.58 (m, 5H), 7.79 (s, 1H).

$^{13}$C NMR : δ 9.75, 29.73, 36.76, 52.14, 128.16, 128.73, 129.27, 129.66, 134.30, 142.34, 168.35, 173.25.

Analysis calcd. for $C_{14}H_{17}NO_3$ : C, 68.00; H, 6.93; N, 5.66.

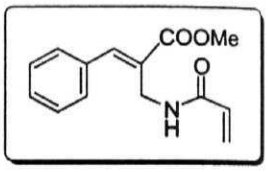
Found : C, 68.20; H, 6.95; N, 5.61.

**Methyl (2*E*)-2-acryloylaminomethyl-3-phenylprop-2-enoate (181):**

This molecule was obtained as colorless solid *via* the reaction between methyl 3-hydroxy-3-phenyl-2-methylenepropanoate (**126a**) and acrylonitrile in the presence of

methanesulfonic acid following similar procedure described for the molecule **177a.**

*E* / *Z* : 87 / 13 [determined by the integration of isomeric olefinic proton singlets at δ 7.82 (*E*-isomer) & δ 7.03 (Z-isomer) in the $^1$H NMR spectrum of the crude sample.. However, the pure *E*-isomer was obtained on column chromatography (30% EtOAc in hexanes)]




Reaction time : 5 h

Yield : 74%

Mp : 90 °C

IR (KBr) : ν 3296, 1712, 1655, 1624 cm$^{-1}$

$^1$H NMR : δ 3.85 (s, 3H), 4.44 (d, 2H, *J* = 5.8 Hz), 5.64 (dd, 1H, *J* = 9.8 Hz, 2.0 Hz), 6.10 (dd, 1H, *J* = 9.8 Hz, 16.6 Hz), 6.21-6.38 (m, 2H), 7.27-7.61 (m, 5H), 7.82 (s, 1H).

$^{13}$C NMR : δ 36.61, 51.92, 125.98, 127.52, 128.47, 129.07, 129.40, 130.75, 133.95, 142.48, 165.09, 167.91.

MS (m/z) : 246 $(M+H)^+$

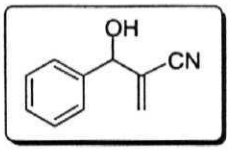
Analysis calcd. for $C_{14}H_{15}NO_3$ : C, 68.56; H, 6.16; N, 5.71.

Found : C, 68.42; H, 6.13; N, 5.75.

**3-Hydroxy-2-methylene-3-phenylpropanenitrile (182a):**

To a solution of benzaldehyde (50 mmol, 5.306 g) in acrylonitrile (75 mmol, 3.975 g), was added DABCO (15 mol%, 7.5 mmol, 0.841 g). After keeping the reaction mixture at room temperature for 2 days, the reaction mixture was diluted with ether (50 mL)

and washed successively with 2N HCl, aqueous $NaHCO_3$ solution and water. Organic layer was dried over anhydrous $Na_2SO_4$. Solvent was evaporated and the residue thus obtained was purified by distillation under reduced pressure to provide the pure product (**182a**) as colorless liquid.




Yield : 77% (6.129 g)

Bp : 118-120 °C/1.2 mm

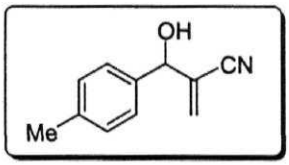
IR (neat) : ν 3447, 2229, 1620 $cm^{-1}$

$^1H$ NMR : δ 2.42 (b, 1H), 5.28 (s, 1H), 6.02 (s, 1H), 6.09 (s, 1H), 7.38 (s, 5H).

$^{13}C$ NMR : δ 73.94, 117.13, 126.33, 126.58, 128.85, 130.22, 139.34.

**3-Hydroxy-2-methylene-3-(4-methylphenyl)propanenitrile (182b):**

This molecule was obtained as a colorless viscous liquid *via* the reaction between 4-methylbenzaldehyde and acrylonitrile under the influence of DABCO following a similar procedure described for the molecule **182a**.




Reaction time : 2 days

Yield : 71%

Bp : 128-130 °C/1.3 mm

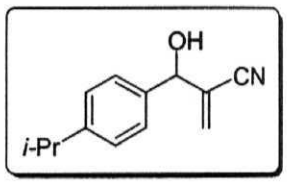
IR (neat) : ν 3427 (b), 2229, 1614 $cm^{-1}$

$^1H$ NMR : δ 2.37 (s, 3H), 3.65 (d, 1H, $J$ = 3.9 Hz), 5.12 (d, 1H, $J$ = 3.9 Hz), 5.92 (s, 1H), 6.01 (d, 1H, $J$ = 1.9 Hz), 7.16-7.28 (m, 4H).

$^{13}$C NMR : δ 21.20, 73.81, 117.21, 126.46, 126.58, 129.55, 129.90, 136.44, 138.63.

**3-Hydroxy-3-(4-isopropylphenyl)-2-methylenepropanenitrile (182c):**

This compound was prepared *via* the Baylis-Hillman coupling of 4-isopropylbenzaldehyde with acrylonitrile in the presence of DABCO, as a colorless viscous liquid, following a similar procedure described for the molecule **182a**.




Reaction time : 2 days

Yield : 72%

IR (neat) : ν 3437, 2229, 1616 cm$^{-1}$

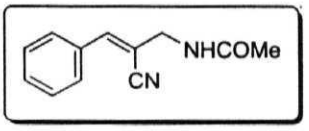
$^{1}$H NMR : δ 1.25 (d, 6H, $J$ = 6.8 Hz), 2.29 (d, 1H, $J$ = 4.0 Hz), 2.92 (sept, 1H, $J$ = 6.8 Hz), 5.29 (d, 1H, $J$ = 4.0 Hz), 6.04 (s, 1H), 6.11 (d, 1H, $J$ = 2.0 Hz), 7.23-7.40 (m, 4H).

$^{13}$C NMR : δ 23.88, 33.86, 73.96, 117.12, 126.59, 126.96, 129.67, 136.72, 149.69.

**(2*Z*)-2-Acetylaminomethyl-3-phenylprop-2-enenitrile (183a):**

This molecule was obtained as a colorless solid *via* the Ritter reaction of 3-hydroxy-2-methylene-3-phenylpropanenitrile (**182a**) with acetonitrile in the presence of methanesulfonic acid following similar procedure described for the molecule **177a**.

*Z* / *E* : 96 / 4 [determined by the integration of isomeric allylic protons doublet at δ 4.14 (*Z*-isomer) & δ 4.29 (E-isomer) in the $^1$H NMR spectrum of the crude sample. However, the pure *E*-isomer was obtained on column chromatography (30% EtOAc in hexanes)]




Reaction time : 5 h

Yield : 82%

Mp : 98-100 $^0$C

IR (KBr) : ν 3302, 2216, 1657, 1620 cm$^{-1}$

$^1$H NMR : δ 2.05 (s, 3H), 4.14 (d, 2H, *J* = 6.0 Hz), 6.13 (b, 1H), 7.16 (s, 1H), 7.34-7.50 (m, 3H), 7.69-7.81 (m, 2H).

$^{13}$C NMR : δ 23.05, 43.42, 107.95, 117.99, 128.86, 130.60, 132.98, 145.30, 170.68.

MS (m/z) : 201 $(M+H)^+$

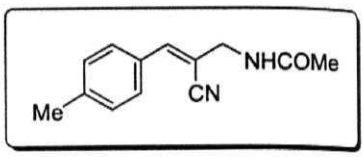
Analysis calcd. for $C_{12}H_{12}N_2O$ : C, 71.98; H, 6.04; N, 13.99

Found : C, 72.22; H, 6.07; N, 14.08

**(2*Z*)-2-Acetylaminomethyl-3-(4-methylphenyl)prop-2-enenitrile (183b):**

This compound was prepared *via* the treatment of 3-hydroxy-3-(4-methylphenyl)-2-methylenepropanenitrile (**182b**) with acetonitrile in the presence of methanesulfonic acid, following similar procedure described for the molecule **177a**, as a colorless solid.

*Z* : *E* : 100 : 0 [In the $^1$H NMR spectrum of the crude product, there were no peaks observed corresponding to the minor *E*-isomer].




Reaction time : 5 h

Yield : 85%

Mp : 108-110 °C

IR (KBr) : ν 3290, 2212, 1649, 1622 $cm^{-1}$

$^1H$ NMR : δ 2.05 (s, 3H), 2.38 (s, 3H), 4.15 (d, 2H, $J$ = 6.2 Hz), 6.05 (b, 1H), 7.13 (s, 1H), 7.21 (d, 2H, $J$ = 8.2 Hz), 7.64 (d, 2H, $J$ = 8.2 Hz).

$^{13}C$ NMR : δ 21.41, 22.98, 43.38, 106.68, 118.22, 128.88, 129.54, 130.32, 141.08, 145.17, 170.74.

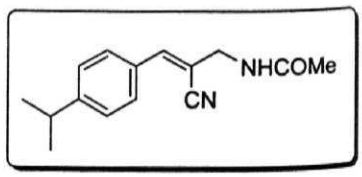
Analysis calcd. for $C_{13}H_{14}N_2O$ : C, 72.87; H, 6.59; N, 13.07

Found : C, 72.65; H, 6.61, N; 13.17

**(2*Z*)-2-Acetylaminomethyl-3-(4-isopropylphenyl)prop-2-enenitrile (183c):**

The Ritter reaction of 3-hydroxy-3-(4-isopropylphenyl)-2-methylenepropanenitrile (**182c**) with acetonitrile in the presence of methanesulfonic acid, following similar procedure described for the molecule **177a**, provided this molecule as a colorless solid.

*Z* : *E* : 100 : 0 [In the $^1H$ NMR spectrum of the crude product, there were no peaks observed corresponding to the minor *E*-isomer].




Reaction time : 5 h

Yield : 83%

Mp : 76-78 °C

IR (KBr) : ν 3302, 2212, 1657, 1625 $cm^{-1}$

$^1H$ NMR : δ 1.25 (d, 6H, $J$ = 7.8 Hz), 2.05 (s, 3H), 2.93 (sept, 1H, $J$ = 7.8 Hz), 4.15 (d, 2H, $J$ = 6.0 Hz), 5.99 (b, 1H), 7.14 (s, 1H), 7.28 (d, 2H, $J$ = 7.8 Hz), 7.68 (d, 2H, $J$ = 7.8 Hz).

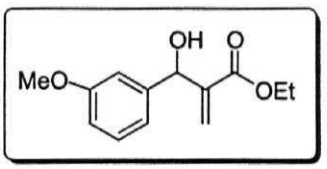
$^{13}C$ NMR : δ 22.90, 23.54, 33.92, 43.28, 106.62, 118.16, 126.82, 128.91, 130.56, 145.09, 151.81, 170.66.

Analysis calcd. for $C_{15}H_{18}N_2O$ : C, 74.35; H, 7.49; N, 11.56.

Found : C, 74.19; H, 7.45; N, 11.48

**Ethyl 3-hydroxy-3-(3-methoxyphenyl)-2-methylenepropanoate (178b):**

This molecule was obtained as a colorless viscous liquid *via* the Baylis-Hillman reaction between 3-methoxybenzaldehyde and ethyl acrylate catalyzed by DABCO following a similar procedure described for the molecule **126a**. The crude product was purified by column chromatography (10% EtOAc in hexanes, silica gel).




Reaction time : 12 days

Yield : 60%

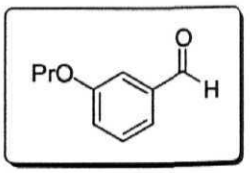
IR (neat) : ν 3458, 1714, 1620 $cm^{-1}$

$^1H$ NMR : δ 1.25 (t, 3H, $J$ = 6.8 Hz), 2.70 (b, 1H), 3.79 (s, 3H), 4.18 (q, 2H, $J$ = 6.8 Hz), 5.53 (s, 1H), 5.80 (s, 1H), 6.33 (s, 1H), 6.75-7.00 (m, 3H), 7.18-7.32 (m, 1H).

$^{13}$C NMR : δ 13.88, 55.04, 60.76, 72.71, 112.15, 113.19, 118.96, 125.44, 129.22, 143.32, 143.15, 159.55, 166.20.

**3-Propoxybenzaldehyde (195a):**

To a stirred solution of 3-hydroxybenzaldehyde (10 mmol, 1.221 g) and anhydrous $K_2CO_3$ (10 mmol, 1.38 g) in acetonitrile (15 mL), was added propyl bromide (10 mmol, 1.23 g) and this suspension was refluxed for 3 hours. Reaction mixture was cooled to room temperature and excess acetonitrile was removed under reduced pressure. The residue thus obtained was diluted with water (25 mL) and extracted with ether (3 x 25 mL). The combined organic layer was dried over anhydrous $Na_2SO_4$. Solvent evaporation followed by column chromatography (silica gel, 3% EtOAc in hexanes) of the resulting crude product provided the desired aldehyde **195a** as a colorless liquid.




Yield : 85%

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

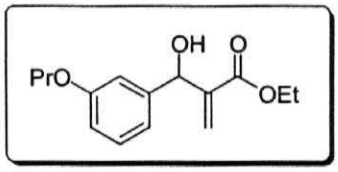
$^1$H NMR : δ 1.05 (t, 3H, $J$ = 7.6 Hz), 1.72-1.94 (m, 2H), 3.98 (t, 2H, $J$ = 6.6 Hz), 7.10-7.24 (m, 1H), 7.33-7.50 (m, 3H), 9.96 (s, 1H).

$^{13}$C NMR : δ 10.38, 22.43, 69.76, 113.04, 121.73, 123.03, 129.92, 137.86, 159.73, 191.93.

**Ethyl 3-hydroxy-2-methylene-3-(3-propoxyphenyl)propanoate (178c):**

This compound was prepared *via* the DABCO catalyzed Baylis-Hillman coupling of 3-

propoxybenzaldehyde (**195a**) with ethyl acrylate following a similar procedure described for the molecule **126a**. The crude product was purified by column chromatography (10% EtOAc in hexanes, silica gel).




Reaction time : 13 days

Yield : 65%

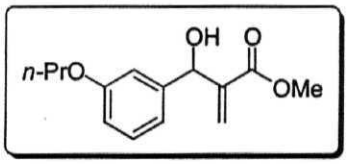
IR (neat) : ν 3456, 1712, 1619 $cm^{-1}$

$^1H$ NMR : δ 1.00 (t, 3H, $J$ = 7.0 Hz), 1.19 (t, 3H, $J$ = 7.6), 1.68-1.92 (m, 2H), 3.51 (b, 1H), 3.87 (t, 2H, $J$ = 6.6 Hz), 4.11 (q, 2H, $J$ = 7.6 Hz), 5.47 (s, 1H), 5.83 (s, 1H), 6.29 (s, 1H), 6.70-6.88 (m, 3H), 7.18-7.28 (m, 1H).

$^{13}C$ NMR : δ 10.48, 13.97, 22.56, 60.79, 69.43, 72.77, 112.89, 113.82, 118.91, 125.41, 129.24, 142.49, 143.22, 159.23, 166.26.

**Methyl 3-hydroxy-2-methylene-3-(3-propoxyphenyl)propanoate (126j):**

This was obtained *via* the Baylis-Hillman reaction between 3-propoxybenzaldehyde (**195a**) and methyl acrylate under the catalytic influence of DABCO, following a similar procedure described for the molecule **126a**, as a colorless viscous liquid. The crude product was purified by column chromatography (10% EtOAc in hexanes, silica gel).




Reaction time : 13 days

Yield : 62%

IR (neat) : ν 3466, 1720, 1630 $cm^{-1}$

$^1H$ NMR : δ 1.10 (t, 3H, $J$ = 7.0 Hz), 1.67-1.89 (m, 2H), 3.38 (b, 1H), 3.66 (s, 3H), 3.88 (q, 2H, $J$ = 6.2 Hz), 5.48 (s, 1H), 5.83 (s, 1H), 6.28 (s, 1H), 6.73-6.97 (m, 3H), 7.17-7.28 (m, 1H).

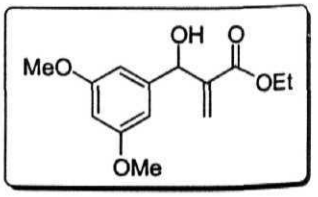
$^{13}C$ NMR : δ 10.46, 22.57, 51.78, 69.47, 72.82, 112.89, 113.91, 118.85, 125.75, 129.29, 142.20, 143.08, 159.27, 166.70.

**Ethyl 3-hydroxy-3-(3,5-dimethoxyphenyl)-2-methylenepropanoate (178d):**

This was prepared according to the procedure developed in our laboratory.[311]

To a solution of 3,5-dimethoxybenzaldehyde (10 mmol, 1.661 g), DABCO (15 mol%, 1.5 mmol, 0.168 g) in ethyl acrylate (15 mmol, 1.5 g), was added silica gel {(>200 mesh), (2.50-2.75 g)} and mixed thoroughly left at room temperature. After 10 days, mixture (silica gel pack) was washed thoroughly with ethyl acetate (4 x 10 mL). 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, 10% ethyl acetate in hexanes) to provide the product (**178d**) as viscous liquid.

Yield : 61% (1.625 g)



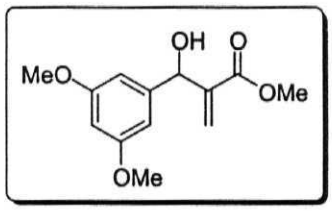

IR (neat) : ν 3476, 1714, 1620 $cm^{-1}$

$^1H$ NMR : δ 1.22 (t, 3H, $J$ = 7.0 Hz), 3.45 (b, 1H), 3.73 (s, 6H), 4.15 (q, 2H, $J$ = 7.0 Hz), 5.46 (s, 1H), 5.81 (s, 1H), 6.29 (s, 1H), 6.27-6.40 (m, 1H), 6.50 (d, 2H, $J$ = 1.6 Hz).

$^{13}$C NMR : δ 14.02, 55.26, 60.90, 73.02, 99.77, 104.64, 125.80, 142.15, 144.02, 160.78, 166.33.

**Methyl 3-hydroxy-3-(3,5-dimethoxyphenyl)-2-methylenepropanoate (126k):**

This molecule was obtained as a colorless viscous liquid *via* the reaction between 3,5-dimethoxybenzaldehyde and methyl acrylate catalyzed by DABCO in silica gel solid phase medium, following a similar procedure described for the molecule **178d**.




Reaction time : 10 days

Yield : 59%

IR (neat) : ν 3435, 1720, 1620 cm$^{-1}$

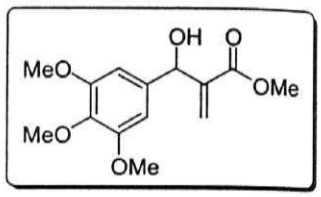
$^{1}$H NMR : δ 3.10 (d, 1H, $J$ = 5.8 Hz), 3.74 (s, 3H), 3.78 (s, 6H), 5.49 (d, 1H, $J$ = 5.8 Hz), 5.83 (s, 1H), 6.34 (s, 1H), 6.37-6.46 (m, 1H), 6.53 (d, 2H, $J$ = 2.8 Hz).

$^{13}$C NMR : δ 51.84, 55.22, 72.76, 99.74, 104.68, 125.92, 142.01, 143.99, 160.75, 166.70.

**Methyl 3-hydroxy-2-methylene-3-(3,4,5-trimethoxyphenyl)propanoate (126l):**

This molecule was obtained *via* the Baylis-Hillman coupling of 3,4,5-trimethoxybenzaldehyde with methyl acrylate under the catalytic influence DABCO in silica gel solid phase medium, following a similar procedure described for the molecule **178d**, as a yellow solid.

Reaction time : 17 days




Yield : 60%

Mp : 48-50 °C

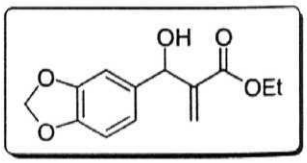
IR (KBr) : ν 3450, 1722, 1630 $cm^{-1}$

$^1$H NMR : δ 3.10 (d, 1H, *J* 5.8 Hz), 3.75 (s, 3H), 3.83 (s, 3H), 3.84 (s, 6H), 5.50 (d, 1H, *J* = 5.8 Hz), 5.83 (s, 1H), 6.33 (s, 1H), 6.59 (s, 2H).

$^{13}$C NMR : δ 51.81, 55.96, 60.60, 72.60, 103.80, 125.51, 137.20, 142.25, 153.02, 166.70.

**Ethyl 3-hydroxy-2-methylene-3-(3,4-methylenedioxyphenyl)propanoate (178e):**

This compound was prepared *via* the DABCO-catalyzed coupling between piperanal and ethyl acrylate, following a similar procedure described for the molecule **126a**, as a colorless viscous liquid.




Reaction time : 45 days

Yield : 60%

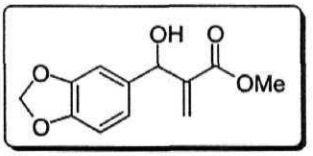
IR (neat) : ν 3464, 1712, 1630 $cm^{-1}$

$^1$H NMR : δ 1.26 (t, 3H, *J* = 7.0 Hz), 2.99 (d, 1H, *J* = 5.2 Hz), 4.19 (q, 2H, *J* = 7.29 Hz), 5.48 (d, 1H, *J* = 5.2 Hz), 5.83 (s, 1H), 5.94 (s, 2H), 6.32 (s, 1H), 6.73-6.95 (m, 3H).

$^{13}$C NMR : δ 13.97, 60.81, 72.79, 100.97, 107.26, 108.00, 120.20, 125.14, 135.63, 142.58, 147.13, 147.70, 166.25.

**Methyl 3-hydroxy-2-methylene-3-(3,4-methylenedioxyphenyl)propanoate (126m):**

This molecule was obtained as a colorless viscous liquid *via* the Baylis-Hillman reaction between piperanal and methyl acrylate in the presence of DABCO following a similar procedure described for the molecule **126a**.




Reaction time : 45 days

Yield : 52%

IR (neat) : ν 3499, 1720, 1630 $cm^{-1}$

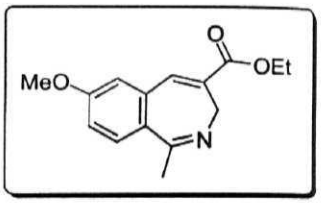
$^{1}H$ NMR : δ 3.08 (b, 1H), 3.69 (s, 3H), 5.44 (s, 1H), 5.84 (s, 1H), 5.89 (s, 2H), 6.28 (s, 1H), 6.66-6.90 (m, 3H).

$^{13}C$ NMR : δ 51.81, 72.72, 100.01, 107.22, 108.04, 120.22, 125.40, 135.50, 142.25, 147.19, 147.73, 166.70.

**3-Aza-5-ethoxycarbonyl-9-methoxy-2-methylbicyclo[5.4.0]undeca-1(7),2,5,8,10-pentaene (184):**

To a stirred solution of ethyl 3-hydroxy-3-(3-methoxyphenyl)-2-methylenepropanoate (**178b**) (2 mmol, 0.472) in acetonitrile (5 mL) was added methanesulfonic acid (3 mL) at 60 °C and immediately temperature was raised to 150 °C. After stirring at 150 °C for 6 h, the reaction mixture was brought to room temperature and diluted with water. Aqueous $K_2CO_3$ solution was added slowly till the acid was neutralized 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, 25% EtOAc in hexanes) to furnish the pure compound (**184**) as light yellow solid.




Yield : 55% (0.286 g)

Mp : 86-88 °C

IR (KBr) : ν 1709, 1630, 1602 $cm^{-1}$

$^1H$ NMR : δ 1.37 (t, 3H, $J$ = 7.4 Hz), 2.36 (s, 3H), 3.88 (s, 3H), 3.92 (s, 2H), 4.31 (q, 2H, $J$ = 7.4 Hz), 6.91-7.06 (m, 2H), 7.64 (d, 1H, $J$ = 8.8 Hz), 7.68 (s, 1H).

$^{13}C$ NMR : δ 14.23, 26.26, 47.22, 55.39, 61.11, 113.68, 115.21, 130.36, 131.44, 133.69, 137.00, 138.35, 159.59, 165.50, 167.09.

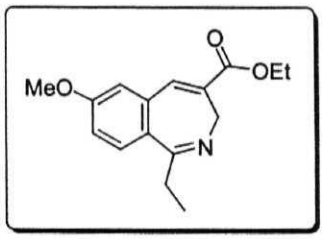
Analysis calcd. for $C_{15}H_{17}NO_3$ : C, 69.48; H, 6.61; N, 5.40.

Found : C, 69.35; H, 6.63; N, 5.45.

**3-Aza-5-ethoxycarbonyl-2-ethyl-9-methoxybicyclo[5.4.0]undeca-1(7),2,5,8,10-pentaene (185):**

This molecule was obtained as a light yellow solid *via* the reaction between ethyl 3-hydroxy-3-(3-methoxyphenyl)-2-methylenepropanoate (**178b**) and propionitrile in the presence of methanesulfonic acid following similar procedure described for the molecule **184**.

Reaction time : 6 h




Yield : 67%

Mp : 89-90 °C

IR (KBr) : ν 1705, 1618, 1602 $cm^{-1}$

$^1H$ NMR : δ 0.97 (t, 3H, $J$ = 7.2 Hz), 1.37 (t, 3H, $J$ = 7.0 Hz), 2.69 (q, 2H, $J$ = 7.2 Hz), 3.87 (s, 3H), 3.92 (s, 2H), 4.31 (q, 2H, $J$ = 7.0 Hz), 6.90-7.06 (m, 2H), 7.63 (d, 1H, $J$ = 8.6 Hz), 7.68 (s, 1H).

$^{13}C$ NMR : δ 11.69, 14.08, 32.13, 46.89, 55.19, 60.92, 113.36, 115.04, 129.82, 130.69, 133.99, 137.33, 138.24, 159.28, 165.36, 171.09.

MS (m/z) : 273 ($M^+$), 272 $(M-1)^+$

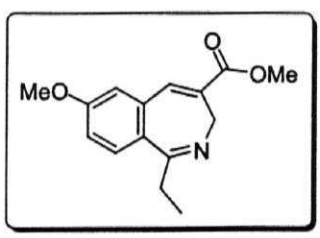
Analysis calcd. for $C_{16}H_{19}NO_3$ : C, 70.31; H, 7.01; N, 5.12.

Found : C, 70.39; H, 7.05; N, 5.15.

**3-Aza-2-ethyl-9-methoxy-5-methoxycarbonylbicyclo[5.4.0]undeca-1(7),2,5,8,10-pentaene (186):**

This compound was prepared *via* the treatment of methyl 3-hydroxy-3-(3-methoxyphenyl)-2-methylenepropanoate (**126h**) with propionitrile in the presence of methanesulfonic acid following similar procedure described for the molecule **184**.

Reaction time : 6 h




Yield : 44%

IR (neat) : ν 1712, 1625, 1602 $cm^{-1}$

$^1H$ NMR : δ 0.93 (t, 3H, $J$ = 7.5 Hz), 2.64 (q, 2H, $J$ = 7.5 Hz), 3.79 (s, 3H), 3.82 (s, 3H), 3.87 (s, 2H), 6.88-7.02 (m, 2H), 7.58 (d, 1H, $J$ = 8.6 Hz), 7.63 (s, 1H).

$^{13}C$ NMR : δ 11.75, 32.22, 47.09, 52.00, 55.33, 113.62, 115.22, 129.94, 130.97, 133.90, 137.45, 138.54, 159.51, 165.97, 171.26.

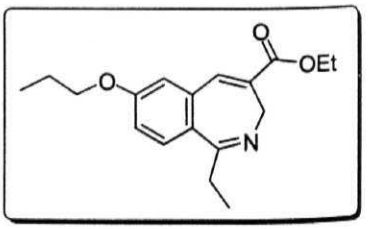
MS (m/z) : 259 ($M^+$), 258 $(M-1)^+$

Analysis calcd. for $C_{15}H_{17}NO_3$ : C, 69.48; H, 6.61; N, 5.40

Found : C, 69.24; H, 6.56; N, 5.34

**3-Aza-5-ethoxycarbonyl-2-ethyl-9-propoxybicyclo[5.4.0]undeca-1(7),2,5,8,10-pentaene (187):**

Treatment of ethyl 3-hydroxy-2-methylene-3-(3-propoxyphenyl)propanoate (**178c**) with propionitrile in the presence of methanesulfonic acid, following similar procedure described for the molecule **184**, provided the desired 2-benzazepine derivative **187** as light brown viscous liquid.




Reaction time : 6 h

Yield : 58%

IR (neat) : ν 1711, 1622, 1602 $cm^{-1}$

$^1H$ NMR : δ 0.95 (t, 3H, $J$ = 7.8 Hz), 1.04 (t, 3H, $J$ = 7.8 Hz), 1.35 (t, 3H, $J$ = 6.8 Hz), 1.73-1.94 (m, 2H), 2.68 (q, 2H, $J$ = 7.8 Hz), 3.90 (s, 2H), 3.97 (t,

2H, $J$ = 6.8 Hz), 4.29 (q, 2H, $J$ = 6.8 Hz), 6.88-7.06 (m, 2H), 7.60 (d, 1H, $J$ = 8.8 Hz), 7.66 (s, 1H).

$^{13}$C NMR : δ 10.41, 11.86, 14.22, 22.44, 32.26, 46.99, 61.08, 69.69, 114.11, 115.66, 129.95, 130.58, 134.02, 137.49, 138.49, 159.06, 165.56, 171.45.

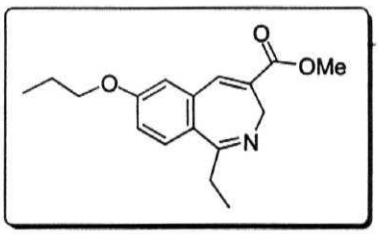
MS (m/z) : 301 ($M^+$), 300 $(M-1)^+$

Analysis calcd. for $C_{18}H_{23}NO_3$ : C, 71.73; H, 7.69; N, 4.65.

Found : C, 71.50; H, 7.61; N, 4.70.

**3-Aza-2-ethyl-5-methoxycarbonyl-9-propoxybicyclo[5.4.0]undeca-1(7),2,5,8,10-pentaene (188):**

This molecule was obtained as light brown viscous liquid *via* the reaction between methyl 3-hydroxy-2-methylene-3-(3-propoxyphenyl)propanoate **(126j)** and propionitrile in the presence of methanesulfonic acid following similar procedure described for the molecule **184**.




Reaction time : 6 h

Yield : 65%

IR (neat) : ν 1714, 1625, 1602 cm$^{-1}$

$^1$H NMR : δ 0.94 (t, 3H, $J$ = 7.2 Hz), 1.02 (t, 3H, $J$ = 7.2 Hz), 1.68-1.91 (m, 2H), 2.66 (q, 2H, $J$ = 7.2 Hz), 3.81 (s, 3H), 3.89 (s, 2H), 3.96 (t, 2H, $J$ = 6.6 Hz), 6.87-7.01 (m, 2H), 7.59 (d, 1H, $J$ = 8.6 Hz), 7.64 (s, 1H).

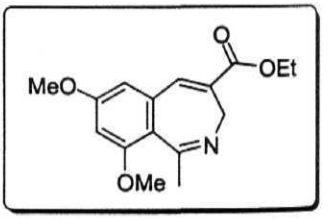
$^{13}$C NMR : δ 10.39, 11.84, 22.45, 32.22, 46.98, 52.09, 69.73, 114.19, 115.72, 129.97, 130.60, 133.70, 137.44, 138.71, 159.13, 166.06, 171.59.

Analysis calcd. for $C_{17}H_{21}NO_3$ : C, 71.06; H, 7.37; N, 4.87.

Found : C, 71.35; H, 7.30; N, 4.81.

**3-Aza-9,11-dimethoxy-5-ethoxycarbonyl-2-methylbicyclo[5.4.0]undeca-1(7),2,5,8,10-pentaene (189)[s]:**

This compound was prepared *via* the treatment of ethyl 3-hydroxy-3-(3,5-dimethoxyphenyl)-2-methylenepropanoate (**178d**) with acetonitrile in the presence of methanesulfonic acid, following similar procedure described for the molecule **184**, as a light brown viscous liquid.




Reaction time : 6 h

Yield : 70%

IR (neat) : ν 1709, 1622, 1599 cm$^{-1}$

$^1$H NMR : δ 1.25 (t, 3H, $J$ = 7.0 Hz), 2.18 (s, 3H), 2.84 (d, 1H, $J$ = 10.8 Hz), 3.75 (s, 3H), 3.78 (s, 3H), 4.18 (q, 2H, $J$ = 7.0 Hz), 4.70 (d, 1H, $J$ = 10.8 Hz), 6.43 (s, 2H), 7.53 (s, 1H).

$^{13}$C NMR : δ 14.17, 25.77, 47.48, 55.40, 55.61, 60.99, 99.50, 104.72, 122.63, 135.39, 137.24, 138.23, 159.49, 160.48, 165.48, 165.62.

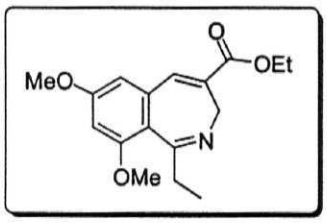
MS (m/z) : 289 ($M^+$)

Analysis calcd. for $C_{16}H_{19}NO_4$ : C, 66.42; H, 6.62; N, 4.84

Found : C, 66.17; H, 6.68; N, 4.77

**3-Aza-9,11-dimethoxy-5-ethoxycarbonyl-2-ethylbicyclo[5.4.0]undeca-1(7),2,5,8,10-pentaene (190)[s]:**

Treatment of ethyl 3-hydroxy-3-(3,5-dimethoxyphenyl)-2-methylenepropanoate (**178d**) with propionitrile in the presence of methanesulfonic acid, following similar procedure described for the molecule **184**, provided the required 2-benzazepine derivative **190** as a light brown viscous liquid.




Reaction time : 6 h

Yield : 74%

IR (neat) : ν 1711, 1620, 1599 $cm^{-1}$

$^1H$ NMR : δ 0.84 (t, 3H, $J$ = 7.6 Hz), 1.32 (t, 3H, $J$ = 6.8 Hz), 2.51-2.78 (m, 2H), 2.91 (d, 1H, $J$ = 10.8 Hz), 3.82 (s, 3H), 3.84 (s, 3H), 4.15-4.36 (m, 2H), 4.80 (d, 1H, $J$ = 10.8 Hz), 6.49 (s, 2H), 7.60 (s, 1H).

$^{13}C$ NMR : δ 12.06, 14.21, 31.67, 47.37, 55.45, 55.72, 61.07, 99.47, 104.75, 121.82, 135.91, 137.95, 138.31, 159.45, 160.59, 165.55, 170.90.

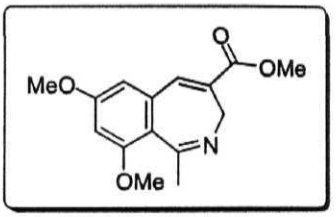
MS (m/z) : 303 ($M^+$)

Analysis calcd. for $C_{17}H_{21}NO_4$ : C, 67.31, H, 6.98, N, 4.62

Found : C, 67.52, H, 6.95, N, 4.68

**3-Aza-9,11-dimethoxy-5-methoxycarbonyl-2-methylbicyclo[5.4.0]undeca-1(7),2,5,8,10-pentaene (191)[$]:**

This molecule was obtained as a light yellow solid *via* the reaction between methyl 3-hydroxy-3-(3,5-dimethoxyphenyl)-2-methylenepropanoate (**126k**) and acetonitrile in the presence of methanesulfonic acid following similar procedure described for the molecule **184**.




Reaction time : 6 h

Yield : 72%

Mp : 108 °C

IR (KBr) : ν 1703, 1628, 1597 $cm^{-1}$

$^1H$ NMR : δ 2.29 (s, 3H), 2.97 (d, 1H, $J$ = 10.8 Hz), 3.84 (s, 3H), 3.86 (s, 3H), 3.89 (s, 3H), 4.81 (d, 1H, $J$ = 10.8 Hz), 6.52 (s, 2H), 7.65 (s, 1H).

$^{13}C$ NMR : δ 25.84, 47.60, 52.03, 55.42, 55.65, 99.58, 104.70, 122.76, 135.10, 137.20, 138.49, 159.52, 160.48, 165.63, 166.00.

MS (m/z) : 275 ($M^+$)

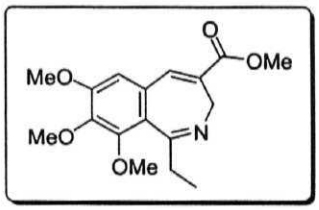
Analysis calcd. for $C_{15}H_{17}NO_4$ : C, 65.44; H, 6.22; N, 5.09

Found : C, 65.35; H, 6.20; N, 5.12

**3-Aza-2-ethyl-5-methoxycarbonyl-9,10,11-trimethoxybicyclo[5.4.0]undeca-1(7),2,5,8,10-pentaene (192)[$]:**

This molecule was obtained *via* the simultaneous Ritter and Houben-Hoesch reactions of methyl 3-hydroxy-2-methylene-3-(3,4,5-trimethoxyphenyl)propanoate (**126l**) with

propionitrile in the presence of methanesulfonic acid, following similar procedure described for the molecule **184**, as a light yellow solid.




Reaction time : 6 h

Yield : 33%

Mp : 140-141 °C

IR (KBr) : ν 1709, 1624, 1591 $cm^{-1}$

$^1H$ NMR : δ 0.88 (t, 3H, $J$ = 7.6 Hz), 2.68 (q, 2H, $J$ = 7.6 Hz), 2.93 (d, 1H, $J$ = 10.8 Hz), 3.84 (s, 3H), 3.91 (s, 6H), 3.94 (s, 3H), 4.88 (d, 1H, $J$ = 10.8 Hz), 6.72 (s, 1H), 7.65 (s, 1H).

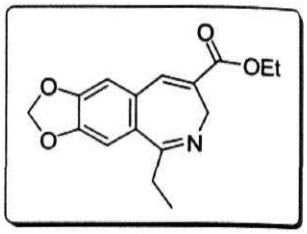
$^{13}C$ NMR : δ 12.06, 31.88, 47.79, 52.19, 56.05, 61.19, 61.67, 107.80, 126.33, 132.02, 134.10, 138.51, 141.92, 152.47, 153.89, 166.18, 170.20.

Analysis calcd. for $C_{17}H_{21}NO_5$ : C, 63.94; H, 6.63; N, 4.39

Found : C, 63.80; H, 6.60; N, 4.37

**3-Aza-5-ethoxycarbonyl-2-ethyl-9,10-methylenedioxybicyclo[5.4.0]undeca-1(7),2,5,8,10-pentaene (193):**

This molecule was obtained as a light yellow solid *via* the treatment of ethyl 3-hydroxy-2-methylene-3-(3,4-methylenedioxyphenyl)propanoate (**178e**) with propionitrile in the presence of methanesulfonic acid following similar procedure described for the molecule **184**.



Reaction time : 6 h

Yield : 48%

Mp : 78-79 °C

IR (KBr) : ν 1701, 1630, 1587 $cm^{-1}$

$^1H$ NMR : δ 0.97 (t, 3H, $J$ = 7.6 Hz), 1.36 (t, 3H, $J$ = 7.0 Hz), 2.65 (q, 2H, $J$ = 7.6 Hz), 3.88 (br s, 2H), 4.29 (q, 2H, $J$ = 7.0 Hz), 6.07 (s, 2H), 6.87 (s, 1H), 7.11 (s, 1H), 7.61 (s, 1H).

$^{13}C$ NMR : δ 11.86, 14.31, 32.47, 47.32, 61.13, 101.93, 107.71, 109.07, 131.39, 131.97, 133.56, 138.10, 147.67, 148.24, 165.69, 170.33.

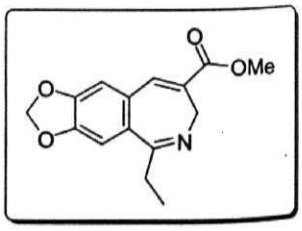
MS (m/z) : 287 ($M^+$), 286 $(M-1)^+$

Analysis calcd. for $C_{16}H_{17}NO_4$ : C, 66.89; H, 5.96; N, 4.87.

Found : C, 66.99; H, 5.94; N, 4.85.

**3-Aza-2-ethyl-5-methoxycarbonyl-9,10-methylenedioxybicyclo[5.4.0]undeca-1(7), 2,5,8,10-pentaene (194):**

Treatment of methyl 3-hydroxy-2-methylene-3-(3,4-methylenedioxyphenyl)propanoate (**126m**) with propionitrile in the presence of methanesulfonic acid, following similar procedure described for the molecule **184**, provided the title compound **194** as a light yellow solid.



Reaction time : 6 h

Yield : 46%

Mp : 126-127 °C

IR (KBr) : ν 1707, 1630, 1585 $cm^{-1}$

$^1H$ NMR : δ 0.97 (t, 3H, *J* = 7.6 Hz), 2.65 (q, 2H, *J* = 7.6 Hz), 3.84 (s, 5H), 6.08 (s, 2H), 6.87 (s, 1H), 7.12 (s, 1H), 7.62 (s, 1H).

$^{13}C$ NMR : δ 11.75, 32.37, 47.28, 52.08, 101.89, 107.61, 108.98, 131.16, 131.42, 133.54, 138.25, 147.64, 148.15, 166.05, 170.18.

Analysis calcd for $C_{15}H_{15}NO_4$ : C, 65.93; H, 5.53; N, 5.13

Found : C, 65.76; H, 5.54; N, 5.10

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[s] *It is interesting to note that in the case of compounds* **189-192** *(having methoxy group at 11 position), one of the ring-allylic methylene protons in $^1H$ NMR spectra appears as a doublet at δ 2.84-2.97 while the other proton appears as a doublet at δ 4.70-4.88. We have in fact confirmed this assignment in one case (compound* **192***) by hydrogen-carbon (hetero) COSY NMR experiment (Spectrum 25) and also by single crystal X-ray data (Fig. X3, Table 8). In the case of all the remaining 2-benzazepine derivatives* **184-188, 193, 194** *(without the methoxy group at 11-position) both the ring allylic methylene protons appear as a singlet at δ 3.84-3.92.*

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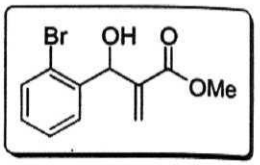
**Methyl 3-hydroxy-3-(2-bromphenyl)-2-methylenepropanoate (126n):**

This molecule was obtained as a colorless viscous liquid *via* the Baylis-Hillman reaction between 2-bromobenzaldehyde and methyl acrylate in the presence of DABCO following a similar procedure described for the molecule **126a**. The crude product was purified by column chromatography (6% EtOAc in hexanes, silica gel).




Reaction time : 9 days

Yield : 70%

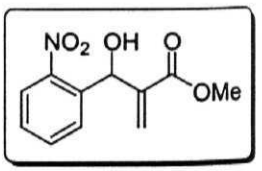
IR (neat) : ν 3447, 1716, 1633 $cm^{-1}$

$^1H$ NMR : δ 3.25 (d, 1H, $J$ = 4.8 Hz), 3.78 (s, 3H), 5.56 (s, 1H), 5.94 (d, 1H, $J$ = 4.8 Hz), 6.34 (s, 1H), 7.10-7.42 (m, 2H), 7.55 (d, 2H, $J$ = 8.6 Hz).

$^{13}C$ NMR : δ 52.08, 71.50, 123.15, 127.02, 127.65, 128.44, 129.33, 132.78, 139.94, 140.79, 166.98.

**Methyl 3-hydroxy-2-methylene-3-(2-nitrophenyl)propanoate (126o):**

This compound was prepared *via* the treatment of 2-nitrobenzaldehyde with methyl acrylate under the influence of DABCO, following a similar procedure described for the molecule **126a**, as a colorless viscous liquid. The crude product was purified by column chromatography (10% EtOAc in hexanes, silica gel).




Reaction time : 2 days

Yield : 60%

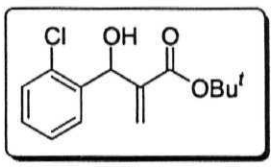
IR (neat) : ν 3447, 1716, 1633 $cm^{-1}$

$^1H$ NMR : δ 3.42 (b, 1H), 3.70 (s, 3H), 5.70 (s, 1H), 6.13 (s, 1H), 6.33 (s, 1H), 7.37-7.68 (m, 2H), 7.73-7.81 (m, 1H), 7.94 (d, 1H, $J$ = 6.8 HZ).

$^{13}C$ NMR : δ 52.11, 67.57, 124.51, 126.35, 128.65, 128.90, 133.38, 136.18, 140.94, 148.33, 166.40.

***tert.* Butyl 3-hydroxy-3-(2-chlorophenyl)-2-methylenepropanoate (126p):**

This was prepared *via* the DABCO-catalyzed Baylis-Hillman coupling between 2-chlorobenzaldehyde and tertiary butyl acrylate in silica gel solid phase medium, following a similar procedure described for the molecule **178d**, as a colorless viscous liquid.




Reaction time : 12 days

Yield : 72%

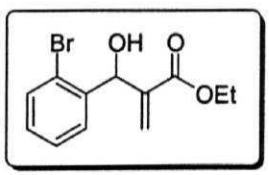
IR (neat) : ν 3447, 1716, 1633 $cm^{-1}$

$^1H$ NMR : δ 1.39 (s, 9H), 3.38 (b, 1H), 5.56 (s, 1H), 5.91 (s, 1H), 6.24 (s, 1H), 7.16-7.53 (m, 4H).

$^{13}C$ NMR : δ 27.95, 69.28, 81.60, 125.46, 126.96, 128.13, 128.90, 129.39, 133.03, 138.90, 142.44, 165.73.

**Ethyl 3-hydroxy-3-(2-bromophenyl)-2-methylenepropanoate (178f):**

This molecule was obtained *via* the Baylis-Hillman reaction between 2-bromobenzaldehyde and ethyl acrylate in the presence of DABCO, following a similar procedure described for the molecule **126a**, as a colorless viscous liquid. The crude product was purified by column chromatography (6% EtOAc in hexanes, silica gel).




Reaction time : 9 days

Yield : 69%

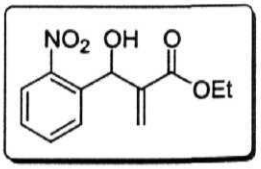
IR (neat) : ν 3458, 1716, 1631 $cm^{-1}$

$^1H$ NMR : δ 1.22 (t, 3H, $J$ = 6.8 Hz), 3.54 (b, 1H), 4.17 (q, 2H, $J$ = 6.8 Hz), 5.58 (s, 1H), 5.93 (s, 1H), 6.33 (s, 1H), 7.05-7.19 (m, 1H), 7.21-7.36 (m, 1H), 7.42-7.56 (m, 2H).

$^{13}C$ NMR : δ 14.04, 61.06, 71.45, 123.23, 126.60, 127.61, 128.44, 129.26, 132.73, 140.14, 141.16, 166.46.

**Ethyl 3-hydroxy-2-methylene-3-(2-nitrophenyl)propanoate (178g):**

This molecule was obtained as a brown viscous liquid *via* the treatment of 2-nitrobenzaldehyde with ethyl acrylate in the presence of DABCO (cat.) following a similar procedure described for the molecule **126a**. The crude product was purified by column chromatography (10% EtOAc in hexanes, silica gel).




Reaction time : 2 days

Yield : 71%

IR (neat) : ν 3476, 1712, 1631 $cm^{-1}$

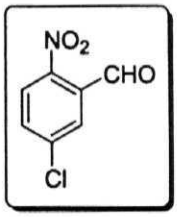
$^1H$ NMR : δ 1.16 (t, 3H, $J$ = 6.8 Hz), 3.69 (b, 1H), 4.12 (q, 2H, $J$ = 6.8 Hz), 5.69 (s, 1H), 6.24 (s, 1H), 6.31 (s, 1H), 7.35-7.47 (m, 1H), 7.53-7.65 (m, 1H), 7.70 (d, 1H, $J$ = 7.8 Hz), 7.88 (d, 1H, $J$ = 7.8 Hz).

$^{13}C$ NMR (400 MHz) : δ 13.19, 61.14, 67.41, 124.47, 126.13, 128.60, 128.87, 133.41, 136.30, 141.09, 148.24, 165.91.

**5-Chloro-2-nitrobenzaldehyde (195b):**

This was prepared according to the literature procedure with little modification.[282]

To a stirred mixture of 3-chlorobenzaldehyde (30 mmol, 4.217 g) and $KNO_3$ (30 mmol, 3.033 g) cooled to 0 °C, was added slowly dropwise, conc. $H_2SO_4$. After stirring for 30 min at the same temperature, the reaction mixture was poured into ice-cold water. The solid obtained after filtration was crystallized from MeOH to provide 5-chloro-2-nitrobenzaldehyde as colorless needles in 80% (4.45 g) yield.




Yield : 70%

Mp : 74-75 °C [literature : 77.5 °C][282]

IR (KBr) : ν 1697, 1602 $cm^{-1}$

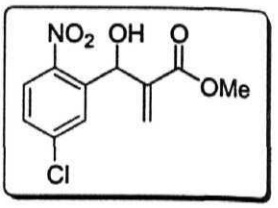
$^1H$ NMR (400 MHz) : δ 7.72 (dd, 1H, $J$ = 8.6 & 2.2 Hz), 7.90 (d, 1H, $J$ = 2.2 Hz), 8.13 (d, 1H, $J$ = 8.6 Hz), 10.42 (s, 1H).

$^{13}C$ NMR : δ 126.19, 129.68, 132.91, 133.44, 141.26, 147.71, 186.71.

**Methyl 3-hydroxy-2-methylene-3-(5-chloro-2-nitrophenyl)propanoate (126q):**

This compound was prepared *via* the Baylis-Hillman coupling of 5-chloro-2-nitrobenzaldehyde (**195b**) with methyl acrylate under the catalytic influence of DABCO following a similar procedure described for the molecule **126a**, as a brown viscous liquid. The crude product was purified by column chromatography (10% EtOAc in hexanes, silica gel).

Reaction time : 4 days




Yield : 74%

IR (neat) : ν 3466, 1716, 1631 $cm^{-1}$

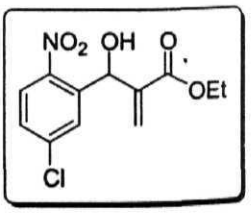
$^1$H NMR : δ 3.68 (b, 1H), 3.72 (s, 3H), 5.65 (s, 1H), 6.20 (s, 1H), 6.31 (s, 1H), 7.42 (dd, 1H, $J$ = 2.4 & 8.8 Hz), 7.74 (d, 1H, $J$ = 2.4 Hz), 7.90 (d, 1H, $J$ = 8.8 Hz).

$^{13}$C NMR : δ 52.27, 67.24, 126.16, 126.60, 128.76, 129.14, 138.49, 140.13, 140.67, 146.26, 166.30.

**Ethyl 3-(5-chloro-2-nitrophenyl)-3-hydroxy-2-methylenepropanoate (178h):**

This molecule was obtained as a brown viscous liquid *via* the reaction between 5-chloro-2-nitrobenzaldehyde (**195b**) and ethyl acrylate in the presence of DABCO (cat.) following a similar procedure described for the molecule **126a**. The crude product was purified by column chromatography (10% EtOAc in hexanes, silica gel).

Reaction time : 4 days




Yield : 71%

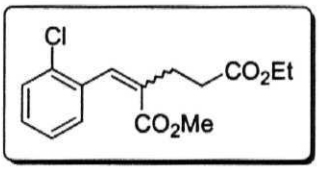
IR (neat) : ν 3468, 1712, 1631 $cm^{-1}$

$^1$H NMR : δ 1.25 (t, 3H, $J$ = 7.0 Hz), 3.52 (b, 1H), 4.21 (q, 2H, $J$ = 7.0 Hz), 5.68 (s, 1H), 6.22 (s, 1H), 6.37 (s, 1H), 7.42 (dd, 1H, $J$ = 8.8 & 2.0 Hz), 7.77 (d, 1H, $J$ = 2.0 Hz), 7.94 (d, 1H, $J$ = 8.8 Hz).

$^{13}$C NMR : δ 13.93, 61.32, 67.19, 126.14, 126.33, 128.66, 129.15, 138.66, 140.06, 140.94, 146.27, 165.82.

**Ethyl 5-(2-chlorophenyl)-4-methoxycarbonylpent-4-enoate (203):**

To a stirred solution of methyl 3-(2-chlorophenyl)-3-hydroxy-2-methylenepropanoate (**126g**) (2 mmol, 0.453 g) in triethyl orthoacetate (2 mL) was added catalytic amount of propanoic acid (3-4 drops). The reaction mixture was heated at 145 °C for 3 hours with stirring. Then the reaction mixture was diluted with water and extracted into ether (3 x 25 mL). Combined organic layer was dried over anhydrous $Na_2SO_5$. Solvent was evaporated and the residue thus obtained was purified by column chromatography (5-6% EtOAc in hexanes) to provide the desired product (**203**) as colorless liquid.




Yield : 87% (0.515 g)

*Z* : *E* : 70 : 30 [*determined by the integration of isomeric olefinic proton singlets at δ 6.89 (Z-isomer) & δ 7.77 (E-isomer) in the $^1$H NMR spectrum of the crude as well as column purified sample. It was further confirmed by integration of isomeric $OCH_3$ proton singlets at δ 3.57 (Z-isomer) & δ 3.84 (E-isomer)*

IR (neat) : ν 1736, 1716, 1641, 1591 cm$^{-1}$

$^1$H NMR (*Z* & *E* mixture) : δ 1.21 & 1.26 (2t, 3H, *J* = 7.8 Hz), 2.46-2.88 (m, 4H), 3.57 & 3.84 (2s, 3H), 4.02-4.26 (m, 2H), 6.89 & 7.77 (2s, 1H), 7.14-7.49 (m, 4H).

*The underlined chemical shift values with low intensity arise due to the presence of minor (E)-isomer*

$^{13}$C NMR (*Z* & *E* mixture) : δ 14.01, 14.08, 23.03, 29.99, 33.27, 51.38, 51.97, 60.24, 60.36, 126.09,

126.60, 128.88, 128.98, 129.51, 129.66, 132.74, 132.96, 133.42, 133.68, 133.85, 134.02, 134.92, 137.54, 167.40, 168.15, 172.15, 172.30.

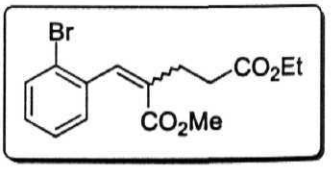
*Major peaks at δ 29.99 (allylic carbon), 51.38 (O<u>C</u>H$_3$), 60.36 (O<u>C</u>H$_2$) and minor peaks at δ 23.03 (allylic carbon), 51.97 (O<u>C</u>H$_3$), 60.24 (O<u>C</u>H$_2$) are attributed to the major Z- and minor E-isomers respectively. Similarly, peaks at δ 168.15, δ 172.15 (with high intensity) and peaks at δ 167.40, 172.30 (with low intensity) are attributed to carbonyl carbons of major and minor isomers respectively.*

Analysis calcd. for $C_{15}H_{17}ClO_4$ : C, 60.71; H, 5.77

Found : C, 60.57; H, 5.71

**Ethyl 5-(2-bromophenyl)-4-methoxycarbonylpent-4-enoate (204):**

This product was obtained as colorless liquid *via* the treatment of methyl 3-(2-bromophenyl)-3-hydroxy-2-methylenepropanoate (**126n**) with triethyl orthoacetate in the presence of propanoic acid (cat.) following similar procedure described for **203**.




Yield : 70%

Reaction time : 3 h

*Z* : *E* : 76 : 24 [*determined by the integration of isomeric olefinic proton singlets at δ 6.84 (Z-isomer) & δ 7.71 (E-isomer) in $^1$H NMR spectrum of the crude as well as column purified sample.*

IR (neat) : ν 1732, 1710, 1639, 1587 cm$^{-1}$

$^1$H NMR (*Z* & *E* mixture) : δ <u>1.20</u> & 1.26 (2t, 3H, *J* = 6.8 Hz), 2.46-2.90 (m, 4H), 3.55 & <u>3.84</u> (2s, 3H), 4.08 & 4.16 (2q, 2H, *J* = 6.8 Hz), 6.85 & <u>7.71</u> (2s, 1H), 7.07-7.44 (m, 3H), 7.54-7.66 (m, 1H).

*The underlined chemical shift values with low intensity arise due to the presence of minor (E)-isomer*

$^{13}$C NMR (*Z* & *E* mixture) : δ 14.12, 14.22, 23.09, 29.93, 33.43, 51.48, 52.06, 60.35, 60.50, 122.89, 123.76, 126.77, 127.30, 129.10, 129.68, 132.25 132.79, 133.90, 135.79, 135.94, 137.01, 139.77, 167.57, 168.15, 172.28, 172.42.

*Major peaks at δ 14.22 ($CH_2\underline{C}H_3$), 29.93 (allylic carbon), 51.48 ($O\underline{C}H_3$), 60.50 ($O\underline{C}H_2$) and minor peaks at δ 14.12 ($CH_2\underline{C}H_3$), 23.09 (allylic carbon), 52.06 ($O\underline{C}H_3$), 60.35 ($O\underline{C}H_2$) are attributed to the major Z- and minor E-isomers respectively. Similarly, peaks at δ 168.15, 172.28 (with high intensity) and peaks at δ 167.15, 172.42 (with low intensity) are attributed to carbonyl carbons of major and minor isomers respectively.*

Analysis calcd. for $C_{15}H_{17}BrO_4$ : C, 52.80; H, 5.02

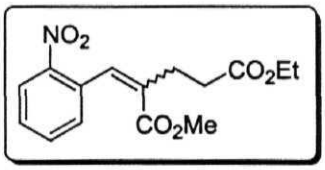
Found : C, 52.64; H, 5.11

**Ethyl 4-methoxycarbonyl-5-(2-nitrophenyl)pent-4-enoate (205):**

This molecule was prepared *via* the treatment of methyl 3-hydroxy-2-methylene-3-(2-nitrophenyl)propanoate (**126o**) with triethyl orthoacetate in the presence of propanoic acid (cat.), following similar procedure described for **203**, as a colorless liquid.

Yield : 77%

Reaction time : 12 h




*Z* : *E* : 77 : 23 [*determined by the integration of isomeric olefinic proton singlets at δ 7.21 (Z-isomer) & δ 7.97 (E-isomer) in $^1$H NMR spectrum of the crude as well as column purified sample. It was further confirmed by integration of isomeric $OCH_3$ proton singlets at 3.48 (Z-isomer) & 3.85.*

IR (neat) : ν 1728, 1711, 1641, 1608 $cm^{-1}$

$^1H$ NMR (*Z* & *E* mixture) : δ 1.19 & 1.27 (2t, 3H, *J* = 6.8 Hz), 2.40-2.91 (m, 4H), 3.49 & 3.85 (2s, 3H), 4.04 & 4.18 (2q, 2H, *J* = 6.8 Hz), 7.22 & 7.97 (2s, 1H), 7.25-7.75 (m, 3H), 8.12 & 8.18 (2d, 1H, *J* = 7.8 Hz).

*The underlined chemical shift values with low intensity arise due to the presence of minor (E)-isomer*

$^{13}C$ NMR (*Z* & *E* mixture) : δ 13.98, 14.07, 23.00, 29.31, 33.02, 33.24, 51.41, 52.04, 60.24, 60.41, 124.20, 124.81, 128.35, 129.15, 130.49, 130.68, 131.50, 132.11, 132.74, 132.91, 133.20, 133.52, 135.24, 137.71, 146.91, 147.39, 167.09, 172.23.

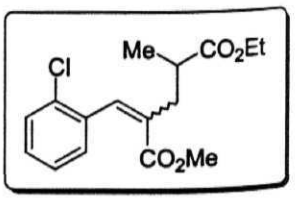
*Major peaks at δ 14.07 ($CH_2\underline{C}H_3$), 29.31 (allylic carbon), 33.24 ($\underline{C}H_2CO_2Et$), 51.41 ($O\underline{C}H_3$), 60.41 ($O\underline{C}H_2$) and minor peaks at δ 13.98 ($CH_2\underline{C}H_3$), 23.00 ( allylic carbon ), 33.02 ($\underline{C}H_2CO_2Et$), 52.04 ($O\underline{C}H_3$), 60.24 ($O\underline{C}H_2$) are attributed to the major Z- and minor E-isomers respectively.*

Analysis calcd. for $C_{15}H_{17}NO_6$ : C, 58.63; H, 5.58; N, 4.56.

Found : C, 58.83; H, 5.55; N, 4.51.

**Ethyl 5-(2-chlorophenyl)-4-methoxycarbonyl-2-methylpent-4-enoate (206):**

This was obtained as colorless liquid *via* the Johnson-Claisen rearrangement of methyl 3-(2-chlorophenyl)-3-hydroxy-2-methylenepropanoate (**126g**) with triethyl orthopropanoate under the catalytic influence of propanoic acid following similar procedure described for **203**.




Yield : 85%

Reaction time : 3 h

$Z:E$ : 69 : 31 [*determined by the integration of isomeric olefinic proton singlets at δ 6.84 (Z-isomer) & δ 7.75 (E-isomer) in $^1H$ NMR spectrum of the crude as well as column purified sample. It was further confirmed by integration of isomeric $OCH_3$ proton singlets δ 3.55 (Z-isomer) & δ 3.81 (E-isomer).*

IR (neat) : ν 1730, 1714, 1639, 1586 $cm^{-1}$

$^1H$ NMR (*Z* & *E* mixture) : δ 0.98-1.38 (m, 6H), 2.45-2.95 (m, 3H), 3.55 & 3.81 (2s, 3H), 3.96-4.22 (m, 2H), 6.84 & 7.75 (2s, 1H), 7.12-7.48 (m, 4H).

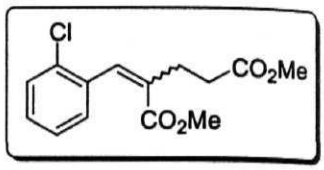
*The underlined chemical shift values (δ) with low intensity arise due to the presence of minor (E)-isomer*

$^{13}C$ NMR (*Z* & *E* mixture) : δ 14.07, 14.20, 16.57, 16.82, 31.10, 38.43, 38.79, 51.46, 52.01, 60.26, 60.41, 126.19, 126.65, 128.98, 129.15, 129.66, 130.07, 132.64, 132.96, 133.42, 133.88, 134.29, 134.56, 135.29, 138.20, 167.84, 168.40, 175.56, 175.63.

*Major peaks at δ 14.20 ($CO_2CH_2\underline{C}H_3$), 16.82 ($CH\underline{C}H_3$), 38.79 (allylic carbon), 51.46 ($O\underline{C}H_3$), 60.41 ($O\underline{C}H_2$) and minor peaks at δ 14.07 ( $CO_2CH_2\underline{C}H_3$), 16.57 ( $CH\underline{C}H_3$), 31.10 (allylic carbon), 52.01 ($O\underline{C}H_3$), 60.26 ($O\underline{C}H_2$) are attributed to the major Z- and minor E-isomers respectively. Similarly, peaks at δ 168.84, 175.56 (with high intensity) and peaks at δ 167.74, 175.63 (with low intensity) are attributed to carbonyl carbons of major and minor isomers respectively.*

**Methyl 5-(2-chlorophenyl)-4-methoxycarbonylpent-4-enoate (207):**

Treatment of methyl 3-(2-chlorophenyl)-3-hydroxy-2-methylenepropanoate (**126g**) with trimethyl orthoacetate in the presence of propanoic acid (cat.), following similar procedure described for **203**, provided this compound as a colorless liquid.




Yield : 83%

Reaction time : 10 h

*Z* : *E* : 70 : 30 [*determined by the integration of isomeric olefinic proton singlets at δ 6.90 (Z-isomer) & δ 7.78 (E-isomer) in $^1$H NMR spectrum of the crude as well as column purified sample*]

IR (neat) : ν 1738, 1714, 1641, 1591 cm$^{-1}$

$^1$H NMR (*Z* & *E* mixture) : δ 2.44-2.88 (m, 4H), 3.57 & 3.84 (2s, 3H), 3.62 & 3.70 (2s, 3H), 6.90 & 7.78 (2s, 1H), 7.16-7.48 (m, 4H).

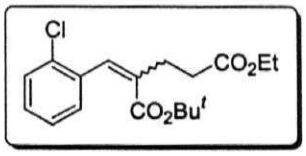
*The underlined chemical shift values with low intensity arise due to the presence of minor (E)-isomer*

$^{13}$C NMR (*Z* & *E* mixture) : δ 23.07, 30.08, 33.07, 33.19, 51.50, 51.60, 52.09, 126.17, 126.68, 129.01, 129.08, 129.61, 132.84, 132.96, 133.71, 133.98, 135.00, 137.81, 167.53, 168.23, 172.74, 172.86.

*Major Peaks at δ 30.08 (allylic carbon), 33.19 (CH$_2$CO$_2$Et) and minor peaks at δ 23.07 ( allylic carbon ), 33.07 (CH$_2$CO$_2$Et) are attributed to the major Z- and minor E-isomers respectively. Similarly, peaks at δ 168.23, 172.74 (with high intensity) and peaks at δ 167.53, 172.86 (with low intensity) are attributed to carbonyl carbons of major and minor isomers respectively.*

**Ethyl 5-(2-chlorophenyl)-4-*t*-butoxycarbonylpent-4-enoate (208):**

This product was obtained as colorless liquid *via* the Johnson-Claisen rearrangement of tertiary-butyl 3-(2-chlorophenyl)-3-hydroxy-2-methylenepropanoate **(126p)** with triethyl orthoacetate under the catalytic influence of propanoic acid following similar procedure described for **203**.




Yield : 86%

Reaction time : 3 h

*Z* : *E* : 80 : 20 [*determined by the integration of isomeric olefinic proton singlets at δ 6.78 (Z-isomer) & δ 7.67 (E-isomer) in $^1$H NMR spectrum of the crude as well as column purified sample*]

IR (neat) : ν 1736, 1707, 1641, 1591 cm$^{-1}$

$^1$H NMR (*Z* & *E* mixture) : δ 1.21-1.35 (m) & 1.55 (s) [12H], 2.45-2.83 (m, 4H), 4.02-4.25 (m, 2H), 6.78 & 7.67 (2s, 1H), 7.15-7.42 (m, 4H).

*The underlined chemical shift values with low intensity arise due to the presence of minor (E)-isomer*

$^{13}$C NMR (*Z* & *E* mixture) : δ 13.93, 14.03, 23.12, 27.39, 27.93, 29.99, 33.24, 60.04, 60.14, 80.81, 125.90, 126.46, 128.42, 128.74, 129.25, 129.39, 129.66, 129.85, 131.84, 132.60, 133.66, 134.22, 134.68, 135.87, 136.14, 136.23, 166.07, 166.73, 172.11, 172.21.

*Major peaks at δ 14.03 ($CH_2\underline{C}H_3$), 29.99 (allylic carbon), 60.14 ($O\underline{C}H_2$) and minor peaks at δ 13.93 ($CH_2\underline{C}H_3$), 23.12 (allylic carbon), 60.04 ($O\underline{C}H_2$) are attributed to the major Z- and minor E-isomers respectively. Similarly, peaks at δ 166.73, 172.11 (with high intensity) and peaks at δ 166.07, 172.21 (with low intensity) are attributed to carbonyl carbons of major and minor isomers respectively.*

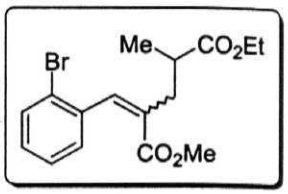
Analysis calcd. for $C_{18}H_{23}ClO_4$ : C, 63.81; H, 6.84

Found : C, 63.56; H, 6.89

**Ethyl 5-(2-bromophenyl)-4-methoxycarbonyl-2-methylpent-4-enoate (209):**

This product was obtained as colorless liquid *via* the treatment of methyl 3-(2-bromophenyl)-3-hydroxy-2-methylenepropanoate (**126n**) with triethyl orthopropanoate

in the presence of propanoic acid (cat.) following similar procedure described for **203**.




Yield : 90%

Reaction time : 3 h

*Z* : *E* : 73 : 27 [*determined by the integration of isomeric olefinic proton singlets at δ 6.82 (Z-isomer) & δ 7.72 (E-isomer) in $^1$H NMR spectrum of the crude as well as column purified sample.*

IR (neat) : ν 1730, 1716, 1639, 1587 cm$^{-1}$

$^1$H NMR (*Z* & *E* mixture) : δ 0.98-1.38 (m, 6H), 2.46-2.96 (m, 3H), 3.54 & 3.84 (2s, 3H), 3.96-4.27 (m, 2H), 6.82 & 7.72 (2s, 1H), 7.06-7.42 (m, 3H), 7.51-7.68 (m, 1H).

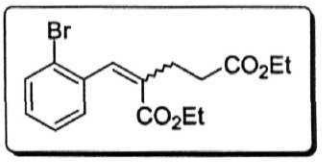
*The underlined chemical shift values with low intensity arise due to the presence of minor (E)-isomer*

$^{13}$C NMR (*Z* & *E* mixture) : δ 14.07, 14.20, 16.57, 16.84, 30.91, 38.31, 38.55, 38.67, 51.48, 52.06, 60.26, 60.43, 122.87, 123.79, 126.77, 127.23, 129.13, 129.64 130.10, 132.23, 132.69, 132.96, 136.02, 136.77, 137.11, 140.29, 167.77, 168.28, 175.56, 175.66

*Major peaks at δ 14.20 ($CO_2CH_2\underline{C}H_3$), 16.84 ($CH\underline{C}H_3$), 38.55 (allylic carbon), 38.67 ($\underline{C}H_2CO_2Et$), 51.48 ($O\underline{C}H_3$), 60.43 ($O\underline{C}H_2$) and minor peaks at δ 14.07 ($CO_2CH_2\underline{C}H_3$), 16.57 ($CH\underline{C}H_3$), 30.91 (allylic carbon), 38.31 ($\underline{C}H_2CO_2Et$), 52.06 ($O\underline{C}H_3$), 60.26 ($O\underline{C}H_2$) are attributed to the major Z- and minor E-isomers respectively. Similarly, peaks at δ 168.28, 175.56 (with high intensity) and peaks at δ 166.77, 175.66 (with low intensity) are attributed to carbonyl carbons of major and minor isomers respectively.*

**Ethyl 5-(2-bromophenyl)-4-ethoxycarbonylpent-4-enoate (210):**

Treatment of ethyl 3-(2-bromophenyl)-3-hydroxy-2-methylenepropanoate (**178f**) with triethyl orthoacetate in the presence of propanoic acid (cat.), following similar procedure described for **203**, provided the desired diester **210** as colorless liquid.




Yield : 83%

Reaction time : 3 h

*Z* : *E* : 79 : 21 [*determined by the integration of isomeric olefinic proton singlets at δ 6.84 (Z-isomer) & δ 7.71 (E-isomer) in $^1$H NMR spectrum of the crude as well as column purified sample*]

IR (neat) : ν 1734, 1711, 1639, 1587 cm$^{-1}$

$^1$H NMR (*Z* & *E* mixture) : δ 0.98, 1.21, 1.27 & 1.36 (4t, 6H, *J* = 7.8 Hz), 2.44-2.88 (m, 4H), 3.95-4.38 (m, 4H), 6.84 & 7.71 (2s, 1H), 7.07-7.40 (m, 3H), 7.54 & 7.61 (2d, 1H, *J* = 7.8 Hz).

*The underlined chemical shift values with low intensity arise due to the presence of minor (E)-isomer]*

$^{13}$C NMR (*Z* & *E* mixture) : δ 13.59, 14.12, 14.22, 23.05, 29.89, 33.33, 33.43, 60.35, 60.50, 60.98, 122.84, 123.81, 126.72, 127.30, 129.00, 129.73, 129.83, 132.15 132.79, 133.08, 134.34, 135.60, 136.04, 137.35, 139.53, 167.09, 167.67, 172.37.

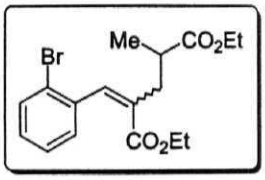
*Major peaks at δ 29.89 (allylic carbon), 33.43 (CH$_2$CO$_2$Et) and minor peaks at δ 23.05 (allylic carbon), 33.33 (CH$_2$CO$_2$Et) are attributed to the major Z- and minor E-isomers respectively. Similarly, peaks at δ 167.69 (with high intensity) and peaks at δ 167.13 (with low intensity) are attributed to one of the carbonyl carbons of major and minor isomers respectively*

Analysis calcd. for $C_{16}H_{19}BrO_4$ : C, 54.10; H, 5.39

Found : C, 54.20; H, 5.32

**Ethyl 5-(2-bromophenyl)-4-ethoxycarbonyl-2-methylpent-4-enoate (211):**

This product was prepared *via* the treatment of ethyl 3-(2-bromophenyl)-3-hydroxy-2-methylenepropanoate (**178f**) with triethyl orthopropanoate in the presence of propanoic acid (cat.), following similar procedure described for **203**, as colorless liquid.




Yield : 80%

Reaction time : 3 h

*Z* : *E* : 77 : 23 [*determined by the integration of isomeric olefinic proton singlets at δ 6.80 (Z-isomer) & δ 7.70 (E-isomer) in $^1$H NMR spectrum of the crude as well as column purified sample*]

IR (neat) : ν 1730, 1716, 1640 $cm^{-1}$

$^1$H NMR (*Z* & *E* mixture) : δ 0.92-1.45 (m, 9H), 2.44-2.95 (m, 3H), 3.95-4.37 (m, 4H), 6.81 & 7.71 (2s, 1H), 7.05-7.39 (m, 3H), 7.51-7.65 (m, 1H).

*The underlined chemical shift values with low intensity arise due to the presence of minor (E)-isomer*

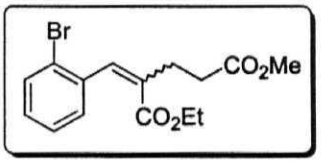
$^{13}$C NMR (*Z* & *E* mixture) : δ 13.06, 13.59, 13.69, 16.06, 16.31, 30.52, 37.80, 38.04, 38.14, 59.63, 59.82, 60.31, 122.26, 123.28, 126.24, 126.77, 128.52, 129.15, 129.35, 129.64, 131.58, 131.96, 132.16, 133.08, 135.55, 135.80, 136.96, 139.24, 166.51, 166.99, 174.71.

*Major peaks at δ 16.31 (CH$\underline{C}$H$_3$), 38.04 (allylic carbon), 38.14 ($\underline{C}$H$_2$CO$_2$Et) and minor peaks at δ 16.06 (CH$\underline{C}$H$_3$), 30.52 (allylic carbon), 37.80 ($\underline{C}$H$_2$CO$_2$Et) are attributed to the major Z- and minor E-isomers respectively. Similarly, peaks at δ 166.99 (with high*

*intensity) and peaks at δ 166.51 (with low intensity) are attributed to one of the carbonyl carbons of major and minor isomers respectively*

**Methyl 5-(2-bromophenyl)-4-ethoxycarbonylpent-4-enoate (212):**

This diester was obtained *via* the Johnson-Claisen rearrangement of ethyl 3-(2-bromophenyl)-3-hydroxy-2-methylenepropanoate (**178f**) with trimethyl orthoacetate in the presence of propanoic acid (cat.) following similar procedure described for **203**, as colorless liquid.




Yield : 65%

Reaction time : 10 h

*Z* : *E* : 78 : 22 [*determined by the integration of isomeric olefinic proton singlets at δ 6.84 (Z-isomer) & δ 7.71 (E-isomer) in $^1$H NMR spectrum of the crude as well as column purified sample*]

IR (neat) : ν 1738, 1707, 1641 cm$^{-1}$

$^1$H NMR (*Z* & *E* mixture) : δ 0.98 & 1.36 (2t, 3H, *J* = 6.8 Hz), 2.43-2.87 (m, 4H), 3.62 & 3.70 (2s, 3H), 4.01 & 4.30 (2q, 2H, *J* = 6.8 Hz), 6.84 & 7.71 (2s, 1H), 7.07-7.39 (m, 3H), 7.54 & 7.61 (2d, 1H, *J* = 7.8 Hz).

*The underlined chemical shift values with low intensity arise due to the presence of minor (E)-isomer*

$^{13}$C NMR (*Z* & *E* mixture) : δ 13.47, 14.10, 22.93, 29.77, 33.04, 51.50, 60.38, 60.87, 122.67, 123.60, 126.60, 127.19, 128.88, 129.68, 131.99, 132.62, 132.89, 134.12, 135.58, 135.89, 137.20, 139.51, 166.87, 167.45, 172.64.

*Major peaks at δ 13.47 ($CO_2CH_2\underline{C}H_3$), 29.77(allylic carbon), 60.38 (with $O\underline{C}H_2$) and minor peaks at δ 14.10 ($CO_2CH_2\underline{C}H_3$), 22.93 ( allylic carbon ), 60.87 ($O\underline{C}H_2$) are attributed to the major Z- and minor E-isomers respectively. Similarly, peaks at δ*

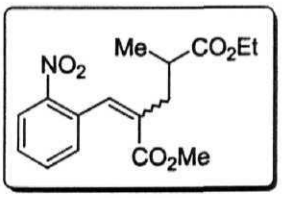
*167.45 (with high intensity) and peaks at δ 166.87 (with low intensity) are attributed to one of the carbonyl carbons of major and minor isomers respectively.*

Analysis calcd. for $C_{15}H_{17}BrO_4$ : C, 52.80; H, 5.02

Found : C, 52.61; H, 5.07

**Ethyl 4-methoxycarbonyl-2-methyl-5-(2-nitrophenyl)pent-4-enoate (213):**

This product was obtained as colorless liquid *via* the Johnson-Claisen rearrangement of methyl 3-hydroxy-2-methylene-3-(2-nitrophenyl)propanoate (**126o**) with triethyl orthopropanoate under the catalytic influence of propanoic acid following similar procedure described for **203**.




Yield : 75%

Reaction time : 12 h

*Z* : *E* : 80 : 20 [*determined by the integration of the separated isomeric $OCH_3$ proton singlets at δ 3.47 (Z-isomer) & δ 3.85 (E-isomer) in $^1H$ NMR spectrum of the crude as well column purified sample. It was further confirmed by integration of isomeric $CO_2\underline{CH_2}CH_3$ peaks at δ 4.17 (Z-isomer) & δ 4.00 (E-isomer).*

IR (neat) : ν 1728, 1714, 1641, 1608 $cm^{-1}$

$^1H$ NMR (*Z* & *E* mixture) : δ 0.91-1.40 (m, 6H), 2.32-2.95 (m, 3H), 3.47 & 3.85 (2s, 3H), 4.00 & 4.17 (2q, 2H, *J* = 7.8 Hz), 7.18 & 7.99 (2s, 1H), 7.27-7.75 (m, 3H), 8.12 & 8.19 (2d, 1H, *J* = 7.8 Hz).

*The underlined chemical shift values correspond to the minor (E)-isomer*

$^{13}C$ NMR (*Z* & *E* mixture) : δ 13.72, 13.84, 16.53, 30.97, 37.74, 38.03, 38.56, 51.05, 51.71, 59.86, 60.08, 123.97, 124.55, 128.21 128.92, 130.35, 130.74, 131.32, 131.44, 132.17, 132.68, 132.99, 133.26, 135.40, 137.89, 146.92, 147.35, 167.05, 175.08.

*Major peaks at δ 13.84 ($CO_2CH_2\underline{C}H_3$), 37.74 (allylic carbon), 38.56 ($\underline{C}H_2CO_2Et$), 51.05 ($O\underline{C}H_3$), 60.08 ($O\underline{C}H_2$) and minor peaks at δ 13.72 ( $CO_2CH_2\underline{C}H_3$), 30.97 (allylic carbon), 38.03 ($\underline{C}H_2CO_2Et$), 51.71 ($O\underline{C}H_3$), 59.86 ($O\underline{C}H_2$) are attributed to the major Z- and minor E-isomers respectively.*

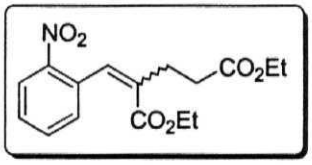
$^1$H NMR and $^{13}$C NMR spectra also indicated inseparable very minor quantities (~ 5%) of unidentified impurity

Analysis calcd. for $C_{16}H_{19}NO_6$ : C, 59.81; H, 5.96; N, 4.36

Found : C, 59.95; H, 5.90; N, 4.31

**Ethyl 4-ethoxycarbonyl-5-(2-nitrophenyl)pent-4-enoate (214):**

This molecule was prepared *via* the treatment of ethyl 3-hydroxy-2-methylene-3-(2-nitrophenyl)propanoate (**178g**) with triethyl orthoacetate in the presence of propanoic acid (cat.), following similar procedure described for **203**, as colorless liquid.




Yield : 80%

Reaction time : 12 h

*Z* : *E* : 84 : 16 [*determined by the integration of isomeric olefinic proton singlets at δ 7.22 (Z-isomer) & δ 7.96 (E-isomer) in $^1$H NMR spectrum of the crude as well column purified sample*]

IR (neat) : ν 1732, 1711, 1641, 1608. cm$^{-1}$

$^1$H NMR (*Z* & *E* mixture) : δ 0.89, 1.19, 1.27 & 1.36 (4t, 6H, *J* = 6.8 Hz), 2.40-2.90 (m, 4H), 3.92, 4.03, 4.18 & 4.30 (4q, 4H, *J* = 6.8 Hz), 7.21 & 7.95 (2s, 1H), 7.24-7.74 (m, 3H), 8.11 & 8.17 (2d, 1H, *J* = 7.8 Hz).

*The underlined chemical shift values with low intensity arise due to the presence of minor (E)-isomer*

$^{13}$C NMR (*Z* & *E* mixture) : δ 13.46, 14.14, 23.07, 29.35, 33.14, 33.31, 60.30, 60.45, 61.06, 124.20, 124.85, 128.30, 129.17, 130.60, 130.80, 131.67, 132.52, 132.96, 133.22, 133.59, 134.90, 137.47, 147.12, 147.51, 166.72, 172.35.

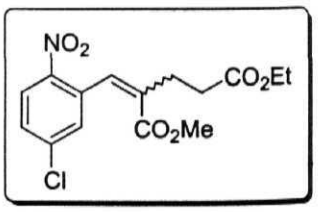
*Major peaks at δ 29.35 (allylic carbon), 33.31 (C̲H$_2$CO$_2$Et) and minor peaks at δ 23.07 (allylic carbon), 33.14 (C̲H$_2$CO$_2$Et) are attributed to the major Z- and minor E-isomers respectively.*

Analysis calcd. for $C_{16}H_{19}NO_6$ : C, 59.81; H, 5.96; N, 4.36

Found : C, 59.57; H, 5.99; N, 4.30

**Ethyl 5-(5-chloro-2-nitrophenyl)-4-methoxycarbonylpent-4-enoate (215):**

This compound was prepared *via* the reaction between methyl 3-(5-chloro-2-nitrophenyl)-3-hydroxy-2-methylenepropanoate (**126q**) and triethyl orthoacetate in the presence of propanoic acid (cat.), following similar reaction procedure described for **203**, as a colorless liquid.




Yield : 72%

Reaction time : 12 h

*Z* : *E* : 86 : 14 [*determined by the integration of isomeric olefinic proton singlets at δ 7.13 (Z-isomer) & δ 7.88 (E-isomer) in the $^1$H NMR spectrum of the crude as well as column purified sample. It was further confirmed by integration of isomeric OCH$_3$ proton singlets at δ 3.53 (Z-isomer) & δ 3.84 (E-isomer).*

IR (neat) : ν 1730, 1718, 1645, 1602 cm$^{-1}$

$^1$H NMR (*Z* & *E* mixture) : δ 1.19 & 1.27 (2t, 3H, *J* = 6.8 Hz), 2.39-2.88 (m, 4H), 3.58 & 3.84 (2s,

3H), 4.04 & 4.17 (2q, 2H, $J$ = 6.8 Hz), 7.13 & 7.88 (2s, 1H), 7.22 & 7.32 (2d, 1H, $J$ = 3.0 Hz), 7.41 & 7.49 (2dd, 1H, $J$ = 8.8 & 3.0 Hz), 8.06 & 8.14 (2d, 1H, $J$ = 8.8 Hz).

*The underlined chemical shift values correspond to the minor (E)-isomer*

$^{13}$C NMR (*Z* & *E* mixture) : δ 14.17, 23.09, 29.28, 32.92, 33.21, 51.69, 52.25, 60.43, 60.57, 125.80, 126.43, 128.44, 129.22, 130.36, 130.60, 132.93, 133.56, 134.27, 135.07, 136.57, 139.33, 139.97, 145.40, 145.81, 166.70, 166.87, 172.25.

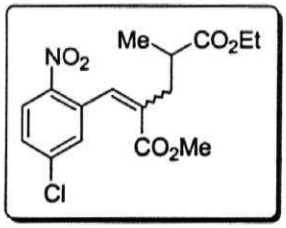
*Major peaks at δ 29.28 (allylic carbon), 33.21 ($\underline{C}H_2CO_2Et$), 51.69 ($O\underline{C}H_3$), 60.57 ($O\underline{C}H_2$) and minor peaks at δ 23.09 (allylic carbon), 32.92 ($\underline{C}H_2CO_2Et$), 52.25 ($O\underline{C}H_3$), 60.43 ($O\underline{C}H_2$) are attributed to the major Z- and minor E-isomers respectively.*

Analysis calcd. for $C_{15}H_{16}ClNO_6$ : C, 52.72; H, 4.72; N, 4.10

Found : C, 52.92; H, 4.75; N, 4.14

**Ethyl 5-(5-chloro-2-nitrophenyl)-4-methoxycarbonyl-2-methylpent-4-enoate (216):**

This product was obtained as colorless liquid *via* the Johnson-Claisen rearrangement of methyl 3-(5-chloro-2-nitrophenyl)-3-hydroxy-2-methylenepropanoate **(126q)** with triethyl orthopropanoate under the influence of propanoic acid (cat.) following similar procedure described for **203**.




Yield : 73%

Reaction time : 12 h

*Z* : *E* : 82 : 18 [*determined by the integration of isomeric olefinic proton singlets at δ 7.11 (Z-isomer) & δ 7.92 (E-isomer) in the $^1$H NMR*

*spectrum of the crude as well as column purified sample. It was further confirmed by integration of isomeric $OCH_3$ singlets at δ 3.53 (Z-isomer) & δ 3.85 (E-isomer).*

IR (neat) : ν 1728, 1643, 1602 1564 $cm^{-1}$

$^1H$ NMR (*Z* & *E* mixture) : δ 0.98-1.40 (m, 6H), 2.45-2.95 (m, 3H), 3.53 & 3.85 (2s, 3H), 4.00 & 4.17 (2q, 2H, *J* = 7.8 Hz), 7.11 & 7.92 (2s, 1H), 7.20 & 7.30 (2d, 1H, *J* = 2.0 Hz), 7.41 & 7.49 (2dd, 1H, *J* = 8.8, 2.0 Hz), 8.08 & 8.17 (2d, 1H, *J* = 8.8 Hz).

*The underlined chemical shift values with low intensity arise due to the presence of minor (E)-isomer*

$^{13}C$ NMR (*Z* & *E* mixture) : δ 14.12, 16.99, 31.27, 37.82, 38.31, 38.79, 51.70, 52.23, 60.28, 60.50, 125.83, 126.41, 128.45, 129.15, 130.36, 130.78, 132.01, 132.91, 133.69, 134.95, 135.09, 137.13, 139.36, 139.95, 145.33, 145.77, 166.87, 167.07, 175.43.

*Major peaks at δ 37.82 (allylic carbon), 38.79 ($\underline{C}H_2CO_2Et$), 51.70 ($O\underline{C}H_3$), 60.50 ($O\underline{C}H_3$) and minor peaks at δ 31.27 (allylic carbon), 38.31 ($\underline{C}H_2CO_2Et$), 52.23 ($O\underline{C}H_3$), 60.28 ($O\underline{C}H_3$) are attributed to the major Z- and minor E-isomers respectively.*

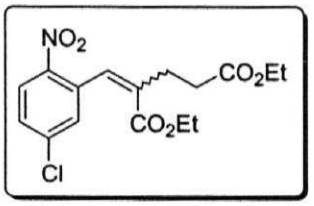
Analysis calcd. for $C_{16}H_{18}ClNO_6$ : C, 54.02; H, 5.10; N, 3.94

Found : C, 54.15; H, 5.17; N, 3.98

**Ethyl 5-(5-chloro-2-nitrophenyl)-4-ethoxycarbonylpent-4-enoate (217):**

Johnson-Claisen rearrangement of ethyl 3-(5-chloro-2-nitrophenyl)-3-hydroxy-2-methylenepropanoate (**178h**) with triethyl orthoacetate under the catalytic influence of

propanoic acid, following similar reaction procedure described for **203**, provided the title product **217** as colorless liquid.




Yield : 71%

Reaction time : 12 h

*Z* : *E* : 85 : 15 [*determined by the integration of isomeric olefinic proton singlets at δ 7.15 (Z-isomer) & δ 7.89 (E-isomer) in the $^1$H NMR spectrum of the crude as well as column purified sample. It was further confirmed by the integration of isomeric H-3 aromatic proton doublets at δ 8.07 (Z-isomer) and δ 8.15 (E-isomer).*

IR (neat) : ν 1732, 1716, 1643, 1602 cm$^{-1}$

$^1$H NMR (*Z* & *E* mixture) : δ 0.97, 1.20, 1.27 & 1.36 (4t, 6H, *J* = 6.8, 6.8, 6.8 & 6.8 Hz), 2.41-2.90 (m, 4H), 3.98, 4.05, 4.18 & 4.31 (4q, 2H, *J* = 6.8, 6.8, 6.8 & 6.8 Hz), 7.15 & 7.89 (2s, 1H), 7.24 & 7.32 (2d, 1H, *J* = 2.0 Hz), 7.41 & 7.49 (2dd, 1H, *J* = 8.8 & 2.0 Hz), 8.07 & 8.15 (2d, 1H, *J* = 8.8 Hz).

*The underlined chemical shift values with low intensity arise due to the presence of minor (E)-isomer*

$^{13}$C NMR (*Z* & *E* mixture) : δ 13.61, 14.22, 23.20, 29.38, 33.04, 33.29, 60.45, 60.60, 60.75, 61.28, 125.78, 126.43, 128.33, 129.20, 130.63, 133.42, 133.61, 134.22, 135.39, 136.19, 139.36, 139.99, 145.55, 145.94, 166.34, 166.43, 172.30.

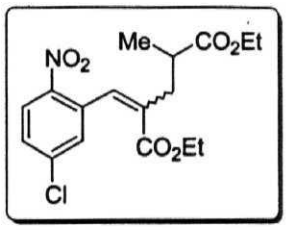
*Major peaks at δ 29.38 (allylic carbon), 33.29 (CH$_2$CO$_2$Et), 60.60 (OCH$_2$), 60.75 (OCH$_2$) and minor peaks at δ 23.20 (allylic carbon), 33.04 (CH$_2$CO$_2$Et), 60.45 (OCH$_2$), 61.28 (OCH$_2$) are attributed to the major Z- and minor E-isomers respectively.*

Analysis calcd. for $C_{16}H_{18}ClNO_6$ : C, 54.02; H, 5.10; N, 3.94

Found : C, 54.18; H, 5.05; N, 3.90

**Ethyl 5-(5-chloro-2-nitrophenyl)-4-ethoxycarbonyl-2-methylpent-4-enoate (218):**

This molecule was prepared *via* the treatment of ethyl 3-(5-chloro-2-nitrophenyl)-3-hydroxy-2-methylenepropanoate (**178h**) with triethyl orthopropanoate in the presence of propanoic acid (cat.), following similar procedure described for **203**, as colorless liquid.




Yield : 71%

Reaction time : 12 h

*Z* : *E* : 85 : 15 [*determined by the integration of isomeric olefinic proton singlets at δ 7.12 (Z-isomer) & δ 7.92 (E-isomer) in the $^1$H NMR spectrum of the crude as well as column purified sample.*

IR (neat) : ν 1726, 1712, 1641, 1602 cm$^{-1}$

$^1$H NMR (*Z* & *E* mixture) : δ 0.89-1.45 (m, 9H), 2.30-2.95 (m, 3H), 3.91-4.39 (m, 4H), 7.12 & 7.91 (2s, 1H), 7.22 & 7.31 (2d, 1H, *J* = 2.0 Hz), 7.41 & 7.49 (2dd, 1H, *J* = 8.8, 2.0 Hz), 8.07 & 8.16 (2d, 1H, *J* = 8.8 Hz).

*The underlined chemical shift values with low intensity are due to the presence of minor (E)-isomer*

$^{13}$C NMR (*Z* & *E* mixture) : δ 13.45, 14.04, 16.83, 31.31, 37.81, 38.32, 38.73, 60.15, 60.32, 60.56, 61.05, 125.67, 126.30, 128.24, 129.02, 130.50, 130.74, 132.58, 133.55, 134.01, 135.25, 136.44, 139.15, 139.74, 145.51, 145.90, 166.35, 175.27.

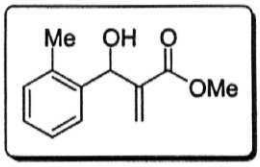
*Major peaks at δ 37.81 (allylic carbon), 38.73 (C̲H$_2$CO$_2$Et), 60.32 (OC̲H$_3$), 61.56 (OC̲H$_2$) and minor peaks at δ 31.31 (allylic carbon), 38.32 (C̲H$_2$CO$_2$Et), 60.15 (OC̲H$_3$), 60.05 (OC̲H$_2$) are attributed to the major Z- and minor E-isomers respectively.*

Analysis calcd. for $C_{17}H_{20}ClNO_6$ : C, 55.21; H, 5.45; N, 3.79

Found : C, 55.42; H, 5.40; N, 3.84

**Methyl 3-hydroxy-2-methylene-3-(2-methylphenyl)propanoate (126r):**

This molecule was obtained as a colorless viscous liquid *via* the reaction between 2-methylbenzaldehyde and methyl acrylate in the presence of DABCO (cat.) following a similar procedure described for the molecule **126a**.




Reaction time : 9 days

Yield : 70%

Bp : 140-142/4.0 mm

IR (neat) : ν 3433, 1722, 1630 $cm^{-1}$

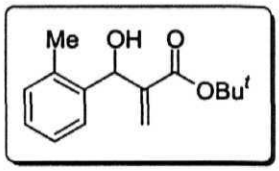
$^1H$ NMR : δ 2.31 (s, 3H), 3.24 (b, 1H), 3.70 (s, 3H), 5.65 (s, 1H), 5.77 (s, 1H), 6.30 (s, 1H), 7.08-7.25 (m, 3H), 7.30-7.44 (m, 1H).

$^{13}C$ NMR : δ 19.02, 51.86, 69.09, 125.85, 126.09, 126.38, 127.74, 130.41, 135.70, 139.04, 142.05, 167.04.

***t*-Butyl 3-hydroxy-2-methylene-3-(2-methylphenyl)propanoate (126s):**

This compound was prepared *via* the DABCO-catalyzed coupling of 2-methylbenzaldehyde with *t*-butyl acrylate in silica gel solid phase medium, following a similar procedure described for the molecule **178d**, as a colorless viscous liquid.

Reaction time : 12 days




Yield : 75%

Mp : 44-45 °C

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

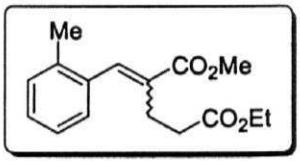
$^1H$ NMR : δ 1.43 (s, 9H), 2.33 (s, 3H), 2.92 (b, 1H), 5.51 (s, 1H), 5.74 (s, 1H), 6.24 (s, 1H), 7.13-7.28 (m, 3H), 7.33-7.45 (m, 1H).

$^{13}C$ NMR : δ 19.08, 28.01, 69.63, 81.47, 124.89, 126.15, 126.35, 127.75, 130.42, 135.76, 139.35, 143.62, 166.08.

**Ethyl 4-methoxycarbonyl-5-(2-methylphenyl)pent-4-enoate (219):**

This product was obtained as colorless liquid *via* the treatment of methyl 3-hydroxy-2-methylene-3-(2-methylphenyl)propanoate (**126r**) with triethyl orthoacetate in the presence of propanoic acid (cat.) following similar procedure described for **203**.

Yield : 91%




Reaction time : 3 h

*Z* : *E* : 38 : 62 [*determined by the integration of isomeric olefinic proton singlets at δ 6.88 (Z-isomer) & δ 7.78 (E-isomer) in the $^1H$ NMR spectrum of the crude as well as column purified sample*]

IR (neat) : ν 1732, 1714, 1635, 1602 $cm^{-1}$

$^1H$ NMR (*Z* & *E* mixture) : δ 1.15-1.36 (m, 3H), 2.26 (s, 3H), 2.40-2.85 (m, 4H), 3.53 & 3.83 (2s, 3H), 4.01-4.26 (m, 2H), 6.88 & 7.78 (2s, 1H), 7.01-7.32 (m, 4H).

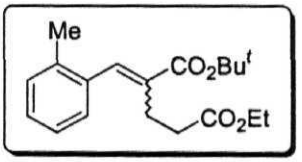
*The underlined chemical shift values (δ) with low intensity arise due to the presence of minor (E)-isomer*

$^{13}$C NMR (*Z* & *E* mixture) : δ 13.99, 19.66, 22.91, 30.00, 33.44, 51.10, 51.73, 60.08, 60.22, 125.18, 125.67, 127.61, 127.80, 127.95, 128.24, 129.45, 129.99, 131.88, 132.90, 134.64, 135.37, 135.86, 136.34, 139.98, 167.78, 168.60, 172.34.

*Major peaks at δ 22.91 (allylic carbon), 51.73 (O<u>C</u>H$_3$), 60.08 (O<u>C</u>H$_2$) and minor peaks at δ 30.00 (allylic carbon), 51.10 (O<u>C</u>H$_3$), 60.22 (O<u>C</u>H$_2$) are attributed to the major E- and minor Z-isomers respectively. Similarly, peak at δ 167.78 (with high intensity) and peak at δ 168.60 (with low intensity) are attributed to <u>C</u>O$_2$Me carbonyl carbon of major and minor isomer respectively*

**Ethyl 4-(*t*-butoxycarbonyl)-5-(2-methyphenyl)pent-4-enoate (220):**

Treatment of *t*-butyl 3-hydroxy-2-methylene-3-(2-methylphenyl)propanoate (**126s**) with triethyl orthoacetate in the presence of propanoic acid, following similar reaction procedure described for **203**, provided the desired diester as colorless liquid.




Yield : 83%

Reaction time : 3 h

*Z* : *E* : 42 : 58 [*determined by the integration of isomeric olefinic proton singlets at δ 6.78 (Z-isomer) & δ 7.68 (E-isomer) in the $^1$H NMR spectrum of the crude as well as column purified sample*]

IR (neat) : ν 1736, 1707, 1637, 1602 cm$^{-1}$

$^1$H NMR (*Z* & *E* mixture) : δ 1.14-1.60 (m, 12H),* <u>2.23</u> & 2.25 (2s, 3H), 2.33-2.80 (m, 4H), 4.06 & 4.15 (2q, 2H, *J* = 6.8 Hz), <u>6.78</u> & 7.69 (2s, 1H), 7.00-7.28 (m, 4H).

* *This multiplet contains singlets at δ 1.17 (with low intensity, minor Z-isomer) and δ 1.55 (with high intensity,) which are attributed to C(CH$_3$)$_3$ protons of minor Z-isomer*

*and major E-isomer repectively. Underlined chemical shift values with low intensity arise due to the presence of minor (E)-isomer*

$^{13}$C NMR (*Z* & *E* mixture) : δ 14.13, 14.23, 19.71, 19.81, 23.16, 27.57, 28.18, 30.07, 33.59, 33.71, 60.20, 60.32, 80.79, 125.23, 125.74, 127.37, 128.17, 128.26, 129.36, 130.03, 133.60, 134.64, 135.10, 135.40, 136.49, 137.02, 138.96, 166.78, 172.61

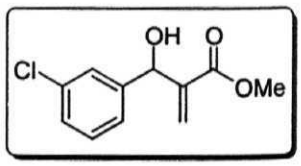
Analysis calcd. for $C_{19}H_{26}O_4$ : C, 71.67; H, 8.23

Found : C, 71.44; H, 8.29

**Methyl 3-(3-chlorophenyl)-3-hydroxy-2-methylenepropanoate (126t):**

This molecule was obtained as a colorless viscous liquid *via* the Baylis-Hillman reaction between 2-chlorobenzaldehyde and methyl acrylate catalyzed by DABCO following a similar procedure described for the molecule **126a**. The crude product was purified by column chromatography (6% EtOAc in hexanes, silica gel).

Reaction time : 8 days




Yield : 65%

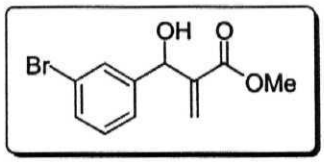
IR (neat) : ν 3468, 1718, 1631 cm$^{-1}$

$^1$H NMR : δ 3.56 (b, 1H), 3.67 (s, 3H), 5.47 (s, 1H), 5.84 (s, 1H), 6.31 (s, 1H), 7.21 (s, 3H), 7.33 (s, 1H).

$^{13}$C NMR : δ 51.87, 72.27, 124.78, 126.24, 126.73, 127.79, 129.56, 134.20, 141.62, 143.56, 166.46

**Methyl 3-(3-bromophenyl)-3-hydroxy-2-methylenepropanoate (126u):**

This compound was obtained *via* the Baylis-Hillman reaction between 3-bromobenzaldehyde and methyl acrylate in the presence of DABCO (cat.), following a similar procedure described for the molecule **126a**, as a colorless viscous liquid. The crude product was purified by column chromatography (5% EtOAc in hexanes, silica gel).




Reaction time : 8 days

Yield : 70%

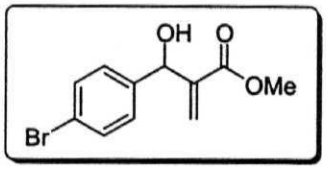
IR (neat) : ν 3466, 1718, 1631 $cm^{-1}$

$^1H$ NMR : δ 3.21 (b, 1H), 3.73 (s, 3H), 5.50 (s, 1H), 5.84 (s, 1H), 6.35 (s, 1H), 7.13-7.48 (m, 3H), 7.53 (s, 1H).

$^{13}C$ NMR : δ 52.01, 72.58, 122.58, 125.27, 126.53, 129.71, 129.98, 130.90, 141.59, 143.80, 166.56.

**Methyl 3-(4-bromophenyl)-3-hydroxy-2-methylenepropanoate (126v):**

This was obtained *via* the DABCO-catalyzed coupling of 4-bromobenzaldehyde with methyl acrylate, following a similar procedure described for the molecule **126a**, as a colorless viscous liquid. The crude product was purified by column chromatography (5% EtOAc in hexanes, silica gel).




Reaction time : 8 days

Yield : 70%

Mp : 56-58 °C

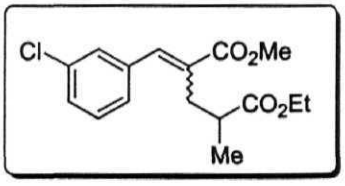
IR (KBr) : ν 3448, 1720, 1635 $cm^{-1}$

$^1H$ NMR : δ 3.16 (b, 1H), 3.72 (s, 3H), 5.50 (s, 1H), 5.82 (s, 1H), 6.33 (s, 1H), 7.24 (d, 2H, $J$ = 8.6 Hz), 7.46 (d, 2H, $J$ = 8.6 Hz),

$^{13}C$ NMR : δ 52.06, 72.76, 121.83, 126.34, 128.40, 131.58, 140.48, 141.76, 166.70.

**Ethyl 5-(3-chlorophenyl)-4-methoxycarbonyl-2-methylpent-4-enoate (221):**

This product was obtained as colorless liquid *via* the Johnson-Claisen rearrangement of methyl 3-(3-chlorophenyl)-3-hydroxy-2-methylenepropanoate (**126t**) with triethyl orthoacetate under the catalytic influence of propanoic acid following similar procedure described for **203**.




Yield : 80%

Reaction time : 3 h

*Z* : *E* : 39 : 61 [*determined by the integration of isomeric olefinic proton singlets at δ 6.65 (Z-isomer) & δ 7.66 (E-isomer) in the $^1H$ NMR spectrum of the crude as well as column purified sample*]

IR (neat) : ν 1728, 1714, 1639, 1593 $cm^{-1}$

$^1H$ NMR (*Z* & *E* mixture) : δ 1.05-1.38 (m, 6H), 2.42-3.00 (m, 3H), 3.65 & 3.82 (2s, 3H), 3.98-4.22 (m, 2H), 6.65 & 7.66 (2s, 1H), 7.03-7.42 (m, 4H).

*The underlined chemical shift values (δ) with low intensity arise due to the presence of minor (E)-isomer*

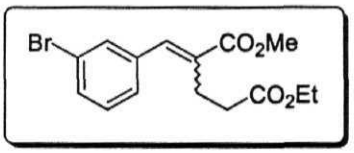
$^{13}C$ NMR (*Z* & *E* mixture) : δ 13.91, 14.03, 16.55, 16.67, 30.86, 38.45, 39.08, 51.41, 51.84, 60.14,

60.19, 126.09, 127.04, 127.67, 127.94, 128.25, 128.84, 129.18, 129.64, 132.09, 132.94, 133.83, 134.29, 137.08, 137.67, 138.85, 167.84, 168.71, 175.22, 175.26.

*Major peaks at δ 13.91, 16.55, 51.84 (O<u>C</u>H$_3$), 60.14 (O<u>C</u>H$_2$) (with high intensity) and minor peaks at δ 14.03 , 16.67, 51.41 (O<u>C</u>H$_3$), 60.19 (O<u>C</u>H$_2$) are attributed to the major E- and minor Z-isomers respectively. Similarly, peaks at δ 167.84, 175.26 (with high intensity) and peaks at δ 168.71, 175.22 (with low intensity) are attributed to carbonyl carbons of major and minor isomer respectively*

**Ethyl 5-(3-bromophenyl)-4-methoxycarbonylpent-4-enoate (222):**

This was obtained *via* the treatment of methyl 3-(3-bromophenyl)-3-hydroxy-2-methylenepropanoate (**126u**) with triethyl orthoacetate in the presence of propanoic acid, following similar procedure described for **203**, as colorless liquid.




Yield : 87%

Reaction time : 3 h

*Z* : *E* : 32 : 68 [*determined by the integration of isomeric olefinic proton singlets at δ 6.67 (Z-isomer) & δ 7.64 (E-isomer) in the $^1$H NMR spectrum of the crude as well as column purified sample*]

IR (neat) : ν 1732, 1712, 1633 cm$^{-1}$

$^1$H NMR (*Z* & *E* mixture) : δ 1.23 & <u>1.25</u> (2t, 3H, *J* = 7.0 Hz), 2.46-2.91 (m, 4H), <u>3.65</u> & 3.82 (2s, 3H), 4.06-4.23 (m, 2H), <u>6.67</u> & 7.64 (2s, 1H), 7.10-7.55 (m, 4H).

*The underlined chemical shift values (δ) with low intensity arise due to the presence of minor (E)-isomer*

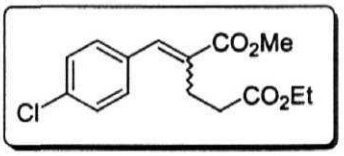
$^{13}$C NMR (*Z* & *E* mixture) : δ 14.05, 22.98, 30.42, 33.07, 33.26, 51.50, 51.94, 60.31, 122.00,

122.53, 126.56, 127.38, 129.47, 129.98, 130.63, 130.92, 131.36, 131.80, 132.62, 133.23, 133.88, 137.23, 137.93, 138.42, 167.60, 168.67, 172.01, 172.16.

*Major peaks at δ 22.98 (allylic carbon), 33.26 (CH$_2$CO$_2$Et), 51.94 (OCH$_3$) and minor peaks at δ 30.42 (allylic carbon), 33.07 (CH$_2$CO$_2$Et), 51.50 (OCH$_3$) are attributed to the major E- and minor Z-isomers respectively. Similarly, peaks at δ 167.60, 172.16 (with high intensity) and peaks at δ 168.67, 172.01 (with low intensity) are attributed to carbonyl carbons of major and minor isomer respectively*

**Ethyl 5-(4-chlorophenyl)-4-methoxycarbonylpent-4-enoate (223):**

The Johnson-Claisen rearrangement of methyl 3-(4-chlorophenyl)-3-hydroxy-2-methylenepropanoate (**126f**) with triethyl orthoacetate in the presence of propanoic acid (cat.), following similar procedure described for **203**, provided the title compound **223** as colorless liquid.




Yield : 89%

Reaction time : 3 h

*Z* : *E* : 35 : 65 [*determined by the integration of isomeric olefinic proton singlets at δ 6.69 (Z-isomer) & δ 7.66 (E-isomer) in the $^1$H NMR spectrum of the crude as well as column purified sample*]

IR (neat) : ν 1732, 1711, 1633, 1593 cm$^{-1}$

$^1$H NMR (*Z* & *E* mixture) : δ 1.23 & 1.25 (2t, 3H, *J* = 6.8 Hz), 2.46-2.94 (m, 4H), 3.65 & 3.82 (2s, 3H), 4.04-4.24 (m, 2H), 6.69 & 7.67 (2s, 1H), 7.12-7.48 (m, 4H).

*The underlined chemical shift values with low intensity arise due to the presence of minor (E)-isomer*

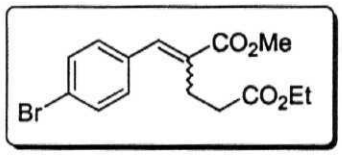
$^{13}$C NMR (*Z* & *E* mixture) : δ 14.07, 23.00, 30.57, 33.26, 51.55, 51.96, 60.36, 128.23, 128.79,

129.42, 130.39, 131.82, 133.06, 133.61, 133.86, 134.34, 134.51, 138.85, 167.87, 168.88, 172.18, 172.35.

*Major peaks at δ 23.00 (allylic carbon), 51.96 (O<u>C</u>H$_3$) and minor peaks at δ 30.57 (allylic carbon), 51.55 (O<u>C</u>H$_3$) are attributed to the major E- and minor Z-isomers respectively. Similarly, peaks at δ 167.87, 172.35 (with high intensity) and peaks at δ 168.88, 172.18 (with low intensity) are attributed to carbonyl carbons of major and minor isomer respectively*

**Ethyl 5-(4-bromophenyl)-4-methoxycarbonylpent-4-enoate (224):**

Treatment of methyl 3-(4-bromophenyl)-3-hydroxy-2-methylenepropanoate (**126v**) with triethyl orthoacetate in the presence of propanoic acid (cat.) following similar procedure described for **203**, provided the desired diester **224** as colorless liquid.




Yield : 82%

Reaction time : 3 h

*Z* : *E* : 38 : 62 [*determined by the integration of isomeric olefinic proton singlets at δ 6.64 (Z-isomer) & δ 7.66 (E-isomer) in the $^1$H NMR spectrum of the crude as well as column purified sample.*

IR (neat) : ν 1738, 1712, 1633, 1585 cm$^{-1}$

$^1$H NMR (*Z* & *E* mixture) : δ 1.21 & <u>1.23</u> (2t, 3H, *J* = 6.8 Hz), 2.44-2.91 (m, 4H), <u>3.63</u> & 3.80 (2s, 3H), 4.01-4.21 (m, 2H), <u>6.64</u> & 7.62 (2s, 1H), <u>7.07</u> & 7.21 (d, 2H, *J* = 8.8 Hz), <u>7.40</u> & 7.50 (d, 2H, *J* = 8.8 Hz).

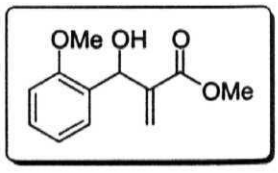
*The underlined chemical shift values with low intensity arise due to the presence of minor (E)-isomer*

$^{13}$C NMR (*Z* & *E* mixture) : δ 14.22, 23.15, 30.72, 33.38, 51.67, 52.09, 60.50, 122.02, 122.89, 129.81, 130.70, 131.31, 131.89, 132.09, 133.30, 134.03, 134.20, 134.92, 139.02, 168.01, 169.01, 172.30, 172.47.

*Major peaks at δ 23.15 (allylic carbon), 52.09 (O<u>C</u>H$_3$) and minor peaks at δ 30.72 (allylic carbon), 51.67 (O<u>C</u>H$_3$) are attributed to the major E- and minor Z-isomers respectively. Similarly, peaks at δ 168.01, 172.47 (with high intensity) and peaks at δ 169.01 & δ 172.30 (with low intensity) are attributed to carbonyl carbons of major and minor isomer respectively*

**Methyl 3-hydroxy-3-(2-methoxyphenyl)-2-methylenepropanenoate (126w):**

This molecule was obtained as a colorless viscous liquid *via* the Baylis-Hillman reaction between 2-methoxybenzaldehyde and methyl acrylate in the presence of DABCO (cat.) following a similar procedure described for the molecule **126a**. The crude product was purified by column chromatography (7% EtOAc in hexanes, silica gel).




Reaction time : 10 days

Yield : 73%

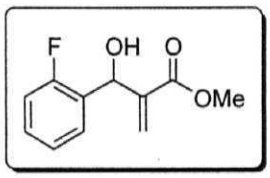
IR (neat) : ν 3468, 1720, 1631 cm$^{-1}$

$^{1}$H NMR : δ 3.42 (d, 1H, *J* = 5.8 Hz), 3.75 (s, 3H), 3.84 (s, 3H), 5.73 (s, 1H), 5.88 (d, 1H, *J* = 5.8 Hz), 6.31 (s, 1H), 6.80-7.18 (m, 2H), 7.23-7.42 (m, 2H).

$^{13}$C NMR : δ 51.75, 55.26, 67.88, 110.50, 120.56, 125.54, 127.50, 128.79, 129.18, 141.47, 156.54, 166.97.

**Methyl 3-(2-fluorophenyl)-3-hydroxy-2-methylenepropanoate (126x):**

This molecule was obtained *via* the BaylisHillman coupling of 2-fluorobenzaldehyde with methyl acrylate under the catalytic influence of DABCO, following a similar procedure described for the molecule **126a**, as a colorless viscous liquid. The crude product was purified by column chromatography (5% EtOAc in hexanes, silica gel).




Reaction time : 8 days

Yield : 70%

IR (neat) : ν 3447, 1716, 1631 $cm^{-1}$

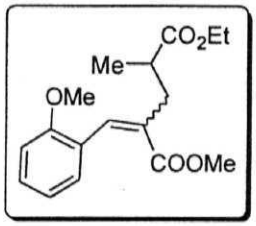
$^1H$ NMR : δ 3.26 (d, 1H, $J$ = 4.8 Hz), 3.70 (s, 3H), 5.79 (s, 1H), 5.89 (d, 1H, $J$ = 4.8 Hz), 6.34 (s, 1H), 6.96-7.60 (m, 4H).

$^{13}C$ NMR : δ 51.92, 66.69 (d, $J$ = 2.4 Hz), 115.25 (d, $J$ = 21.8 Hz), 124.14 (d, $J$ = 3.6 Hz), 126.26, 128.13 (d, $J$ = 3.6 Hz), 128.27 (d, $J$ = 13.3 Hz),* 129.38 (d, $J$ = 8.4 Hz), 140.94, 159.96 ($J$ = 245.0 Hz), 166.70.

* One peak of this doublet is mixed with peak at δ 128.13

**Ethyl 4-methoxycarbonyl-5-(2-methoxyphenyl)-2-methylpent-4-enoate (225):**

This product was obtained as colorless liquid *via* the Johnson-Claisen rearrangement of methyl 3-hydroxy-2-methylene-3-(2-methoxyphenyl)propanoate (**126w**) with triethyl orthopropanoate under the catalytic influence of propanoic acid following similar procedure described for **203**.




Yield : 95%

Reaction time : 3 h

*Z* : *E* : 55 : 45 [*determined by the integration of isomeric olefinic proton singlets at δ 6.78 (Z-isomer) & δ 7.69 (E-isomer) in the $^1H$ NMR spectrum of the crude as well as column purified sample.*

IR (neat) : ν 1730, 1714, 1633, 1599 $cm^{-1}$

$^1H$ NMR (*Z* & *E* mixture) (400 MHz) : δ 1.00-1.30 (m, 6H), 2.31-2.91 (m, 4H), 3.59-4.21 (m, 8H), 6.84 & 7.84 (2s, 1H), 6.84-7.40 (m, 4H).

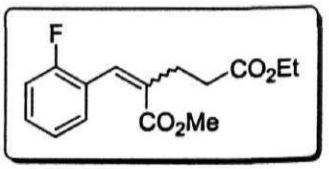
*The underlined chemical shift values with low intensity arise due to the presence of minor (E)-isomer*

$^{13}C$ NMR (*Z* & *E* mixture) (400 MHz) : δ 14.07, 14.19, 16.53, 16.75, 31.20, 38.52, 38.92, 39.28, 51.36, 51.89, 55.31, 55.39, 60.21, 60.33, 110.35, 110.55, 120.06, 120.30, 124.48, 125.28, 129.35, 129.43, 129.59, 129.93, 130.56, 131.22, 133.08, 137.38, 156.69, 157.42, 168.44, 169.44, 175.86, 176.01.

*$^1H$ and $^{13}C$ NMR data indicated that the molecule is contaminated with 5% unidentified impurity*

**Ethyl 5-(2-fluoriphenyl)-4-methoxycarbonylpent-4-enoate (226):**

This compound was obtained *via* the treatment of methyl 3-(2-flourophenyl)-3-hydroxy-2-methylenepropanoate (**126x**) with triethyl orthoacetate in the presence of catalytic amount of propanoic acid, following similar procedure described for **203**, as colorless liquid.




Yield : 92%

Reaction time : 3 h

*Z* : *E* : 54 : 46 [*determined by the integration of isomeric olefinic proton singlets at δ 6.78 (Z-isomer) & δ 7.69 (E-isomer) in the $^1H$ NMR spectrum of the crude as well as column purified sample.*

IR (neat) : ν 1734, 1716, 1641, 1610 $cm^{-1}$

$^1H$ NMR (*Z* & *E* mixture) : δ 1.15-131 (m, 3H), 2.48-2.90 (m, 4H), 3.64 & 3.83 (2s, 3H), 4.06-4.26 (m, 2H), 6.77 & 7.73 (2s, 1H), 6.96-7.44 (m, 4H).

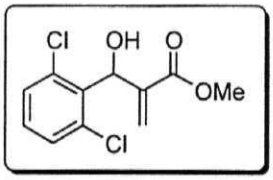
*The underlined chemical shift values (δ) are attributed to the minor (E)-isomer*

$^{13}C$ NMR (*Z* & *E* mixture) : δ 14.15, 23.54, 30.52, 33.24, 33.43, 51.53, 52.04, 60.36, 60.45, 115.27 (d, $J$ = 24.2 Hz), 115.75 (d, $J$ = 24.2 Hz), 123.09, 123.35, 123.62 (d, $J$ = 2.4 Hz), 124.10 (d, $J$ = 2.4 Hz), 128.86, 129.54, 129.71, 129.78, 129.95, 130.32, 130.49, 133.18, 133.61, 134.61, 159.85 (d, $J$ = 246.2 Hz), 160.20 (d, $J$ = 246.2 Hz), 167.62, 168.50, 172.33, 172.57.

The underlined chemical shifts include peaks due to major *Z*- and minor *E*-isomer along with peaks due to C-F coupling

**Methyl 3-(2,6-dichlorophenyl)-3-hydroxy-2-methylenepropanoate (126y):**

This molecule was obtained as a colorless solid *via* the Baylis-Hillman coupling between 2,6-dichlorobenzaldehyde and methyl acrylate under the catalytic influence of DABCO in silica gel solid phase medium, following a similar procedure described for the molecule **178d**.




Reaction time : 10 days

Yield : 80%

Mp : 66-68 °C

IR (KBr) : ν 3501, 1707, 1633 $cm^{-1}$

$^1H$ NMR : δ 3.35 (d, 1H, $J$ = 7.8 Hz), 3.74 (s, 3H), 5.57 (d, 1H, $J$ = 2.0 Hz), 6.30-6.45 (m, 2H), 7.11-7.39 (m, 3H).

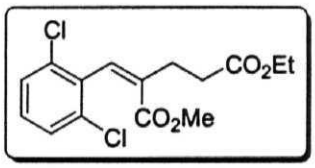
$^{13}$C NMR : δ 51.87, 69.68, 126.53, 129.32, 129.38, 135.39, 135.48, 139.30, 166.41.

**Ethyl (4*Z*)-5-(2,6-dichlorophenyl)-4-methoxycarbonylpent-4-enoate (227):**

This product was obtained as colorless liquid *via* the treatment of methyl 3-(2,6-dichlorophenyl)-3-hydroxy-2-methylenepropanoate (**126y**) with triethyl orthoacetate in the presence of propanoic acid (cat.) following similar procedure described for **203**.

Yield : 77%

Reaction time : 3 h




*Z* : *E* : 100 : 0 (*determined by absence of E-olefinic proton singlet in $^1$H NMR spectrum of the crude as well as column purified sample*)

IR (neat) : ν 1732, 1716, 1647, 1556 cm$^{-1}$

$^1$H NMR (*Z*-isomer) : δ 1.26 (t, 3H, *J* = 6.8 Hz), 2.58-2.73 (m, 2H), 2.79-2.93 (m, 2H), 3.57 (s, 3H), 4.16 (q, 2H, *J* = 6.8 Hz), 6.73 (s, 1H), 7.08-7.38 (m, 3H).

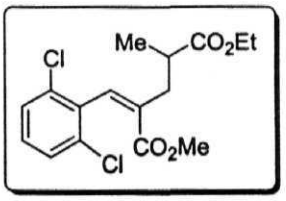
$^{13}$C NMR (Z-isomer) : δ 14.22, 29.33, 33.67, 51.72, 60.52, 127.52, 128.66, 133.49, 135.11, 135.87, 166.53, 172.45.

Analysis calcd. for $C_{15}H_{16}Cl_2O_4$ : C, 54.40; H, 4.87

Found : C, 54.21; H, 4.82

**Ethyl (4*Z*)-5-(2,6-dichlorophenyl)-4-methoxycarbonyl-2-methylpent-4-enoate (228):**

This molecule was obtained *via* the Johnson-Claisen rearrangement of methyl 3-(2,6-dichlorophenyl)-3-hydroxy-2-methylenepropanoate (**126y**) with triethyl orthopropanoate under the catalytic influence of propanoic acid, following similar procedure described for **203**, as colorless liquid.




Yield : 86%

Reaction time : 3 h

*Z* : *E* : 100 : 0 (*determined by absence of E-olefinic proton singlet in $^1$H NMR spectrum of the crude as well as column purified sample*)

IR (neat) : ν 1730, 1716, 1645, 1579 $cm^{-1}$

$^1$H NMR (*Z*-isomer) : δ 1.25 (t, 3H, *J* = 6.8 Hz) 1.26 (d, 3H, *J* = 6.8 Hz), 2.51-3.04 (m, 3H), 3.55 (s, 3H), 4.14 (q, 2H, *J* = 6.8 Hz), 6.70 (s, 1H), 7.07-7.36 (m, 3H).

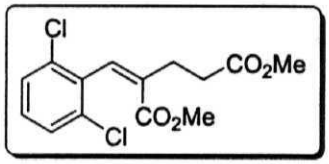
$^{13}$C NMR (*Z*-isomer) : δ 14.03, 16.89, 37.73, 38.70, 51.53, 60.28, 127.40, 128.54, 133.47, 134.00, 134.92, 135.02, 166.48, 175.51.

Analysis calcd. for $C_{16}H_{18}Cl_2O_4$ : C, 55.67; H, 5.26

Found : C, 55.81; H, 5.30

**Methyl (4*Z*)-5-(2,6-dichlorophenyl)-4-methoxycarbonylpent-4-enoate (229):**

Treatment of methyl 3-(2,6-dichlorophenyl)-3-hydroxy-2-methylenepropanoate (**126y**) with trimethyl orthoacetate in the presence of propanoic acid (cat), following similar procedure described for **203**, provided the title compound **229** as colorless liquid.




Yield : 62%

Reaction time : 3 h

*Z* : *E* : 100 : 0 (*determined by absence of E-olefinic proton singlet in $^1$H NMR spectrum of the crude as well as column purified sample*)

IR (neat) : ν 1736, 1724, 1649, 1579 $cm^{-1}$

$^1$H NMR (*Z*-isomer) : δ 2.60-2.74 (m, 2H), 2.78-2.96 (m, 2H), 3.56 (s, 3H), 3.70 (s, 3H), 6.73 (s, 1H), 7.08-7.40 (m, 3H).

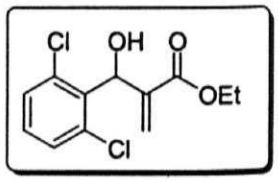
$^{13}$C NMR (*Z*-isomer) : δ 29.43, 33.46, 51.75, 127.55, 128.69, 133.59, 135.09, 135.77, 166.51, 172.89.

Analysis calcd. for $C_{14}H_{14}Cl_2O_4$ : C, 53.02; H, 4.45

Found : C, 53.24; H, 4.40

**Ethyl 3-(2,6-dichlorophenyl)-3-hydroxy-2-methylenepropanoate (178i):**

This compound was obtained *via* the treatment of 2,6-dichlorobenzaldehyde with ethyl acrylate in the presence of DABCO (cat.) in silica gel solid phase medium, following a similar procedure described for the molecule **88d**, as a colorless solid.




Reaction time : 10 days

Yield : 77%

Mp : 68-70 °C

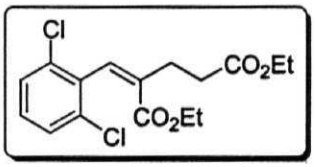
IR (KBr) : ν 3501, 1697, 1620 $cm^{-1}$

$^1$H NMR : δ 1.23 (t, 3H, $J$ = 6.8 Hz), 3.34 (d, 1H, $J$ = 7.8 Hz), 4.11-4.31 (m, 2H), 5.78 (d, 1H, $J$ = 2.0 Hz), 6.33 (dd, 1H, $J$ = 7.8 & 2.0 Hz), 6.41 (d, 1H, $J$ = 2.0 Hz), 7.10-7.40 (m, 3H).

$^{13}$C NMR : δ 13.95, 60.91, 69.83, 126.17, 129.31, 135.53, 139.74, 165.99.

**Ethyl (4*Z*)-5-(2,6-dichlorophenyl)-4-ethoxycarbonylpent-4-enoate (230):**

This product was obtained as colorless liquid *via* the treatment of ethyl 3-(2,6-dichlorophenyl)-3-hydroxy-2-methylenepropanoate (**178i**) with triethyl orthoacetate in the presence of propanoic acid (cat.) following similar procedure described for **203**.




Yield : 77%

Reaction time : 3 h

*Z* : *E* : 100 : 0 (*determined by absence of E-olefinic proton singlet in $^1$H NMR spectrum of the crude as well as column purified sample*)

IR (neat) : ν 1732, 1712, 1630, 1579 cm$^{-1}$

$^1$H NMR (*Z*-isomer) : δ 0.94 (t, 3H, $J$ = 6.8 Hz) 1.26 (t, 3H, $J$ = 6.8 Hz), 2.58-2.72 (m, 2H), 2.79-2.92 (m, 2H), 4.00 (q, 2H, $J$ = 6.8 Hz), 4.16 (q, 2H, $J$ = 6.8 Hz), 6.74 (s, 1H), 7.08-7.33 (m, 3H).

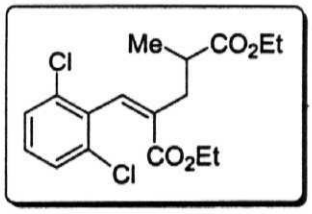
$^{13}$C NMR (*Z*-isomer) : δ 13.44, 14.17, 29.28, 33.62, 60.50, 127.40, 128.54, 133.03, 133.59, 135.45, 136.18, 166.04, 172.40.

Analysis calcd. for $C_{16}H_{18}Cl_2O_4$ : C, 55.67; H, 5.26

Found : C, 55.48; H, 5.20

**Ethyl (4*Z*)-5-(2,6-dichlorophenyl)-4-ethoxycarbonyl-2-methylpent-4-enoate) (231):**

The Johnson-Claisen rearrangement of ethyl 3-(2,6-dichlorophenyl)-3-hydroxy-2-methylenepropanoate (**178i**) with triethyl orthopropanoate under the catalytic influence of propanoic acid, following similar procedure described for **203**, provided this product as colorless liquid.




Yield : 80%

Reaction time : 3 h

*Z* : *E* : 100 : 0 (*determined by absence of E-olefinic proton singlet in $^1$H NMR spectrum of the crude as well as column purified sample*)

IR (neat) : ν 1730, 1714, 1641, 1579 $cm^{-1}$

$^1$H NMR (*Z*-isomer) : δ 0.93 (t, 3H, *J* = 6.8 Hz), 1.20-1.35 (m, 6H), 2.51-3.02 (m, 3H), 3.99 (q, 2H, *J* = 6.8 Hz), 4.14 (q, 2H, *J* = 6.8 Hz), 6.70 (s, 1H), 7.07-7.36 (m, 3H).

$^{13}$C NMR (*Z*-isomer) : δ 13.49, 14.22, 17.08, 37.90, 38.87, 60.45, 60.55, 127.45, 128.57, 133.71, 133.86, 135.46, 135.55, 166.26, 175.82.

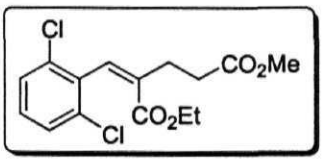
Analysis calcd. for $C_{17}H_{20}Cl_2O_4$ : C, 56.84; H, 5.61

Found : C, 56.99; H, 5.54

**Methyl (4*Z*)-5-(2,6-dichlorophenyl)-4-ethoxycarbonylpent-4-enoate (232):**

This product was obtained as colorless liquid *via* the Johnson-Claisen rearrangement of ethyl 3-(2,6-dichlorophenyl)-3-hydroxy-2-methylenepropanoate (**178i**) with trimethyl

orthoacetate in the presence of propanoic acid (cat.) following similar procedure described for **203**.




Yield : 74%

Reaction time : 3 h

*Z* : *E* : 100 : 0 (*determined by absence of E-olefinic proton singlet in $^1H$ NMR spectrum of the crude as well as column purified sample*)

IR (neat) : ν 1739, 1712, 1647, 1579 $cm^{-1}$

$^1H$ NMR (*Z*-isomer) : δ 0.93 (t, 3H, *J* = 7.8 Hz), 2.60-2.72 (m, 2H), 2.78-2.92 (m, 2H), 3.69 (s, 3H), 3.99 (q, 2H, *J* = 7.8 Hz), 6.72 (s, 1H), 7.07-7.35 (m, 3H).

$^{13}C$ NMR (*Z*-isomer) : δ 13.37, 29.28, 33.31, 51.55, 60.48, 127.36, 128.50, 133.10, 133.49, 135.36, 135.99, 165.95, 172.79.

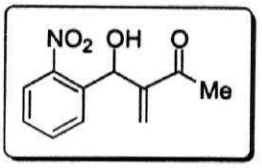
Analysis calcd. for $C_{15}H_{16}Cl_2O_4$ : C, 54.40; H, 4.87

Found : C, 54.26; H, 4.92

**4-Hydroxy-3-methylene-4-(2-nitrophenyl)butan-2-one (233a):**

To a solution of 2-nitrobenzaldehyde (10 mmol, 1.511 g) and methyl vinyl ketone (10 mmol, 0.709 g) in THF, was added DABCO (1.5 mmol, 0.168 g) and the reaction mixture was kept at room temperature for 6 days. The reaction mixture was diluted with ether (50 mL) and washed successively with 2N HCl, aqueous $NaHCO_3$ solution and water. Organic layer was dried over anhydrous $Na_2SO_4$. Solvent was evaporated and the residue thus obtained was purified by column chromatography, followed by

crystallization (10% EtOAc in hexanes) to provide the desired product **233a** as a light yellow solid in 60 % (1.33 g) yield.




Mp : 78-80 °C

IR (KBr) : ν 3350, 1662, 1625 $cm^{-1}$

$^1H$ NMR : δ 2.36 (s, 3H), 3.58 (d, 1H, $J$ = 4.8 Hz), 5.79 (s, 1H), 6.16 (s, 1H), 6.21 (d, 1H, $J$ = 4.8 Hz), 7.38-7.55 (m, 1H), 7.59-7.72 (m, 1H), 7.77 (d, 1H, $J$ = 7.8 Hz), 7.92-8.04 (m, 1H).

$^{13}C$ NMR : δ 25.77, 66.71, 124.37, 126.34, 128.30, 128.69, 133.25, 136.60, 147.80, 149.02, 199.50.

**Ethyl 4-acetyl-5-(2-nitrophenyl)pent-4-enoate (234):**

To a stirred solution of 4-hydroxy-3-methylene-4-(2-nitrophenyl)butan-2-one (**233a**) (1 mmol, 0.221 g) in triethyl orthoacetate (1 mL) was added catalytic amount of propanoic acid (2-3 drops). After heating at 145 °C for 12 hours, the reaction mixture was diluted with water and extracted into ether (3 x 15 mL). Combined organic layer was dried over anhydrous $Na_2SO_5$. Careful silica gel column purification (5-6% EtOAc in hexanes) of the crude product, obtained after solvent evaporation, provided the pure *Z*-isomer (**234-*Z***) and *E*-isomer (**234-*E***) as colorless liquids.

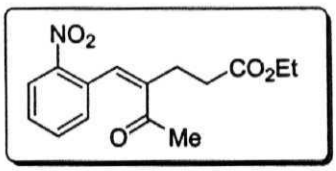
Yield : 85% (combined yield of isolated *Z*- (**234-*Z***) and *E*-isomers (**234-*E***)

Reaction time : 12 h

*Z* : *E* : 56 : 44 [*determined by the integration of isomeric olefinic proton singlets at δ 7.08 (Z-isomer) & δ 7.85 (E-isomer) in the $^1H$ NMR spectrum of the crude as well as column purified sample*]

Fortunately, (*Z*)- and (*E*)-isomers were separated by careful column chromatography (silica gel, 3% EtOAc in hexanes)

**Spectral data of pure *Z*-isomer (234-*Z*):**



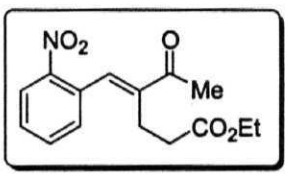

Yield : 48%

IR (neat) : ν 1734, 1684, 1606, 1572 $cm^{-1}$

$^1H$ NMR (*Z*-isomer) : δ 1.25 (t, 3H, *J* = 7.8 Hz), 1.85 (s, 3H), 2.50-2.64 (m, 2H), 2.70-2.84 (m, 2H), 4.16 (q, 2H, *J* = 7.8Hz), 7.07 (s, 1H), 7.22 (dd, 1H, *J* = 6.8, 2.0 Hz), 7.44-7.64 (m, 2H), 8.13 (dd, 1H, *J* = 7.8, 2.0 Hz).

$^{13}C$ NMR (*Z*-isomer) : δ 14.25, 29.80, 30.57, 33.17, 60.68, 124.98, 129.28, 129.91, 131.99, 132.58, 133.60, 143.40, 147.15, 172.36, 204.16.

**Spectral data of pure *E*-isomer (234-*E*):**




Yield : 37%

IR (neat) : ν 1734, 1674, 1608, 1572 $cm^{-1}$

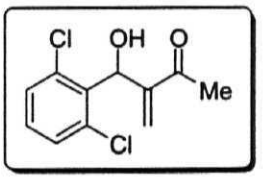
$^1H$ NMR (*E*-isomer) : δ 1.18 (t, 3H, *J* = 7.8 Hz), 2.28-2.45 (m, 2H), 2.49-2.68 (m, 5H), 4.10

(q, 2H, $J$ = 7.8 Hz), 7.35 (d, 1H, $J$ = 7.8 Hz), 7.52-7.78 (m, 2H), 7.85 (s, 1H), 8.22 (dd, 1H, $J$ = 8.0, 2.0 Hz).

$^{13}$C NMR (*E*-isomer) : δ 14.20, 22.10, 26.18, 33.07, 60.41, 125.15, 129.47, 130.82, 131.80, 133.81, 138.30, 141.16, 147.42, 172.62, 199.33.

**4-(2,6-Dichlorophenyl)-4-hydroxy-3-methylenebutan-2-one (233b):**

This molecule was obtained as a colorless viscous liquid *via* the Baylis-Hillman reaction between 2,6-dichlorobenzaldehyde and methyl vinyl ketone catalyzed by DABCO following a similar procedure described for the molecule **126a**. The crude product was purified by column chromatography (10% EtOAc in hexanes, silica gel).




Reaction time : 10 days

Yield : 65%

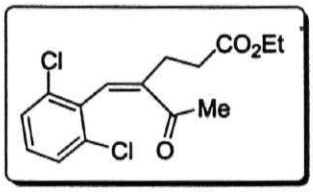
IR (neat) : υ 3443, 1674, 1562 cm$^{-1}$

$^{1}$H NMR : δ 2.39 (s, 3H), 3.37 (d, 1H, $J$ = 6.8 Hz), 5.90 (s, 1H), 6.23 (s, 1H), 6.35 (d, 1H, $J$ = 6.8 Hz), 7.09-7.44 (m, 3H).

$^{13}$C NMR : δ 26.57, 69.96, 125.97, 129.37, 135.53, 135.89, 147.80, 199.74.

**Ethyl (4*Z*)-4-acetyl-5-(2,6-dichlorophenyl)pent-4-enoate (235):**

Treatment of 4-(2,6-dichlorophenyl)-4-hydroxy-3-methylenebutan-2-one (**233b**) with triethyl orthoacetate in the presence of propanoic acid (cat.), following similar procedure described for **234**, provided **235** as colorless liquid.




Yield : 84%

Reaction time : 3 h

*Z* : *E* : 100 : 0 (*determined by absence of E-olefinic proton singlet in $^1$H NMR spectrum of the crude as well as column purified sample*)

IR (neat) : ν 1734, 1678, 1621, 1579 $cm^{-1}$

$^1$H NMR (*Z*-isomer) : δ 1.26 (t, 3H, *J* = 6.8 Hz) 1.89 (s, 3H), 2.58 (t, 2H, *J* = 7.8 Hz), 2.80 (t, 2H, *J* = 7.8 Hz), 4.15 (q, 2H, *J* = 6.8 Hz), 6.72 (s, 1H), 7.16-7.40 (m, 3H).

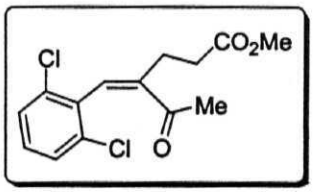
$^{13}$C NMR (*Z*-isomer) : δ 14.24, 29.11, 29.41, 33.67, 60.53, 128.11, 129.56, 130.19, 134.20, 134.90, 144.48, 172.50, 200.86.

Analysis calcd. for $C_{15}H_{16}Cl_2O_3$ : C, 57.16; H, 5.12

Found : C, 56.97; H, 5.18

**Methyl (4*Z*)-4-acetyl-5-(2,6-dichlorophenyl)pent-4-enoate (236):**

This molecule was obtained *via* the Johnson-Claisen rearrangement of 4-(2,6-dichlorophenyl)-4-hydroxy-3-methylenebutan-2-one (**233b**) with trimethyl orthoacetate under the catalytic influence of propanoic acid, following similar procedure described for **234**, as colorless liquid.




Yield : 70%

Reaction time : 3 h

*Z* : *E* : 100 : 0 (*determined by absence of E-olefinic proton singlet in $^1$H NMR*

*spectrum of the crude as well as column purified sample*)

IR (neat) : ν 1738, 1678, 1620, 1579 $cm^{-1}$

$^1H$ NMR (*Z*-isomer) : δ 1.89 (s, 3H), 2.60 (t, 2H, *J* = 6.8 Hz), 2.81 (t, 2H, *J* = 6.8 Hz), 3.70 (s, 3H), 6.73 (s, 1H), 7.14-7.40 (m, 3H).

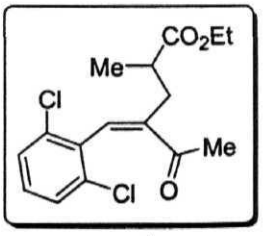
$^{13}C$ NMR (*Z*-isomer) : δ 29.14, 29.48, 33.43, 51.67, 128.11, 129.59, 130.34, 134.17, 134.88, 144.36, 172.96, 200.81

Analysis calcd. for $C_{14}H_{14}Cl_2O_3$ : C, 55.83; H, 4.69

Found : C, 55.72; H, 4.62

**Ethyl (4*Z*)-4-acetyl-5-(2,6-dichlorophenyl)-2-methylpent-4-enoate (237):**

This was prepared as colorless liquid *via* the reaction between 4-(2,6-dichlorophenyl)-4-hydroxy-3-methylenebutan-2-one (**233b**) and triethyl orthopropanoate under the catalytic influence of propanoic acid following similar procedure described for **234**.




Yield : 83%

Reaction time : 3 h

*Z* : *E* : 100 : 0 (*determined by absence of E-olefinic proton singlet in $^1H$ NMR spectrum of the crude as well as column purified sample*)

IR (neat) : ν 1732, 1680, 1625, 1579 $cm^{-1}$

$^1H$ NMR (*Z*-isomer) : δ 1.26 (t, 6H, J = 7.0 Hz)* 1.90 (s, 3H), 2.49-2.95 (m, 3H), 4.06-4.28 (m, 2H), 6.69 (s, 1H), 7.16-7.45 (m, 3H)

* *The doublet of $CH\underline{CH_3}$ is hidden in this triplet*

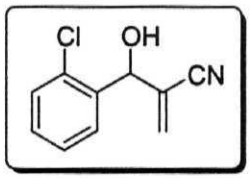
$^{13}$C NMR (*Z*-isomer) : δ 14.14, 17.10, 29.01, 38.06, 38.84, 60.38, 128.06, 129.49, 130.63, 134.19, 134.90, 143.75, 175.60, 200.90.

Analysis calcd. for $C_{16}H_{18}Cl_2O_3$ : C, 58.37; H, 5.51

Found : C, 58.22; H, 5.55

**3-(2-Chlorophenyl)-3-hydroxy-2-methylenepropanenitrile (282d):**

This molecule was obtained as a colorless viscous liquid *via* the reaction between 2-chlorobenzaldehyde and acrylonitrile catalyzed by DABCO following a similar procedure described for the molecule **282a**. The crude product was purified by column chromatography (5% EtOAc in hexanes, silica gel).




Reaction time : 2 days

Yield : 70%

IR (neat) : ν 3458, 2227, 1622 cm$^{-1}$

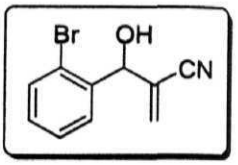
$^{1}$H NMR (400 MHz) : δ 2.92 (d, 1H, *J* = 4.0 Hz), 5.77 (d, 1H, *J* = 4.0 Hz), 6.07 (s, 2H), 7.27-7.45 (m, 3H), 7.62-7.70 (m, 1H).

$^{13}$C NMR : δ 70.59, 116.71, 124.78, 127.62, 128.06, 129.83, 130.05, 131.31, 132.69, 136.60.

**3-(2-Bromophenyl)-3-hydroxy-2-methylenepropanenitrile (282e):**

This compound was prepared *via* the Baylis-Hillman coupling between 2-bromobenzaldehyde and acrylonitrile under the influence of DABCO, following a similar

procedure described for the molecule **282a**, as a colorless viscous liquid. The crude product was purified by column chromatography (5% EtOAc in hexanes, silica gel).




Reaction time : 2 days

Yield : 70%

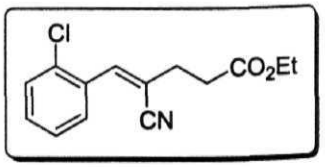
IR (neat) : ν 3441, 2231, 1622 $cm^{-1}$

$^1H$ NMR : δ 3.83 (b, 1H), 5.64 (s, 1H), 6.00 (s, 1H), 6.01 (s, 1H), 7.12-7.27 (m, 1H), 7.31-7.48 (m, 1H), 7.50-7.65 (m, 2H).

$^{13}C$ NMR : δ 72.48, 116.84, 122.71, 124.62, 128.17, 128.34, 130.27, 131.85, 132.99, 138.16.

**Ethyl (4*Z*)-5-(2-chlorophenyl)-4-cyanopent-4-enoate (238):**

This product was obtained as colorless liquid *via* the treatment of 3-(2-chlorophenyl)-3-hydroxy-2-methylenepropanenitrile (**282d**) with triethyl orthoacetate in the presence of propanoic acid (cat.) following similar reaction procedure described for **203**.




Yield : 71%

Reaction time : 3 h

*Z* : *E* :100 : 0 (*determined by the absence of any isomeric peaks in $^1H$ NMR spectrum of the crude as well as pure sample*).

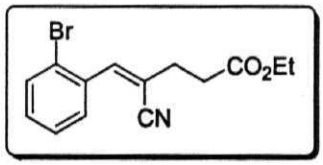
IR (neat) : ν 2214, 1736, 1626, 1591 $cm^{-1}$

$^1$H NMR : δ 1.26 (t, 3H, $J$ = 6.8 Hz), 2.56-2.87 (m, 4H), 4.17 (q, 2H, $J$ = 6.8 Hz), 7.20-7.46 (m, 4H), 7.82-7.98 (m, 1H).

$^{13}$C NMR : δ 14.17, 31.08, 32.70, 60.82, 113.09, 117.51, 127.11, 129.20, 129.73, 130.99, 132.04, 134.00, 141.04, 171.38.

**Ethyl (4*Z*)-5-(2-Bromophenyl)-4-cyanopent-4-enoate (239):**

This molecule was prepared *via* the Johnson-Claisen rearrangement of 3-(2-bromophenyl)-3-hydroxy-2-methylenepropanenitrile (**182e**) with triethyl orthoacetate under the catalytic influence of propanoic acid, following similar reaction procedure described for **203**, as colorless liquid.




Yield : 88%

Reaction time : 3 h

*Z* : *E* :100 : 0 (*determined by the absence of any isomeric peaks in $^1$H NMR spectrum of the crude as well as pure sample*)

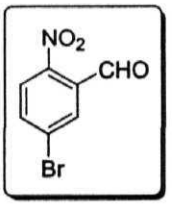
IR (neat) : ν 2214, 1734, 1620, 1587 cm$^{-1}$

$^1$H NMR : δ 1.27 (t, 3H, $J$ = 7.8 Hz), 2.58-2.90 (m, 4H), 4.17 (q, 2H, $J$ = 6.8 Hz), 7.18-7.48 (m, 3H), 7.61 (d, 1H, $J$ = 7.8 Hz), 7.85 (dd, 1H, $J$ = 7.8, 2.0 Hz).

$^{13}$C NMR : δ 14.06, 30.73, 32.50, 60.61, 113.08, 117.23, 123.92, 127.56, 129.31, 130.96, 132.78, 133.67, 143.28, 171.15.

**5-Bromo-2-nitrobenzaldehyde (195c):**

This was prepared from the 3-bromobenzaldehyde following the literature procedure with slight modifications[282] following a similar procedure as described for the aldehyde **195b**.




Reaction time : 30 min

Yield : 62%

Mp : 70-72 °C [literature : 74 °C][282]

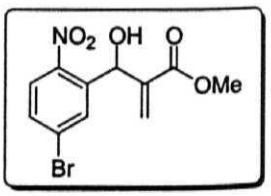
IR (NEAT) : ν 1697, 1599 $cm^{-1}$

$^1H$ NMR : δ 7.70-8.15 (m, 3H), 10.40 (s, 1H)

$^{13}C$ NMR : δ 126.12, 129.45, 132.55, 136.51, 148.04, 186.77.

**Methyl 3-(5-bromo-2-nitrophenyl)-3-hydroxy-2-methylenepropanoate (126z):**

This molecule was obtained as a brown viscous liquid *via* the reaction between 5-bromo-2-nitrobenzaldehyde and methyl acrylate catalyzed by DABCO following a similar procedure described for the molecule **126a**. The crude product was purified by column chromatography (10% EtOAc in hexanes, silica gel).




Reaction time : 4 days

Yield : 66%

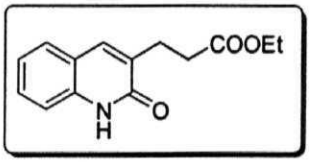
IR (neat) : ν 3468, 1716, 1631 $cm^{-1}$

$^1$H NMR : δ 2.85 (b, 1H), 3.76 (s, 3H), 5.69 (s, 1H), 6.22 (s, 1H), 6.36 (s, 1H), 7.60 (dd, 1H, $J$ = 7.8 Hz & 2.0 Hz), 7.85 (d, 1H, $J$ = 7.8 Hz), 7.93 (d, 1H, $J$ = 2.0 Hz).

$^{13}$C NMR : δ 52.28, 67.10, 126.12, 126.63, 128.57, 131.77, 132.09, 138.39, 140.65, 146.71, 166.24.

**Ethyl 3-(1,2-dihydro-2-oxo-3-quinolinyl)propanoate (257):**

A solution of methyl 3-hydroxy-2-methylene-3-(2-nitrophenyl)propanoate (**126o**) (1 mmol, 0.237 g) in triethyl orthoacetate (1 mL) was heated at 145 °C in the presence of catalytic amount of propanoic acid (2-3 drops) for 12 hours. Excess orthoacetate was distilled off under reduced pressure. The residue, thus obtained, was diluted with acetic acid (5 mL) and the resulting solution was heated at 110 °C for 1 hour in the presence of Fe powder (electrolytic, 6 mmol, 0.335 g). Then the reaction mixture was cooled to room temperature and diluted with ethyl acetate (10 mL). Reaction mixture was filtered and precipitate was washed twice with ethyl acetate (10 mL). Filtrate and washings were combined and dried over $Na_2SO_4$ (anhydrous). Solvent was evaporated and the residue thus obtained was purified by column chromatography (30% EtOAc in hexanes) to provide the **257** as colorless solid.




Yield : 69% (0.170 g)

Mp : 128-130 °C

IR (KBr) : ν 3200-2800 (multiple bands), 1730, 1657, 1620 $cm^{-1}$

$^1H$ NMR : δ 1.23 (t, 3H, $J$ = 6.8 Hz), 2.77 (t, 2H, $J$ = 7.0 Hz), 3.01 (t, 2H, $J$ = 7.0 Hz), 4.13 (q, 2H, $J$ = 6.8 Hz), 7.14-7.56 (m, 4H), 7.69 (s, 1H), 11.81 (b, 1H)

$^{13}C$ NMR : δ 14.22, 26.25, 32.90, 60.36, 115.81, 120.08, 122.41, 127.16, 129.64, 131.96, 137.69, 137.84, 164.23, 173.06.

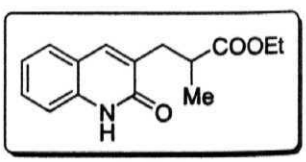
MS (m/z) : 245 ($M^+$)

Analysis calcd. for $C_{14}H_{15}NO_3$ : C, 68.56; H, 6.16; N, 5.71

Found : C, 68.62; H, 6.20; N, 5.68

**Ethyl 3-(1,2-dihydro-2-oxo-3-quinolinyl)-2-methylpropanoate (258):**

This molecule was obtained as colorless solid *via* the Johnson-Claisen rearrangement of methyl 3-hydroxy-2-methylene-3-(2-nitrophenyl)propanoate (**126o**) with triethyl orthopropanoate and subsequent reductive cyclization using Fe / AcOH following similar procedure described for **257**.




Reaction time : 13 h

Yield : 70%

Mp : 126-128 °C

IR (KBr) : ν 3180-2850 (multiple bands), 1732, 1653, 1610 $cm^{-1}$

$^1$H NMR : δ 1.16 (t, 3H, $J$ = 6.8 Hz), 1.27 (d, 3H, $J$ = 6.8 Hz), 2.74-3.20 (m, 3H), 4.08 (q, 2H, $J$ = 6.8 Hz), 7.14-7.25 (m, 1H), 7.32-7.56 (m, 3H), 7.64 (s, 1H), 11.82 (b, 1H)

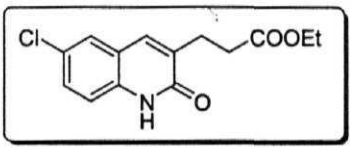
$^{13}$C NMR : 14.15, 17.37, 34.81, 38.48, 60.19, 115.76, 120.03, 122.36, 127.11, 129.64, 131.09, 137.91, 138.37, 164.35, 176.19.

Analysis calcd. for $C_{15}H_{17}NO_3$ : C, 69.48; H, 6.61; N, 5.40

Found : C, 69.63; H, 6.63; N, 5.41

**Ethyl 3-(7-chloro-1,2-dihydro-2-oxo-3-quinolinyl)propanoate (259):**

This compound was obtained from methyl 3-(5-chloro-2-nitrophenyl)-3-hydroxy-2-methylenepropanoate (**126q**) *via* the one-pot Johnson-Claisen rearrangement / reductive cyclization strategy, following similar procedure described for **257** as a colorless solid.




Reaction time : 13 h

Yield : 62%

Mp : 152-154 °C

IR (KBr) : ν 3190-2850 (multiple bands), 1728, 1655, 1614 cm$^{-1}$

$^1$H NMR : δ 1.23 (t, 3H, $J$ = 7.8 Hz), 2.76 (t, 2H, $J$ = 8.0 Hz), 3.00 (t, 2H, $J$ = 8.0 Hz), 4.13 (q, 2H, $J$ = 7.8 Hz), 7.28-7.54 (m, 3H), 7.62 (s, 1H), 12.15 (b, 1H)

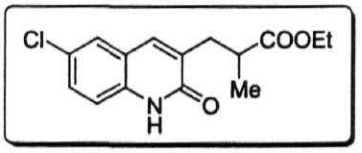
$^{13}$C NMR : δ 14.32, 26.32, 32.83, 60.55, 117.19, 121.15, 126.48, 127.91, 130.00, 133.57, 136.31, 136.70, 164.03, 172.91.

Analysis calcd. for $C_{14}H_{14}ClNO_3$ : C, 60.11; H, 5.04; N, 5.01

Found : C, 60.00; H, 5.00; N, 5.04

**Ethyl 3-(7-chloro-1,2-dihydro-2-oxo-3-quinolinyl)-2-methylpropanoate (260):**

This was obtained *via* the treatment of methyl 3-(5-chloro-2-nitrophenyl)-3-hydroxy-2-methylenepropanoate (**126q**) with triethyl orthopropanoate in the presence of propanoic acid (cat.) and subsequent treatment with Fe / AcOH, following similar procedure described for **257**, as colorless solid.




Reaction time : 13 h

Yield : 68%

Mp : 158-160 °C

IR (KBr) : ν 3200-2850 (multiple bands), 1720, 1658, 1620 cm$^{-1}$

$^1$H NMR : δ 1.17 (t, 3H, $J$ = 6.8 Hz), 1.26 (d, 3H, $J$ = 6.8 Hz), 2.72-3.18 (m, 3H), 4.09 (q, 2H, $J$ = 6.8 Hz), 7.29-7.54 (m, 3H), 7.57 (s, 1H), 12.37 (b, 1H)

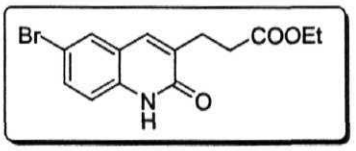
$^{13}$C NMR : δ 14.22, 17.50, 34.74, 38.40, 60.33, 117.22, 120.93, 126.26, 127.67, 129.88, 132.47, 136.28, 137.25, 164.18, 176.02.

Analysis calcd. for $C_{15}H_{16}ClNO_3$ : C, 61.33; H, 5.49; N, 4.77

Found : C, 61.50; H, 5.46; N, 4.76

**Ethyl 3-(7-bromo-1,2-dihydro-2-oxo-3-quinolinyl)propanoate (261):**

This product was prepared *via* the Johnson-Claisen rearrangement of methyl 3-(5-bromo-2-nitrophenyl)-3-hydroxy-2-methylenepropanoate (**126z**) with triethyl orthoacetate and subsequent treatment with Fe / AcOH, following similar procedure described for **257**, as colorless solid.




Reaction time : 13 h

Yield : 59%

Mp : 168-170 °C

IR (KBr) : ν 3200-2850 (multiple bands), 1726, 1653, 1616 $cm^{-1}$

$^1H$ NMR : δ 1.24 (t, 3H, *J* = 7.8 Hz), 2.75 (t, 2H, *J* = 6.8 Hz), 3.00 (t, 2H, *J* = 6.8 Hz), 4.14 (q, 2H, *J* = 7.8 Hz), 7.23 (d, 1H, *J* = 6.8 Hz), 7.49-7.73 (m, 3H), 11.64 (b, 1H).

$^{13}C$ NMR : δ 14.34, 26.30, 32.78, 60.58, 115.20, 117.36, 121.61, 129.61, 132.69, 133.52, 136.62, 163.89, 172.94.

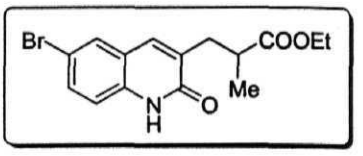
Analysis calcd. for $C_{14}H_{14}BrNO_3$ : C, 51.87; H, 4.35; N, 4.32

Found : C, 51.94; H, 4.36; N, 4.35

**Ethyl 3-(7-bromo-1,2-dihydro-2-oxo-2-methyl-3-quinolinyl)propanoate (262):**

This molecule was obtained as colorless solid *via* the Johnson-Claisen rearrangement of methyl 3-(5-bromo-2-nitrophenyl)-3-hydroxy-2-methylenepropanoate (**126z**) with

triethyl orthopropanoate and subsequent reductive cyclization using Fe / AcOH following similar procedure described for **257**.




Reaction time : 13 h

Yield : 62%

Mp : 128-130 °C

IR (KBr) : ν 3200-2700 (multiple bands), 1728, 1657, 1616 $cm^{-1}$

$^1H$ NMR : δ 1.17 (t, 3H, *J* = 6.8 Hz), 1.27 (d, 3H, *J* = 6.8 Hz), 2.72-3.19 (m, 3H), 4.09 (q, 2H, *J* = 6.8 Hz), 7.27 (d, 1H, *J* = 8.8 Hz), 7.51-7.61 (m, 2H), 7.65 (d, 1H, *J* = 2.0 Hz), 12.23 (b, 1H)

$^{13}C$ NMR : δ 14.27, 17.54, 34.79, 38.50, 60.38, 115.13, 117.46, 121.53, 129.47, 132.64, 136.70, 137.23, 164.18, 176.04.

Analysis calcd. for $C_{15}H_{16}BrNO_3$ : C, 53.27; H, 4.77; N, 4.14

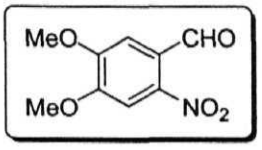
Found : C, 53.08; H, 4.72; N, 4.12

**4,5-Dimethoxy-2-nitrobenzaldehyde (195d):**

This was prepared according to the literature procedure with slight modification[282].

To 3,4-dimethoxybenzaldehyde (30 mmol, 4.98 g), was added conc. $HNO_3$ (30 mL) while the reaction mixture was stirring at room temperature. After heating the reaction mixture at 40 °C for 30 min, it was poured into ice-cold water. The yellow precipitate thus formed was filtered. The precipitate was washed with aqueous $NaHSO_4$ solution and filtered to remove any insoluble impurities. The filtrate was treated with aqueous

KOH solution to generate the aldehyde as yellow solid. The crude solid on crystallization from methanol at 0 °C provided the pure **195d** as yellow crystalline solid in 3.16 g.




Reaction time : 30 min

Yield : 49.92%

Mp : 125-127 °C [literature : 128 °C][308]

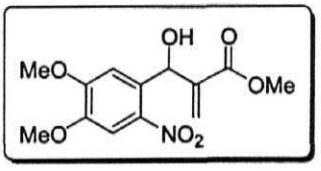
IR (NEAT) : ν 1687, 1604 $cm^{-1}$

$^1H$ NMR : δ 4.03 (s, 3H), 4.04 (s, 3H), 7.42 (s, 1H), 7.62 (s, 1H), 10.45 (s, 1H).

$^{13}C$ NMR : δ 56.72, 107.22, 109.78, 125.53, 143.86, 150.42, 153.24, 187.60.

**Methyl 3-(3,4-dimethoxyphenyl)-3-hydroxy-2-methylenepropanoate (263):**

This compound was prepared DABCO-catalyzed Baylis-Hillman coupling of 3,4-dimethoxy-2-nitrobenzaldehyde with methyl acrylate, following a similar procedure described for the molecule **126a**, as a brown viscous liquid. The crude product was purified by column chromatography (10% EtOAc in hexanes, silica gel).




Reaction time : 14 days

Yield : 65%

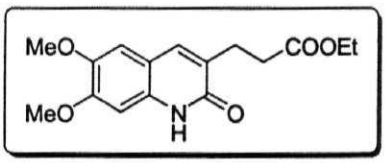
IR (neat) : ν 3504, 1726, 1625 $cm^{-1}$

$^1$H NMR : δ 3.72 (s, 3H), 3.90 (s, 3H), 3.92 (s, 3H), 4.02 (b, 1H), 5.50 (s, 1H), 6.22 (s, 1H), 6.26 (s, 1H), 7.21 (s, 1H), 7.56 (s, 1H).

$^{13}$C NMR : δ 52.09, 56.23, 56.31, 67.42, 107.78, 109.89, 125.59, 131.48, 139.95, 141.52, 147.88, 153.29, 166.63.

**Ethyl 3-(7,8-dimehtoxy-1,2-dihydro-2-oxo-3-quinolinyl)propanoate (264):**

This molecule was prepared *via* the treatment of methyl 3-(3,4-dimethoxy-2-nitrophenyl)-3-hydroxy-2-methylenepropanoate (**263**) with triethyl orthoacetate and subsequent reductive cyclization using Fe / AcOH, following similar procedure described for **257**, as colorless solid.




Reaction time : 13 h

Yield : 64%

Mp : 154-156 °C.

IR (KBr) : ν 3200-2800 (multiple bands), 1736, 1662, 1620 cm$^{-1}$

$^1$H NMR : δ 1.21 (t, 3H, $J$ = 6.8 Hz), 2.76 (t, 2H, $J$ = 6.8 Hz), 2.98 (t, 2H, $J$ = 6.8 Hz), 3.92 (s, 3H), 3.99 (s, 3H), 4.11 (q, 2H, $J$ = 6.8 Hz), 6.85 (s, 1H), 6.90 (s, 1H), 7.62 (s, 1H), 12.14 (b, 1H),

$^{13}$C NMR : δ 14.12, 26.35, 32.95, 56.06, 60.21, 97.98, 107.54, 113.46, 128.64, 133.54, 137.40, 145.72, 151.90, 164.11, 173.03.

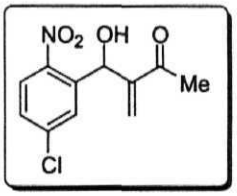
MS (m/z) : 306 $(M+1)^+$

Analysis calcd. for $C_{16}H_{19}NO_5$ : C, 62.94; H, 6.27; N, 4.59

Found : C, 62.82; H, 6.32; N, 4.62

**4-(5-Chloro-2-nitrophenyl)-4-hydroxy-3-methylenebutan-2-one (233c):**

This molecule was obtained as a light yellow solid *via* the Baylis-Hillman coupling between 5-chloro-2-nitrobenzaldehyde (**195b**) and methyl vinyl ketone under the catalytic influence of DABCO following a similar procedure described for the molecule **233a.**




Reaction time : 7 days

Yield : 58%

Mp : 68-70 °C

IR (KBr) : ν 3360, 1666, 1602 $cm^{-1}$

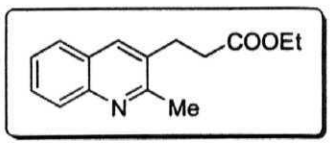
$^1H$ NMR : δ 2.38 (s, 3H), 3.53 (b, 1H), 5.77 (s, 1H), 6.17 (s, 1H), 6.24 (s, 1H), 7.42 (dd, 1H, $J$ = 8.8 Hz & 2.0 Hz), 7.79 (d, 1H, $J$ = 2.0 Hz), 7.96 (d, 1H, $J$ = 8.8 Hz).

$^{13}C$ NMR : δ 25.89, 66.88, 126.23, 126.57, 128.59, 129.09, 138.93, 140.21, 146.03, 148.74, 199.63.

**Ethyl 3-(2-methyl-3-quinolinyl)propanoate (265):**

This molecule was obtained as brown liquid *via* the Johnson-Claisen rearrangement of 4-hydroxy-3-methylene-4-(2-nitrophenyl)butan-2-one (**233a**) with triethyl orthoacetate

and subsequent reductive cyclization using Fe / AcOH following similar reaction procedure described for **257**.




Reaction time : 13 h

Yield : 79%

IR (neat) : ν 1734, 1620, 1602 $cm^{-1}$

$^1H$ NMR : δ 1.23 (t, 3H, *J* = 6.8 Hz), 2.71 (t, 2H, *J* = 7.8 Hz)*, 2.75 (s, 3H), 3.12 (t, 2H, *J* = 7.8 Hz), 4.15 (q, 2H, *J* = 6.8 Hz), 7.41-7.52 (m, 1H), 7.58-7.69 (m, 1H), 7.72 (d, 1H, *J* = 7.8 Hz), 7.87 (s, 1H), 8.00 (d, 1H, *J* = 8.8 Hz).

** One of the three peaks of this triplet is merged with singlet at δ 2.75.*

$^{13}C$ NMR : δ 14.15, 23.05, 27.76, 33.87, 60.58, 125.78, 126.94, 127.19, 128.20, 128.76, 132.26, 134.51, 146.47, 158.16, 172.40.

MS (m/z) : 243 ($M^+$)

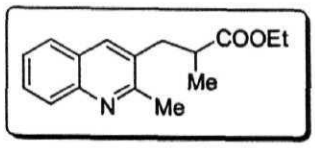
Analysis calcd. for $C_{15}H_{17}NO_2$ : C, 74.05; H, 7.04; N, 5.76

Found : C, 73.74; H, 7.09; N, 5.70

**Ethyl 2-methyl-3-(2-methyl-3-quinolinyl)propanoate (266):**

The Johnson-Claisen rearrangement of 4-hydroxy-3-methylene-4-(2-nitrophenyl)-butan-2-one (**233a**) with triethyl orthopropanoate and subsequent treatment with Fe / AcOH, following similar procedure described for **257**, provided molecule **266** as brown liquid.

Reaction time : 13 h




Yield : 83%

IR (neat) : ν 1732, 1622, 1601 $cm^{-1}$

$^1H$ NMR : δ 1.13 (t, 3H, *J* = 6.8 Hz), 1.25 (d, 3H, *J* = 6.8 Hz), 2.66-2.95 (m, 5H), 3.13-3.31 (m, 1H), 4.07 (q, 2H, *J* = 6.8 Hz), 7.40-7.52 (m, 1H), 7.57-7.68 (m, 1H), 7.71 (d, 1H, *J* = 7.8 Hz), 7.84 (s, 1H), 7.99 (d, 1H, *J* = 7.8 Hz).

$^{13}C$ NMR : δ 14.00, 17.16, 23.17, 36.59, 39.69, 60.33, 125.66, 126.90, 128.20, 128.69, 131.26, 135.55, 146.57, 158.26, 175.51.

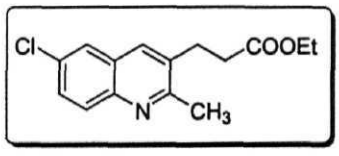
MS (m/z) : 258 $(M+1)^+$

Analysis calcd. for $C_{16}H_{19}NO_2$ : C, 74.68; H, 7.44, N; 5.44

Found : C, 74.88; H, 7.50, N; 5.40

**Ethyl 3-(7-chloro-2-methyl-3-quinolinyl)propanoate (267):**

This compound was prepared *via* the treatment of 4-(5-chloro-2-nitrophen-yl)-4-hydroxy-3-methylenebutan-2-one (**233c**) with triethyl orthoacetate followed by reductive cyclization using Fe / AcOH, following similar procedure described for **257**, as brown liquid.




Reaction time : 13 h

Yield : 73%

IR (neat) : ν 1732, 1595, 1601 $cm^{-1}$

$^1H$ NMR : δ 1.25 (t, 3H, $J$ = 6.8 Hz), 2.65-2.83 (m, 5H), 3.12 (t, 2H, $J$ = 7.8 Hz), 4.16 (q, 2H, $J$ = 6.8 Hz), 7.57 (dd, 1H, $J$ = 8.8 Hz and 2.0 Hz), 7.71 (d, 1H, $J$ = 2.0 Hz), 7.78 (s, 1H), 7.92 (d, 1H, $J$ = 8.8 Hz).

$^{13}C$ NMR : δ 14.15, 23.10, 27.68, 33.67, 60.65, 125.61, 127.74, 129.56, 129.93, 131.33, 133.32, 133.42, 144.85, 158.60, 172.23.

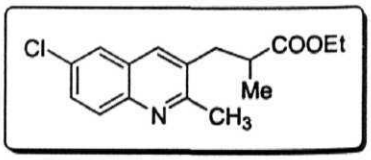
MS (m/z) : 278 $(M+1)^+$, 279 $(M+2)^+$, 281 $(M+4)^+$

Analysis calcd. for $C_{15}H_{16}ClNO_2$ : C, 64.87; H, 5.81; N, 5.04

Found : C, 64.59; H, 5.82; N, 5.12

**Ethyl 2-methyl-3-(7-chloro-2-methyl-3-quinolinyl)propanoate (268):**

This molecule was obtained as brown liquid *via* the Johnson-Claisen rearrangement of 4-(5-chloro-2-nitrophenyl)-4-hydroxy-3-methylenebutan-2-one (**233c**) with triethyl orthopropanoate and subsequent reductive cyclization using Fe / AcOH following similar procedure described for **257**.




Reaction time : 13 h

Yield : 76%

IR (neat) : ν 1730, 1651, 1601 $cm^{-1}$

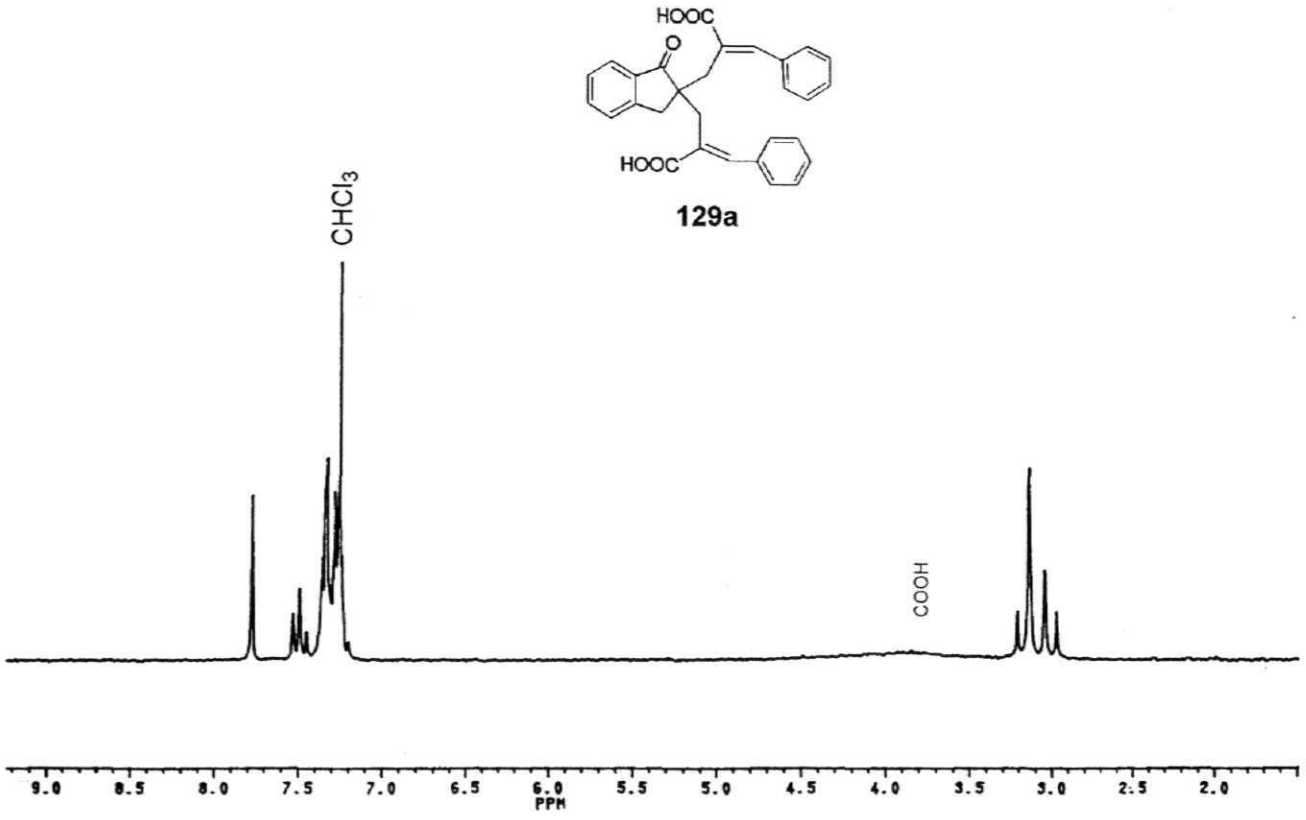
$^{1}$H NMR : δ 1.13 (t, 3H, $J$ = 6.8 Hz), 1.25 (d, 3H, $J$ = 6.8 Hz), 2.70-2.93 (m, 5H), 3.11-3.28 (m, 1H), 4.06 (q, 2H, $J$ = 6.8 Hz), 7.54 (dd, 1H, $J$ = 8.6 Hz & 2.0 Hz) 7.68 (d, 1H, $J$ = 2.0 Hz), 7.73 (s, 1H), 7.90 (d, 1H, $J$ = 8.6 Hz).

$^{13}$C NMR : δ 14.07, 17.30, 23.20, 36.56, 39.62, 60.48, 125.59, 127.62, 129.59, 129.90, 131.31, 132.43, 134.58, 144.89, 158.74, 175.41.

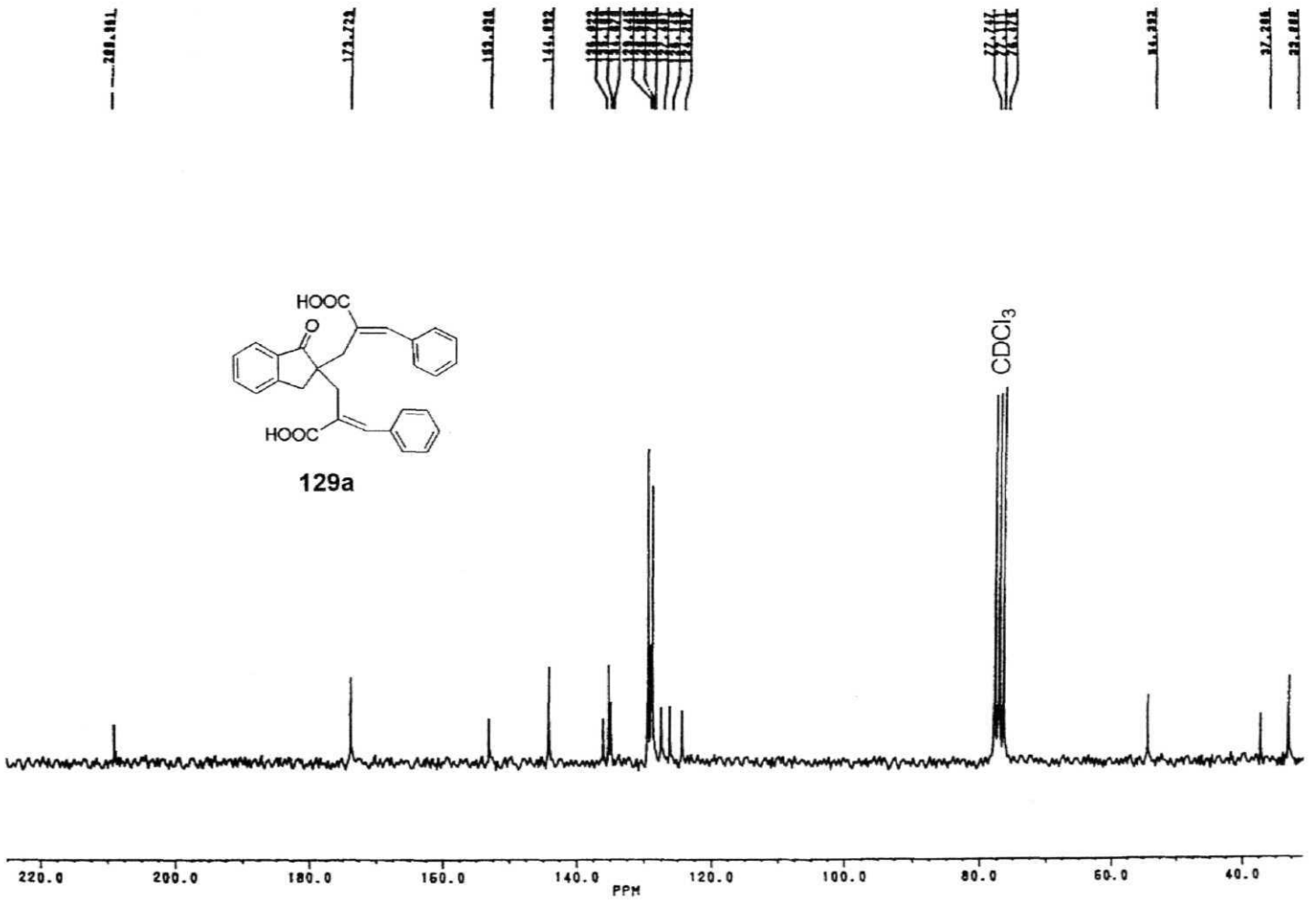
MS (m/z) : 292 $(M+1)^+$, 293 $(M+2)^+$, 295 $(M+4)^+$

Analysis calcd. for $C_{16}H_{18}ClNO_2$ : C, 65.86; H, 6.22, 4.80

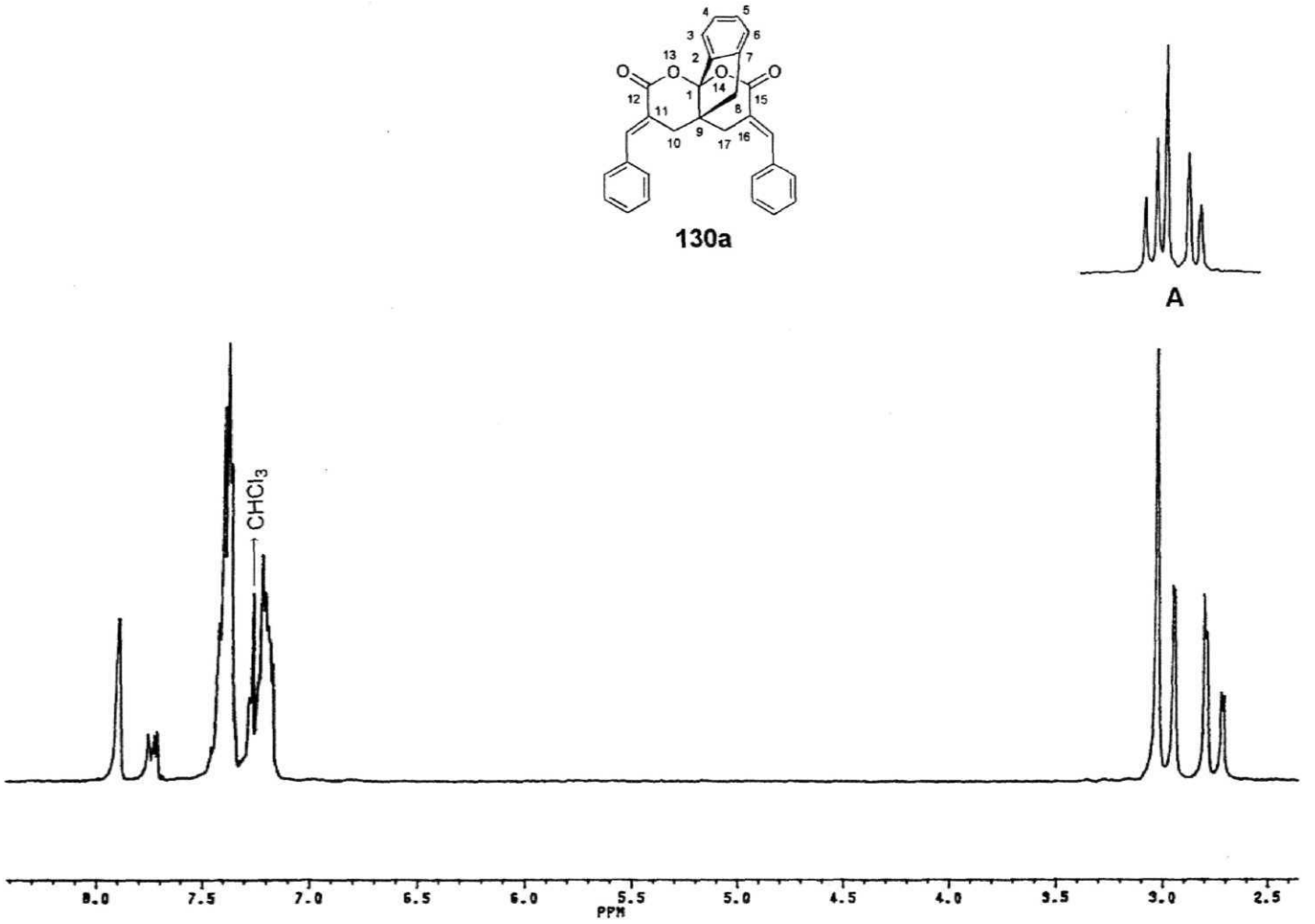
Found : C, 65.60; H, 6.26, 4.75



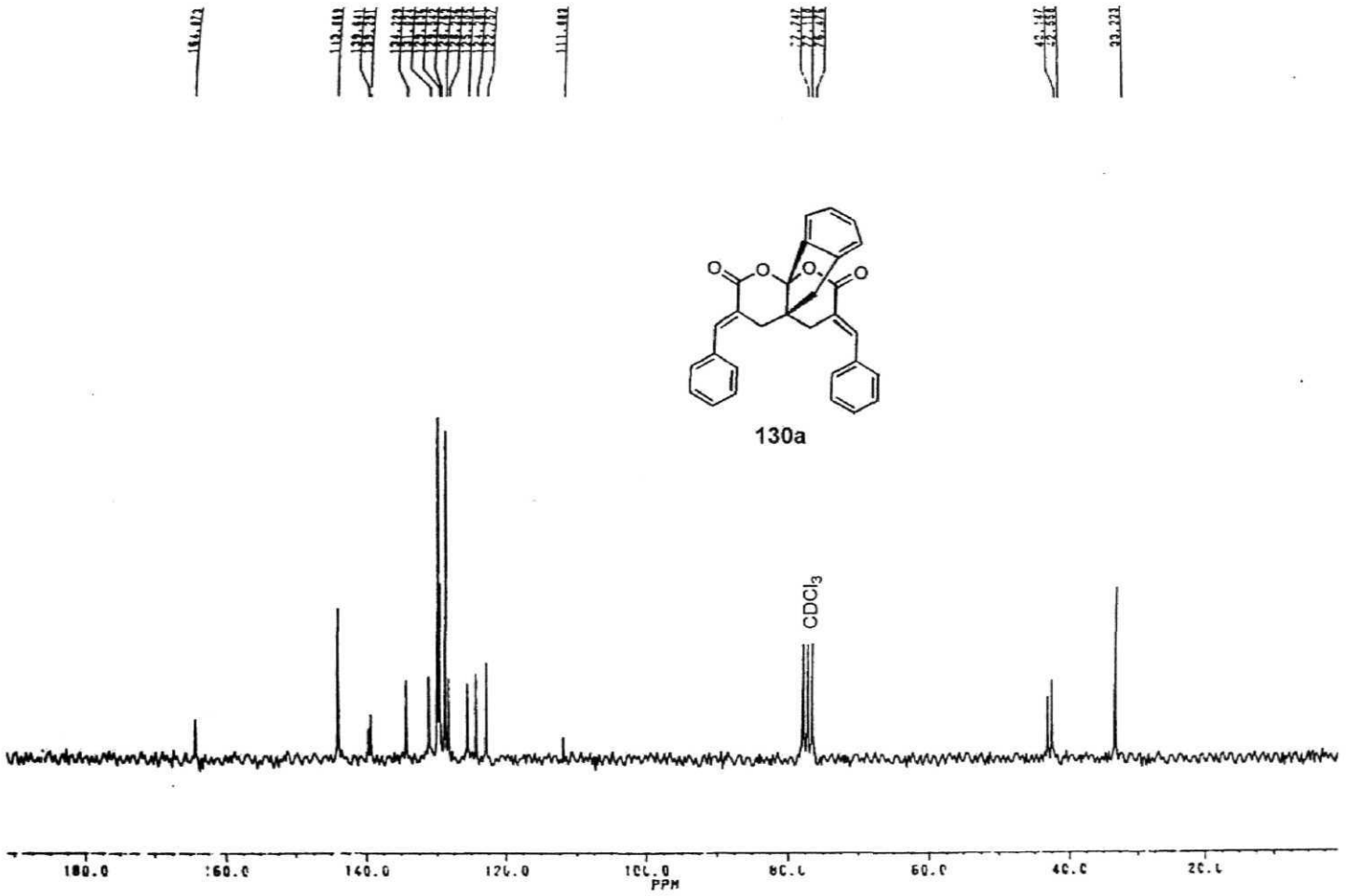

Spectrum 1: $^{1}H$ NMR spectrum of **129a**




Spectrum 2: $^{13}C$ NMR spectrum of **129a**

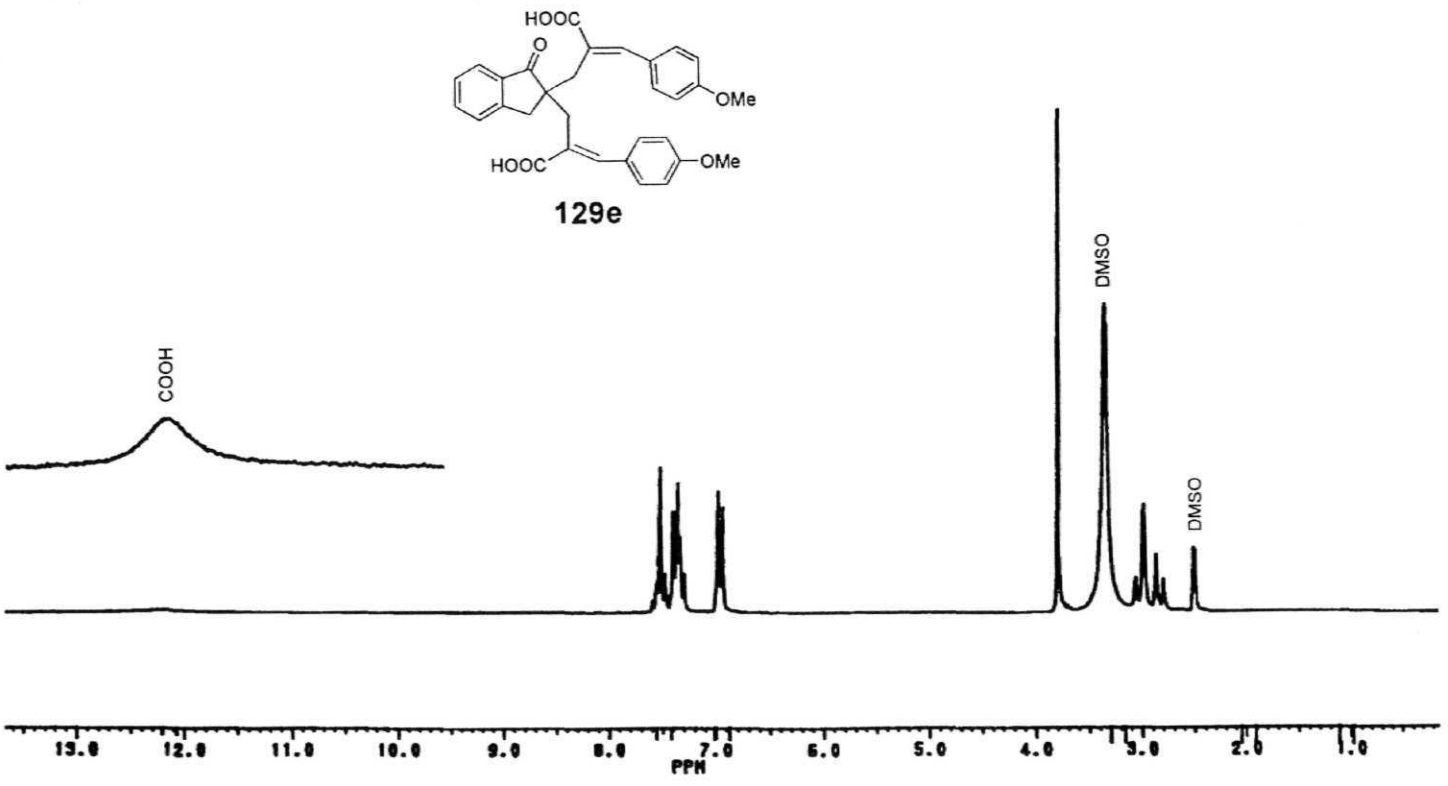



Spectrum 3: $^1$H NMR spectrum of **130a**
**A:** Splitting of the benzylic $CH_2$ singlet (at C-8) from the AB quartet of allylic $CH_2$ protons (C-10 & C-17) in the presence of $Eu(fod)_3$.

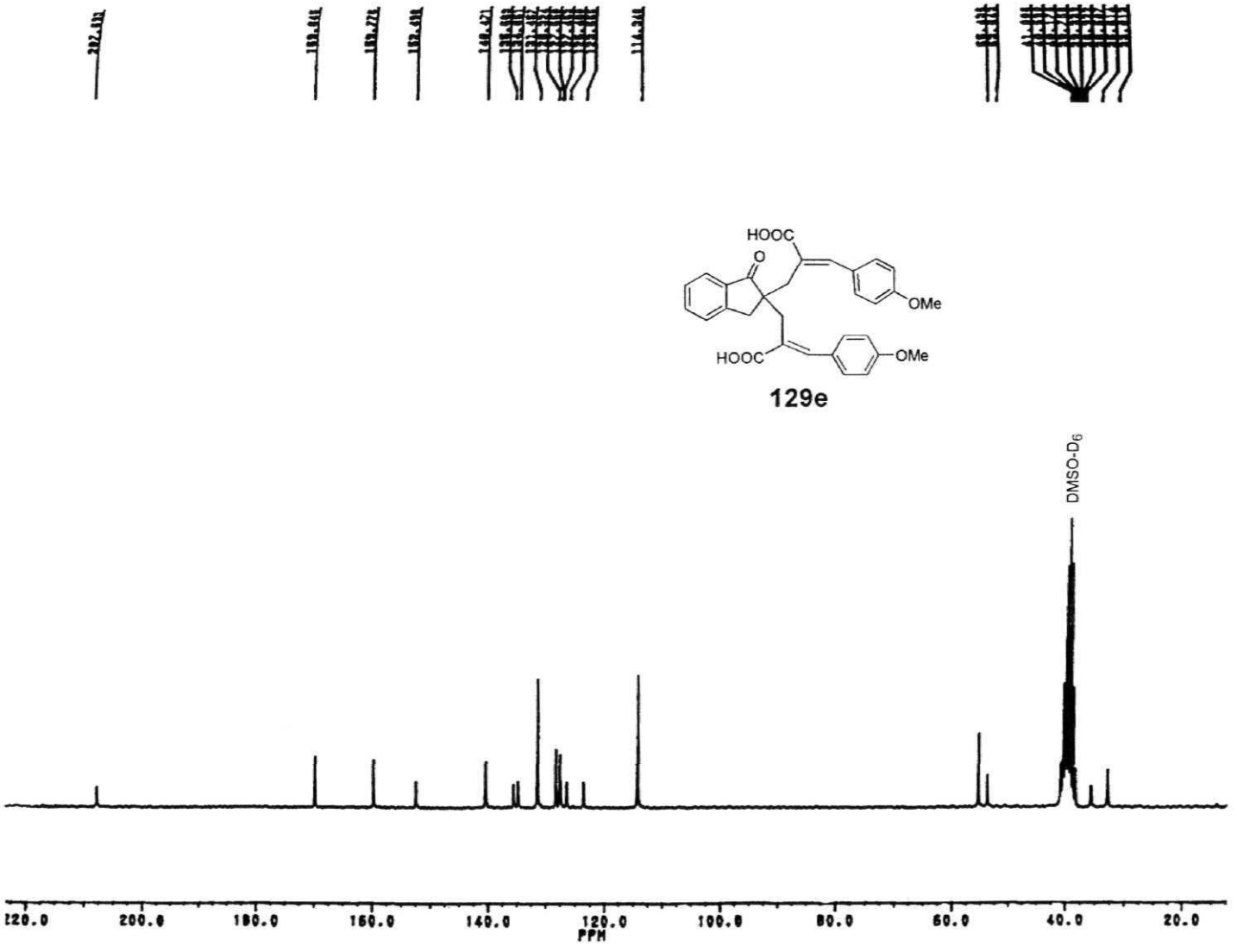



130a

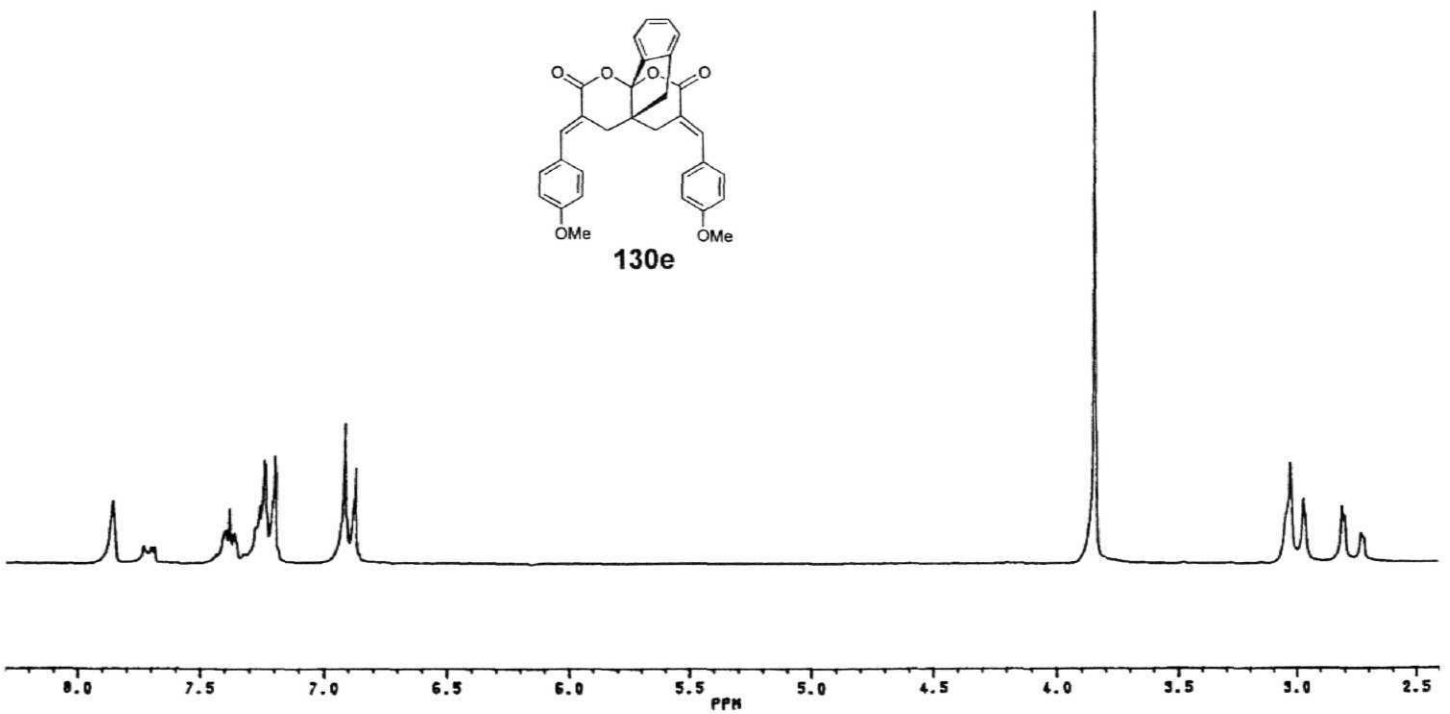
Spectrum 4: $^{13}C$ NMR spectrum of **130a**



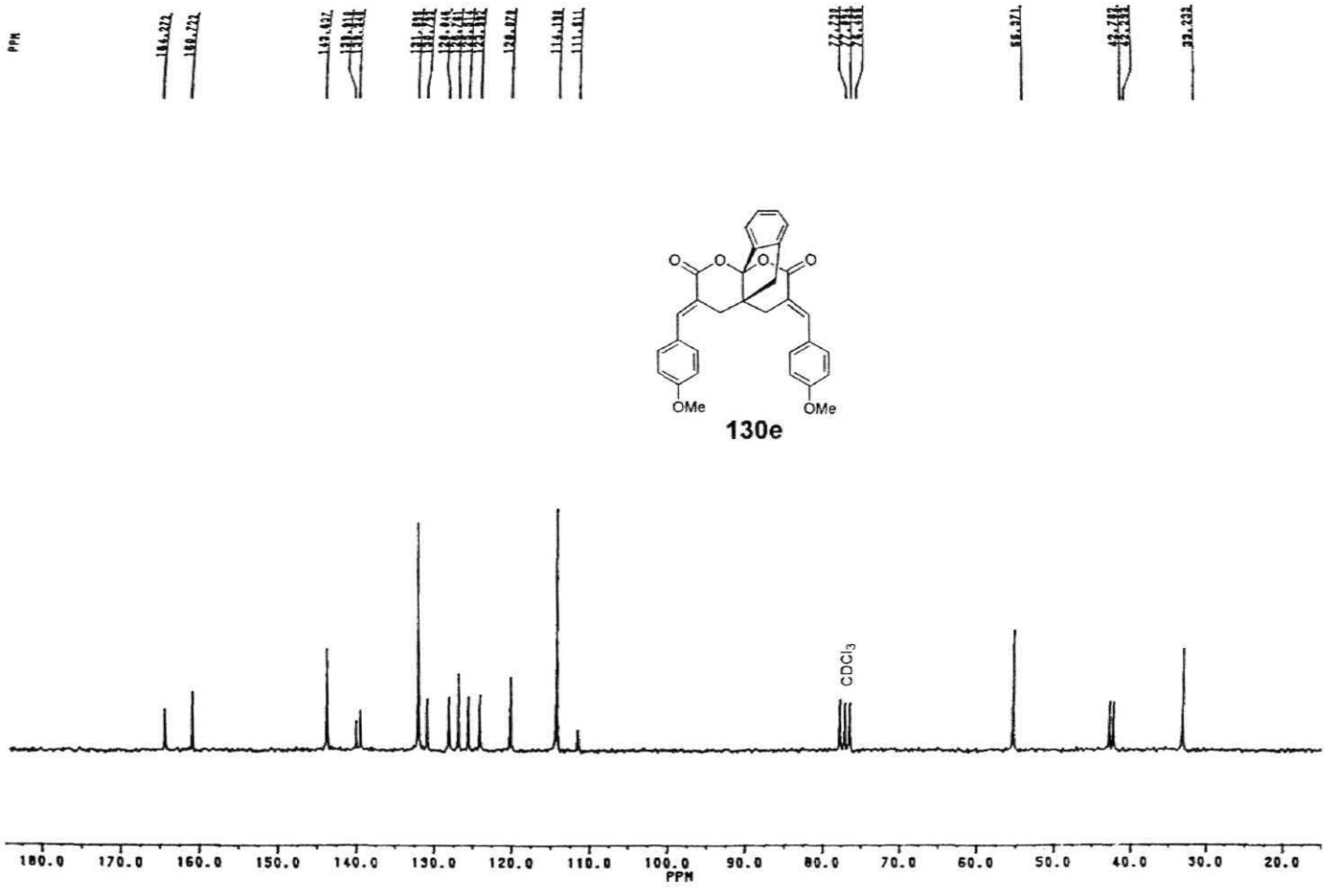

Spectrum 5: $^{1}$H NMR spectrum of **129e**



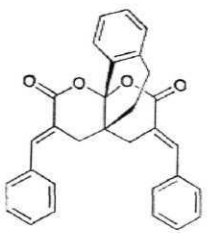

Spectrum 6: $^{13}C$ NMR spectrum of **129e**



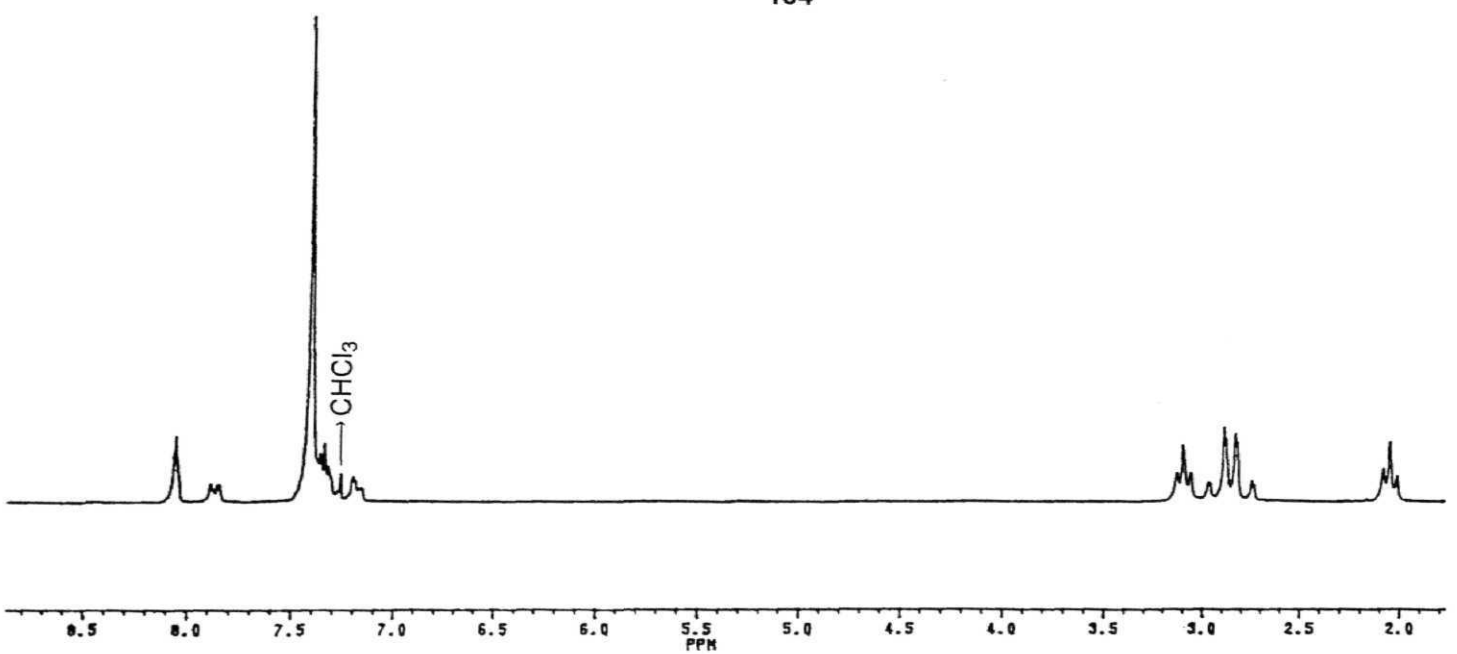

Spectrum 7: $^{1}$H NMR spectrum of **130e**



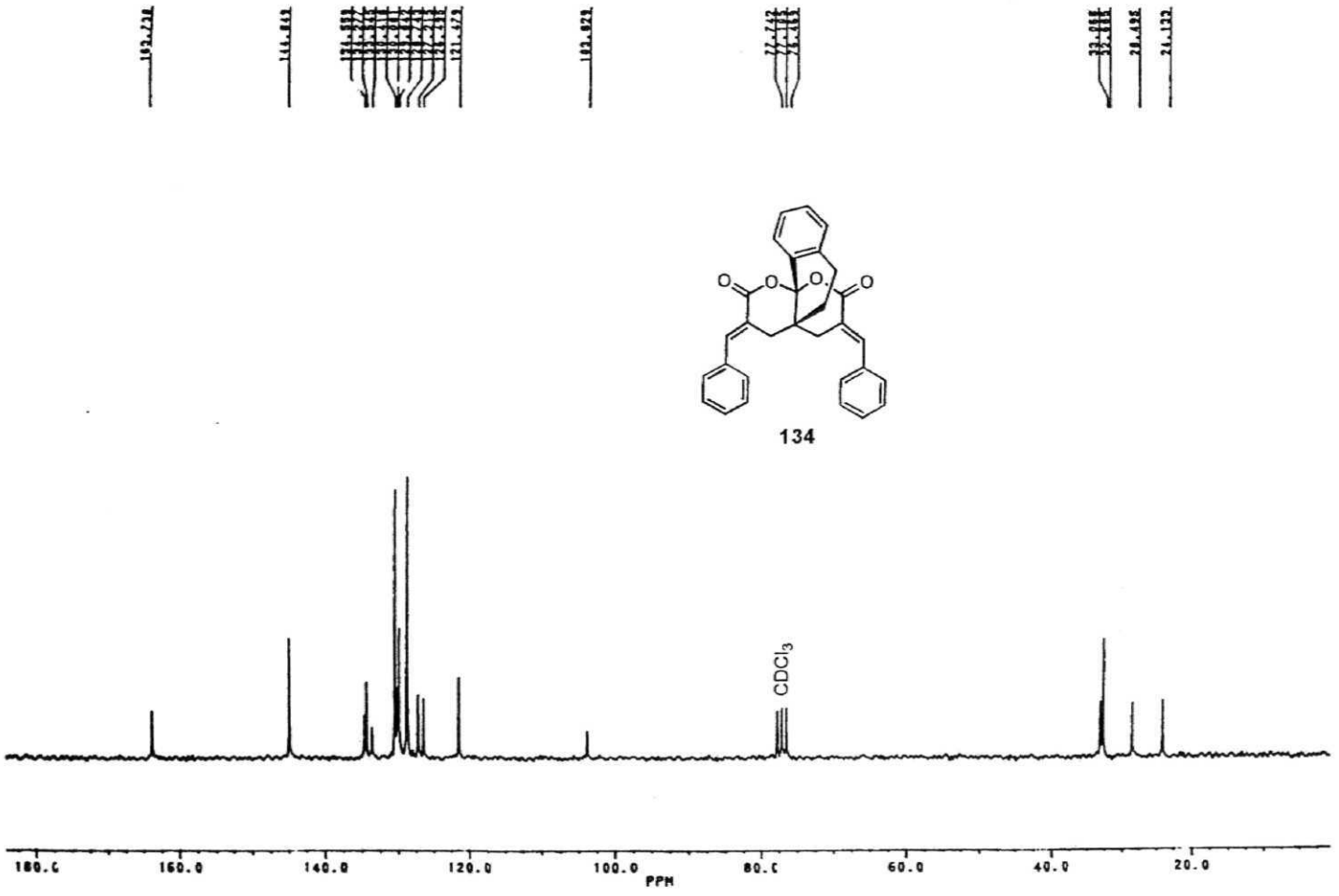

Spectrum 8: $^{13}C$ NMR spectrum of **130e**



**134**

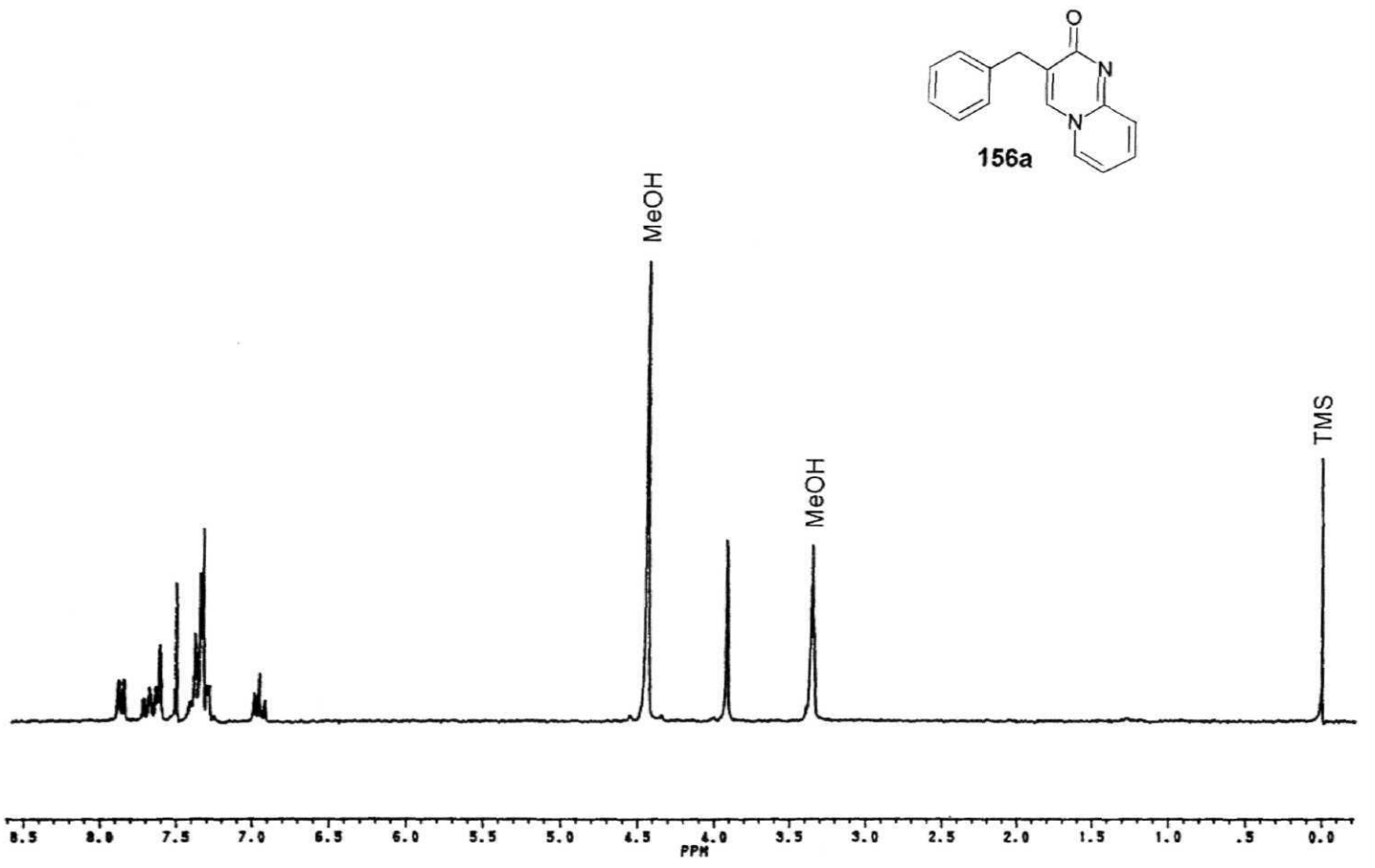



Spectrum 9: $^{1}$H NMR spectrum of **134**

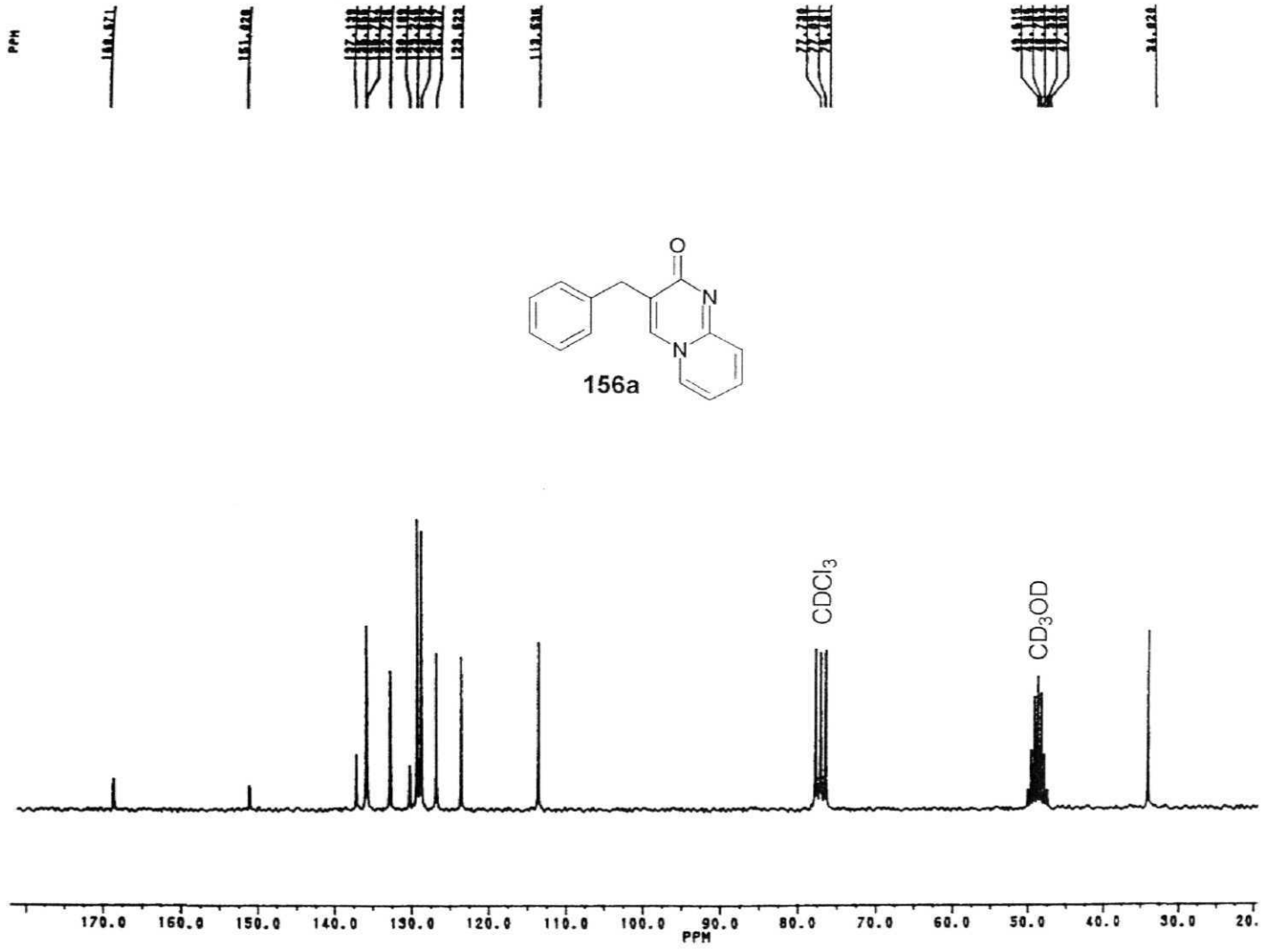



134

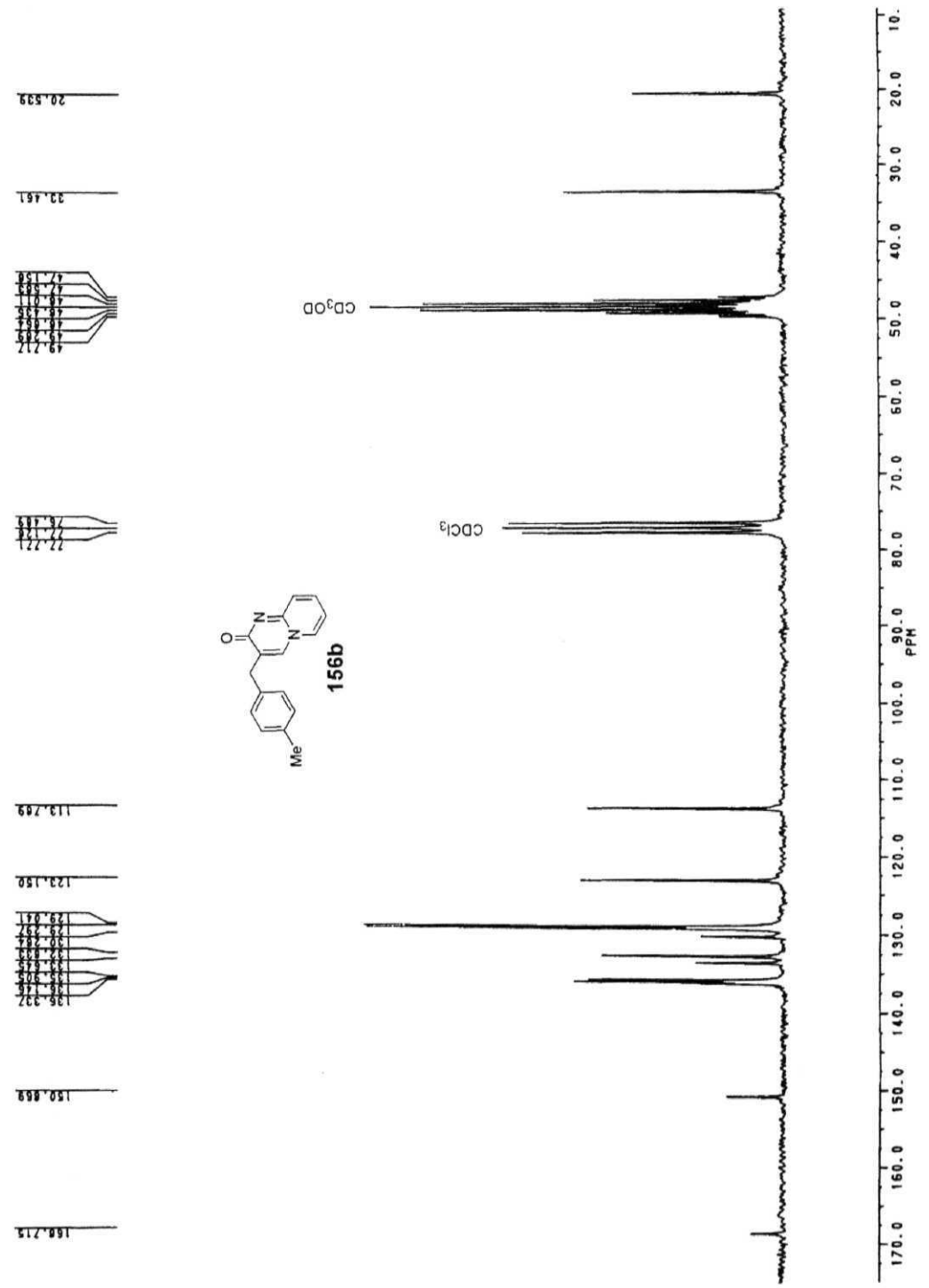
Spectrum 10: $^{13}C$ NMR spectrum of **134**



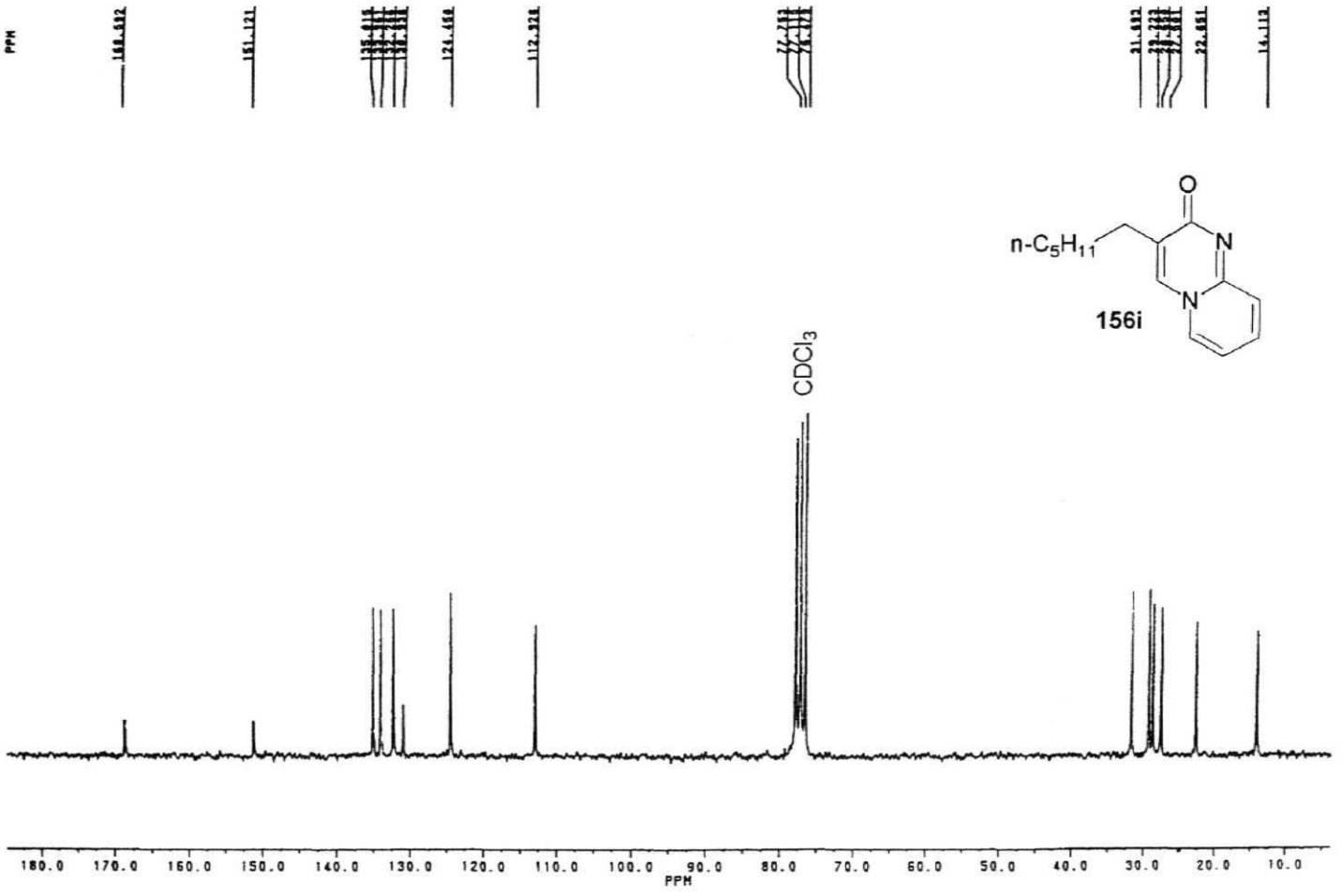

Spectrum 11: $^{1}$H NMR spectrum of **156a**



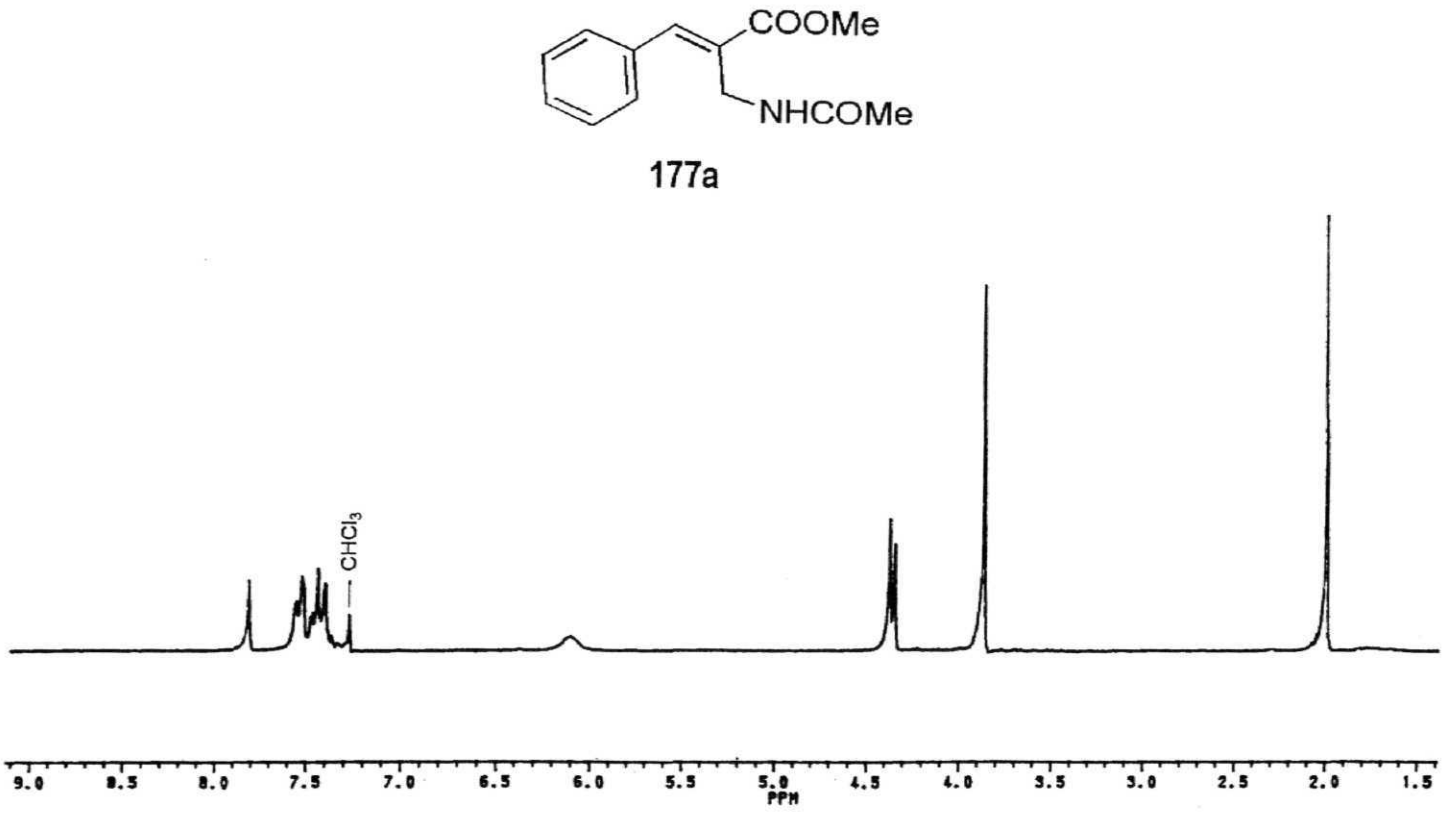

Spectrum 12: $^{13}C$ NMR spectrum of **156a**



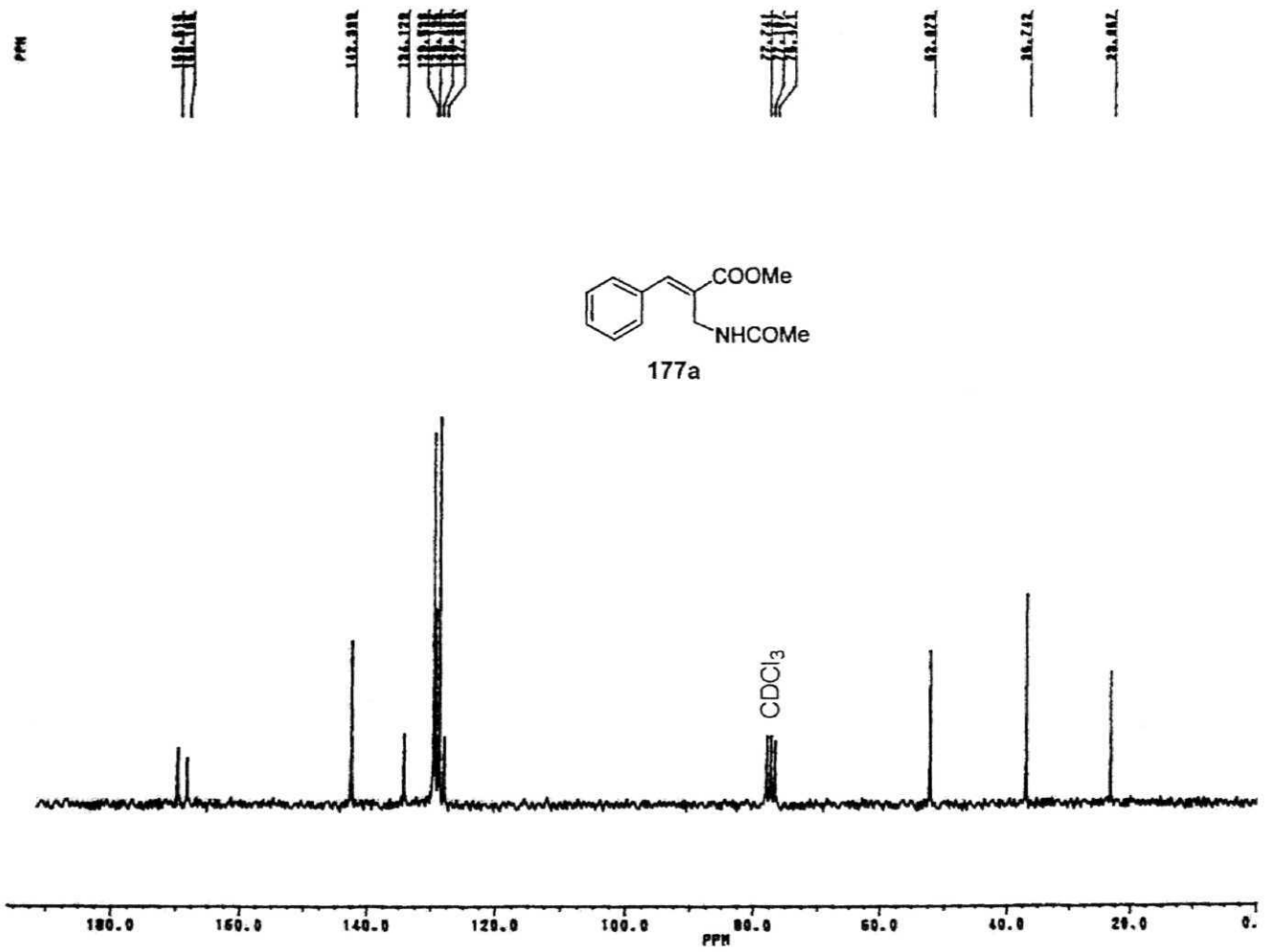

Spectrum 13: $^{13}$CNMR spectrum of **156b**



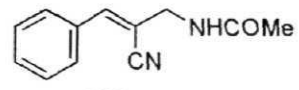

Spectrum 14: $^{13}C$ NMR spectrum of **156i**



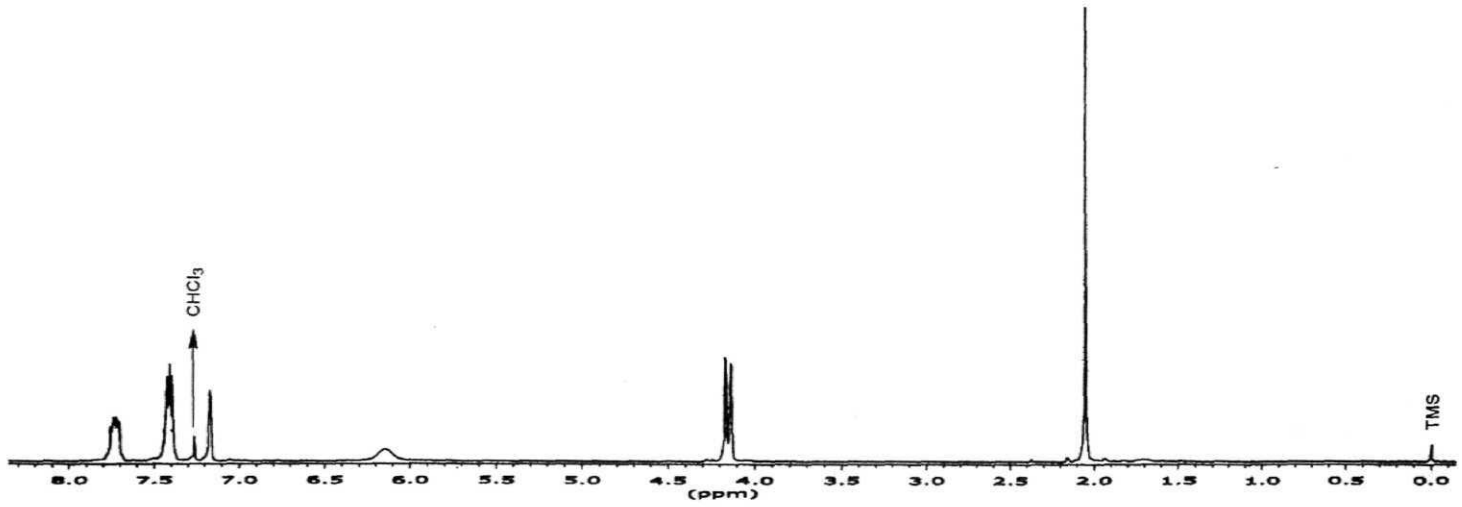

Spectrum 15: $^{1}$H NMR spectrum of **177a**



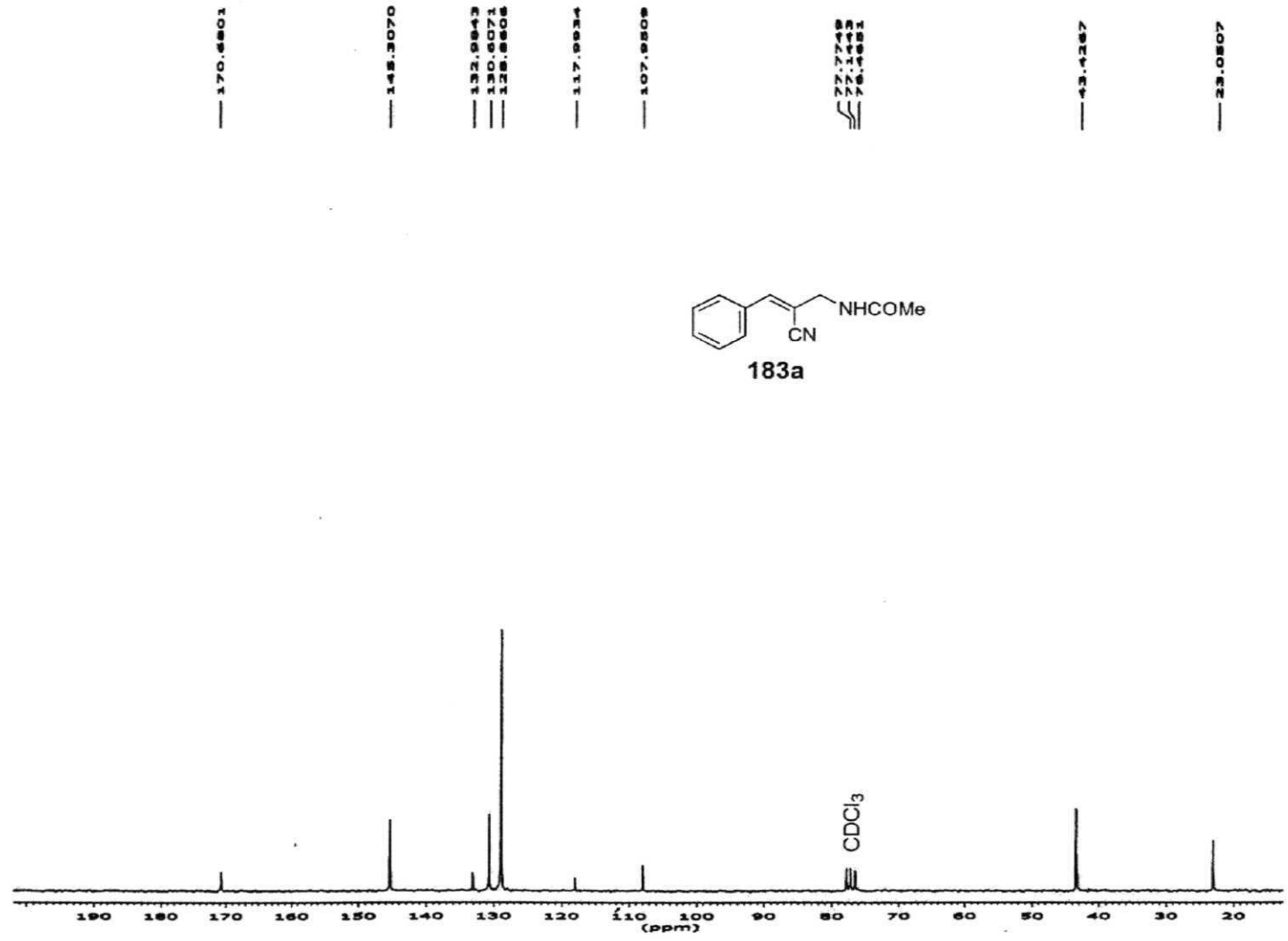

Spectrum 16: $^{13}C$ NMR spectrum of **177a**



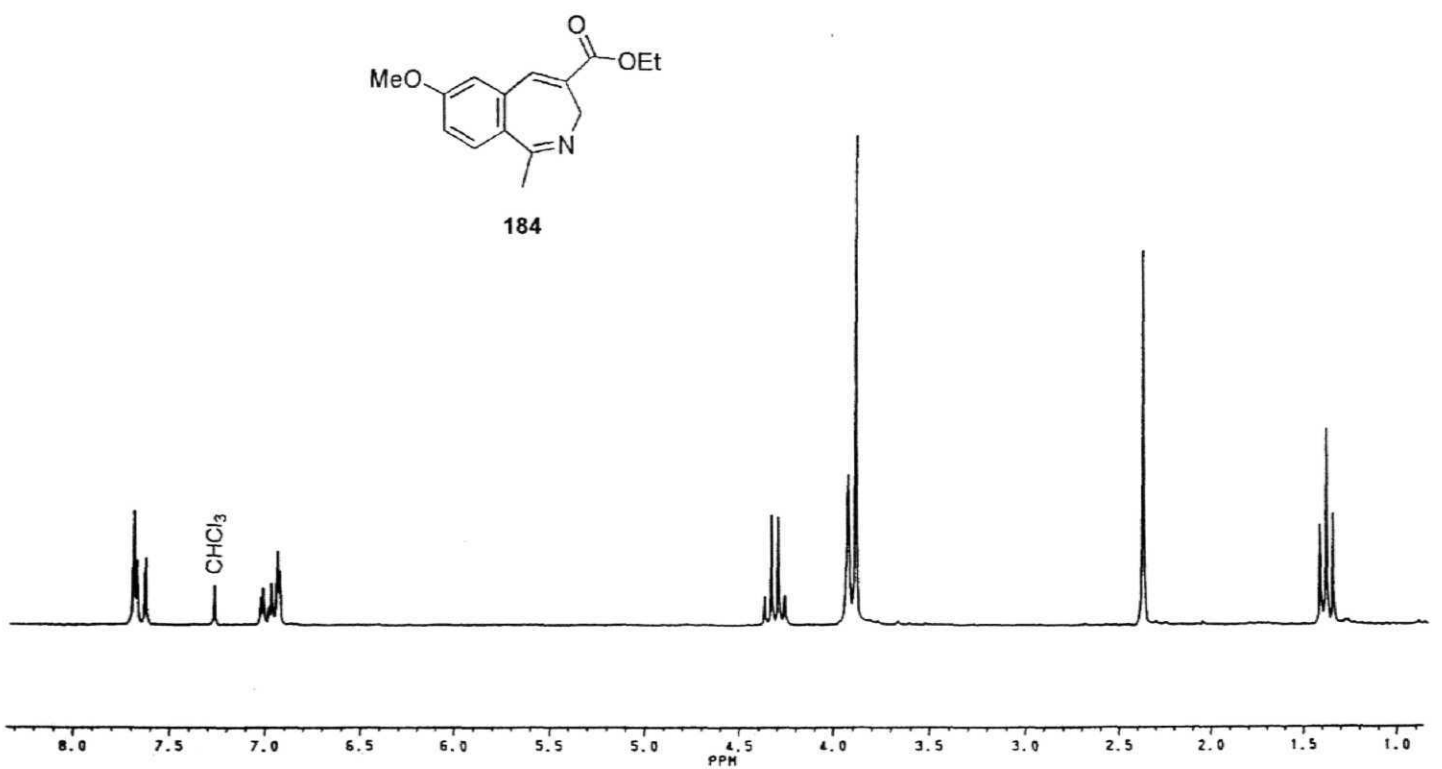

**183a**




Spectrum 17: $^{1}$H NMR spectrum of **183a**

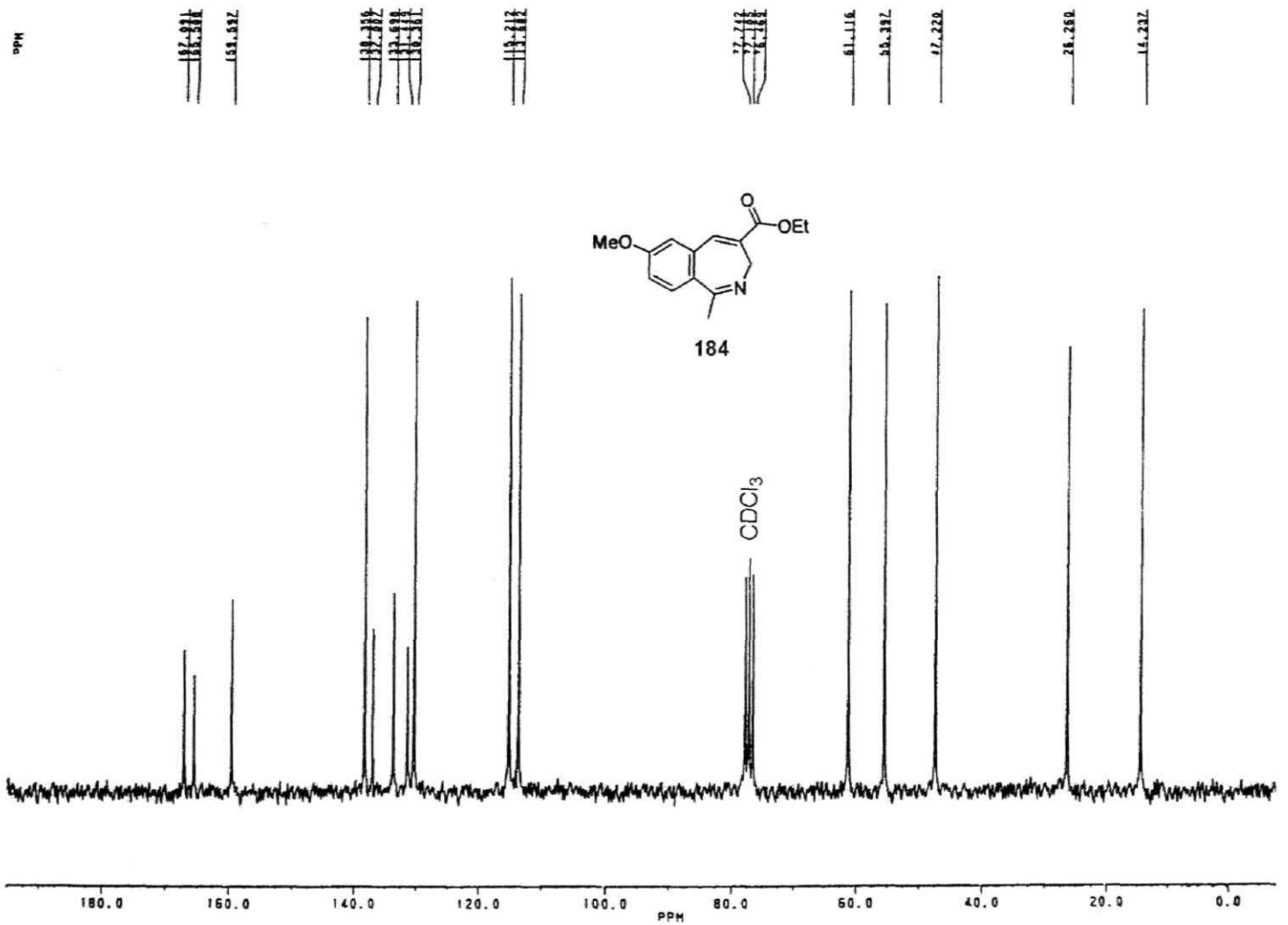



Spectrum 18: $^{13}C$ NMR spectrum of **183a**

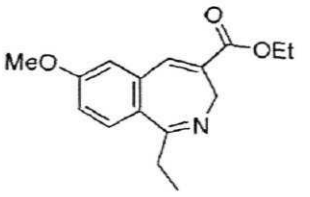



**184**

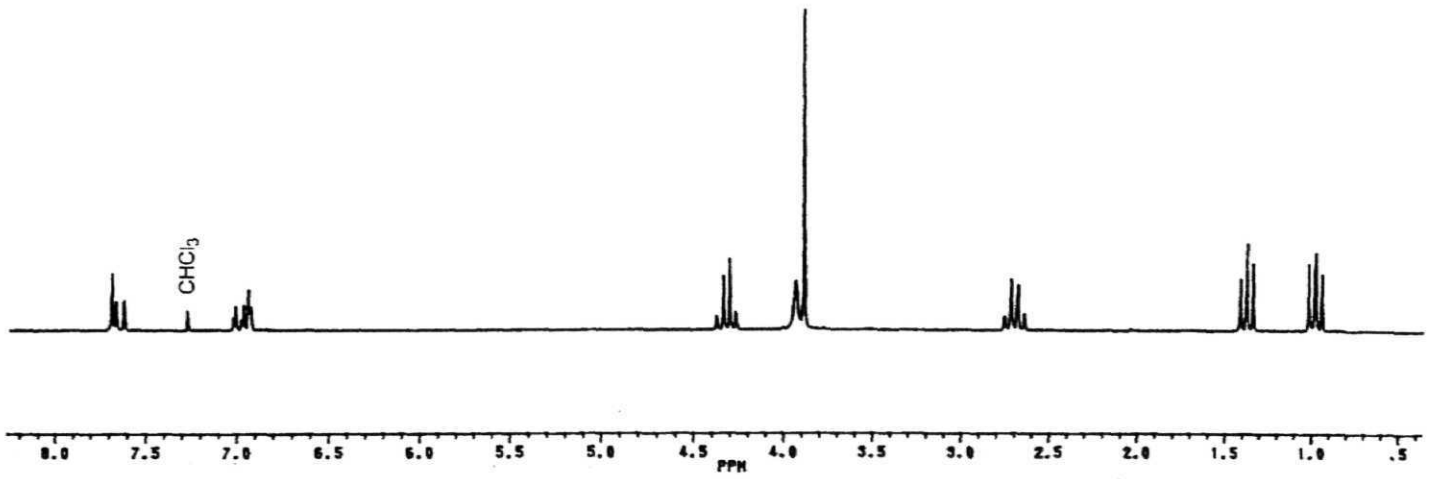
Spectrum 19: $^{1}$H NMR spectrum of **184**



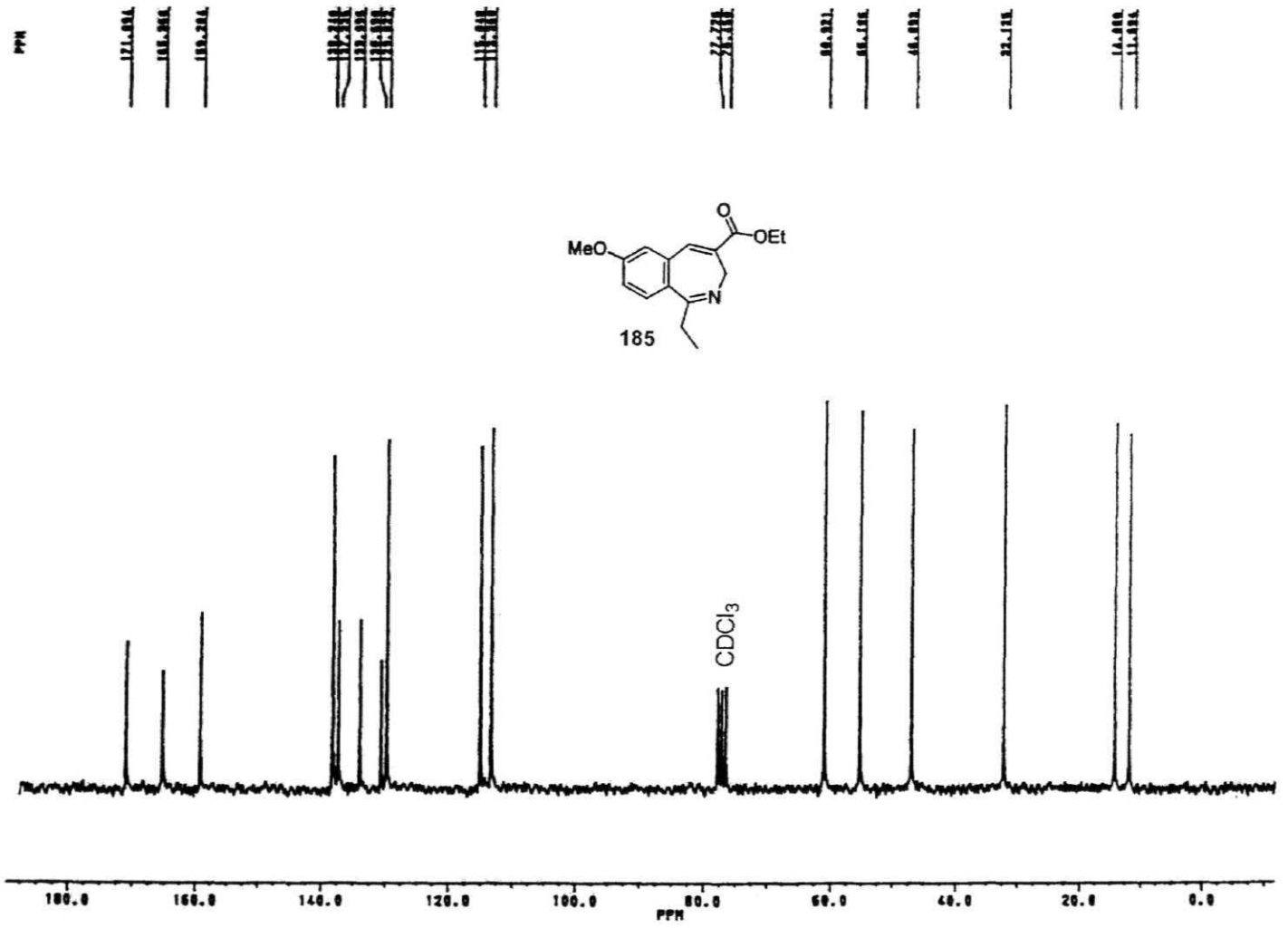

Spectrum 20: $^{13}C$ NMR spectrum of **184**



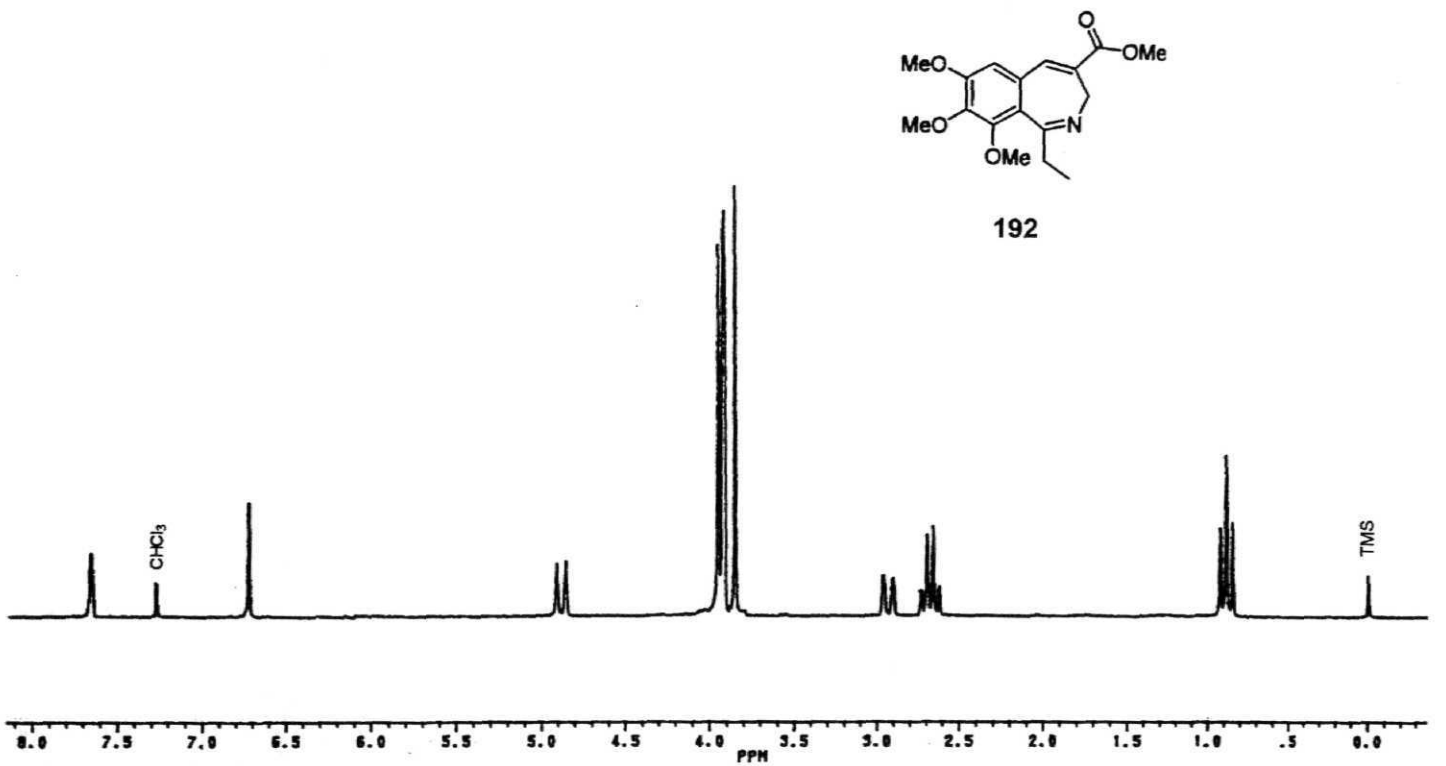

**185**



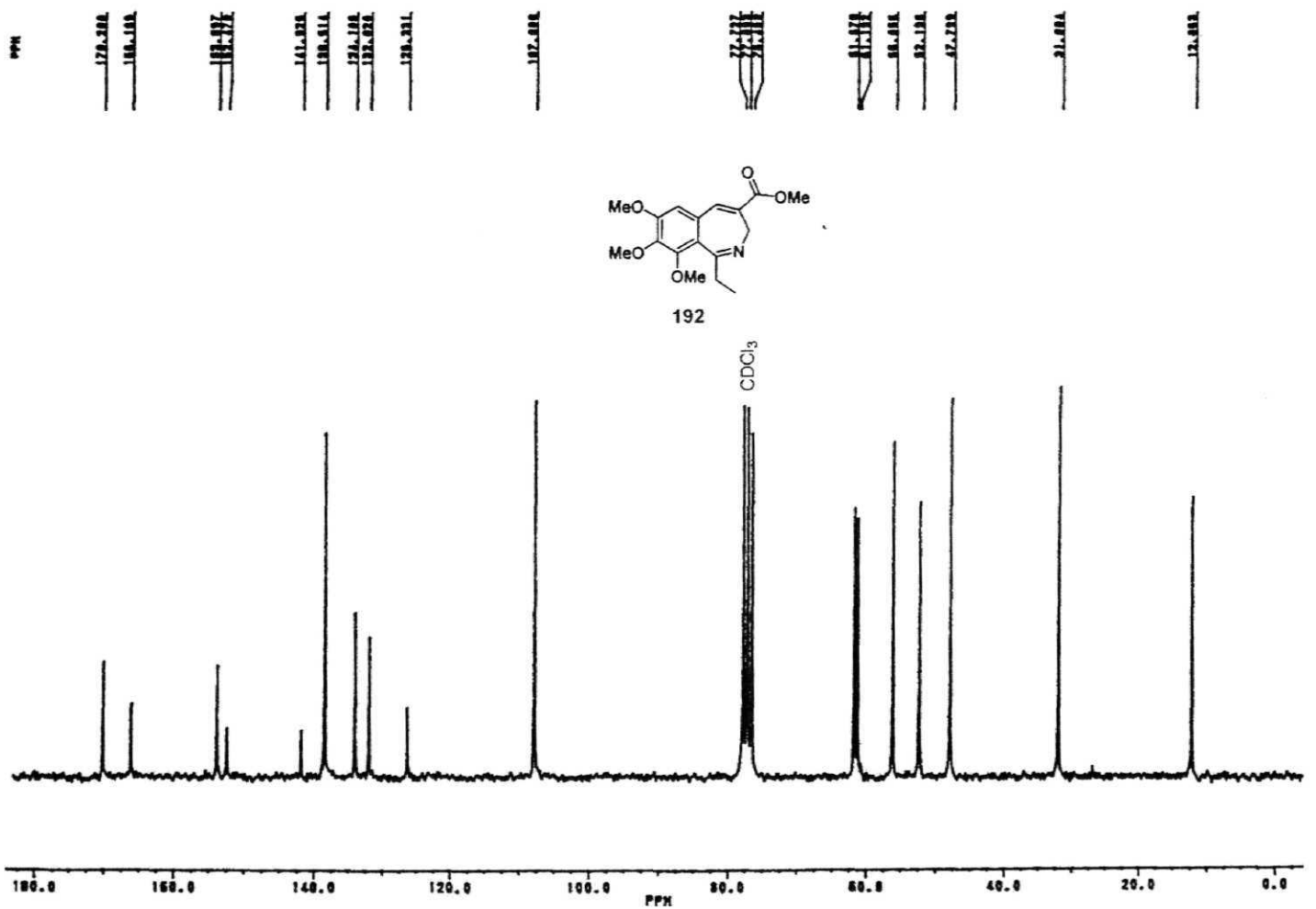

Spectrum 21: $^{1}$H NMR spectrum of **185**



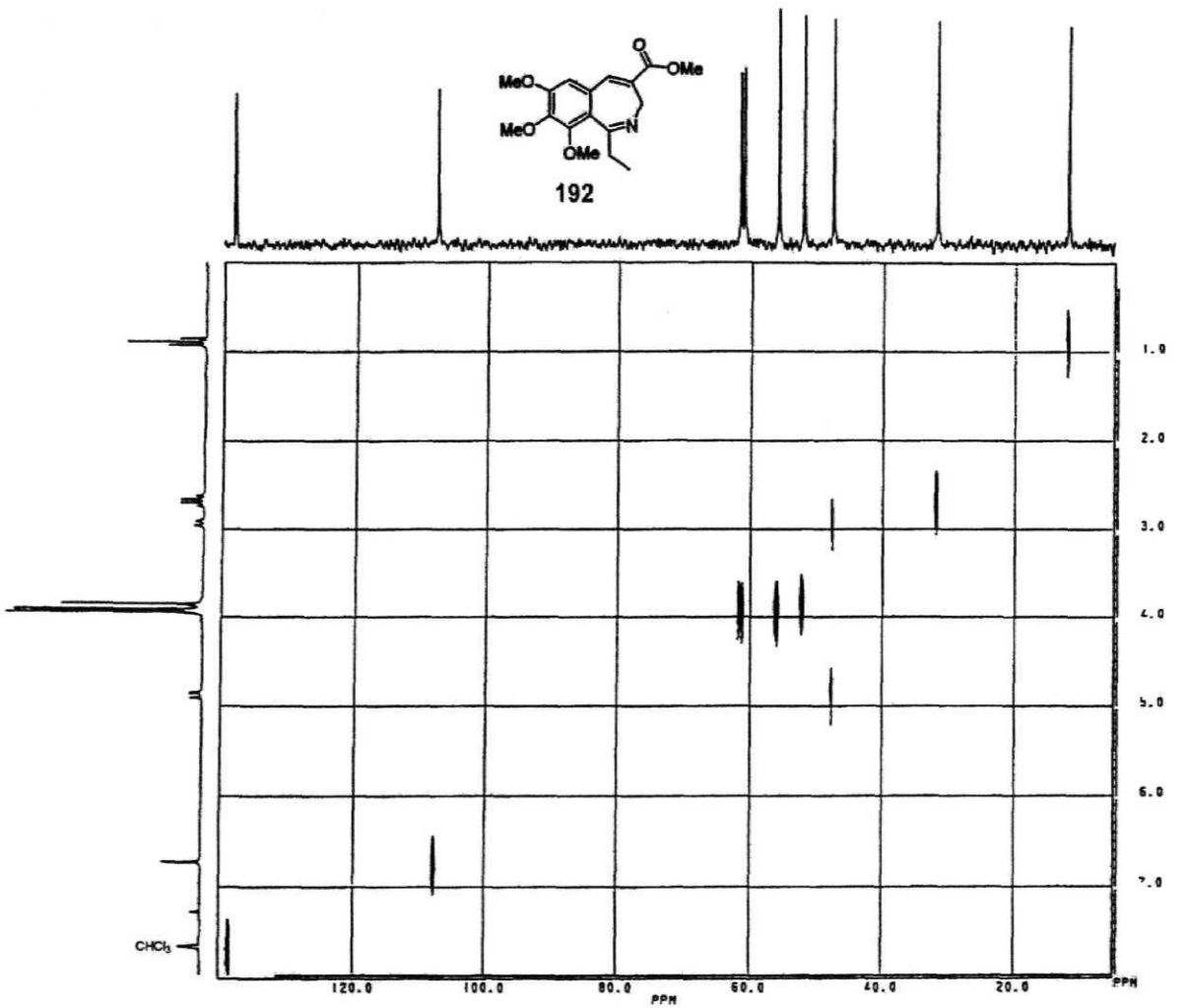

Spectrum 22: $^{13}C$ NMR spectrum of **185**



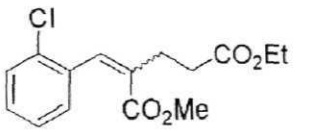

Spectrum 23: $^{1}$H NMR spectrum of **192**




Spectrum 24: $^{13}C$ NMR spectrum of **192**



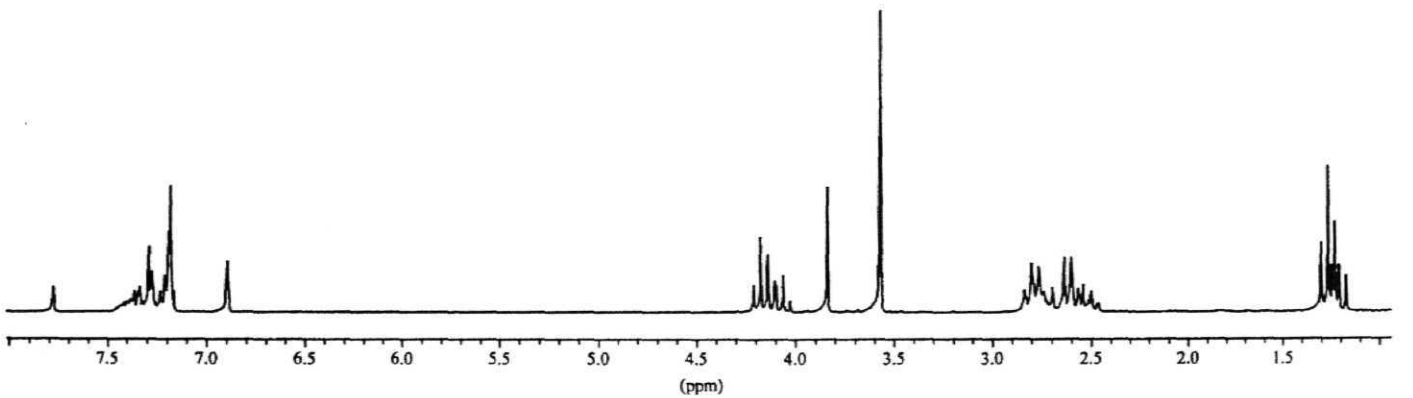

Spectrum 25: HX-COSY spectrum of **192**



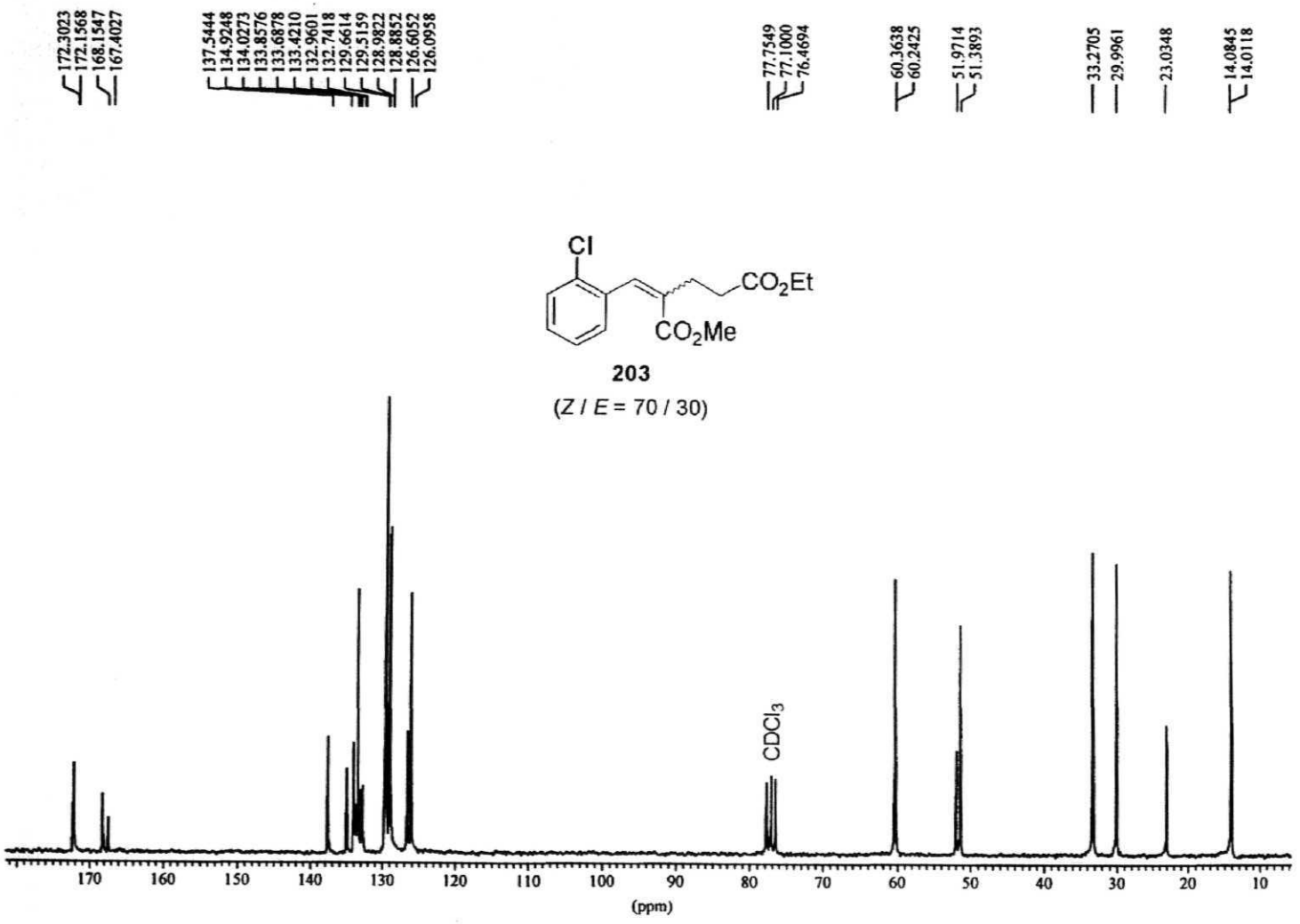

**203**

(*Z* / *E* = 70 / 30)

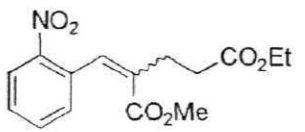





Spectrum 26: $^{1}$H NMR spectrum of **203**

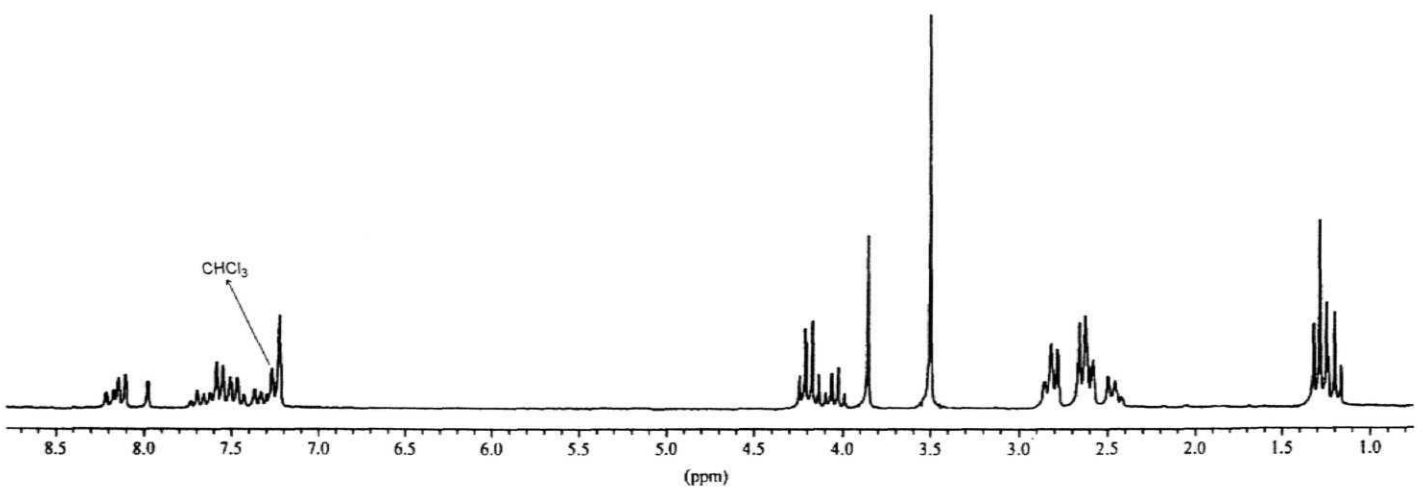



Spectrum 27: $^{13}C$ NMR spectrum of **203**

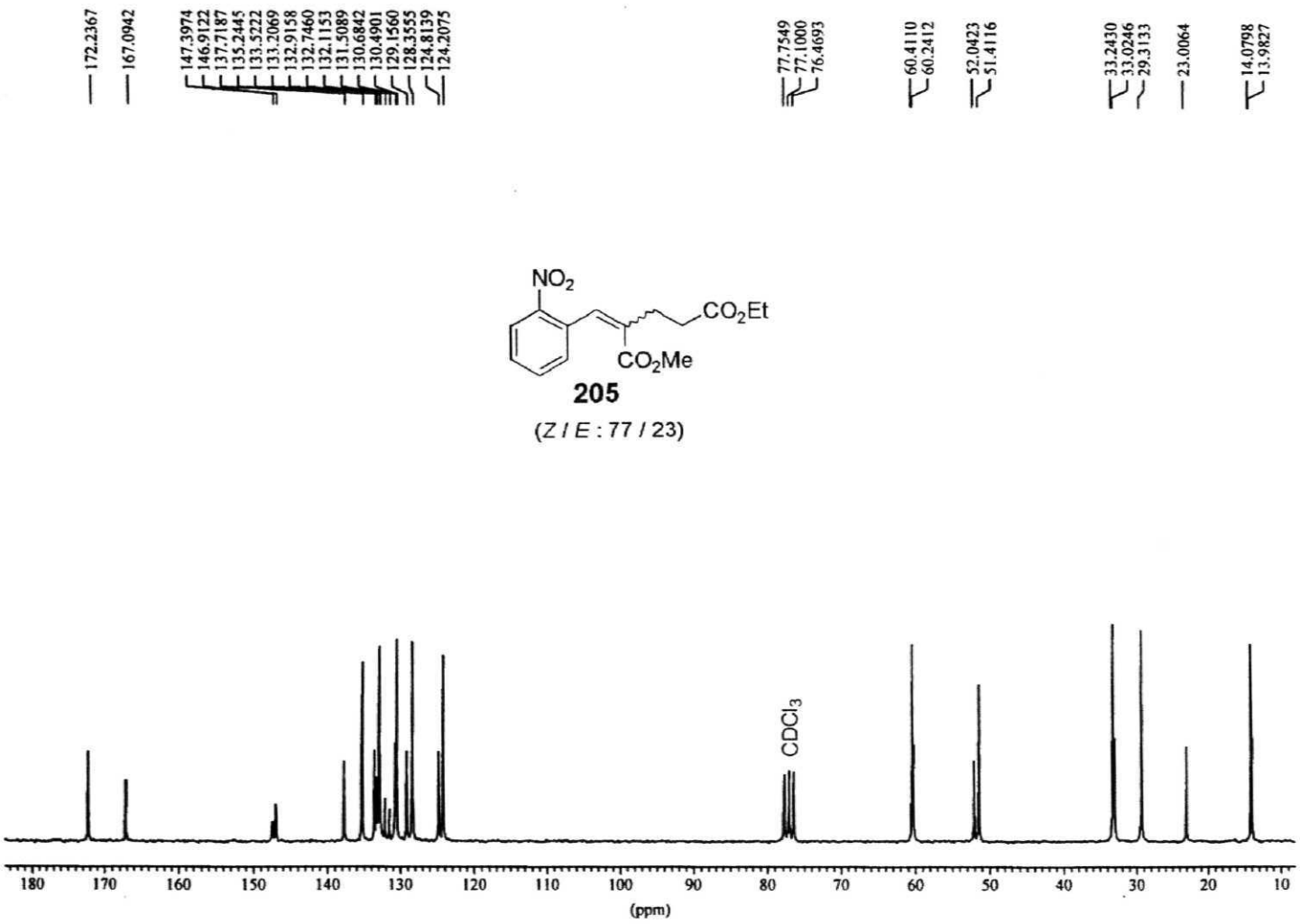



**205**

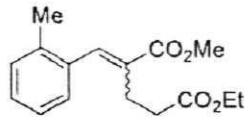
(*Z* / *E* : 77 / 23)




Spectrum 28: $^{1}$H NMR spectrum of **205**

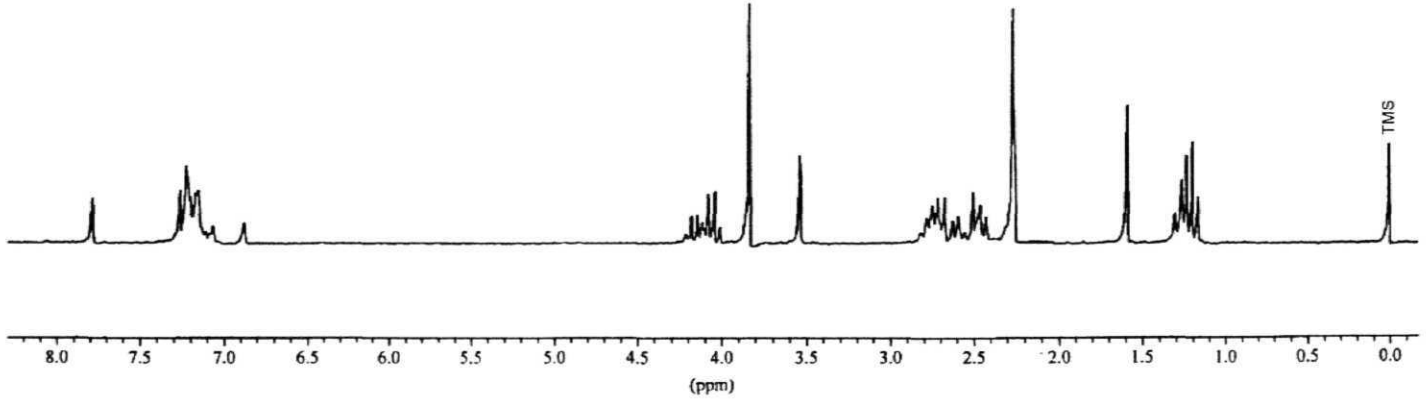



Spectrum 29: $^{13}C$ NMR spectrum of **205**

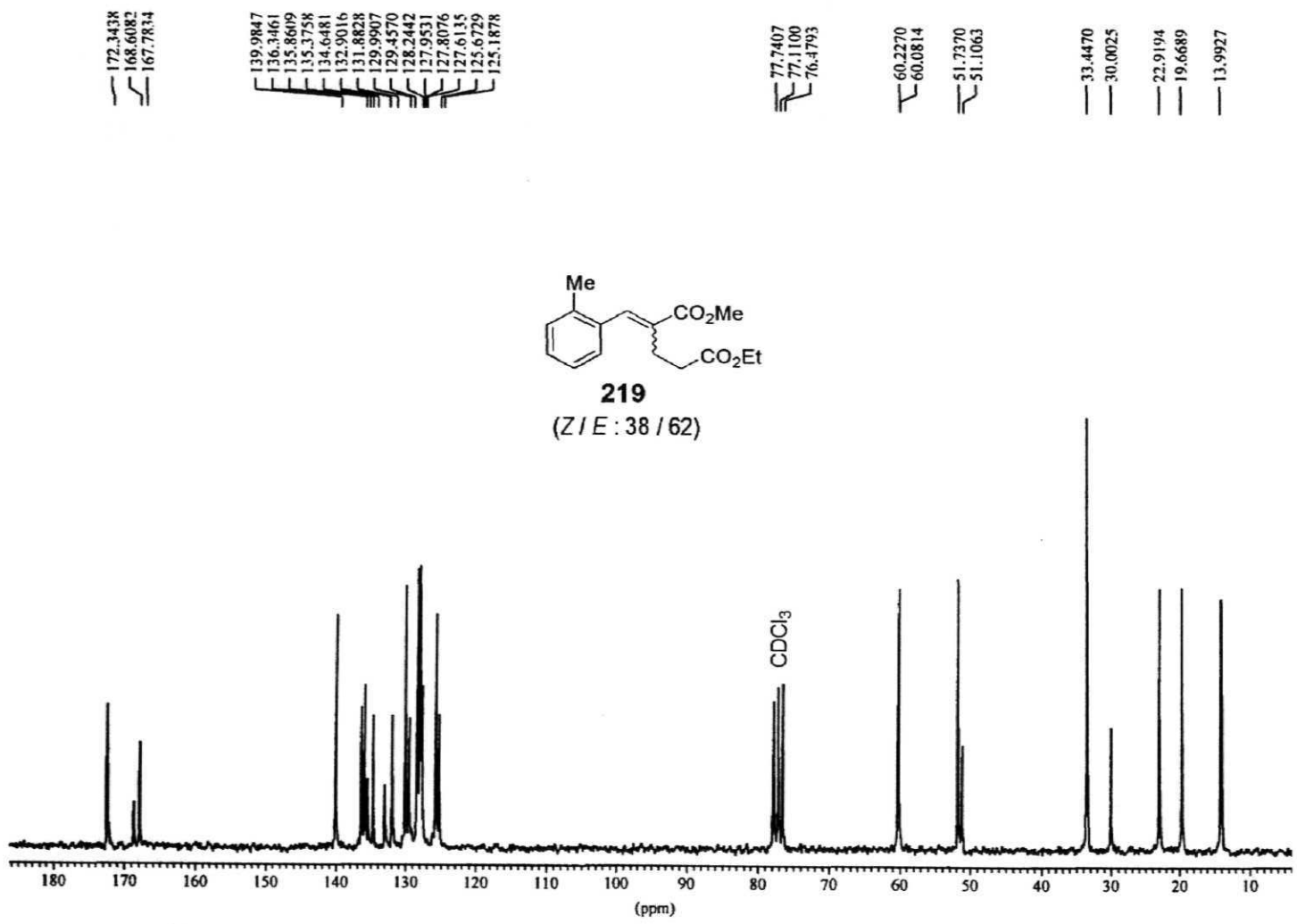



**219**

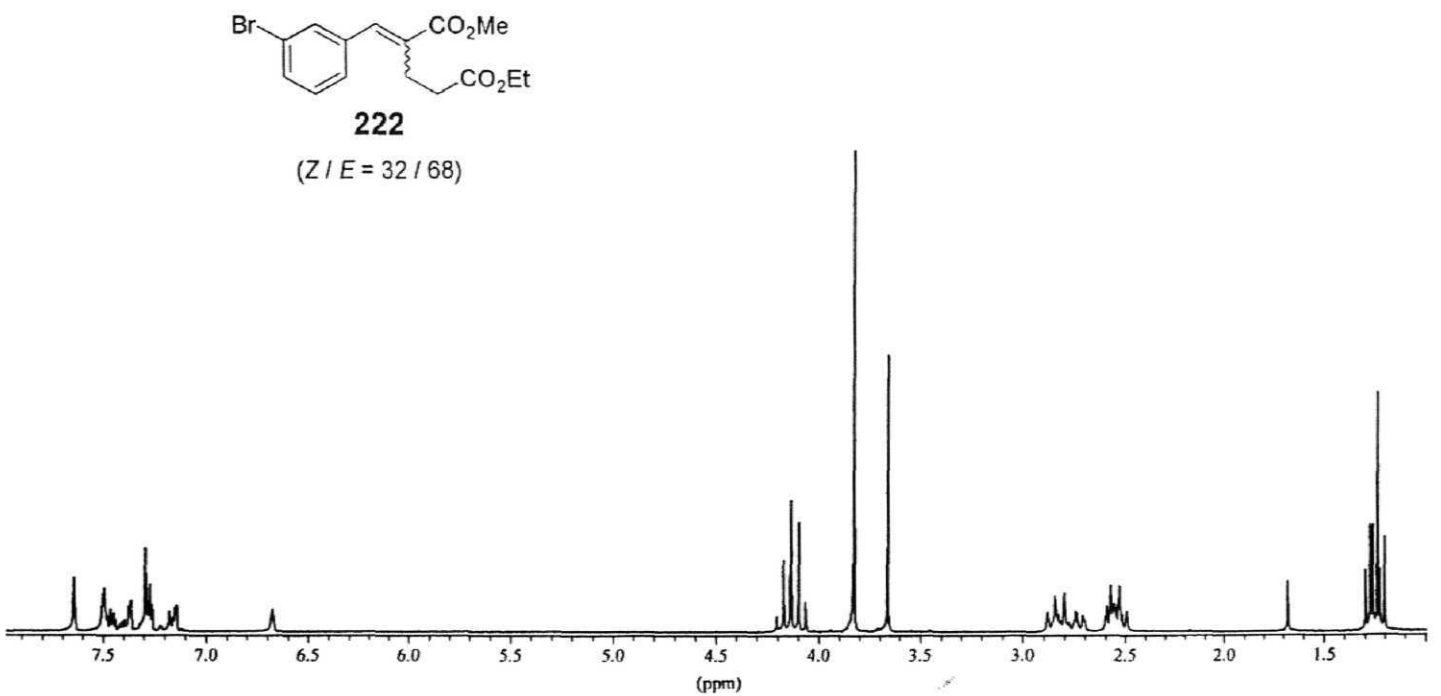
(*Z* / *E* : 38 / 62)



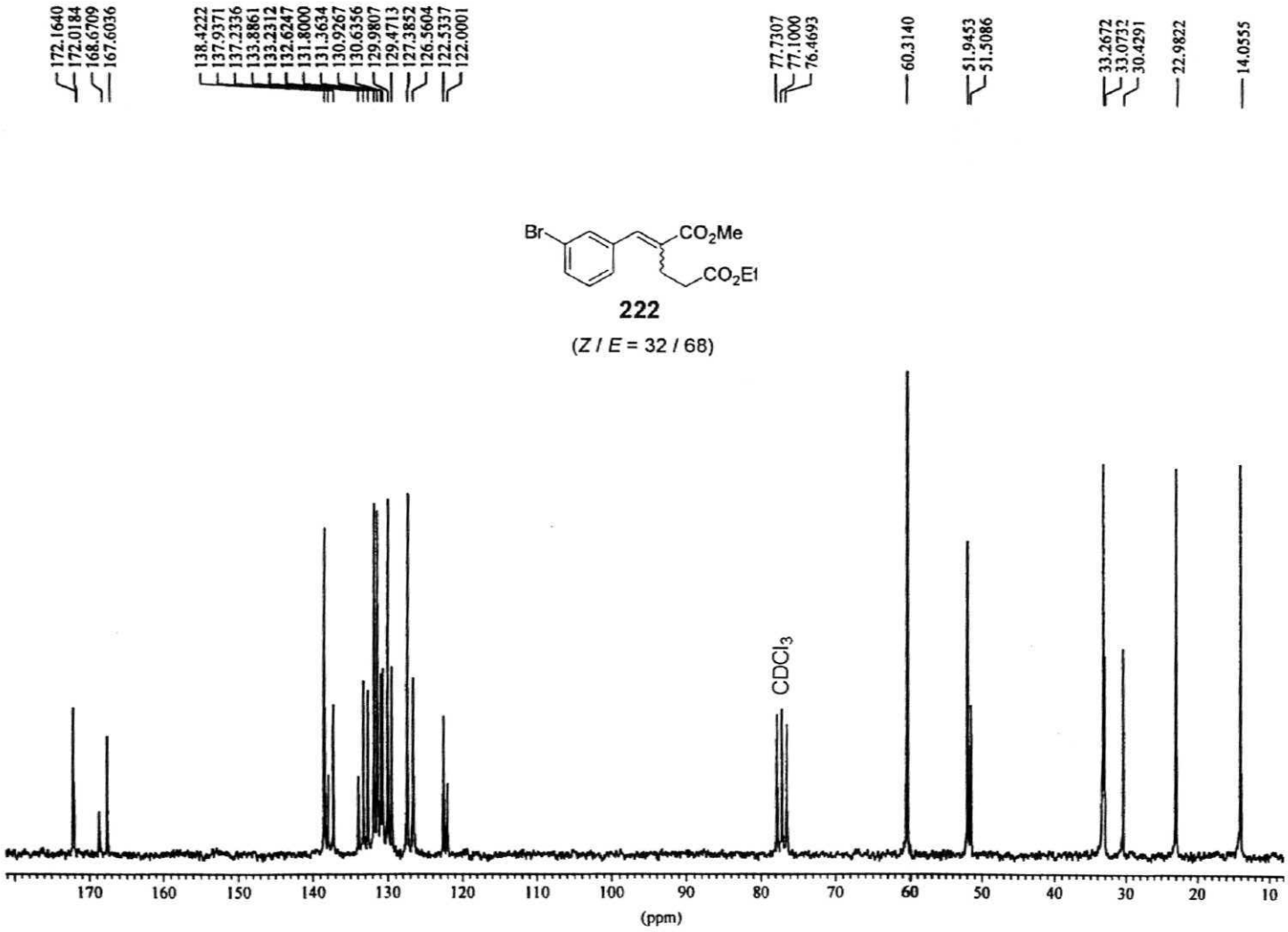

Spectrum 30: $^{1}$H NMR spectrum of **219**



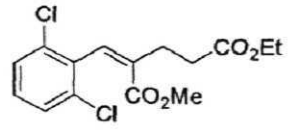

Spectrum 31: $^{13}C$ NMR spectrum of **219**



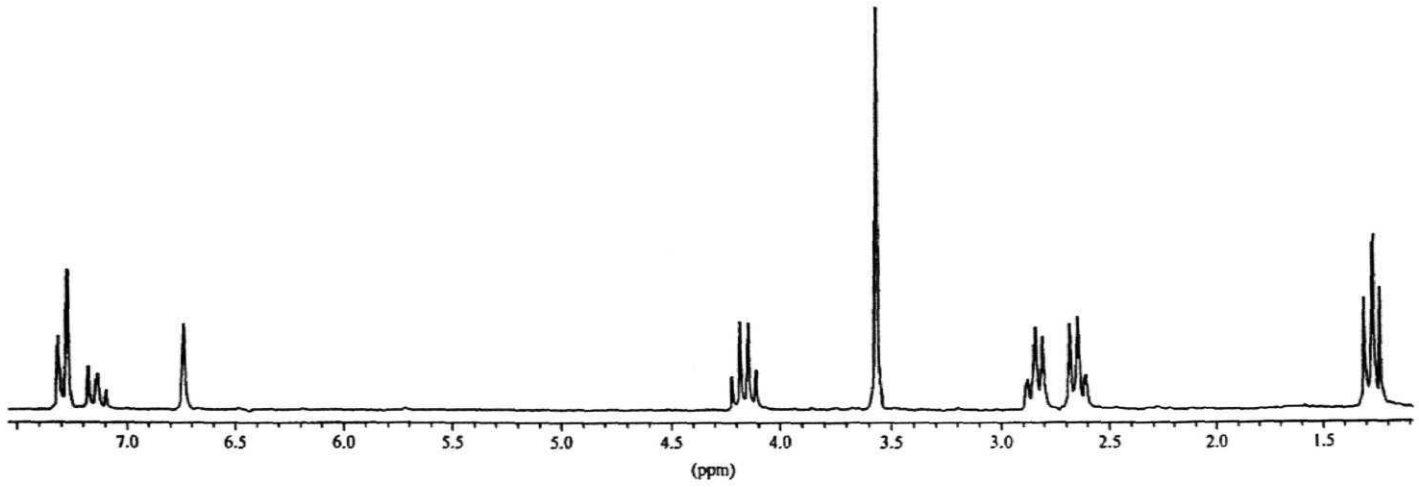

Spectrum 32: $^{1}$H NMR spectrum of **222**



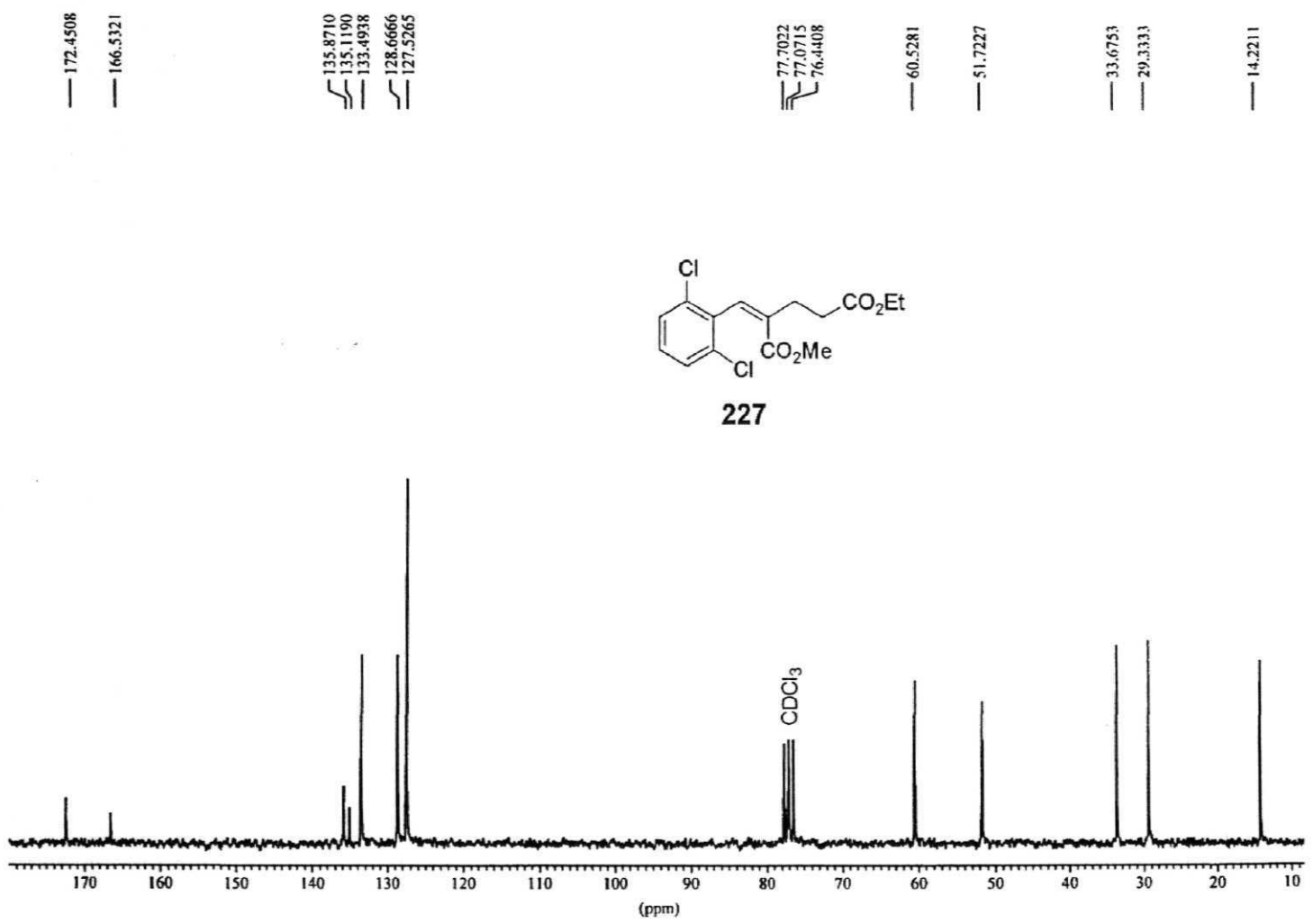

Spectrum 33: $^{13}C$ NMR spectrum of **222**




**227**

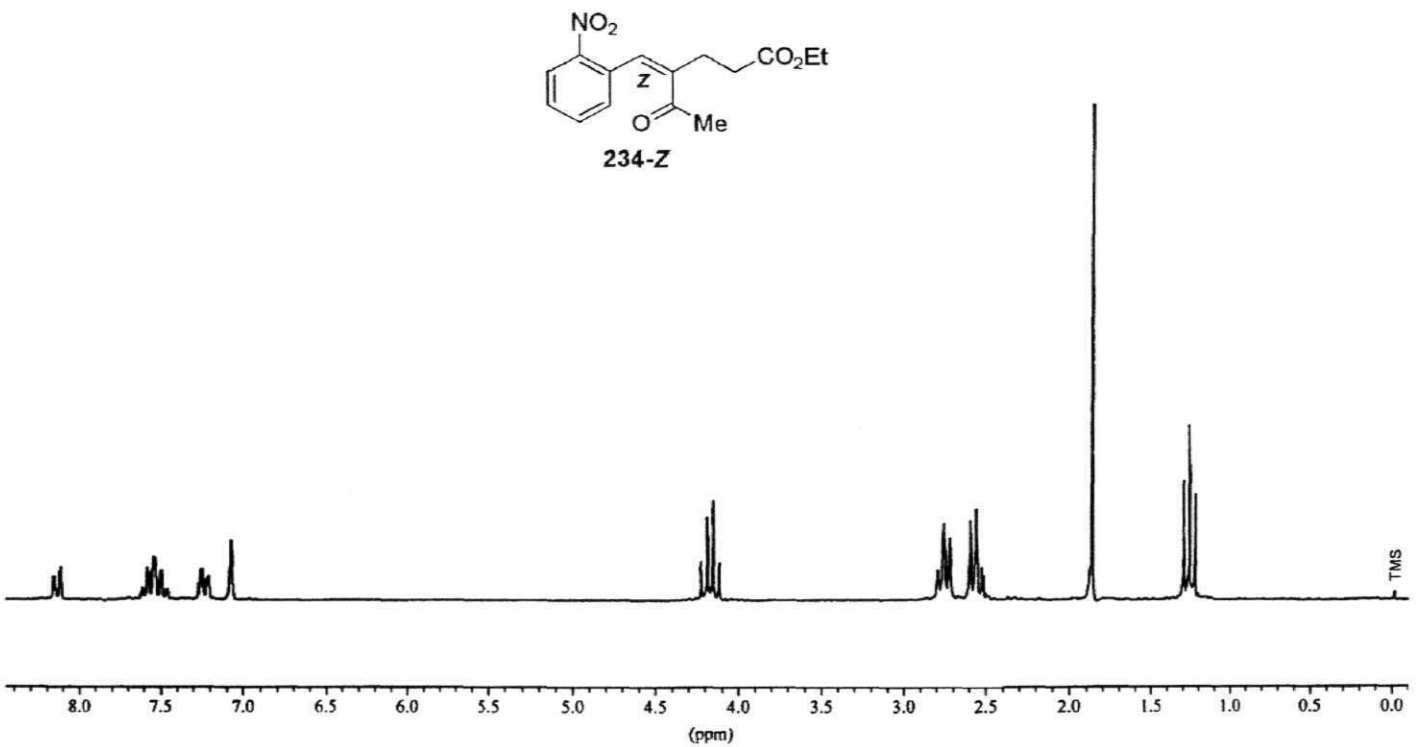



Spectrum 34: $^{1}$H NMR spectrum of **227**

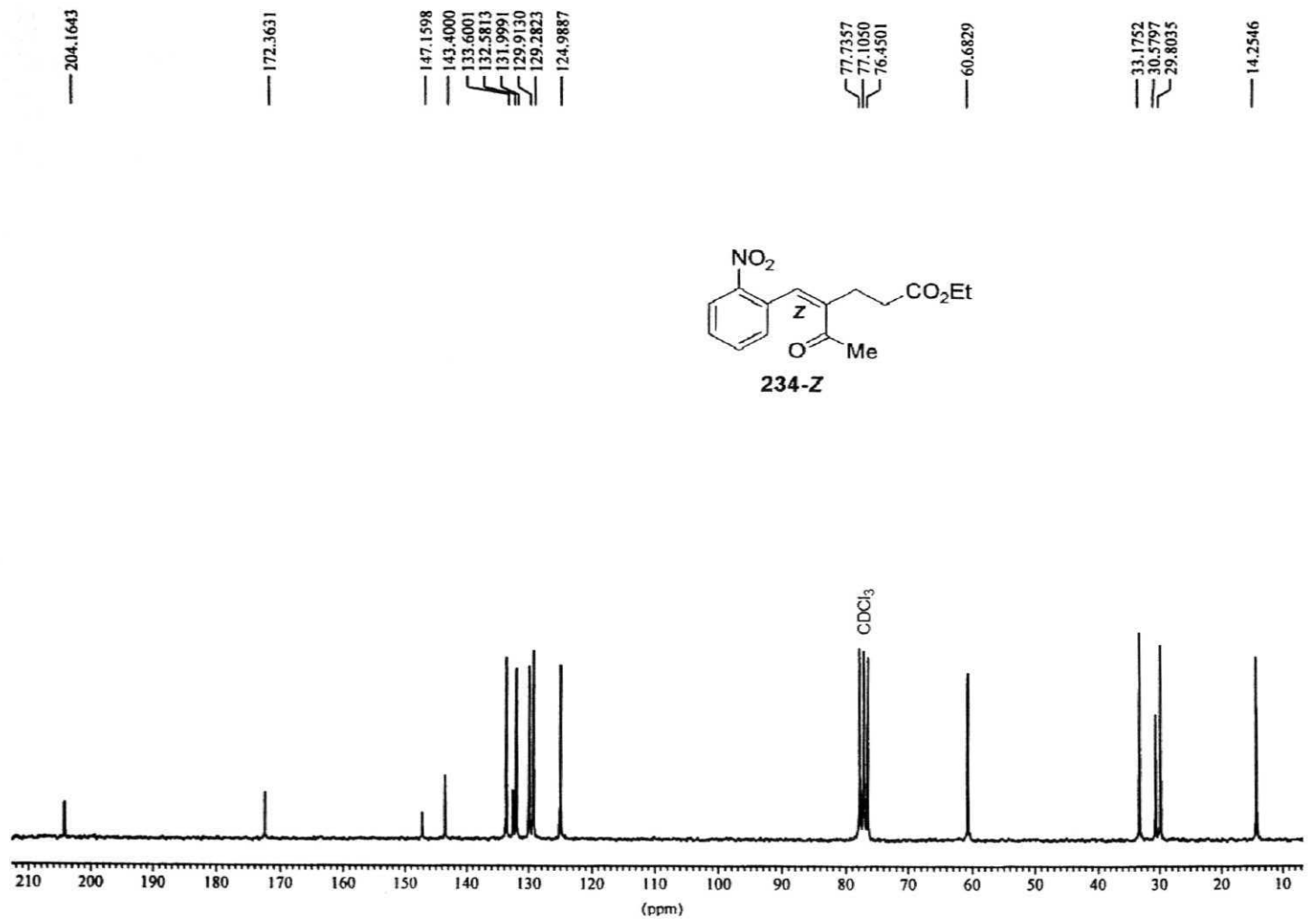



**227**

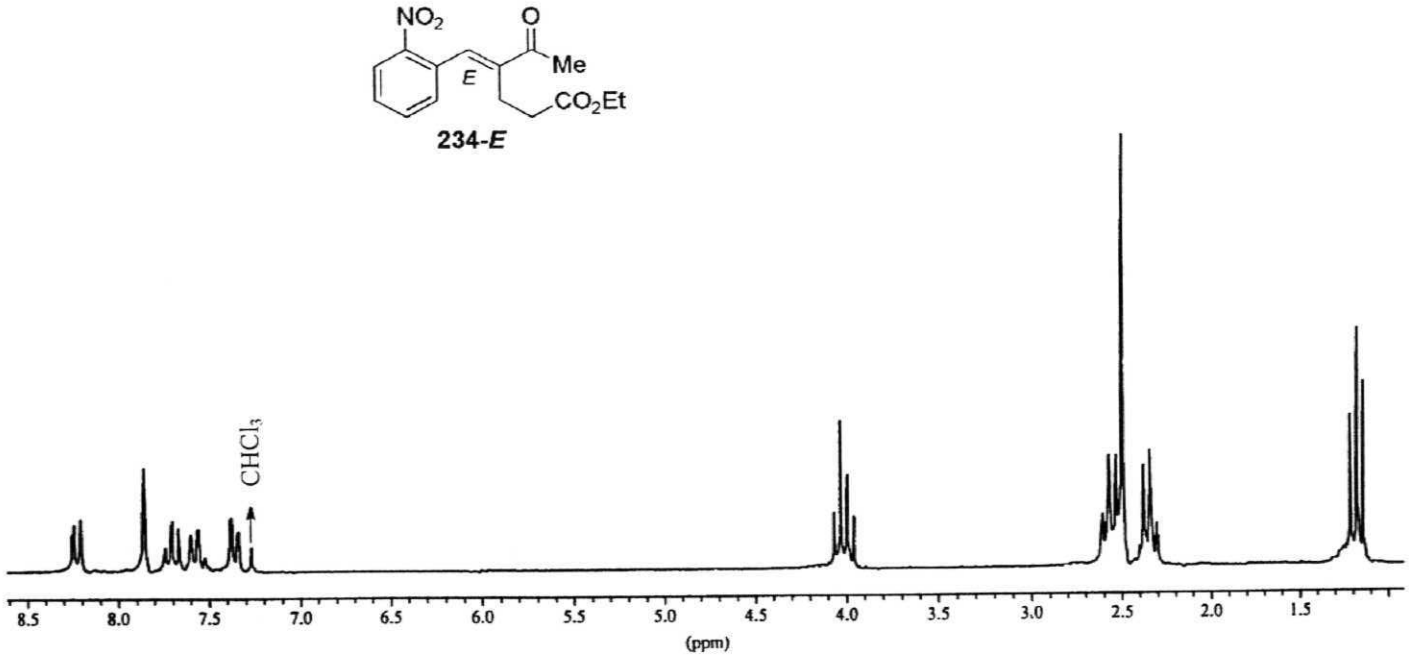
Spectrum 35: $^{13}C$ NMR spectrum of **227**



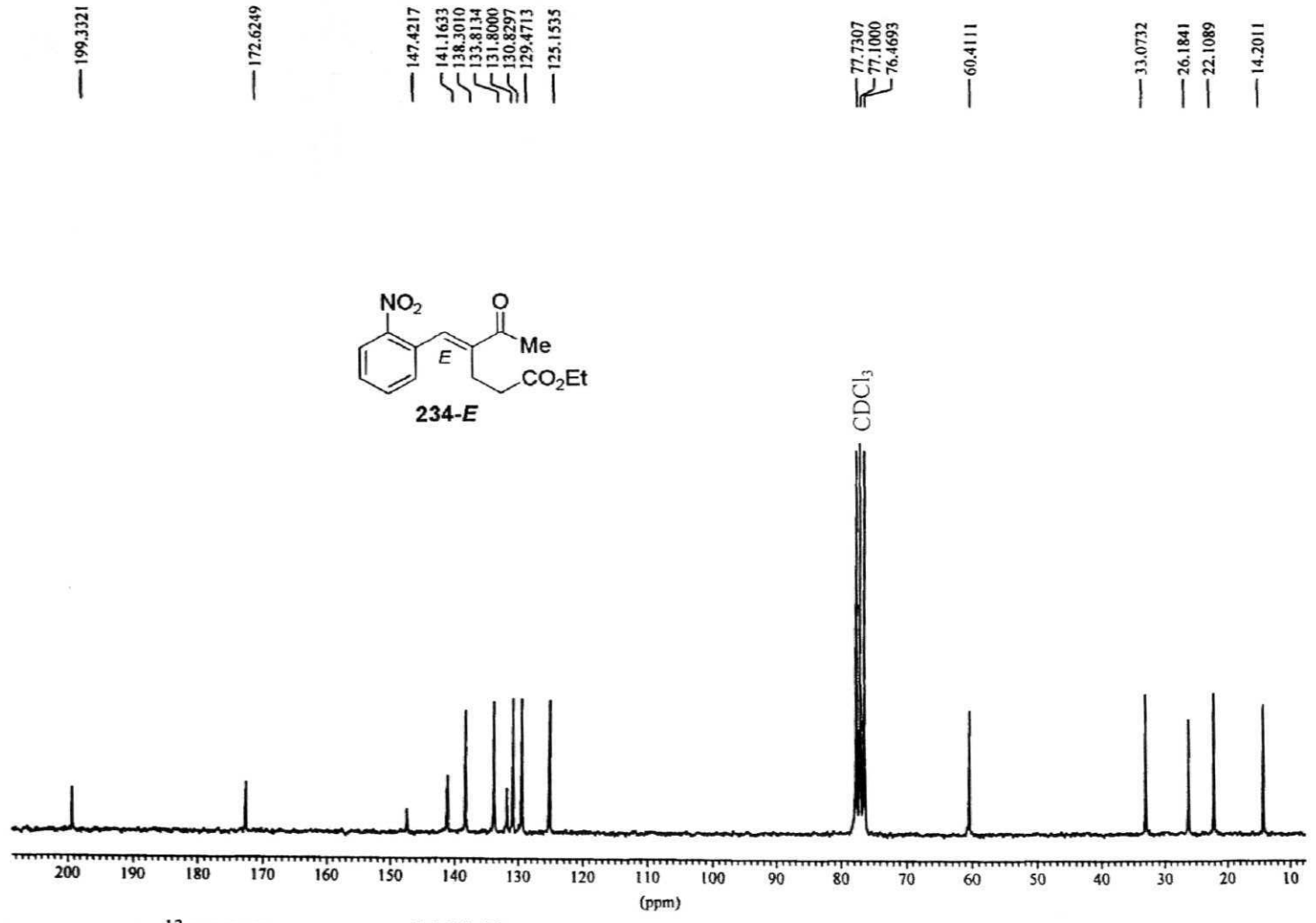

Spectrum 36: $^{1}$H NMR spectrum of **234-*Z***



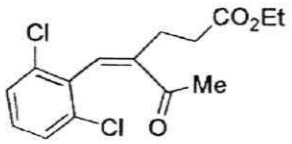

Spectrum 37: $^{13}$C NMR spectrum of **234-*Z***



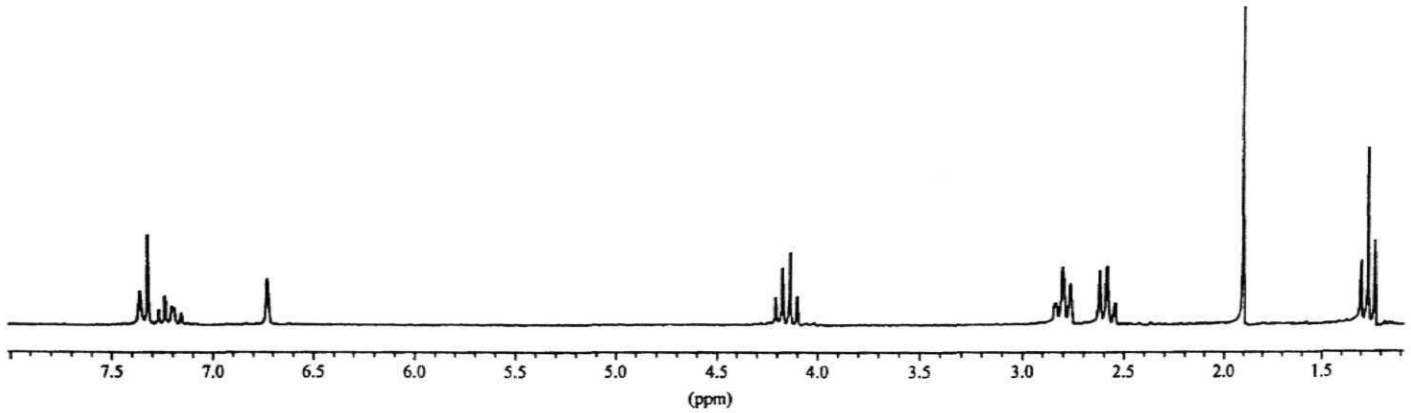

Spectrum 38: $^{1}$H NMR spectrum of **234-*E***



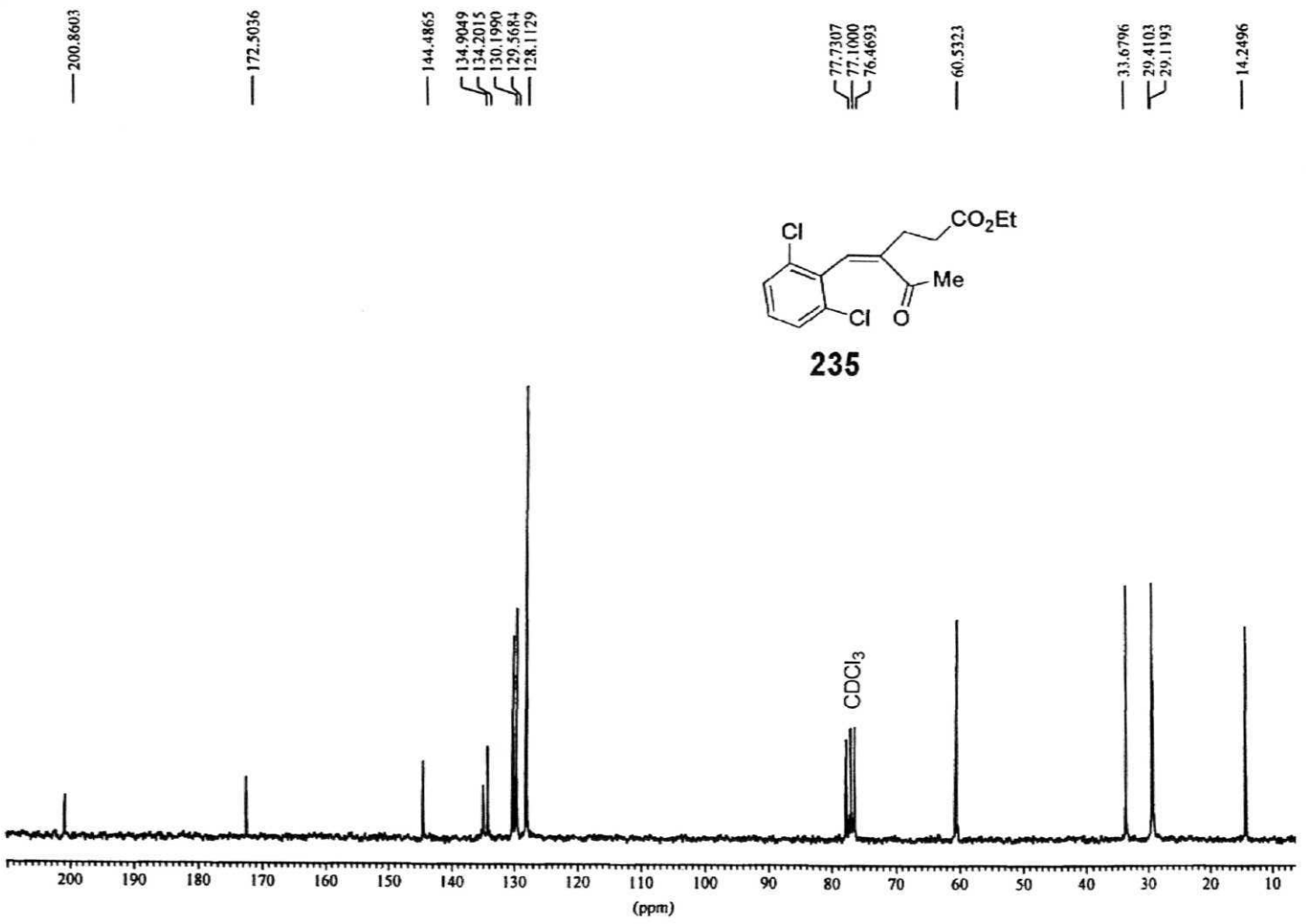

Spectrum 39: $^{13}C$ NMR spectrum of **234-*E***



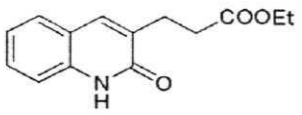

**235**




Spectrum 40: $^{1}$H NMR spectrum of **235**

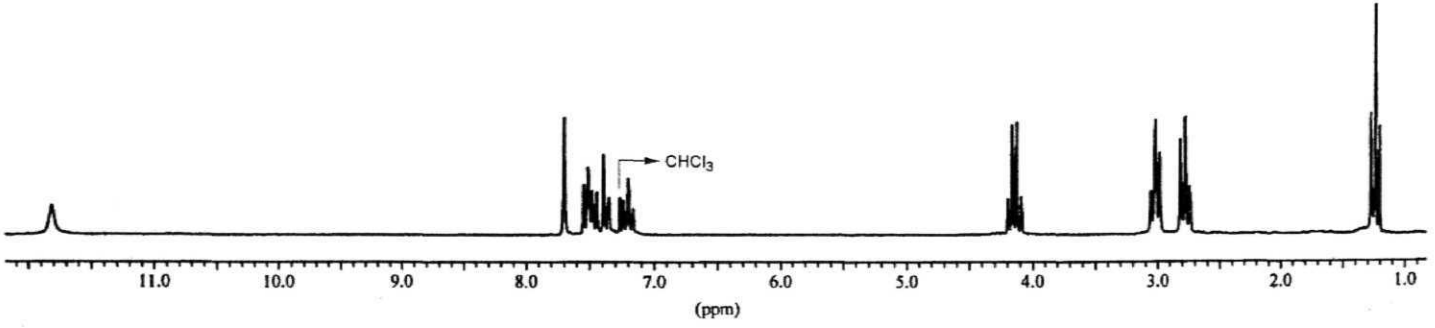



Spectrum 41: $^{13}C$ NMR spectrum of **235**

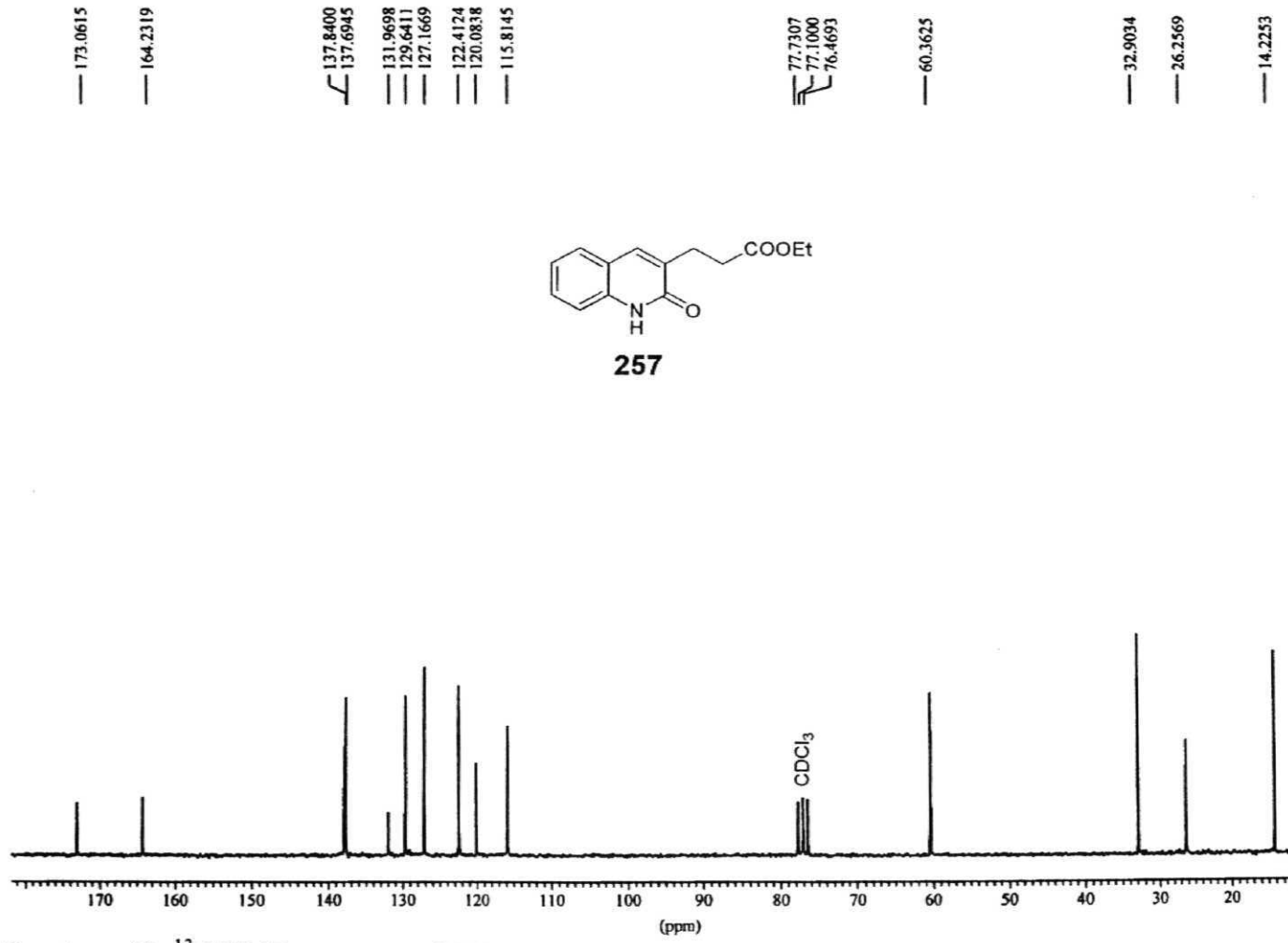



**257**

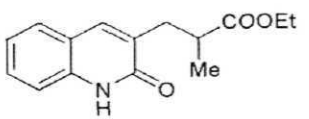




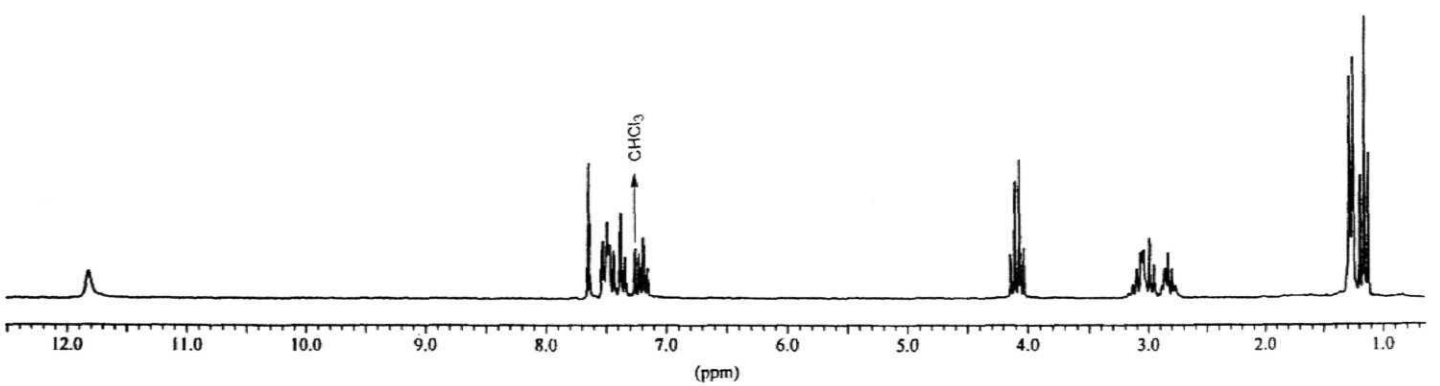

Spectrum 42: $^{1}$H NMR spectrum of **257**



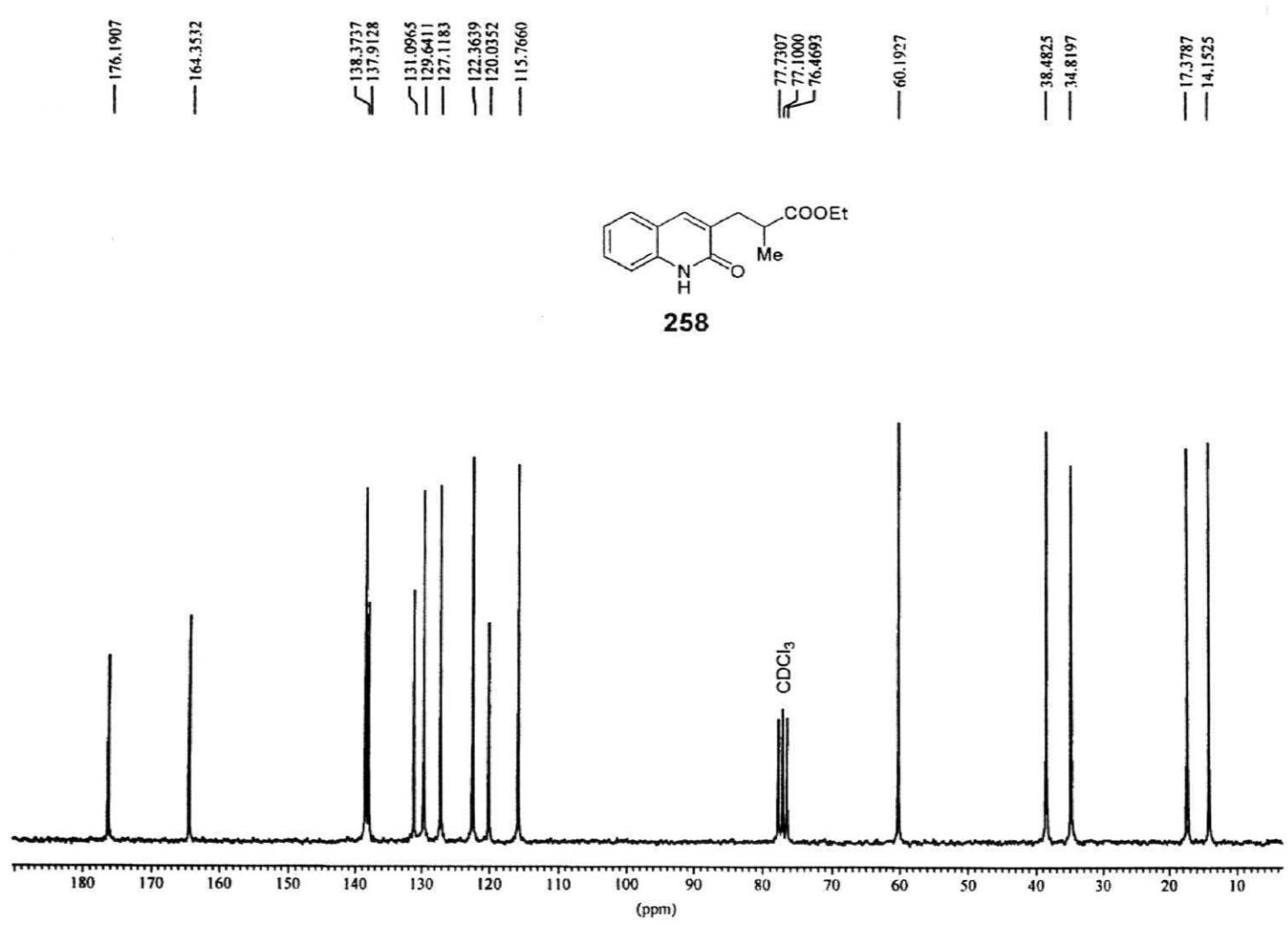

Spectrum 43: $^{13}C$ NMR spectrum of **257**




**258**

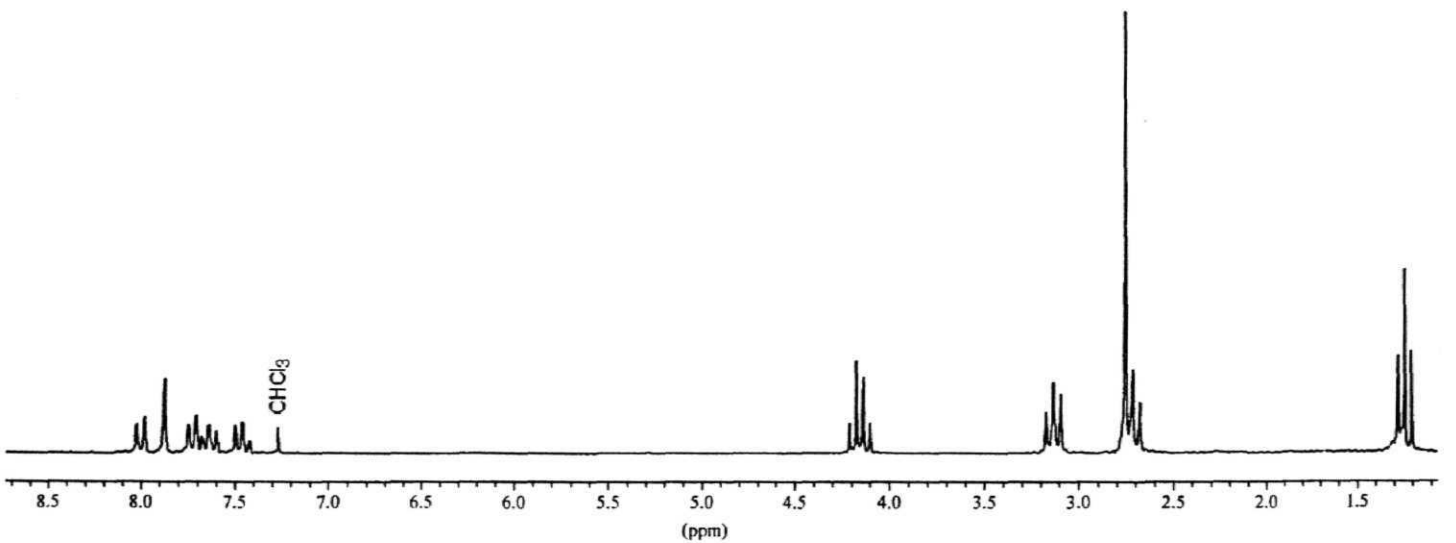



Spectrum 44: $^{1}$H NMR spectrum of **258**

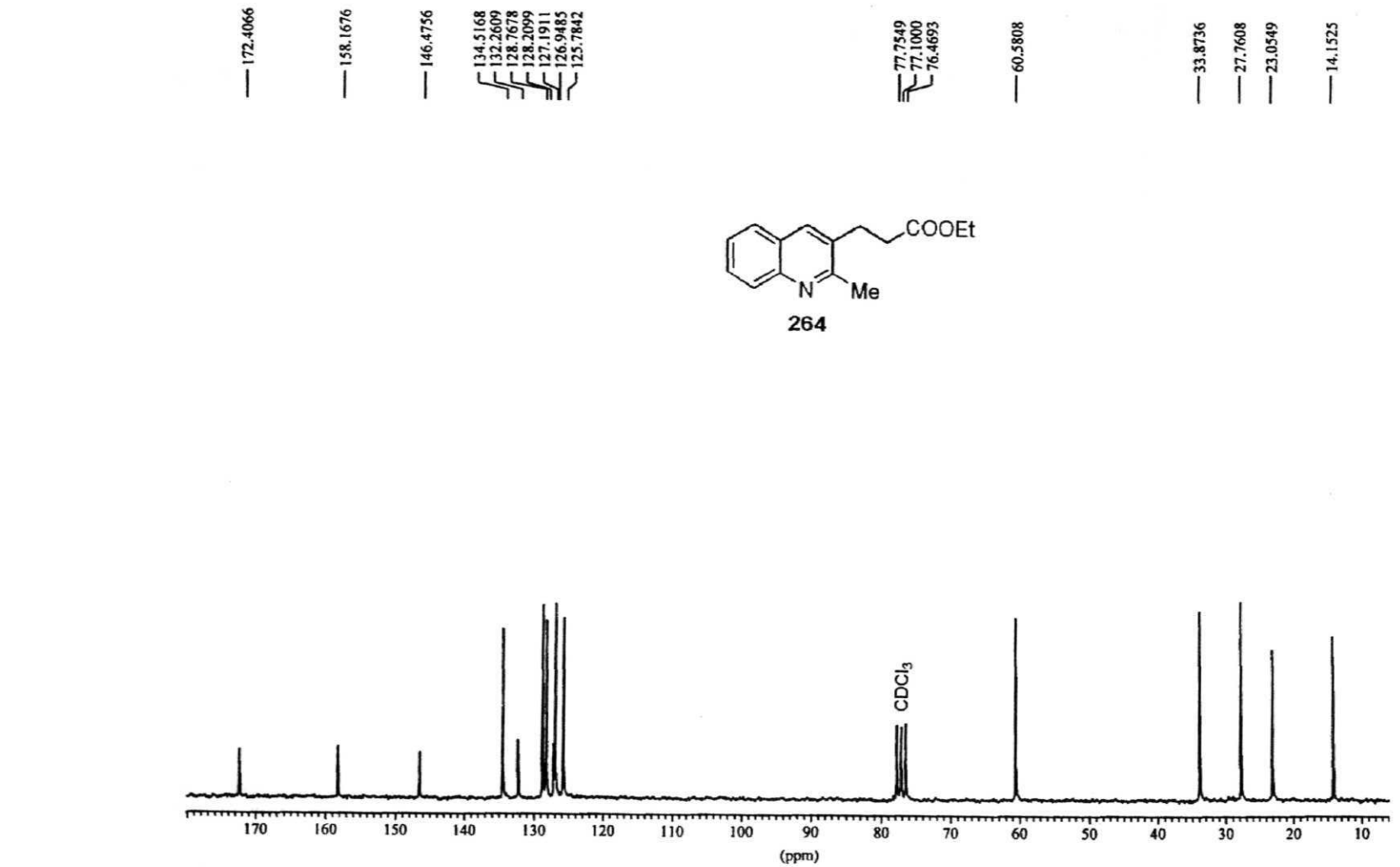



Spectrum 45: $^{13}C$ NMR spectrum of **258**


**264**




Spectrum 46: $^{1}$H NMR spectrum of **264**




Spectrum 47: $^{13}C$ NMR spectrum of 264

# APPENDIX

## (X-RAY CRYSTALLOGRAPHIC DATA)

**Table I**: Atomic coordinates (x $10^4$) and equivalent isotropic displacement parameters ($A^2$ x $10^3$) for molecule **130d**. U(eq) is defined as one third of the trace of the orthogonalized $U_{ij}$ tensor.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| O(1) | 2956(2) | 6585(3) | 136(2) | 76(1) |
| O(2) | 3769(2) | 6188(2) | 1233(2) | 74(1) |
| O(3) | 2466(2) | 6179(3) | -1083(2) | 92(1) |
| O(4) | 4701(2) | 4713(3) | 1445(2) | 103(1) |
| C(1) | 2998(2) | 6713(4) | -675(3) | 63(1) |
| C(2) | 3680(2) | 7437(3) | -982(2) | 49(1) |
| C(3) | 3599(2) | 7753(4) | -1764(2) | 54(1) |
| C(4) | 4154(2) | 8455(3) | -2247(2) | 49(1) |
| C(5) | 3821(2) | 9196(4) | -2894(2) | 62(1) |
| C(6) | 4305(3) | 9906(4) | -3354(2) | 74(1) |
| C(7) | 5136(3) | 9920(4) | -3222(3) | 68(1) |
| C(8) | 5479(2) | 9157(4) | -2602(2) | 63(1) |
| C(9) | 5006(2) | 8435(4) | -2124(2) | 53(1) |
| C(10) | 4381(2) | 7746(4) | -394(2) | 50(1) |
| C(11) | 4569(3) | 5810(4) | 1280(3) | 67(1) |

| | | | | |
|---|---|---|---|---|
| C(12) | 5176(2) | 6824(4) | 1174(2) | 55(1) |
| C(13) | 5960(2) | 6475(4) | 1160(2) | 64(1) |
| C(14) | 6667(2) | 7315(4) | 1095(2) | 59(1) |
| C(15) | 6803(2) | 8370(4) | 1594(2) | 70(1) |
| C(16) | 7485(3) | 9116(5) | 1552(3) | 77(1) |
| C(17) | 8068(3) | 8866(5) | 1014(3) | 74(1) |
| C(18) | 7929(3) | 7812(5) | 524(3) | 81(1) |
| C(19) | 7252(2) | 7036(4) | 561(2) | 72(1) |
| C(20) | 4846(2) | 8159(3) | 1055(2) | 49(1) |
| C(21) | 4108(2) | 8146(3) | 429(2) | 45(1) |
| C(22) | 3461(2) | 7232(3) | 743(2) | 51(1) |
| C(23) | 2927(2) | 8065(3) | 1210(2) | 45(1) |
| C(24) | 2354(2) | 7709(4) | 1741(2) | 65(1) |
| C(25) | 1902(3) | 8655(5) | 2080(3) | 79(1) |
| C(26) | 2016(2) | 9923(5) | 1888(3) | 74(1) |
| C(27) | 2580(2) | 10285(4) | 1354(2) | 59(1) |
| C(28) | 3038(2) | 9337(3) | 1015(2) | 48(1) |
| C(29) | 3679(2) | 9465(3) | 412(2) | 49(1) |
| C(30) | 5674(4) | 10732(5) | -3728(3) | 124(2) |
| C(31) | 6183(4) | 10034(6) | -4228(4) | 159(3) |
| C(32) | 5808(4) | 11996(6) | -3438(4) | 148(3) |
| C(33) | 8826(3) | 9707(6) | 986(4) | 122(2) |
| C(34) | 8710(4) | 10919(8) | 673(6) | 242(6) |
| C(35) | 9516(4) | 9238(10) | 1324(7) | 320(8) |

**Table II**: Atomic coordinates (x $10^4$) and equivalent isotropic displacement parameters ($A^2$ x $10^3$) for molecule **134**. U(eq) is defined as one third of the trace of the orthogonalized $U_{ij}$ tensor.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| O(1) | 5408(3) | 8204(2) | 869(1) | 58(1) |
| O(2) | 4435(2) | 7791(2) | 1792(1) | 52(1) |
| O(3) | 4096(3) | 8701(2) | 17(1) | 76(1) |
| O(4) | 3133(3) | 7438(2) | 2591(1) | 73(1) |
| C(1) | 4172(4) | 7952(3) | 2399(2) | 50(1) |
| C(2) | 5170(3) | 8733(2) | 2782(2) | 44(1) |
| C(3) | 5136(4) | 8607(3) | 3401(2) | 51(1) |
| C(4) | 5993(4) | 9127(3) | 3920(2) | 55(1) |
| C(5) | 5958(6) | 8608(3) | 4499(2) | 83(1) |
| C(6) | 6803(8) | 8999(4) | 5015(2) | 122(2) |
| C(7) | 7704(7) | 9919(5) | 4961(2) | 122(2) |
| C(8) | 7721(6) | 10475(4) | 4403(2) | 104(2) |
| C(9) | 6881(5) | 10097(3) | 3884(2) | 70(1) |
| C(10) | 6171(4) | 9525(3) | 2448(1) | 47(1) |
| C(11) | 4384(4) | 8899(3) | 563(2) | 58(1) |
| C(12) | 3733(4) | 9843(3) | 923(2) | 51(1) |

| | | | | |
|---|---|---|---|---|
| C(13) | 2536(4) | 10334(3) | 628(2) | 58(1) |
| C(14) | 1536(4) | 11220(3) | 820(2) | 57(1) |
| C(15) | 391(5) | 11533(4) | 385(2) | 88(1) |
| C(16) | -703(6) | 12316(4) | 527(3) | 97(2) |
| C(17) | -639(6) | 12802(4) | 1109(3) | 100(2) |
| C(18) | 473(5) | 12500(3) | 1538(2) | 79(1) |
| C(19) | 1514(4) | 11716(3) | 1404(2) | 65(1) |
| C(20) | 4433(4) | 10137(3) | 1555(2) | 55(1) |
| C(21) | 5893(4) | 9516(2) | 1737(1) | 48(1) |
| C(22) | 7228(4) | 10026(3) | 1419(2) | 64(1) |
| C(23) | 8686(5) | 9348(4) | 1539(2) | 78(1) |
| C(24) | 8512(4) | 8099(3) | 1633(2) | 64(1) |
| C(25) | 9786(5) | 7413(5) | 1725(2) | 88(1) |
| C(26) | 9651(6) | 6287(5) | 1849(2) | 99(2) |
| C(27) | 8290(6) | 5779(4) | 1872(2) | 84(1) |
| C(28) | 7014(4) | 6441(3) | 1774(2) | 63(1) |
| C(29) | 7113(4) | 7594(3) | 1659(2) | 52(1) |
| C(30) | 5732(4) | 8296(3) | 1526(2) | 49(1) |

**Table III**: Atomic coordinates (x $10^4$) and equivalent isotropic displacement parameters ($A^2$ x $10^3$) for molecule **192**. U(eq) is defined as one third of the trace of the orthogonalized $U_{ij}$ tensor.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| C(1) | 7227(2) | 10038(2) | 8334(2) | 46(1) |
| C(2) | 7110(3) | 10081(2) | 7158(2) | 47(1) |
| C(3) | 7582(3) | 10897(2) | 6619(2) | 51(1) |
| C(4) | 8160(3) | 11725(2) | 7253(2) | 52(1) |
| C(5) | 8304(3) | 11695(2) | 8397(2) | 50(1) |
| C(6) | 7886(3) | 10848(2) | 8954(2) | 46(1) |
| C(7) | 8197(3) | 10840(2) | 10180(2) | 52(1) |
| C(8) | 8419(3) | 9993(2) | 10802(2) | 51(1) |
| C(9) | 8315(3) | 8959(2) | 10250(3) | 53(1) |
| C(10) | 6517(3) | 9262(2) | 8911(2) | 49(1) |
| C(11) | 5108(3) | 9161(3) | 8479(3) | 64(1) |
| C(12) | 4508(3) | 8194(3) | 8781(4) | 86(1) |
| C(13) | 7204(5) | 8399(3) | 6443(4) | 96(1) |
| C(14) | 6426(4) | 11171(3) | 4802(3) | 84(1) |
| C(15) | 9235(4) | 13328(3) | 7231(3) | 76(1) |
| C(16) | 8740(3) | 10125(3) | 12041(3) | 63(1) |

| | | | | |
|---|---|---|---|---|
| C(17) | 9111(4) | 9275(3) | 13798(3) | 89(1) |
| O(1) | 6502(2) | 9311(2) | 6500(2) | 64(1) |
| O(2) | 7568(2) | 10883(2) | 5475(2) | 71(1) |
| O(3) | 8562(2) | 12500(2) | 6636(2) | 69(1) |
| O(4) | 8893(4) | 10929(2) | 12520(2) | 115(1) |
| O(5) | 8829(2) | 9226(2) | 12582(2) | 68(1) |
| N(1) | 6969(2) | 8770(2) | 9797(2) | 53(1) |

**Table IV**: Atomic coordinates (x $10^4$) and equivalent isotropic displacement parameters ($A^2$ x $10^3$) for molecule **194**. U(eq) is defined as one third of the trace of the orthogonalized $U_{ij}$ tensor.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| N(1) | 9735(1) | 1776(1) | 6726(1) | 39(1) |
| O(1) | 7537(2) | 1294(1) | 291(1) | 61(1) |
| O(2) | 9237(2) | 2419(1) | 772(1) | 63(1) |
| O(3) | 6353(2) | -448(1) | 6832(1) | 65(1) |
| O(4) | 8586(2) | -125(1) | 8309(1) | 56(1) |
| C(1) | 8980(2) | 1846(1) | 4266(1) | 38(1) |
| C(2) | 9435(2) | 2320(1) | 3213(1) | 47(1) |
| C(3) | 8904(2) | 2072(1) | 1937(1) | 46(1) |

| | | | | |
|---|---|---|---|---|
| C(4) | 7899(2) | 1396(1) | 1648(1) | 45(1) |
| C(5) | 7413(2) | 926(1) | 2624(1) | 42(1) |
| C(6) | 8006(2) | 1136(1) | 3966(1) | 37(1) |
| C(7) | 7483(2) | 605(1) | 4983(1) | 39(1) |
| C(8) | 8361(2) | 479(1) | 6194(1) | 38(1) |
| C(9) | 10007(2) | 899(1) | 6577(1) | 41(1) |
| C(10) | 9322(2) | 2183(1) | 5653(1) | 37(1) |
| C(11) | 9071(2) | 3093(1) | 5763(2) | 46(1) |
| C(12) | 9309(3) | 3433(1) | 7152(2) | 63(1) |
| C(13) | 8126(3) | 2019(1) | -265(2) | 62(1) |
| C(14) | 7643(2) | -78(1) | 7115(1) | 42(1) |
| C(15) | 7953(3) | -643(1) | 9271(2) | 74(1) |

**Table V**: Atomic coordinates (x $10^4$) and equivalent isotropic displacement parameters ($A^2$ x $10^3$) for molecule **263**. U(eq) is defined as one third of the trace of the orthogonalized $U_{ij}$ tensor.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| O(1) | 5569(18) | 10690(14) | 5762(9) | 60(3) |
| O(2) | 2134(17) | 12464(14) | 5965(9) | 55(3) |
| O(3) | 3645(15) | 16341(11) | 10553(10) | 61(3) |

| | | | | |
|---|---|---|---|---|
| O(4) | 12285(18) | 12939(17) | 11386(12) | 79(4) |
| O(5) | 9771(17) | 14850(12) | 12102(9) | 56(3) |
| N(1) | 3242(16) | 15029(12) | 9081(11) | 43(3) |
| C(1) | 3814(18) | 13964(14) | 8310(10) | 32(3) |
| C(2) | 2602(19) | 13839(14) | 7580(11) | 38(3) |
| C(3) | 3250(20) | 12716(19) | 6738(12) | 48(4) |
| C(4) | 5110(20) | 11678(17) | 6647(14) | 54(4) |
| C(5) | 6290(20) | 11834(17) | 7392(10) | 41(4) |
| C(6) | 5744(17) | 12982(13) | 8227(11) | 31(3) |
| C(7) | 6830(20) | 13228(18) | 8981(13) | 50(4) |
| C(8) | 6302(14) | 14278(11) | 9769(10) | 24(3) |
| C(9) | 4290(20) | 15282(18) | 9750(14) | 56(4) |
| C(10) | 7530(30) | 9690(20) | 5654(16) | 78(6) |
| C(11) | 200(20) | 13160(20) | 6144(14) | 55(4) |
| C(12) | 7479(19) | 14518(16) | 10593(10) | 37(3) |
| C(13) | 9476(17) | 13510(13) | 10492(11) | 29(3) |
| C(14) | 10740(20) | 13743(18) | 11362(12) | 44(4) |
| C(15) | 10820(30) | 15030(20) | 12975(16) | 77(6) |
| C(16) | 9440(30) | 16420(20) | 13695(18) | 93(7) |

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# LIST OF PUBLICATIONS

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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
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D. Basavaiah, **T. Satyanarayana**, B. Devender and K. R. Reddy (*manuscript under preparation*).