APPLICATION OF BAYLIS-HILLMAN ACETATES: STUDIES TOWARDS DEVELOPMENT OF STRATEGIES FOR SYNTHESIS OF SUBSTITUTED INDENES, [1,2,3]-TRIAZOLO-[1,4]-BENZOXAZONINES AND PYRIMIDIN-4(3*H*)-ONES

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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

MARCH, 2012 **BHAVANAM SEKHARA REDDY**

CERTIFICATE

Certified that the work embodied in this thesis entitled "**Application of Baylis-Hillman Acetates: Studies Towards Development of Strategies for Synthesis of Substituted Indenes, [1,2,3]-Triazolo-[1,4]-benzoxazonines and Pyrimidin-4(3*H*)-ones**" has been carried out by **Mr. Bhavanam Sekhara Reddy** under my supervision and the same has not been submitted elsewhere for a degree.

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B. Sekhara Reddy

ABBREVIATIONS

Ac	acetyl
AcOH	acetic acid
aq.	aqueous
Ar	aryl
Bn	benzyl
Boc	*tert*-butoxycarbonyl
Bs	benzenesulfonyl
Bu	*n*-butyl
^{t}Bu or Bu^{t}	*tert*-butyl
cat.	catalyst
Cbz	benzyloxycarbonyl
Conc.	concentrated
m-CPBA	*meta*-chloroperbenzoic acid
CRF	corticotropin-releasing factor
DABCO	1,4-diazabicyclo(2.2.2)octane
DABOs	dihydroalkoxybenzyloxopyrimidines
DBU	1,8-diazabicyclo(5.4.0)undec-7-ene
DCE	1,2-dichloroethane
DCM	dichloromethane
de	diastereomeric excesses
DMAP	dimethylaminopyridine
DMF	*N*,*N*-dimethylformamide

DMSO	dimethyl sulfoxide
dr	diastereomeric ratio
ee	enantiomeric excesses
Eq.	equation
eq.	equivalent(s)
Et	ethyl
EWG	electron withdrawing group
Hex	hexyl
HMT	hexamethylenetetramine
3-HQD	3-hydroxyquinuclidine
HIV	Human immunodeficiency virus
LAH	lithium aluminum hydride
LDA	lithium diisopropylamide
Me	methyl
Mp	melting point
Ms	mesyl
MVK	methyl vinyl ketone
MW	microwave
NHC	*N*-heterocyclic carbene
NMP	*N*-methyl 2-pyrrolidinone
NPth	phthalimide
Nu	nucleophile
ORTEP	Oak Ridge Thermal Ellipsoid Plot
PEG	poly ethyleneglycol

Pg	protecting group
Ph	phenyl
PIFA	phenyliodine(III) bis(trifluoroacetate)
PMP	*p*-methoxyphenyl
^{i}Pr	*iso*-propyl
Pr	propyl
PTA	1,3,5-triaza-7-phosphaadamantane
QS	quaternary salt
rt	room temperature
SES	2-trimethylsilylethanesulfonyl
TBAB	tetrabutylammonium bromide
TBAF	tetrabutylammonium fluoride
TBDMS/TBS	*tert*-butyldimethylsilyl
Tf	trifluoromethanesulfonyl
TFA	trifluoroacetic acid
TFAA	trifluoroacetic anhydride
TFSA	trifluoromethanesulfonic acid
THF	tetrahydrofuran
TMEDA	tetramethylethylenediamine
TMG	1,1,3,3-tetramethylguanidine
TMPDA	1,1,3,3-tetramethylpropane-1,3-diamine
TMS	trimethylsilyl
Tol	*p*-tolyl
Ts	*p*-toluenesulfonyl

ABSTRACT

Construction of C-C bonds is the fundamental reaction in organic chemistry. Functional groups play a crucial role in organic synthesis as it depends mostly on the functional group transformations. Therefore it will be interesting and challenging to develop reactions which should involve C-C bond formation leading to the production of densely functionalized molecules. Baylis-Hillman reaction is one such reaction developed in recent years.[1-9] It is a three component C-C bond forming reaction and provides diverse classes of densely functionalized molecules *via* the coupling of α-position of activated alkene with electrophile under the catalytic conditions. Our research group has been working for last 28 years on various aspects of Baylis-Hillman reaction with main aim of developing this reaction as a powerful synthetic tool in organic chemistry.

This thesis deals with the applications of the Baylis-Hillman adducts in synthesis of carbocyclic and heterocyclic molecules and is divided into three chapters 1) Introduction 2) Objectives, Results & Discussion and 3) Experimental. The first chapter, *i.e.* Introduction describes a brief account of literature on the development of the reaction and on the applications of the Baylis-Hillman adducts for synthesis of various valuable carbocyclic and heterocyclic compounds with an emphasis on recent developments.

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

1) To use the Baylis-Hillman adducts as probes in understanding the chemoselectivity in the intramolecular Friedel-Crafts reaction of substrates containing keto and ester functionalities in a similar environment and subsequently use this chemoselective cyclization methodology in developing a facile protocol for synthesis of functionalized indene derivatives.
2) To use the Baylis-Hillman acetates for construction of [1,2,3]-triazolo-[1,4]-benzoxazonine system employing Huisgen reaction (Click reaction) for construction of 9-membered ring.
3) To develop a simple methodology for synthesis of 2,5,6-trisubstituted pyrimidin-4(3*H*)-one derivatives from Baylis-Hillman acetates.

Towards developing the Baylis-Hillman adducts as probes in understanding the chemoselectivity in the intramolecular Friedel-Crafts reaction of substrates containing keto and ester functionalities: Development of a facile methodology for synthesis of functionalized indene derivatives

Intramolecular Friedel-Crafts reaction is an important and useful reaction for obtaining various classes of both carbocyclic and heterocyclic molecules. In these reactions, usually the functional groups such as ketones, esters/acids/acid chlorides and nitriles are used for intramolecular Friedel-Crafts reaction with aromatic ring. It will be highly interesting to examine the competition for cyclization between nitrile and ester, nitrile and keto, ester and keto groups with aromatic ring in a substrate containing such two or three groups in a similar environment.

In this direction we have selected alkyl 4-alkoxycarbonyl-3-aryl-2-methylene-5-oxohexanoate (**92**), molecules containing one keto group and two ester groups in

similar environment, for intramolecular Friedel-Crafts cyclization with aromatic ring. In principle there are three possible cyclizations in this case to produce three types of compounds **93**, **93A** & **93B** (Scheme 51).

When we examined the intramolecular Friedel-Crafts cyclization of substrate containing unsubstituted aromatic ring (**92a**, R = H, R' = R" = Me) the expected ring formation did not occur under various conditions (Scheme 53). At this stage it occurred to us that the substrate containing electron donating group on the aromatic ring may facilitate the intramolecular Friedel-Crafts cyclization. Accordingly such a compound (**92b**, R = 3-OMe, R' = R" = Me) was prepared and subjected for intramolecular Friedel-Crafts cyclization. In this direction the best results were obtained when the substrate was treated with $TiCl_4$ at room temperature (addition at 0 ^oC) thus providing the desired indene in 96% [*para* cyclized product (**93b**) 76% and *ortho* cyclized product (***ortho*-93b**) 20% yield] (Table 1). The generality of this strategy was demonstrated by selecting various acetates (**94c-k**) of the BH-alcohols (**95c-k**) derived from aromatic aldehydes (**96b-f**), having appropriate electron donating groups (Scheme 56 & 59). The resulting indenes (**93c-o** & ***ortho*-93k-o**) were obtained in excellent yields (Table 4 & Table 7). In some cases we have also obtained the *ortho*-directed Friedel-Crafts cyclized products (***ortho*-93k-o,** Table 7).

From these studies it is clear that ketone takes part exclusively in the Friedel-Crafts cyclization in preference over ester function even in the presence of two ester functionalities.

Development of a simple protocol for synthesis of [1,2,3]-triazolo-[1,4]-benzoxazonine derivatives from the Baylis-Hillman acetates

[1,2,3]-Triazole framework has attracted attention of synthetic chemists in recent years as this skeleton is present in many bioactive molecules (Figure 7). Therefore there has been increasing interest in the synthesis of [1,4]-oxazo cyclic systems containing 6/7/8-membered cyclic systems (**A, B, & C**) (Figure 8) fused with [1,2,3]-triazole framework. However there is not much literature available for synthesis of [1,2,3]-triazolo-[1,4]-oxazonine (**D**) systems (Figures 8 & 9).

We have developed a simple methodology for synthesis of [1,2,3]-triazolo-[1,4]-benzoxazonine derivatives (**114a-i**) starting from Baylis-Hillman acetates (**116a-i**). The strategy involves the preparation of azido-alkynes by treatment of Baylis-Hillman acetates (**116a-i**) with sodium azide. The resulting azido-alkynes obtained (after aqueous work-up) were successfully transformed into [1,4]-benzoxazonine ring fused with triazole derivatives (**114a-i**) in moderate to high yields by heating in toluene under reflux (Scheme 70 & Table 13).

Development of a simple methodology for synthesis of tri-substituted pyrimidin-4(3*H*)-one derivatives from Baylis-Hillman acetates

Pyrimidin-4(3*H*)-one skeleton is yet an important framework present in various pharmacologically active compounds (Figure 10). Due to their remarkable biological activities there has been increasing interest in the synthesis of pyrimidin-4(3*H*)-one derivatives. It is interesting to note that there is no report on the synthesis of 2,5,6-trisubstituted pyrimidin-4(3*H*)-one derivatives using Baylis-Hillman acetates.

We have therefore undertaken this task and developed a facile methodology for synthesis of pyrimidin-4(3*H*)-one derivatives (**133a-l**) from Baylis-Hillman acetates (**94a-d, 94g, 94h, 94l-q**) in one-pot operation (Scheme 77, Eq.34 and Table 15). Treatment of the *in situ* generated quaternary salt (**QS**), obtained *via* the reaction of Baylis-Hillman acetates (**94a-d, 94g, 94h, 94l-q**) with DABCO, with benzamidine hydrochloride in refluxing ethanol produced pyrimidin-4(3*H*)-one derivatives (**133a-l**) in high yields.

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

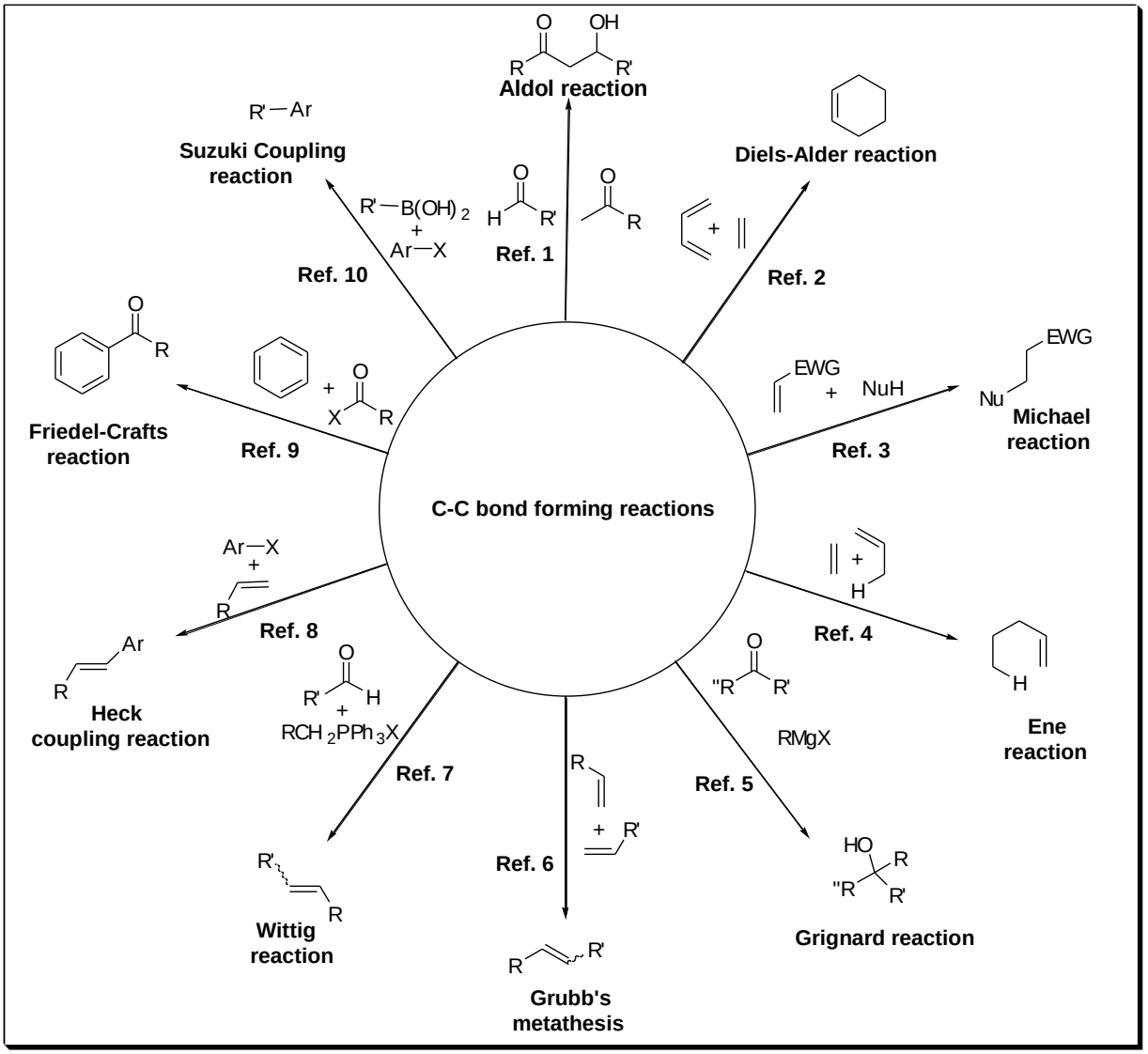
CONTENTS

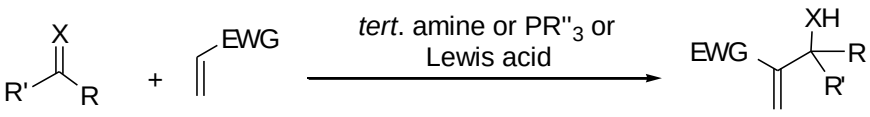
Introduction

Organic chemistry is one of the most successful branches of science addressing human well-being. In fact organic chemistry is like an ocean and provides un-ending source of inspiration and generates un-ending opportunities for research in both fundamental and applied aspects. Construction of C-C bonds is the most fundamental reaction in organic chemistry. Many C-C bond forming reactions have been discovered during the last several decades and their applications have been well documented in the literature. Some of the most important C-C bond forming reactions are aldol reaction,[1] Diels-Alder reaction,[2] Michael reaction,[3] Ene reaction[4] (atom economy reactions) and Grignard reaction,[5] Grubb's metathesis,[6] Wittig reaction,[7] Heck reaction,[8] Friedel-Crafts reaction[9] and Suzuki coupling[10] (non-atom economy reactions) *etc*. (Figure 1).

Functional groups play a crucial role in organic chemistry and organic synthesis depends mostly on the functional group transformations. The key functional groups in organic chemistry are carbonyl (ketone, aldehyde, acid, ester, amide etc.), nitrile, hydroxyl, amine, alkene, alkyne. Therefore it will be interesting and challenging to develop reactions which involve C-C bond formation leading to the production of densely functionalized molecules. Baylis-Hillman reaction[11,12] is one such reaction developed in recent years. It is a three component C-C bond forming reaction and provides diverse classes of densely functionalized molecules *via* the coupling of α-position of activated alkene with electrophile under the influence of a catalyst (Eq. 1). It is worth mentioning here that Rauhut and Currier[13] in the year 1963 and Morita[14a,b] in the year 1968 reported similar reactions even before Baylis and Hillman.

Figure 1





Eq. 1

R = alkyl, aryl, heteroaryl
R' = H, COOR, alkyl; R'' = alkyl, aryl
EWG = electron withdrawing group : CHO, COR, COOR, CN, $CONR_2$
SO_3Ph, $PO(OEt)_2$, etc.
X = O, NTs, $NP(=O)R_2$, NCOOR etc.

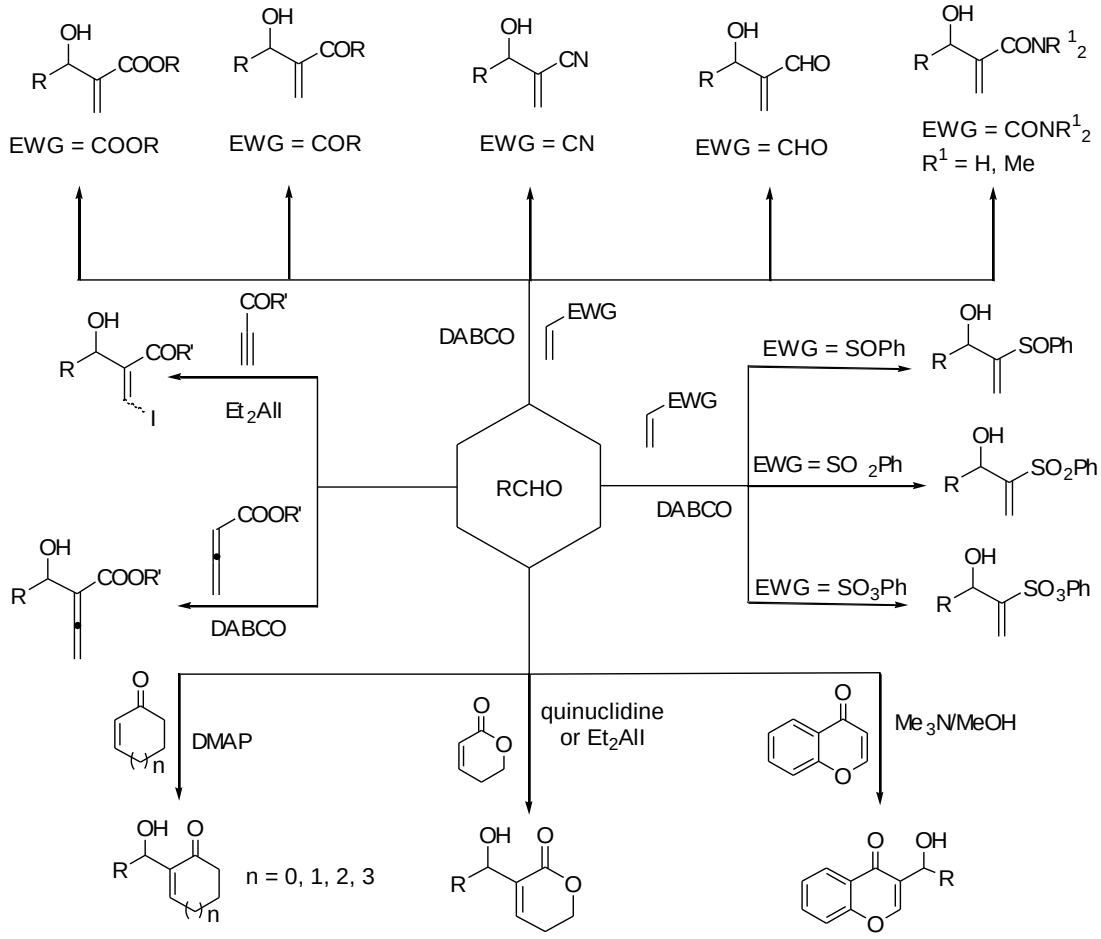
The important features of this reaction are i) It creates a carbon-carbon bond ii) It is an atom economy reaction iii) It generates a chiral center in the resulting adducts iv) It provides multi functional molecules v) It is an organo catalytic reaction (in the case of *tert*-amine or trialkyl/arylphosphine catalysts). During the last three decades the reaction has grown from a un-known patent level to the level of high synthetic popularity as evidenced by the publication of large number of research papers (more than 2000), several major[15-21] and mini reviews.[22-26] Since the thesis deals with the applications of the Baylis-Hillman adducts this section briefly describes the developments of Baylis-Hillman reaction with respect to all the three essential components and applications of the Baylis-Hillman adducts in organic synthesis.

Baylis-Hillman reaction

Activated alkenes/alkynes and cyclic activated alkenes[15-21]

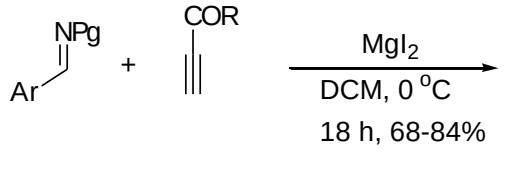
A large number of activated alkenes (alkynes) have been employed for coupling with different electrophiles to provide densely functionalized molecules (Figure 2).[15-21] Some of the recent and important developments are described in Eq. 2 & Scheme 1-4.

Figure 2



Recent developments

Stereoselective synthesis of β-iodo Baylis-Hillman adducts (**1**) *via* treatment of acetylenic esters/ketones with *N*-protected imines in the presence of magnesium iodide was reported by Li and co-workers (Eq. 2).[27]



Eq. 2

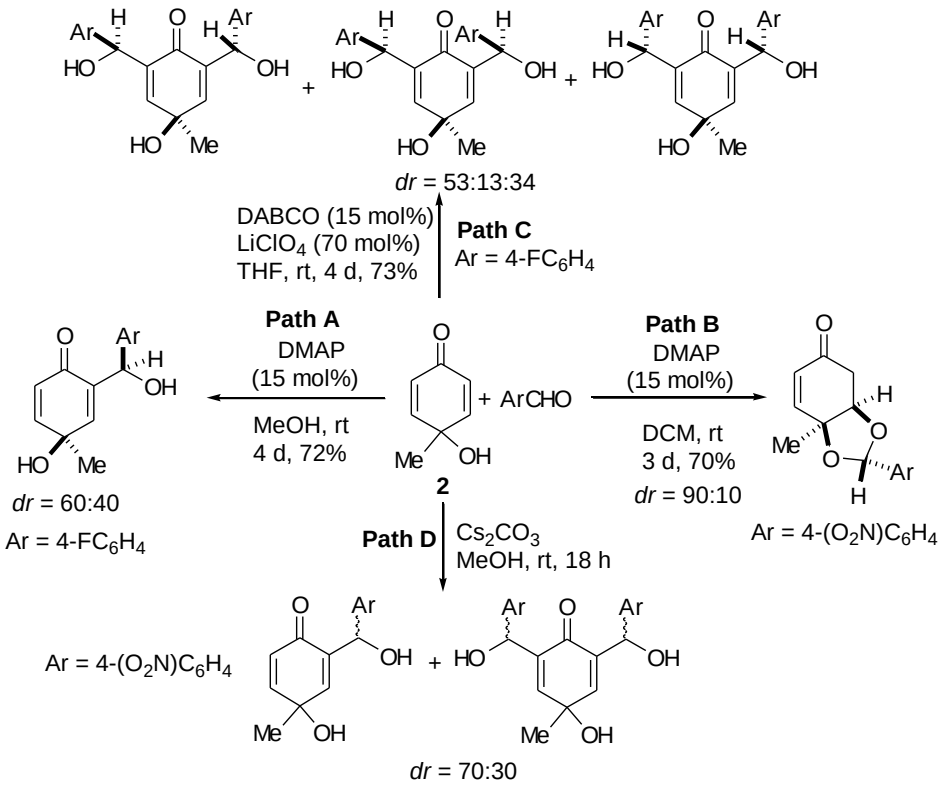
1

Ar = C_6H_5, 4-MeC_6H_4, 4-$(MeO)C_6H_4$, 3-$(BnO)C_6H_4$, 4-FC_6H_4, 4-ClC_6H_4, Fur-2-yl, Thiophen-2-yl
R = Me,OMe, OEt
Pg = Ts, Ms, Bs

Z:E =17:1 to 20:1

Redondo and co-workers[28] have for the first time reported *p*-methylquinol (**2**) as an activated alkene for coupling with various aromatic aldehydes under Baylis-Hillman reaction conditions. In these studies when DMAP is used as a catalyst they observed that protic solvents (MeOH) gave mono Baylis-Hillman adduct (Path A) and the aprotic solvents (DCM) provided ketal derivatives (Path B). The presence of $LiClO_4$ as an additive (along with DABCO as catalyst) provided double Baylis-Hillman adducts (Path C). Non-nucleophilic base (Cs_2CO_3) provided both mono and di-Baylis-Hillman adducts (Path D). One example for each class is presented in Scheme 1.

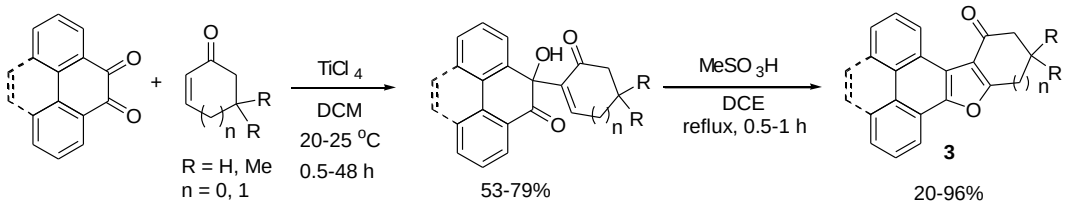
Scheme 1



Recently our research group[29] has reported the Baylis-Hillman reaction between aromatic cyclic 1,2-diones and cycloalk-2-enones under the influence of $TiCl_4$. The resulting Baylis-Hillman adducts were conveniently transformed into pentacyclic and

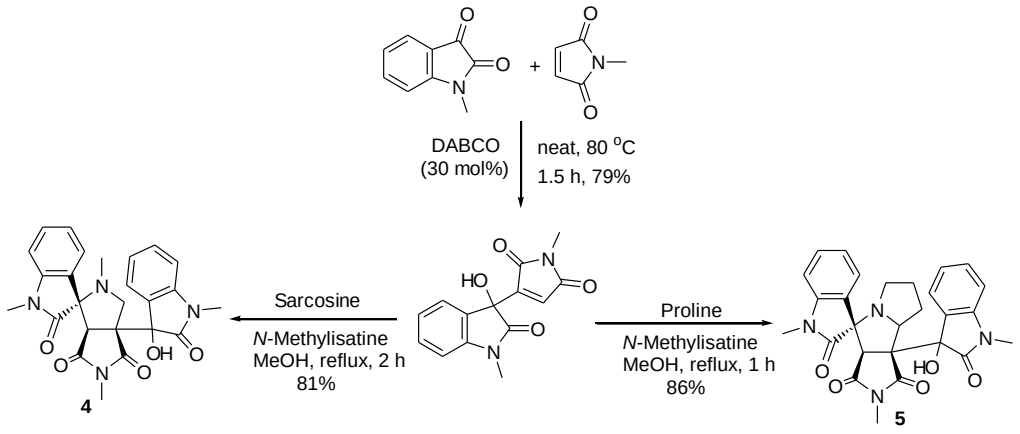
hexacyclic fused furan derivatives (**3**) by treatment with methanesulfonic acid (Scheme 2).

Scheme 2



Perumal and co-workers[30] have used *N*-methylmaleimide as an activated alkene for coupling with isatin derivatives. The Baylis–Hillman adducts thus obtained were subsequently converted into various spiropyrrolidines (**4**) and spiropyrrolizidines (**5**) stereoselectively through an intermolecular 1,3-dipolar cycloaddition with azomethine ylides generated from sarcosine and proline respectively. One representative example for each class is shown in Scheme 3.

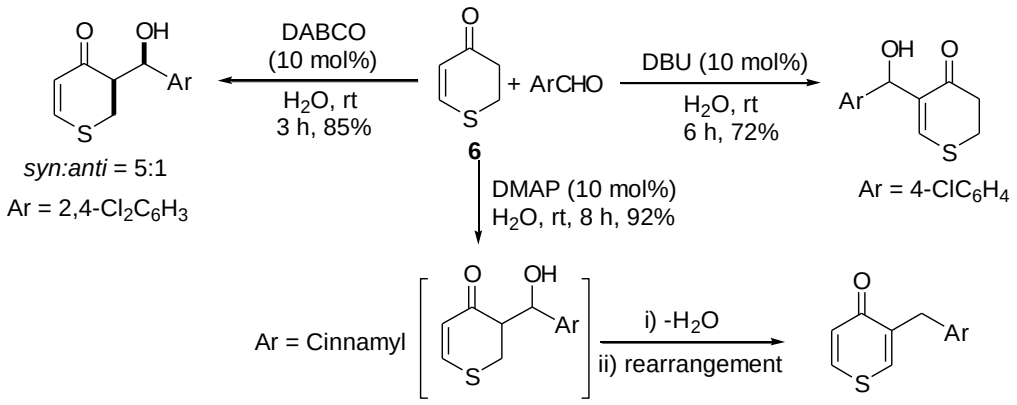
Scheme 3



Abaee and co-workers[31] used dihydrothiopyran-4-one (**6**) as an activated alkene for Baylis-Hillman reaction with aldehydes. In aqueous medium DBU provided the Baylis-Hillman adducts while DABCO and DMAP gave the aldol products. In the case of DMAP the resulting aldol product further underwent dehydration and isomerization to

provide 3-arylmethyl-4*H*-thiopyran-4-one derivatives. One example for each class is presented in Scheme 4.

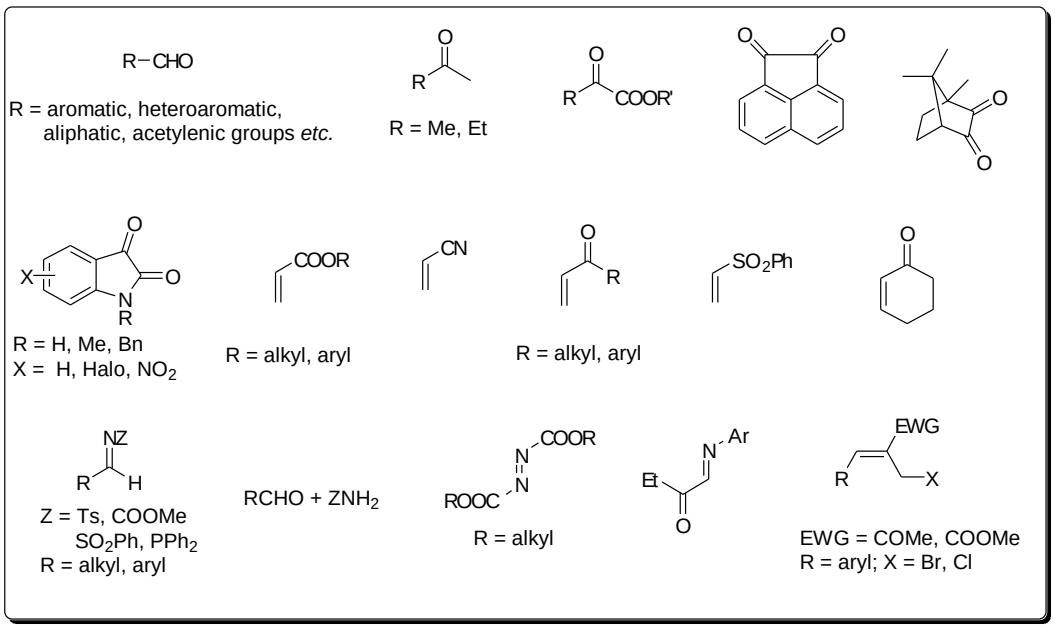
Scheme 4



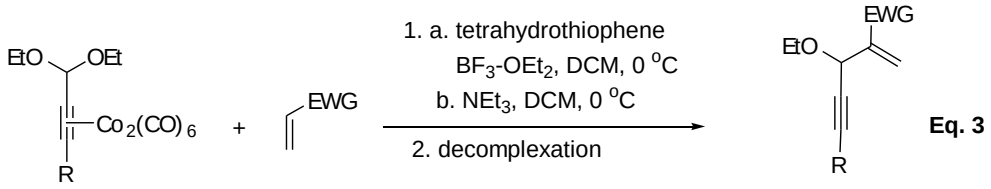
Electrophiles

A number of electrophiles have been systematically employed for coupling with various activated alkenes to provide a variety of densely functionalized molecules (Figure 3).[15-21] Selected represented examples are described in Eq. 3-5 & Scheme 5.

Figure 3

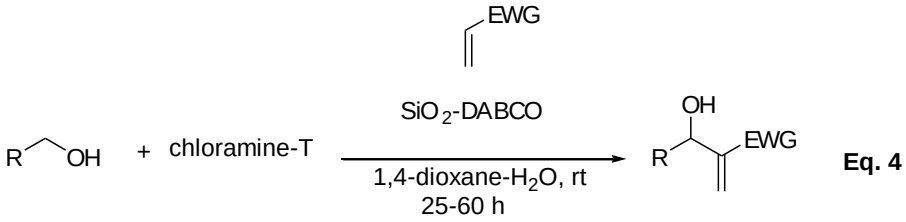


Krafft and co-workers[32] have used acetylenic acetals (**7**), complexed with dicobalthexacarbonyl, as the electrophiles for Baylis-Hillman reaction with various activated alkenes under the catalytic influence of BF_3-OEt_2 and tetrahydrothiophene system (Eq. 3).



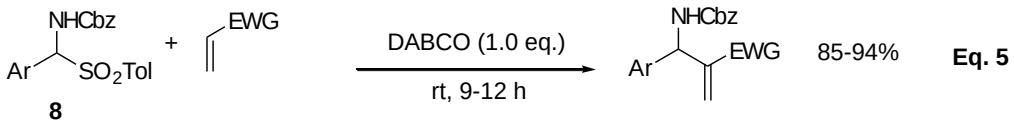
R = C_6H_5, 4-$(O_2N)C_6H_4$, Me, Et, ^nPr
EWG = COMe, COEt, COPh

Yadav and co-workers[33] have reported alcohols as substrates (*via in situ* oxidation with chloramine-T) for Baylis–Hillman reaction with acrylonitrile/methyl acrylate under the catalytic influence of silica gel-DABCO (Eq. 4).



R = C_6H_5, 4-BrC_6H_4, 4-$(MeO)C_6H_4$, 3-$(O_2N)C_6H_4$, 4-ClC_6H_4, $PhCH_2CH_2$, Fur-2-yl, Et, ^{n}Pent
EWG = CO_2Me, CN

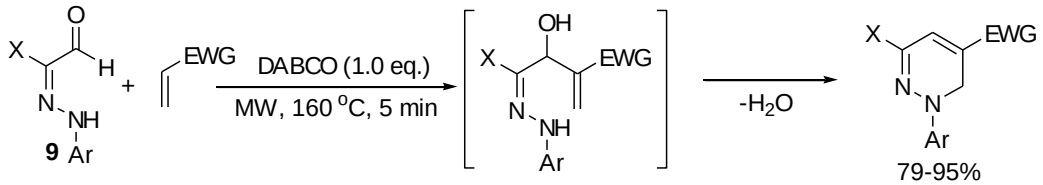
Recently Das and co-workers[34] have used *α*-aminosulfones as electrophiles (**8**) for coupling with alkyl acrylates in the presence of DABCO to produce β-amino esters (Eq. 5).



Ar = C_6H_5, 4-MeC_6H_4, 4-$^iPrC_6H_4$, 4-ClC_6H_4, 4-$(MeO)C_6H_4$, 3-$(O_2N)C_6H_4$, 4-$(O_2N)C_6H_4$, Naphth-2-yl, 3,4-$(MeO)_2C_6H_3$, 3,4,5-$(MeO)_3C_6H_2$, Fur-2-yl, Thiophen-2-yl, Vanilyl
EWG = COOMe, COOEt

Awadi and co-workers[35] have employed arylhydrazonals (**9**) for coupling with acrylonitrile or methyl vinyl ketone under the influence of DABCO to provide dihydropyridazine derivatives (Scheme 5).

Scheme 5

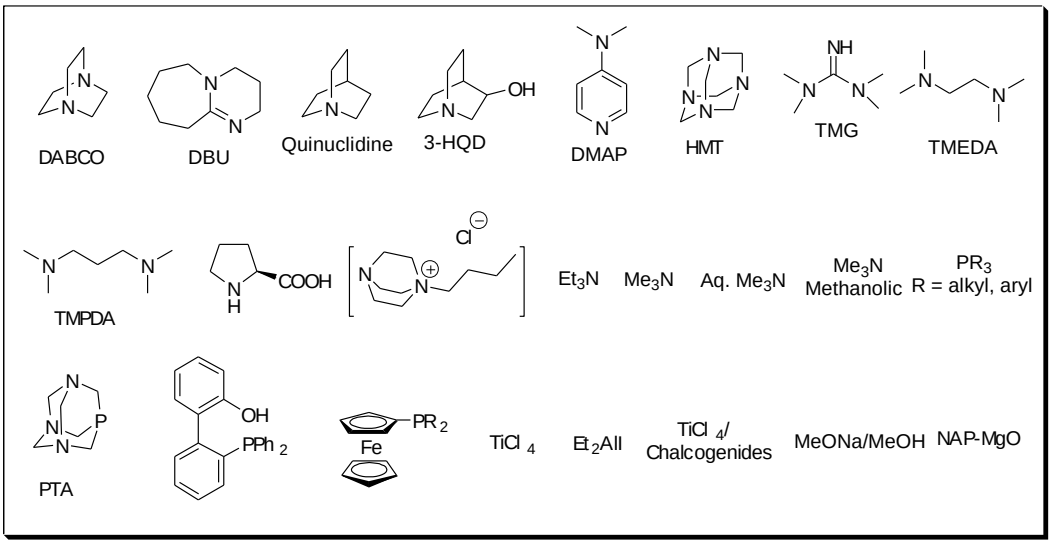


X = COC_6H_5, $CO(4\text{-}ClC_6H_4)$, COOEt, Thiophene-2-carbonyl, Furan-2-carbonyl
Ar = C_6H_5, $4\text{-}MeC_6H_4$, $4\text{-}ClC_6H_4$
EWG = CN, COMe

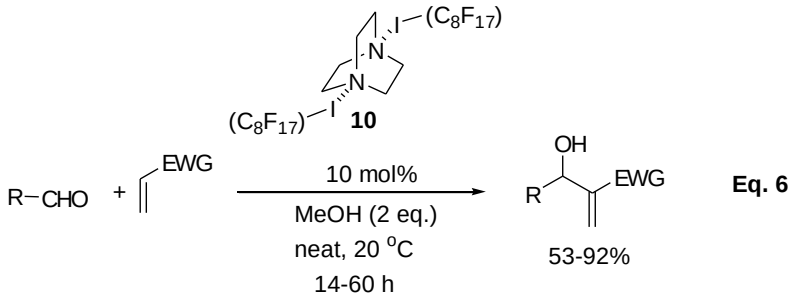
Catalysts/ Catalytic systems

Various amine and non-amine derivatives have been employed as catalysts for Baylis-Hillman reaction (Figure 4).[15-21] Recent developments have been described in Eq. 6-9 & Scheme 6.

Figure 4



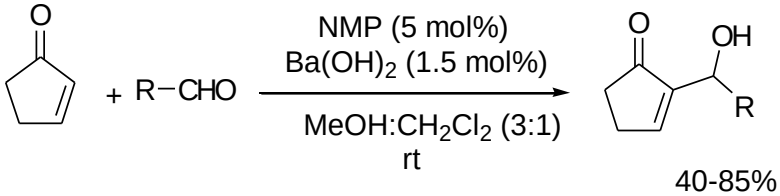
Legros and co-workers[36] have employed fluorous tagged DABCO [DABCO-$(C_8F_{17}I)_2$] (**10**), as an efficient organocatalyst for the Baylis-Hillman reaction. The main advantage of this catalyst is its recoverability by filtration (Eq. 6).



Eq. 6

R = C_6H_5, 3-$(O_2N)C_6H_4$, 4-$(O_2N)C_6H_4$, 4-ClC_6H_4, Fur-2-yl, 2,4-$Cl_2C_6H_3$
EWG = CO_2Me, COMe, CN

Guerra and Afonso[37] have studied the application of NMP/$Ba(OH)_2$ as a catalytic system for performing the Baylis-Hillman reaction between 2-cyclopenten-1-one and various aromatic / aliphatic aldehydes (Eq. 7).

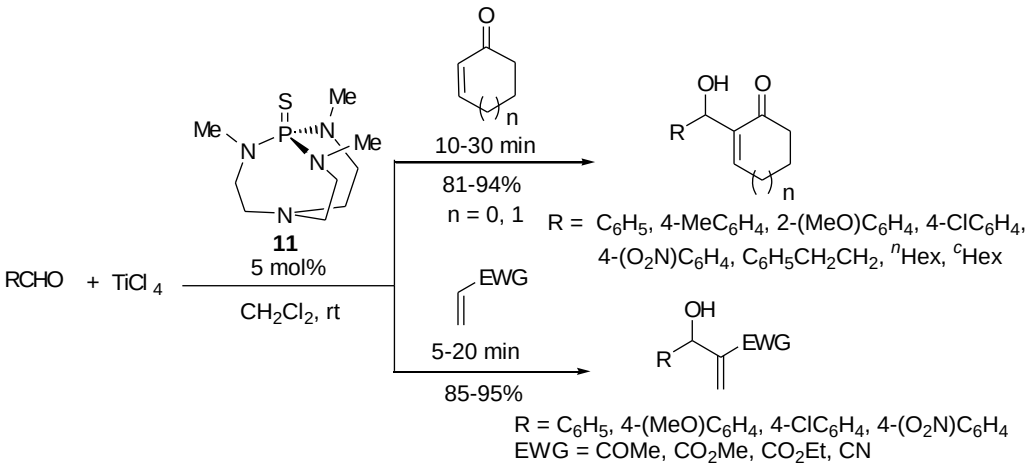


Eq. 7

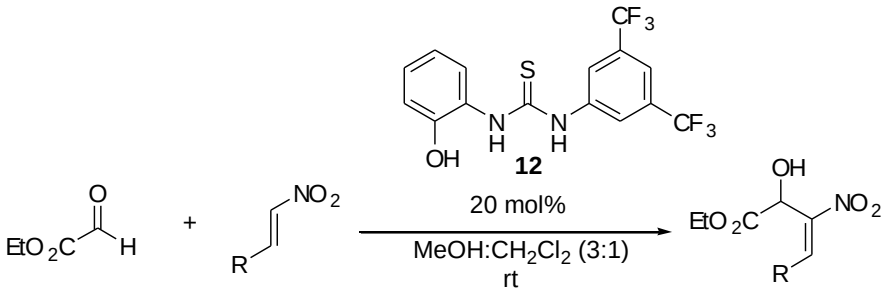
R = C_6H_5, 4-$(MeO)C_6H_4$, 4-$(O_2N)C_6H_4$, Fur-2-yl, Naphth-2-yl, Me, Et

Verkade and co-workers[38] have used proazaphosphatrane sulfide (**11**) as an efficient catalyst in the Baylis-Hillman coupling of various aromatic / aliphatic aldehydes with acrylates, cyclic/acyclic alkyl vinyl ketones, and acrylonitrile in the presence of $TiCl_4$. The resulting BH adducts were obtained in excellent yields in short interval of time (Scheme 6).

Scheme 6



Chen and co-workers[39] have studied the application of thioureas (**12**) as co-catalysts for coupling of nitroalkenes with ethyl glyoxylate in the presence of DMAP or imidazole to provide the resulting allyl alcohols in moderate to high yields (Eq. 8).

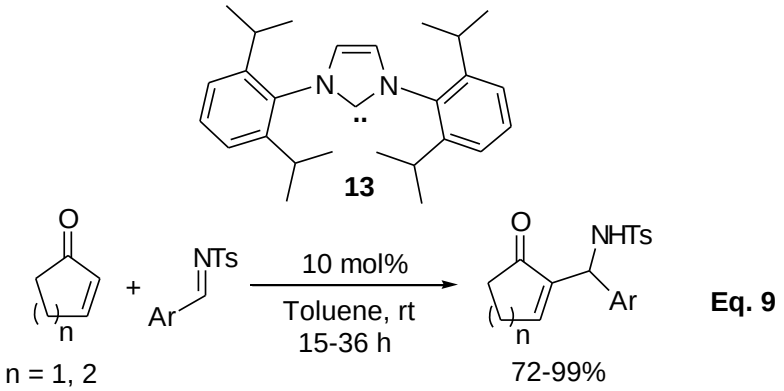


Eq. 8

cat.	cat. (mol%)	time (h)	yield (%)
DMAP, neat	20	0.5-1.5	56-92
Imidazole	100	1.0-12	35-88

R = C_6H_5, 2-(F_3C)C_6H_4, 3-(F_3C)C_6H_4, 3-ClC_6H_4, 4-ClC_6H_4, 2-BrC_6H_4, 3-BrC_6H_4, 4-BrC_6H_4, 4-MeC_6H_4, 2-(MeO)C_6H_4, 3-(MeO)C_6H_4, 4-(MeO)C_6H_4, Thiophen-2-yl, Fur-2-yl, Dihydrocinnamyl, ^{i}Bu

Ye and co-workers[40] have used *N*-heterocyclic carbenes (NHC) (**13**) as catalysts for performing Baylis-Hillman reaction between cyclic activated alkenes and *N*-tosylated imines. Representative examples are given in Eq. 9.



Ar = C_6H_5, 4-MeC_6H_4, 2-$(MeO)C_6H_4$, 3-$(MeO)C_6H_4$, 4-$(MeO)C_6H_4$, 4-FC_6H_4, 3-ClC_6H_4, 4-ClC_6H_4, 4-$(O_2N)C_6H_4$, Fur-2-yl

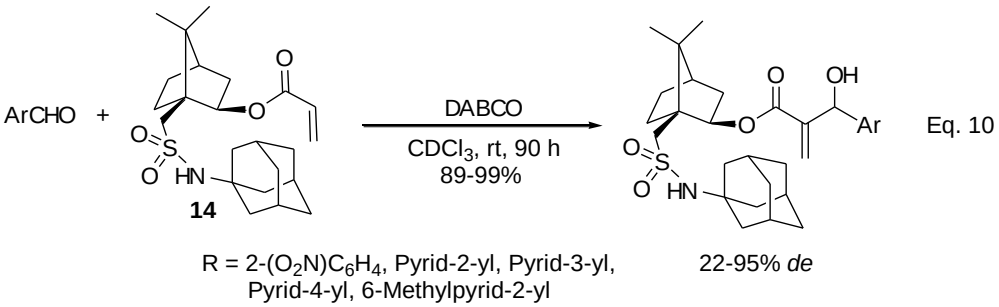
Asymmetric Baylis-Hillman reaction

The asymmetric Baylis-Hillman reaction can be in principle achieved using chiral activated alkenes, chiral electrophiles, chiral catalysts or a chiral medium and has attracted the attention of several leading research groups and significant developments have been achieved in this direction.[15-21] It is not possible to describe all these developments in this section, however selected examples with respective all the three essential components, chiral activated alkenes, chiral electrophiles, chiral catalysts and chiral medium were presented.

Recent developments

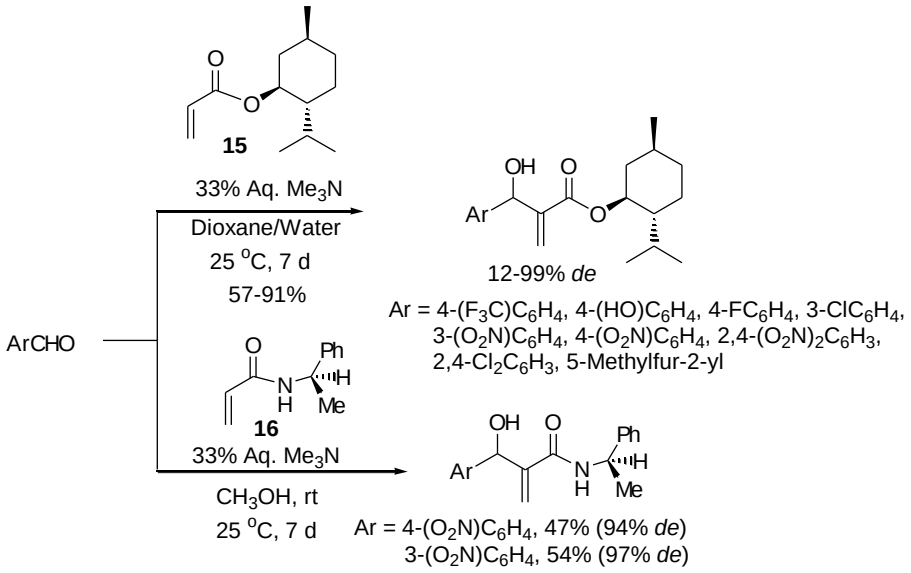
Chiral activated alkenes/alkynes

2-*exo*-Acryloyloxy-*N*-(1-adamantyl)bornane-10-sulfonamide (**14**) was used an activated alkene in Baylis-Hillman reaction with various aldehydes by Duggan and Kaye.[41] The resulting adducts were obtained in low to high diastereoselectivities (Eq 10).



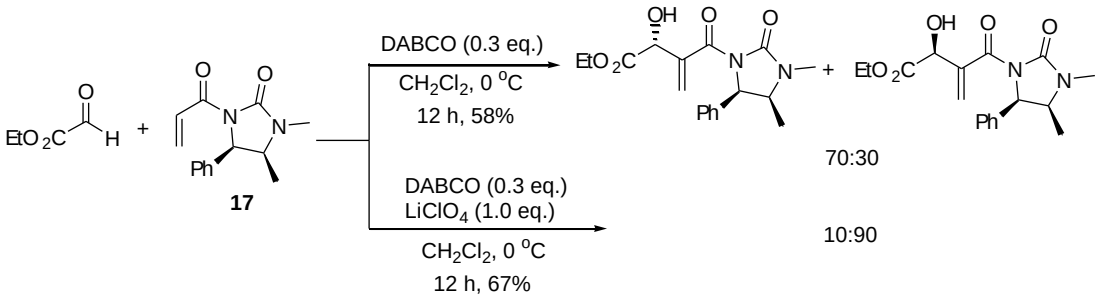
Zhou and co-workers[42,43] have used chiral acrylates, *L*-menthyl acrylate (**15**) (derived from (*L*)-menthol) and *α*-phenylethyl acrylamide (**16**) (derived from *α*-phenylethylamine) as chiral activated alkenes for the Baylis-Hillman reaction with various aromatic aldehydes under the influence of aq. trimethyl amine. The resulting Baylis-Hillman adducts were obtained in low to high diastereoselectivities (Scheme 7).

Scheme 7



Orena and co-workers[44] reported diastereoselective Baylis-Hillman reaction between the chiral acrylimide **17** and ethyl glyoxalate in the presence of DABCO (cat.). In these studies they have observed an interesting reversal of stereoselectivity of resulting adduct when they added $LiClO_4$. One such example is shown in Scheme 8.

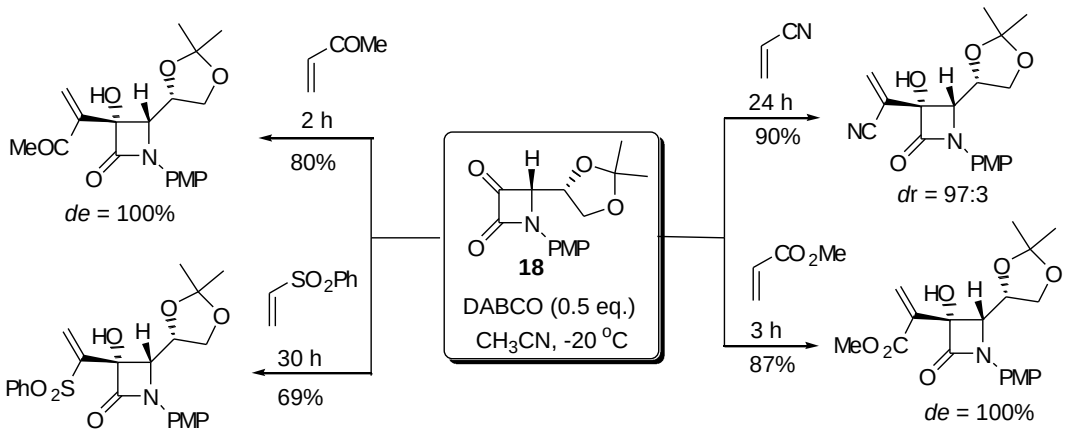
Scheme 8



Chiral electrophiles

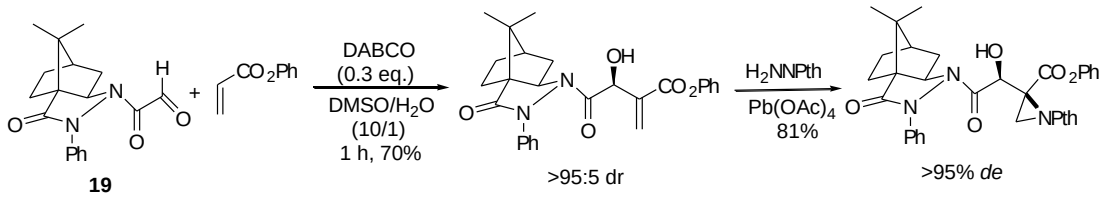
Highly substituted 3-hydroxy-β-lactams were synthesized by Alcaide and co-workers[45] *via* the coupling of chiral azetidine-2,3-diones (**18**) with various activated alkenes under the catalytic influence of DABCO. Representative examples are shown in Scheme 9.

Scheme 9

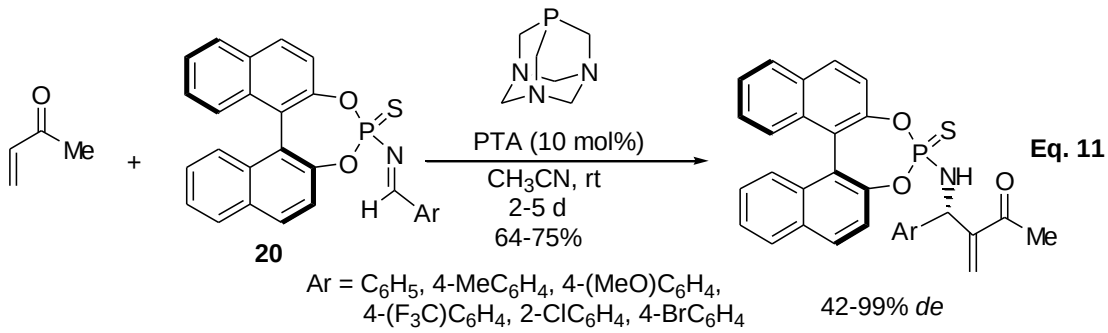


N-Glyoxyloylcamphorpyrazolidinone (**19**) was used as an electophile for coupling with various activated alkenes under the catalytic influence of DABCO to provide the resulting adducts in high diastereoselectives.[46] One such adduct is transformed into *N*-phthalimidoaziridine derivative by treatment with *N*-aminophthalimide (Scheme 10).

Scheme 10



An interesting Baylis-Hillman reaction between chiral thiophosphorylimines (**20**) and MVK under the catalytic influence of PTA was reported by Zhou and co-workers.[47] The resulting Baylis-Hillman adducts were obtained in moderate to high diastereoselectivities (Eq 11).

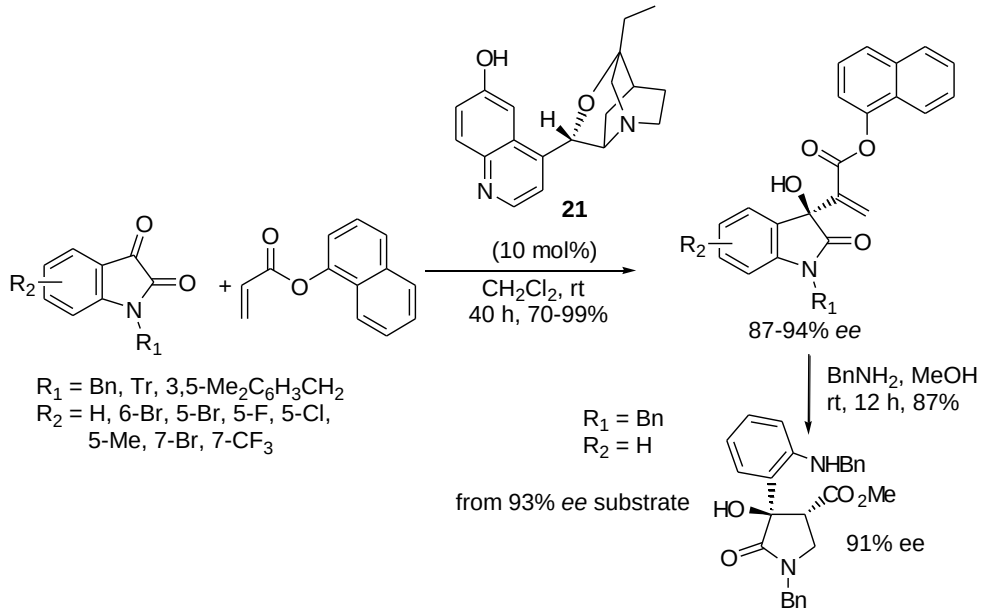


Eq. 11

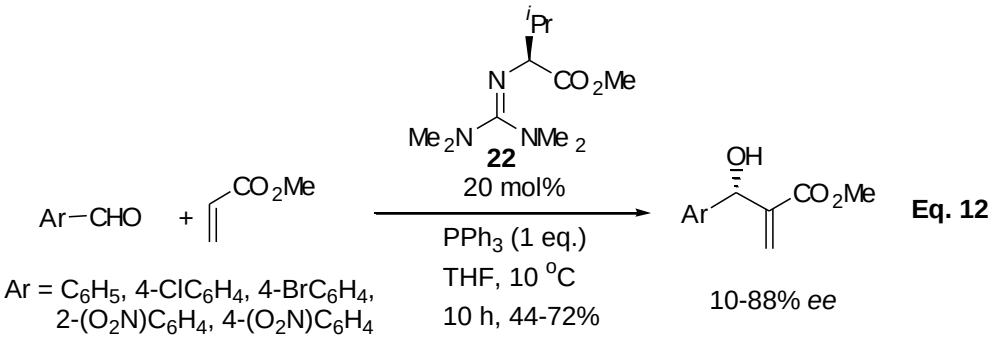
Chiral catalysts/ Catalytic systems

Shi and co-workers[48] reported the asymmetric Baylis-Hillman reaction of isatin derivatives with naphth-1-yl acrylate in the presence of 4-(3-ethyl-4-oxa-1-azatricyclo[4,4,0,$0^{3,8}$]dec-5-yl)quinolin-6-ol (**21**) as a chiral catalyst, to afford the resulting adducts containing quaternary stereogenic center with high enantioselectivities (Scheme 11). One of these oxindole derivatives was subsequently transformed into 3-aryl-3-hydroxypyrrolidin-2-one framework (precursors of promising drug candidates for the treatment of HIV-1 infection).

Scheme 11



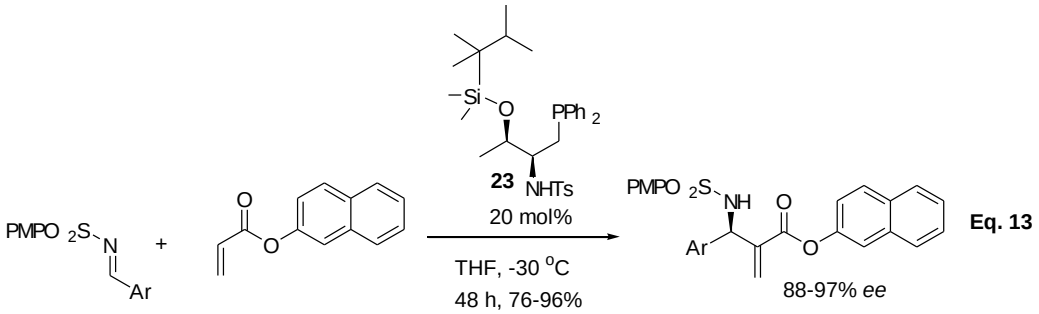
Liebscher and co-workers[49] have studied the applicability of combination of chiral guanidine (**22**) and triphenylphosphine as a novel dual catalytic system for performing asymmetric Baylis-Hillman reaction between aromatic aldehydes and methyl acrylate The resulting adducts were obtained in low to high enantioselectivities (up to 88%) (Eq. 12).



Eq. 12

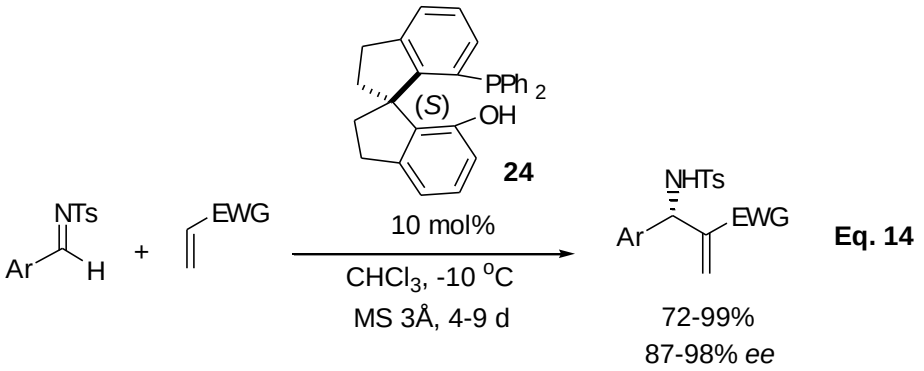
Lu and co-workers[50] have successfully used *L*-threonine-derived phosphine-sulfonamide (**23**), bifunctional catalyst for asymmetric Baylis-Hillman reaction of

various *N*-(*p*-methoxybenzenesulfonyl)imines with acrylates to provide the resulting adducts in high enantioselectivities up to 97% (Eq. 13).



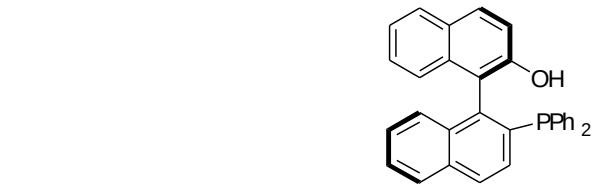
Ar = C_6H_5, 4-MeC_6H_4, 4-EtC_6H_4, 4-FC_6H_4, 4-BrC_6H_4, 4-ClC_6H_4, 4-$(F_3C)C_6H_4$, 4-$(O_2N)C_6H_4$, 3-MeC_6H_4, 3-ClC_6H_4, 2-$(F_3C)C_6H_4$, 2-FC_6H_4, 2-BrC_6H_4, 2-ClC_6H_4, Fur-2-yl, Thiophen-2-yl, Naphth-2-yl

Sasai and co-workers[51] have developed a new spiro-type bifunctional phosphine organocatalyst (**24**) for performing Baylis-Hillman reaction of aromatic aldehydes with alkyl vinyl ketones to provide the resultant adducts in excellent enantioselectivities (up to 98% ee) (Eq. 14).



Ar = 4-ClC_6H_4, 3-ClC_6H_4, 2-ClC_6H_4, 4-FC_6H_4, 4-BrC_6H_4, 4-$(NC)C_6H_4$, 3-$(NC)C_6H_4$, 2-$(NC)C_6H_4$, 4-$(O_2N)C_6H_4$, 3-$(O_2N)C_6H_4$, 2-$(O_2N)C_6H_4$
EWG = COMe, COEt

Shi and co-workers[52] have used *in situ* generated *N*-protected imines (generated from *N*-protected α-amidoalkyl phenyl sulfones or α-amidoalkyl *p*-tolyl sulfones) as elecrophiles under the mild reaction conditions for asymmetric Baylis-Hillman reaction with MVK under the catalytic influence of chiral phosphine (**25**) to yield the resultant adducts in high *ee* (Eq. 15).



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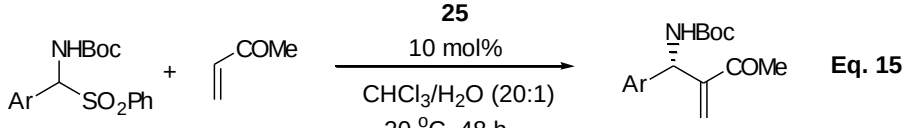
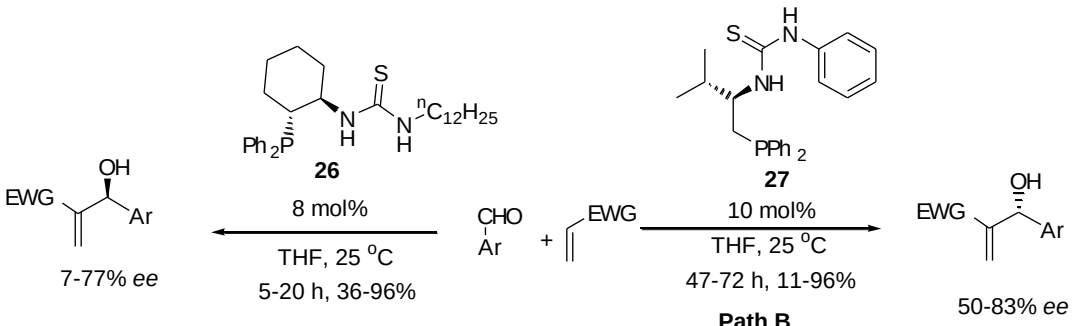


Eq. 15

Ar = 4-$(F_3C)C_6H_4$, 3-MeC_6H_4, 3-ClC_6H_4, 2-$(MeO)C_6H_4$, 2-ClC_6H_4, Fur-2-yl

Wu and co-workers[53] used various chiral bifunctional phosphinothiourea organocatalysts [obtained from (*R*,*R*)-2-amino-1-(diphenylphosphino)cyclohexane] (**26**) for the asymmetric Baylis-Hillman reaction between various aromatic aldehydes and acrylates. The resulting Baylis-Hillman adducts were obtained in good enantioselectivities (Path A, Scheme 12). Wu and co-workers[54] have also observed that chiral bifunctional phosphinothiourea derivatives (**27**) prepared from *L*-valine offered better selectivities in the Baylis-Hillman reaction of aromatic aldehydes with acrylates (Path B, Scheme 12).

Scheme 12



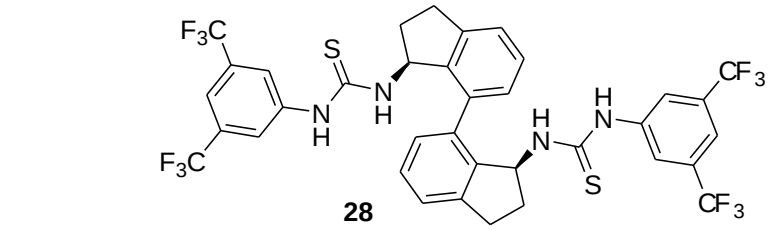
Ar = 2-$(O_2N)C_6H_4$, 3-$(O_2N)C_6H_4$, 4-$(O_2N)C_6H_4$, 4-$(F_3C)C_6H_4$, 4-ClC_6H_4, 2,4-$Cl_2C_6H_3$, 4-BrC_6H_4, Fur-2-yl

EWG = CO_2Et, CO_2Bu^n

Ar = C_6H_5, 2-$(O_2N)C_6H_4$, 3-$(O_2N)C_6H_4$, 4-$(O_2N)C_6H_4$, 4-$(F_3C)C_6H_4$, 4-BrC_6H_4

EWG = CO_2Me, CO_2Et, CO_2Bu^n

Ito and co-workers[55] have used chiral bis(thiourea) (**28**) and DABCO as catalytic system for Baylis-Hillman reaction of 2-cyclohexen-1-one with both aromatic and aliphatic aldehydes to produce the resulting adducts in 62-96% enantioselectivities (Eq. 16).



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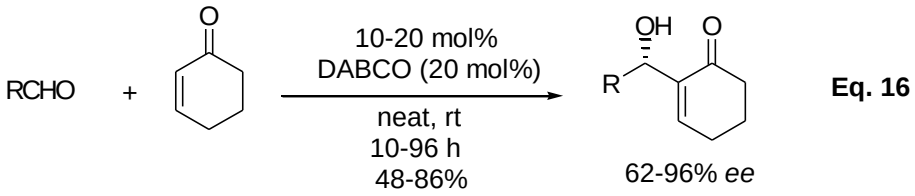


Eq. 16

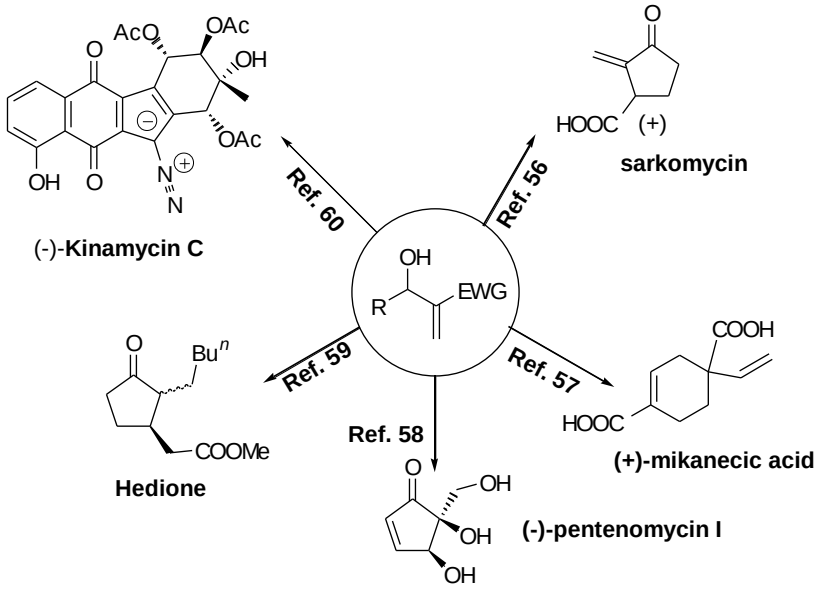
R = C_6H_5, 4-(MeO)C_6H_4, 4-FC_6H_4, 4-(O_2N)C_6H_4,
3-ClC_6H_4, 3-FC_6H_4, PhCH_2CH_2, ^{i}Pr, ^{n}Hex, ^{c}Hex

Applications of Baylis-Hillman adducts and their derivatives: Earlier developments

The Baylis-Hillman adducts contain a minimum of three functional groups in close proximity. In fact, this close proximity made these adducts very important substrates for many organic transformations as they can be tuned and manipulated with high degree of flexibility.[15-21] Thus various organic methodologies have been developed using Baylis-Hillman adducts as substrates.[15-21] These adducts have also been transformed into various carbocyclic & heterocyclic molecules of medicinal importance. These are pictorially presented in Figure 5 & 6. Since this thesis will deal with the transformation of Baylis-Hillman adducts into carbocyclic & heterocyclic molecules, some of recent and relevant literature reports related to transformations of BH adducts into carbocyclic & heterocyclic molecules are presented in this section.

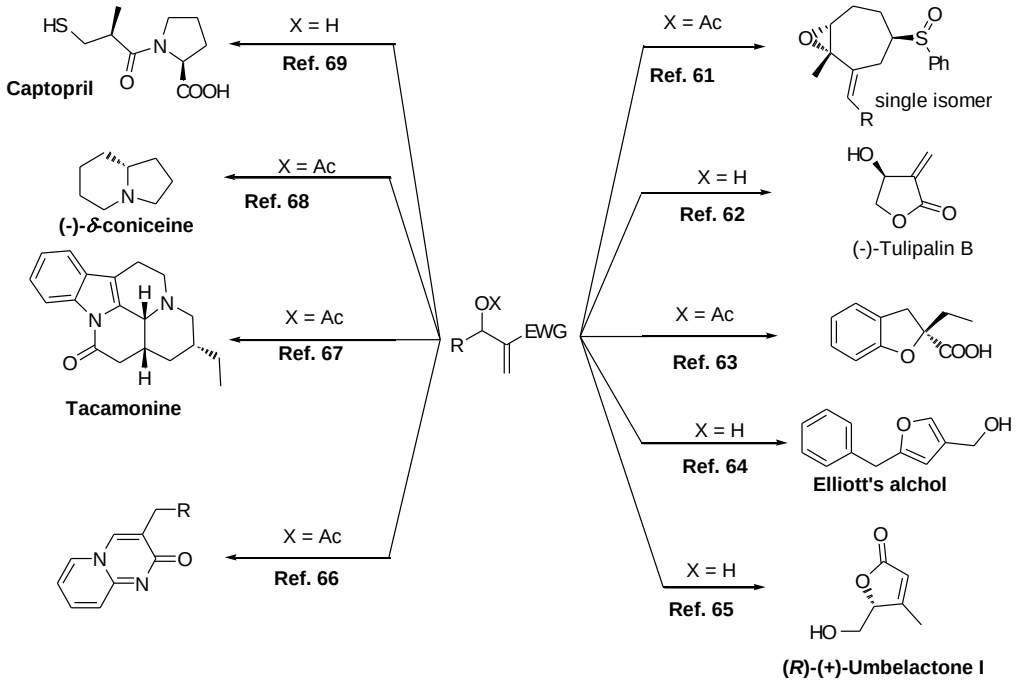
Synthesis of carbocyclic compounds from Baylis-Hillman adducts: Earlier reports

Figure 5



Synthesis of heterocyclic compounds from Baylis-Hillman adducts/ acetates: Earlier reports

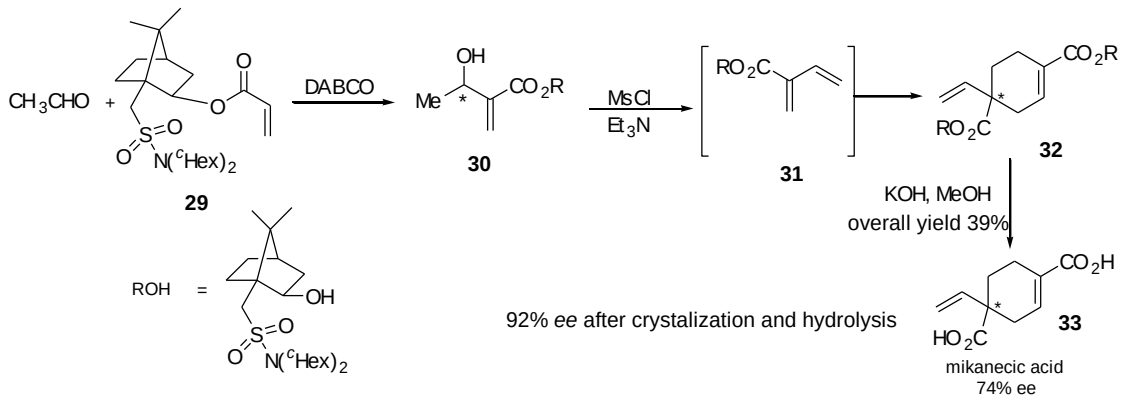
Figure 6



Carbocyclic compounds

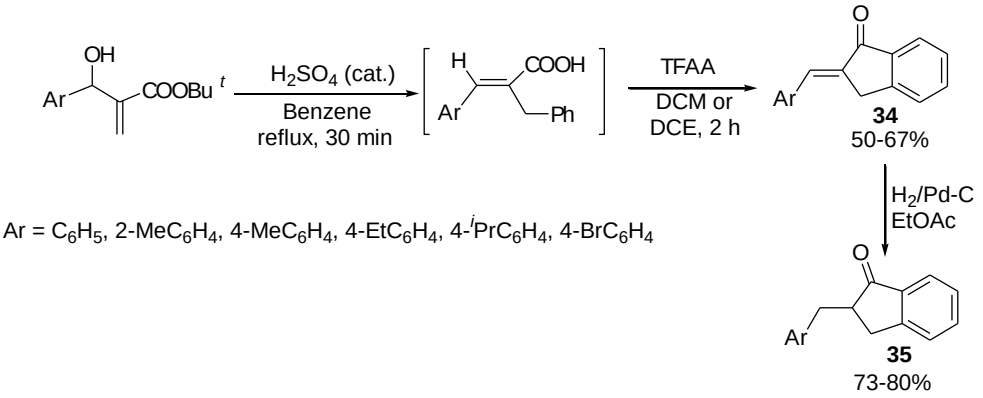
Our research group[70] has reported an interesting synthesis of enantiomerically enriched mikanecic acid (**33**), a terpene dicarboxylic acid having vinylic quarternary chiral center, from the Baylis-Hillman adduct (**30**) (derived from acetaldehyde and chiral acrylate, **29**). Thus, treatment of **30** with methanesulfonyl chloride provided the mikanecic acid (**33**) in 92% enantiomeric purity after crystallization and hydrolysis of the resulting diester **32**. This reaction is believed to proceed through the formation of the diene carboxylate **31**, which is not stable and underwent spontaneous Diels-Alder dimerization to provide the corresponding adduct **32** (Scheme 13).

Scheme 13



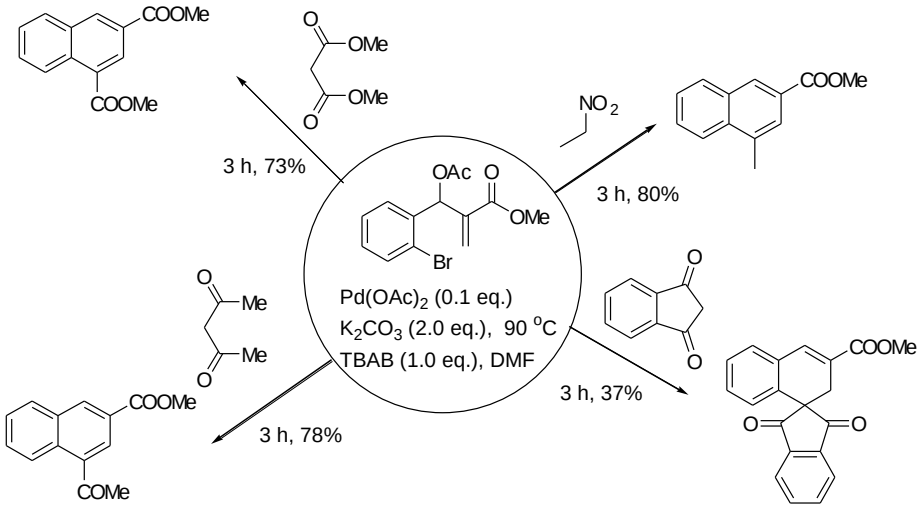
Our research group[71] has successfully transformed *tert*-butyl 3-aryl-3-hydroxy-2-methylenepropanoates, the Baylis-Hillman adducts obtained from *tert*-butyl acrylate and aromatic aldehydes, into (*E*)-2-arylideneindan-1-ones (**34**) *via* the one-pot procedure (simultaneously) involving one inter- and one intramolecular Friedel-Crafts reactions according to the Scheme 14. These compounds were further transformed into the corresponding 2-arylmethylindan-1-ones (**35**) *via* the catalytic hydrogenation in the presence of 5% Pd/C catalyst (Scheme 14).

Scheme 14



Kim and co-workers[72] have transformed acetate of the Baylis-Hillman alcohols (derived from 2-bromobenzaldehyde and methyl acrylate) into various carbocyclic and spiro carbocyclic molecules by treatment with 1,3-dicarbonyl compounds or nitroalkanes followed by intramolecular Heck strategy. Representative examples are given in Scheme 15.

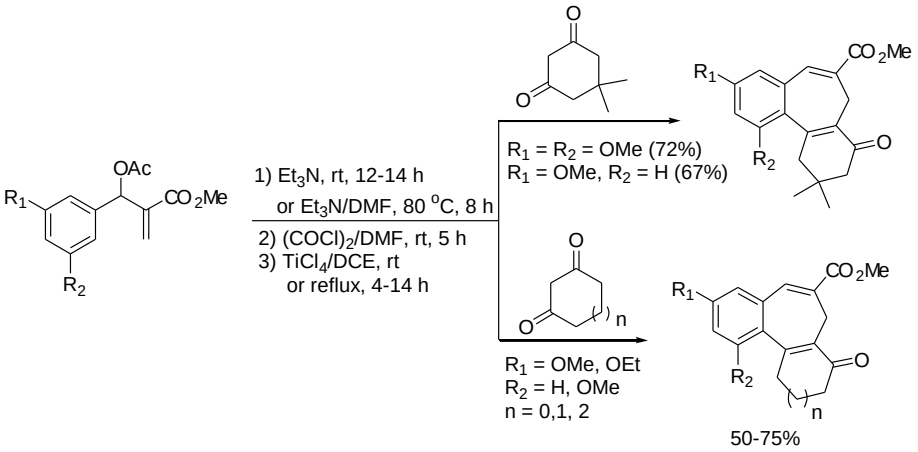
Scheme 15



An interesting one-pot synthesis of angularly fused [6-7-5], [6-7-6], and [6-7-7] carbocyclic ring systems from Baylis-Hillman acetates through a strategy involving

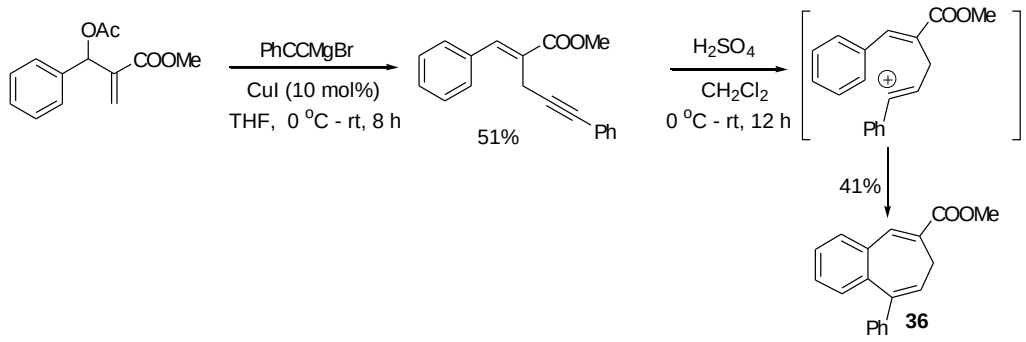
alkylation, formation of a vinyl chloride, and intramolecular cyclization (Friedel-Crafts) has been developed by our research group (Scheme 16).[73]

Scheme 16

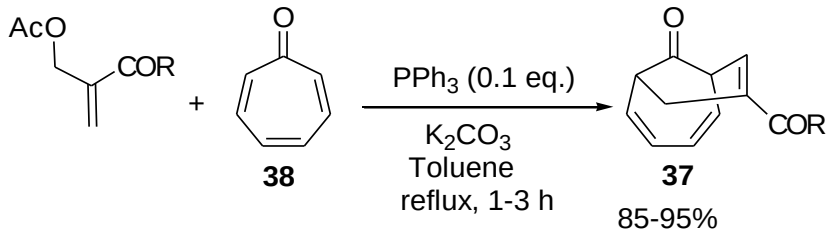


Kim and co-workers[74] have successfully employed the Baylis-Hillman acetates for synthesis of 9-phenyl-7*H*-benzocycloheptene derivatives (**36**) *via* the treatment with alkynyl Grignard reagents followed by intramolecular Friedel-Crafts reaction. One representative example is shown in Scheme 17.

Scheme 17



Lu and co-workers[75] have synthesized bridged nine-membered carbocyclic compounds (**37**) *via* the reaction of tropone (**38**) with various Baylis-Hillman acetates under the catalytic influence of PPh_3 (Eq. 17). This reaction involves [3+6] annulation strategy.

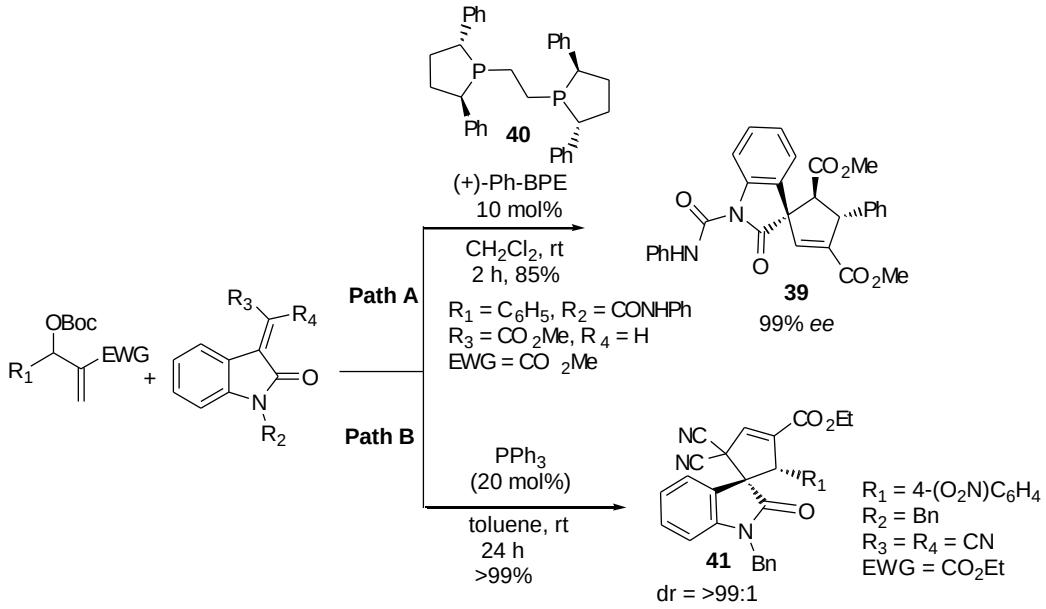


Eq. 17

R = MeO, C_6H_5, 4-MeC_6H_4, 4-$(MeO)C_6H_4$, 4-ClC_6H_4, 4-BrC_6H_4

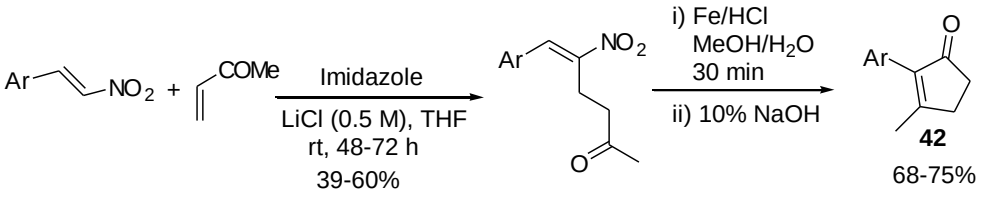
An enantioselective synthesis of spirocyclopenteneoxindoles (**39)** was developed by Barbas III and co-workers[76] *via* [3+2] cycloaddition reaction between methyleneindolinones and Baylis-Hillman carbonates using chiral phosphine, **40** as a catalyst (Path A). About the same time Shi and co-workers[77] have also reported a diastereoselective synthesis of spirocyclopenteneoxindole derivates, **41** from the Baylis-Hillman carbonates by treatment with isatylidene malononitriles under the catalytic influence of triphenylphosphine (Path B). One example in each case is presented in Scheme 18.

Scheme 18



Recently Namboothiri and co-workers[78] have used nitroalkenes as activated alkenes for Baylis-Hillman reaction with methyl vinyl ketone under the influence of imidazole-LiCl system. The resulting adducts were transformed into corresponding 2,3-disubstituted cyclopent-2-enones (**42**) by reduction of the nirtogroup to aminogroup followed by hydrolysis and cyclization (Scheme 19).

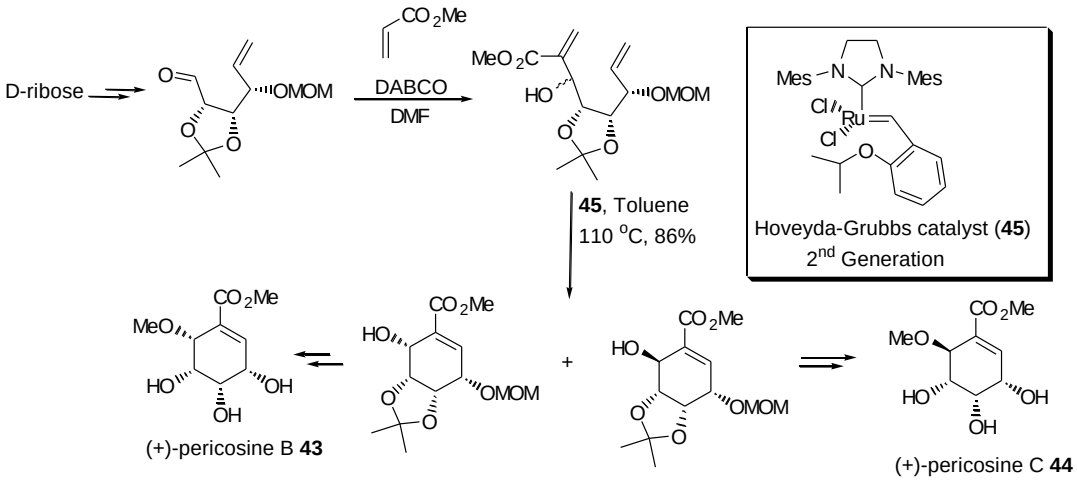
Scheme 19



Ar = C_6H_5, 4-(MeO)C_6H_4, 3,4-(OCH_2O)C_6H_3, 3,4-$(MeO)_2C_6H_3$, Thiophen-2-yl

Vankar and co-workers[79] have developed facile synthesis of (+)-pericosine B (**43**) and (+)-pericosine C (**44**) starting from D-ribose using the Baylis-Hillman reaction and RCM as the key steps (Scheme 20).

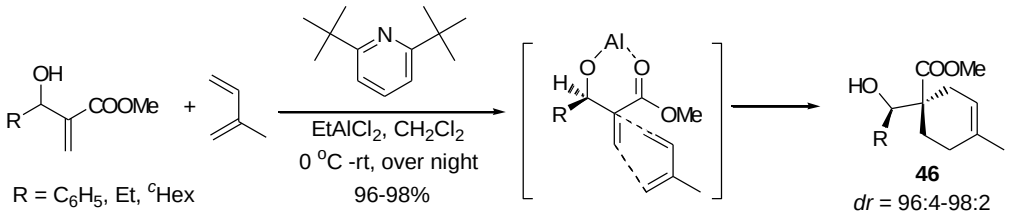
Scheme 20



Aggarwal and co-workers[80] reported a facile procedure for synthesis of substituted cyclohexene derivatives (**46**) in high diastereoselectivity, from the Baylis-Hillman

alcohols by treatment with dienes in the presence of ethylaluminium dichloride. The reaction is believed to proceed through [4+2] cycloaddition pathway Representative examples are shown in Scheme 21.

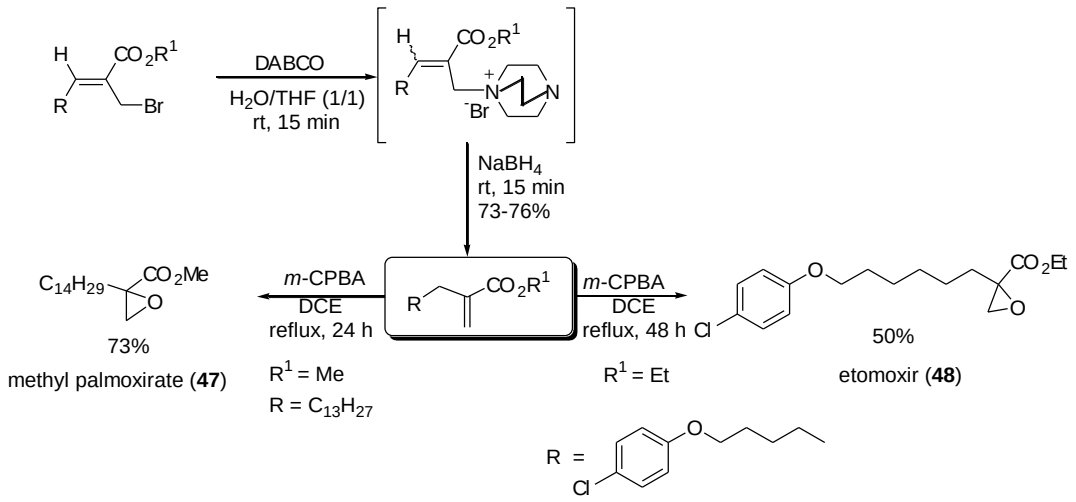
Scheme 21



Oxygen heterocyclic compounds

Our research group[81] has reported an interesting protocol for synthesis of two hypoglycemic agents methyl palmoxirate (**47**), and etomoxir (**48**) from the Baylis-Hillman bromides following the reaction strategy shown in Scheme 22.

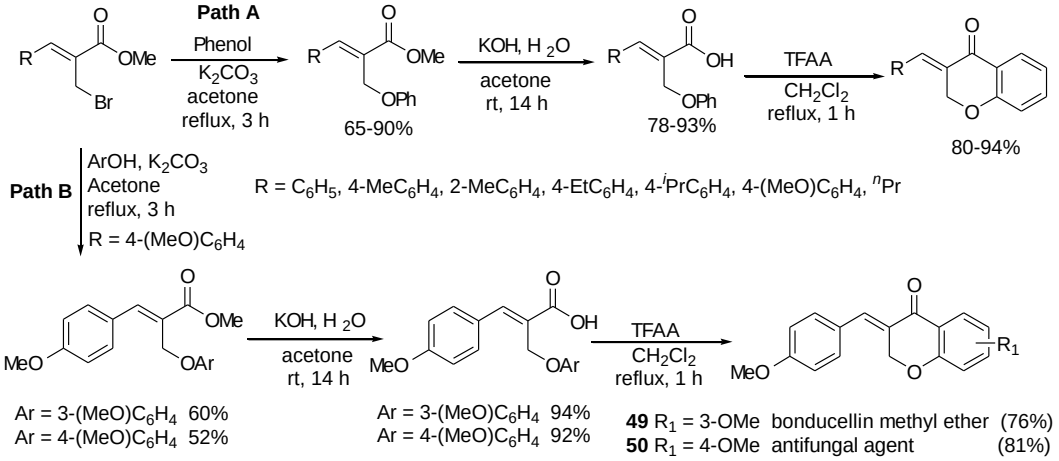
Scheme 22



A simple strategy for synthesis of 3-benzylidenechroman-4-ones from the Baylis-Hillman bromides (derived from aromatic/ aliphatic aldehydes and methyl acrylate) *via* the treatment with phenols followed by hydrolysis and intra-molecular Friedel-Crafts reaction (Path A, Scheme 23) has been developed by our research group.[82] The

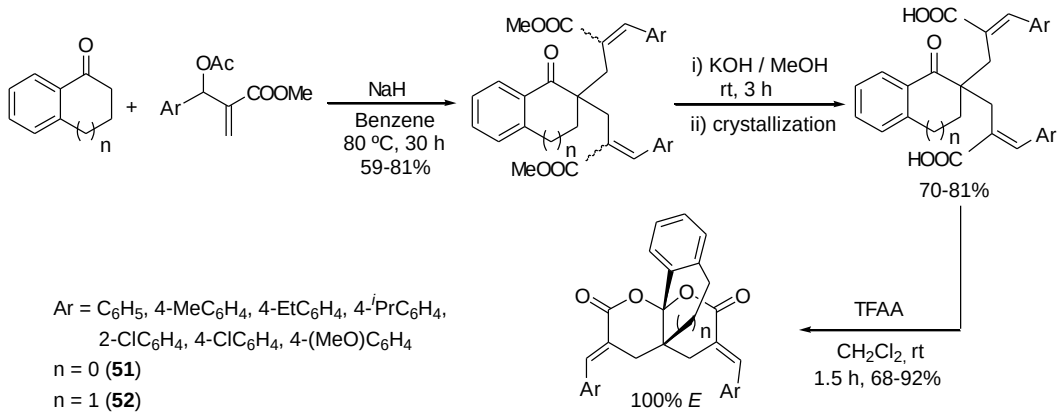
efficiency of this methodology was demonstrated by the synthesis of two natural products such as bonducellin methyl ether (**49**) and antifungal agent (**50**) (Path B, Scheme 23).

Scheme 23



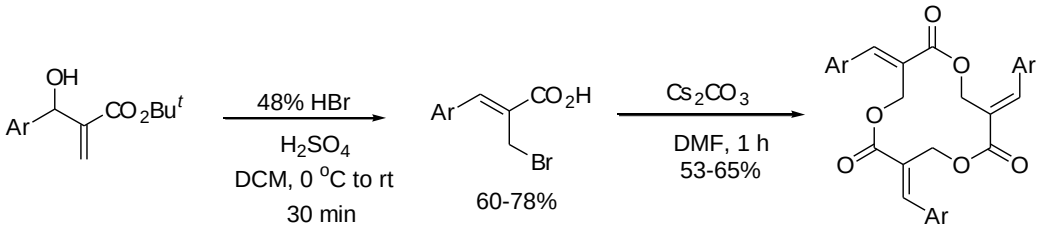
A novel synthetic strategy for obtaining substituted propellano-bislactones *i.e.* 2,10-dioxa[4.4.3]propellane-3,9-diones (**51**) and 2,10-dioxa[4.4.4]propellane-3,9-diones (**52**) from the Baylis-Hillman acetates has been developed by our research group.[83] This protocol proceeds through the bisalkylation of cycloalkanones with Baylis-Hillman acetates followed by hydrolysis and bislactonization (Scheme 24).

Scheme 24

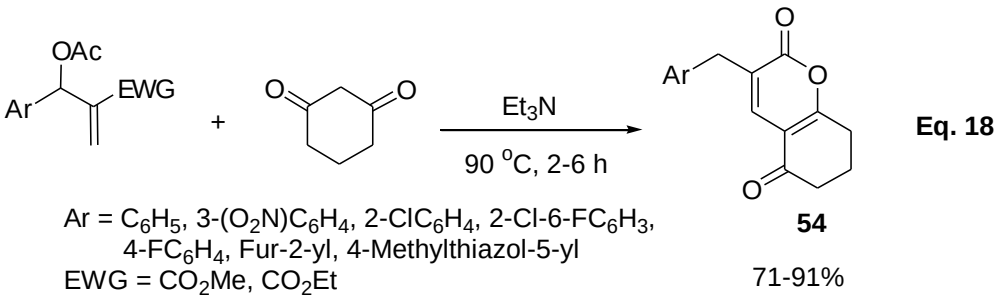


A facile synthesis of triolides (**53**) has been developed by Zulykama and Perumal[84] starting from Baylis–Hillman bromides following the reaction sequence shown in Scheme 25.

Scheme 25



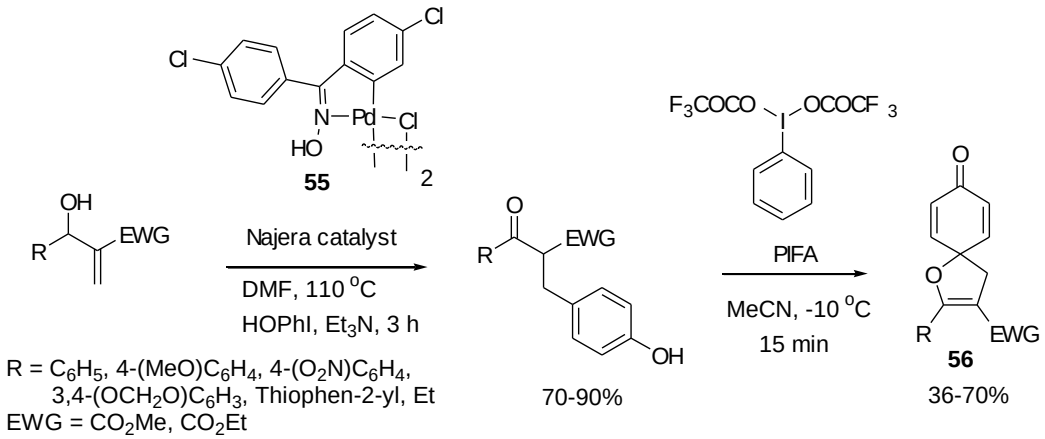
A simple synthesis of 3-arylmethyl-7,8-dihydro-6H-chromene-2,5-diones (**54**) from the acetates of Baylis-Hillman alcohols (derived from aromatic aldehydes and alkyl acrylates) by treating with cyclohexane-1,3-diones in the presence of triethylamine under solvent free conditions was reported by Su and co-workers.[85]



Eq. 18

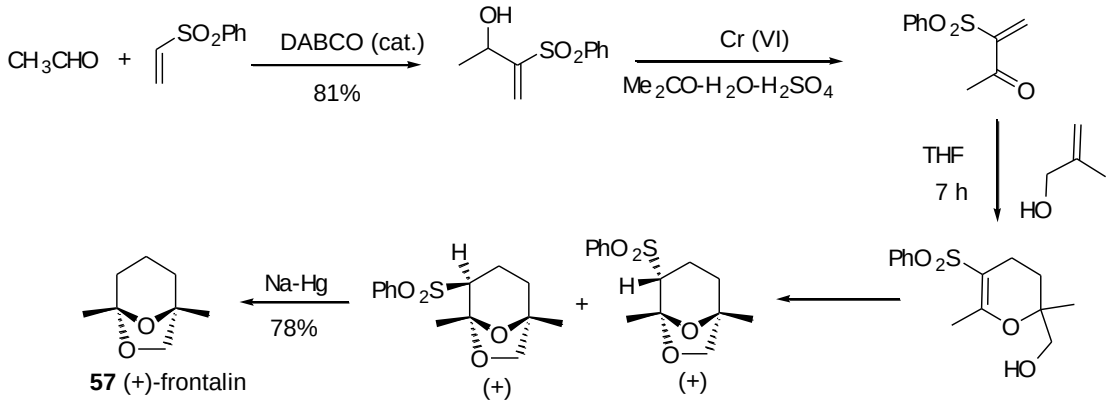
Coelho and co-workers[86] have used Najera's catalyst (**55**) for performing intermolecular Heck reaction between Baylis-Hillman adducts and *p*-(hydroxy)phenyliodide to provide α-(4-hydroxy)benzyl-β-keto esters which on subsequent treatment with phenyliodine bis(trifluoroacetate) gave spirocyclohexadienones (**56**), an interesting structural moiety present in several biologically active natural products (Scheme 26).

Scheme 26



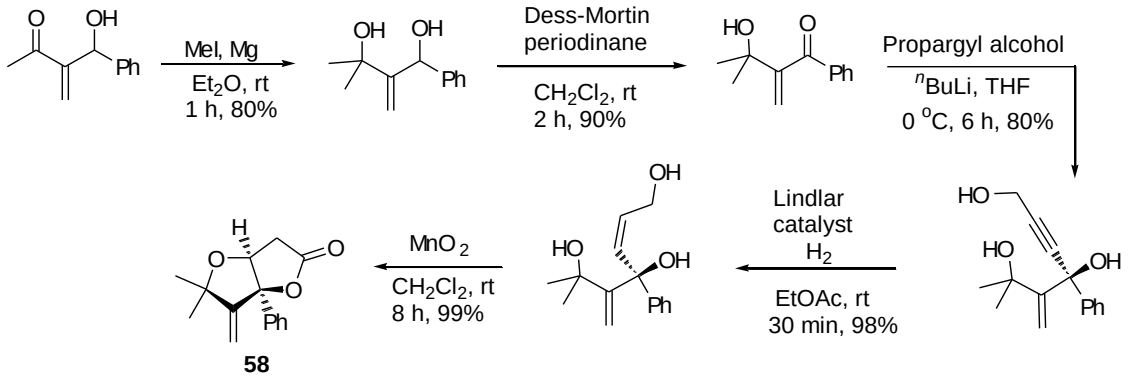
Weichert and Hoffmann[87] have described a facile synthesis of racemic frontalin (**57**) starting from the Baylis-Hillman adduct, derived from acetaldehyde and phenyl vinyl sulfone according to the reaction strategy shown in Scheme 27.

Scheme 27



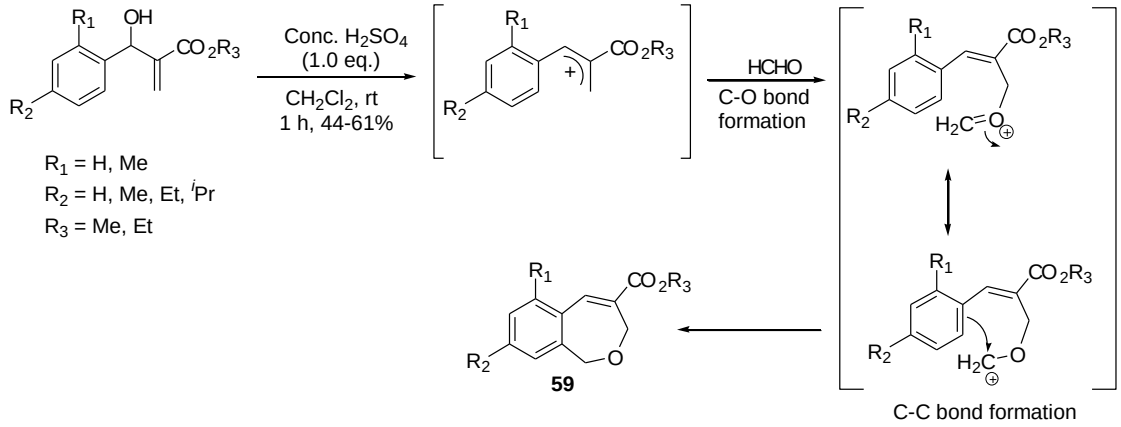
Mehta and co-workers[88] have used the Baylis-Hillman adducts obtained *via* the coupling of methyl vinyl ketone and aliphatic/aromatic aldehydes for synthesis of furo[3,2-*b*]furanone frameworks (**58**). One representative example is shown in Scheme 28.

Scheme 28



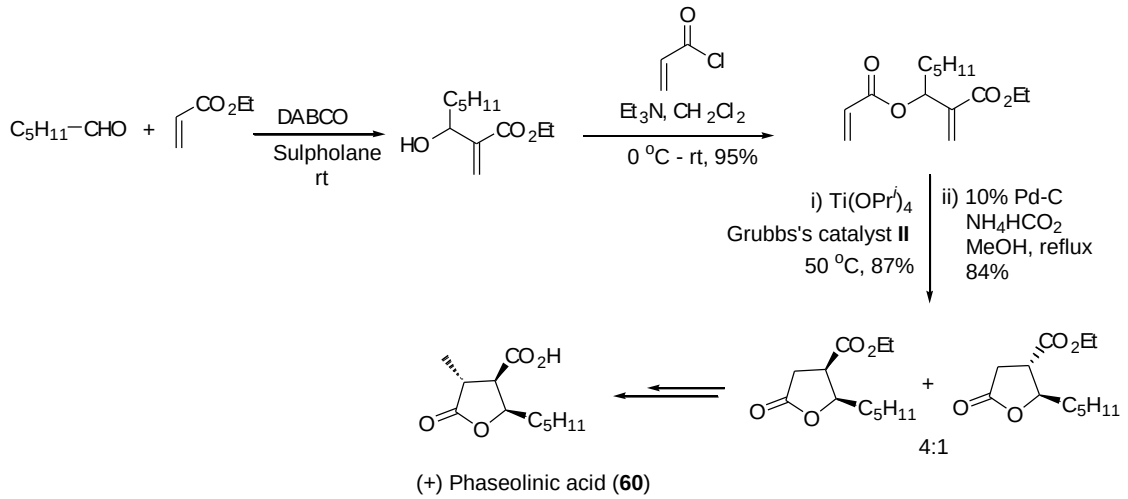
Our research group[89] has developed a simple protocol for obtaining benzoxepine derivatives (**59**) *via* treatment of Baylis-Hillman alcohols with formaldehyde in the presence of H_2SO_4. The reaction proceeds through simultaneous formation of C-O (Prins-type reaction) and C-C bonds (Friedel-Crafts reaction) (Scheme 29).

Scheme 29



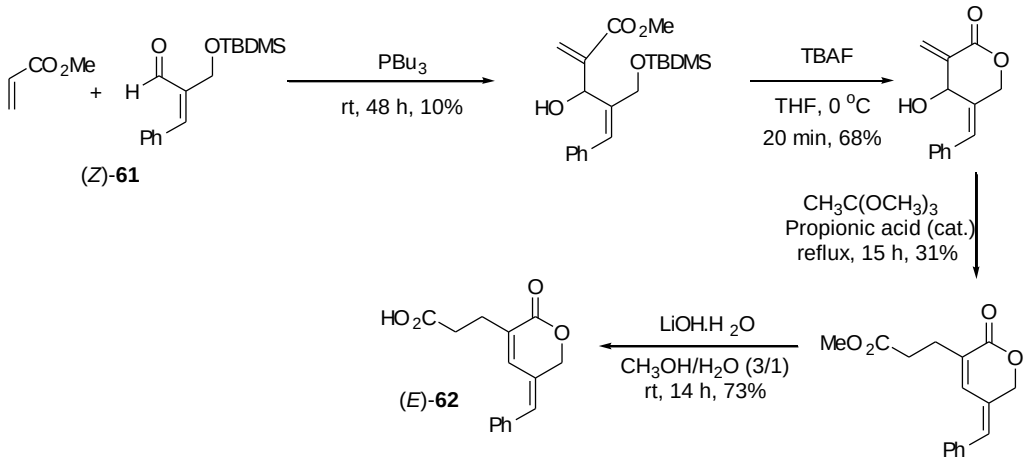
The Baylis-Hillman adduct derived from hexanal and ethyl acrylate, has been converted into phaseolinic acid (**60**) by Selvakumar and co-workers.[90] This methodology involves RCM as the key step (Scheme 30).

Scheme 30



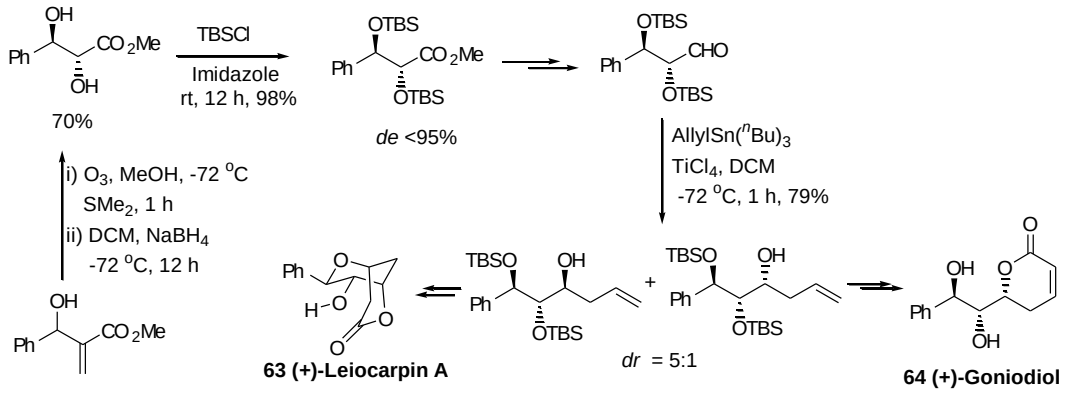
Ko and co-workers[91] have transformed the Baylis-Hillman adduct, derived from the aldehyde (*Z*)-**61** and methyl acrylate, into a MMP-inhibitory active gelastain analogue (*E*)-**62** according to the reaction sequence shown in Scheme 31.

Scheme 31



Paioti and Coelho[92] have reported a facile total synthesis of two styryl lactones (±)-Leiocarpin A (**63**) and (±)-Goniodiol (**64**) from the Baylis-Hillman adduct, derived from benzaldehyde and methyl acrylate, following the reaction sequence shown in Scheme 32.

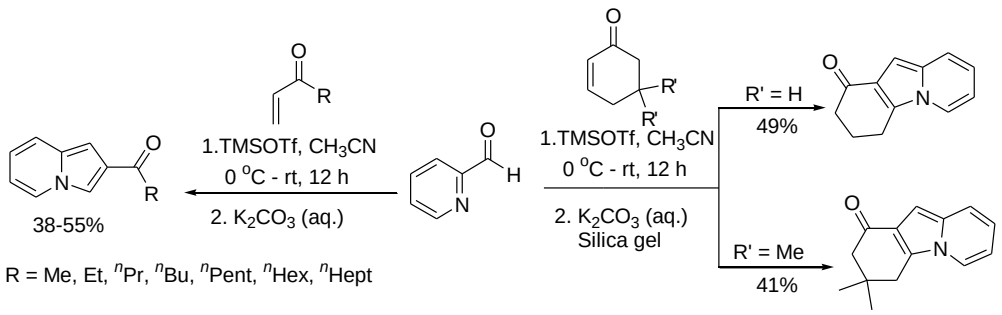
Scheme 32



Nitrogen heterocyclic compounds

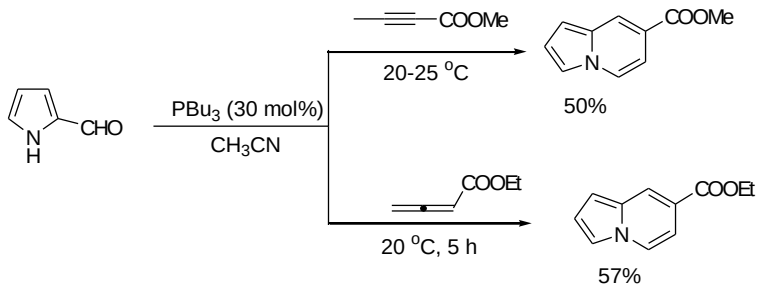
Our research group[93] have reported a simple and one-pot strategy for synthesis of indolizine derivatives *via* the treatment of pyridine-2-carboxaldehyde with vinyl ketones (both cyclic and acyclic) in the presence of trimethylsilyl trifluoromethanesulfonate (TMSOTf) (Scheme 33). In this strategy aldehyde group of the pyridine-2-carboxaldehyde serves as electrophilic component while nitrogen of the pyridine ring induces the Baylis-Hillman coupling with alkyl vinyl ketones.

Scheme 33



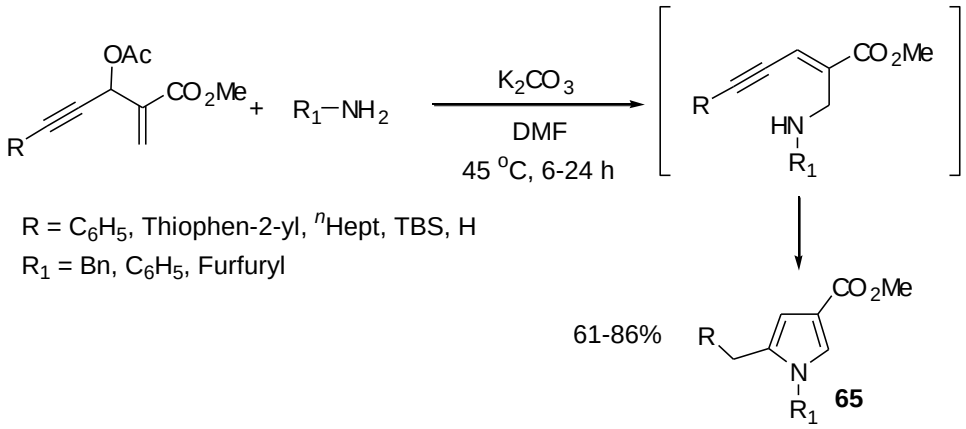
Virieux and co-workers[94] have developed a facile methodology for synthesis of indolizine-7-carboxylates from 2-pyrrolecarboxaldehyde *via* the treatment with allene or propiolate derivatives under the catalytic influence of tributylphosphine. Representative examples are given in Scheme 34.

Scheme 34



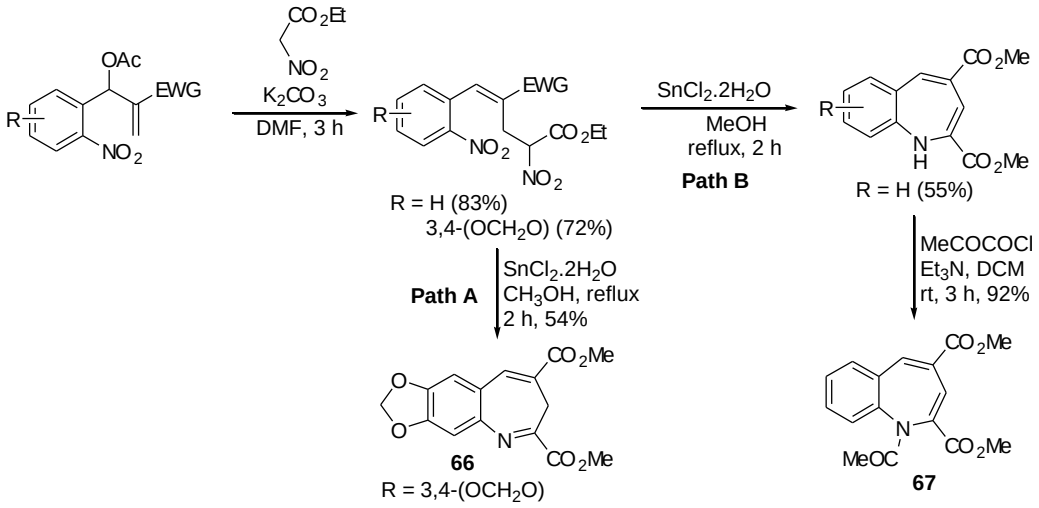
Reddy and co-workers[95] have described a novel methodology for the synthesis of substituted pyrroles (**65**) starting from the acetates of Baylis-Hillman alcohols obtained from acetylenic aldehydes and methyl acrylate, by treating with amines in the presence of K_2CO_3 (Scheme 35).

Scheme 35



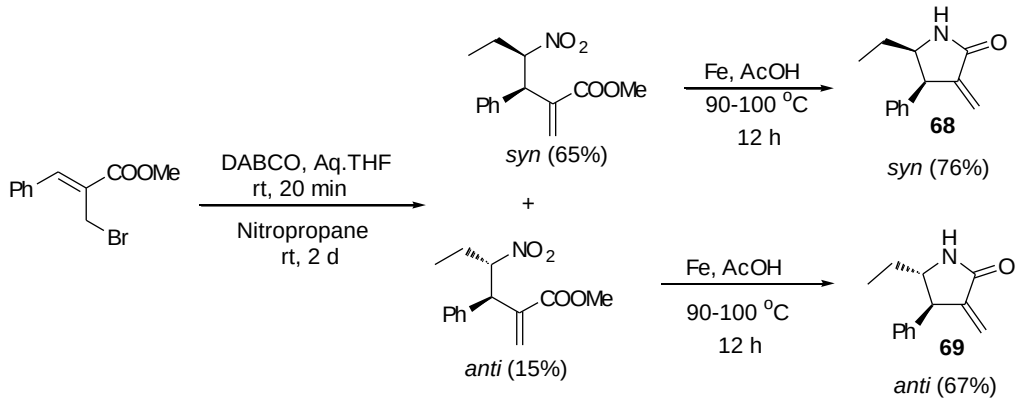
Singh and Batra[96] have synthesized 1H- and 3*H*-1-benzazepines (Scheme 36) from Baylis-Hillman acetates (derived from aromatic aldehydes) by treatment with nitro alkanes followed by reduction of nitrogroup with $SnCl_2$. If the electron donating group present on aromatic ring of Baylis-Hillman acetates, 3*H*-1-benzazepines (**66**) are obtained as the products (Path A) while in the absence of such electron donating group the Baylis-Hillman acetates provided 1*H*-1-benzazepines (**67**) (Path B). One representative example is shown in Scheme 36 for each case.

Scheme 36



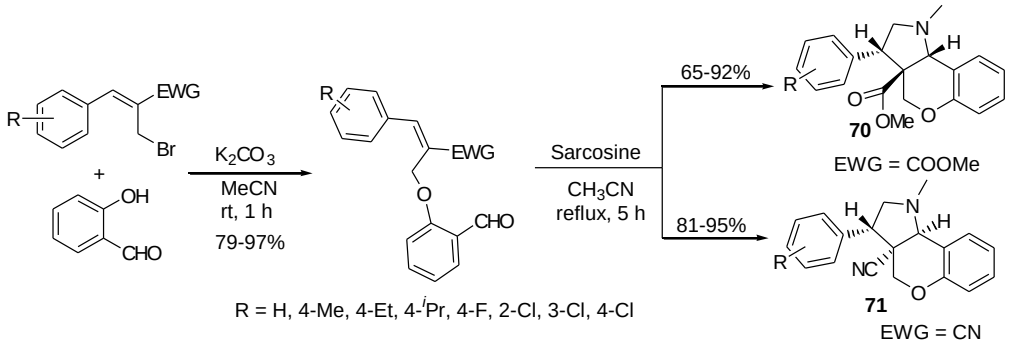
Kim and co-workers[97] reported a simple strategy for obtaining β,γ-disubstituted α-methylene γ-butyrolactams (**68** & **69**) from the Baylis-Hillman bromide *via* treatment with nitroalkanes followed by reductive cyclization (Scheme 37).

Scheme 37



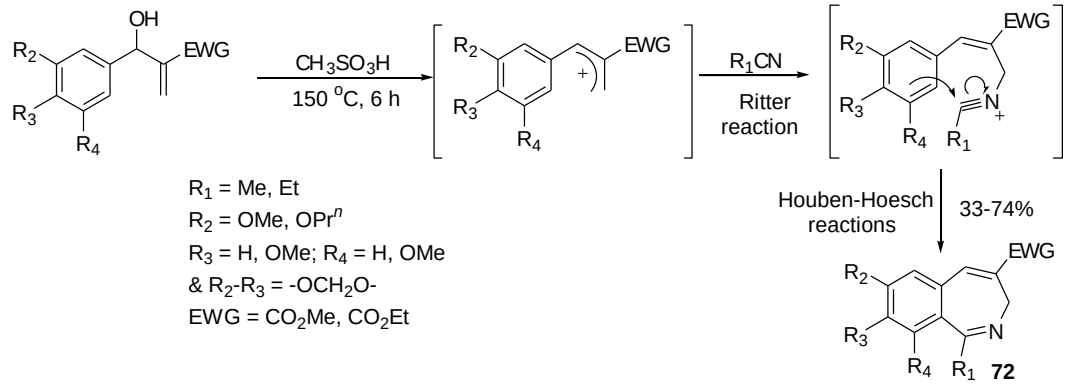
Bakthadoss and co-workers[98] have reported regio and stereoselective route for the synthesis of tricyclic chromeno-pyrrolidines (**70** & **71**) starting from Baylis-Hillman bromides according to the reaction sequence described in Scheme 38.

Scheme 38



Our research group[99] have developed an interesting strategy for conversion of Baylis-Hillman alcohols (derived from aryl aldehydes, containing electron donating group, and alkyl acrylates) into 2-benzazepine derivatives (**72**) *via* the treatment with alkylnitriles in the presence of methanesulfonic acid (Scheme 39). This reaction involves the simultaneous Ritter (C-N bond formation) and Houben-Hoesch (C-C bond formation) reactions.

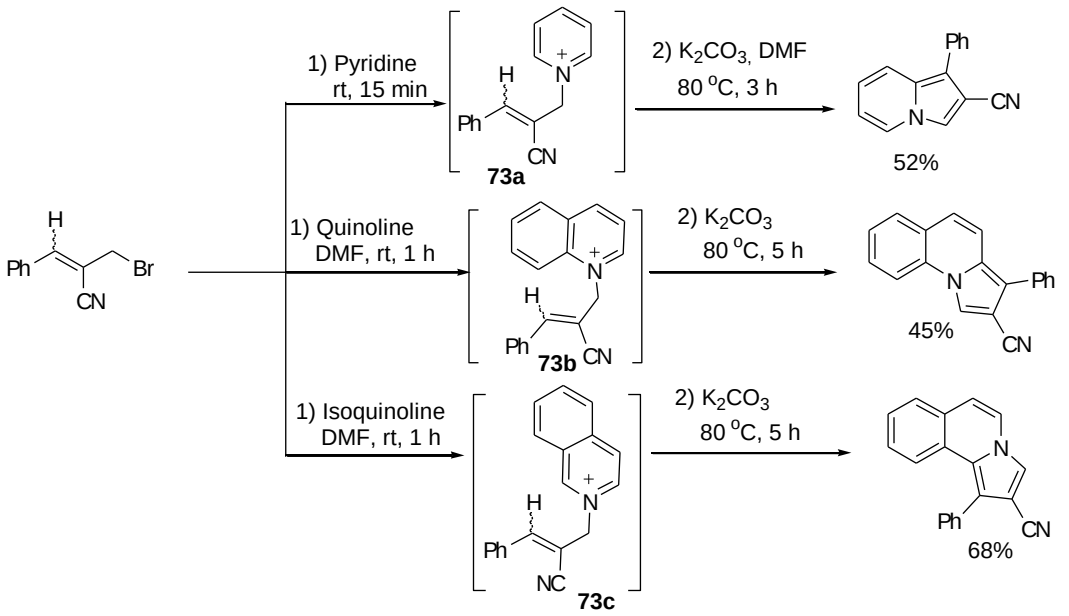
Scheme 39



A convenient protocol for synthesis of indolizine and benzofused indolizine derivatives was reported from Baylis-Hillman bromides *via* reaction with pyridine and quinoline/isoquinoline respectively by our research group.[100] This reaction proceeds *via*

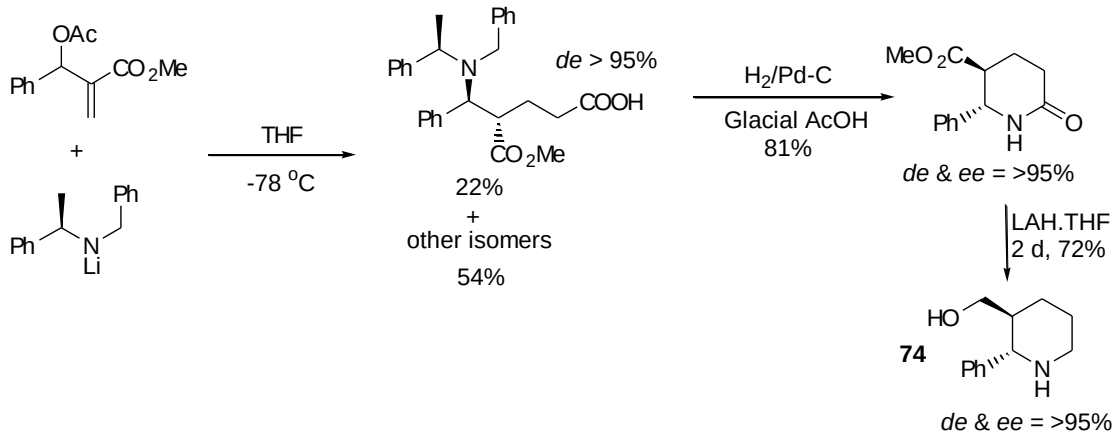
1,5-cyclization of the initially formed pyridinium/quinolinium/isoquinolinium salts (**73a**/**73b**/**73c**). One example for each case is shown in Scheme 40.

Scheme 40



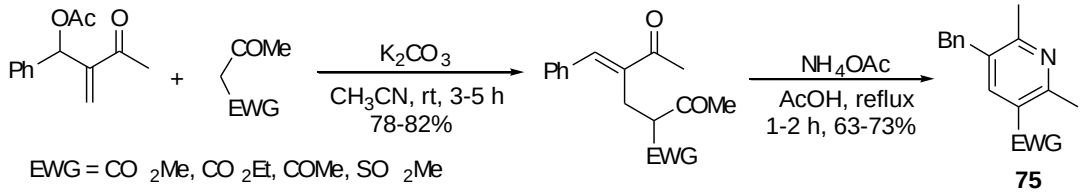
Highly enantioselective and diastereoselective synthesis of 2,3-disubstituted piperidines (**74**) was reported by Garrido and co-workers[101] using Baylis-Hillman acetates as starting material according to the reaction sequence shown in Scheme 41 (one selective example is presented).

Scheme 41



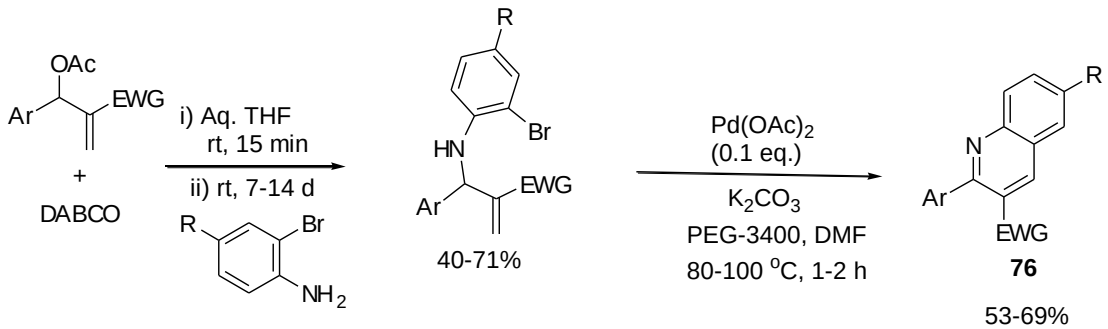
Baylis-Hillman acetates have been conveniently transformed into tetra-substituted pyridine derivatives (**75**) by reaction with active methylene compounds like alkylaceto acetate, acetyl acetone, β-sulfonyl ketones followed by treatment with ammonium acetate according to the reaction sequence as shown in Scheme 42.[102]

Scheme 42



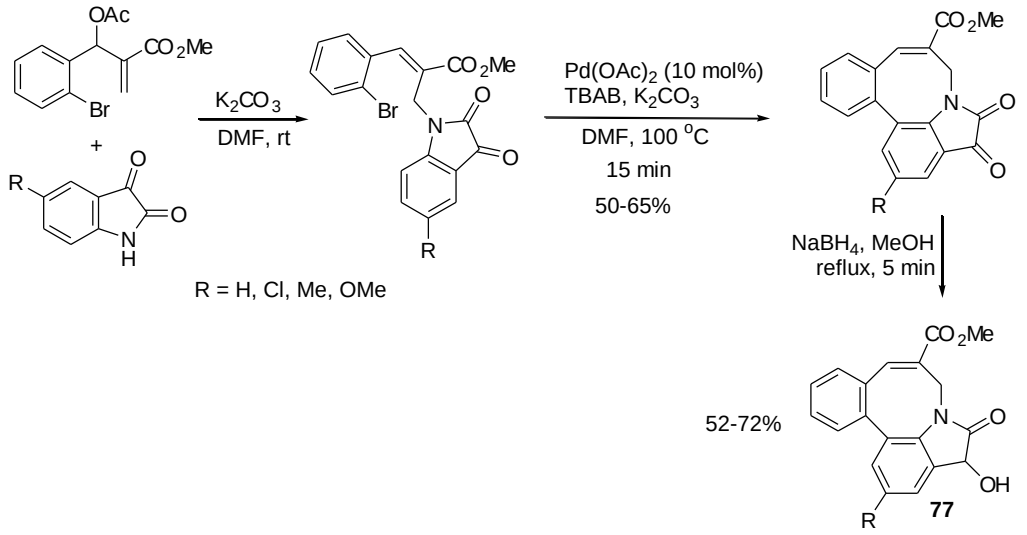
Kim and co-workers[103] have reported a facile synthesis of 2-arylquinolines (**76**) from the Baylis-Hillman acetates *via* the reaction with 2-bromoarylamines followed by intramolecular Heck reaction (Scheme 43).

Scheme 43



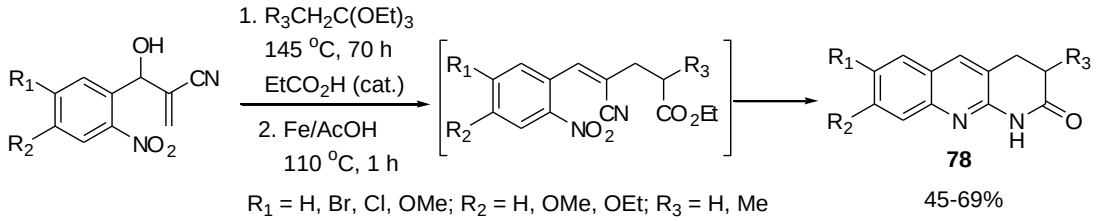
Kim and co-workers[104] have also synthesized 3-hydroxyoxindole derivatives (**77**) starting from acetates of Baylis-Hillman alcohols (derived from 2-bromobenzaldehyde and methyl acrylate) following the reaction sequence as described in Scheme 44.

Scheme 44



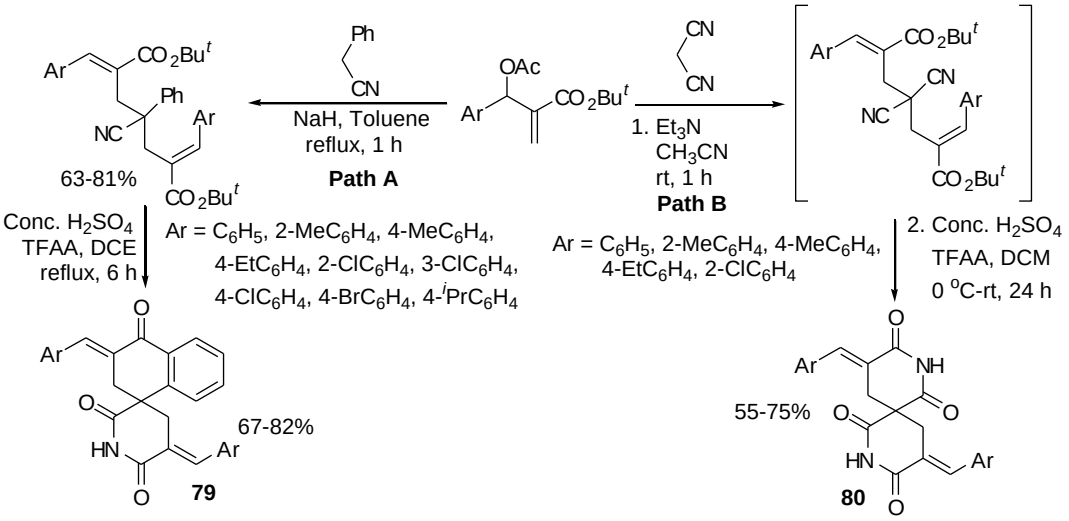
Our research group[105] has developed a simple, facile and one-pot procedure for the synthesis of tricyclic heterocyclic systems containing [1,8]naphthyridin-2-one framework (**78**) from the Baylis-Hillman alcohols following the reaction sequence presented in Scheme 45.

Scheme 45

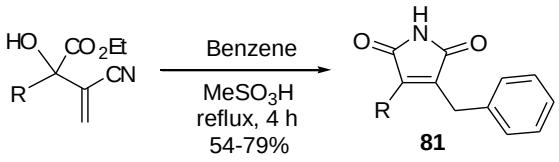


A convenient methodology has been developed for synthesis of di(*E*)-arylidene-tetralone-spiro-glutarimides (**79**) from the acetates of Baylis-Hillman alcohols (obtained from *tert*-butyl acrylate and arylaldehydes) and benzyl cyanide in a two step-protocol by our research group[106] (Path A, Scheme 46). Our research group also reported a one-pot strategy for obtaining di(*E*)-arylidene-spiro-bisglutarimides (**80**) from the Baylis-Hillman acetates (Path B, Scheme 46).

Scheme 46



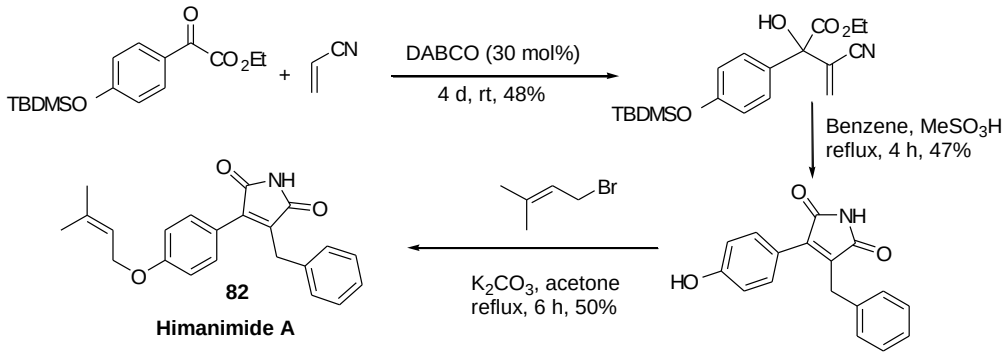
Our research group[107] has reported a facile route for obtaining 3,4-disubstituted maleimide derivatives (**81**) from the Baylis-Hillman alcohols derived from α-keto esters and acrylonitrile (Eq. 19). This methodology has been successfully extended for synthesis of Himanimide A (**82**), an important bioactive molecule according to the reaction sequence as shown in Scheme 47.



Eq. 19

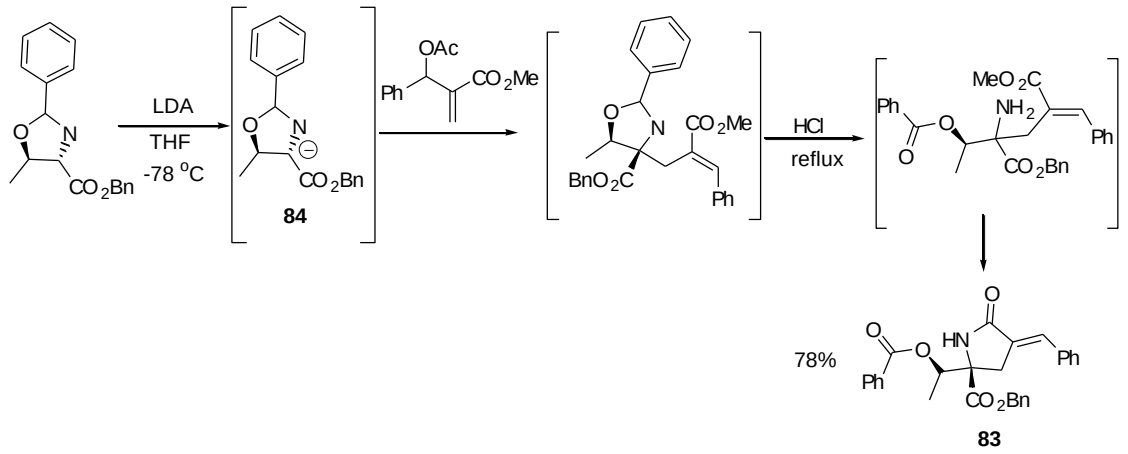
R = C_6H_5, 2-MeC_6H_4, 2-(MeO)C_6H_4, 3-MeC_6H_4, 3-(MeO)C_6H_4, 4-MeC_6H_4, 4-(MeO)C_6H_4, 4-(EtO)C_6H_4, 4-BrC_6H_4, 4-ClC_6H_4, Me, Et, ^{n}Pr

Scheme 47



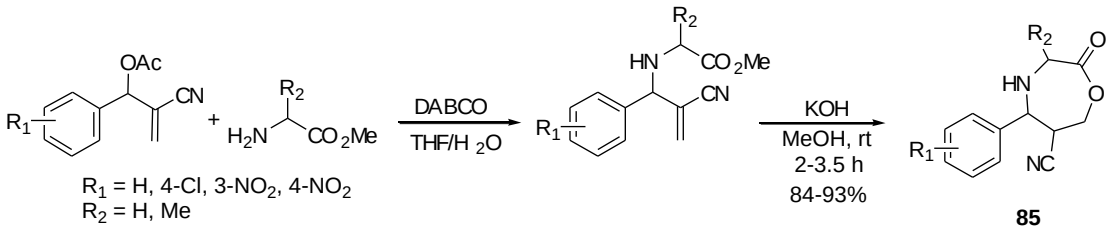
Mereddy and co-workers[108] have reported an interesting synthesis of functionalized pyroglutamates (**83**) from Baylis-Hillman acetates *via* the reaction with the anion **84**, generated from threonine oxazoline. One representative example is shown in Scheme 48.

Scheme 48



Yadav and co-workers[109] have conveniently converted the Baylis-Hillman acetates into substituted [1,4]oxazepin-2-one derivatives (**85**), *via* the reaction with amino ester followed by hydrolysis and cyclization. Representative examples are presented in Scheme 49.

Scheme 49



OBJECTIVES, RESULTS AND DISCUSSION

The previous section clearly demonstrates the importance of Baylis-Hillman reaction as an useful carbon-carbon bond forming reaction providing diverses classes of multi-functional molecules whose applications in several organic transformations and in synthesis of a number of carbocyclic and heterocyclic compounds have been well documented.[15-21] Our research group has been working for last 28 years on various aspects of Baylis-Hillman reaction with main aim of developing this reaction as useful as the Diels-Alder reaction (which is believed to be the most popular and useful reaction) for assembling carbon framework. In continution of our research program in this direction we have undertaken this thesis work with the following objectives.

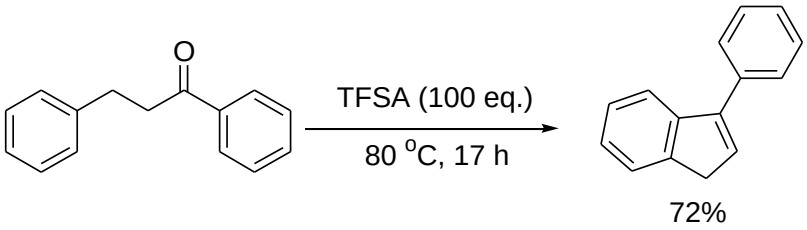
OBJECTIVES

1) To use the Baylis-Hillman adducts as probes in understanding the chemoselectivity in the intramolecular Friedel-Crafts reaction of substrates containing keto and ester functionalities in a similar environment and subsequently use this chemoselective cyclization methodology in developing a facile protocol for synthesis of functionalized indene derivatives.
2) To use the Baylis-Hillman acetates for construction of [1,2,3]-triazolo-[1,4]-benzoxazonine system employing Huisgen reaction (Click reaction) for construction of 9-membered ring.
3) To develop a simple methodology for synthesis of 2,5,6-trisubstituted pyrimidin-4(3*H*)-one derivatives from Baylis-Hillman acetates.

RESULTS AND DISCUSSION

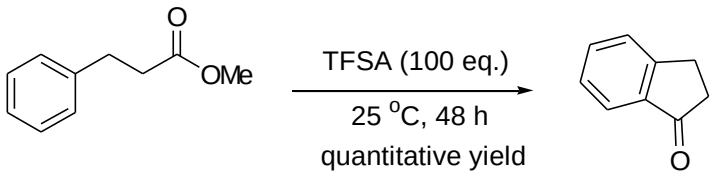
Towards developing the Baylis-Hillman adducts as probes in understanding the chemoselectivity in the intramolecular Friedel-Crafts reaction of substrates containing keto and ester functionalities: Development of a facile methodology for synthesis of functionalized indene derivatives

3-Arylpropionitriles/3-arylpropan-1-ones/3-arylpropyl esters are well known synthons for obtaining various indanone derivatives *via* the treatment with appropriate acid. To mention a few examples, the Friedel-Crafts reaction of 1,3-diphenylpropan-1-one in the presence of trifluoromethanesulfonic acid provided 3-phenyl-1H-indene (Eq. 20).[110]



Eq. 20

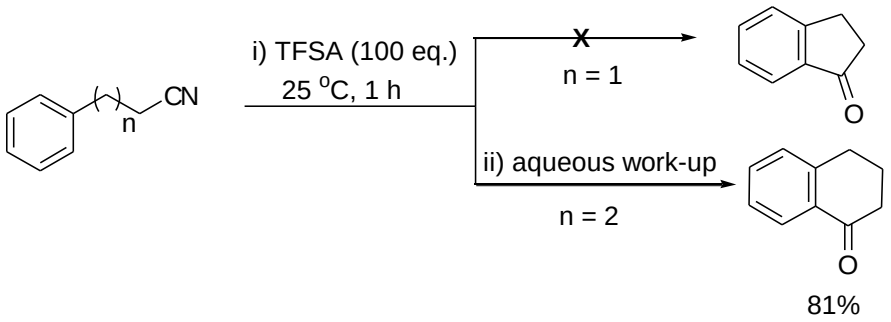
The Friedel-Crafts reaction of methyl 3-phenylpropionoate with TFSA furnishes 1-indanone in quantitative yields (Eq. 21).[112]



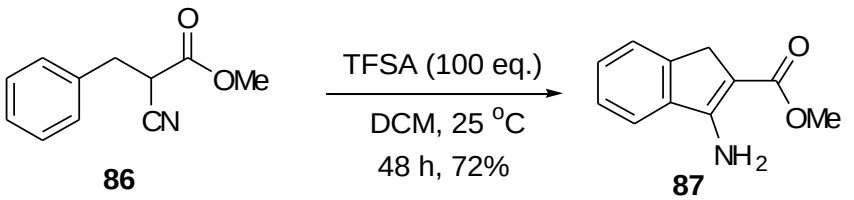
Eq. 21

It is interesting to note that when 3-phenylpropionitrile was treated with TFSA, expected five-membered-ring (indanone) was not formed where as in the case of 4-phenylbutyronitrile six-membered-ring (1-tetralone) was formed in 81% yield after aqueous work-up (Scheme 50).[112]

Scheme 50

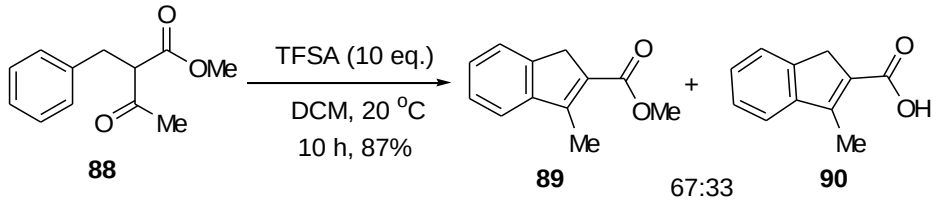


It will be highly interesting to examine the competition for cyclization with aromatic ring between nitrile and ester, nitrile and keto, ester and keto groups in a substrate containing such two or three groups in a similar environment. Some examples for such competitive cyclization reactions are known in the literature. Arylcyanopropionate (**86**) in the presence of TFSA provided five-membered β-enamino esters (**87**) exclusively (Eq. 22). This reaction clearly indicates that nitrile underwent faster cyclization with aromatic ring than that of the ester group.[112]

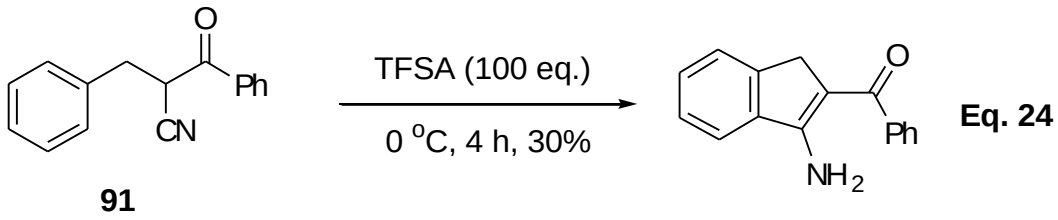


Eq. 22

Similarly Friedel-Crafts reaction of 2-aceto-3-arylpropionates (**88**), containing both keto and ester gave 2-(alkoxycarbonyl)-3-methyl-1H-indene derivatives (**89** & **90**) on treatment with TFSA.[111] One such example is given in Eq. 23. This clearly indicates that keto cyclization is higly preferred over ester cyclization in the case of competitive intramolecular Friedel-Crafts reaction.

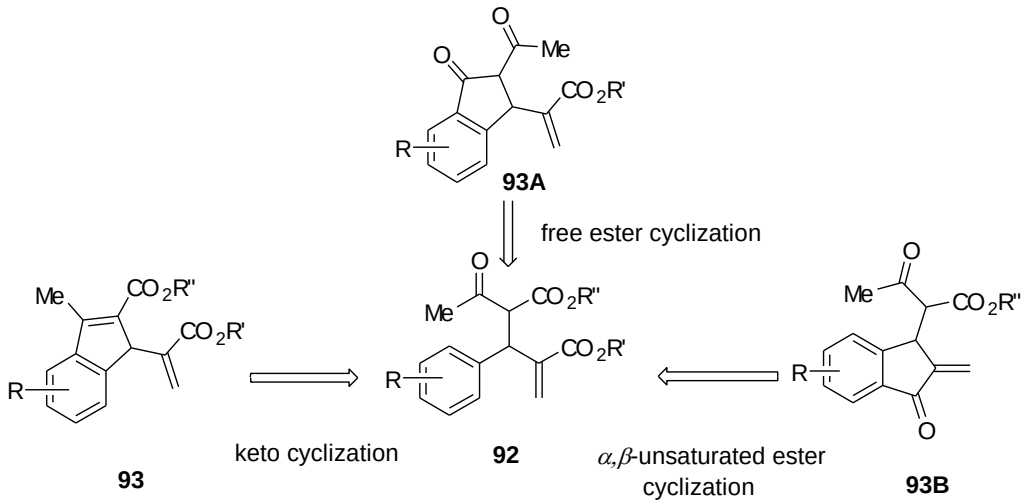


In the case of 2-benzyl-3-oxo-3-phenylpropionitrile (**91**), containing nitrile and keto groups, it is interesting to note that nitrile group underwent cyclization producing 3-amino-2-benzoyl-1H-indene (Eq. 24). This reaction clearly shows that nitrile cyclization is preferred over keto cyclization with aromatic ring in this substrate.[112]



In view of the above interesting reports we have directed our efforts towards understanding the competition between keto cyclization and ester cyclization with aromatic ring if the substrate conatains two ester groups and one keto group in a similar environment. For this purpose we have selected alkyl 4-alkoxycarbonyl-3-aryl-2-methylene-5-oxohexanoate (**92**) as substrates. In principle there are three possible cyclizations in this case to produce three types of compounds (**93**, **93A** & **93B**). We plan to examine the competition between ester and keto groups for Friedel-Crafts cyclization and then appropriately utilize this metodology for syntheis of indene derivatives (Scheme 51).

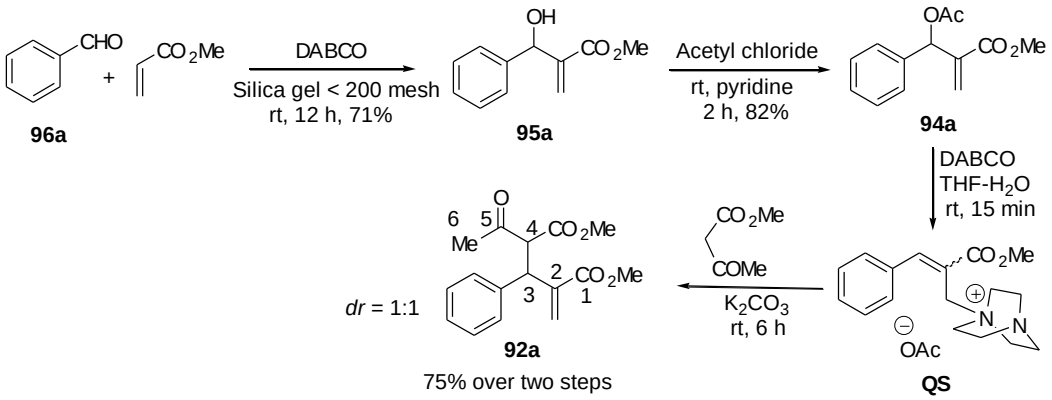
Scheme 51



Accordingly, we have first selected methyl 4-methoxycarbonyl-2-methylene-5-oxo-3-phenylhexanoate (**92a**) as a substrate for our studies. This diester **92a** was prepared from methyl 3-acetoxy-2-methylene-3-phenylpropanoate (**94a**) (Scheme 52). Thus treatment of methyl 3-acetoxy-2-methylene-3-phenylpropanoate (**94a**) (10 mmol), with DABCO (10 mmol) for 15 min at room temperature provided quaternary salt (**QS**). Subsequent treatment of the *in situ* generated quaternary salt (**QS**) with methyl acetoacetate (11 mmol) in presence of K_2CO_3 (11 mmol) at room temperature for 6 h provided methyl 4-methoxycarbonyl-2-methylene-5-oxo-3-phenylhexanoate (**92a**), in 75% isolated yield [*dr* ≈ 1:1, the diastereomeric ratio was determined by the integration ratio of diastereomeric acetyl methyl group protons at δ 1.96 (s) & δ 2.27 (s)] (Scheme 52). Structure of this molecule was established with the IR, ^{1}H NMR, ^{13}C NMR, mass spectral data and elemental analysis. The required methyl 3-acetoxy-2-methylene-3-phenylpropanoate (**94a**) was prepared *via* the acetylation of methyl 3-hydroxy-2-methylene-3-phenylpropanoate (**95a**), which in turn was obtained *via* the Baylis-

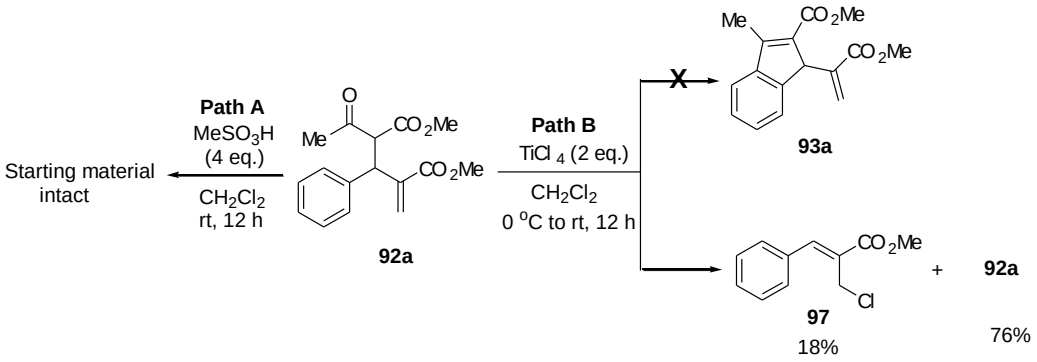
Hillman coupling of benzaldehyde (**96a**) and methyl acrylate under the influence of DABCO, following the known procedure (Scheme 52).[113]

Scheme 52



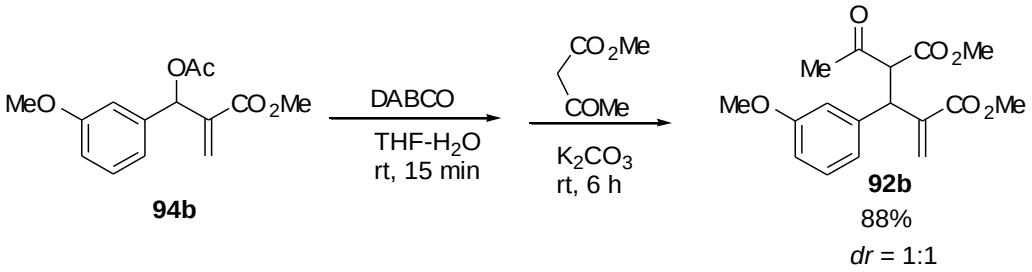
We then examined the intramolecular Friedel-Crafts reaction of methyl 4-methoxycarbonyl-2-methylene-5-oxo-3-phenylhexanoate (**92a**) with methanesulfonic acid. Unfortunately the expected cyclization did not proceed. Most of the starting material was intact (Path A, Scheme 53). We have also used $TiCl_4$ as a reagent to perform the intramolecular Friedel-Crafts reaction of methyl 4-methoxycarbonyl-2-methylene-5-oxo-3-phenylhexanoate (**92a**). In this case also the desired cyclization did not occur. Interestingly methyl (2*Z*)-2-(chloromethyl)-3-phenylprop-2-enoate (**97**) was obtained in poor yield (18%) along with un-reacted methyl 4-methoxycarbonyl-2-methylene-5-oxo-3-phenylhexanoate (**92a**) (in 76% recovered yield) (Path B, Scheme 53). The structure of allyl chloride **97** was established by IR, ^{1}H NMR, ^{13}C NMR analysis. It has been well documented in the literature that treatment of Baylis-Hillman acetates with Lewis acid like $AlCl_3$ provides the corresponding allyl chlorides.[114]

Scheme 53



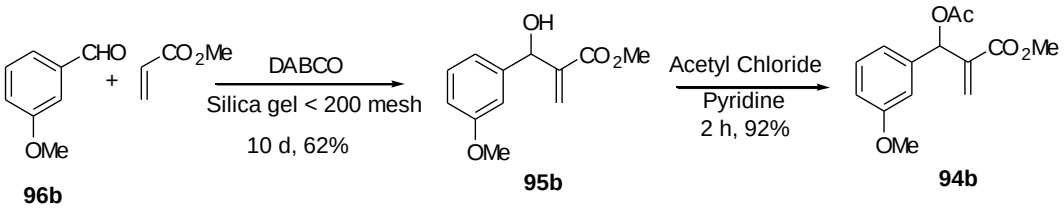
At this stage, it occured to us that electron donating group on aromatic ring may facilitate the intramolecular Friedel-Crafts cyclization process. Accordingly we selected methyl 4-methoxycarbonyl-3-(3-methoxyphenyl)-2-methylene-5-oxohexanoate (**92b**) as a substrate to examine the intramolecular Friedel-Crafts reaction. The required methyl 4-methoxycarbonyl-3-(3-methoxyphenyl)-2-methylene-5-oxohexanoate (**92b**) was prepared from methyl 3-acetoxy-3-(3-methoxyphenyl)-2-methylenepropanoate (**94b**) according the reaction strategy followed for synthesis of methyl 4-methoxycarbonyl-2-methylene-5-oxo-3-phenylhexanoate (**92a**). Thus the treatment of methyl 3-acetoxy-3-(3-methoxyphenyl)-2-methylenepropanoate (**94b**) (5 mmol), with DABCO (5 mmol) for 15 min at room temperature followed by reaction with methyl acetoacetate (5.5 mmol), in presence of K_2CO_3 (5.5 mmol) at room temperature for 6 h provided methyl 4-methoxycarbonyl-3-(3-methoxyphenyl)-2-methylene-5-oxohexanoate (**92b**), in 88% isolated yield (*dr* ≈ 1:1, the diastereomeric ratio was determined by the integration ratio of diastereomeric acetyl methyl group protons at δ 1.99 & δ 2.27) (Scheme 54). Structure of this molecule was established by IR, ^{1}H NMR [see Spectrum 1], ^{13}C NMR [see Spectrum 2], mass spectral data and elemental analysis.

Scheme 54



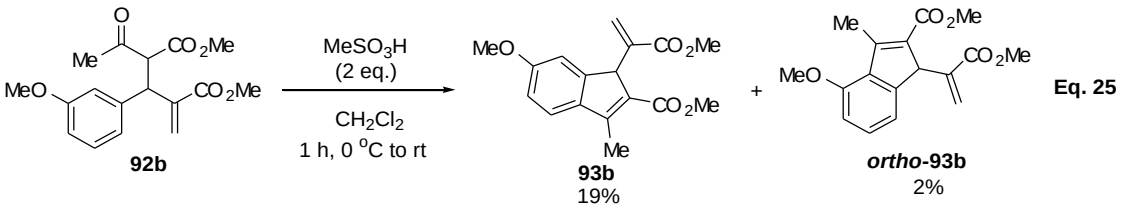
Required methyl 3-acetoxy-3-(3-methoxyphenyl)-2-methylenepropanoate (**94b**) was prepared *via* the acetylation of methyl 3-hydroxy-3-(3-methoxyphenyl)-2-methylene-propanoate (**95b**). This allyl alcohol was obtained *via* the Baylis-Hillman coupling of 3-methoxybenzaldehyde (**96b**) with methyl acrylate in presence of DABCO (Scheme 55).

Scheme 55



We have then treated methyl 4-methoxycarbonyl-3-(3-methoxyphenyl)-2-methylene-5-oxohexanoate (**92b)**, (1 mmol), with methanesulfonic acid (2 mmol) in anhydrous dichloromethane (2 mL), at room temperature for 1 h (addition at 0 ^{o}C) to provide methyl 6-methoxy-1-(1-methoxycarbonylethenyl)-3-methyl-1H-indene-2-carboxylate (**93b) (***para* cyclization product) and methyl 4-methoxy-1-(1-methoxycarbonylethenyl)-3-methyl-1H-indene-2-carboxylate (***ortho*-93b**) (*ortho* cyclization product) in 19% and 2% isolated yields respectively (entry 1, Table 1, Eq. 25) along with un-reacted starting material **92b** in 65% recovered yield. Structures of **93b** and ***ortho*-93b** were established by IR, ^{1}H NMR [for compounds **93b** and ***ortho*-93b** see Spectrums 3 & 5 respectively], ^{13}C NMR [for compounds **93b** and ***ortho*-93b** see Spectrums 4 & 6 respectively], mass

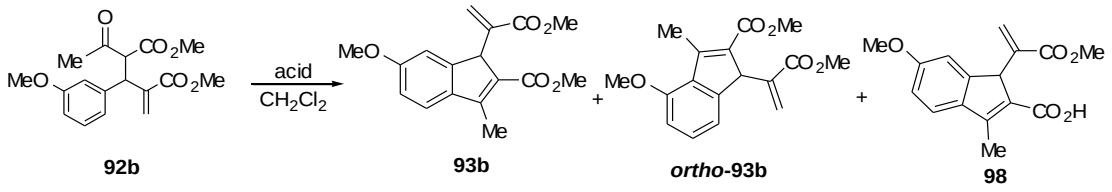
spectral data and elemental data and were further confirmed by single crystal X-ray data analyses (for ORTEP diagrams of **93b** & ***ortho*-93b** see Fig. X1 & X2 and Table I & Table II respectively).



This reaction is indeed encouraging and clearly indicates that ketone takes part in Friedel-Crafts cyclization in preference over ester function even in the presence of two ester functionalities. With a view to increase the yield of the indene derivatives in this reaction strategy, we have examined applicability of various acids and Lewis acids. In this direction we realized that $TiCl_4$ offers better yields (entry 5, Table 1). Thus, treatment of **92b** (1 mmol) with $TiCl_4$ (2 mmol, 2 M solution in DCM) as a Lewis acid in dichloromethane (DCM) at room temperature for 1 h, provided methyl 6-methoxy-1-(1-methoxycarbonylethenyl)-3-methyl-1H-indene-2-carboxylate (**93b**) (*para* cyclization product) in 76% and methyl 4-methoxy-1-(1-methoxycarbonylethenyl)-3-methyl-1H-indene-2-carboxylate (***ortho*-93b**) (*ortho* cyclization product) in 20% isolated yields after usual work-up followed by column chromatography. When H_2SO_4 used as a reagent for cyclization, ester group attached active methylene group underwent hydrolysis to give 6-methoxy-1-(1-methoxycarbonylethenyl)-3-methyl-1H-indene-2-carboxylic acid (**98**) in 35% yield along with expected indene esters **93b** & ***ortho*-93b** in 46 & 10% respectively. The structure of molecule **98** was established by IR, ^{1}H NMR [see Spectrums 7], ^{13}C NMR [see Spectrums 8], mass spectral data and

elemental data. Structure of **98** was further confirmed by single crystal X-ray data analysis (for ORTEP diagram of **98** see Fig. X3 and for table see Table III).

Table 1. **Optimization: Synthesis of highly functionalized indenes *via* the intramolecular Friedel-Crafts cyclization of 92b**®,[a]



92b **93b** ***ortho*-93b** **98**

Entry	Conditon(s)	Product Yield (%)[b,c]		
		93b	***ortho*-93b**	**98**[d]
1	$MeSO_3H$ (2 eq.), 0 °C to rt, 1 h	19	2	-
2	H_2SO_4 (2 eq.), 0 °C to rt, 1 h	46	10	35
3[e]	H_2SO_4 (1 eq.), 0 °C to rt, 1 h	61	10	7
4	$BF_3.OEt_2$ (2 eq.), 0 °C to rt, 1h	60	7	-
5	$TiCl_4$ (2 eq.), 0 °C to rt, 1 h	**76**	**20**	-
6[e]	$TiCl_4$ (1eq.), 0 °C to rt, 4 h	61	8	-

(a) All reactions were carried out on 1 mmol scale of keto-diester (**92b**) with 2 mmol of acid in CH_2Cl_2 (2 mL) for 1 h at room temperature.

(b) All the compounds (**93b, *ortho*-93b** & **98**) were obtained as a solids and gave satisfactory IR, ^1H NMR, ^{13}C NMR, mass spectral data and elemental analyses.

(c) Yields were based on keto-diester **92b**.

(d) Structure of the compound **98** was further confirmed by single crystal X-ray data (Fig. X3).

(e) These reactions were carried out on 1 mmol scale of keto-diester (**92b**) with 1 mmol of acid in CH_2Cl_2 (2 mL) for 1-4 h at room temperature.

® For continuity and better understandings we have numbered keto-diester as **92b** and indene derivatives as **93b, *ortho*-93b** & **98**.

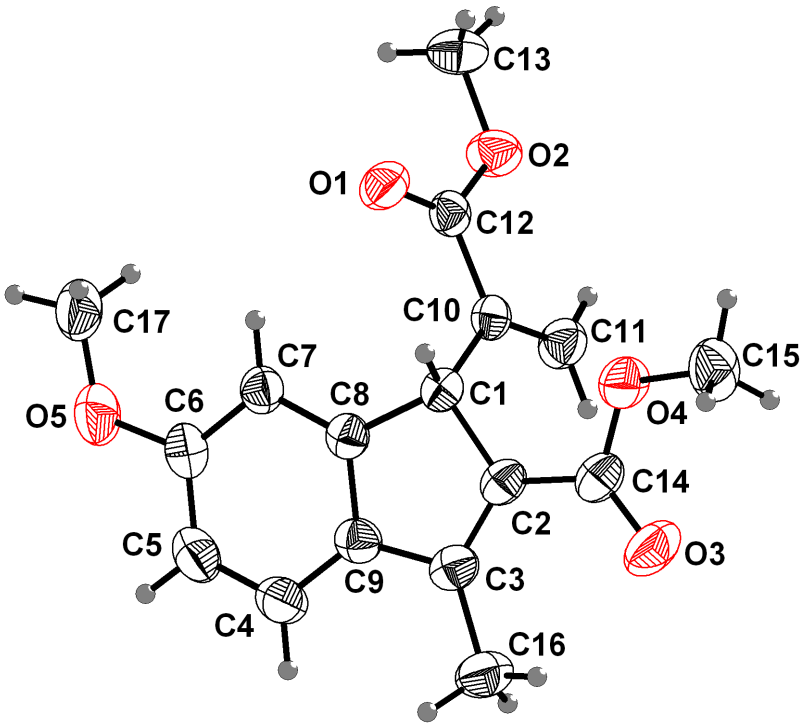


Fig. X1 ORTEP diagram of the compound **93b**

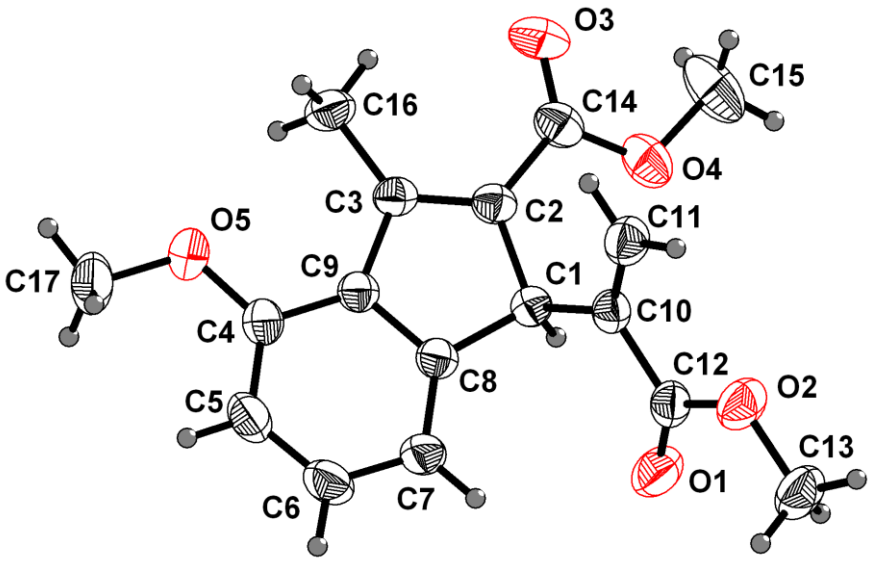


Fig. X2 ORTEP diagram of the compound ***ortho*-93b**

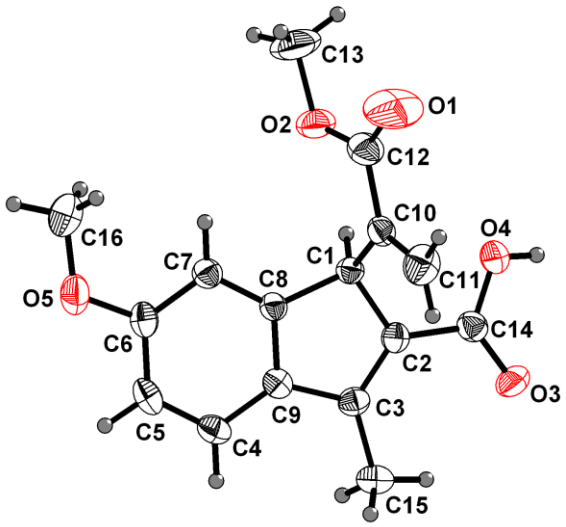
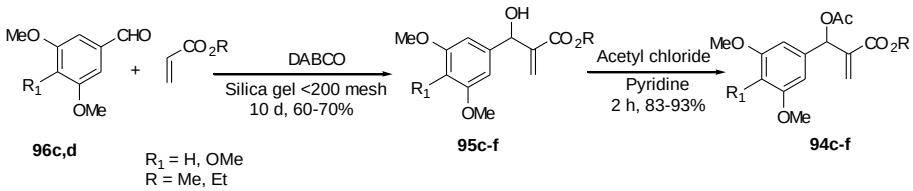


Fig. X3 ORTEP diagram of the compound **98**

With a view to understand the generality of this reaction we have prepared various Baylis-Hillman alcohols (**95c-f**), from representative alkoxy-benzaldehydes (**96c** & **96d**) and alkyl acrylates (methyl acrylate or ethyl acrylate). These alcohols (**95c-f**) were subsequently converted into their corresponding acetates (**94c-f**) (Scheme 56 and Table 2).

Scheme 56



These Baylis-Hillman acetates (**94c-f**), were on treatment with DABCO & methyl/ethyl acetoacetate under the influence of K_2CO_3 at room temperature for 6 h provided the corresponding keto-diesters (**92c-j**), in 88-93% isolated yields (dr ≈ 1:1) (Scheme 57, Table 3). Structures of these compounds were conformed with IR, ^{1}H NMR [for compound **92i** see Spectrums 9], ^{13}C NMR [for compound **92i** see Spectrums 10], mass spectral data and elemental analyses.

Table I. Crystal data and structure refinement for 93b

Identification code	: **93b**
Empirical formula	: $C_{17}\ H_{18}\ O_5$
Formula weight	: 302.31
Temperature	: 298(2) K
Wavelength	: 0.71073 Å
Crystal system	: Triclinic
Space group	: P-1
Unit cell dimensions	: a = 9.6539(10) Å; α = 68.543(2) deg.
	b = 9.7867(10) Å; β = 64.2280(10) deg.
	c = 10.5569(11) Å; γ = 61.3790(10) deg.
Volume	: 772.63(14) $Å^3$
Z, Calculated density	: 2, 1.299 Mg/m^3
Absorption coefficient	: 0.096 mm^{-1}
F(000)	: 320
Crystal size	: 0.52 x 0.40 x 0.28 mm
Theta range for data collection	: 2.19 to 25.05 deg.
Limiting indices	: -11<=h<=11, -11<=k<=11, -12<=l<=12
Reflections collected / unique	: 7513 / 2735 [R(int) = 0.0191]
Completeness to theta = 25.05	: 99.7 %
Max. and min. transmission	: 0.9737 and 0.9520
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 2735 / 0 / 203
Goodness-of-fit on F^2	: 1.060
Final R indices [I>2sigma(I)]	: R1 = 0.0473, wR2 = 0.1224
R indices (all data)	: R1 = 0.0534, wR2 = 0.1276
Largest diff. peak and hole	: 0.188 and -0.253 e. $Å^{-3}$

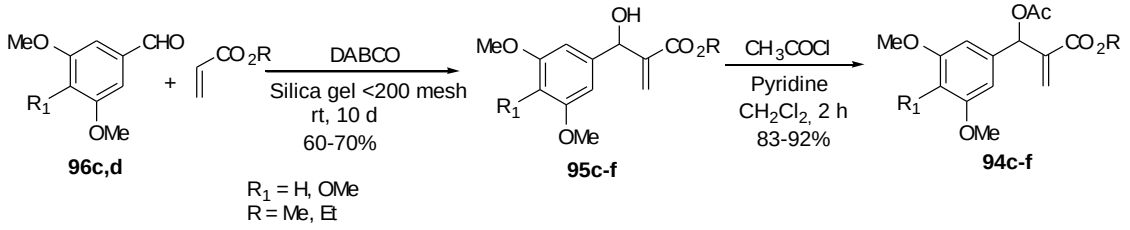
Table II. Crystal data and structure refinement for *ortho*-93b

Identification code	: ***ortho*-93b**
Empirical formula	: $C_{17}\ H_{18}\ O_5$
Formula weight	: 302.31
Temperature	: 298(2) K
Wavelength	: 0.71073 Å
Crystal system	: Triclinic
Space group	: P-1
Unit cell dimensions	: a = 8.9453(10) Å; α = 106.120(2) deg.
	: b = 9.4121(11) Å; β = 108.691(2) deg.
	: c = 10.5433(12) Å; γ = 103.365(2) deg.
Volume	: 756.17(15) $Å^3$
Z, Calculated density	: 2, 1.328 Mg/m^3
Absorption coefficient	: 0.098 mm^{-1}
F(000)	: 320
Crystal size	: 0.60 x 0.38 x 0.20 mm
Theta range for data collection	: 2.21 to 25.04 deg.
Limiting indices	: -10<=h<=10, -11<=k<=11, -12<=l<=12
Reflections collected / unique	: 7327 / 2671 [R(int) = 0.0237]
Completeness to theta = 25.04	: 99.4 %
Max. and min. transmission	: 0.9807 and 0.9437
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 2671 / 0 / 203
Goodness-of-fit on F^2	: 1.062
Final R indices [I>2sigma(I)]	: R1 = 0.0456, wR2 = 0.1208
R indices (all data)	: R1 = 0.0494, wR2 = 0.1249
Largest diff. peak and hole	: 0.237 and -0.238 e. $Å^{-3}$

Table III. Crystal data and structure refinement for 98

Identification code	: **98**
Empirical formula	: C_{16} H_{16} O_5
Formula weight	: 288.29
Temperature	: 298(2) K
Wavelength	: 0.71073 Å
Crystal system	: Triclinic
Space group	: P -1
Unit cell dimensions	: a = 8.515(3) Å; α = 64.63(4) deg.
	: b = 9.887(4) Å; β = 78.40(3) deg.
	: c = 10.222(4) Å; γ = 67.65(4) deg.
Volume	: 718.4(5) $Å^3$
Z, Calculated density	: 2, 1.333 Mg/m^3
Absorption coefficient	: 0.099 mm^{-1}
F(000)	: 304
Crystal size	: 0.42 x 0.38 x 0.28 mm
Theta range for data collection	: 3.33 to 26.37 deg.
Limiting indices	: -10<=h<=10, -12<=k<=9, -12<=l<=12
Reflections collected / unique	: 6265 / 2940 [R(int) = 0.0540]
Completeness to theta = 26.37	: 99.8 %
Max. and min. transmission	: 0.9727 and 0.9595
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 2940 / 0 / 195
Goodness-of-fit on F^2	:0.810
Final R indices [I>2sigma(I)]	: R1 = 0.0498, wR2 = 0.0936
R indices (all data)	: R1 = 0.1286, wR2 = 0.1081
Extinction coefficient	: 0.008(2)
Largest diff. peak and hole	: 0.170 and -0.183 e. $Å^{-3}$

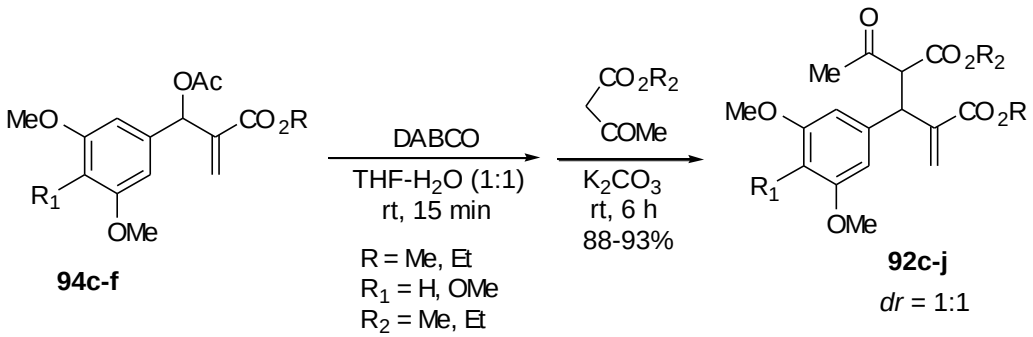
Table 2. Preparation of Baylis-Hillman alcohols (95c-f)[Φ,a] and acetates (94c-f)[Φ,b]



Aldehyde	R_1	R	B-H alcohol[c]	Yield (%)[d]	B-H acetate[c]	Yield (%)[e]
96c	H	Me	**95c**	64	**94c**	92
96d	OMe	Me	**95d**	60	**94d**	85
96c	H	Et	**95e**	60	**94e**	83
96d	OMe	Et	**95f**	70	**94f**	86

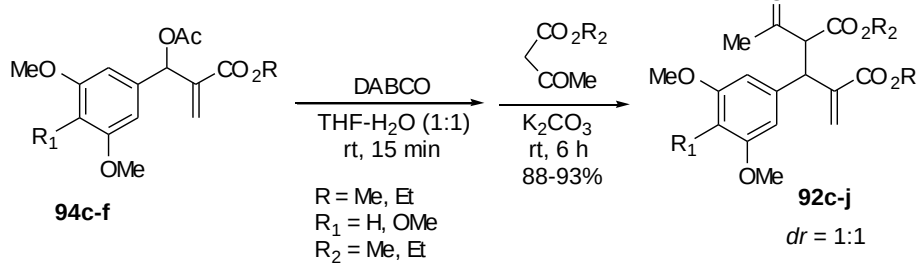
(a) All reactions were carried out on 20 mmol scale of aldehydes (**96c** & **96d**) with 30 mmol of methyl/ethyl acrylates, under influence of DABCO (15 mol%) in the silica gel-solid phase medium (mesh <200-400) at room temperature for 10 days.
(b) All reactions were carried out on 10 mmol scale of Baylis-Hillman alcohols (**95c-f**) with acetyl chloride, in presence of pyridine at room temperature for 2 h.
(c) All the compounds gave satisfactory IR, ^{1}H NMR & ^{13}C NMR spectral data.
(d) Yields are based on aldehydes.
(e) Yields are based on Baylis-Hillman alcohols.

Scheme 57



[Φ] For continuity and better understanding we have numbered the B-H alcohols derived from the aldehydes (**96c** & **96d**) and methyl acrylate or ethyl acrylate as **95c-f** and the corresponding B-H acetates as **94c-f** respectively.

Table 3. Synthesis of keto-diesters (92c-j)[#,a]



B-H acetate	R_1	R	R_2	Product[b,c]	Yield (%)[d]
94c	H	Me	Me	**92c**	93
94d	OMe	Me	Me	**92d**	88
94e	H	Et	Me	**92e**	92
94f	OMe	Et	Me	**92f**	90
94c	H	Me	Et	**92g**	90
94d	OMe	Me	Et	**92h**	93
94e	H	Et	Et	**92i**	92
94f	OMe	Et	Et	**92j**	90

(a) All reactions were carried out on 5 mmol scale of Baylis-Hillman acetates (**94c-f**) with 5 mmol of DABCO in THF-H_2O (5+5 mL) at rt for 15 min followed by addition of 5.5 mmol of keto ester under influence of K_2CO_3 (5.5 mmol) and stirred at room temperature for 6 h.

(b) All the keto-diesters (**92c-j**) were gave satisfactory IR, ^{1}H NMR, ^{13}C NMR mass spectral data and elemental analyses and all the compounds were obtained in keto form.

(c) Yields are based on B-H acetates.

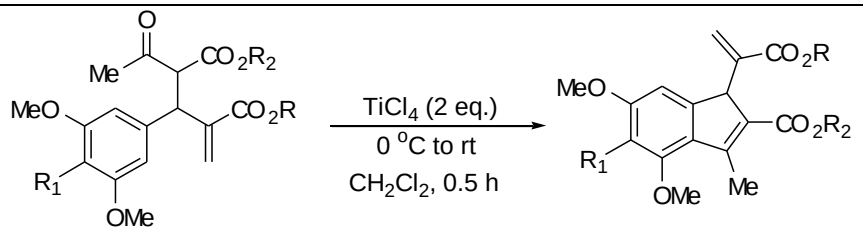
(d) The diastereomeric ratio was determined by the integration ratio of diastereomeric acetyl methyl group protons.

Subsequent treatment of these keto-diesters (**92c-j**) with $TiCl_4$ at room temperature provided the resulting indene derivatives (**93c-j**) in 91-95% isolated yields (Table 4). Structures of these compounds were established by IR, ^{1}H NMR [for compound **93c, 93f** & **93g** see Spectrums 11, 13 & 15 respectively], ^{13}C NMR [for compound **93c, 93f**

For continuity and better understandings we have numbered keto-diesters obtained from the reaction of B-H acetates (**94c-f)** with methyl acetoacetate as **92c-f** and keto-diesters obtained *via* the reaction of **94c-f** with ethyl acetoacetate as **92g-j** respectively.

& **93g** see Spectrums 12, 14 & 16 respectively], mass spectral data and elemental analyses. Structures of the molecules **93c**, **93h** were further confirmed by single crystal X-ray data analyses (for tables see Table IV and Table V). For ORTEP diagram of **93c** & **93h** see Fig. X4 and Fig. X5 respectively.

Table 4. Synthesis of highly functionalized indene derivatives (93c-j)[®,a]



92c-j **93c-j**

Keto-diester	R_1	R	R_2	Product	Yield (%)[b,c]
92c	H	Me	Me	**93c**[d]	94
92d	OMe	Me	Me	**93d**	92
92e	H	Et	Me	**93e**	93
92f	OMe	Et	Me	**93f**	93
92g	H	Me	Et	**93g**	95
92h	OMe	Me	Et	**93h**[d]	91
92i	H	Et	Et	**93i**	94
92j	OMe	Et	Et	**93j**	93

(a) All reactions were carried out on 1.0 mmol scale of keto-diesters (**92c-j**) with 2 mmol of $TiCl_4$ (1 mL, 2 M solution in CH_2Cl_2) in CH_2Cl_2 (2 mL) at room temperature for 0.5 h.

(b) All the compounds (**93c-j**) were fully characterized by IR, ^{1}H NMR, ^{13}C NMR, mass spectra data and elemental analyses.

(c) Yields are based on keto-diesters.

(d) Compounds **93c** & **93h** were further characterized by single crystal X-ray data.

® For clarity and better understandings we have numbered indene derivatives derived from keto-diesters **92c-j** as **93c-j**

.

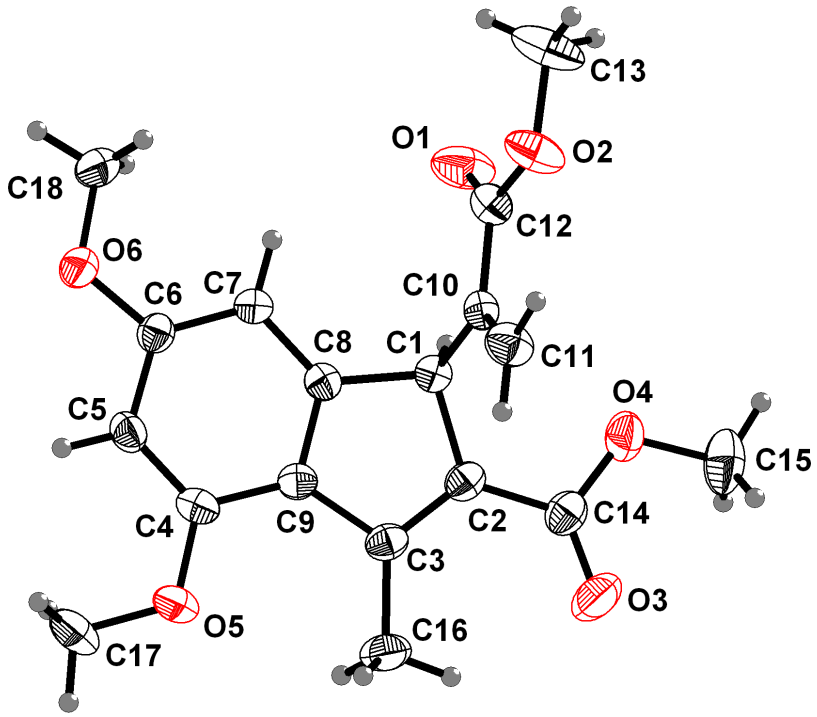


Fig. X4 ORTEP diagram of the compound **93c**

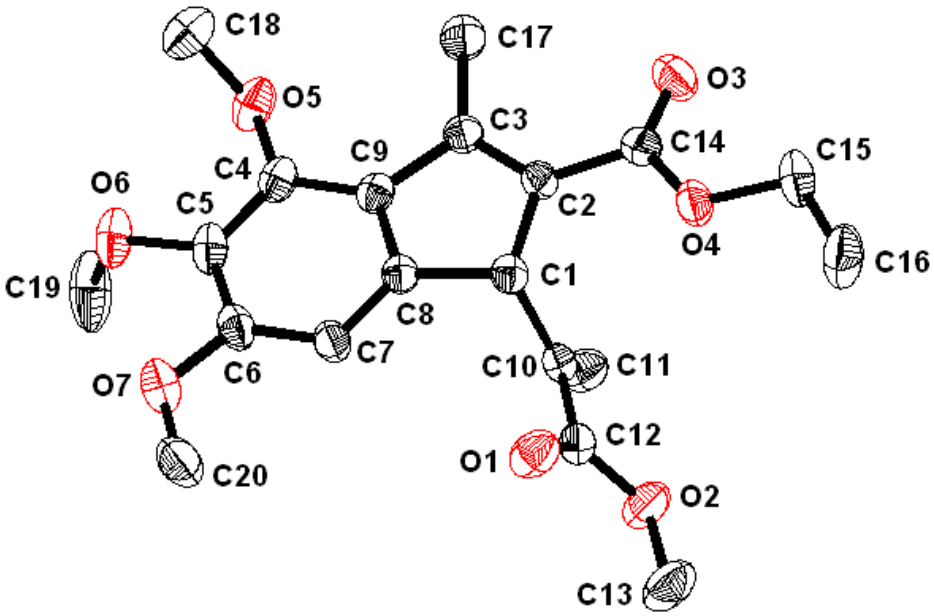


Fig. X5 ORTEP diagram of the compound **93h**

(hydrogen atoms were omitted for clarity)

Table IV. Crystal data and structure refinement for 93c

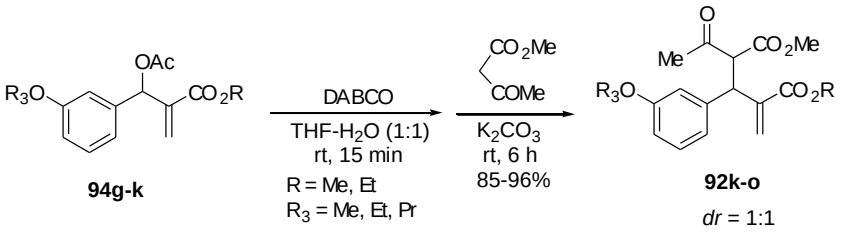
Identification code	: **93c**
Empirical formula	: $C_{18}\ H_{20}\ O_6$
Formula weight	: 332.34
Temperature	: 298(2) K
Wavelength	: 0.71073 Å
Crystal system	: Monoclinic
Space group	: C 1 2/c 1
Unit cell dimensions	: a = 19.345(3) Å; α = 90 deg.
	b = 9.5690(11) Å; β = 122.10(2) deg.
	c = 21.222(4) Å; γ = 90 deg.
Volume	: 3327.8(9) $Å^3$
Z, Calculated density	: 8, 1.327 Mg/m^3
Absorption coefficient	: 0.100 mm^{-1}
F(000)	: 1408
Crystal size	: 0.36 x 0.32 x 0.28 mm
Theta range for data collection	: 2.87 to 26.36 deg.
Limiting indices	: -23<=h<=24, -11<=k<=8, -26<=l<=26
Reflections collected / unique	: 7221 / 3403 [R(int) = 0.0239]
Completeness to theta = 26.36	: 99.9 %
Max. and min. transmission	: 0.9726 and 0.9650
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 3403 / 0 / 222
Goodness-of-fit on F^2	: 1.056
Final R indices [I>2sigma(I)]	: R1 = 0.0472, wR2 = 0.1149
R indices (all data)	: R1 = 0.0711, wR2 = 0.1304
Largest diff. peak and hole	: 0.186 and -0.207 e. $Å^{-3}$

Table V. Crystal data and structure refinement for 93h

Identification code	: **93h**
Empirical formula	: $C_{20}\ H_{24}\ O_7$
Formula weight	: 376.39
Temperature	: 298(2) K
Wavelength	: 0.71073 Å
Crystal system	: Monoclinic
Space group	: P2(1)/c
Unit cell dimensions	: a = 10.0264(11) Å; α = 90 deg.
	b = 16.1212(17) Å; β = 107.732(2) deg.
	c = 12.7802(13) Å; γ = 90 deg.
Volume	: 1967.6(4) $Å^3$
Z, Calculated density	: 4, 1.271 Mg/m^3
Absorption coefficient	: 0.096 mm^{-1}
F(000)	: 800
Crystal size	: 0.52 x 0.40 x 0.28 mm
Theta range for data collection	: 2.10 to 25.05 deg.
Limiting indices	: -11<=h<=11, -19<=k<=19, -15<=l<=15
Reflections collected / unique	: 18745 / 3484 [R(int) = 0.0819]
Completeness to theta = 25.05	: 99.9 %
Max. and min. transmission	: 0.9736 and 0.9518
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 3484 / 0 / 250
Goodness-of-fit on F^2	: 1.137
Final R indices [I>2sigma(I)]	: R1 = 0.0852, wR2 = 0.1469
R indices (all data)	: R1 = 0.1370, wR2 = 0.1666
Largest diff. peak and hole	: 0.169 and -0.135 e. $Å^{-3}$

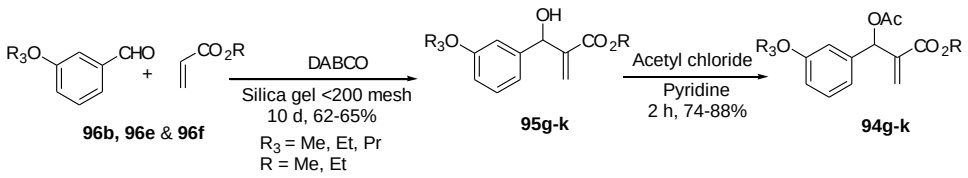
In order to examine the *ortho-para* cyclization selectivity we have selected un-symmetrically substituted aryl aldehydes to obtain the keto-diesters (**92k-o**). The desired keto-diesters (**92k-o**) were prepared from the corresponding Baylis-Hillman acetates (**94g-k**) by treating with DABCO, followed by the reaction with methyl acetoacetate under the influence of K_2CO_3 at room temperature for 6 h, in 85-96% isolated yields (in 1:1 diastereomeric ratio) (Scheme 58, Table 5). Structures of these compounds are established with IR, ^{1}H NMR, ^{13}C NMR, mass spectral data and elemental analyses.

Scheme 58

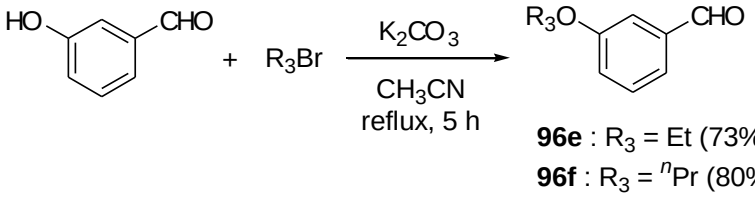


The required B-H acetates (**94g-k**) were prepared *via* the acetylation of corresponding B-H alcohols (**95g-k**), which in turn were obtained *via* the coupling of arylaldehydes (**96b, 96e** & **96f**) and methyl acrylate or ethyl acrylate under the catalytic influence of DABCO (Scheme 59, Table 6).

Scheme 59



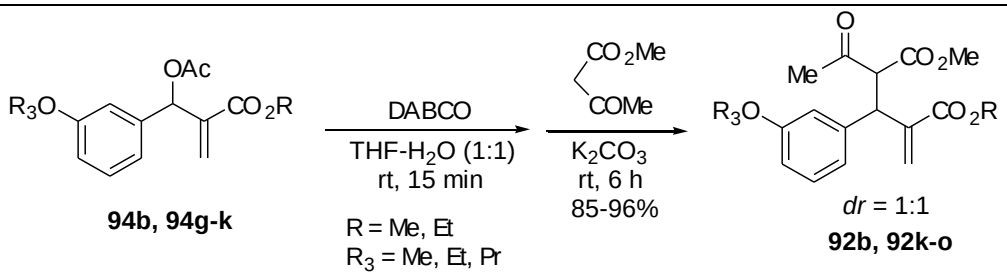
3-Ethoxybenzaldehyde (**96e**), and 3-propoxybenzaldehyde (**96f**) were prepared from 3-hydroxybenzaldehyde by alkylation with ethyl bromide and propyl bromide respectively according to the Eq. 26.



Eq. 26

In order to understand the *ortho-para* selectivity we have treated keto-diesters (**92k-o**) with $TiCl_4$ at room temperature. The resulting indene derivatives, *para*-cyclized derivatives (**93k-o)** and *ortho*-cyclized derivatives (***ortho*-93k-o**) were obtained in 72-76% and 17-21% isolated yields respectively (Table 7). Structures of these compounds are confirmed using IR, ^{1}H NMR [for compound **93n** and ***ortho*-93n** see Spectrums 17

Table 5. Synthesis of keto-diesters (92b, 92k-o)[#,a]



B-H acetate	R_3	R	Product[b,c]	Yield (%)[d]	M.p (^{o}C)
94b	Me	Me	**92b**	88	-
94g	Et	Me	**92k**	90	64-66
94h	Pr	Me	**92l**	96	-
94i	Me	Et	**92m**	85	-
94j	Et	Et	**92n**	86	-
94k	Pr	Et	**92o**	90	-

(a) All reactions were carried out on 5 mmol scale of Baylis-Hillman acetates (**94b, 94g-k**) with 5 mmol of DABCO in THF-H_2O (5+5 mL) at rt for 15 min followed by addition of 5.5 mmol of methyl acetoacetate under influence of K_2CO_3 (5.5 mmol) and stirred at room temperature for 6 h.

(b) All the compounds (**92b, 92k-o**) were gave satisfactory IR, ^{1}H NMR, ^{13}C NMR mass spectral data and elemental analyses and all the compounds were obtained in keto form.

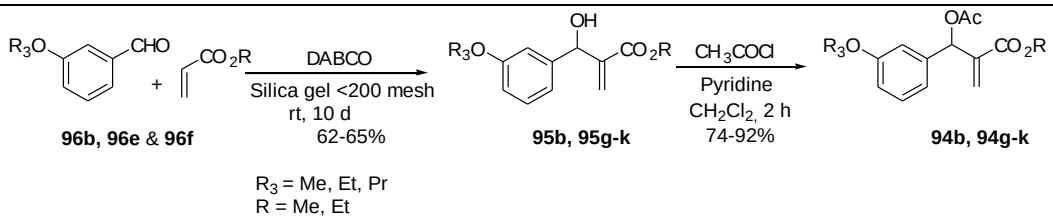
(c) The diastereomeric ratio was determined by the integration ratio of diastereomeric acetyl methyl group protons.

(d) Yields are based on B-H acetates.

For continuity and better understandings we have numbered keto-diester obtained from the reaction of **94b, 94g-k** with methyl acetoacetate as **92b, 92k-o** respectively.

& 19 respectively], ^{13}C NMR [for compound **93n** and ***ortho*-93n** see spectrums 18 & 20 respectively], mass spectral data and elemental analyses. Structures of the molecules **93k**, ***ortho*-93k** were further established by single crystal X-ray data analyses (for ORTEP diagram of **93k** & ***ortho*-93k** see Fig. X6 and Fig. X7). For tables see Table VI and Table VII respectively.

Table 6. Synthesis of Baylis-Hillman alcohols (95b, 95g-k)[Φ,a] and acetates (94b, 94g-k)[Φ,b]



Aldehyde	R_3	R	B-H alcohol[e]	Yield (%)[c]	B-H acetate[e]	Yield (%)[d]
96b	Me	Me	**95b**	62	**94b**	92
96e	Et	Me	**95g**	65	**94g**	86
96f	Pr	Me	**95h**	62	**94h**	86
96b	Me	Et	**95i**	65	**94i**	88
96e	Et	Et	**95j**	62	**94j**	74
96f	Pr	Et	**95k**	65	**94k**	80

(a) All reactions were carried out on 100 mmol scale of aldehydes with 150 mmol of methyl/ethyl acrylates, under influence of DABCO (15 mol%) in the silica gel-solid phase medium (mesh <200-400) at room temperature for 10 days.

(b) All reactions were carried out on 10 mmol scale of Baylis-Hillman alcohols (**95b, 95g-k**) with acetyl chloride, in presence of pyridine at room temperature for 2 h.

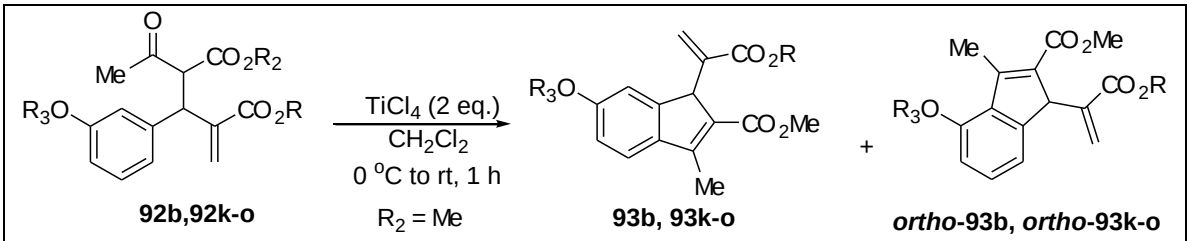
(c) Yields are based on aldehydes.

(d) Yields are based on Baylis-Hillman alcohols.

(e) All the compounds gave satisfactory IR, ^{1}H NMR, ^{13}C NMR spectral data.

Φ For continuity and better understanding we have numbered the B-H alcohols derived from the aldehydes (**96b, 96e** & **96f**) and methyl acrylate or ethyl acrylate as **95b, 95g-k** respectively and the corresponding B-H acetates as **94b, 94g-k** respectively.

Table 7. Synthesis of indene derivatives (93b, 93k-o, *ortho*-93b & *ortho*-93k-o)®,a



92b,92k-o **93b, 93k-o** ***ortho*-93b, *ortho*-93k-o**

Keto-diester	R_3	R	Product	Yield (%)[b,c]	Product	Yield (%)[b,c]
92b	Me	Me	**93b**	76	***ortho*-93b**	20
92k	Et	Me	**93k**[d]	73	***ortho*-93k**[d]	21
92l	Pr	Me	**93l**	75	***ortho*-93l**	19
92m	Me	Et	**93m**	75[d]	***ortho*-93m**	17
92n	Et	Et	**93n**	76	***ortho*-93n**	17
92o	Pr	Et	**93o**	72	***ortho*-93o**	17

(a) All reactions were carried out on 1.0 mmol scale of keto-diesters (**92b, 92k-o**) with 2 mmol of $TiCl_4$ (1 mL, 2 M solution in CH_2Cl_2) in CH_2Cl_2 (2 mL) at room temperature for 1 h.

(b) All the compounds (**93b, 93k-o, *ortho*-93b** & ***ortho*-93k-o**) were fully characterized using IR, ^{1}H NMR, ^{13}C NMR, mass spectra data and elemental analyses.

(c) Yields are based on keto-diesters.

(d) Compounds **93k** & ***ortho*-93k** were further characterized by single crystal X-ray data.

® For clarity and better understandings we have numbered for *para/ortho*-cyclized products derived from **92b, 92k-o** as **93b, 93k-o** and ***ortho*-93b** & ***ortho*-93k-o** respectively.

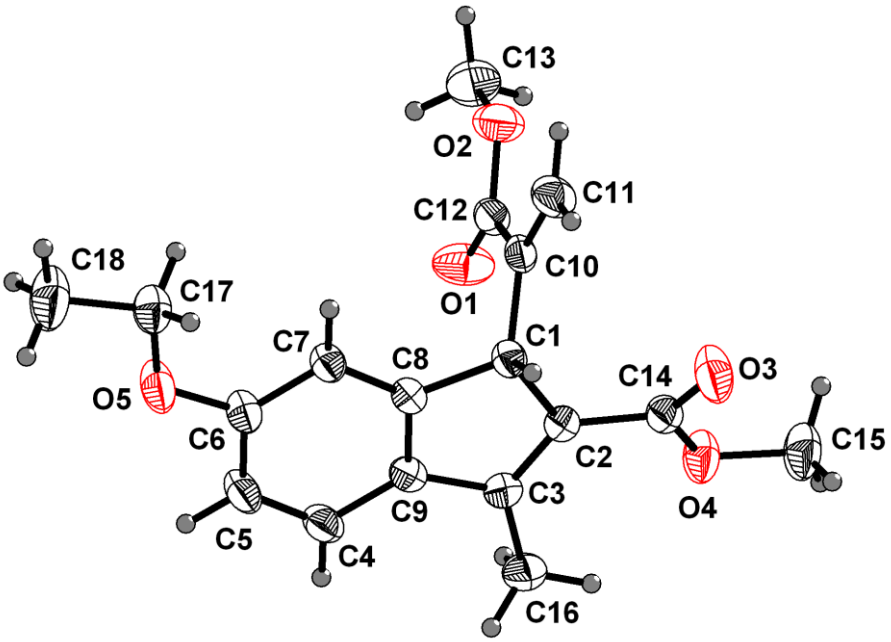


Fig. X6 ORTEP diagram of the compound **93k**

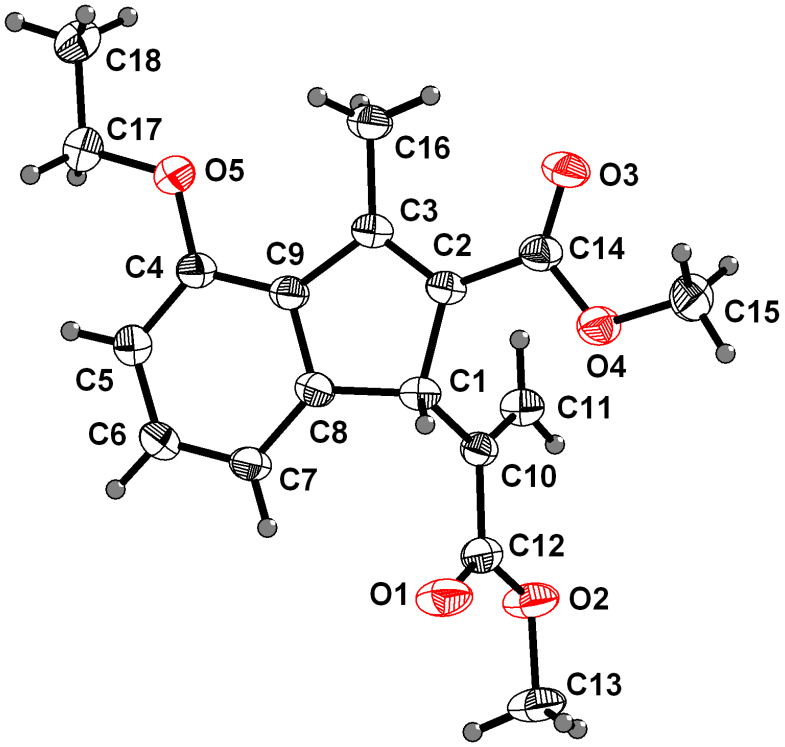


Fig. X7 ORTEP diagram of the compound ***ortho*-93k**

Table VI. Crystal data and structure refinement for 93k

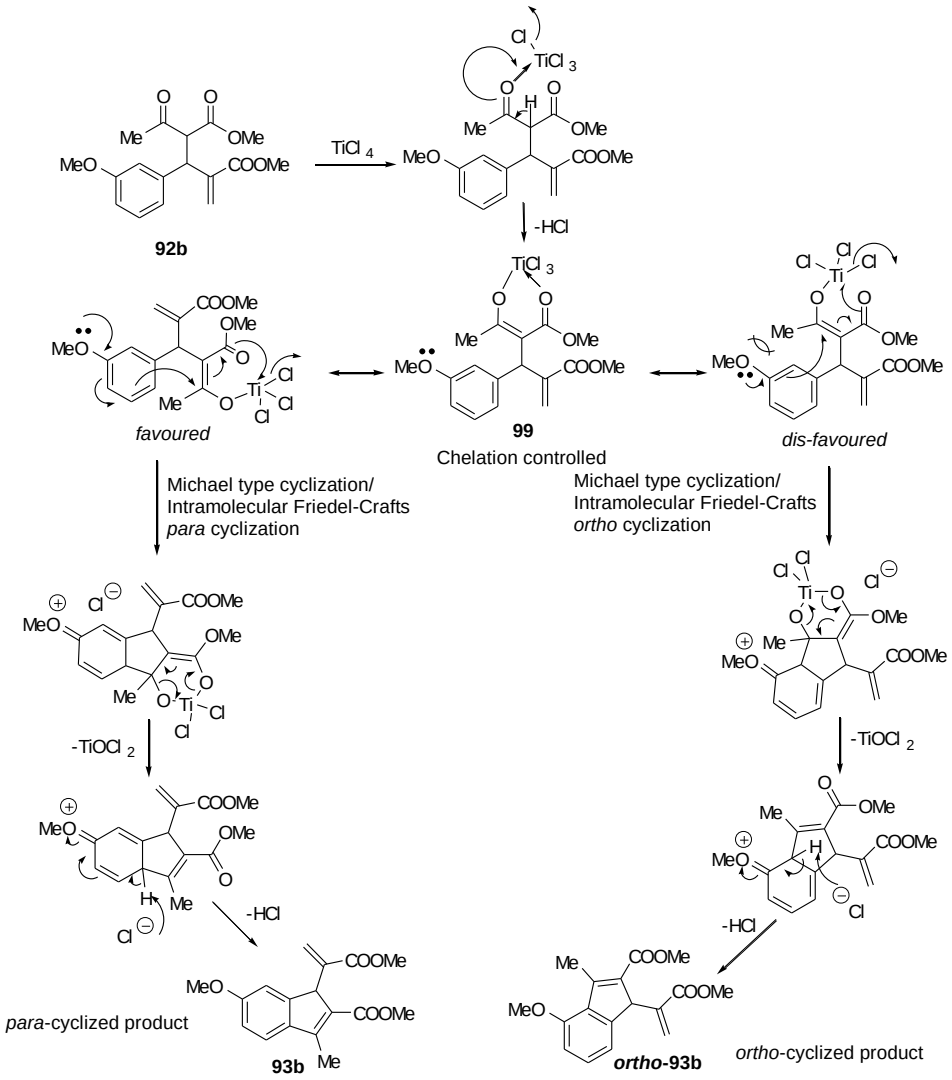
Identification code	: **93k**
Empirical formula	: C_{18} H_{20} O_5
Formula weight	: 316.34
Temperature	: 298(2) K
Wavelength	: 0.71073 Å
Crystal system	: Triclinic
Space group	: P-1
Unit cell dimensions	: a = 5.7636(8) Å; α = 91.482(2) deg.
	b = 9.3432(13) Å; β = 92.853(3) deg.
	c = 15.310(2) Å; γ = 91.267(2) deg.
Volume	: 822.9(2) $Å^3$
Z, Calculated density	: 2, 1.277 Mg/m^3
Absorption coefficient	: 0.093 mm^{-1}
F(000)	: 336
Crystal size	: 0.60 x 0.28 x 0.08 mm
Theta range for data collection	: 1.33 to 25.08 deg.
Limiting indices	: -6<=h<=6, -11<=k<=11, -18<=l<=18
Reflections collected / unique	: 8031 / 2913 [R(int) = 0.0413]
Completeness to theta = 25.08	: 99.7 %
Max. and min. transmission	: 0.9926 and 0.9464
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 2913 / 0 / 212
Goodness-of-fit on F^2	: 1.040
Final R indices [I>2sigma(I)]	: R1 = 0.0622, wR2 = 0.1512
R indices (all data)	: R1 = 0.0792, wR2 = 0.1638
Largest diff. peak and hole	: 0.262 and -0.359 e. $Å^{-3}$

Table VII. Crystal data and structure refinement for *ortho*-93k

Identification code	: ***ortho*-93k**
Empirical formula	: $C_{18}\ H_{20}\ O_5$
Formula weight	: 316.34
Temperature	: 298(2) K
Wavelength	: 0.71073 Å
Crystal system	: Triclinic
Space group	: P-1
Unit cell dimensions	: a = 6.965(4) Å; α = 78.010(9) deg.
	b = 7.746(4) Å; β = 89.915(10) deg.
	c = 15.540(8) Å; γ = 80.114(9) deg.
Volume	: 807.4(7) $Å^3$
Z, Calculated density	: 2, 1.301 Mg/m^3
Absorption coefficient	: 0.095 mm^{-1}
F(000)	: 336
Crystal size	: 0.36 x 0.32 x 0.32 mm
Theta range for data collection	: 1.34 to 25.14 deg.
Limiting indices	: -8<=h<=8, -9<=k<=9, -18<=l<=18
Reflections collected / unique	: 7635 / 2855 [R(int) = 0.0441]
Completeness to theta = 25.14	: 98.6 %
Max. and min. transmission	: 0.9704 and 0.9667
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 2855 / 0 / 212
Goodness-of-fit on F^2	: 1.009
Final R indices [I>2sigma(I)]	: R1 = 0.0499, wR2 = 0.1196
R indices (all data)	: R1 = 0.0769, wR2 = 0.1372
Largest diff. peak and hole	: 0.155 and -0.194 e. $Å^{-3}$

Mechanism for the formation of highly functionalized indene derivatives from the keto-diesters is presented in Scheme 60, by taking reaction between methyl 4-methoxycarbonyl-3-(3-methoxyphenyl)-2-methylene-5-oxohexanoate (**92b**) and $TiCl_4$ as a model case. Treatment keto-diester with $TiCl_4$ would generate titanium enolate intermediate (**99**) that might undergo further intramolecular Friedel-Crafts reactions leading to the formation of the indene derivatives, **93b** & ***ortho*-93b**. It is believed that chelation controlled titanium species directs the mode of cyclization.

Scheme 60: Plausible Mechanism



In conclusion we have examined the competition between keto cyclization and ester cyclization for intramolecular Friedel-Crafts reaction with aromatic ring by taking alkyl 4-alkoxycarbonyl-3-(alkoxyphenyl)-2-methylene-5-oxohexanoates (**92**) as substrates containing two ester groups and one keto group in a similar environment, thus demonstrating the importance of the Baylis-Hillman acetates as probes to understanding these intramolecular Friedel-Crafts reactions. We have used this strategy for developing a convenient, operationally simple synthesis of highly functionalized indene derivatives from the acetates of the Baylis-Hillman adducts in a two step protocol.

Development of a simple protocol for synthesis of [1,2,3]-triazolo-[1,4]-benzoxazonine derivatives from the Baylis-Hillman acetates

[1,2,3]-Triazole framework has attracted attention of synthetic chemists in recent years as this skeleton is present in many bioactive molecules showing various activities like anti-HIV (**100**),[115] anti-allergic (**101**),[116] anti-bacterial (**102**[117] & **103**),[118] human β_3-adrenergic receptor agonists (**104**)[119](Figure 7). Therefore there has been increasing interest in the synthesis of [1,4]-oxazo cyclic systems fused with [1,2,3]-triazole framework containing 6/7/8-membered cyclic systems (**A, B, C**) (Figure 8) and in the study of their biological properties. Some such recent strategies are described in this section.

Figure 7

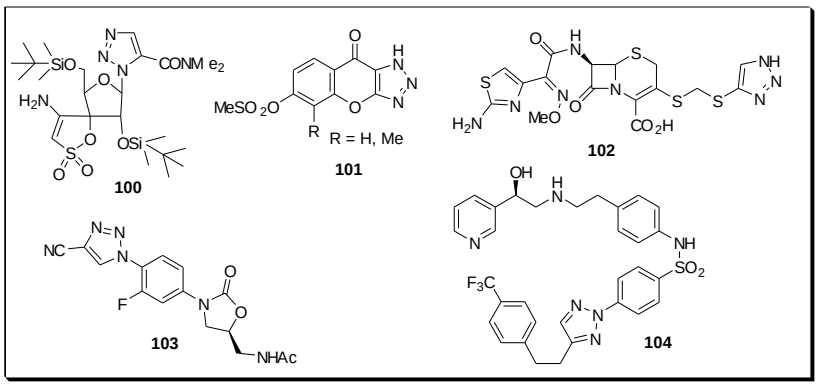
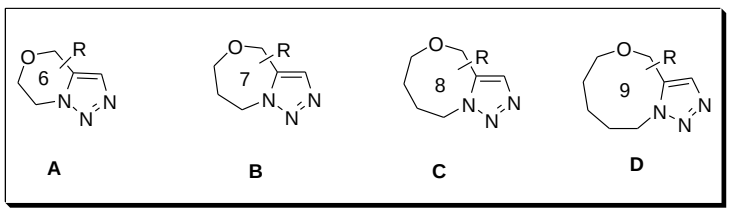


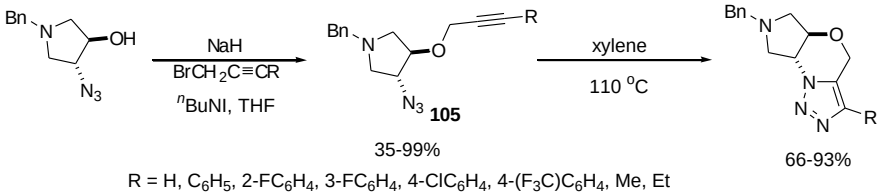
Figure 8



Pericas and co-workers[120] have reported an interesting synthesis of triazolo-[1,4]-oxazine framework *via* the intramolecular cyclization (Huisgen reaction) of the

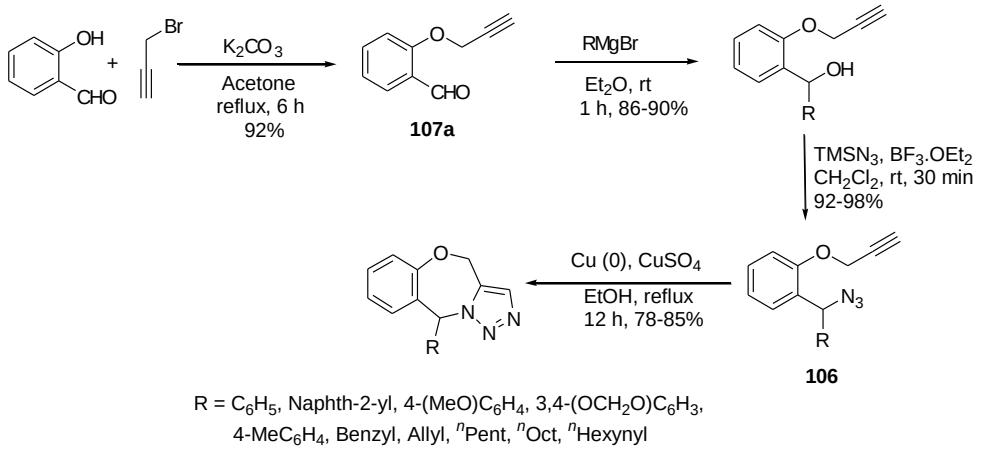
substrate **105**, containing alkyne-azide units (Scheme 61). Some of these compounds exhibit significant affinity for the sigma-1 receptor.

Scheme 61

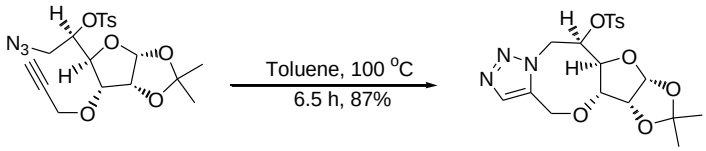


A facile synthesis of triazolo-benzoxazepine derivatives have been developed by Chandrasekhar and co-workers[121] *via* the intramolecular Cu(0)/$CuSO_4$ catalyzed 1,3-dipolar cycloaddition of azide **106**, starting from salicylaldehyde, according to the reaction sequence shown in Scheme 62. Some of these compounds were subjected for anti-microbial activity studies.

Scheme 62



Fused triazolo-[1,4]-oxazazocine derivatives (**108**) were synthesized using carbohydrate-derived azido-alkynes under reagent free conditions by Hotha and co-workers.[122] One example is presented in Eq. 27.

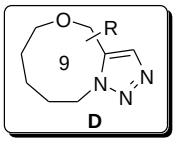


Eq. 27

108

We became interested in triazolo-[1,4]-benzoxazonine system because there is not much literature was available about this framework and also due to the challenges in the construction of 9-membered ring *i.e.* [1,4]-oxazonine ring. Therefore our objective is directed towards development of triazolo-[1,4]-benzoxazonine system **D** (Figure 8 & 9) using Baylis-Hillman adducts. It is appropriate to mention here the utility of Baylis-Hillman adducts for preparation of triazole and benzofused triazole systems using Huisgen (Click) reaction as the key step. Some recent and relevant literature reports are summarized in the following.

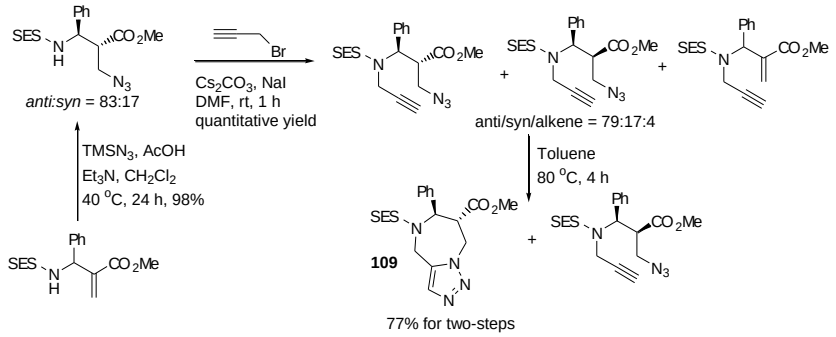
Figure 9



D

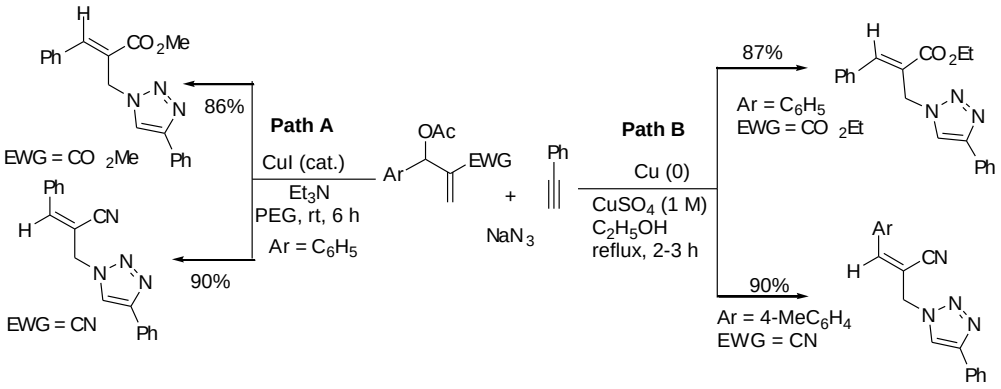
Lamaty and co-workers[123] have used [3+2] Huisgen cycloaddition reaction for synthesis of triazolodiazepines (**109**) from the Baylis-Hillman adducts following the reaction sequence as shown in Scheme 63.

Scheme 63



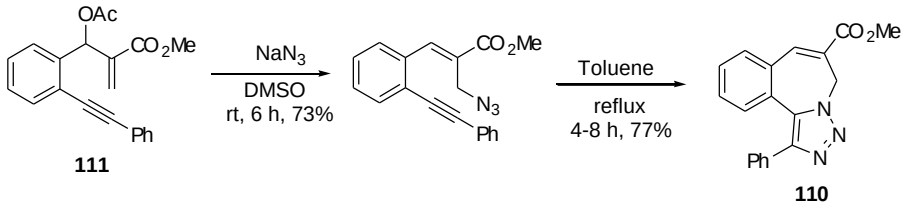
One-pot synthesis of triazole derivatives has been reported from the Baylis-Hillman acetates by treatment with sodium azide and phenylacetylene under the influence of CuI (Paths A)[124] and also using Cu(0)/$CuSO_4$ (Path B).[125] Selected examples are shown in Scheme 64.

Scheme 64



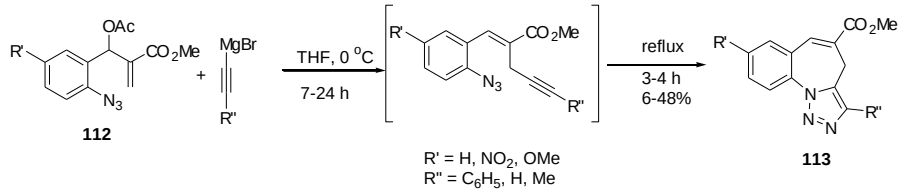
5H-1,2,3-Triazolo[4,3-a][2]benzazepines (**110**) have been synthesized by the intramolecular 1,3-dipolar cycloaddition reaction as the key step starting from the Baylis-Hillman acetates **111** following the reaction sequence as shown in Scheme 65 (one example is presented) by Ko and Lee.[126]

Scheme 65



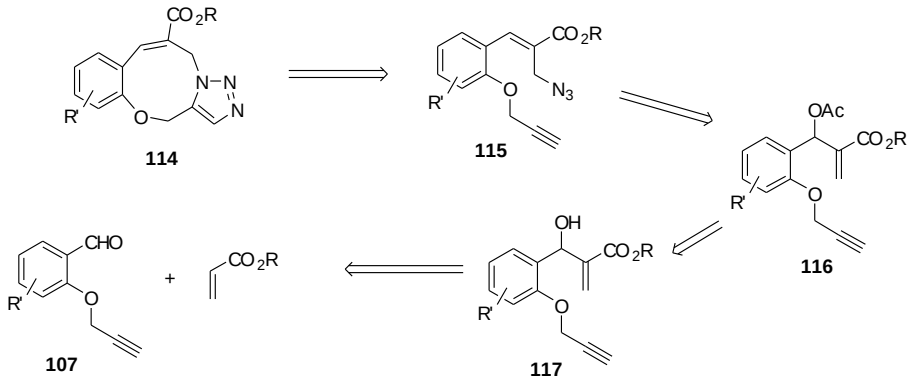
Acetates (**112**) of the Baylis-Hillman alcohols derived from 2-azidobenzaldehyde have been conveniently transformed into 4H-[1,2,3]-triazolo[1,5-a][1]benzazepines (**113**) according to the synthetic sequence shown in Scheme 66 by Song and Lee.[127]

Scheme 66



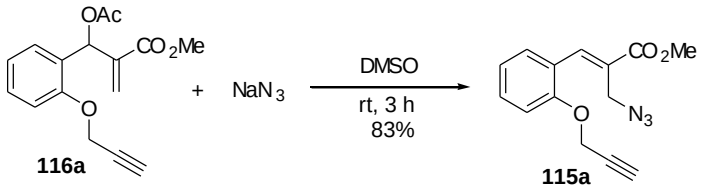
Based on literature reports and also on our experience on the Baylis-Hillman reaction we directed our studies towards synthesis of [1,2,3]-triazolo-[1,4]-benzoxazonine derivatives (**114**) according to the retro-synthetic sequence shown in Scheme 67.

Scheme 67: Retro-synthetic strategy



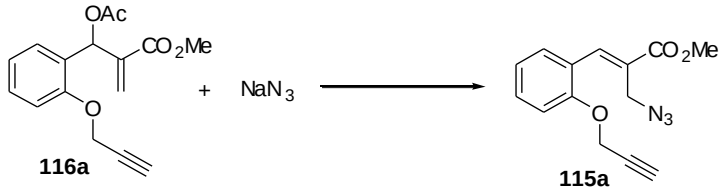
Accordingly we have first selected methyl 3-acetoxy-2-methylene-3-[2-(prop-2-ynyloxy)phenyl]propanoate (**116a**), the Baylis-Hillman acetate, as a substrate for reaction with sodium azide. This reaction was tried under different conditions and the best results were obtained when the reaction was performed in DMSO as a solvent at room temperature (entry 6, Table 8). Thus the treatment of methyl 3-acetoxy-2-methylene-3-[2-(prop-2-ynyloxy)phenyl]propanoate (**116a**) (5 mmol), with sodium azide (7.5 mmol), in DMSO at room temperature for 3 h provided methyl 2-(azidomethyl)-3-[2-(prop-2-ynyloxy)phenyl]propenoate (**115a**), in 83% isolated yield (Eq. 28). Structure of this molecule was established by IR, ^{1}H NMR [for compound

115a see Spectrum 21], ^{13}C NMR [for compound **115a** see Spectrum 22], mass spectral data and elemental analysis.



Eq. 28

Table 8. **Optimization: Synthesis of azido alkyne 115a**®,a



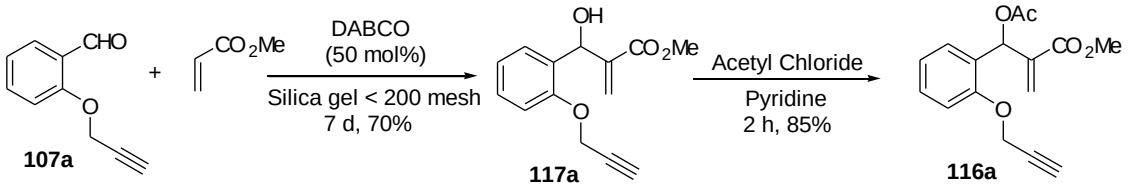
Entry	Condition(s)	Yield (%)[b,c]
1	Toluene, rt, 1 day	-
2	Toluene-H_2O, rt, 1 day	11
3	THF-H_2O (1:1), rt, 1 day	-
4	DMSO-H_2O, rt, 12 h	23
5	DMSO, rt, 2 h	65
6	DMSO, rt, 3 h	**83**
7	DMSO, rt, 12 h	73

(a) All reactions were carried out on 5 mmol scale of BH acetate (**116a**) with sodium azide (1.5 eq.) at room temperature.
(b) Yields were based on BH acetate **116a**.

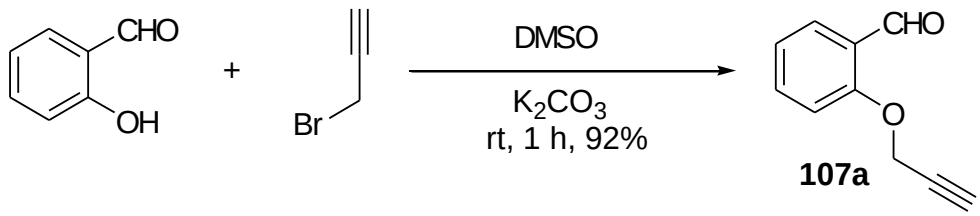
Required methyl 3-acetoxy-2-methylene-3-[2-(prop-2-ynyloxy)phenyl]propanoate (**116a**) was prepared *via* the acetylation of methyl 3-hydroxy-2-methylene-3-[2-(prop-2-ynyloxy)phenyl]propanoate (**117a**). This allyl alcohol **117a** was obtained *via* the coupling of 2-(prop-2-ynyloxy)benzaldehyde (**107a**) with methyl acrylate in presence of DABCO (Scheme 68).[113]

® For continuity and better understandings we have numbered BH acetate as **116a** and azide-alkyne as **115a**.

Scheme 68



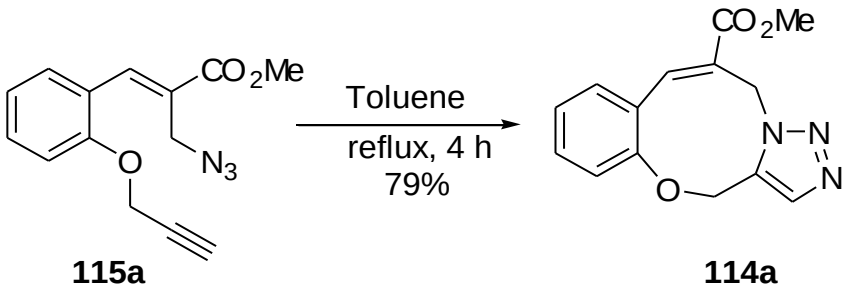
2-(Prop-2-ynyloxy)benzaldehyde (**107a**) was prepared *via* the *O*-propargylation of 2-hydroxybenzaldehyde, with propargyl bromide in presence of K_2CO_3 in DMSO at room temperature according to the Eq. 29. Structure of **107a**, **116a** and **117a** was established using IR, ^{1}H NMR, and ^{13}C NMR spectral analysis.



Eq. 29

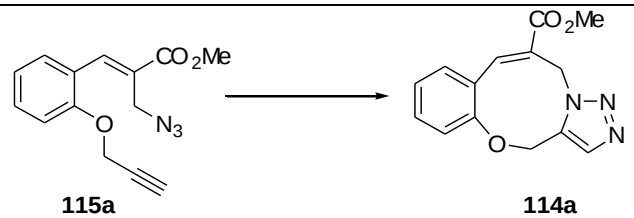
After having azido alkyne (**115a**) in our hand, we tried for intramolecular [3+2] Huisgen cyclization under usual conditions using Cu(0)/$CuSO_4$ as a catalytic system (entry 1, Table 9). The desired triazole was obtained in less yield, 30% (Entry 1, Table 9). In order to increase the yield of the desired triazolo-[1,4]-benzoxazonine, we have examined this reaction under different conditions and observed that just refluxing in toluene provided better yields (Entry 4, Table 9). Thus heating methyl 2-(azidomethyl)-3-[2-(prop-2-ynyloxy)phenyl]-propenoate (**115a**) (1 mmol) in refluxing toluene for 4 h provided 10-methoxycarbonyl-2-oxa-6,7,8-triazatricyclo[10,4,0,$0^{4,8}$]hexadeca-4,6,10,12,14,16(1)-hexaene (**114a**) in 79% isolated yield (Eq. 30). Structure of this molecule was established by IR, ^{1}H NMR [for compound **114a** see Spectrum 23], ^{13}C NMR [for compound **114a** see Spectrum 24], mass spectral data and elemental

analysis. We have also obtained single crystal for this compound and further confirmed the structure of the molecule **114a** by single crystal X-ray data analysis (see Fig. X8, for ORTEP diagram of molecule **114a**, Table VIII).



Eq 30

Table 9. **Optimization**: **Synthesis of triazolo-[1,4]-benzoxazonine 114a**®,a



Entry	Condition(s)	Yield (%)[b,c]
1	Cu/$CuSO_4$, EtOH, reflux, 4 h	30
2	DMSO, reflux, 4 h	67
3	Toluene, reflux, 2 h	59
4	Toluene, reflux, 4 h	**79**

(a) All reactions were carried out on 1 mmol scale of azido-alkyne (**115a**).
(b) Yields were based on azido-alkyne **115a**.

® For continuity and better understandings we have numbered azido-alkyne as **115a** and triazolo-[1,4]-benzoxazonine derivarive as **114a**.

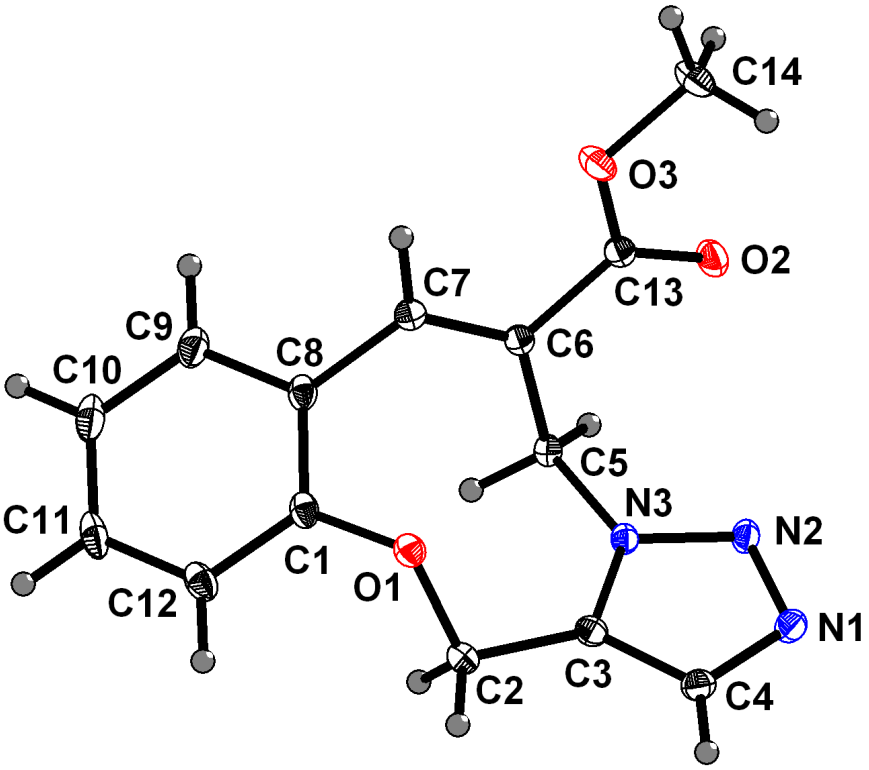


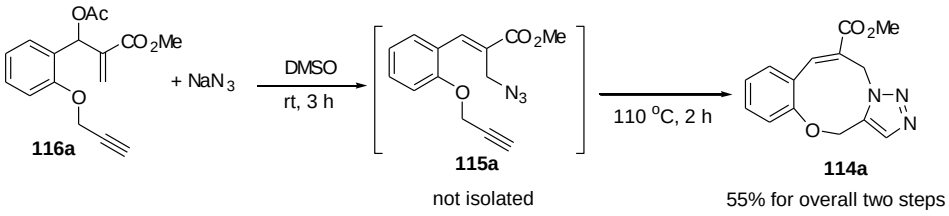
Fig. X8 ORTEP diagram of the compound **114a**

Encouraged by this success in obtaining [1,2,3]-triazolo-[1,4]-benzoxazonine in reasonably high yields we turned our attention to achieve the same without purifying the intermediate azido-alkyne **115a**. In this direction we have performed the reaction between Baylis-Hillman acetate **116a** and sodium azide in DMSO as a solvent. We have then treated methyl 3-acetoxy-2-methylene-3-[2-(prop-2-ynyloxy)phenyl]-propanoate (**116a**) with sodium azide in DMSO for 3 h at room temperature and then heating the resulting mixture for 2 h at 110 ^{o}C in the same solvent to provide 10-methoxycarbonyl-2-oxa-6,7,8-triazatricyclo[10,4,0,0^{4,8}]hexadeca-4,6,10,12,14,16(1)-hexaene (**114a)**, only in 55% isolated yield (Scheme 69, entry 5, Table 10).

Table VIII. Crystal data and structure refinement for 114a

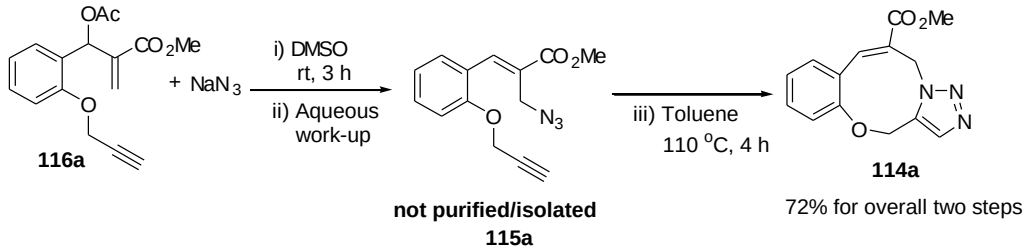
Identification code	: **114a**
Empirical formula	: $C_{14}\ H_{13}\ N_3\ O_3$
Formula weight	: 271.27
Temperature	: 100(2) K
Wavelength	: 0.71073 Å
Crystal system	: Monoclinic
Space group	: C2/c
Unit cell dimensions	: a = 19.4754(15) Å; α = 90 deg.
	b = 10.3699(8) Å; β = 125.1930(10) deg.
	c = 15.3638(12) Å; γ = 90 deg.
Volume	: 2535.7(3) $Å^3$
Z, Calculated density	: 8, 1.421 Mg/m^3
Absorption coefficient	: 0.103 mm^{-1}
F(000)	: 1136
Crystal size	: 0.52 x 0.48 x 0.40 mm
Theta range for data collection	: 2.34 to 25.92 deg.
Limiting indices	: -23<=h<=23, -12<=k<=12, -18<=l<=18
Reflections collected / unique	: 12686 / 2475 [R(int) = 0.0292]
Completeness to theta = 25.92	: 100.0 %
Max. and min. transmission	: 0.9601 and 0.9485
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 2475 / 0 / 182
Goodness-of-fit on F^2	: 1.051
Final R indices [I>2sigma(I)]	: R1 = 0.0384, wR2 = 0.0941
R indices (all data)	: R1 = 0.0399, wR2 = 0.0958
Largest diff. peak and hole	: 0.263 and -0.351 e. $Å^{-3}$

Scheme 69: One-pot transformation



Since in the two pot operation, second step using toluene as a solvent (under reflux) gave high yields (entry 4, Table 9) we have treated methyl 3-acetoxy-2-methylene-3-[2-(prop-2-ynyloxy)phenyl]propanoate (**116a**) with sodium azide in DMSO for 3 h at room temperature. The resulting crude compound methyl 2-(azidomethyl)-3-[2-(prop-2-ynyloxy)phenyl]propenoate (**115a**), after aqueous work-up, without further purification was heated in toluene under reflux for 4 h at 110 ^{o}C to provide 10-methoxycarbonyl-2-oxa-6,7,8-triazatricyclo[10,4,0,0^{4,8}]hexadeca-4,6,10,12,14,16(1)-hexaene (**114a**), in 72% overall isolated yield for two steps (Scheme 70, Entry 7, Table 10).

Scheme 70



With a view to understand the generality of this reaction we have prepared various Baylis-Hillman alcohols (**117b-i**), from substituted benzaldehydes (**107a-e**) (Scheme 71, Table 11) and alkyl acrylates, which were subsequently converted into their corresponding acetates (**116b-i**) (Scheme 71, Table 12).

Scheme 71

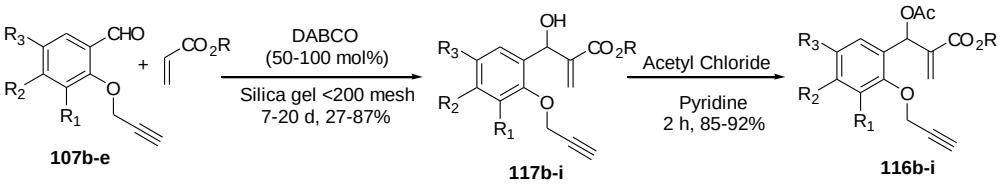
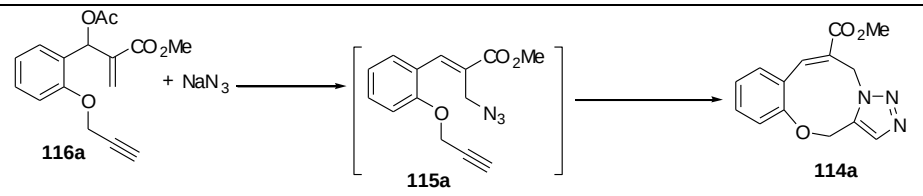


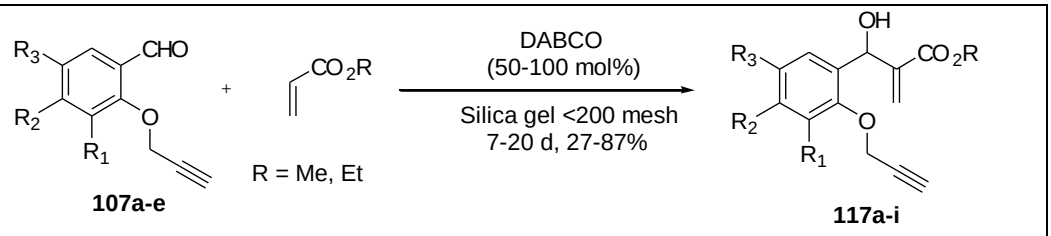
Table 10. **Optimization**: **Synthesis of triazolo-[1,4]-benzoxazonine from BH acetate 116a**[a]



Entry	Conditon(s)	Yield (%)		
		116a[c]	**115a**[d]	**114a**[e]
1	i) DMSO, rt, 2 h, ii) 110 ^{o}C, 3 h[b]	43	-	30
2	i) DMSO, rt, 3 h, ii) 70 ^{o}C, 6 h[b]	-	12	54
3	i) DMSO, rt, 3 h, ii) 110 ^{o}C, 6 h[b]	-	-	55
4	i) DMSO, rt, 3 h, ii) 110 ^{o}C, 4 h[b]	-	-	50
5	i) DMSO, rt, 3 h, ii) 110 ^{o}C, 2 h[b]	-	-	55
6	i) DMSO, rt, 3 h, ii) work-up, iii) Toluene, reflux, 3 h[f]	-	17	63
7	i) DMSO, rt, 3 h, ii) work-up, iii) Toluene, reflux, 4 h[f]	-	-	**72**
8	i) DMSO, rt, 3 h, ii) work-up, iii) Toluene, reflux, 5 h[f]	-	-	68

(a) All reactions were carried out on 1.0 mmol scale of BH acetate (**116a**) with sodium azide (1.5 mmol) in DMSO (2 mL).
(b) All reactions were carried out on in DMSO (2 mL) for 2-3 h at room temperature followed by heating at 70-110 ^{o}C.
(c) Recovered B-H acetate **115a**.
(d) Recovered azido-alkyne
(e) Yields are based on B-H acetate.
(f) All reactions were carried out in DMSO (2 mL) for 3 h at room temperature followed by aqueous work-up and heating the resulting crude in toluene (2 mL) at 110 ^{o}C.

Table 11. Synthesis of Baylis-Hillman alcohols (117a-i)[©,a]



Aldehyde	R_1	R_2	R_3	R	Product [b]	Yield (%)[c]
107a	H	H	H	Me	**117a**	70
107b	OMe	H	H	Me	**117b**	57
107c[d]	H	OMe	H	Me	**117c**	27
107d	H	H	Br	Me	**117d**	83
107e	H	H	Cl	Me	**117e**	65
107a	H	H	H	Et	**117f**	81
107b	OMe	H	H	Et	**117g**	71
107c[d]	H	OMe	H	Et	**117h**	36
107d	H	H	Br	Et	**117i**	87

(a) All reactions were carried out on 20 mmol scale of aldehydes (**107a,107b,107d,107e**) with 30 mmol of alkyl acrylates, under influence of DABCO (50 mol%) in the silica gel-solid phase medium (mesh <200-400) at room temperature for 7-14 days

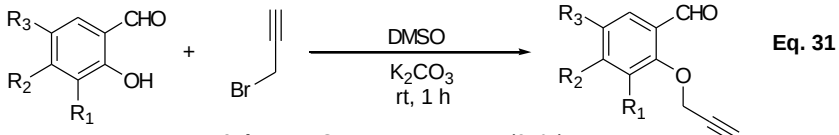
(b) All the compounds (**117a-i**) were viscous liquids and gave satisfactory IR, ^{1}H NMR, ^{13}C NMR spectral data.

(c) Yields are based on aldehydes.

(d) These reactions were carried out on 20 mmol scale of aldehyde **107c** with 30 mmol of alkyl acrylates, under influence of DABCO (100 mol%) in the silica gel-solid phase medium (mesh <200-400) at room temperature for 20 days

Required 2-(prop-2-ynyloxy)benzaldehyde derivatives (**107b-e**) were prepared *via* the *O*-propargylation of corresponding 2-hydroxybenzaldehyds, with propargyl bromide in presence of K_2CO_3 in DMSO according to the Eq. 31.

© For continuity and easy understandings we have numbered various aromatic aldehydes and Baylis-Hillman alcohols (obtained from methyl acrylate and ethyl acrylate) as **107a-e** and **117a-i** respectively.



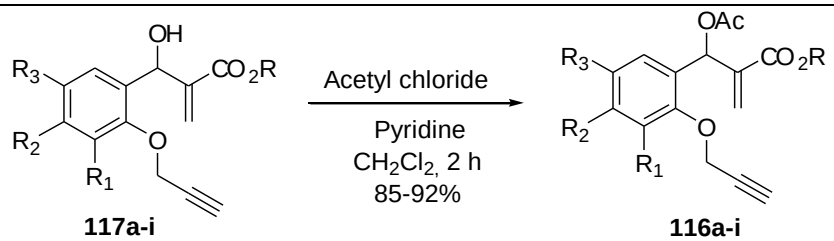
Eq. 31

107b: R_1 = OMe, R_2 = R_3 = H (95%)
107c: R_1 = R_3= H, R_2 = OMe (85%)
107d: R_1 = R_2= H, R_3 = Br (83%)
107e: R_1 = R_2= H, R_3 = Cl (80%)

107b-e

These Baylis-Hillman acetates (**116b-i**), were converted into the desired triazolo-[1,4]-benzoxazonine derivatives (**114b-i)** in 57-71% isolated yield (for two steps) *via* the treatment with sodium azide in DMSO and then heating the resulting crude (after work-up) in toluene under reflux (Table 13).

Table 12. **Synthesis of Baylis-Hillman acetates (116a-i)**[€,a]



117a-i **116a-i**

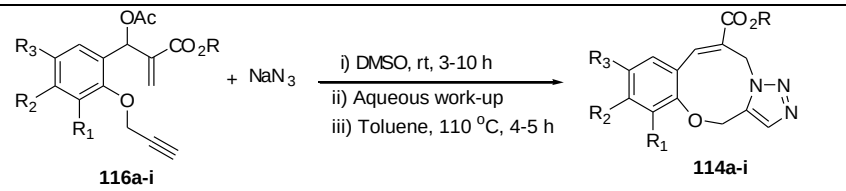
B-H alcohol	R_1	R_2	R_3	R	B-H acetate[b]	Yield (%)[c]
117a	H	H	H	Me	**116a**	85
117b	OMe	H	H	Me	**116b**	90
117c	H	OMe	H	Me	**116c**	85
117d	H	H	Br	Me	**116d**	90
117e	H	H	Cl	Me	**116e**	91
117f	H	H	H	Et	**116f**	88
117g	OMe	H	H	Et	**116g**	87
117h	H	OMe	H	Et	**116h**	87
117i	H	H	Br	Et	**116i**	92

(a) All reactions were carried out on 10 mmol scale of Baylis-Hillman alcohols (**117a-i**) with acetyl chloride, in presence of pyridine at at room temperature for 2 h.
(b) All the compounds (**116a-i**) were viscous liquids and gave satisfactory IR, ^{1}H NMR, ^{13}C NMR spectral data.
(c) Yields are based on B-H alcohols.

€ For continuity and better understandings we have numbered Baylis-Hillman alcohols and Baylis-Hillman acetates as **117a-i** and **116a-i** respectively.

Structures of all these compounds are established with IR, ^{1}H NMR [for compounds **114e & 114h** see Spectrum 25 & 27 respectively], ^{13}C NMR [for compounds **114e** & **114h** see Spectrum 26 & 28 respectively], mass spectral data and elemental analyses.

Table 13. Synthesis of triazolo-[1,4]-benzoxazonine derivatives (114a-i)[¢,a]



116a-i **114a-i**

57-72% for overall two steps

B-H acetate	R	Product	Yield (%)[b,c]	M.p °C
116a	Me	**114a**	72	148-150
116b	Me	**114b**	68	185-188
116c	Me	**114c**	63	145-148
116d	Me	**114d**	57	212-214
116e	Me	**114e**	62	204-206
116f	Et	**114f**	58	88-89
116g	Et	**114g**	65	160-162
116h	Et	**114h**	68	140-142
116i	Et	**114i**	71	166-169

(a) All reactions were carried out on 1.0 mmol scale of B-H acetate (**116a-i**) with sodium azide (1.5 mmol) in DMSO (2 mL) for 3-10 h at room temperature followed by aqueous work-up and heating the resulting crude in toluene (2 mL) for 4-5 h under reflux.

(b) All the compounds (**114a-i**) were colorless solids and were characterized (with IR, ^{1}H NMR, ^{13}C NMR, mass spectral data and elemental analyses

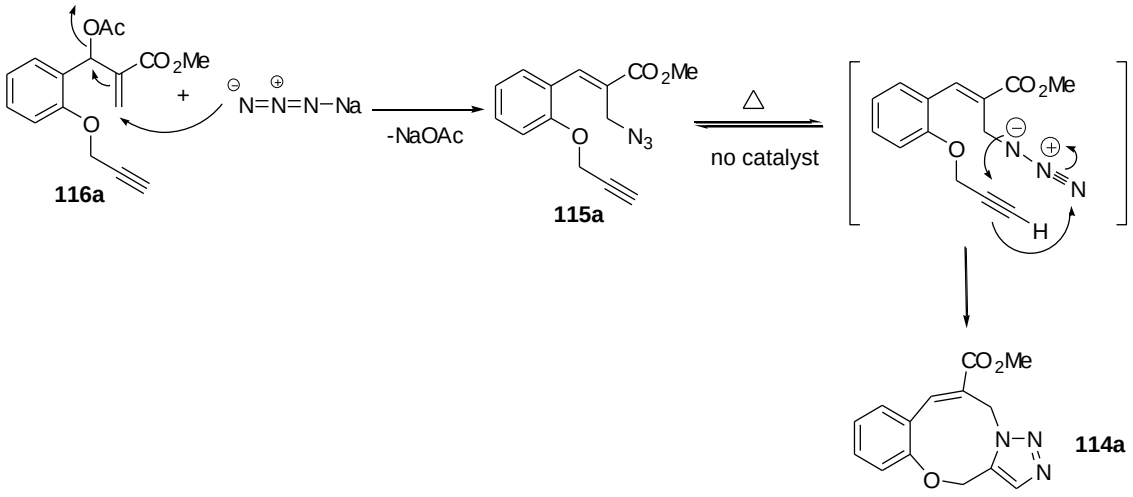
(c) Yields are based on B-H acetates.

Mechanism for the formation of triazolo-[1,4]-benzoxazonine derivatives from the Baylis-Hillman acetates is presented in Scheme 72 by taking reaction between methyl 3-acetoxy-2-methylene-3-[2-(prop-2-ynyloxy)phenyl]propanoate (**116a**) and NaN_3 as a model case. Treatment of 3-acetoxy-2-methylene-3-[2-(prop-2-ynyloxy)phenyl]-propanoate (**116a**) with NaN_3 provided alkynyl-azide **115a** intermediate, that will

¢ For clarity and better understandings we have numbered triazolo-[1,4]-benzoxazonine derivatives derived from **116a-i** as **114a-i** respectively.

undergo further intramolecular [3+2] cycloaddition reaction leading to the formation of the triazole derivative **114a**.

Scheme 72: Plausible Mechanism

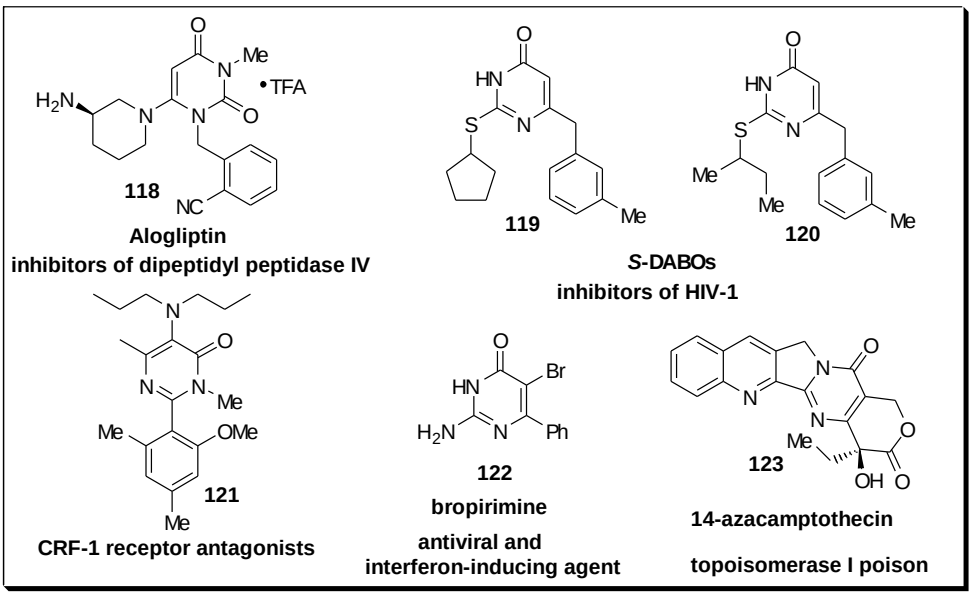


In conclusion, we have developed a facile synthetic strategy for obtaining [1,2,3]-triazolo-[1,4]-benzoxazonine framework by treating Baylis-Hillman acetates with sodium azide and subsequent [3+2] cyclization of the resulting crude in refluxing toluene. This methodology demonstrates the applicability of Baylis-Hillman adducts for synthesis of larger rings containing [1,4]-benzoxazonine framework fused with [1,2,3]-triazole skeleton. It is interesting to note that [3+2] cyclization (Click reaction) occurs without copper catalyst.

Development of a simple methodology for synthesis of tri substituted pyrimidin-4(3*H*)-one derivatives from Baylis-Hillman acetates

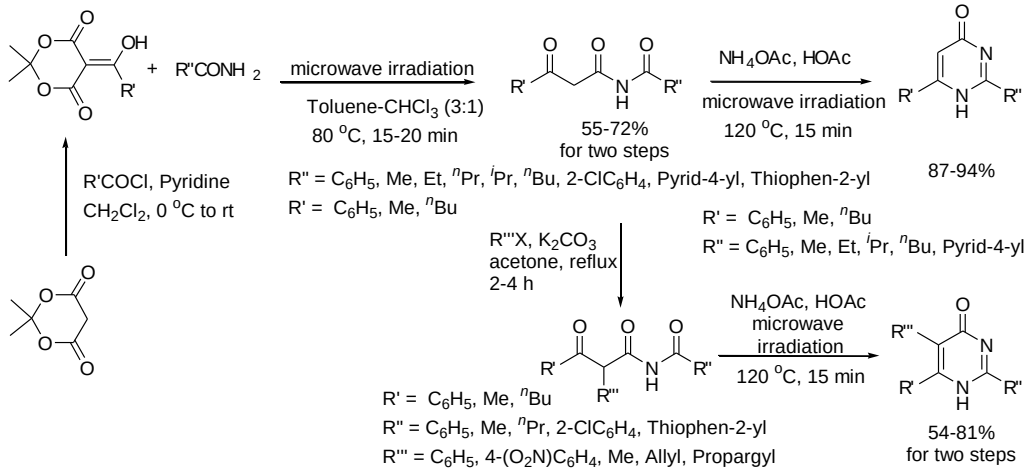
Pyrimidin-4(3*H*)-one skeleton is an important framework present in various pharmacologically active compounds. For example alogliptin (**118**)[128] is a potent selective inhibitor of serine protease dipeptidyl peptidase IV (DPP-4), *S*-DABOs (**119** & **120**)[129] are known as inhibitors of human immunodeficiency virus type-1, 2-aryl-3,6-dialkyl-5-dialkylaminopyridin-4-ones (**121**)[130] is found to be CRF-1 receptor antagonists. Bropirimine (**122**)[131] is an antiviral and interferon-inducing agent. 14-Azacamptothecin (**123**)[132] is known to be water-soluble topoisomerase I poison (Figure 10). Due to their remarkable biological properties there has been increasing interest in the synthesis of pyrimidin-4(3*H*)-one derivatives. Some of the recent and interesting strategies for synthesis of these molecules are presented in this section.

Figure 10

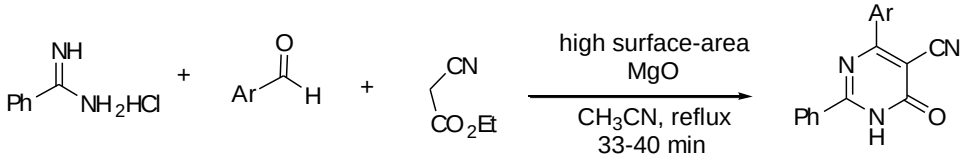


Guo[133] reported an interesting facile synthesis of 2,6-disubstituted pyrimidin-4(1*H*)-ones and 2,5,6-trisubstituted pyrimidin-4(1*H*)-ones starting from Meldrum's acid following the reaction strategy shown in Scheme 73.

Scheme 73



Sheibani and co-workers[134] have reported three-component reaction of aldehydes, amidine hydrochloride, and ethyl cyanoacetate for synthesis of pyrimidin-4(3*H*)-ones (**124**) under the catalytic influence of high surface-area magnesium oxide under heterogeneous conditions (Eq. 32).



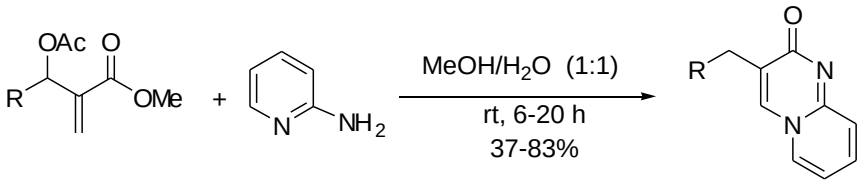
Ar = C_6H_5, 4-ClC_6H_4, 3-$(F_3C)C_6H_4$, 4-$(F_3C)C_6H_4$, 2,4-$Cl_2C_6H_3$, 4-$(O_2N)C_6H_4$

124

82-89%

Eq. 32

The Baylis-Hillman adducts have also been used as synthons for obtaining substituted pyrimidin-4-one derivatives (**125**). Our research group has reported a facile one-pot synthesis of fused pyrimidones *via* the treatment of the Baylis-Hillman acetates with 2-aminopyridine according to the following reaction sequence as shown in Eq. 33.[135]



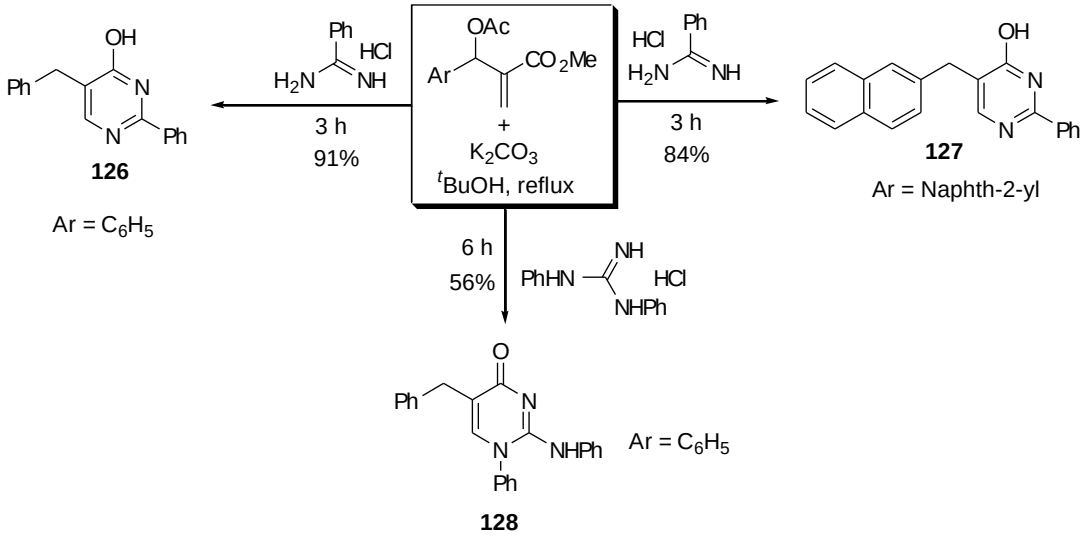
Eq. 33

R_1 = C_6H_5, 4-MeC_6H_4, 4-EtC_6H_4, 4-$^{i}PrC_6H_4$, 2-ClC_6H_4, 4-ClC_6H_4, 3-(MeO)C_6H_4, 4-(MeO)C_6H_4, ^{n}Pent

125

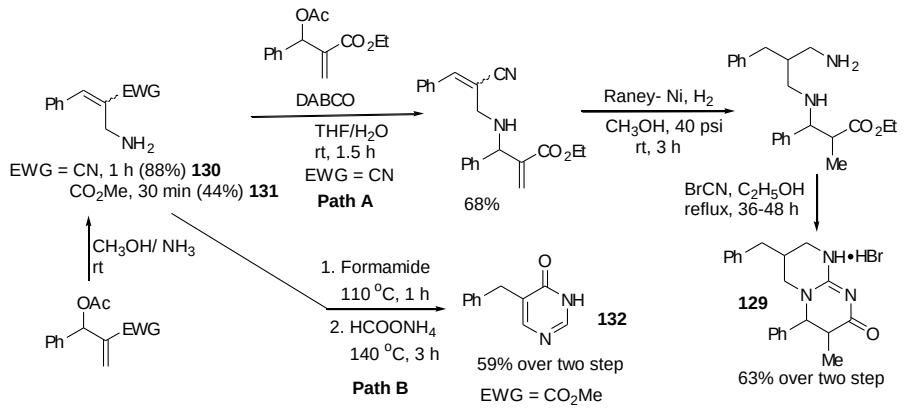
Baylis-Hillman acetates have been used as starting materials for obtaining pyrimidine derivatives (**126-128**) by Kim and co-workers.[136] Selected examples are presented in Scheme 74.

Scheme 74



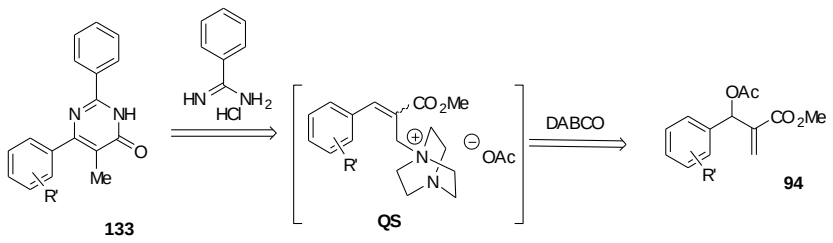
Pathak and Batra[137] have reported an interesting synthesis of fused pyrimidin-4-one derivatives (**129**) from the allyl amines (**130**, EWG = CN) (derived from BH acetates by treatment with methanolic ammonia), according to the Path A, Scheme 75. Later on they[138] have also used the allylamines (**131**, EWG = CO_2Me) for synthesis of various pyrimidin-4(3*H*)-one (**132**) derivatives by treatment with formamide followed by the reaction with ammonium acetate according to the reaction sequence as shown in Path B, Scheme 75.

Scheme 75



It is interesting to note that there is no report on the synthesis of 2,5,6-trisubstituted pyrimidin-4(3*H*)-one derivatives using Baylis-Hillman adducts. We have earlier demonstrated the application of the quaternary salt (**QS**) (derived from Baylis-Hillman bromides and DABCO) for various organic transformations.[81,139,140] On the basis of this experience it occurred to us that the quaternary salts (**QS**) (pages 45 & 46) generated from the B-H acetates (**94**) would serve as appropriate synthons for preparation of 2,5,6-trisubstituted pyrimidin-4(3*H*)-ones (**133**) according to the retro-synthetic sequence shown in Scheme 76.

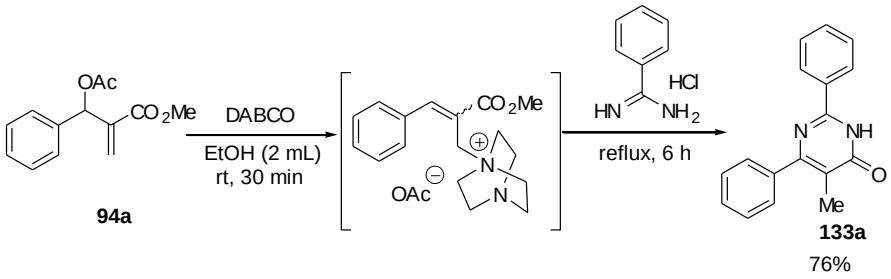
Scheme 76: Retro-synthetic strategy



Accordingly, we have first selected methyl 3-acetoxy-2-methylene-3-phenylpropanoate (**94a**) the Baylis-Hillman acetate, as a substrate. Treatment of methyl 3-acetoxy-2-methylene-3-phenylpropanoate (**94a**) (1 mmol), with DABCO (2.5 mmol) in ethanol at room temperature for 30 min. provided the required quaternary ammonium salt (**QS**, R

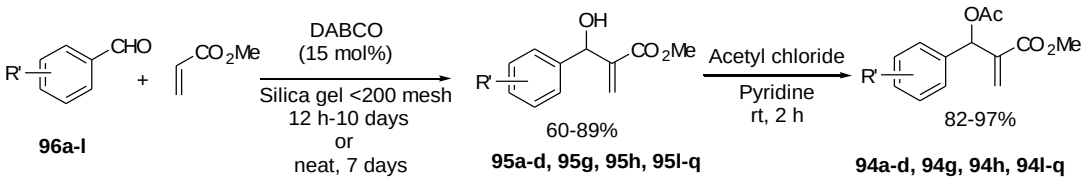
= H). Subsequent reaction of *in situ* generated salt with benzamidine hydrochloride (1.5 mmol) at refluxing temperature (in ethanol) provided 2,6-diphenyl-5-methyl-pyrimidin-4(3*H*)-one (**133a**), in 76% isolated yield (Scheme 77). Structure of this molecule was established by IR, ^{1}H NMR [for compound **133a** see Spectrum 29], ^{13}C NMR [for compound **133a** see Spectrum 30], mass spectral data and elemental analysis.

Scheme 77



To examined the generality of this strategy we have selected various Baylis-Hillman acetates (**94a-d, 94g, 94h, 94l-q**). The required B-H acetates were prepared from the corresponding B-H alcohols (**95a-d, 95g, 95h, 95l-q**)[#] by acetylation with acetyl chloride in the presence of pyridine (Scheme 78, Table 14). The required allylalcohols (**95a-d, 95g, 95h, 95l-q**) were conveniently prepared by B-H reaction of aryl aldehydes (**96a-l**) with methyl acrylate under the catalytic influence of DABCO (Scheme 78, Table 14). Structures of all these alcohols and acetates are complete agreement with IR, ^{1}H NMR and ^{13}C NMR.

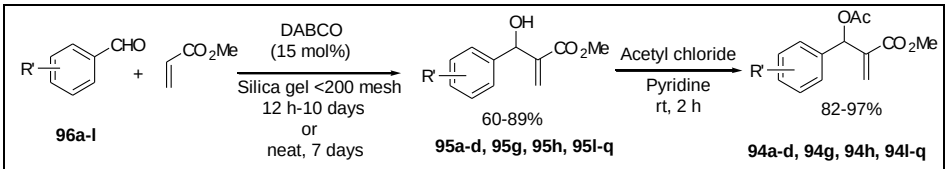
Scheme 78[#]



The yields of B-H alcohols **95a-d, 95g** & **95h** and acetates **94a-d, 94g** & **94h** are already reported in the first section (Schemes 52, 55, 56 & 59, Tables 2 & 6)

After having B-H acetates (**94a-d, 94g, 94h, 94l-q**) in our hand, we have transformed them into pyrimidin-4(3*H*)-one derivatives (**133a-l**) in 65-90% isolated yields *via* the reaction with DABCO and then treating the resulting salt with benzamidine hydrochloride in (Eq. 34 & Table 15). Structures of these compounds are in complete agreement with IR, ^{1}H NMR [for compounds **133c** & **133k** see Spectrum 31 & 33], ^{13}C

Table 14. Synthesis of Baylis-Hillman alcohols (95l-q)$^{\Phi}$ and acetates (94l-q)$^{\Phi,\#}$



96a-l

95a-d, 95g, 95h, 95l-q

94a-d, 94g, 94h, 94l-q

Aldehyde	R'	B-H alcohol	Yield (%)[c]	B-H acetate[d]	Yield (%)[e]
96g[a]	4-OMe	**95l**	61	**94l**	90
96h[a]	3,4-$(OMe)_2$	**95m**	61	**94m**	95
96i[b]	4-Me	**95n**	66	**94n**	83
96j[b]	4-Et	**95o**	67	**94o**	96
96k[b]	2-Cl	**95p**	89	**94p**	90
96l[b]	3-Br	**95q**	83	**94q**	97

(a) All reactions were carried out on 20 mmol scale of aldehydes with 30 mmol of methyl acrylate under influence of DABCO (15 mol%) in the silica gel-solid phase medium (mesh <200-400) at room temperature for 10 days.

(b) All reactions were carried out on 20 mmol scale of aldehydes with 30 mmol of methyl acrylate under influence of DABCO (15 mol%) in neat condition at room temperature for 7 days.

(c) Yields are based on aldehydes.

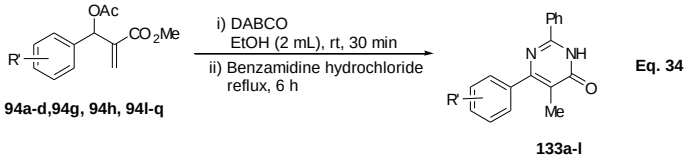
(d) All reactions were carried out on 10 mmol scale of Baylis-Hillman alcohols (**95l-q**) with acetyl chloride, in presence of pyridine at room temperature for 2 h.

(e) Yields are based on Baylis-Hillman alcohols.

Φ For continuity and better understanding we have numbered the B-H alcohols derived from the aldehydes (**96g-l**) and methyl acrylate as **95l-q** and the corresponding B-H acetates as **94l-q** respectively.

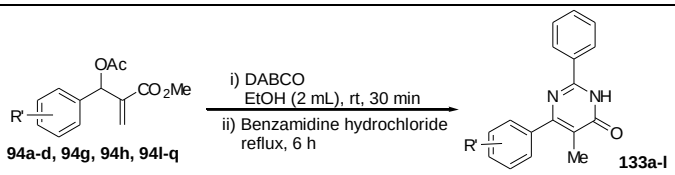
\# The yields of BH alcohols **95a-d, 95g** & **95h** and BH acetates **94a-d, 94g** & **94h** are already reported in the first section [Schemes 52 (Page No 46), 55 (Page No 48), 56 (Page No 52) & 59 (Page No 62), Table 2 (Page No 56) & Table 6 (Page No 64)].

NMR [for compounds **133c** & **133k** see Spectrums 32 & 34], mass spectral data and elemental analyses. Structures of the molecules **133e** & **133f** were further confirmed by single crystal X-ray data analyses [Table IX & Table X. For ORTEP diagrams see Figs X9 & Fig. X10 respectively.



Eq. 34

Table 15. Synthesis of trisubstituted pyrimidin-4(3*H*)-one derivatives (133a-l)®,[a]



B-H acetate	R'	Product[b]	Yield (%)[c]	M.p ^{o}C
94a	H	**133a**	76	262-263
94b	3-OMe	**133b**	70	197-198
94c	3,5-$(OMe)_2$	**133c**	65	237-238
94d	3,4,5-$(OMe)_3$	**133d**	67	235-236
94g	3-OEt	**133e**[d]	73	190-191
94h	3-OPr	**133f**[d]	69	194-195
94l	4-OMe	**133g**	80	274-275
94m	3,4-$(OMe)_2$	**133h**	68	224-225
94n	4-Me	**133i**	90	273-274
94o	4-Et	**133j**	76	267-269
94p	2-Cl	**133k**	80	247-249
94q	3-Br	**133l**	73	210-212

(a) All reactions were carried out on 1.0 mmol scale of BH acetate (**94a-d, 94g, 94h, 94l-q**) with DABCO (2.5 mmol) in ethanol (2 mL) for 30 min at room temperature followed by the treatment with benzamidine hydrochloride (1.5 mmol) heating for 6 h under reflux.

(b) All the compounds **133a-l** was colorless solids.

(c) Yields are based on B-H acetate.

(d) Compounds **133e** & **133f** were further characterized by single crystal X-ray data.

® For clarity and better understandings we have numbered pyrimidin-4-one derivatives derived from B-H acetates **94a-d, 94g, 94h, 94l-q** as **133a-l**.

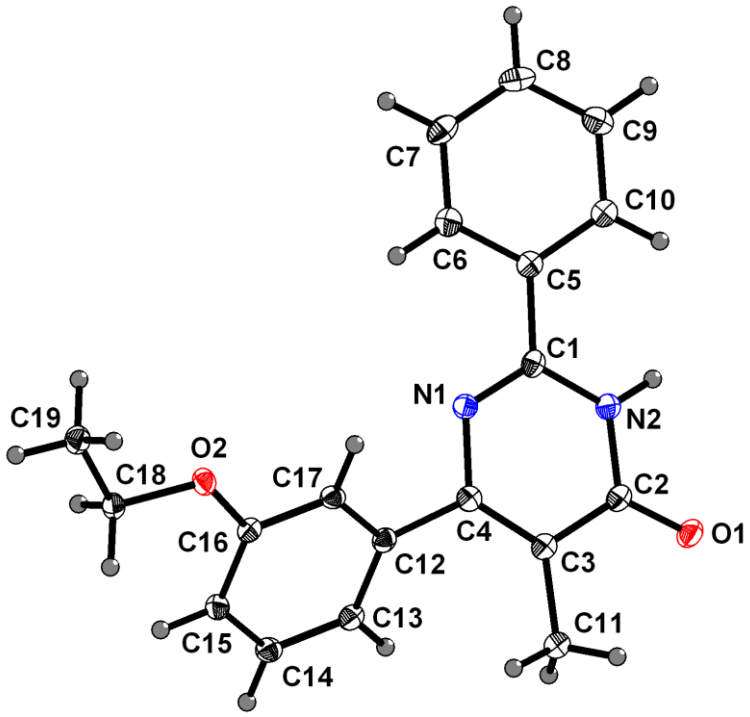


Fig. X9 ORTEP diagram of the compound **133e**

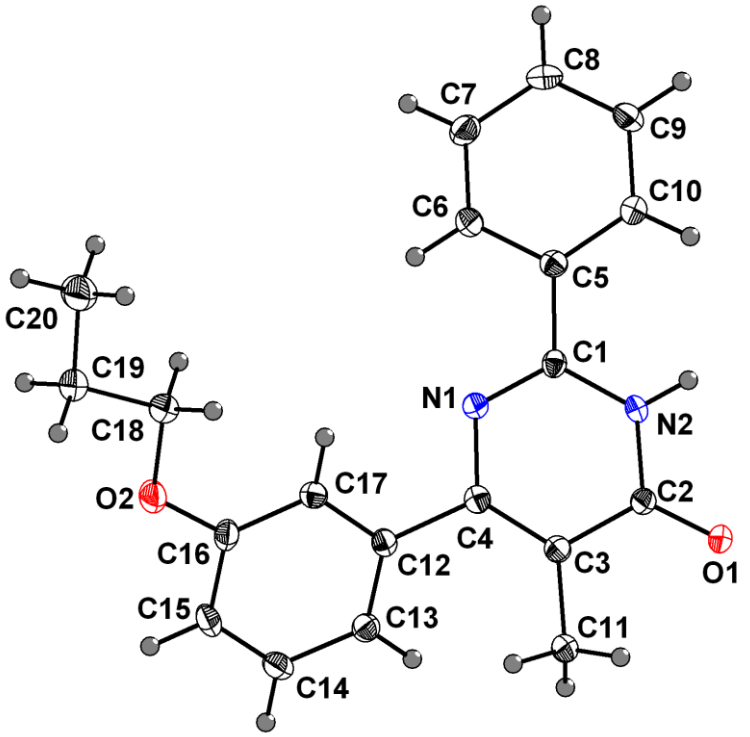


Fig. X10 ORTEP diagram of the compound **133f**

Table IX. Crystal data and structure refinement for 133e

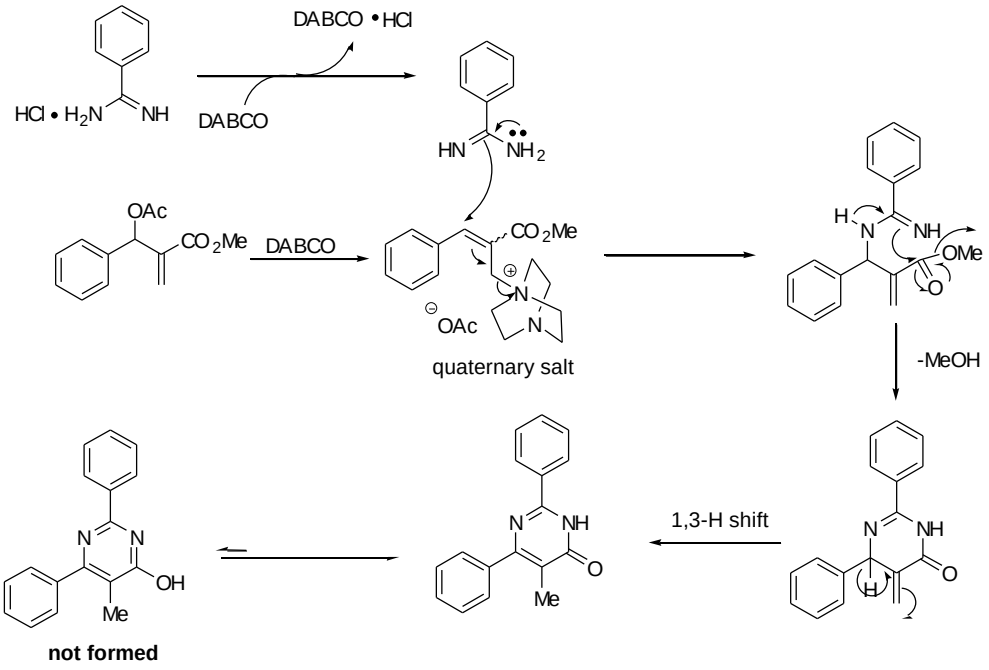
Identification code	: **133e**
Empirical formula	: $C_{19}\ H_{18}\ N_2\ O_2$
Formula weight	: 306.35
Temperature	: 100(2) K
Wavelength	: 0.71073 Å
Crystal system	: Triclinic
Space group	: P-1
Unit cell dimensions	: a = 6.4911(8) Å; α = 87.445(2) deg.
	b = 7.3443(9) Å; β = 79.872(2) deg.
	c = 17.743(2) Å; γ = 67.551(2) deg.
Volume	: 769.34(16) $Å^3$
Z, Calculated density	: 2, 1.322 Mg/m^3
Absorption coefficient	: 0.087 mm^{-1}
F(000)	: 324
Crystal size	: 0.36 x 0.24 x 0.16 mm
Theta range for data collection	: 1.17 to 26.02 deg.
Limiting indices	: -7<=h<=7, -9<=k<=9, -21<=l<=21
Reflections collected / unique	: 7893 / 2993 [R(int) = 0.0234]
Completeness to theta = 26.02	: 99.4 %
Max. and min. transmission	: 0.9862 and 0.9694
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 2993 / 0 / 214
Goodness-of-fit on F^2	: 1.054
Final R indices [I>2sigma(I)]	: R1 = 0.0437, wR2 = 0.1071
R indices (all data)	: R1 = 0.0512, wR2 = 0.1112
Largest diff. peak and hole	: 0.241 and -0.198 e. $Å^{-3}$

Table X. Crystal data and structure refinement for 133f

Identification code	: **133f**
Empirical formula	: C_{20} H_{20} N_2 O_2
Formula weight	: 320.38
Temperature	: 100(2) K
Wavelength	: 0.71073 Å
Crystal system	: Monoclinic
Space group	: P2(1)/n
Unit cell dimensions	: a = 11.2055(8) Å; α = 90 deg.
	b = 7.4037(6) Å; β = 99.6800(10) deg.
	c = 19.6368(15) Å; γ = 90 deg.
Volume	: 1605.9(2) $Å^3$
Z, Calculated density	: 4, 1.325 Mg/m^3
Absorption coefficient	: 0.086 mm^{-1}
F(000)	: 680
Crystal size	: 0.24 x 0.12 x 0.08 mm
Theta range for data collection	: 1.96 to 26.06 deg.
Limiting indices	: -13<=h<=13, -9<=k<=9, -24<=l<=24
Reflections collected / unique	: 16082 / 3173 [R(int) = 0.0364]
Completeness to theta = 26.06	: 99.8 %
Max. and min. transmission	: 0.9931 and 0.9796
Refinement method	: Full-matrix least-squares on F^2
Data / restraints / parameters	: 3173 / 0 / 223
Goodness-of-fit on F^2	: 1.047
Final R indices [I>2sigma(I)]	: R1 = 0.0482, wR2 = 0.1193
R indices (all data)	: R1 = 0.0586, wR2 = 0.1256
Largest diff. peak and hole	: 0.519 and -0.235 e. $Å^{-3}$

Mechanism for the formation of 2,5,6-trisubstituted pyrimidin-4(3*H*)-ones from the Baylis-Hillman acetates is presented in Scheme 79 by taking reaction between methyl 3-acetoxy-2-methylene-3-phenylpropanoate (**94a**) and benzamidine hydrochloride as a model case. It is interesting to note that all the compounds (**133a-l**) are obtained as pyrimidin-4(3*H*)-one derivatives but not as 4-hydroxy pyrimidines.

Scheme 79: Plausible Mechanism



In conclusion, we have developed a simple, facile one-pot methodology for synthesis of 2,5,6-trisubstituted pyrimidin-4(3*H*)-one derivatives from the Baylis-Hillman acetates in good yields. This strategy involves the formation of quaternary salt by the treatment of B-H acetate with DABCO and then the reaction of *in situ* generated salt with benzamidine hydrochloride at reflux temperature for 6 hours in ethanol.

CONCLUSIONS

In conclusion we have achieved considerable successes in all the three objectives that have been mentioned in the beginning of this chapter. We have successfully used the Baylis-Hillman adducts as probes in understanding the chemoselectivity in the case of intramolecular Friedel-Crafts reaction of substrates having two ester functionalities and one keto functionality in a similar environment. We found that in these intramolecular Friedel-Crafts reactions the cyclization occurs predominantly with keto group rather than ester groups even though there are two ester groups. We have also used this strategy to synthesize representative classes of highly substituted indene derivatives.

The Baylis-Hillman acetates have been also employed as useful synthones for obtaining [1,2,3]-triazolo-[1,4]-benzoxazonine framework. In this strategy the key step is the formation of [1,4]-oxazonine ring using Click reaction. It needs to be mentioned here that [1,2,3]-triazolo-[1,4]-oxazonine framework is an interesting structural organization that is not well studied in the literature and is believed to be an attractive framework in the field of medicinal chemistry. It is interesting to note that the simultaneous formation of oxazonine ring and triazole ring does not require any catalyst (normally Click reaction requires copper catalyst).

We have developed a facile and simple synthesis of 2,5,6-trisubstituted pyrimidin-4(3*H*)-one derivatives employing Baylis-Hillman acetates as starting materials. The strategy involves the treatment of Baylis-Hillman acetates with DABCO followed by the reaction with benzamidine hydrochloride. Our studies clearly demonstrate the applicability of Baylis-Hillman adducts/acetates for synthesis of carbocyclic/heterocyclic compounds, thus further expanding the scope of the Baylis-Hillman reaction in organic synthesis.

EXPERIMENTAL

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

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

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

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

Nuclear Magnetic Resonance Spectra: Proton magnetic resonance spectra and carbon-13 magnetic resonance spectra were recorded on BRUKER-AVANCE-400 spectrometers. ^{1}H NMR (400 MHz) spectra for all the samples were measured in chloroform-*d* with TMS (δ = 0 ppm) as an internal standard. ^{13}C NMR (100 MHz) spectra for all the samples were measured in chloroform-*d* with its middle peak of the triplet (δ = 77.10 ppm) as an internal standard. Spectral assignments are as follows: (1) chemical shifts on the δ scale, (2) standard abbreviation for multiplicity, that is, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublet, b s = broad singlet, dABq = doublet of AB quartet, (3) number of hydrogens integrated for the signal, (4) coupling constant *J* in Hertz.

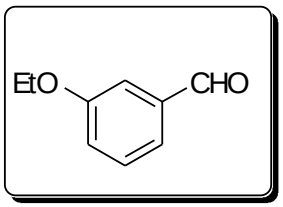
X-ray Crystallographic Study: Single crystal X-ray data for all the eight compounds (**93b, *ortho*-93b, 93h, 93k, *ortho*-93k, 114a, 133e** and **133f**) were collected on a Bruker SMART APEX CCD area detector system [λ(Mo-Kα) = 0.71073 Å] (**93b, *ortho*-93b, 93h, 93k** and ***ortho*-93k)** at 298K, (**114a, 133e *and* 133f)** at 100K respectively, graphite monochromator with a ω scan width of 0.3^{o}, crystal-detector distance 60 mm, collimator 0.5 mm. The SMART software (Version 5.630) was used for the intensity data acquisition and the SAINTPLUS Software (Version 6.45) was used for the data extraction. In each case, absorption correction was performed with the help of SADABS program, an empirical absorption correction using equivalent reflections was performed with the program. Single crystal X-ray data for the compounds **93c** and **98** were collected on Oxford Diffraction Xcalibur Eos Gemini diffractometer with graphite-monochromated Mo *Kα* radiation with the wavelength of 0.71073 Å at 298K. Data were analyzed with ‘‘CrysAlis PRO’’ software and the collected data was reduced by using the ‘‘CrysAlis PRO’’ program. An empirical absorption correction using spherical harmonics was implemented in ‘‘SCALE3 ABSPACK’’ scaling algorithm. The structurs wwer solved using SHELXS-97, and full-matrix least-squares refinement against F^2 was carried out using SHELXL-97. All non-hydrogen atoms were refined anisotropically. The software used to prepare the material is *WinGx* v1.70.01 (L. Farrugia, 2005). The DIAMOND (Version 2.1e) software was used for molecular graphics.

Mass Spectral Analysis: Mass seectra were recorded on Shimadzu LCMS 2010A mass spectrometer.

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

3-Ethoxybenzaldehyde (96e)

To a stirred suspension of 3-hydroxybenzaldehyde (100 mmol, 12.21 g) and anhydrous K_2CO_3 (150 mmol, 20.73 g) in acetonitrile (150 mL) was added bromoethane (150 mmol, 16.34 g). Then reaction mixture was heated under reflux for 5 h. Reaction mixture was cooled to room temperature and acetonitrile was removed under reduced pressure. The residue was diluted with water (50 mL) and extracted with diethyl ether (3X100 mL). Combined organic layer was dried over anhydrous Na_2SO_4. Crude product obtained, after solvent evaporation, was purified by column chromatography (5% EtOAc in hexanes) to provide the desired product as a color less liquid.



Reaction time : 5 h

Yield : 73% (10.96 g)

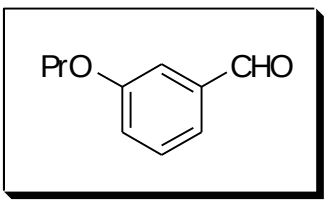
IR (neat) : ν 2727, 1699, 1599 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.44 (t, 3H, *J* = 6.8 Hz), 4.10 (q, 2H, *J* = 6.8 Hz), 7.14-7.22 (m, 1H), 7.38 (s, 1H), 7.41-7.50 (m, 2H), 9.97 (s, 1H)

^{13}C NMR (100 MHz) : δ 14.51, 63.54, 112.67, 121.64, 123.05, 129.85, 137.64, 159.35, 191.98

3-Propoxybenzaldehyde (96f)

This was obtained as a colorless liquid *via* the treatment of 3-hydroxybenzaldehyde with 1-bromopropane in presence of K_2CO_3 in acetonitrile at reflux temperature following similar procedure described for the molecule **96e**.



Reaction time : 5 h

Yield : 80% (13.13 g)

IR (neat) : ν 2727, 1697, 1599 cm^{-1}

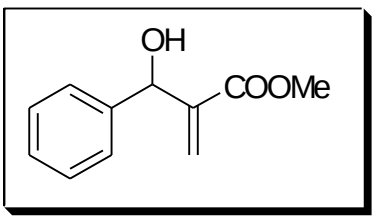
^{1}H NMR (400 MHz) : δ 1.05 (t, 3H, *J* = 7.2 Hz), 1.78-1.90 (m, 2H), 3.98 (t, 2H, *J* = 6.4 Hz), 7.14-7.22 (m, 1H), 7.38 (s, 1H), 7.42-7.49 (m, 2H), 9.97 (s, 1H)

^{13}C NMR (100 MHz) : δ 10.39, 22.39, 69.65, 112.77, 121.79, 123.14, 129.91, 137.70, 159.62, 192.12

Methyl 3-hydroxy-2-methylene-3-phenylpropanoate (95a)

This compound was prepared according to the procedure known in the literature[113]

To a solution of benzaldeyhde (**96a**) (100 mmol, 10.61 g) in methyl acrylate (150 mmol, 12.91 g) was added DABCO (15 mmol, 1.68 g) at room temperature. Then 10 g of silicagel (>200 mesh) was added and throughly mixed. The resulting solid reaction mixture was kept at room temperature for 12 hours. The reaction mixture was washed with ethyl acetate (3X60 mL). Combined organic layer was washed successively, with 2N HCl (30 mL), saturated $NaHCO_3$ solution (30 mL), water (30 mL) and then dried over anhydrous Na_2SO_4. Solvent was evaporated and the crude thus obtained was purified by column chromatography to provide the desired product as a colorless liquid in 71% (13.61 g) isolated yield.



Reaction time : 12 h

Yield : 71%

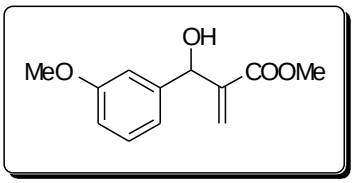
IR (neat) : ν 3466, 1716, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.01 (d, 1H, *J* = 5.6 Hz), 3.73 (s, 3H), 5.57 (d, 1H, *J* = 5.6 Hz), 5.83 (s, 1H), 6.34 (s, 1H), 7.27-7.41 (m, 5H)

^{13}C NMR (100 MHz) : δ 51.97, 73.17, 126.11, 126.62, 127.84, 128.44, 141.29, 141.97, 166.78

Methyl 3-hydroxy-3-(3-methoxyphenyl)-2-methylenepropanoate (95b)

This was prepared as a colorless liquid *via* the coupling of 3-methoxybenzaldeyhde (**96b**) with methyl acrylate under the catalytical influence of DABCO in silica gel solid phase medium at room temperature following the similar procedure described for molecule **95a**.



Reaction time : 10 d

Yield : 62%

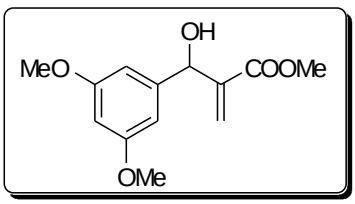
IR (neat) : ν 3443, 1722, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.13 (d, 1H, *J* = 5.6 Hz), 3.72 (s, 3H), 3.79 (s, 3H), 5.52 (d, 1H, *J* = 5.6 Hz), 5.83 (s, 1H), 6.33 (s, 1H), 6.82 (dd, 1H, *J* = 1.6 Hz & 8.4 Hz), 6.88-6.98 (m, 2H), 7.19-7.29 (m, 1H)

^{13}C NMR (100 MHz) : δ 52.03, 55.26, 73.20, 112.12, 113.39, 118.93, 126.34, 129.50, 141.83, 142.97, 159.74, 166.84

Methyl 3-(3,5-dimethoxyphenyl)-3-hydroxy-2-methylenepropanoate (95c)

This compound was prepared as a colorless liquid *via* DABCO catalyzed Baylis-Hillman coupling of 3,5-dimethoxybenzaldehyde (**96c**) with methyl acrylate following a similar procedure described for the molecule **95a**.



Reaction time : 10 d

Yield : 64%

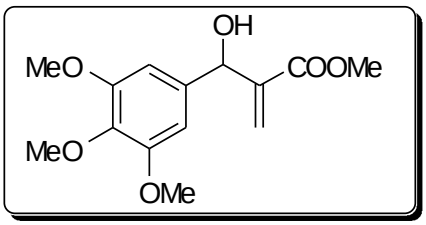
IR (neat) : ν 3477, 1714, 1620 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.06 (d, 1H, *J* = 6.0 Hz), 3.74 (s, 3H), 3.78 (s, 6H), 5.49 (d, 1H, *J* = 6.0 Hz), 5.82 (s, 1H), 6.34 (s, 1H), 6.38 (s, 1H), 6.54 (s, 2H)

^{13}C NMR (100 MHz) : δ 52.04, 55.35, 73.22, 99.78, 104.55, 126.45, 141.65, 143.81, 160.84, 166.83

Methyl 3-hydroxy-2-methylene-3-(3,4,5-trimethoxyphenyl)propanoate (95d)

This molecule was obtained as a white solid *via* the Baylis–Hillman coupling reaction of 3,4,5-trimethoxybenzaldehyde (**96d**) with methyl acrylate in the presence of DABCO (cat.) in silica gel solid phase medium, following a similar procedure described for the molecule **95a**.



Reaction time : 10 d

Yield : 60%

Mp : 58-60 ^{0}C

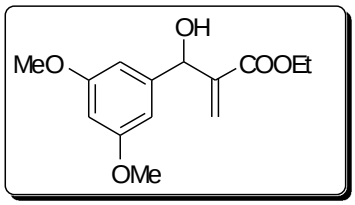
IR (KBr) : ν 3443, 1728, 1631 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.09 (d, 1H, *J* = 5.6 Hz), 3.75 (s, 3H), 3.83 (s, 3H), 3.85 (s, 6H), 5.50 (d, 1H, *J* = 5.6 Hz), 5.83 (s, 1H), 6.34 (s, 1H), 6.60 (s, 2H)

^{13}C NMR (100 MHz) : δ 51.96, 55.94, 60.70, 72.92, 103.43, 125.97, 136.96, 137.15, 141.85, 153.04, 166.77

Ethyl 3-(3,5-dimethoxyphenyl)-3-hydroxy-2-methylenepropanoate (95e)

This Baylis-Hillman alcohol was obtained as colorless viscous liquid *via* the treatment of of 3,5-dimethoxybenzaldehyde (**96c**) with ethyl acrylate under the catalytical influence of DABCO following similar procedure described for molecule **95a**.



Reaction time : 10 d

Yield : 60%

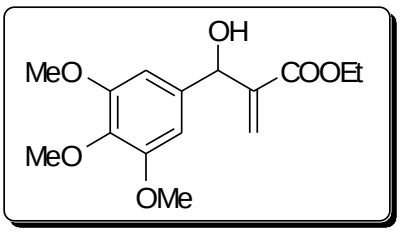
IR (neat) : ν 3479, 1714, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.26 (t, 3H, *J* = 7.2 Hz), 3.13 (d, 1H, *J* = 6.0 Hz), 3.78 (s, 6H), 4.19 (q, 2H, *J* = 7.2 Hz), 5.48 (d, 1H, *J* = 6.0 Hz), 5.80 (d, 1H, *J* = 0.8 Hz), 6.33 (s, 1H), 6.37-6.40 (m, 1H), 6.54 (d, 2H, *J* = 2.4 Hz)

^{13}C NMR (100 MHz) : δ 14.11, 55.37, 61.03, 73.35, 99.78, 104.54, 126.24, 141.88, 143.90, 160.84, 166.43

Ethyl 3-hydroxy-2-methylene-3-(3,4,5-trimethoxyphenyl)propanoate (95f)

This compound was prepared as a white solid *via* DABCO catalyzed Baylis-Hillman coupling of 3,4,5-trimethoxybenzaldehyde (**96d**) with ethyl acrylate, following a similar procedure described for the molecule **95a**.



Reaction time : 10 d

Yield : 70%

Mp : 87-89 ^{0}C

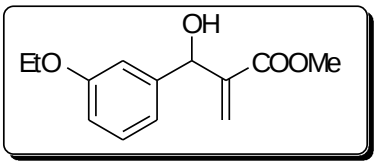
IR (KBr) : ν 3479, 1716, 1625 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.27 (t, 3H, *J* = 7.2 Hz), 3.20 (d, 1H, *J* = 5.6 Hz), 3.83 (s, 3H), 3.85 (s, 6H), 4.20 (q, 2H, *J* = 7.2 Hz), 5.50 (d, 1H, *J* = 4.8 Hz), 5.81 (s, 1H), 6.34 (s, 1H), 6.60 (s, 2H)

^{13}C NMR (100 MHz) : δ 14.08, 56.01, 60.78, 61.00, 73.16, 103.48, 125.88, 137.04, 137.24, 142.09, 153.12, 166.43

Methyl 3-(3-ethoxyphenyl)-3-hydroxy-2-methylenepropanoate (95g)

This compound was obtained as a colorless liquid by the Baylis–Hillman coupling of 3-ethoxybenzaldehyde (**96e**) and methyl acrylate in presence of DABCO as a catalyst, following similar procedure described for the molecule **95a**.



Reaction time : 10 d

Yield : 65%

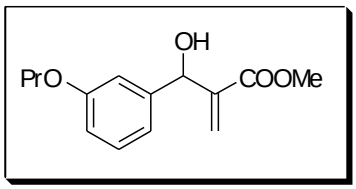
IR (neat) : ν 3466, 1714, 1631 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.40 (t, 3H, *J* = 6.8 Hz), 3.03 (d, 1H, *J* = 5.6 Hz), 3.73 (s, 3H), 4.03 (q, 2H, *J* = 6.8 Hz), 5.53 (d, 1H, *J* = 5.6 Hz), 5.83 (s, 1H), 6.33 (s, 1H), 6.81 (d, 1H, *J* = 8.0 Hz), 6.90-6.97 (m, 2H), 7.20-7.29 (m, 1H)

^{13}C NMR (100 MHz) : δ 14.86, 52.02, 63.42, 73.21, 112.71, 113.89, 118.81, 126.29, 129.47, 141.83, 142.93, 159.10, 166.82

Methyl 3-hydroxy-2-methylene-3-(3-propoxyphenyl)propanoate (95h)

Baylis–Hillman coupling of 3-propoxybenzaldehyde (**96f**) with methyl acrylate in presence of DABCO as a catalyst following the similar procedure described for the molecule **95a**, provided the title compound as a colorless liquid.



Reaction time : 10 d

Yield : 62%

IR (neat) : ν 3477, 1714, 1630 cm^{-1}

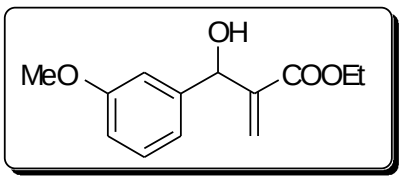
^{1}H NMR (400 MHz) : δ 1.03 (t, 3H, *J* = 7.2 Hz), 1.74-1.86 (m, 2H), 3.04 (b s, 1H), 3.73 (s, 3H), 3.91 (t, 2H, *J* = 6.8 Hz), 5.52 (s, 1H),

5.83 (s, 1H), 6.33 (s, 1H), 6.81 (d, 1H, *J* = 7.6 Hz), 6.90-6.96 (m, 2H), 7.20-7.28 (m, 1H)

^{13}C NMR (100 MHz) : δ 10.55, 22.60, 51.97, 69.45, 73.11, 112.71, 113.89, 118.74, 126.21, 129.41, 141.85, 142.89, 159.27, 166.80

Ethyl 3-hydroxy-3-(3-methoxyphenyl)-2-methylenepropanoate (95i)

This was obtained *via* the DABCO catalyzed coupling of 3-methoxybenzaldehyde (**96b**) with ethyl acrylate, following a similar procedure described for the molecule **95a** as a colorless liquid.



Reaction time : 10 d

Yield : 65%

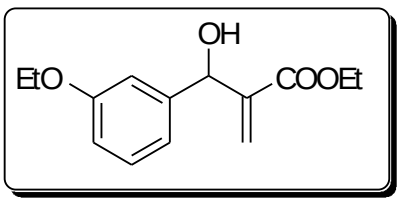
IR (neat) : ν 3472, 1712, 1625 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.25 (t, 3H, *J* = 7.2 Hz), 3.10 (d, 1H, *J* = 6.0 Hz), 3.80 (s, 3H), 4.18 (q, 2H, *J* = 7.2 Hz), 5.53 (d, 1H, *J* = 6.0 Hz), 5.80 (s, 1H), 6.33 (s, 1H), 6.82 (d, 1H, *J* = 8.0 Hz), 6.92-6.98 (m, 2H), 7.22-7.30 (m, 1H)

^{13}C NMR (100 MHz) : δ 14.09, 55.24, 61.00, 73.24, 112.10, 113.37, 118.95, 126.03, 129.44, 142.11, 143.08, 159.72, 166.40

Ethyl 3-(3-ethoxyphenyl)-3-hydroxy-2-methylenepropanoate (95j)

This was obtained as a colorless liquid *via* DABCO catalyzed coupling of 3-ethoxybenzaldehyde (**96e**) with ethyl acrylate following the similar procedure described for the molecule **95a**.



Reaction time : 10 d

Yield : 62%

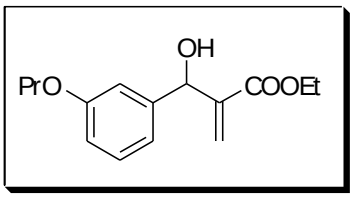
IR (neat) : ν 3479, 1716, 1624 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.25 (t, 3H, *J* = 6.8 Hz), 1.40 (t, 3H, *J* = 6.8 Hz), 3.05 (d, 1H, *J* = 5.2 Hz), 4.02 (q, 2H, *J* = 6.8 Hz), 4.18 (q, 2H, *J* = 6.8 Hz), 5.52 (s, 1H), 5.80 (s, 1H), 6.33 (s, 1H), 6.81 (d, 1H, *J* = 8.0 Hz), 6.91-6.98 (m, 2H), 7.21-7.30 (m, 1H)

^{13}C NMR (100 MHz) : δ 14.06, 14.83, 60.95, 63.37, 73.19, 112.66, 113.83, 118.82, 125.95, 129.39, 142.09, 143.02, 159.04, 166.36

Ethyl 3-hydroxy-2-methylene-3-(3-propoxyphenyl)propanoate (95k)

This compound was obtained as a colorless liquid *via* the treatment of 3-propoxybenzaldehyde (**96f**) with ethyl acrylate under the catalytical influence of DABCO in silica gel solid phase medium, following a similar procedure described for the molecule **95a**.



Reaction time : 10 d

Yield : 65%

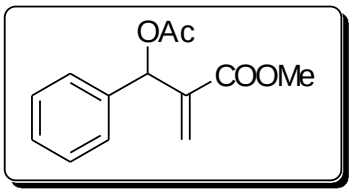
IR (neat) : ν 3483, 1714, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.02 (t, 3H, *J* = 7.2 Hz), 1.25 (t, 3H, *J* = 7.2 Hz), 1.74-1.86 (m, 2H), 3.07 (d, 1H, *J* = 5.6 Hz), 3.91 (t, 2H, *J* = 6.4 Hz), 4.18 (q, 2H, *J* = 7.2 Hz), 5.52 (d, 1H, *J* = 5.6 Hz), 5.81 (s, 1H), 6.33 (s, 1H), 6.81 (d, 1H, *J* = 8.0 Hz), 6.90-6.97 (m, 2H), 7.20-7.28 (m, 1H)

^{13}C NMR (100 MHz) : δ 10.56, 14.08, 22.62, 60.97, 69.47, 73.25, 112.70, 113.89, 118.77, 126.00, 129.39, 142.10, 142.99, 159.28, 166.40

Methyl 3-acetoxy-2-methylene-3-phenylpropanoate (94a)

To a stirred solution of methyl 3-hydroxy-2-methylene-3-phenylpropanoate (**95a**) (50 mmol, 9.61 g) in dichloromethane (100 mL) was added pyridine (100 mmol, 7.91 g) followed by acetyl chloride (100 mmol, 7.85 g) at 0 ^{o}C and stirring continued at room temperature for 2 h. Reaction mixture was diluted with diethyl ether (100 mL) and 2N HCl (50 mL). Organic layer was separated and was washed successively with saturated aq. $NaHCO_3$ solution, water and dried over anhydrous Na_2SO_4. Crude product thus obtained after solvent evaporation, was purified by column chromatography (10% EtOAc in hexanes) to provide the title compound as a colorless viscous liquid in 82% (9.60 g) isolated yield.



Reaction time : 2 h

Yield : 82%

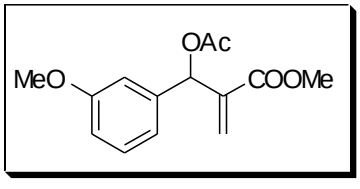
IR (neat) : ν 1745, 1732, 1633 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.10 (s, 3H), 3.70 (s, 3H), 5.86 (s, 1H), 6.39 (s, 1H), 6.68 (s, 1H), 7.27-7.41 (m, 5H)

^{13}C NMR (100 MHz) : δ 21.04, 51.96, 73.10, 125.77, 127.64, 128.37, 128.44, 137.78, 139.66, 165.40, 169.41

Methyl 3-acetoxy-3-(3-methoxyphenyl)-2-methylenepropanoate (94b)

This was prepared as a colorless liquid *via* the treatment of methyl 3-hydroxy-3-(3-methoxyphenyl)-2-methylenepropanoate (**95b**) with acetyl chloride in presence of pyridine following the similar procedure described for molecule **94a**.



Reaction time : 2 h

Yield : 92%

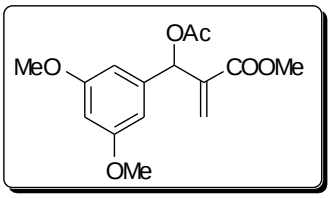
IR (neat) : ν 1745, 1726, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.10 (s, 3H), 3.71 (s, 3H), 3.79 (s, 3H), 5.85 (s, 1H), 6.39 (s, 1H), 6.65 (s, 1H), 6.83 (dd, 1H, *J* = 2.0 Hz & 8.0 Hz), 6.89-6.94 (m, 1H), 6.96 (d, 1H, *J* = 8.0 Hz), 7.22-7.30 (m, 1H)

^{13}C NMR (100 MHz) : δ 21.08, 52.02, 55.21, 72.91, 113.35, 113.71, 119.94, 126.02, 129.52, 139.30, 139.53, 159.59, 165.42, 169.43

Methyl 3-acetoxy-3-(3,5-dimethoxyphenyl)-2-methylenepropanoate (94c)

Treatment of methyl 3-(3,5-dimethoxyphenyl)-3-hydroxy-2-methylenepropanoate (**95c**) with acetyl chloride in the presence of pyridine following the similar procedure described for the molecule **94a** provided the title compound as a colorless viscous liquid.



Reaction time : 2 h

Yield : 92%

IR (neat) : ν 1743, 1728, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.11 (s, 3H), 3.73 (s, 3H), 3.78 (s, 6H), 5.84 (s, 1H), 6.40 (s, 2H), 6.520 (s, 1H), 6.525 (s, 1H), 6.62 (s, 1H)

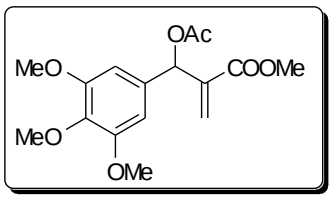
^{13}C NMR (100 MHz) : δ 21.10, 52.06, 55.35, 72.88, 100.18, 105.69, 126.26, 139.45, 140.08, 160.79, 165.46, 169.44

Methyl 3-acetoxy-2-methylene-3-(3,4,5-trimethoxyphenyl)propanoate (94d)

This was prepared as a white solid *via* the acetylation of methyl 3-hydroxy-2-methylene-3-(3,4,5-trimethoxyphenyl)propanoate (**95d)** with acetyl chloride in the presence of pyridine following a similar procedure described for molecule **94a**.

Reaction time : 2 h

Yield : 85%



Mp : 65-66 ^{0}C

IR (KBr) : ν 1745, 1707, 1635 cm^{-1}

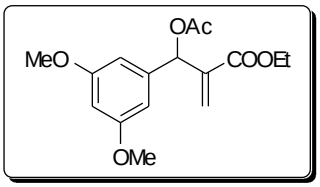
^{1}H NMR (400 MHz) : δ 2.12 (s, 3H), 3.73 (s, 3H), 3.83 (s, 3H), 3.85 (s, 6H), 5.86 (s, 1H), 6.40 (s, 1H), 6.59 (s, 2H), 6.62 (s, 1H)

^{13}C NMR (100 MHz) : δ 21.08, 52.02, 56.05, 60.70, 73.08, 104.74, 125.67, 133.12, 137.91, 139.44, 153.14, 165.38, 169.39

Ethyl 3-acetoxy-3-(3,5-dimethoxyphenyl)-2-methylenepropanoate (94e)

Treatment of ethyl 3-(3,5-dimethoxyphenyl)-3-hydroxy-2-methylenepropanoate (**95e**) with acetyl chloride in the presence of pyridine following the similar procedure described for the molecule **94a** provided the title compound as a colorless viscous liquid.

Reaction time : 2 h



Yield : 83%

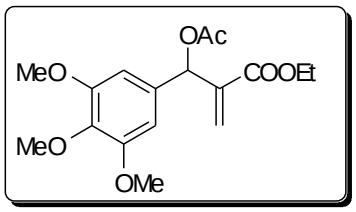
IR (neat) : ν 1747, 1714, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.24 (t, 3H, *J* = 7.2 Hz), 2.11 (s, 3H), 3.78 (s, 6H), 4.18 (q, 2H, *J* = 7.2 Hz), 5.80 (s, 1H), 6.39 (s, 2H), 6.520 (s, 1H), 6.526 (s, 1H), 6.62 (s, 1H)

^{13}C NMR (100 MHz) : δ 14.06, 21.10, 55.33, 61.00, 72.92, 100.14, 105.68, 126.03, 139.67, 140.12, 160.73, 164.99, 169.45

Ethyl 3-acetoxy-2-methylene-3-(3,4,5-trimethoxyphenyl)propanoate (94f)

This was prepared *via* the acetylation of ethyl 3-hydroxy-2-methylene-3-(3,4,5-trimeth-oxyphenyl)propanoate (**95f)** with acetyl chloride in the presence of pyridine following a similar procedure described for molecule **94a** as a low melting white solid.



Reaction time : 2 h

Yield : 86%

Mp : 41-43 ^{0}C

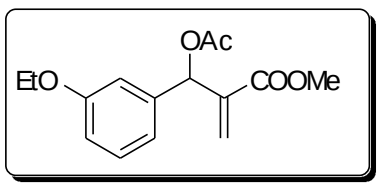
IR (neat) : ν 1745, 1720, 1633 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.24 (t, 3H, *J* = 7.2 Hz), 2.12 (s, 3H), 3.83 (s, 3H), 3.85 (s, 6H), 4.18 (q, 2H, *J* = 7.2 Hz), 5.82 (s, 1H), 6.39 (s, 1H), 6.59 (s, 2H), 6.63 (s, 1H)

^{13}C NMR (100 MHz) : δ 13.97, 21.03, 55.99, 60.65, 60.90, 73.08, 104.74, 125.38, 133.19, 137.84, 139.67, 153.07, 164.88, 169.34

Methyl 3-acetoxy-3-(3-ethoxyphenyl)-2-methylenepropanoate (94g)

This was prepared as a colorless liquid *via* the acetylation of Baylis-Hillman alcohol, methyl 3-(3-ethoxyphenyl)-3-hydroxy-2-methylenepropanoate (**95g**), with acetyl chloride in the presence of pyridine following the similar procedure described for molecule **94a**.



Reaction time : 2 h

Yield : 86%

IR (neat) : ν 1749, 1732, 1625 cm^{-1}

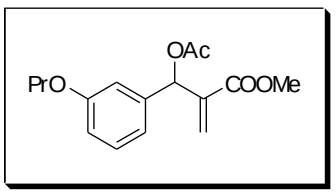
^{1}H NMR (400 MHz) : δ 1.40 (t, 3H, *J* = 6.8 Hz), 2.10 (s, 3H), 3.71 (s, 3H), 4.02 (q, 2H, *J* = 6.8 Hz), 5.84 (s, 1H), 6.39 (s, 1H), 6.64

(s, 1H), 6.83 (d, 1H, *J* = 8.4 Hz), 6.90 (s, 1H), 6.94 (d, 1H, *J* = 7.6 Hz), 7.21-7.29 (m, 1H)

^{13}C NMR (100 MHz) : δ 14.79, 21.08, 52.00, 63.39, 72.93, 113.91, 114.19, 119.83, 125.97, 129.48, 139.25, 139.57, 158.98, 165.43, 169.42

Methyl 3-acetoxy-2-methylene-3-(3-propoxyphenyl)propanoate (94h)

This was prepared as a colorless liquid *via* the treatment of methyl 3-hydroxy-2-methylene-3-(3-propoxyphenyl)propanoate (**95h)** with acetyl chloride in presence of pyridine following the similar procedure described for molecule **94a**.



Reaction time : 2 h

Yield : 86%

IR (neat) : ν 1747, 1726, 1633 cm^{-1}

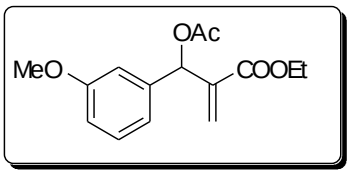
^{1}H NMR (400 MHz) : δ 1.03 (t, 3H, *J* = 7.2 Hz), 1.74-1.85 (m, 2H), 2.10 (s, 3H), 3.71 (s, 3H), 3.90 (t, 2H, *J* = 6.4 Hz), 5.85 (s, 1H), 6.39 (s, 1H), 6.64 (s, 1H), 6.83 (d, 1H, *J* = 8.0 Hz), 6.90 (s, 1H), 6.94 (d, 1H, *J* = 7.6 Hz), 7.21-7.29 (m, 1H)

^{13}C NMR (100 MHz) : δ 10.59, 21.16, 22.63, 52.07, 69.50, 73.01, 113.97, 114.30, 119.83, 126.04, 129.51, 139.26, 139.61, 159.23, 165.51, 169.50

Ethyl 3-acetoxy-3-(3-methoxyphenyl)-2-methylenepropanoate (94i)

This compound was prepared as a colorless liquid *via* the treatment of ethyl 3-hydroxy-3-(3-methoxyphenyl)-2-methylenepropanoate (**95i**) with acetyl chloride, in the presence of pyridine, following a similar procedure described for the molecule **94a**.

Reaction time : 2 h



Yield : 88%

IR (neat) : ν 1747, 1730, 1630 cm^{-1}

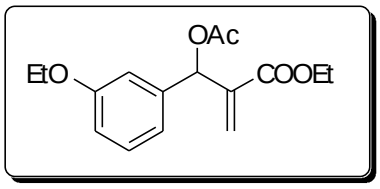
^{1}H NMR (400 MHz) : δ 1.23 (t, 3H, *J* = 7.2 Hz), 2.11 (s, 3H), 3.80 (s, 3H), 4.17 (q, 2H, *J* = 7.2 Hz), 5.82 (s, 1H), 6.39 (s, 1H), 6.66 (s, 1H), 6.84 (dd, 1H, *J* = 1.6 Hz & 8.0 Hz), 6.91 (s, 1H), 6.96 (d, 1H, *J* = 7.6 Hz), 7.22-7.30 (m, 1H)

^{13}C NMR (100 MHz) : δ 13.91, 20.93, 55.06, 60.84, 72.86, 113.26, 113.59, 119.87, 125.62, 129.36, 139.28, 139.73, 159.48, 164.83, 169.28

Ethyl 3-acetoxy-3-(3-ethoxyphenyl)-2-methylenepropanoate (94j)

Treatment of ethyl 3-(3-ethoxyphenyl)-3-hydroxy-2-methylenepropanoate (**95j**) with acetyl chloride in the presence of pyridine following the similar procedure described for the molecule **94a** provided the title compound as a low melting white solid.

Reaction time : 2 h



Yield : 74%

Mp : 47-48 ^{0}C

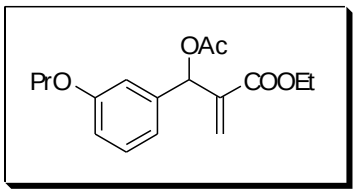
IR (KBr) : ν 1738, 1724, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.23 (t, 3H, *J* = 6.8 Hz), 1.40 (t, 3H, *J* = 6.8 Hz), 2.10 (s, 3H), 4.01 (q, 2H, *J* = 6.8 Hz), 4.16 (q, 2H, *J* = 6.8 Hz), 5.81 (s, 1H), 6.39 (s, 1H), 6.64 (s, 1H), 6.82 (d, 1H, *J* = 7.6 Hz), 6.90 (s, 1H), 6.94 (d, 1H, *J* = 7.2 Hz), 7.19-7.30 (m, 1H)

^{13}C NMR (100 MHz) : δ 14.06, 14.83, 21.14, 61.00, 63.41, 73.02, 113.93, 114.21, 119.94, 125.77, 129.46, 139.34, 139.83, 158.97, 165.01, 169.47

Ethyl 3-acetoxy-2-methylene-3-(3-propoxyphenyl)propanoate (94k)

This compound was obtained as a colorless liquid *via* the treatment of ethyl 3-hydroxy-2-methylene-3-(3-propoxyphenyl)propanoate (**95k**) with acetyl chloride, in the presence of pyridine, following a similar procedure described for the molecule **94a**.



Reaction time : 2 h

Yield : 80%

IR (neat) : ν 1747, 1722, 1631 cm^{-1}

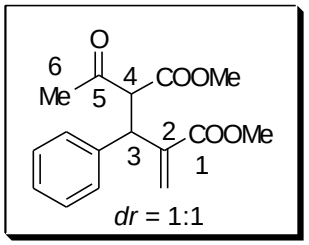
^{1}H NMR (400 MHz) : δ 1.03 (t, 3H, *J* = 7.2 Hz), 1.23 (t, 3H, *J* = 7.2 Hz), 1.74-1.86 (m, 2H), 2.11 (s, 3H), 3.90 (t, 2H, *J* = 6.4 Hz), 4.16 (q, 2H, *J* = 7.2 Hz), 5.82 (s, 1H), 6.39 (s, 1H), 6.65 (s, 1H), 6.83 (dd, 1H, *J* = 1.6 Hz & 8.0 Hz), 6.90 (s, 1H), 6.94 (d, 1H, *J* = 7.6 Hz), 7.19-7.29 (m, 1H)

^{13}C NMR (100 MHz) : δ 10.54, 14.02, 21.10, 22.56, 60.96, 69.40, 73.00, 113.91, 114.21, 119.83, 125.72, 129.41, 139.26, 139.80, 159.13, 164.98, 169.44

Methyl 4-methoxycarbonyl-2-methylene-5-oxo-3-phenylhexanoate (92a)

To a stirred solution of methyl 3-acetoxy-2-methylene-3-phenylpropanoate (**94a**) (10 mmol, 2.34 g) in THF-H_2O (20 mL, 1:1) was added DABCO (10 mmol, 1.12 g) at room temperature and reaction mixture was stirred at the same temperature for 15 min (up to complete formation of salt monitered by TLC). Methyl acetoacetate (11 mmol,

1.27 g) and K_2CO_3 (11 mmol, 1.52 g) were added and stirring was continued for further 6 h at room temperature. Reaction mixture was quenched by adding 2N HCl (10 mL), and extracted with diethyl ether (3X40 mL). Combined organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and crude product obtained was purified by column chromatography to provide the title compound as a colorless viscous liquid in 75% (2.18 g) isolated yield.



Reaction time : 15 min + 6 h

Yield : 75%

IR (neat) : ν 1743, 1716, 1630 cm^{-1}

^1H NMR (400 MHz) : δ 1.96 & 2.27 (2s, 3H), 3.47, 3.67, 3.68 & 3.70 (4s, 6H), 4.36-4.45 (m, 1H), 4.68-4.77 (m, 1H), 5.70 & 5.76 (2s, 1H), 6.27 & 6.29 (2s, 1H), 7.17-7.31 (m, 5H)

^{13}C NMR (100 MHz) : δ 28.96, 30.55, 46.00, 46.12, 51.95, 52.01, 52.41, 52.64, 63.27, 64.38, 124.22, 125.15, 127.21, 127.29, 128.17, 128.38, 128.42, 128.59, 138.41, 138.76, 140.59, 141.22, 166.22, 166.37, 167.91, 167.99, 201.20, 201.33

^1H & ^{13}C NMR clearly indicate that it is a mixture of two diastereomers almost in 1:1 ratio. The diastereomeric ratio was determined by the integration ratio of diastereomeric acetyl methyl group protons.

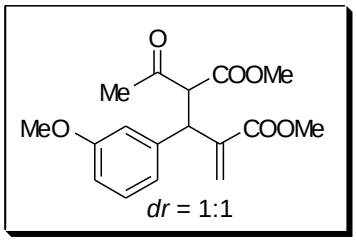
LCMS (m/z) : 289 $(M-H)^+$

Anal calc'd for $C_{16}H_{18}O_5$: C, 66.19; H, 6.25

Found : C, 66.31; H, 6.22

Methyl 4-methoxycarbonyl-3-(3-methoxyphenyl)-2-methylene-5-oxohexanoate (92b)

Treatment of methyl 3-acetoxy-3-(3-methoxyphenyl)-2-methylenepropanoate (**94b**) with DABCO in THF-H_2O system, and then reaction of resulting salt with methyl acetoacetate in the presence of K_2CO_3, following a similar procedure described for the molecule **92a**, provided the title compound as a colorless viscous liquid.



Reaction time : 15 min + 6 h

Yield : 88%

IR (neat) : ν 1745, 1724, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.99 & 2.27 (2s, 3H), 3.50, 3.68, 3.69 & 3.70 (4s, 6H), 3.76 & 3.77 (2s, 3H), 4.35-4.45 (m, 1H), 4.65-4.75 (m, 1H), 5.68 & 5.74 (2s, 1H), 6.27 & 6.29 (2s, 1H), 6.71-6.90 (m, 3H), 7.15-7.22 (m, 1H)

^{13}C NMR (100 MHz) : δ 28.91, 30.50, 45.94, 46.06, 51.90, 51.95, 52.38, 52.55, 55.04, 63.21, 64.31, 112.41, 114.07, 114.42, 120.41, 120.57, 124.33, 125.27, 129.34, 129.52, 140.08, 140.44, 140.55, 141.17, 159.49, 159.58, 166.20, 166.35, 167.85, 167.92, 201.06, 201.18

^{1}H & ^{13}C NMR clearly indicate that it is a mixture of two diastereomers almost in 1:1 ratio

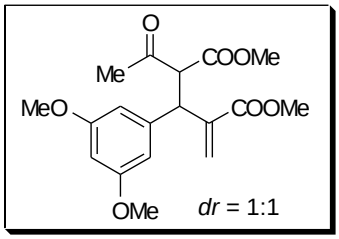
LCMS (m/z) : 319 $(M-H)^+$

Anal calc'd for $C_{17}H_{20}O_6$: C, 63.74; H, 6.29

Found : C, 63.72; H, 6.33

Methyl 3-(3,5-dimethoxyphenyl)-4-methoxycarbonyl-2-methylene-5-oxohexanoate (92c)

This compound was obtained as a white solid *via* the treatment of the salt obtained *via* the reaction of methyl 3-acetoxy-3-(3,5-dimethoxyphenyl)-2-methylenepropanoate (**94c**), with DABCO in THF-H_2O system, with methyl acetoacetate in the presence of K_2CO_3, following a similar procedure described for the molecule **92a**.



Reaction time : 15 min + 6 h

Yield : 94%

Mp : 83-85 ^{0}C

IR (KBr) : ν 1747, 1714, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.02 & 2.26 (2s, 3H), 3.54 & 3.70 (2s, 6H), 3.75 (s, 6H), 4.32-4.42 (m, 1H) 4.60-4.71 (m, 1H), 5.67 & 5.73 (2s, 1H), 6.25-6.33 (m, 2H), 6.39 & 6.41 (2s, 2H)

^{13}C NMR (100 MHz) : δ 29.05, 30.81, 46.07, 46.20, 52.07, 52.12, 52.59, 52.70, 55.25, 63.22, 64.38, 98.94, 99.00, 106.34, 106.65, 124.55, 125.58, 140.43, 140.91, 141.07, 141.29, 160.65, 160.76, 166.30, 166.47, 167.93, 201.28, 201.41

^{1}H & ^{13}C NMR clearly indicate that it is a mixture of two diastereomers almost in 1:1 ratio

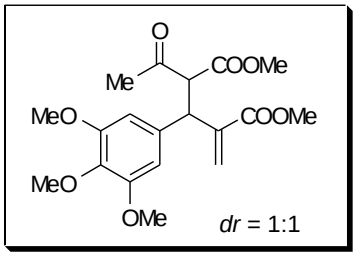
LCMS (m/z) : 349 $(M-H)^+$

Anal calc'd for $C_{18}H_{22}O_7$: C, 61.71; H, 6.33

Found : C, 61.85; H, 6.27

Methyl 4-methoxycarbonyl-2-methylene-5-oxo-3-(3,4,5-trimethoxyphenyl)hexano-ate (92d)

Treatment of methyl 3-acetoxy-2-methylene-3-(3,4,5-trimethoxyphenyl)propanoate (**94d**) with DABCO in THF-H_2O system followed by reaction of the resulting salt with methyl acetoacetate in the presence of K_2CO_3, following a similar procedure described for the molecule **92a**, provided the title compound as a white solid.



Reaction time : 15 min + 6 h

Yield : 88%

Mp : 64-65 ^{0}C

IR (KBr) : ν 1747, 1718, 1625 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.01 & 2.27 (2s, 3H), 3.53, 3.70, 3.71 & 3.72 (4s, 6H), 3.79 & 3.80 (2s, 3H), 3.82 (s, 6H), 4.35-4.43 (m, 1H), 4.61-4.69 (m, 1H), 5.69 & 5.74 (2s, 1H), 6.27 & 6.29 (2s, 1H), 6.45 & 6.47 (2s, 2H)

^{13}C NMR (100 MHz) : δ 28.97, 30.75, 46.31, 46.45, 52.04, 52.10, 52.55, 52.68, 56.00, 56.05, 60.70, 63.23, 64.35, 105.15, 105.43, 124.36, 125.38, 133.95, 134.36, 136.92, 137.03, 140.45, 141.07, 152.94, 153.09, 166.30, 166.47, 167.86, 167.94, 201.16, 201.45

^{1}H & ^{13}C NMR clearly indicate that it is a mixture of two diastereomers almost in 1:1 ratio

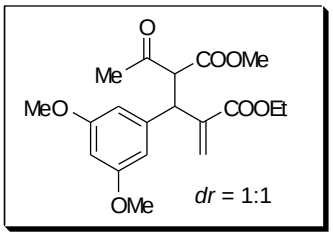
LCMS (m/z) : 379 $(M-H)^+$

Anal calc'd for $C_{19}H_{24}O_8$: C, 59.99; H, 6.36

Found : C, 60.15; H, 6.41

Ethyl 3-(3,5-dimethoxyphenyl)-4-methoxycarbonyl-2-methylene-5-oxohexanoate (92e)

This compound was obtained as a colorless viscous liquid *via* the reaction of ethyl 3-acetoxy-3-(3,5-dimethoxyphenyl)-2-methylenepropanoate (**94e**) with DABCO in THF-H_2O system, and subsequent treatment of the resulting salt with methyl acetoacetate in the presence of K_2CO_3, following a similar procedure described for the molecule **92a**.



Reaction time : 15 min + 6 h

Yield : 92%

IR (neat) : ν 1745, 1718, 1625 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.23 & 1.24 (2t, 3H, *J* = 7.2 Hz), 2.01 & 2.26 (2s, 3H), 3.54 & 3.69 (2s, 3H), 3.74 & 3.75 (2s, 6H), 4.07-4.22 (m, 2H), 4.32-4.40 (m, 1H), 4.60-4.70 (m, 1H) 5.65 & 5.70 (2s, 1H), 6.25-6.32 (m, 2H), 6.37-6.44 (m, 2H)

^{13}C NMR (100 MHz) : δ 14.02, 29.01, 30.80, 46.09, 46.22, 52.54, 52.65, 55.22, 60.97, 61.03, 63.20, 64.35, 98.93, 98.98, 106.34, 106.67, 124.23, 125.29, 140.66, 141.00, 141.30, 141.37, 160.60, 160.72, 165.81, 165.98, 167.96, 201.27, 201.45

^{1}H & ^{13}C NMR clearly indicate that it is a mixture of two diastereomers almost in 1:1 ratio

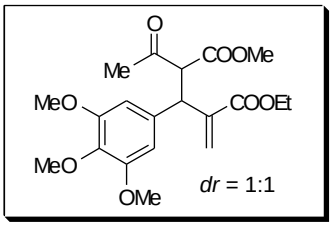
LCMS (m/z) : 363 $(M-H)^+$

Anal calc'd for $C_{19}H_{24}O_7$: C, 62.63; H, 6.64

Found : C, 62.51; H, 6.68

Ethyl 4-methoxycarbonyl-2-methylene-5-oxo-3-(3,4,5-trimethoxyphenyl)hexanoate (92f)

Treatment of ethyl 3-acetoxy-2-methylene-3-(3,4,5-trimethoxyphenyl)propanoate (**94f**) with DABCO in THF-H_2O system and then the reaction of the resulting salt with methyl acetoacetate in the presence of K_2CO_3, following a similar procedure described for the molecule **92a**, provided the title compound as a colorless viscous liquid.



Reaction time : 15 min + 6 h

Yield : 90%

IR (neat) : ν 1745, 1716, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.24 & 1.25 (2t, 3H, *J* = 6.8 Hz), 2.00 & 2.27 (2s, 3H), 3.53 & 3.70 (2s, 3H), 3.79, 3.80 & 3.82 (3s, 9H), 4.07-4.26 (m, 2H), 4.34-4.44 (m, 1H), 4.59-4.69 (m, 1H), 5.66 & 5.71 (2s, 1H), 6.27 & 6.29 (2s, 1H), 6.45 & 6.48 (2s, 2H)

^{13}C NMR (100 MHz) : δ 14.02, 28.97, 30.81, 46.38, 46.52, 52.55, 52.67, 56.10, 56.06, 60.73, 61.00, 61.06, 63.27, 64.39, 105.22, 105.50, 124.09, 125.15, 134.10, 134.50, 136.95, 137.05, 140.72, 141.34, 152.94, 153.09, 165.87, 166.04, 167.90, 168.00, 201.21, 201.54

^{1}H & ^{13}C NMR clearly indicate that it is a mixture of two diastereomers almost in 1:1 ratio

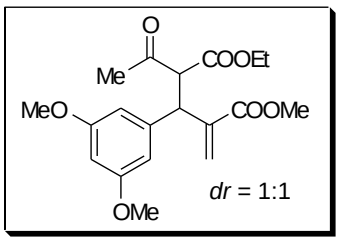
LCMS (m/z) : 393 $(M-H)^+$

Anal calc'd for $C_{20}H_{26}O_8$: C, 60.90; H, 6.64

Found : C, 61.02; H, 6.58

Methyl 3-(3,5-dimethoxyphenyl)-4-ethoxycarbonyl-2-methylene-5-oxohexanoate (92g)

This compound was obtained as a white solid *via* treatment of the salt, obtained from methyl 3-acetoxy-3-(3,5-dimethoxyphenyl)-2-methylenepropanoate (**94c**) by reaction with DABCO in THF-H_2O system, with ethyl acetoacetate in the presence of K_2CO_3, following a similar procedure described for the molecule **92a**.



Reaction time : 15 min + 6 h

Yield : 90%

Mp : 59-61 ^{0}C

IR (KBr) : ν 1741, 1712, 1625 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.03 & 1.22 (2t, 3H, *J* = 6.8 Hz), 2.03 & 2.26 (2s, 3H), 3.700 & 3.707 (2s, 3H), 3.74 (s, 6H), 3.98 & 4.15 (2q, 2H, *J* = 6.8 Hz), 4.30-4.40 (m, 1H), 4.60-4.71 (m, 1H), 5.67& 5.74 (2s, 1H), 6.23-6.33 (m, 2H), 6.37-6.46 (m, 2H)

^{13}C NMR (100 MHz) : δ 13.79, 13.99, 28.97, 30.69, 46.04, 46.09, 52.04, 52.10, 55.26, 61.54, 61.66, 63.48, 64.52, 98.95, 99.02, 106.50, 106.63, 124.58, 125.40, 140.60, 141.09, 141.14, 141.30, 160.62, 160.75, 166.33, 166.50, 167.47, 201.35, 201.41

^{1}H & ^{13}C NMR clearly indicate that it is a mixture of two diastereomers almost in 1:1 ratio

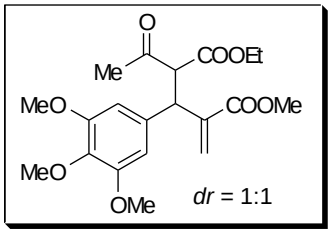
LCMS (m/z) : 363 $(M-H)^+$

Anal calc'd for $C_{19}H_{24}O_7$: C, 62.63; H, 6.64

Found : C, 62.73; H, 6.59

Methyl 4-ethoxycarbonyl-2-methylene-5-oxo-3-(3,4,5-trimethoxyphenyl)hexanoate (92h)

Reaction of methyl 3-acetoxy-2-methylene-3-(3,4,5-trimethoxyphenyl)propanoate (**94d**) with DABCO in THF-H_2O system and then the treatment of the resulting salt with ethyl acetoacetate in the presence of K_2CO_3, following a similar procedure described for the molecule **92a**, provided the title compound as a low melting white solid.



Reaction time : 15 min + 6 h

Yield : 93%

Mp : 48-50 ^{0}C

IR (neat) : ν 1747, 1718, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.02 & 1.23 (2t, 3H, *J* = 7.2 Hz), 2.02 & 2.27 (2s, 3H), 3.71, 3.72, 3.79 & 3.82 (4s, 12H), 3.97 & 4.16 (2q, 2H, *J* = 7.2 Hz), 4.32-4.42 (m, 1H), 4.61-4.70 (m, 1H), 5.69 & 5.75 (2s, 1H), 6.26 & 6.29 (2s, 1H), 6.47 & 6.49 (2s, 2H)

^{13}C NMR (100 MHz) : δ 13.82, 13.99, 28.93, 30.69, 46.35, 46.39, 52.07, 52.13, 56.07, 56.10, 60.75, 61.54, 61.69, 63.55, 64.54, 105.40, 105.47, 124.43, 125.24, 134.16, 134.44, 137.03 140.64, 141.18, 152.96, 153.12, 166.37, 166.53, 167.39, 167.54, 201.30, 201.50

^{1}H & ^{13}C NMR clearly indicate that it is a mixture of two diastereomers almost in 1:1 ratio

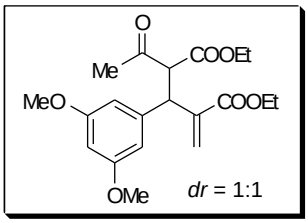
LCMS (m/z) : 393 $(M-H)^{+}$

Anal calc'd for $C_{20}H_{26}O_8$: C, 60.90; H, 6.64

Found : C, 61.05; H, 6.56

Ethyl 3-(3,5-dimethoxyphenyl)-4-ethoxycarbonyl-2-methylene-5-oxohexanoate (92i)

This compound was obtained as a colorless viscous liquid *via* the reaction of the salt (formed *in situ* by treating ethyl 3-acetoxy-3-(3,5-dimethoxyphenyl)-2-methylene-propanoate (**94e**) with DABCO in THF-H_2O system) with ethyl acetoacetate in the presence of K_2CO_3, following a similar procedure described for the molecule **92a**.



Reaction time : 15 min + 6 h

Yield : 92%

IR (neat) : ν 1741, 1716, 1625 cm^{-1}

^{1}H NMR (400 MHz) : δ [1.03 (t, *J* = 7.2 Hz) & 1.19-1.29 (m) (6H)], 2.02 & 2.26 (2s, 3H), 3.74 (s, 6H), 3.98 (q, 1H, *J* = 7.2 Hz), 4.07-4.22 (m, 3H), 4.30-4.39 (m, 1H), 4.61-4.69 (m, 1H), 5.65 & 5.71 (2s, 1H), 6.24-6.33 (m, 2H), 6.37-6.45 (m, 2H)

^{13}C NMR (100 MHz) : δ 13.76, 13.96, 14.03, 28.93, 30.70, 46.04, 46.10, 55.21, 60.94, 61.01, 61.49, 61.61, 63.45, 64.49, 98.92, 98.99, 106.50, 106.64, 124.26, 125.11, 140.80, 141.14, 141.37, 160.57, 160.70, 165.83, 166.01, 167.44, 167.49, 201.36, 201.47

^{1}H & ^{13}C NMR clearly indicate that it is a mixture of two diastereomers almost in 1:1 ratio

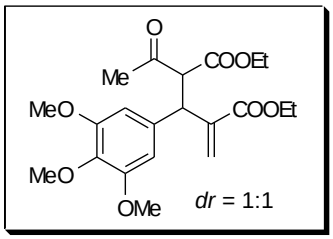
LCMS (m/z) : 377 $(M-H)^{+}$

Anal calc'd for $C_{20}H_{26}O_7$: C, 63.48; H, 6.93

Found : C, 63.41; H, 6.86

Ethyl 4-ethoxycarbonyl-2-methylene-5-oxo-3-(3,4,5-trimethoxyphenyl)hexanoate (92j)

Treatment of ethyl 3-acetoxy-2-methylene-3-(3,4,5-trimethoxyphenyl)propanoate (**94f**) with DABCO in THF-H_2O system and then the reaction of the *in situ* generated quaternary salt with ethyl acetoacetate in the presence of K_2CO_3, following a similar procedure described for the molecule **92a**, provided the title compound as a low melting white solid.



Reaction time : 15 min + 6 h

Yield : 90%

Mp : 45-47 ^{0}C

IR (neat) : ν 1743, 1716, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ [1.01 (t, *J* = 7.2 Hz) & 1.19-1.31 (m) (6H)], 2.01 & 2.27 (2s, 3H), 3.79, 3.821 & 3.825 (3s, 9H), 3.97 (q, 1H, *J* = 7.2 Hz), 4.10-4.22 (m, 3H), 4.32-4.41 (m, 1H), 4.61-4.69 (m, 1H), 5.66 & 5.73 (2s, 1H), 6.26 & 6.29 (2s, 1H), 6.46 & 6.49 (2s, 2H)

^{13}C NMR (100 MHz) : δ δ 13.75, 13.92, 13.99, 28.86, 30.68, 46.29, 46.35, 55.98, 60.67, 60.92, 61.00, 61.43, 61.59, 63.47, 64.47,

105.37, 105.45, 124.08, 124.89, 134.22, 134.50, 136.94, 140.82, 141.36, 152.86, 153.03, 165.84, 166.01, 167.33, 167.52, 201.23, 201.51

^{1}H & ^{13}C NMR clearly indicate that it is a mixture of two diastereomers almost in 1:1 ratio

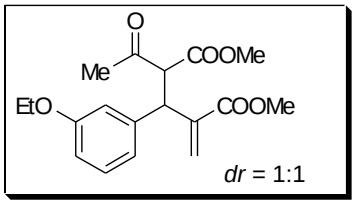
LCMS (m/z) : 407 $(M-H)^{+}$

Anal calc'd for $C_{21}H_{28}O_8$: C, 61.75; H, 6.91

Found : C, 61.85; H, 6.94

Methyl 3-(3-ethoxyphenyl)-4-methoxycarbonyl-2-methylene-5-oxohexanoate (92k)

This compound was obtained as a white solid *via* the treatment of quaternary salt (formed from methyl 3-acetoxy-3-(3-ethoxyphenyl)-2-methylenepropanoate (**94g**) by reaction with DABCO in THF-H_2O system) with methyl acetoacetate in the presence of K_2CO_3, following a similar procedure described for the molecule **92a**.



Reaction time : 15 min + 6 h

Yield : 90%

Mp : 64-66 ^{0}C

IR (KBr) : ν 1753, 1716, 1631 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.39 (t, 3H, *J* = 6.8 Hz), 1.98 & 2.27 (2s, 3H), 3.50, 3.68, 3.693 & 3.698 (4s, 6H), 3.93-4.04 (m, 2H), 4.33-4.42 (m, 1H), 4.63-4.74 (m, 1H), 5.68 & 5.73 (2s, 1H), 6.27 & 6.29 (2s, 1H), 6.69-6.87 (m, 3H), 7.12-7.21 (m, 1H)

^{13}C NMR (100 MHz) : δ 14.80, 29.02, 30.71, 46.05, 46.16, 52.06, 52.12, 52.55, 52.72, 63.36, 64.50, 113.16, 114.60, 114.94, 120.44, 120.61, 124.38, 125.41, 129.44, 129.63, 140.05, 140.41, 140.60, 141.25, 158.95, 159.05, 166.33, 166.49, 167.99, 168.06, 201.33, 201.44

^{1}H & ^{13}C NMR clearly indicate that it is a mixture of two diastereomers almost in 1:1 ratio

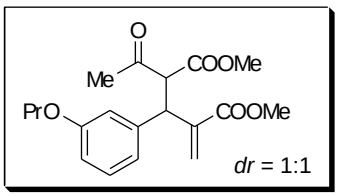
LCMS (m/z) : 333 $(M-H)^+$

Anal calc'd for $C_{18}H_{22}O_6$: C, 64.66; H, 6.63

Found : C, 64.59; H, 6.68

Methyl 4-methoxycarbonyl-2-methylene-5-oxo-3-(3-propoxyphenyl)hexanoate (92l)

Reaction of methyl 3-acetoxy-2-methylene-3-(3-propoxyphenyl)propanoate (**94h**) with DABCO in THF-H_2O system and then the treatment of the resulting quaternary salt with methyl acetoacetate in the presence of K_2CO_3, following a similar procedure described for the molecule **92a**, provided the title compound as a colorless viscous liquid.



Reaction time : 15 min + 6 h

Yield : 96%

IR (neat) : ν 1741, 1722, 1635 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.02 (t, 3H, *J* = 7.2 Hz), 1.72-1.85 (m, 2H), 1.98 & 2.27 (2s, 3H), 3.50 & 3.69 (2s, 6H), 3.83-3.91 (m, 2H), 4.33-4.42 (m, 1H), 4.63-4.73 (m, 1H), 5.68 & 5.74 (2s,

1H), 6.27 & 6.29 (2s, 1H), 6.69-6.86 (m, 3H), 7.12-7.20 (m, 1H)

^{13}C NMR (100 MHz) : δ 10.53, 22.56, 29.03, 30.74, 46.00, 46.13, 52.06, 52.12, 52.55, 52.72, 63.34, 64.49, 69.36, 113.17, 114.56, 114.87, 120.34, 120.51, 124.38, 125.41, 129.41, 129.60, 139.98, 140.34, 140.55, 141.21, 159.11, 159.21, 166.32, 166.48, 167.98, 168.05, 201.36, 201.48

^{1}H & ^{13}C NMR clearly indicate that it is a mixture of two diastereomers almost in 1:1 ratio

LCMS (m/z) : 347 $(M-H)^+$

Anal calc'd for $C_{19}H_{24}O_6$: C, 65.50; H, 6.94

Found : C, 65.41; H, 6.88

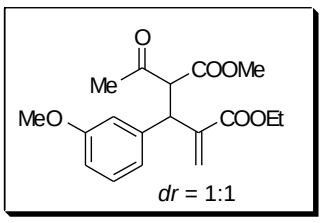
Ethyl 4-methoxycarbonyl-3-(3-methoxyphenyl)-2-methylene-5-oxohexanoate (92m)

This compound was obtained as a colorless viscous liquid *via* the treatment of the salt (generated form ethyl 3-acetoxy-3-(3-methoxyphenyl)-2-methylenepropanoate (**94i**) by reaction with DABCO in THF-H_2O system) with methyl acetoacetate in the presence of K_2CO_3, following a similar procedure described for the molecule **92a**.

Reaction time : 15 min + 6 h

Yield : 85%

IR (neat) : ν 1747, 1718, 1625 cm^{-1}



^{1}H NMR (400 MHz) : δ 1.22 & 1.23 (2t, 3H, *J* = 7.2 Hz), 1.98 & 2.27 (2s, 3H), 3.50 & 3.70 (2s, 3H), 3.76 & 3.77 (2s, 3H), 4.05-

4.21 (m, 2H), 4.33-4.43 (m, 1H), 4.63-4.74 (m, 1H), 5.66 & 5.72 (2s, 1H), 6.27 & 6.29 (2s, 1H), 6.70-6.88 (m, 3H), 7.13-7.22 (m, 1H)

^{13}C NMR (100 MHz) : δ 14.00, 29.02, 30.74, 46.00, 46.13, 52.51, 52.68, 55.11, 60.98, 61.04, 63.27, 64.40, 112.44, 114.08, 114.46, 120.51, 120.70, 124.12, 125.15, 129.38, 129.56, 140.14, 140.51, 140.73, 141.37, 159.48, 159.57, 165.80, 165.95, 167.96, 168.01, 201.32, 201.47

^{1}H & ^{13}C NMR clearly indicate that it is a mixture of two diastereomers almost in 1:1 ratio

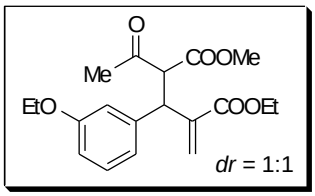
LCMS (m/z) : 333 $(M-H)^+$

Anal calc'd for $C_{18}H_{22}O_6$: C, 64.66; H, 6.63

Found : C, 64.51; H, 6.67

Ethyl 3-(3-ethoxyphenyl)-4-methoxycarbonyl-2-methylene-5-oxohexanoate (92n)

Treatment of ethyl 3-acetoxy-3-(3-ethoxyphenyl)-2-methylenepropanoate (**94j**) with DABCO in THF-H_2O system and then the reaction of the *in situ* formed salt with methyl acetoacetate in the presence of K_2CO_3, following a similar procedure described for the molecule **92a**, provided the title compound as a colorless viscous liquid.



Reaction time : 15 min + 6 h

Yield : 86%

IR (neat) : ν 1743, 1718, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.21 & 1.22 (2t, 3H, *J* = 7.2 Hz), 1.38 (t, 3H, *J* = 6.8 Hz), 1.97 & 2.27 (2s, 3H), 3.50 & 3.70 (2s, 3H), 3.94-

4.04 (m, 2H), 4.07-4.20 (m, 2H), 4.33-4.41 (m, 1H), 4.63-4.73 (m, 1H), 5.65 & 5.71 (2s, 1H), 6.27 & 6.29 (2s, 1H), 6.69-6.87 (m, 3H), 7.12-7.21 (m, 1H)

^{13}C NMR (100 MHz) : δ 13.98, 14.74, 28.98, 30.74, 45.98, 46.10, 52.49, 52.65, 60.95, 61.01, 63.26, 64.42, 113.04, 114.52, 114.87, 120.43, 120.62, 124.02, 125.07, 129.33, 129.52, 140.04, 140.41, 140.73, 141.38, 158.84, 158.93, 165.78, 165.94, 167.95, 168.01, 201.33, 201.50

^{1}H & ^{13}C NMR clearly indicate that it is a mixture of two diastereomers almost in 1:1 ratio

LCMS (m/z) : 347 $(M-H)^+$

Anal calc'd for $C_{19}H_{24}O_6$: C, 65.50; H, 6.94

Found : C, 65.51; H, 6.88

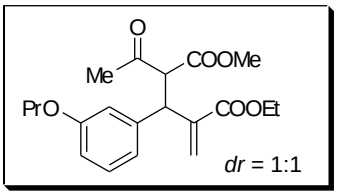
Ethyl 4-methoxycarbonyl-2-methylene-5-oxo-3-(3-propoxyphenyl)hexanoate (92o)

This compound was obtained as a colorless viscous liquid *via* the treatment of the salt (formed by the reaction of ethyl 3-acetoxy-2-methylene-3-(3-propoxyphenyl)-propanoate (**94k**) with DABCO in THF-H_2O system) with methyl acetoacetate in the presence of K_2CO_3, following a similar procedure described for the molecule **92a**.

Reaction time : 15 min + 6 h

Yield : 90%

IR (neat) : ν 1747, 1718, 1625 cm^{-1}



^{1}H NMR (400 MHz) : δ 1.02 (t, 3H, *J* = 7.2 Hz), 1.22 & 1.23 (2t, 3H, *J* = 7.2 Hz), 1.72-1.84 (m, 2H), 1.97 & 2.27 (2s, 3H), 3.50 &

3.70 (2s, 3H), 3.82-3.91 (m, 2H), 4.06-4.20 (m, 2H), 4.33-4.41 (m, 1H), 4.62-4.73 (m, 1H), 5.66 & 5.71 (2s, 1H), 6.27 & 6.29 (2s, 1H), 6.68-6.86 (m, 3H), 7.11-7.20 (m, 1H)

^{13}C NMR (100 MHz) : δ 10.50, 14.00, 22.53, 29.00, 30.76, 46.00, 46.14, 52.51, 52.66, 60.97, 61.04, 63.29, 64.45, 69.32, 113.11, 114.56, 114.88, 120.36, 120.55, 124.06, 125.12, 129.33, 129.51, 140.03, 140.40, 140.75, 141.40, 159.05, 159.15, 165.83, 165.98, 167.99, 168.04, 201.38, 201.55

^{1}H & ^{13}C NMR clearly indicate that it is a mixture of two diastereomers almost in 1:1 ratio

LCMS (m/z) : 361 $(M-H)^+$

Anal calc'd for $C_{20}H_{26}O_6$: C, 66.28; H, 7.23

Found : C, 66.21; H, 7.25

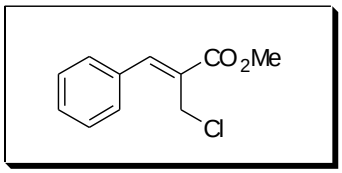
Treatment of methyl 4-methoxycarbonyl-2-methylene-5-oxo-3-phenylhexanoate (92a) with $TiCl_4$:

Methyl (2*Z*)-2-(chloromethyl)-3-phenylprop-2-enoate (97)

To a stirred solution of methyl 4-methoxycarbonyl-2-methylene-5-oxo-3-phenylhexanoate (**92a**) (1 mmol, 0.290 g), in anhydrous dichloromethane (2 mL), $TiCl_4$ (2 mmol, 1 mL, 2M solution in dichloromethane) was added at 0 ^{o}C. Reaction mixture was stirred at room temperature for 12 h. Then the reaction mixture was cooled to 0 ^{o}C and quenched with water (2 mL) and extracted with ethyl acetate (3x20 mL). Combined organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and the

residue thus obtained on purification by column chromatography provided methyl (2*Z*)-2-(chloromethyl)-3-phenylprop-2-enoate (**97**) in 18% (0.038 g) isolated yield as a colorless liquid. We have also recovered un-reacted methyl 4-methoxycarbonyl-2-methylene-5-oxo-3-phenylhexanoate (**92a**) in 76% (0.220 g) isolated yield.

Reaction time : 12 h



Yield : 18%

IR (neat) : ν 1718, 1630 cm^{-1}

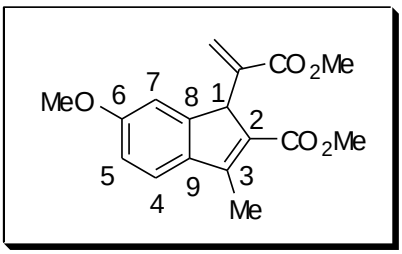
^{1}H NMR (400 MHz) : δ 3.80 (s, 3H), 4.39 (s, 2H), 7.29-7.43 (m, 3H), 7.43-7.52 (m, 2H), 7.80 (s, 1H)

^{13}C NMR (100 MHz) : δ 39.22, 52.56, 128.42, 128.95, 129.70, 129.80, 134.19, 143.89, 166.82

Intramolecular Friedel-Crafts reaction of methyl 4-methoxycarbonyl-3-(3-methoxyphenyl)-2-methylene-5-oxohexanoate (92b) with $TiCl_4$:

To a stirred solution of methyl 4-methoxycarbonyl-3-(3-methoxyphenyl)-2-methylene-5-oxohexanoate (**92b**) (1 mmol, 0.320 g), in anhydrous dichloromethane (2 mL), $TiCl_4$ (2 mmol, 1 mL, 2M solution in dichloromethane) was added at 0 ^{o}C. After stirring at room temperature for 1 h, reaction mixture was cooled to 0 ^{o}C and quenched with water (2 mL) and extracted with ethyl acetate (3x20 mL). Combined organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated. Residue thus obtained was purified by column chromatography (5% EtOAc in hexanes) to provide methyl 6-methoxy-1-(1-methoxycarbonylethenyl)-3-methyl-1H-indene-2-carboxylate (**93b**) and methyl 4-methoxy-1-(1-methoxycarbonylethenyl)-3-methyl-1H-indene-2-carboxylate (***ortho*-93b**) in 76% and 20% isolated yields respectively.

Methyl 6-methoxy-1-(1-methoxycarbonylethenyl)-3-methyl-1H-indene-2-carboxylate (93b)



Reaction time : 1 h

Yield : 76% (0.230 g)

Color : white

Mp : 88-90 ^{0}C

IR (KBr) : ν 1693, 1602 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.54 (d, 3H, *J* = 2.4 Hz), 3.74 (s, 3H), 3.80 (s, 3H), 3.81 (s, 3H), 4.85 (s, 1H, multiplicity not resolved properly), 5.39 (s, 1H), 6.11 (s, 1H), 6.89 (dd, 1H, *J* = 2.0 Hz & 8.4 Hz), 6.93 (d, 1H, *J* = 2.0 Hz), 7.37 (d, 1H, *J* = 8.4 Hz)

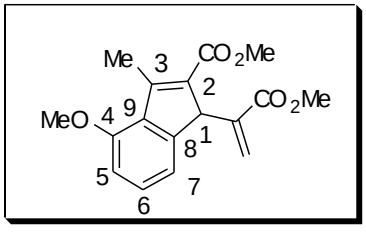
^{13}C NMR (100 MHz) : δ 12.68, 50.88, 51.08, 52.16, 55.54, 109.39, 113.19, 122.28, 124.71, 130.61, 136.70, 139.08, 149.67, 152.91, 160.73, 165.66, 167.37

LCMS (m/z) : 301 $(M-H)^+$

Anal calc'd for $C_{17}H_{18}O_5$: C, 67.54; H, 6.00

Found : C, 67.72; H, 6.05

Methyl 4-methoxy-1-(1-methoxycarbonylethenyl)-3-methyl-1H-indene-2-carboxylate (*ortho*-93b)



Yield : 20% (0.060 g)

Color : pale yellow

Mp : 76-77 ^{0}C

IR (KBr) : ν 1703, 1599 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.76 (d, 3H, *J* = 2.4 Hz), 3.73 (s, 3H), 3.80 (s, 3H), 3.87 (s, 3H), 4.84-4.89 (m, 1H, multiplicity not resolved properly), 5.38 (s, 1H), 6.08 (s, 1H), 6.80 (d, 1H, *J* = 8.4 Hz), 6.94 (d, 1H, *J* = 7.6 Hz), 7.22-7.30 (m, 1H)

^{13}C NMR (100 MHz) : δ 15.80, 51.08, 51.13, 52.15, 55.31, 109.52, 116.11, 124.59, 129.86, 130.87, 131.10, 139.14, 149.88, 154.33, 156.44, 165.78, 167.37

LCMS (m/z) : 301 $(M-H)^{+}$

Anal calc'd for $C_{17}H_{18}O_5$: C, 67.54; H, 6.00

Found : C, 67.42; H, 5.96

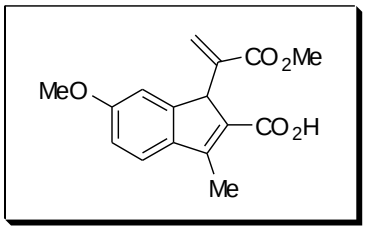
Treatment of methyl 4-methoxycarbonyl-3-(3-methoxyphenyl)-2-methylene-5-oxohexanoate (92b) with H_2SO_4:

To a stirred solution of methyl 4-methoxycarbonyl-3-(3-methoxyphenyl)-2-methylene-5-oxohexanoate (**92b**) (1 mmol, 0.320 g), in anhydrous dichloromethane (2 mL), H_2SO_4 (2 mmol, 0.196 g) was added at 0 ^{o}C. After stirring at room temperature for 1 h, reaction mixture was cooled to 0 ^{o}C, quenched with water (2 mL) and extracted with ethyl acetate (3x20 mL). Combined organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated, residue thus obtained was subjected to column chromatography to furnish methyl 6-methoxy-1-(1-methoxycarbonylethenyl)-3-methyl-1H-indene-2-carboxylate (**93b**) in 46% (0.139 g), methyl 4-methoxy-1-(1-methoxycarbonyl-ethenyl)-3-methyl-1H-indene-2-carboxylate (***ortho*-93b**) in 10%

(0.029 g), and 6-methoxy-1-(1-methoxycarbonylethenyl)-3-methyl-1H-indene-2-carboxylic acid (**98**) in 35% (0.100 g) isolated yields.

*The both compounds **93b** & **ortho-93b** have identical ^{1}H NMR, ^{13}C NMR spectral data as that are obtained in the procedure mentioned in page132.*

6-Methoxy-1-(1-methoxycarbonylethenyl)-3-methyl-1H-indene-2-carboxylic acid (98)



Reaction time : 1 h

Yield : 35%

Color : pale yellow

Mp : 176-178 ^{0}C

IR (KBr) : ν 2800-3200 (b), 1718, 1657, 1601 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.58 (d, 3H, *J* = 2.0 Hz), 3.80 (s, 3H), 3.82 (s, 3H), 4.85 (s, 1H, multiplicity not resolved properly), 5.47 (s, 1H), 6.15 (s, 1H), 6.90 (dd, 1H, *J* = 2.0 Hz & 8.4 Hz), 6.95 (s, 1H, unresolved doublet), 7.40 (d, 1H, *J* = 8.4 Hz),

^{13}C NMR (100 MHz) : δ 12.95, 50.91, 52.17, 55.55, 109.36, 113.41, 122.65, 125.04, 129.94, 136.52, 138.73, 150.19, 155.71, 161.09, 167.28, 170.81

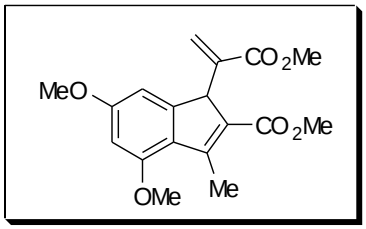
LCMS (m/z) : 289 $(M+H)^{+}$

Anal calc'd for $C_{16}H_{16}O_5$: C, 66.66; H, 5.59

Found : C, 66.51; H, 5.62

Methyl 4,6-dimethoxy-1-(1-methoxycarbonylethenyl)-3-methyl-1H-indene-2-carboxylate (93c)

Treatment of methyl 3-(3,5-dimethoxyphenyl)-4-methoxycarbonyl-2-methylene-5-oxo-hexanoate (**92c**) with $TiCl_4$ in dichloromethane following the similar procedure described for the molecule **93b** (treatment of **92b** with $TiCl_4$), provided the tille compound as a white solid.



Reaction time : 0.5 h

Yield : 94% (0.312 g)

Mp : 130-132 ^{0}C

IR (KBr) : ν 1697, 1597 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.73 (d, 3H, *J* = 2.0 Hz), 3.71 (s, 3H), 3.80 (s, 3H), 3.81 (s, 3H), 3.84 (s, 3H), 4.81 (s, 1H), 5.37 (s, 1H), 6.09 (s, 1H), 6.36 (d, 1H, *J* = 1.6 Hz), 6.50 (s, 1H)

^{13}C NMR (100 MHz) : δ 15.63, 50.91, 51.15, 52.15, 55.30, 55.58, 97.63, 100.56, 124.52, 124.68, 128.79, 139.43, 151.69, 154.72, 157.16, 162.08, 165.75, 167.53

LCMS (m/z) : 333 $(M+H)^+$

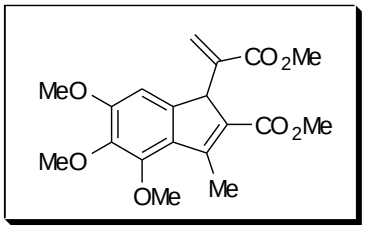
Anal calc'd for $C_{18}H_{20}O_6$: C, 65.05; H, 6.07

Found : C, 64.98; H, 6.15

Methyl 1-(1-methoxycarbonylethenyl)-3-methyl-4,5,6-trimethoxy-1H-indene-2-carboxylate (93d)

This was prepared as a pale yellow solid by the treatment of methyl 4-methoxycarbonyl-2-methylene-5-oxo-3-(3,4,5-trimethoxyphenyl)hexanoate (**92d**) with

$TiCl_4$ in dichloromethane following the similar procedure described for the molecule **93b** (treatment of **92b** with $TiCl_4$).



Reaction time : 0.5 h

Yield : 92% (0.331 g)

Mp : 80-83 ^{0}C

IR (KBr) : ν 1699, 1599 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.73 (d, 3H, *J* = 2.4 Hz), 3.72 (s, 3H), 3.81 (s, 3H), 3.85 (s, 3H), 3.86 (s, 3H), 3.95 (s, 3H), 4.79 (s, 1H) , 5.38 (s, 1H), 6.10 (s, 1H), 6.70 (s, 1H)

^{13}C NMR (100 MHz) : δ 14.70, 50.97, 51.06, 52.11, 56.13, 60.86, 61.41, 103.11, 124.62, 128.58, 130.51, 139.25, 141.61, 144.47, 150.09, 153.73, 154.78, 165.49, 167.49

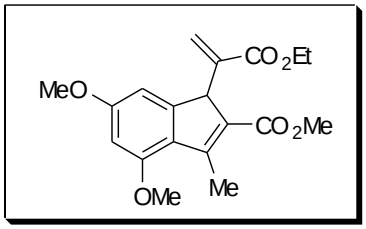
LCMS (m/z) : 361 $(M-H)^+$

Anal calc'd for $C_{19}H_{22}O_7$: C, 62.97; H, 6.12

Found : C, 63.25; H, 5.96

Methyl 4,6-dimethoxy-1-(1-ethoxycarbonylethenyl)-3-methyl-1H-indene-2-carboxylate (93e)

Treatment of ethyl 3-(3,5-dimethoxyphenyl)-4-methoxycarbonyl-2-methylene-5-oxohexanoate (**92e**) with $TiCl_4$ in dichloromethane following the similar procedure described for the molecule **93b** (treatment of **92b** with $TiCl_4$), provided the tille compound as a white solid.



Reaction time : 0.5 h

Yield : 93% (0.320 g)

Mp : 70-72 ^{0}C

IR (KBr) : ν 1697, 1599 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.28 (t, 3H, *J* = 7.2 Hz), 2.72 (d, 3H, *J* = 2.0 Hz), 3.71 (s, 3H), 3.79 (s, 3H), 3.84 (s, 3H), 4.17-4.30 (m, 2H), 4.80 (s, 1H, not resolved properly), 5.38 (s, 1H), 6.11 (s, 1H), 6.36 (d, 1H, *J* = 1.6 Hz), 6.52 (s, 1H)

^{13}C NMR (100 MHz) : δ 14.10, 15.49, 50.74, 51.22, 55.17, 55.43, 60.79, 97.50, 100.42, 124.47, 128.69, 139.60, 151.58, 154.50, 157.05, 161.98, 165.62, 166.89

LCMS (m/z) : 347 $(M+H)^+$

Anal calc'd for $C_{19}H_{22}O_6$: C, 65.88; H, 6.40

Found : C, 65.76; H, 6.21

Methyl 1-(1-ethoxycarbonylethenyl)-3-methyl-4,5,6-trimethoxy-1H-indene-2-carboxylate (93f)

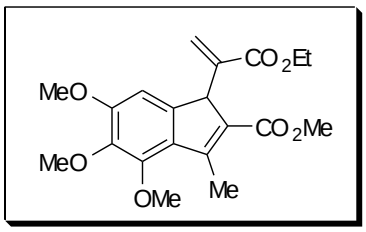
This was obtained as a white solid by the treatment of ethyl 4-methoxycarbonyl-2-methylene-5-oxo-3-(3,4,5-trimethoxyphenyl)hexanoate (**92f**) with $TiCl_4$ in dichloromethane following the similar procedure described for the molecule **93b** (treatment of **92b** with $TiCl_4$).

Reaction time : 0.5 h

Yield : 93% (0.350 g)

Mp : 100-103 ^{0}C

IR (KBr) : ν 1701, 1599 cm^{-1}



^{1}H NMR (400 MHz) : δ 1.28 (t, 3H, *J* = 7.2 Hz), 2.73 (d, 3H, *J* = 2.4 Hz), 3.73 (s, 3H), 3.85 (s, 3H), 3.86 (s, 3H), 3.95 (s, 3H), 4.23 (q, 2H, *J* = 7.2 Hz), 4.77 (s, 1H, multiplicity not resolved), 5.41 (s, 1H), 6.13 (s, 1H), 6.71 (s, 1H)

^{13}C NMR (100 MHz) : δ 14.16, 14.70, 50.97, 51.30, 56.14, 60.89, 61.43, 103.10, 124.71, 128.65, 130.51, 139.46, 141.61, 144.46, 150.11, 153.65, 154.76, 165.54, 166.98

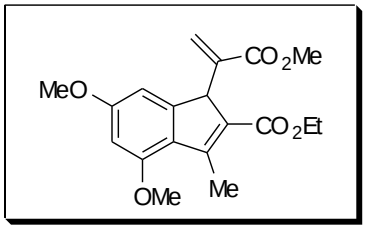
LCMS (m/z) : 375 $(M-H)^{+}$

Anal calc'd for $C_{20}H_{24}O_7$: C, 63.82; H, 6.43

Found : C, 63.82; H, 6.41

Ethyl 4,6-dimethoxy-1-(1-methoxycarbonylethenyl)-3-methyl-1H-indene-2-carboxylate (93g)

Treatment of methyl 3-(3,5-dimethoxyphenyl)-4-ethoxycarbonyl-2-methylene-5-oxohexanoate (**92g**) with $TiCl_4$ in dichloromethane following the similar procedure described for the molecule **93b** (treatment of **92b** with $TiCl_4$), provided the tille compound as a brick red solid.



Reaction time : 0.5 h

Yield : 95% (0.328 g)

Mp : 74-76 ^{0}C

IR (KBr) : ν 1728, 1678, 1599 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.24 (t, 3H, *J* = 7.2 Hz), 2.73 (s, 3H), 3.800 (s, 3H), 3.806 (s, 3H), 3.84 (s, 3H), 4.07-4.28 (m, 2H), 4.81 (s, 1H), 5.36 (s, 1H), 6.10 (s, 1H), 6.36 (s, 1H), 6.49 (s, 1H)

^{13}C NMR (100 MHz) : δ 14.24, 15.52, 51.04, 52.07, 55.25, 55.53, 59.55, 97.57, 100.50, 124.61, 124.71, 129.17, 139.55, 151.75, 154.38, 157.07, 162.00, 165.23, 167.48

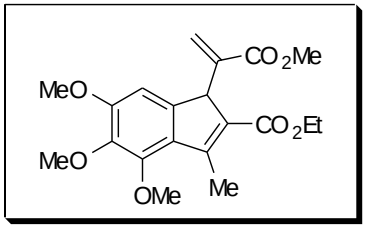
LCMS (m/z) : 347 $(M+H)^+$

Anal calc'd for $C_{19}H_{22}O_6$: C, 65.88; H, 6.40

Found : C, 65.81; H, 6.43

Ethyl 1-(1-methoxycarbonylethenyl)-3-methyl-4,5,6-trimethoxy-1H-indene-2-carboxylate (93h)

This was obtained as a white solid by the reaction of methyl 4-ethoxycarbonyl-2-methylene-5-oxo-3-(3,4,5-trimethoxyphenyl)hexanoate (**92h**) with $TiCl_4$ in dichloromethane following the similar procedure described for the molecule **93b** (treatment of **92b** with $TiCl_4$).



Reaction time : 0.5 h

Yield : 91% (0.341 g)

Mp : 72-74 ^{0}C

IR (KBr) : ν 1691, 1599 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.25 (t, 3H, *J* = 7.2 Hz), 2.73 (d, 3H, *J* = 2.4 Hz), 3.81 (s, 3H), 3.85 (s, 3H), 3.86 (s, 3H), 3.95 (s, 3H), 4.10-4.29 (m, 2H), 4.80 (s, 1H, multiplicity not resolved), 5.37 (s, 1H), 6.11 (s, 1H), 6.69 (s, 1H)

^{13}C NMR (100 MHz) : δ 14.18, 14.62, 50.96, 52.05, 56.11, 59.67, 60.83, 61.39, 103.07, 124.70, 128.69, 130.90, 139.36, 141.56, 144.55, 150.01, 153.40, 154.69, 164.99, 167.46

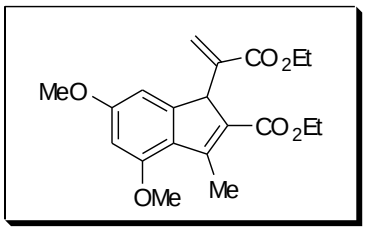
LCMS (m/z) : 377 $(M+H)^+$

Anal calc'd for $C_{20}H_{24}O_7$: C, 63.82; H, 6.43

Found : C, 63.56; H, 6.68

Ethyl 4,6-dimethoxy-1-(1-ethoxycarbonylethenyl)-3-methyl-1H-indene-2-carboxyl-ate (93i)

Treatment of ethyl 3-(3,5-dimethoxyphenyl)-4-ethoxycarbonyl-2-methylene-5-oxohexanoate (**92i**) with $TiCl_4$ in dichloromethane following the similar procedure described of the molecule **93b** (treatment of **92b** with $TiCl_4$), provided the tille compound as a brick red solid.



Reaction time : 0.5 h

Yield : 94% (0.337 g)

Mp : 56-58 ^{0}C

IR (KBr) : ν 1716, 1689, 1599 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.25 (t, 3H, *J* = 7.2 Hz), 1.28 (t, 3H, *J* = 7.2 Hz), 2.73 (d, 3H, *J* = 2.0 Hz), 3.79 (s, 3H), 3.84 (s, 3H), 4.08-4.30 (m, 4H), 4.80 (s, 1H, multiplicity not resolved properly), 5.38 (s, 1H), 6.12 (s, 1H), 6.36 (s, 1H), 6.50 (s, 1H)

^{13}C NMR (100 MHz) : δ 14.18, 14.27, 15.53, 51.26, 55.29, 55.56, 59.55, 60.85, 97.61, 100.48, 124.69, 129.16, 139.76, 151.77, 154.34, 157.10, 161.99, 165.30, 167.01

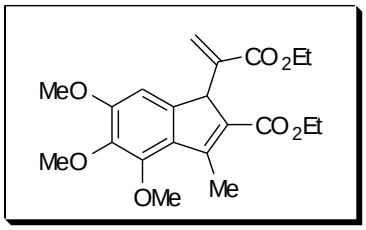
LCMS (m/z) : 361 $(M+H)^+$

Anal calc'd for $C_{20}H_{24}O_6$: C, 66.65; H, 6.71

Found : C, 66.72; H, 6.58

Ethyl 1-(1-ethoxycarbonylethenyl)-3-methyl-4,5,6-trimethoxy-1H-indene-2-carboxylate (93j)

This was prepared as a pale yellow solid by the treatment of ethyl 4-ethoxycarbonyl-2-methylene-5-oxo-3-(3,4,5-trimethoxy-phenyl)hexanoate (**92j**) with $TiCl_4$ in dichloromethane following the similar procedure described for the molecule **93b** (treatment of **92b** with $TiCl_4$).



Reaction time : 0.5 h

Yield : 93% (0.363 g)

Mp : 39-40 ^{0}C

IR (KBr) : ν 1697, 1599 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.26 (t, 3H, *J* = 7.2 Hz), 1.27 (t, 3H, *J* = 7.2 Hz), 2.73 (d, 3H, *J* = 2.4 Hz), 3.85 (s, 3H), 3.86 (s, 3H), 3.95 (s, 3H), 4.10-4.30 (m, 4H), 4.78 (d, 1H, *J* = 1.6 Hz, multiplicity not resolved properly), 5.40 (s, 1H), 6.14 (s, 1H), 6.70 (s, 1H)

^{13}C NMR (100 MHz) : δ 14.09, 14.18, 14.59, 51.23, 56.08, 59.63, 60.79, 60.82, 61.36, 103.03, 124.73, 128.71, 130.81, 139.53, 141.54, 144.48, 150.00, 153.30, 154.64, 165.01, 166.90

LCMS (m/z) : 391 $(M+H)^+$

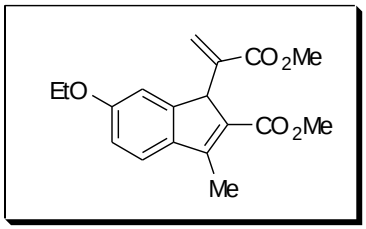
Anal calc'd for $C_{21}H_{26}O_7$: C, 64.60; H, 6.71

Found : C, 64.58; H, 6.71

Reaction of methyl 3-(3-ethoxyphenyl)-4-methoxycarbonyl-2-methylene-5-oxohexanoate (92k) with $TiCl_4$:

Treatment of methyl 3-(3-ethoxyphenyl)-4-methoxycarbonyl-2-methylene-5-oxohexanoate (**92k**) with $TiCl_4$ in dichloromethane following the similar procedure described for obtaining **93b** and ***ortho*-93b** (from **92b**), provided methyl 6-ethoxy-1-(1-methoxycarbonyl-ethenyl)-3-methyl-1H-indene-2-carboxylate (**93k**) and methyl 4-ethoxy-1-(1-methoxycarbonylethenyl)-3-methyl-1H-indene-2-carboxylate (***ortho*-93k**) in 73% and 21% isolated yields respectively.

Methyl 6-ethoxy-1-(1-methoxycarbonylethenyl)-3-methyl-1H-indene-2-carboxylate (93k)



Reaction time : 1 h

Yield : 73% (0.231 g)

Color : white

Mp : 79-80 ^{0}C

IR (KBr) : ν 1724, 1685, 1602 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.41 (t, 3H, *J* = 6.8 Hz), 2.54 (d, 3H, *J* = 2.4 Hz), 3.74 (s, 3H), 3.80 (s, 3H), 4.03 (q, 2H, *J* = 6.8 Hz), 4.84 (s, 1H, multiplicity not resolved properly), 5.38 (s, 1H), 6.10 (s, 1H), 6.87 (dd, 1H, *J* = 2.0 Hz & 8.4 Hz), 6.92 (d, 1H, *J* = 2.0 Hz), 7.36 (d, 1H, *J* = 8.4 Hz)

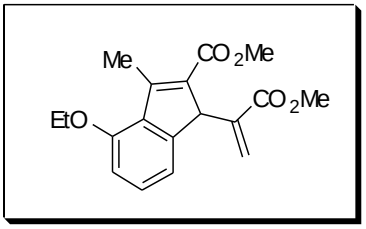
^{13}C NMR (100 MHz) : δ 12.71, 14.85, 50.87, 51.11, 52.19, 63.76, 110.00, 113.62, 122.30, 124.71, 130.53, 136.57, 139.12, 149.70, 153.02, 160.13, 165.72, 167.41

LCMS (m/z) : 315 $(M-H)^+$

Anal calc'd for $C_{18}H_{20}O_5$: C, 68.34; H, 6.37

Found : C, 68.22; H, 6.41

Methyl 4-ethoxy-1-(1-methoxycarbonylethenyl)-3-methyl-1H-indene-2-carboxylate (*ortho*-93k)



Yield : 21% (0.067 g)

Color : pale yellow

Mp : 78-79 ^{0}C

IR (KBr) : ν 1722, 1697, 1597 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.47 (t, 3H, *J* = 6.8 Hz), 2.78 (d, 3H, *J* = 2.4 Hz), 3.73 (s, 3H), 3.80 (s, 3H), 4.09 (q, 2H, *J* = 6.8 Hz), 4.85 (d, 1H, *J* = 2.0 Hz, unresolved quatret), 5.38 (s, 1H), 6.08 (s, 1H), 6.77 (d, 1H, *J* = 8.4 Hz), 6.93 (d, 1H, *J* = 7.2 Hz), 7.19-7.26 (m, 1H)

^{13}C NMR (100 MHz) : δ 14.84, 15.80, 51.06, 52.15, 63.72, 110.25, 115.95, 124.53, 129.84, 130.78, 131.04, 139.19, 149.87, 154.53, 155.83, 165.81, 167.40

LCMS (m/z) : 315 $(M-H)^+$

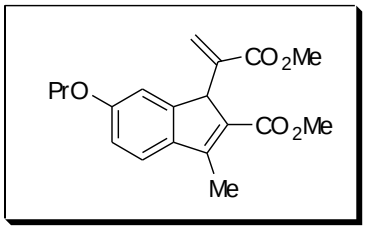
Anal calc'd for $C_{18}H_{20}O_5$: C, 68.34; H, 6.37

Found : C, 68.21; H, 6.25

Treatment of methyl 4-methoxycarbonyl-2-methylene-5-oxo-3-(3-propoxyphenyl)-hexanoate (92l) with $TiCl_4$:

Reaction of methyl 4-methoxycarbonyl-2-methylene-5-oxo-3-(3-propoxyphenyl)-hexanoate (**92l**) with $TiCl_4$ in dichloromethane following the similar procedure described for obtaining **93b** and ***ortho*-93b** (from **92b**), gave methyl 1-(1-methoxycarbonyl-ethenyl)-3-methyl-6-propoxy-1H-indene-2-carboxylate (**93l**) and methyl 1-(1-methoxycarbonylethenyl)-3-methyl-4-propoxy-1H-indene-2-carboxylate (***ortho*-93l**) in 75% and 19% isolated yields respectively.

Methyl 1-(1-methoxycarbonylethenyl)-3-methyl-6-propoxy-1H-indene-2-carboxylate (93l)



Reaction time : 1 h

Yield : 75% (0.247 g)

Color : pale yellow

Mp : 77-79 ^{0}C

IR (KBr) : ν 1722, 1685, 1602 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.03 (t, 3H, *J* = 7.2 Hz), 1.75-1.86 (m, 2H), 2.54 (d, 3H, *J* = 2.4 Hz), 3.74 (s, 3H), 3.81 (s, 3H), 3.92 (t, 2H, *J* = 6.4 Hz), 4.82-4.88 (m, 1H, multiplicity not resolved properly), 5.39 (s, 1H), 6.11 (s, 1H), 6.88 (dd, 1H, *J* = 2.0 Hz & 8.4 Hz), 6.92 (s, 1H, unresolved doublet), 7.36 (d, 1H, *J* = 8.4 Hz)

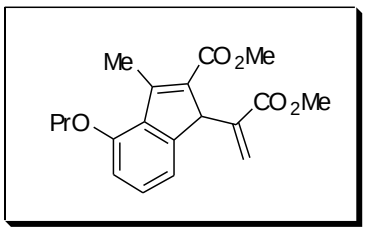
^{13}C NMR (100 MHz) : δ 10.53, 12.65, 22.58, 50.82, 51.03, 52.13, 69.73, 109.97, 113.58, 122.23, 124.65, 130.46, 136.47, 139.11, 149.64, 152.97, 160.30, 165.65, 167.36

LCMS (m/z) : 331 $(M+H)^+$

Anal calc'd for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71

Found : C, 69.18; H, 6.67

Methyl 1-(1-methoxycarbonylethenyl)-3-methyl-4-propoxy-1H-indene-2-carboxylate (*ortho*-93l)



Yield : 19% (0.062 g)

Color : pale yellow

Mp : 77-79 ^{0}C

IR (KBr) : ν 1718, 1697, 1597 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.09 (t, 3H, *J* = 7.2 Hz), 1.82-1.93 (m, 2H), 2.79 (d, 3H, *J* = 2.4 Hz), 3.73 (s, 3H), 3.80 (s, 3H), 3.99 (t, 2H, *J* = 6.4 Hz), 4.86 (d, 1H, *J* = 2.0 Hz, unresolved quatret) , 5.38 (s, 1H), 6.08 (s, 1H), 6.77 (d, 1H, *J* = 8.4 Hz), 6.92 (d, 1H, *J* = 7.2 Hz), 7.19-7.26 (m, 1H)

^{13}C NMR (100 MHz) : δ 10.88, 15.83, 22.67, 51.00, 51.14, 52.08, 69.65, 110.15, 115.89, 124.46, 129.82, 130.83, 131.07, 139.27, 149.89, 154.39, 156.00, 165.77, 167.37

LCMS (m/z) : 329 $(M-H)^+$

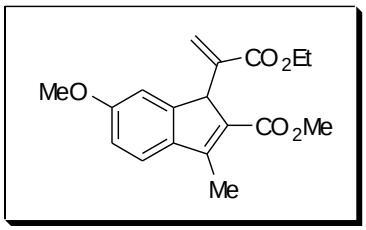
Anal calc'd for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71

Found : C, 68.95; H, 6.63

Treatment of ethyl 4-methoxycarbonyl-3-(3-methoxyphenyl)-2-methylene-5-oxohexanoate (92m) with $TiCl_4$:

Reaction of ethyl 4-methoxycarbonyl-3-(3-methoxyphenyl)-2-methylene-5-oxohexanoate (**92m**) with $TiCl_4$ in dichloromethane following the similar procedure described for obtaining **93b** and ***ortho*-93b** (from **92b**), furnished methyl 1-(1-ethoxy-carbonylethenyl)-6-methoxy-3-methyl-1H-indene-2-carboxylate (**93m**) and methyl 1-(1-ethoxycarbonylethenyl)-4-methoxy-3-methyl-1H-indene-2-carboxylate (***ortho*-93m**) in 75% and 17% isolated yields respectively.

Methyl 1-(1-ethoxycarbonylethenyl)-6-methoxy-3-methyl-1H-indene-2-carboxylate (93m)



Reaction time : 1 h

Yield : 75% (0.238 g)

Color : pale yellow

Mp : 60-62 ^{0}C

IR (KBr) : ν 1695, 1602 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.27 (t, 3H, *J* = 7.2 Hz), 2.54 (d, 3H, *J* = 2.0 Hz), 3.75 (s, 3H), 3.81 (s, 3H), 4.18-4.28 (m, 2H), 4.81-4.87 (m, 1H, multiplicity not resolved), 5.41 (s, 1H), 6.13 (s, 1H), 6.89 (dd, 1H, *J* = 2.0 Hz & 8.4 Hz), 6.94 (d, 1H, *J* = 1.6 Hz, not properly resolved), 7.37 (d, 1H, *J* = 8.4 Hz)

^{13}C NMR (100 MHz) : δ 12.59, 14.12, 51.00, 55.46, 60.87, 109.26, 113.18, 122.17, 124.65, 130.60, 136.71, 139.29, 149.64, 152.75, 160.68, 165.62, 166.81

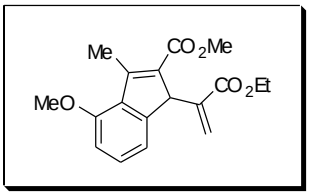
LCMS (m/z) : 315 $(M-H)^+$

Anal calc'd for $C_{18}H_{20}O_5$: C, 68.34; H, 6.37

Found : C, 68.26; H, 6.31

Methyl 1-(1-ethoxycarbonylethenyl)-4-methoxy-3-methyl-1H-indene-2-carboxylate (*ortho*-93m)

Yield : 17% (0.053 g)



Color : pale yellow

Mp : 44-45 ^{0}C

IR (KBr) : ν 1716, 1697, 1601 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.26 (t, 3H, *J* = 7.2 Hz), 2.76 (d, 3H, *J* = 2.4 Hz), 3.73 (s, 3H), 3.88 (s, 3H), 4.22 (q, 2H, *J* = 7.2 Hz), 4.83-4.89 (m, 1H, multiplicity not resolved), 5.40 (s, 1H), 6.11 (s, 1H), 6.80 (d, 1H, *J* = 8.0 Hz), 6.95 (d, 1H, *J* = 7.6 Hz), 7.22-7.30 (m, 1H)

^{13}C NMR (100 MHz) : δ 14.15, 15.76, 51.03, 51.27, 55.29, 60.89, 109.46, 116.09, 124.58, 129.80, 130.92, 131.15, 139.36, 149.88, 154.19, 156.42, 165.79, 166.85

LCMS (m/z) : 315 $(M-H)^+$

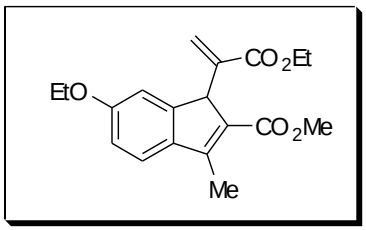
Anal calc'd for $C_{18}H_{20}O_5$: C, 68.34; H, 6.37

Found : C, 68.21; H, 6.38

Treatment of ethyl 3-(3-ethoxyphenyl)-4-methoxycarbonyl-2-methylene-5-oxohexanoate (92n) with $TiCl_4$:

Reaction of ethyl 3-(3-ethoxyphenyl)-4-methoxycarbonyl-2-methylene-5-oxohexanoate (**92n**) with $TiCl_4$ in dichloromethane following the similar procedure described for obtaining **93b** and ***ortho*-93b** (from **92b**), provided methyl 6-ethoxy-1-(1-ethoxycarbonyl-ethenyl)-3-methyl-1H-indene-2-carboxylate (**93n**) and methyl 4-ethoxy-1-(1-ethoxy-carbonylethenyl)-3-methyl-1H-indene-2-carboxylate (***ortho*-93n**) in 76% and 17% isolated yields respectively.

Methyl 6-ethoxy-1-(1-ethoxycarbonylethenyl)-3-methyl-1H-indene-2-carboxylate (93n)



Reaction time : 1 h

Yield : 76% (0.251 g)

Color : pale yellow

Mp : 58-59 ^{0}C

IR (KBr) : ν 1718, 1685, 1604 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.26 (t, 3H, *J* = 7.2 Hz), 1.40 (t, 3H, *J* = 6.8 Hz), 2.53 (d, 3H, *J* = 2.0 Hz), 3.74 (s, 3H), 4.03 (q, 2H, *J* = 6.8 Hz), 4.18-4.27 (m, 2H), 4.82 (d, 1H, *J* = 2.0 Hz, not resolved properly), 5.40 (s, 1H), 6.12 (s, 1H), 6.87 (dd, 1H, *J* = 2.4 Hz & 8.4 Hz), 6.92 (d, 1H, *J* = 2.0 Hz, not resolved properly), 7.36 (d, 1H, *J* = 8.4 Hz)

^{13}C NMR (100 MHz) : δ 12.61, 14.13, 14.79, 51.00, 60.86, 63.68, 109.85, 113.64, 122.18, 124.64, 130.53, 136.58, 139.34, 149.66, 152.83, 160.07, 165.66, 166.83

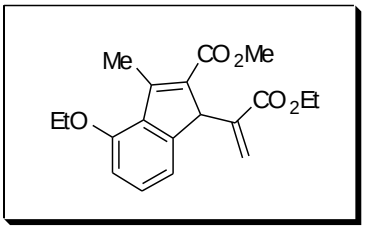
LCMS (m/z) : 331$(M+H)^+$

Anal calc'd for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71

Found : C, 69.25; H, 6.59

Methyl 4-ethoxy-1-(1-ethoxycarbonylethenyl)-3-methyl-1H-indene-2-carboxylate (*ortho*-93n)

Yield : 17**%** (0.054 g)



Color : pale yellow

Mp : 43-45 ^{0}C

IR (KBr) : ν 1712, 1630, 1597 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.27 (t, 3H, *J* = 7.2 Hz), 1.46 (t, 3H, *J* = 7.2 Hz), 2.78 (d, 3H, *J* = 2.4 Hz), 3.73 (s, 3H), 4.09 (q, 2H, *J* = 7.2 Hz), 4.22 (q, 2H, *J* = 7.2 Hz), 4.84 (d, 1H, *J* = 2.0 Hz, not resolved properly), 5.39 (s, 1H), 6.10 (s, 1H), 6.77 (d, 1H, *J* = 8.0 Hz), 6.93 (d, 1H, *J* = 7.6 Hz), 7.19-7.26 (m, 1H)

^{13}C NMR (100 MHz) : δ 14.18, 14.85, 15.77, 51.04, 51.22, 60.91, 63.74, 110.25, 115.96, 124.53, 129.79, 130.88, 131.15, 139.46, 149.92, 154.41, 155.83, 165.85, 166.91

LCMS (m/z) : 329 $(M-H)^+$

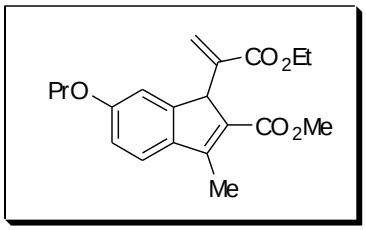
Anal calc'd for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71

Found : C, 69.21; H, 6.63

Reaction of ethyl 4-methoxycarbonyl-2-methylene-5-oxo-3-(3-propoxyphenyl)-hexanoate (92o) with $TiCl_4$:

Ethyl 4-methoxycarbonyl-2-methylene-5-oxo-3-(3-propoxyphenyl)hexanoate (**92o**) on treatment with $TiCl_4$ in dichloromethane following the similar procedure described for obtaining **93b** and ***ortho*-93b** (from **92b**), provided methyl 1-(1-ethoxycarbonylethenyl)-3-methyl-6-propoxy-1H-indene-2-carboxylate (**93o**) and methyl 1-(1-ethoxycarbonylethenyl)-3-methyl-4-propoxy-1H-indene-2-carboxylate (***ortho*-93o**) in 72% and 17% isolated yields respectively.

Methyl 1-(1-ethoxycarbonylethenyl)-3-methyl-6-propoxy-1H-indene-2-carboxylate (93o)



Reaction time : 1 h

Yield : 72% (0.249 g)

Color : pale yellow

Mp : 41-43 ^{0}C

IR (KBr) : ν 1716, 1685, 1601 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.03 (t, 3H, *J* = 7.2 Hz), 1.26 (t, 3H, *J* = 7.2 Hz), 1.75-1.86 (m, 2H), 2.53 (d, 3H, *J* = 2.0 Hz), 3.74 (s, 3H), 3.92 (t, 2H, *J* = 6.4 Hz), 4.18-4.28 (m, 2H), 4.82 (d, 1H, *J* = 2.0 Hz, not resolved properly), 5.40 (s, 1H), 6.12 (s, 1H), 6.88 (dd, 1H, *J* = 2.4 Hz & 8.4 Hz), 6.93 (d, 1H, *J* = 1.6 Hz, not resolved properly), 7.35 (d, 1H, *J* = 8.4 Hz)

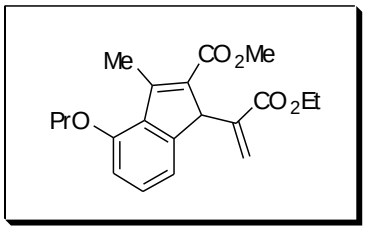
^{13}C NMR (100 MHz) : δ 10.52, 12.63, 14.14, 22.59, 51.01, 60.89, 69.75, 109.90, 113.68, 122.17, 124.67, 130.52, 136.55, 139.37, 149.66, 152.87, 160.30, 165.69, 166.87

LCMS (m/z) : 345 $(M+H)^+$

Anal calc'd for $C_{20}H_{24}O_5$: C, 69.75; H, 7.02

Found : C, 69.71; H, 7.18

Methyl 1-(1-ethoxycarbonylethenyl)-3-methyl-4-propoxy-1H-indene-2-carboxylate (*ortho*-93o)



Yield : 17% (0.057 g)

Color : pale yellow

Mp : 50-51 ^{0}C

IR (KBr) : ν 1714, 1695, 1599 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.09 (t, 3H, *J* = 7.2 Hz), 1.27 (t, 3H, *J* = 7.2 Hz), 1.81-1.93 (m, 2H), 2.79 (d, 3H, *J* = 2.0 Hz), 3.73 (s, 3H), 3.99 (t, 2H, *J* = 6.4 Hz), 4.22 (q, 2H, *J* = 6.8 Hz), 4.85 (s, 1H), 5.39 (s, 1H), 6.11 (s, 1H), 6.77 (d, 1H, *J* = 8.4 Hz), 6.93 (d, 1H, *J* = 7.2 Hz), 7.19-7.26 (m, 1H)

^{13}C NMR (100 MHz) : δ 10.85, 14.11, 15.78, 22.61, 50.95, 51.22, 60.83, 69.56, 110.03, 115.82, 124.46, 129.75, 130.79, 131.05, 139.42, 149.84, 154.29, 155.92, 165.76, 166.83

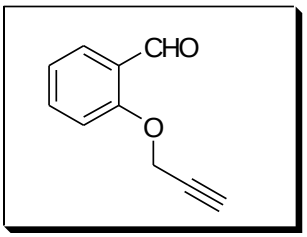
LCMS (m/z) : 345 $(M+H)^+$

Anal calc'd for $C_{20}H_{24}O_5$: C, 69.75; H, 7.02

Found : C, 69.82; H, 6.91

2-(Prop-2-ynyloxy)benzaldehyde (107a)

To a solution of 2-hydroxybenzaldehyde (12.21 g, 100 mmol) and K_2CO_3 (27.64 g, 200 mmol) in DMSO (50 mL), propargyl bromide (17.84 g, 150 mmol, 80% in toluene) was added. After stirring for 1 hour at room temperature, the reaction mixture was diluted with ethyl acetate (150 mL) and washed with water (3X50 mL) to remove DMSO and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the residue thus obtained was purified by column chromatography (10% ethyl acetate in hexanes) on silica gel to afford 14.78 g (92%) of the title compound as a pale yellow solid.



Reaction time : 1 h

Yield : 92%

Mp : 67-69 ^{o}C

IR (KBr) : ν 3271, 2874, 2116, 1684, 1599 cm^{-1}

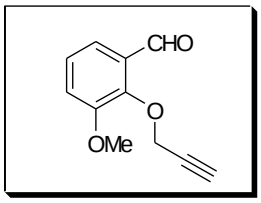
^{1}H NMR (400 MHz) : δ 2.57 (t, 1H, *J* = 2.4 Hz), 4.83 (d, 2H, *J* = 2.4 Hz), 7.06-7.16 (m, 2H), 7.54-7.62 (m, 1H), 7.86 (dd, 1H, *J* = 1.6 Hz & 7.6), 10.48 (s, 1H)

^{13}C NMR (100 MHz) : δ 56.23, 76.50, 77.61, 113.11, 121.48, 125.25, 128.29, 135.62, 159.60, 189.28

3-Methoxy-2-(prop-2-ynyloxy)benzaldehyde (107b)

This was obtained as a pale yellow solid *via* the treatment of 3-methoxy-2-hydroxybenzaldehyde with propargyl bromide in the presence of K_2CO_3 in DMSO following similar procedure described for the molecule **107a**.

Reaction time : 1 h



Yield : 95%

Mp : 46-48 ^{o}C

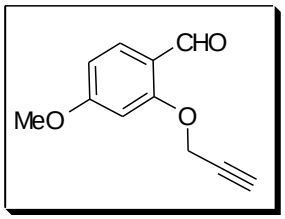
IR (KBr) : ν 3269, 2945, 2119, 1687, 1583 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.48 (t, 1H, *J* = 2.4 Hz), 3.91 (s, 3H), 4.88 (d, 2H, *J* = 2.4), 7.14-7.23 (m, 2H), 7.46 (dd, 1H, *J* = 2.0 Hz & 7.2 Hz), 10.50 (s, 1H)

^{13}C NMR (100 MHz) : δ 55.67, 60.49, 76.80, 78.10, 117.56, 118.34, 124.61, 130.71, 149.14, 152.54, 190.13

4-Methoxy-2-(prop-2-ynyloxy)benzaldehyde (107c)

Treatment of 4-methoxy-2-hydroxybenzaldehyde with propargyl bromide in presence of K_2CO_3 in DMSO, following the similar procedure described for the molecule **107a**, provided the title compound as a pale yellow solid.



Reaction time : 1 h

Yield : 85%

Mp : 84-86 ^{0}C

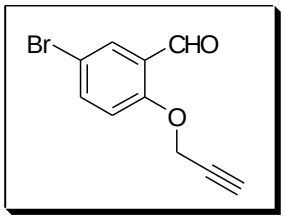
IR (KBr) : ν 3232, 2961, 2125, 1672, 1604 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.58 (t, 1H, *J* = 2.4 Hz), 3.88 (s, 3H), 4.80 (d, 2H, *J* = 2.4 Hz), 6.58-6.63 (m, 2H), 7.84 (d, 1H, *J* = 9.2 Hz), 10.30 (s, 1H)

^{13}C NMR (100 MHz) : δ 55.59, 56.26, 76.61, 77.52, 99.26, 106.81, 119.30, 130.42, 161.39, 165.82, 187.92

5-Bromo-2-(prop-2-ynyloxy)benzaldehyde (107d)

This was obtained as a pale yellow solid *via* the treatment of 5-bromo-2-hydroxy benzaldehyde with propargyl bromide in presence of K_2CO_3 in DMSO following similar procedure described for the molecule **107a**.



Reaction time : 1 h

Yield : 83%

Mp : 94-96 ^{o}C

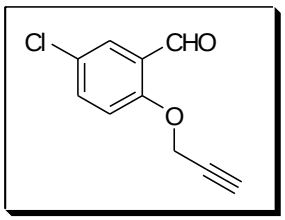
IR (KBr) : ν 3285, 2872, 2119, 1684, 1589 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.58 (t, 1H, *J* = 2.0 Hz), 4.82 (d, 2H, *J* = 2.0 Hz), 7.03 (d, 1H, *J* = 8.8 Hz), 7.65 (dd, 1H, *J* = 2.4 Hz & 8.8 Hz), 7.95 (d, 1H, *J* = 2.4 Hz), 10.39 (s, 1H)

^{13}C NMR (100 MHz) : δ 56.67, 77.04, 77.19, 114.52, 115.36, 126.71, 131.04, 138.06, 158.58, 188.03

5-Chloro-2-(prop-2-ynyloxy)benzaldehyde (107e)

Reaction of 5-chloro-2-hydroxybenzaldehyde with propargyl bromide in presence of K_2CO_3 in DMSO, following the similar procedure described for the molecule **107a**, provided the title compound as a pale yellow solid.



Reaction time : 1 h

Yield : 80%

Mp : 69-70 ^{0}C

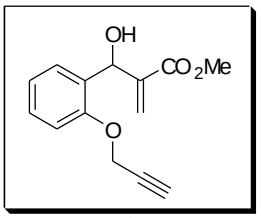
IR (KBr) : ν 3244, 2878, 2118, 1674, 1595 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.58 (t, 1H, *J* = 2.4 Hz), 4.83 (d, 2H, *J* = 2.4 Hz), 7.09 (d, 1H, *J* = 8.8 Hz), 7.51 (dd, 1H, *J* = 2.8 Hz & 8.8 Hz), 7.81 (d, 1H, *J* = 2.8 Hz), 10.41 (s, 1H)

^{13}C NMR (100 MHz) : δ 56.76, 77.00, 77.24, 115.02, 126.37, 127.39, 128.03, 135.20, 158.14, 188.17

Methyl 3-hydroxy-2-methylene-3-[2-(prop-2-ynyloxy)phenyl]propanoate (117a)

To a solution of 2-(prop-2-ynyloxy)benzaldehyde (**107a**) (20 mmol, 3.20 g) in methyl acrylate (30 mmol, 2.58 g) was added DABCO (10 mmol, 1.12 g) at room temperature. Then silica gel (>200 mesh) was added and throughly mixed. After keeping the resulting solid at room temperature for 7 days, the reaction mixture was washed with ethyl acetate (3X20 mL). Combined organic layer was washed successively, with 2N HCl (15 mL), saturated $NaHCO_3$ solution (15 mL), water (15 mL) and then dried over anhydrous Na_2SO_4. Solvent was evaporated and the crude thus obtained was purified by column chromatography to provide the title compound as a pale yellow viscous liquid in 70% (3.44 g) isolated yield.



Reaction time : 7 days

Yield : 70%

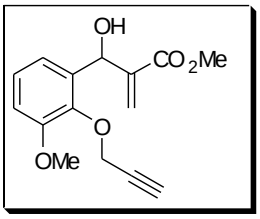
IR (neat) : ν 3466, 3287, 2953, 2121, 1712, 1631 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.50 (t, 1H, *J* = 2.4 Hz), 3.35 (d, 1H, *J* = 6.4 Hz), 3.74, (s, 3H), 4.71 (d, 2H, *J* = 2.4 Hz), 5.75 (s, 1H), 5.89 (d, 1H, *J* = 6.0 Hz), 6.31 (s, 1H), 6.96-7.06 (m, 2H), 7.27-7.31 (m, 1H), 7.41 (d, 1H, *J* = 7.6 Hz)

^{13}C NMR (100 MHz) : δ 51.67, 55.87, 67.32, 75.61, 78.35, 112.04, 121.44, 125.77, 127.59, 128.55, 129.94, 141.24, 154.42, 166.81

Methyl 3-hydroxy-3-[3-methoxy-2-(prop-2-ynyloxy)phenyl]-2-methylenepropanoate (117b)

This compound was obtained as a colorless viscous liquid by the Baylis-Hillman reaction of 3-methoxy-2-(prop-2-ynyloxy)benzaldehyde (**107b**) with methyl acrylate in presence of DABCO as a catalyst, following similar procedure described for the molecule **117a**.



Reaction time : 14 days

Yield : 57%

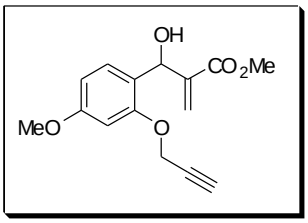
IR (neat) : ν 3489, 3287, 2951, 2123, 1716, 1631 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.51 (t, 1H, *J* = 2.4 Hz), 3.22 (d, 1H, *J* = 5.2 Hz), 3.72 (s, 3H), 3.86 (s, 3H), 4.74 & 4.82 (dABq, 2H, *J* = 2.4 Hz & 15.2 Hz**),** 5.86-5.89 (m, 1H), 6.01 (d, 1H, *J* = 5.6 Hz), 6.36 (s, 1H), 6.87 (dd, 1H, *J* = 1.6 Hz & 8.0 Hz), 6.97 (dd, 1H, *J* = 1.6 Hz & 8.0 Hz), 7.05-7.12 (m, 1H)

^{13}C NMR (100 MHz) : δ 51.83, 55.74, 59.91, 67.63, 75.45, 79.55, 111.93, 119.33, 124.64, 126.00, 135.58, 141.40, 144.01, 152.25, 166.80

Methyl 3-hydroxy-3-[4-methoxy-2-(prop-2-ynyloxy)phenyl]-2-methylenepropanoate (117c)

This molecule was obtained as a colorless viscous liquid *via* the Baylis–Hillman reaction of 4-methoxy-2-(prop-2-ynyloxy)benzaldehyde (**107c**) with methyl acrylate in the presence of DABCO (1 eq.) in silica gel solid phase medium, following a similar procedure described for the molecule **117a**.



Reaction time : 20 days

Yield : 27%

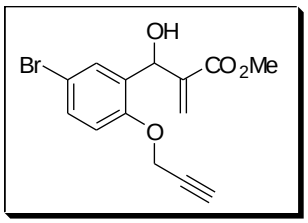
IR (neat) : ν 3493, 3287, 2953, 2121, 1722, 1612 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.52 (t, 1H, *J* = 2.4 Hz), 3.25 (d, 1H, *J* = 6.0 Hz), 3.73 (s, 3H), 3.80 (s, 3H), 4.69 (d, 2H, *J* = 2.4 Hz), 5.78 (s, 1H), 5.82 (d, 1H, *J* = 6.0 Hz), 6.31 (s, 1H), 6.53 (dd, 1H, *J* = 2.4 Hz & 8.8 Hz), 6.57 (d, 1H, *J* = 2.4 Hz), 7.27 (d, 1H, *J* = 8.8 Hz)

^{13}C NMR (100 MHz) : δ 51.76, 55.26, 56.05, 67.32, 75.80, 78.27, 99.96, 105.38, 122.43, 125.56, 128.41, 141.43, 155.59, 160.15, 166.95

Methyl 3-[5-bromo-2-(prop-2-ynyloxy)phenyl]-3-hydroxy-2-methylenepropanoate (117d)

This compound was prepared as a pale yellow viscous liquid *via* DABCO catalyzed Baylis–Hillman reaction of 5-bromo-2-(prop-2-ynyloxy)benzaldehyde (**107d**) with methyl acrylate following a similar procedure described for the molecule **117a**.



Reaction time : 14 days

Yield : 83%

IR (neat) : ν 3466, 3292, 2953, 2121, 1716, 1631 cm^{-1}

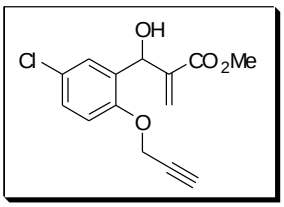
^{1}H NMR (400 MHz) : δ 2.50 (t, 1H, *J* = 2.4 Hz), 3.33 (d, 1H, *J* = 5.6 Hz), 3.77 (s, 3H), 4.69 (d, 2H, *J* = 2.4 Hz), 5.70 (s, 1H), 5.85 (d,

1H, *J* = 5.6 Hz), 6.32 (s, 1H), 6.87 (d, 1H, *J* = 8.8 Hz), 7.38 (dd, 1H, *J* = 2.4 Hz & 8.8 Hz), 7.55 (d, 1H, *J* = 2.4 Hz)

^{13}C NMR (100 MHz) : δ 52.05, 56.25, 67.23, 76.10, 77.94, 113.94, 114.25, 126.62, 130.67, 131.42, 132.25, 140.59, 153.50, 166.89

Methyl 3-[5-chloro-2-(prop-2-ynyloxy)phenyl]-3-hydroxy-2-methylenepropanoate (117e)

This molecule was obtained as a pale yellow viscous liquid *via* the Baylis–Hillman reaction of 5-chloro-2-(prop-2-ynyloxy)benzaldehyde (**107e**) with methyl acrylate in the presence of DABCO (cat.) in silica gel solid phase medium, following a similar procedure described for the molecule **117a**.



Reaction time : 14 days

Yield : 65%

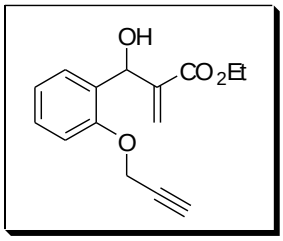
IR (neat) : ν 3470, 3294, 2953, 2121, 1718, 1631 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.50 (t, 1H, *J* = 2.4 Hz), 3.34 (d, 1H, *J* = 5.6 Hz), 3.76 (s, 3H), 4.69 (d, 2H, *J* = 2.4 Hz), 5.71 (s, 1H), 5.85 (d, 1H, *J* = 5.6 Hz), 6.32 (s, 1H), 6.92 (d, 1H, *J* = 8.8 Hz), 7.23 (dd, 1H, *J* = 2.8 Hz & 8.8 Hz), 7.41 (d, 1H, *J* = 2.8 Hz)

^{13}C NMR (100 MHz) : δ 52.00, 56.32, 67.20, 76.04, 78.00, 113.50, 126.55, 126.79, 127.78, 128.40, 131.91, 140.63, 152.99, 166.87

Ethyl 3-hydroxy-2-methylene-3-[2-(prop-2-ynyloxy)phenyl]propanoate (117f)

This was obtained *via* the DABCO catalyzed coupling of 2-(prop-2-ynyloxy)-benzaldehyde (**107a**) with ethyl acrylate, following a similar procedure described for the molecule **117a** as a pale yellow viscous liquid.



Reaction time : 7 days

Yield : 81%

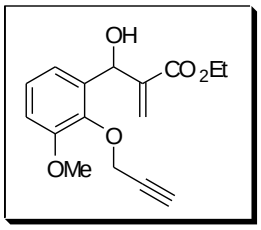
IR (neat) : ν 3468, 3288, 2984, 2121, 1712, 1631 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.25 (t, 3H, *J* = 7.2 Hz), 2.50 (t, 1H, *J* = 2.4 Hz), 3.40 (d, 1H, *J* = 6.4 Hz), 4.19 (q, 2H, *J* = 7.2 Hz), 4.71 (d, 2H, *J* = 2.4 Hz), 5.74 (s, 1H), 5.89 (d, 1H, *J* = 6.0 Hz), 6.31 (s, 1H), 6.96-7.05 (m, 2H), 7.24-7.31 (m, 1H), 7.41 (dd, 1H, *J* = 1.2 Hz & 7.6 Hz)

^{13}C NMR (100 MHz) : δ 13.95, 55.99, 60.71, 67.66, 75.63, 78.41, 112.10, 121.56, 125.60, 127.76, 128.64, 130.06, 141.48, 154.56, 166.51

Ethyl 3-hydroxy-3-[3-methoxy-2-(prop-2-ynyloxy)phenyl]-2-methylenepropanoate (117g)

This was obtained as a pale yellow viscous liquid *via* DABCO catalyzed coupling of 3-methoxy-2-(prop-2-ynyloxy)benzaldehyde (**107b**) with ethyl acrylate following the similar procedure described for the molecule **117a**.



Reaction time : 14 days

Yield : 71%

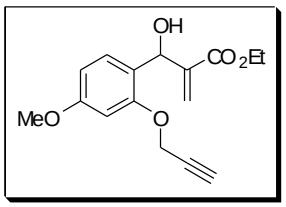
IR (neat) : ν 3489, 3287, 2939, 2119, 1714, 1631 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.23 (t, 3H, *J* = 7.2 Hz), 2.51 (t, 1H, *J* = 2.4 Hz), 3.27 (d, 1H, *J* = 5.2 Hz), 3.86 (s, 3H), 4.13-4.22 (m, 2H), 4.74 & 4.82 **(**dABq, 2H, *J* = 2.4 Hz & 15.6 Hz**),** 5.84 (s, 1H), 6.01 (d, 1H, *J* = 5.2 Hz), 6.35 (s, 1H), 6.87 (d, 1H, *J* = 8.0 Hz), 6.98 (d, 1H, *J* = 7.6 Hz), 7.05-7.11 (m, 1H)

^{13}C NMR (100 MHz) : δ 14.01, 55.73, 59.89, 60.71, 67.65, 75.42, 79.56, 111.88, 119.36, 124.58, 125.66, 135.67, 141.66, 144.01, 152.22, 166.35

Ethyl 3-hydroxy-3-[4-methoxy-2-(prop-2-ynyloxy)phenyl]-2-methylenepropanoate (117h)

This compound was obtained as a pale yellow viscous liquid *via* the treatment of 4-methoxy-2-(prop-2-ynyloxy)benzaldehyde (**107c**) with ethyl acrylate under the influence of DABCO (1 eq.) in silica gel solid phase medium, following a similar procedure described for the molecule **117a**.



Reaction time : 20 days

Yield : 36%

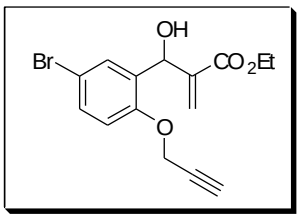
IR (neat) : ν 3477, 3287, 2982, 2121, 1711, 1612cm^{-1}

^{1}H NMR (400 MHz) : δ 1.25 (t, 3H, *J* = 7.2 Hz), 2.51 (t, 1H, *J* = 2.4 Hz), 3.24 (b s, 1H), 3.80 (s, 3H), 4.18 (q, 2H, *J* = 7.2 Hz), 4.69 (d, 2H, *J* = 2.4), 5.76 (s, 1H), 5.82 (s, 1H), 6.31 (s, 1H), 6.53 (dd, 1H, *J* = 2.4 Hz & 8.4 Hz), 6.57 (d, 1H, *J* = 2.4 Hz), 7.28 (d, 1H, *J* = 8.4 Hz)

^{13}C NMR (100 MHz) : δ 13.96, 55.24, 56.05, 60.65, 67.28, 75.78, 78.29, 99.90, 105.35, 122.52, 125.20, 128.43, 141.71, 155.59, 160.11, 166.51

Ethyl 3-[5-bromo-2-(prop-2-ynyloxy)phenyl]-3-hydroxy-2-methylenepropanoate (117i)

This Baylis-Hillman alcohol was prepared as a pale yellow viscous liquid *via* the treatment of of 5-bromo-2-(prop-2-ynyloxy)benzaldehyde (**107d**) with ethyl acrylate under the catalytical influence of DABCO following similar procedure described for molecule **117a**.



Reaction time : 14 days

Yield : 87%

IR (neat) : ν 3460, 3294, 2982, 2121, 1709, 1630 cm^{-1}

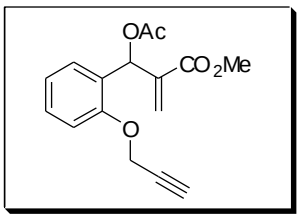
^{1}H NMR (400 MHz) : δ 1.28 (t, 3H, *J* = 7.2 Hz), 2.50 (t, 1H, *J* = 2.4 Hz), 3.37 (d, 1H, *J* = 6.0 Hz), 4.22 (q, 2H, *J* = 7.2 Hz), 4.69 (d, 2H, *J* = 2.4 Hz), 5.70 (s, 1H), 5.84 (d, 1H, *J* = 6.0 Hz), 6.32 (s, 1H), 6.87 (d, 1H, *J* = 8.8 Hz), 7.38 (dd, 1H, *J* = 2.4 Hz & 8.8 Hz), 7.56 (d, 1H, *J* = 2.4 Hz)

^{13}C NMR (100 MHz) : δ 14.08, 56.26, 61.03, 67.36, 76.09, 77.95, 113.92, 114.22, 126.33, 130.76, 131.38, 132.33, 140.82, 153.54, 166.45

Methyl 3-acetoxy-2-methylene-3-[2-(prop-2-ynyloxy)phenyl]propanoate (116a)

To a stirred solution of methyl 3-hydroxy-2-methylene-3-[2-(prop-2-ynyloxy)-phenyl]propanoate (**117a**) (10 mmol, 2.46 g) in dichloromethane (10 mL) was added

pyridine (20 mmol, 1.58 g) followed by acetyl chloride (20 mmol, 1.57 g) at 0 ^{o}C. After stirring at room temperature for 2 h, reaction mixture was diluted with diethyl ether (20 mL) and 2N HCl (15 mL). Organic layer was separated and was washed successively with saturated aq. $NaHCO_3$ solution, water and dried over anhydrous Na_2SO_4. Crude product thus obtained after solvent evaporation, was purified by column chromatography (5% EtOAc in hexanes) to provide the desired product as a colorless viscous liquid in 85% (2.46 g) isolated yield.



Reaction time : 2 h

Yield : 85%

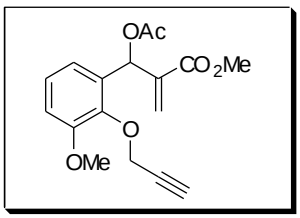
IR (neat) : ν 3287, 2955, 2121, 1739, 1728, 1635 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.10 (s, 3H), 2.47 (t, 1H, *J* = 2.4 Hz), 3.73 (s, 3H), 4.72 (d, 2H, *J* = 2.4 Hz), 5.67 (s, 1H), 6.41 (s, 1H), 6.97-7.06 (m, 3H), 7.27-7.34 (m, 2H)

^{13}C NMR (100 MHz) : δ 20.86, 51.84, 55.99, 67.89, 75.51, 78.37, 112.40, 121.30, 126.63, 127.10, 127.77, 129.34, 138.80, 154.81, 165.52, 169.25

Methyl 3-acetoxy-3-[3-methoxy-2-(prop-2-ynyloxy)phenyl]-2-methylenepropano-ate (116b)

This was prepared as a pale yellow viscous liquid *via* the treatment of methyl 3-hydroxy-3-[3-methoxy-2-(prop-2-ynyloxy)phenyl]-2-methylenepropanoate (**117b**) with acetyl chloride in presence of pyridine following the similar procedure described for molecule **116a**.



Reaction time : 2 h

Yield : 90%

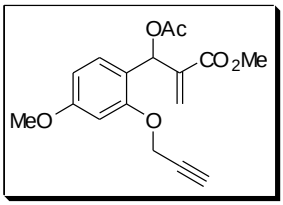
IR (neat) : ν 3288, 2951, 2125, 1736, 1720, 1635 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.10 (s, 3H), 2.49 (t, 1H, *J* = 2.4 Hz), 3.72 (s, 3H), 3.86 (s, 3H), 4.74 &4.81 (dABq, 2H, *J* = 2.4 Hz & 15.2 Hz**)**, 5.69 (d, 1H, *J* = 0.8 Hz), 6.41 (s, 1H), 6.87-6.92 (m, 2H), 7.03-7.10 (m, 2H)

^{13}C NMR (100 MHz) : δ 20.91, 51.81, 55.68, 59.88, 68.43, 75.13, 79.14, 112.46, 119.49, 124.33, 127.07, 131.81, 138.90, 144.54, 152.44, 165.41, 169.16

Methyl 3-acetoxy-3-[4-methoxy-2-(prop-2-ynyloxy)phenyl]-2-methylenepropano-ate (116c)

Acetylation of Baylis-Hillman alcohol, methyl 3-hydroxy-3-[4-methoxy-2-(prop-2-ynyloxy)phenyl]-2-methylenepropanoate (**117c**), with acetyl chloride in the presence of pyridine following the similar procedure described for molecule **116a** provided the title compound as a pale yellow viscous liquid.



Reaction time : 2 h

Yield : 85**%**

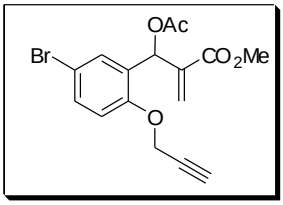
IR (neat) : ν 3285, 2955, 2121, 1739, 1728, 1614 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.08 (s, 3H), 2.49 (t, 1H, *J* = 2.0 Hz.), 3.71 (s, 3H), 3.80 (s, 3H), 4.70 (s, 2H, *J* = 2.0 Hz), 5.71 (d, 1H, *J* = 0.8 Hz), 6.40 (s, 1H), 6.51 (dd, 1H, *J* = 2.0 Hz & 8.4 Hz), 6.60 (d, 1H, *J* = 2.0 Hz), 6.96 (s, 1H), 7.17 (d, 1H, *J* = 8.4 Hz)

^{13}C NMR (100 MHz) : δ 20.87, 51.80, 55.24, 56.10, 67.80, 75.65, 78.28, 100.11, 105.41, 118.92, 126.39, 128.80, 138.99, 156.04, 160.76, 165.55, 169.32

Methyl 3-acetoxy-3-[5-bromo-2-(prop-2-ynyloxy)phenyl]-2-methylenepropanoate (116d)

This was prepared as a pale yellow viscous liquid *via* the treatment of methyl 3-[5-bromo-2-(prop-2-ynyloxy)phenyl]-3-hydroxy-2-methylenepropanoate (**117d**) with acetyl chloride in presence of pyridine following the similar procedure described for molecule **116a**.



Reaction time : 2 h

Yield : 90%

IR (neat) : ν 3292, 2953, 2123, 1743, 1732, 1635 cm^{-1}

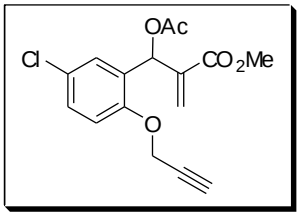
^{1}H NMR (400 MHz) : δ 2.11 (s, 3H), 2.49 (s, 1H), 3.74 (s, 3H), 4.71 (s, 2H), 5.68 (s, 1H), 6.42 (s, 1H), 6.91 (d, 1H, *J* = 8.4 Hz), 6.97 (s, 1H), 7.36-7.44 (m, 2H)

^{13}C NMR (100 MHz) : δ 20.93, 52.01, 56.33, 67.34, 76.01, 77.92, 113.83, 114.33, 127.62, 129.11, 130.69, 132.07, 138.34, 153.87, 165.32, 169.20

Methyl 3-acetoxy-3-[5-chloro-2-(prop-2-ynyloxy)phenyl]-2-methylenepropanoate (116e)

Treatment of methyl 3-[5-chloro-2-(prop-2-ynyloxy)phenyl]-3-hydroxy-2-methylene-propanoate (**117e**) with acetyl chloride in the presence of pyridine following the similar

procedure described for the molecule **116a** provided the title compound as a colorless viscous liquid.



Reaction time : 2 h

Yield : 91%

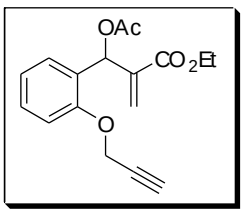
IR (neat) : ν 3292, 2953, 2123, 1743, 1728, 1635 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.11 (s, 3H), 2.49 (s, 1H), 3.74 (s, 3H), 4.71 (s, 2H), 5.68 (s, 1H), 6.42 (s, 1H), 6.94-7.00 (m, 2H), 7.23-7.29 (m, 2H)

^{13}C NMR (100 MHz) : δ 20.94, 52.04, 56.43, 67.44, 75.97, 77.99, 113.91, 126.54, 127.65, 127.86, 128.74, 129.11, 138.37, 153.39, 165.38, 169.25

Ethyl 3-acetoxy-2-methylene-3-[2-(prop-2-ynyloxy)phenyl]propanoate (116f)

This compound was prepared as a pale yellow viscous liquid *via* the reaction of ethyl 3-hydroxy-2-methylene-3-[2-(prop-2-ynyloxy)phenyl]propanoate (**117f**) with acetyl chloride, in the presence of pyridine, following a similar procedure described for the molecule **116a**.



Reaction time : 2 h

Yield : 88%

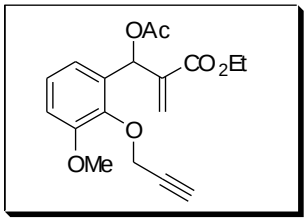
IR (neat) : ν 3287, 2984, 2121, 1743, 1720, 1637 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.23 (t, 3H, *J* = 7.2 Hz), 2.10 (s, 3H), 2.47 (s, 1H), 4.18 (q, 2H, *J* = 7.2 Hz), 4.72 (s, 2H), 5.63 (s, 1H), 6.40 (s, 1H), 6.93-7.07 (m, 3H), 7.22-7.34 (m, 2H)

^{13}C NMR (100 MHz) : δ 13.97, 20.93, 56.07, 60.77, 67.98, 75.52, 78.44, 112.43, 121.34, 126.77, 126.82, 127.91, 129.34, 139.13, 154.88, 165.14, 169.30

Ethyl 3-acetoxy-3-[3-methoxy-2-(prop-2-ynyloxy)phenyl]-2-methylenepropanoate (116g)

Treatment of ethyl 3-hydroxy-3-[3-methoxy-2-(prop-2-ynyloxy)phenyl]-2-methylene-propanoate (**117g**) with acetyl chloride in the presence of pyridine following the similar procedure described for the molecule **116a** provided the title compound as a pale yellow viscous liquid.



Reaction time : 2 h

Yield : 87%

IR (neat) : ν 3285, 2982, 2945, 2125, 1743, 1722, 1637 cm^{-1}

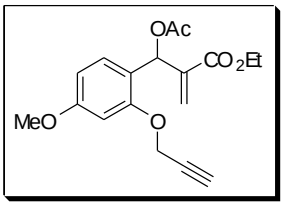
^{1}H NMR (400 MHz) : δ 1.23 (t, 3H, *J* = 7.2 Hz), 2.10 (s, 3H), 2.48 (t, 1H, *J* = 2.4 Hz), 3.86 (s, 3H), 4.18 (q, 2H, *J* = 7.2 Hz), 4.74 & 4.81 (dABq, 2H, *J* = 2.4 Hz & 15.2 Hz), 5.66 (s, 1H), 6.41 (s, 1H), 6.87-9.93 (m, 2H), 7.03-7.10 (m, 2H)

^{13}C NMR (100 MHz) : δ 14.09, 21.10, 55.83, 60.05, 60.86, 68.67, 75.16, 79.31, 112.51, 119.72, 124.45, 127.04, 132.09, 139.27, 144.70, 152.57, 165.14, 169.34

Ethyl 3-acetoxy-3-[4-methoxy-2-(prop-2-ynyloxy)phenyl]-2-methylenepropanoate (116h)

This compound was obtained as a pale yellow viscous liquid *via* the treatment of ethyl 3-hydroxy-3-[4-methoxy-2-(prop-2-ynyloxy)phenyl]-2-methylenepropanoate (**117h**)

with acetyl chloride, in the presence of pyridine, following a similar procedure described for the molecule **116a**.



Reaction time : 2 h

Yield : 87%

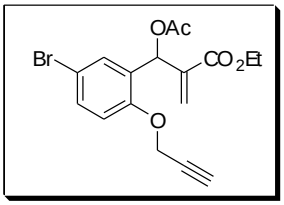
IR (neat) : ν 3283, 2982, 2123, 1743, 1724, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.22 (t, 3H, *J* = 7.2 Hz), 2.08 (s, 3H), 2.49 (t, 1H, *J* = 2.4 Hz), 3.80 (s, 3H), 4.16 (q, 2H, *J* = 7.2 Hz), 4.70 (d, 2H, *J* = 1.2 Hz), 5.67 (s, 1H), 6.39 (s, 1H), 6.51 (dd, 1H, *J* = 2.4 Hz & 8.4 Hz), 6.61 (d, 1H, *J* = 2.4 Hz), 6.96 (s, 1H), 7.17 (d, 1H, *J* = 8.4 Hz)

^{13}C NMR (100 MHz) : δ 13.89, 20.84, 55.19, 56.06, 60.64, 67.77, 75.64, 78.26, 100.01, 105.36, 118.95, 126.00, 128.81, 139.25, 156.00, 160.69, 165.05, 169.24

Ethyl 3-acetoxy-3-[5-bromo-2-(prop-2-ynyloxy)phenyl]-2-methylenepropanoate (116i)

Treatment of ethyl 3-[5-bromo-2-(prop-2-ynyloxy)phenyl]-3-hydroxy-2-methylene-propanoate (**117i**) with acetyl chloride in the presence of pyridine following the similar procedure described for the molecule **116a** provided the title compound as a pale yellow viscous liquid.



Reaction time : 2 h

Yield : 92%

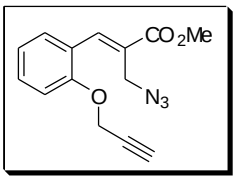
IR (neat) : ν 3292, 2984, 2123, 1745, 1722, 1635 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.25 (t, 3H, *J* = 7.2 Hz), 2.11 (s, 3H), 2.49 (t, 1H, *J* = 1.6 Hz), 4.19 (q, 2H, *J* = 7.2 Hz), 4.71 (d, 2H, *J* = 1.6 Hz), 5.66 (s, 1H), 6.42 (s, 1H), 6.91 (d, 1H, *J* = 8.4 Hz), 6.97 (s, 1H), 7.37-7.44 (m, 2H)

^{13}C NMR (100 MHz) : δ 14.03, 20.95, 56.36, 60.95, 67.44, 76.01, 77.94, 113.82, 114.31, 127.37, 129.19, 130.81, 132.04, 138.59, 153.91, 164.90, 169.20

Methyl 2-(azidomethyl)-3-[2-(prop-2-ynyloxy)phenyl]propenoate (115a)

To the stirred solution of methyl 3-acetoxy-2-methylene-3-[2-(prop-2-ynyloxy)phenyl]-propanoate (**116a**) (5 mmol, 1.44 g) in DMSO (10 mL) was added sodium azide (7.5 mmol, 0.48 g) and stirred for 3 h at room temperature. Then the reaction mixture was diluted with ethyl acetate (50 mL) and washed with water (3X10 mL) (to remove of the DMSO) and dried over anhydrous Na_2SO_4. The solvent was removed in vacuo. Residue[#] thus obtained was purified by column chromatography (10% ethyl acetate in hexanes) on silica gel to afford 83% (1.130 g) of the title compound as a colorless viscous liquid.



Reaction time : 3 h

Yield : 83%

IR (neat) : ν 3292, 2951, 2094, 1714, 1633 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.52 (t, 1H, *J* = 2.4 Hz), 3.88 (s, 3H), 4.14 (s, 2H), 4.76 (d, 2H, *J* = 2.4 Hz), 7.02-7.11 (m, 2H), 7.35-7.43 (m, 2H), 8.11 (s, 1H)

Residue was subjected to next step without purification (Method B, Page No. 171)

^{13}C NMR (100 MHz) : δ 47.48, 52.33, 56.04, 76.08, 78.12, 112.26, 121.50, 123.81, 126.84, 130.35, 131.02, 140.27, 155.66, 167.45

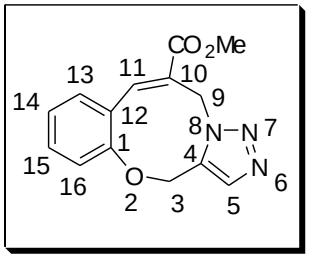
LCMS (m/z) : 272 $(M+H)^+$

Anal calc'd for $C_{14}H_{13}N_3O_3$: C, 61.99; H, 4.83; N, 15.49

Found : C, 61.85; H, 4.78; N, 15.38

10-Methoxycarbonyl-2-oxa-6,7,8-triazatricyclo[10,4,0,0^{4,8}]hexadeca-4,6,10,12,14,16(1)-hexaene (114a)

Method A: A stirred solution of methyl 2-(azidomethyl)-3-[2-(prop-2-ynyloxy)phenyl]propenoate (**115a**) (1 mmol, 0.271 g) in toluene (2 ml) was heated under reflux for 4 hour (reaction was monitered by TLC) and reaction mixture was cooled to room temperature. Solvent was removed in vacuo and purification of the residue by column chromatography (60% ethyl acetate in hexanes) on silica gel afforded 0.215 g (79%) of the title compound as a white solid.



Reaction time : 4 h

Yield : 79%

Mp : 148-150 ^oC

IR (KBr) : ν 1714, 1628 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.85 (s, 3H), 5.28 (s, 2H), 5.38 (s, 2H), 7.16-7.22 (m, 2H,), 7.29-7.34 (m, 1H), 7.37-7.44 (m, 1H), 7.57 (s, 1H), 7.87 (s, 1H)

^{13}C NMR (100 MHz) : δ 46.45, 52.64, 64.86, 121.43, 124.29, 124.87, 125.92, 131.60, 132.09, 132.67, 133.65, 140.96, 157.16, 166.38

LCMS (m/z) : 272 $(M+H)^+$

Anal calc'd for $C_{14}H_{13}N_3O_3$: C, 61.99; H, 4.83; N, 15.49

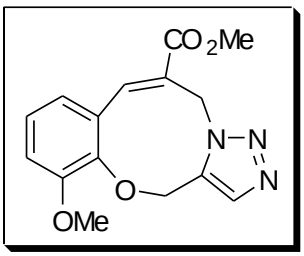
Found : C, 62.12; H, 4.76; N, 15.39

Method B: The crude product **115a**, obtained after usual work-up (Page No. 169), dissolved in toluene (2 ml) and refluxed for 4 hour and reaction mixture was cooled to room temperature and solvent was removed in vacuo and purification of the residue by column chromatography (60% ethyl acetate in hexanes) on silica gel afforded 0.195 g (72%) of the title compound as a white solid for overall two steps from methyl 2-(azidomethyl)-3-[2-(prop-2-ynyloxy)phenyl]propenoate (**115a**).

*The compound **114a** have identical ^1H NMR, ^{13}C NMR spectral data as that obtained in the procedure **Method A**.*

16-Methoxy-10-methoxycarbonyl-2-oxa-6,7,8-triazatricyclo[10,4,0,$0^{4,8}$]hexadeca-4,6,10,12,14,16(1)-hexaene (114b)

Treatment of methyl 3-acetoxy-3-[3-methoxy-2-(prop-2-ynyloxy)phenyl]-2-methylene-propanoate (**116b**) with sodium azide in DMSO and then heating the crude thus obtained (after aqueous work-up) in toluene according to the similar procedure described for the molecule **114a**, in **Method B**, provided the title compound as a white solid.



Reaction time : 3 h + 4 h

Yield : 68%

Mp : 185-188 ^oC

IR (KBr) : ν 1709, 1631 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.88 (s, 3H), 3.93 (s, 3H), 5.27 (s, 4H), 6.81-6.86 (m, 1H), 6.98 (dd, 1H, *J* = 1.2 Hz & 8.4 Hz)), 7.10-7.17 (m, 1H), 7.56 (s, 1H), 7.77 (s, 1H)

^{13}C NMR (100 MHz) : δ 46.03, 52.41, 55.86, 64.37, 113.21, 122.20, 124.63, 126.94, 127.24, 132.08, 134.84, 140.36, 145.29, 152.46, 166.20

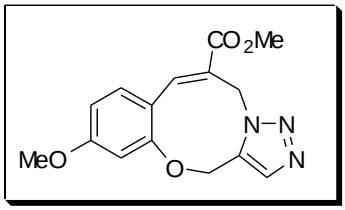
LCMS (m/z) : 302 $(M+H)^{+}$

Anal calc'd for $C_{15}H_{15}N_3O_4$: C, 59.79; H, 5.02; N, 13.95

Found : C, 59.85; H, 5.06; N, 14.12

15-Methoxy-10-methoxycarbonyl-2-oxa-6,7,8-triazatricyclo[10,4,0,0^{4,8}]hexadeca-4,6,10,12,14,16(1)-hexaene (114c)

This was prepared as a white solid *via* the treatment of Baylis-Hillman acetate, methyl 3-acetoxy-3-[4-methoxy-2-(prop-2-ynyloxy)phenyl]-2-methylenepropanoate (**116c**) with sodium azide in DMSO, and then refluxing the crude thus obtained after aqueous work-up in toluene following the similar procedure described for molecule **114a**, in **Method B**.



Reaction time : 4 h + 4 h

Yield : 63%

Mp : 145-148 ^{o}C

IR (KBr) : ν 1714, 1632 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.83 (s, 3H), 3.84 (s, 3H), 5.25 (s, 2H), 5.43 (s, 2H), 6.69 (d, 1H, *J* = 2.8 Hz), 6.74 (dd, 1H, *J* = 2.8 Hz & 8.8 Hz), 7.25 (d, 1H, *J* = 8.8 Hz, one of the peak of the

doublet is merging with [$CDCl_3$] $CHCl_3$ peak), 7.57 (s, 1H), 7.85 (s, 1H)

^{13}C NMR (100 MHz) : δ 46.36, 52.41, 55.51, 64.64, 107.10, 110.41, 116.90, 123.13, 131.92, 133.01, 134.65, 141.40, 158.69, 162.16, 166.60

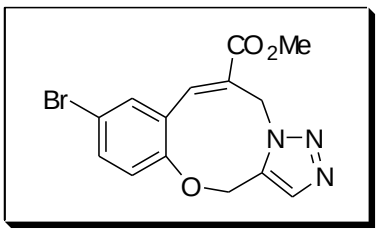
LCMS (m/z) : 302 $(M+H)^+$

Anal calc'd for $C_{15}H_{15}N_3O_4$: C, 59.79; H, 5.02; N, 13.95

Found : C, 59.65; H, 5.08; N, 14.07

14-Bromo-10-methoxycarbonyl-2-oxa-6,7,8-triazatricyclo[10,4,0,0^{4,8}]hexadeca-4,6,10,12,14,16(1)-hexaene (114d)

Treatment of methyl 3-acetoxy-3-[5-bromo-2-(prop-2-ynyloxy)phenyl]-2-methylene-propanoate (**116d**) with sodium azide in DMSO and then heating the crude (after aqueous work-up) in toluene under reflux following the similar procedure described for the molecule **114a** in **Method B**, provided the title compound as a white solid.



Reaction time : 3 h + 5 h

Yield : 57%

Mp : 212-214 ^oC

IR (KBr) : ν 1711, 1631 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.86 (s, 3H), 5.27 (s, 2H), 5.35 (s, 2H), 7.06 (d, 1H, *J* = 8.8 Hz), 7.43 (d, 1H, *J* = 2.4 Hz), 7.49 (dd, 1H, *J* = 2.4 Hz & 8.8 Hz), 7.57 (s, 1H), 7.76 (s, 1H)

^{13}C NMR (100 MHz) : δ 46.40, 52.82, 65.00, 116.87, 123.20, 126.97, 127.24, 132.27, 133.44, 134.30, 134.84, 139.14, 156.15, 166.01

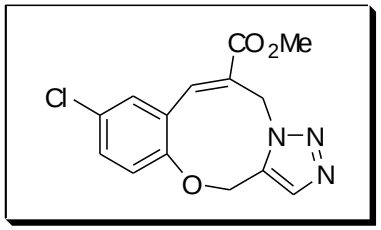
LCMS (m/z) : 350 $(M+H)^+$, 352 $(M+H+2)^+$

Anal calc'd for $C_{14}H_{12}BrN_3O_3$: C, 48.02; H, 3.45; N, 12.00

Found : C, 48.13; H, 3.41; N, 12.07

14-Chloro-10-methoxycarbonyl-2-oxa-6,7,8-triazatricyclo[10,4,0,$0^{4,8}$]hexadeca-4,6,10,12,14,16(1)-hexaene (114e)

This was prepared as a white solid *via* the treatment of Baylis-Hillman acetate, methyl 3-acetoxy-3-[5-chloro-2-(prop-2-ynyloxy)phenyl]-2-methylenepropanoate (**116e**) with sodium azide in DMSO, and then heating the crude (after aqueous work-up) in toluene under frelux following the similar procedure described for molecule **114a**, in **Method B**.



Reaction time : 3 h + 4 h

Yield : 62%

Mp : 204-206 ^oC

IR (KBr) : ν 1711, 1633 cm^{-1}

^1H NMR (400 MHz) : δ 3.86 (s, 3H), 5.27 (s, 2H), 5.36 (s, 2H), 7.11(d, 1H, *J* = 8.8 Hz), 7.28 (d, 1H, *J* = 2.4 Hz), 7.35 (dd, 1H, *J* = 2.4 Hz & 8.8 Hz), 7.57 (s, 1H), 7.75 (s, 1H)

^{13}C NMR (100 MHz) : δ 46.32, 52.73, 65.00, 122.79, 126.49, 127.19, 129.37, 131.29, 131.75, 132.19, 133.48, 139.14, 155.52, 165.97

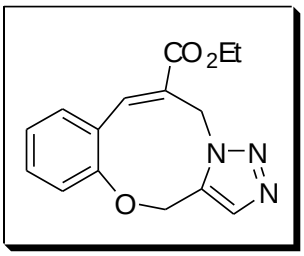
LCMS (m/z) : 306 $(M+H)^+$, 308 $(M+H+2)^+$

Anal calc'd for $C_{14}H_{12}ClN_3O_3$: C, 55.00; H, 3.96; N, 13.74

Found : C, 55.11; H, 3.89; N, 13.65

10-Ethoxycarbonyl-2-oxa-6,7,8-triazatricyclo[10,4,0,$0^{4,8}$]hexadeca-4,6,10,12,14,16(1)-hexaene (114f)

Treatment of ethyl 3-acetoxy-2-methylene-3-[2-(prop-2-ynyloxy)phenyl]propanoate (**116f**) with sodium azide in DMSO and then refluxing the crude thus obtained (after aqueous work-up) in toluene following the similar procedure described for the molecule **114a** in **Method B**, provided the title compound as a white solid.



Reaction time : 4 h + 4 h

Yield : 58%

Mp : 88-89 ^{o}C

IR (KBr) : ν 1709, 1639 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.35 (t, 3H, *J* = 7.2 Hz), 4.30 (q, 2H, *J* = 7.2 Hz), 5.29 (s, 2H), 5.38 (s, 2H), 7.15-7.22 (m, 2H,), 7.31 (d, 1H, *J* = 6.8 Hz), 7.37-7.43 (m, 1H), 7.57 (s, 1H), 7.86 (s, 1H)

^{13}C NMR (100 MHz) : δ 14.20, 46.51, 61.79, 64.88, 121.51, 124.31, 124.93, 126.19, 131.55, 132.11, 132.77, 133.59, 140.66, 157.19, 165.93

LCMS (m/z) : 284 $(M-H)^{+}$

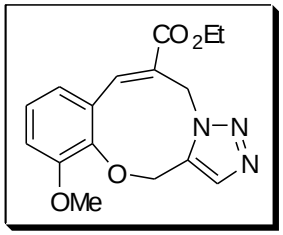
Anal calc'd for $C_{15}H_{15}N_3O_3$: C, 63.15; H, 5.30; N, 14.73

Found : C, 63.29; H, 5.36; N, 14.61

10-Ethoxycarbonyl-16-methoxy-2-oxa-6,7,8-triazatricyclo[10,4,0,$0^{4,8}$]hexadeca-4,6,10,12,14,16(1)-hexaene (114g)

This was prepared as a white solid *via* the treatment of Baylis-Hillman acetate, ethyl 3-acetoxy-3-[3-methoxy-2-(prop-2-ynyloxy)phenyl]-2-methylenepropanoate (**116g**) with

sodium azide in DMSO, followed by refluxing the crude (after aqueous work-up) in toluene according to the similar procedure described for molecule **114a**, in **Method B**.



Reaction time : 3 h + 4 h

Yield : 65%

Mp : 160-162 ^{o}C

IR (KBr) : ν 1705, 1633 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.37 (t, 3H, *J* = 7.2 Hz), 3.93 (s, 3H), 4.33 (q, 2H, *J* = 7.2 Hz), 5.27 (s, 2H), 5.28 (s, 2H), 6.81-6.86 (m, 1H), 6.98 (dd, 1H, *J* = 1.2 Hz & 8.4 Hz), 7.10-7.16 (m, 1H), 7.56 (s, 1H), 7.76 (s, 1H)

^{13}C NMR (100 MHz) : δ 14.09, 46.09, 55.89, 61.53, 64.38, 113.19, 122.31, 124.63, 127.07, 127.55, 132.10, 134.78, 139.98, 145.34, 152.52, 165.75

LCMS (m/z) : 316 $(M+H)^{+}$

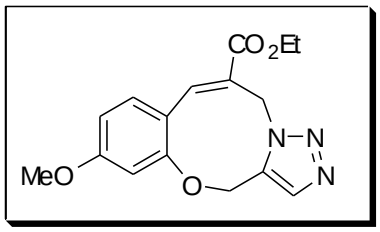
Anal calc'd for $C_{16}H_{17}N_3O_4$: C, 60.94; H, 5.43; N, 13.33

Found : C, 60.88; H, 5.39; N, 13.26

10-Ethoxycarbonyl-15-methoxy-2-oxa-6,7,8-triazatricyclo[10,4,0,0^{4,8}]hexadeca-4,6,10,12,14,16(1)-hexaene (114h)

Treatment of ethyl 3-acetoxy-3-[4-methoxy-2-(prop-2-ynyloxy)phenyl]-2-methylene-propanoate (**116h**) with sodium azide in DMSO and then refluxing the crude (after aqueous work-up) in toluene following the similar procedure described for the molecule **114a** in **Method B**, provided the title compound as a white solid.

Reaction time : 10 h + 4 h



Yield : 68%

Mp : 140-142 ^{o}C

IR (KBr) : ν 1703, 1610 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.33 (t, 3H, *J* = 7.2 Hz), 3.84 (s, 3H), 4.27 (q, 2H, *J* = 7.2 Hz), 5.25 (s, 2H), 5.43 (s, 2H), 6.69 (d, 1H, *J* = 2.4 Hz), 6.74 (dd, 1H, *J* = 2.4 Hz & 8.8 Hz), 7.25 (d, 1H, *J* = 8.8 Hz), 7.57 (s, 1H), 7.84 (s, 1H)

^{13}C NMR (100 MHz) : δ 14.19, 46.53, 55.63, 61.63, 64.78, 107.26, 110.54, 117.06, 123.56, 132.06, 132.97, 134.86, 141.20, 158.86, 162.22, 166.25

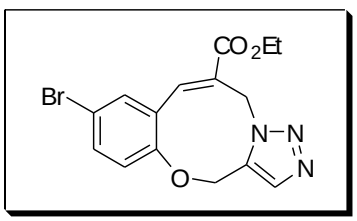
LCMS (m/z) : 316 $(M+H)^{+}$

Anal calc'd for $C_{16}H_{17}N_3O_4$: C, 60.94; H, 5.43; N, 13.33

Found : C, 60.85; H, 5.51; N, 13.26

14-Bromo-10-ethoxycarbonyl-2-oxa-6,7,8-triazatricyclo[10,4,0,0^{4,8}]hexadeca-4,6,10,12,14,16(1)-hexaene (114i)

This was prepared as a white solid *via* the treatment of Baylis-Hillman acetate, ethyl 3-acetoxy-3-[5-bromo-2-(prop-2-ynyloxy)phenyl]-2-methylenepropanoate (**116i**) with sodium azide in DMSO, followed by refluxing the crude thus obtained (after aqueous work-up) in toluene following the similar procedure described for molecule **114a,** in **Method B**.



Reaction time : 3 h + 4 h

Yield : 71%

Mp : 166-169 ^{o}C

IR (KBr) : ν 1712, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.35 (t, 3H, *J* = 6.8 Hz), 4.30 (q, 2H, *J* = 6.8 Hz), 5.27 (s, 2H), 5.36 (s, 2H), 7.06 (d, 1H, *J* = 8.8 Hz), 7.44 (s, 1H), 7.48 (d, 1H, *J* = 8.8 Hz), 7.57 (s, 1H), 7.75 (s, 1H)

^{13}C NMR (100 MHz) : δ 14.11, 46.33, 61.87, 64.91, 116.74, 123.16, 126.97, 127.44, 132.18, 133.37, 134.14, 134.74, 138.68, 156.05, 165.42

LCMS (m/z) : 364$(M+H)^+$, 366 $(M+H+2)^+$

Anal calc'd for $C_{15}H_{14}BrN_3O_3$: C, 49.47; H, 3.87; N, 11.54

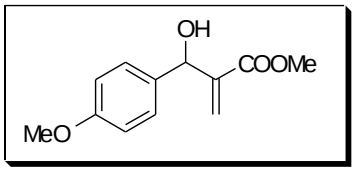
Found : C, 49.36; H, 3.81; N, 11.65

Methyl 3-hydroxy-3-(4-methoxyphenyl)-2-methylenepropanoate (95l)

This molecule was obtained as a colorless liquid *via* the Baylis–Hillman reaction of 4-methoxybenzaldehyde (**96g**) with methyl acrylate catalyzed by DABCO in silica gel solid phase medium, following a similar procedure described for the molecule **95a**.

Reaction time : 10 d

Yield : 61%



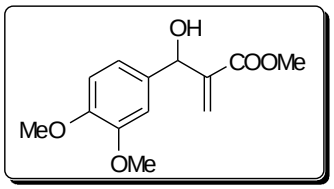
IR (neat) : ν 3348, 1714, 1625 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.87 (d, 1H, *J* = 5.2 Hz), 3.72 (s, 3H), 3.80 (s, 3H), 5.53 (d, 1H, *J* = 5.2 Hz), 5.84 (s, 1H), 6.32 (s, 1H), 6.87 (d, 2H, *J* = 8.4 Hz), 7.29 (d, 2H, *J* = 8.4 Hz)

^{13}C NMR (100 MHz) : δ 51.90, 55.22, 72.58, 113.78, 125.49, 127.93, 133.50, 142.20, 159.16, 166.77

Methyl 3-(3,4-dimethoxyphenyl)-3-hydroxy-2-methylenepropanoate (95m)

This compound was prepared as a colorless solid *via* DABCO catalyzed Baylis-Hillman reaction of 3,4-dimethoxybenzaldehyde (**96h**) with methyl acrylate following a similar procedure described for the molecule **95a**.



Reaction time : 10 d

Yield : 61%

Mp : 55-57 ^{0}C

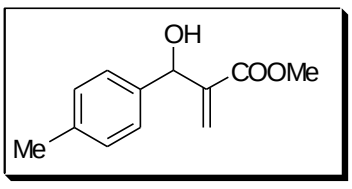
IR **(**KBr**)** : ν 3481, 1722, 1631 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.97 (d, 1H, *J* = 4.0 Hz), 3.73 (s, 3H), 3.87 (s, 3H), 3.88 (s, 3H), 5.53 (s, 1H), 5.83 (s, 1H), 6.33 (s, 1H), 6.83 (d, 1H, *J* = 8.4 Hz), 6.89 (dd, 1H, *J* = 2.0 Hz & 8.4 Hz), 6.93 (d, 1H, *J* = 2.0 Hz)

^{13}C NMR (100 MHz) : δ 51.88, 55.75, 55.79, 72.71, 109.75, 110.83, 118.92, 125.58, 133.86, 142.11, 148.51, 148.85, 166.76

Methyl 3-hydroxy-2-methylene-3-(4-tolyl)propanoate (95n)

A solution of 4-methylbenzaldeyhde (**96i**) (100 mmol, 12.01 g) and methyl acrylate (150 mmol, 12.91 g), DABCO (15 mmol, 1.68 g) was added and kept at room temperature. After 7 days the resulting mixture was diluted with ether (100 mL) and washed with 2N HCl (50ml), water (50 mL) and saturated $NaHCO_3$ solution (50 mL), in that order and then dried over anhydrous Na_2SO_4. Solvent was evaporated. The residue thus obtained was purified by column chromatography to provide title compound **95n** as a colorless loquid.



Reaction time : 7 d

Yield : 13.51 g (66%)

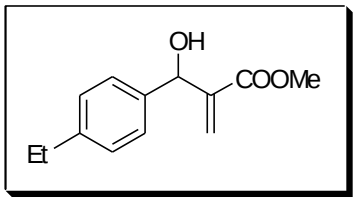
IR (neat) : ν 3447, 1718, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.33 (s, 3H), 2.91 (d, 1H, *J* = 5.6 Hz), 3.72 (s, 3H), 5.54 (d, 1H, *J* = 5.6 Hz), 5.84 (s, 1H), 6.33 (s, 1H), 7.15 (d, 2H, *J* = 8.0 Hz), 7.26 (d, 2H, *J* = 8.0 Hz)

^{13}C NMR (100 MHz) : δ 21.03, 51.78, 72.66, 125.51, 126.54, 129.00, 137.35, 138.39, 142.11, 166.66

Methyl 3-(4-ethylphenyl)-3-hydroxy-2-methylenepropanoate (95o)

Baylis–Hillman reaction of 4-ethylbenzaldehyde (**96j**) with methyl acrylate in presence of DABCO as a catalyst following the similar procedure described for the molecule **95n**, provided the title compound as a colorless liquid.



Reaction time : 7 d

Yield : 67%

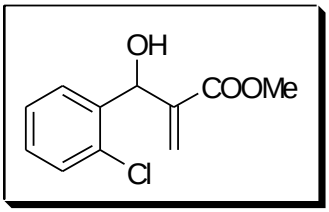
IR (neat) : ν 3445, 1716, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.22 (t, 3H, *J* = 7.6 Hz), 2.63 (q, 2H, *J* = 7.6 Hz), 2.92 (d, 1H, *J* = 5.2 Hz), 3.72 (s, 3H), 5.54 (d, 1H, *J* = 5.2 Hz), 5.85 (s, 1H), 6.33 (s, 1H), 7.17 (d, 2H, *J* = 8.0 Hz), 7.28 (d, 2H, *J* = 8.0 Hz)

^{13}C NMR (100 MHz) : δ 15.43, 28.45, 51.80, 72.73, 125.56, 126.61, 127.82, 138.61, 142.12, 143.72, 166.69

Methyl 3-(2-chlorophenyl)-3-hydroxy-2-methylenepropanoate (95p)

This compound was prepared as a colorless liquid *via* DABCO catalyzed Baylis-Hillman reaction of 2-chlorobenzaldehyde (**96k**) with methyl acrylate following a similar procedure described for the molecule **95n**.



Reaction time : 7 d

Yield : 89%

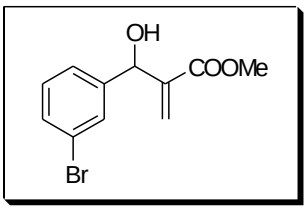
IR **(**neat**)** : ν 3439, 1714, 1631 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.30 (d, 1H, *J* = 4.8 Hz), 3.78 (s, 3H), 5.58 (s, 1H), 5.98 (d, 1H, *J* = 4.8 Hz), 6.33 (s, 1H), 7.22-7.41 (m, 3H), 7.56 (d, 1H, *J* = 7.6 Hz)

^{13}C NMR (100 MHz) : δ 51.98, 68.88, 126.80, 126.89, 128.05, 128.87, 129.32, 132.71, 138.35, 140.70, 166.81

Methyl 3-(3-bromophenyl)-3-hydroxy-2-methylenepropanoate (95q)

This compound was prepared as a colorless viscous liquid *via* DABCO catalyzed Baylis-Hillman reaction of 3-bromobenzaldehyde (**96l**) with methyl acrylate following a similar procedure described for the molecule **95n**.



Reaction time : 7 d

Yield : 83%

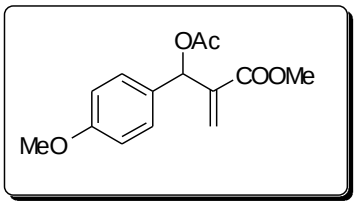
IR **(**neat**)** : ν 3443, 1714, 1631 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.15 (d, 1H, *J* = 6.0 Hz), 3.74 (s, 3H), 5.51 (d, 1H, *J* = 6.0 Hz), 5.84 (s, 1H), 6.36 (s, 1H), 7.18-7.25 (m, 1H), 7.30 (d, 1H, *J* = 8.0 Hz), 7.41 (d, 1H, *J* = 8.0 Hz), 7.53 (s, 1H)

^{13}C NMR (100 MHz) : δ 52.04, 72.36, 122.48, 125.27, 126.54, 129.63, 129.94, 130.82, 141.37, 143.68, 166.49

Methyl 3-acetoxy-3-(4-methoxyphenyl)-2-methylenepropanoate (94l)

Treatment of methyl 3-hydroxy-3-(4-methoxyphenyl)-2-methylenepropanoate (**95l**) with acetyl chloride in the presence of pyridine following the similar procedure described for the molecule **94a** provided the title compound as a colorless viscous liquid.



Reaction time : 2 h

Yield : 90%

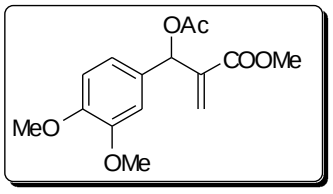
IR (neat) : ν 1743, 1730, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.09 (s, 3H), 3.70 (s, 3H), 3.79 (s, 3H), 5.87 (s, 1H), 6.38 (s, 1H), 6.63 (s, 1H), 6.86 (d, 2H, *J* = 8.4 Hz), 7.30 (d, 2H, *J* = 8.4 Hz)

^{13}C NMR (100 MHz) : δ 21.07, 51.91, 55.18, 72.81, 113.81, 125.07, 129.12, 129.78, 139.71, 159.60, 165.41, 169.41

Methyl 3-acetoxy-3-(3,4-dimethoxyphenyl)-2-methylenepropanoate (94m)

Treatment of methyl 3-(3,4-dimethoxyphenyl)-3-hydroxy-2-methylenepropanoate (**95m**) with acetyl chloride in the presence of pyridine following the similar procedure described for the molecule **94a** provided the title compound as a colorless viscous liquid.



Reaction time : 2 h

Yield : 95%

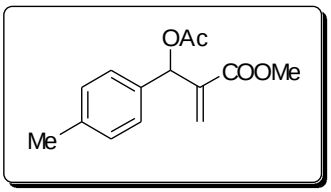
IR (neat) : ν 1745, 1732, 1633 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.10 (s, 3H), 3.71 (s, 3H), 3.86 (s, 3H), 3.87 (s, 3H), 5.87 (s, 1H), 6.39 (s, 1H), 6.64 (s, 1H), 6.83 (d, 1H, *J* = 8.4 Hz), 6.88 (d, 1H, *J* = 2.0 Hz, 6.94 (dd, 1H, *J* = 2.0 Hz & 8.4 Hz)

^{13}C NMR (100 MHz) : δ 21.15, 52.01, 55.86, 73.02, 110.89, 110.97, 120.35, 125.27, 130.11, 139.64, 148.86, 149.12, 165.48, 169.50

Methyl 3-acetoxy-2-methylene-3-(4-tolyl)propanoate (94n)

Treatment of methyl 3-hydroxy-2-methylene-3-(4-tolyl)propanoate (**95n**) with acetyl chloride in the presence of pyridine following the similar procedure described for the molecule **94a** provided the title compound as a colorless viscous liquid.



Reaction time : 2 h

Yield : 83%

IR (neat) : ν 1745, 1728, 1633 cm^{-1}

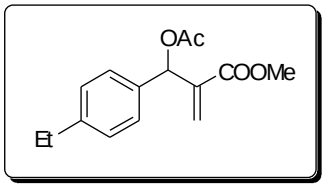
^{1}H NMR (400 MHz) : δ 2.09 (s, 3H), 2.33 (s, 3H), 3.70 (s, 3H), 5.86 (s, 1H), 6.38 (s, 1H), 6.64 (s, 1H), 7.14 (d, 2H, *J* = 7.6 Hz), 7.26 (d, 2H, *J* = 7.6 Hz)

^{13}C NMR (100 MHz) : δ 21.12, 51.91, 72.98, 125.41, 127.65, 129.14, 134.78, 138.20, 139.68, 165.40, 169.38

Methyl 3-acetoxy-3-(4-ethylphenyl)-2-methylenepropanoate (94o)

Treatment of methyl 3-(4-ethylphenyl)-3-hydroxy-2-methylenepropanoate (**95o**) with acetyl chloride in the presence of pyridine following the similar procedure described for the molecule **94a** provided the title compound as a colorless viscous liquid.

Reaction time : 2 h



Yield : 96%

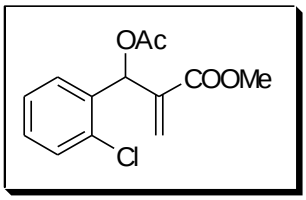
IR (neat) : ν 1745, 1724, 1633 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.22 (t, 3H, *J* = 7.6 Hz), 2.09 (s, 3H), 2.63 (q, 2H, *J* = 7.6 Hz), 3.70 (s, 3H), 5.86 (s, 1H), 6.38 (s, 1H), 6.65 (s, 1H), 7.17 (d, 2H, *J* = 8.0 Hz), 7.28 (d, 2H, *J* = 8.0 Hz)

^{13}C NMR (100 MHz) : δ 15.25, 20.90, 28.40, 51.77, 72.88, 125.26, 127.59, 127.82, 134.88, 139.64, 144.31, 165.27, 169.24

Methyl 3-acetoxy-3-(2-chlorophenyl)-2-methylenepropanoate (94p)

Treatment of methyl 3-(2-chlorophenyl)-3-hydroxy-2-methylenepropanoate (**95p**) with acetyl chloride in the presence of pyridine following the similar procedure described for the molecule **94a** provided the title compound as a colorless viscous liquid.



Reaction time : 2 h

Yield : 90%

IR (neat) : ν 1745, 1728, 1635 cm^{-1}

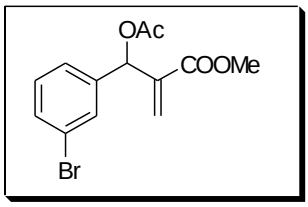
^{1}H NMR (400 MHz) : δ 2.12 (s, 3H), 3.74 (s, 3H), 5.65 (s, 1H), 6.47 (s, 1H), 7.04 (s, 1H), 7.24-7.30 (m, 2H), 7.33-7.42 (m, 2H)

^{13}C NMR (100 MHz) : δ 20.81, 52.09, 70.03, 126.88, 127.85, 128.38, 129.60, 129.83, 133.63, 135.31, 138.15, 165.31, 169.15

Methyl 3-acetoxy-3-(3-bromophenyl)-2-methylenepropanoate (94q)

Treatment of methyl 3-(3-bromophenyl)-3-hydroxy-2-methylenepropanoate (**95q**) with acetyl chloride in the presence of pyridine following the similar procedure described for the molecule **94a** provided the title compound as a colorless viscous liquid.

Reaction time : 2 h



Yield : 97%

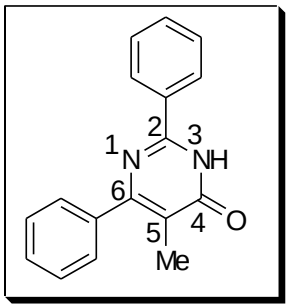
IR (neat) : ν 1747, 1730, 1633 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.12 (s, 3H), 3.72 (s, 3H), 5.89 (d, 1H, *J* = 0.4 Hz), 6.42 (d, 1H, *J* = 0.4 Hz), 6.61 (s, 1H), 7.18-7.24 (m, 1H), 7.29-7.35 (m, 1H), 7.40-7.46 (m, 1H), 7.48-7.52 (m, 1H)

^{13}C NMR (100 MHz) : δ 20.91, 51.97, 72.19, 122.37, 126.14, 126.38, 129.95, 130.42, 131.38, 138.95, 140.07, 164.99, 169.11

2,6-diphenyl-5-methylpyrimidin-4(3*H*)-one (133a)

To a stirred solution of methyl 3-acetoxy-2-methylene-3-phenylpropanoate (**94a**) (1 mmol, 0.234 g) in EtOH (2 mL) was added DABCO (2.5 mmol, 0.280 g) at room temperature and reaction mixture was stirred at the same temperature for 30 min (acetate completely disappered as monitered by TLC, indicating the formation of quaternary salt). Then benzamidine hydrochloride (1.5 mmol, 0.234 g) was then added and heated under reflux with stirring for 6 h. Solvent was evaporated and crude product obtained was purified by column chromatography (60% ethyl acetate in haxenes) to provide the title compound as a white solid in 76% (0.199 g) isolated yield.



Reaction time : 30 min + 6 h

Yield : 76%

Mp : 262-263 ^{0}C

IR (KBr) : ν 3059, 2926, 1641. 1595 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.26 (s, 3H), 7.42-7.58 (m, 6H), 7.65-7.72 (m, 2H), 8.31-8.38 (m, 2H), 13.20 (b s, 1H)

^{13}C NMR (100 MHz) : δ 12.87, 119.11, 127.61, 128.23, 128.90, 129.09, 129.19, 131.68, 132.34, 138.75, 153.14, 161.25, 166.22

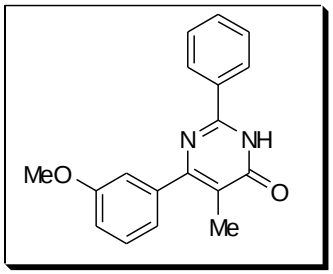
LCMS (m/z) : 263 $(M+H)^+$

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

Found : C, 77.68; H, 5.31; N, 10.59

6-(3-Methoxyphenyl)-5-methyl-2-phenylpyrimidin-4(3*H*)-one (133b)

Treatment of methyl 3-acetoxy-3-(3-methoxyphenyl)-2-methylenepropanoate (**94b**) with DABCO in EtOH and then reaction of the resulting salt with benzamidine hydrochloride following similar procedure described for the molecule **133a**, provided the title compound as a white solid.



Reaction time : 30 min + 6 h

Yield : 70%

Mp : 197-198 ^{0}C

IR (KBr) : ν 3067, 2920, 1655, 1593 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.25 (s, 3H), 3.88 (s, 3H), 6.97-7.03 (m, 1H), 7.20-7.26 (m, 2H), 7.37-7.44 (m, 1H), 7.49-7.59 (m, 3H), 8.26-8.34 (m, 2H), 12.71 (b s, 1H)

^{13}C NMR (100 MHz) : δ 12.80, 55.40, 114.58, 114.73, 119.07, 121.57, 127.73, 128.76, 129.20, 131.58, 132.29, 140.11, 153.21, 159.40, 161.05, 166.41

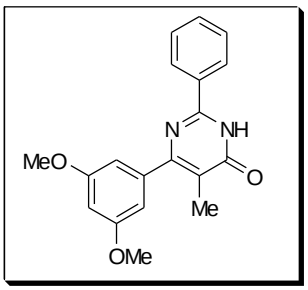
LCMS (m/z) : 293 $(M+H)^+$

Anal calc'd for $C_{18}H_{16}N_2O_2$: C, 73.95; H, 5.52; N, 9.58

Found : C, 73.91; H, 5.58; N, 9.51

6-(3,5-Dimethoxyphenyl)-5-methyl-2-phenylpyrimidin-4(3*H*)-one (133c)

Methyl 3-acetoxy-3-(3,5-dimethoxyphenyl)-2-methylenepropanoate (**94c**) on reaction with DABCO and then the treatment of the resulting salt with benzamidine hydrochloride, following a similar procedure described for the molecule **133a**, provided the title compound as a white solid.



Reaction time : 30 min + 6 h

Yield : 65%

Mp : 237-238 ^{0}C

IR (KBr) : ν 3072, 2939, 1651, 1597 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.24 (s, 3H), 3.85 (s, 6H), 6.55 (t, 1H, *J* = 2.4 Hz), 6.78 (d, 2H, *J* = 2.4 Hz), 7.48-7.58 (m, 3H), 8.28-8.34 (m, 2H), 12.97 (b s, 1H)

^{13}C NMR (100 MHz) : δ 12.81, 55.54, 101.04, 107.28, 119.17, 127.74, 128.79, 131.62, 132.29, 140.71, 153.24, 160.60, 161.22, 166.33

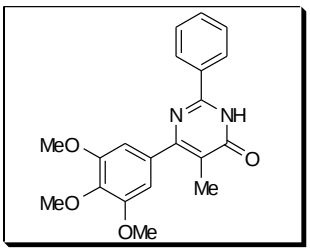
LCMS (m/z) : 323 $(M+H)^+$

Anal calc'd for $C_{19}H_{18}N_2O_3$: C, 70.79; H, 5.63; N, 8.69

Found : C, 70.65; H, 5.68; N, 8.75

5-Methyl-2-phenyl-6-(3,4,5-trimethoxyphenyl)pyrimidin-4(3*H*)-one (133d)

This compound was obtained as a white solid *via* the reaction of the salt (formed *via* treatment of methyl 3-acetoxy-2-methylene-3-(3,4,5-trimethoxyphenyl)propanoate (**94d**) with DABCO) with benzamidine hydrochloride, following a similar procedure described for the molecule **133a**.



Reaction time : 30 min + 6 h

Yield : 67%

Mp : 235-236 ^{0}C

IR (KBr) : ν 3078, 2930, 1658, 1597 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.28 (s, 3H), 3.92 (s, 3H), 3.92 (s, 6H), 6.89 (s, 2H), 7.50-7.60 (m, 3H), 8.24-8.32 (m, 2H), 12.42 (b s, 1H)

^{13}C NMR (100 MHz) : δ 12.90, 56.25, 60.90, 106.55, 118.69, 127.69, 128.73, 131.60, 132.22, 134.12, 138.74, 152.93, 153.16, 161.05, 166.31

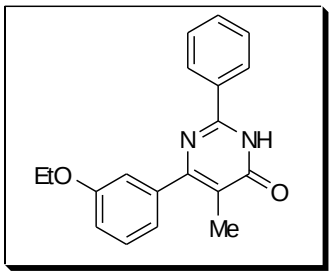
LCMS (m/z) : 353 $(M+H)^+$

Anal calc'd for $C_{20}H_{20}N_2O_4$: C, 68.17; H, 5.72; N, 7.95

Found : C, 68.25; H, 5.65; N, 8.07

6-(3-Ethoxyphenyl)-5-methyl-2-phenylpyrimidin-4(3*H*)-one (133e)

This compound was obtained as a white solid *via* the treatment of the salt, derived *via* the reaction of methyl 3-acetoxy-3-(3-ethoxyphenyl)-2-methylenepropanoate (**94g**) with DABCO, with benzamidine hydrochloride following a similar procedure described for the molecule **133a**.



Reaction time : 30 min + 6 h

Yield : 73%

Mp : 190-191 ^{0}C

IR (KBr) : ν 3067, 2916, 1645, 1604 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.45 (t, 3H, *J* = 6.8 Hz), 2.25 (s, 3H), 4.10 (q, 2H, *J* = 6.8 Hz), 6.96-7.02 (m, 1H), 7.19-7.25 (m, 2H), 7.35-7.42

(m, 1H), 7.48-7.58 (m, 3H), 8.28-8.33 (m, 2H), 12.82 (b s, 1H)

^{13}C NMR (100 MHz) : δ 12.79, 14.88, 63.58, 115.16, 115.30, 119.01, 121.43, 127.73, 128.73, 129.15, 131.53, 132.30, 140.07, 153.17, 158.77, 161.12, 166.41

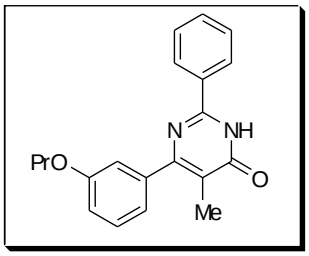
LCMS (m/z) : 307 $(M+H)^+$

Anal calc'd for $C_{19}H_{18}N_2O_2$: C, 74.49; H, 5.92; N, 9.14

Found : C, 74.65; H, 5.85; N, 9.07

5-Methyl-2-phenyl-6-(3-propoxyphenyl)pyrimidin-4(3*H*)-one (133f)

Reaction of methyl 3-acetoxy-2-methylene-3-(3-propoxyphenyl)propanoate (**94h**) with DABCO and then the treatment of the resulting salt with benzamidine hydrochloride following a similar procedure described for the molecule **133a**, provided the title compound as a white solid.



Reaction time : 30 min + 6 h

Yield : 69%

Mp : 194-195 ^{0}C

IR (KBr) : ν 3074, 2959, 1635, 1595 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.06 (t, 3H, *J* = 7.2 Hz), 1.79-1.90 (m, 2H), 2.25 (s, 3H), 3.99 (t, 2H, *J* = 6.8 Hz), 6.96-7.01 (m, 1H), 7.18-7.23 (m, 2H), 7.35-7.41 (m, 1H), 7.48-7.57 (m, 3H), 8.28-8.34 (m, 2H), 12.94 (b s, 1H)

^{13}C NMR (100 MHz) : δ 10.60, 12.81, 22.65, 69.67, 115.22, 115.32, 119.04, 121.38, 127.74, 128.77, 129.15, 131.56, 132.33, 140.07, 153.17, 159.00, 161.23, 166.42

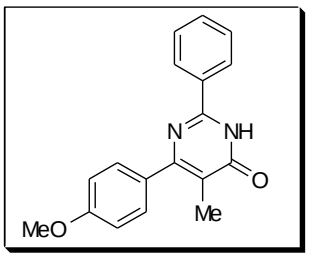
LCMS (m/z) : 321 $(M+H)^+$

Anal calc'd for $C_{20}H_{20}N_2O_2$: C, 74.98; H, 6.29; N, 8.74

Found : C, 75.12; H, 6.21; N, 8.81

6-(4-Methoxyphenyl)-5-methyl-2-phenylpyrimidin-4(3*H*)-one (133g)

This compound was obtained as a white solid *via* the reaction of methyl 3-acetoxy-3-(4-methoxyphenyl)-2-methylenepropanoate (**94l**) with DABCO and then treatment of the resulting salt with benzamidine hydrochloride following a similar procedure described for the molecule **133a.**



Reaction time : 30 min + 6 h

Yield : 80%

Mp : 274-275 ^{0}C

IR (KBr) : ν 3072, 2953, 1645, 1606 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.28 (s, 3H), 3.88 (s, 3H), 7.01 (d, 2H, *J* = 8.8 Hz), 7.49-7.56 (m, 3H), 7.67 (d, 2H, *J* = 8.8 Hz), 8.24-8.30 (m, 2H), 12.43 (b s, 1H)

^{13}C NMR (100 MHz) [$CDCl_3$+DMSO-d_6 (4:1)] : δ 12.13, 54.40, 112.47, 117.15, 126.66, 127.65, 129.73, 130.28, 131.82, 152.18, 158.39, 159.06, 164.23

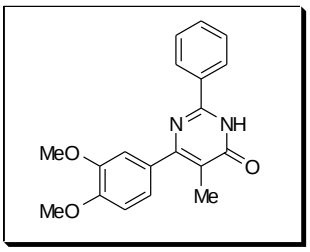
LCMS (m/z) : 293 $(M+H)^+$

Anal calc'd for $C_{18}H_{16}N_2O_2$: C, 73.95; H, 5.52; N, 9.58

Found : C, 73.85; H, 5.56; N, 9.49

6-(3,4-Dimethoxyphenyl)-5-methyl-2-phenylpyrimidin-4(3*H*)-one (133h)

This compound was obtained as a white solid *via* the reaction of the quartenary ammonium salt (derived from methyl 3-acetoxy-3-(3,4-dimethoxyphenyl)-2-methylenepropanoate (**94m**) in reaction with DABCO) with benzamidine hydrochloride, following a similar procedure described for the molecule **133a**.



Reaction time : 30 min + 6 h

Yield : 68%

Mp : 224-225 ^{0}C

IR (KBr) : ν 2912, 1660, 1599 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.29 (s, 3H), 3.95 (s, 6H), 6.97 (d, 1H, *J* = 8.0 Hz), 7.25-7.31 (m, 2H), 7.49-7.59 (m, 3H), 8.26-8.32 (m, 2H), 12.68 (b s, 1H)

^{13}C NMR (100 MHz) : δ 12.99, 56.00, 56.04, 110.53, 112.52, 118.25, 122.37, 127.62, 128.79, 131.31, 131.57, 132.31, 148.63, 149.85, 152.93, 160.86, 166.44

LCMS (m/z) : 323 $(M+H)^{+}$

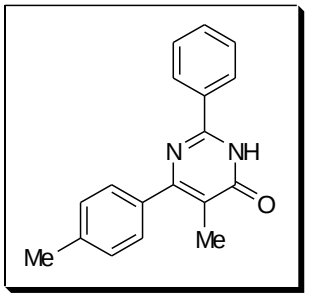
Anal calc'd for $C_{19}H_{18}N_2O_3$: C, 70.79; H, 5.63; N, 8.69

Found : C, 70.65; H, 5.68; N, 8.76

5-Methyl-6-(4-methylphenyl)-2-phenylpyrimidin-4(3*H*)-one (133i)

Treatment of methyl 3-acetoxy-2-methylene-3-(4-tolyl)propanoate (**94n**) with DABCO and then the reaction of the resulting salt with benzamidine hydrochloride, following a similar procedure described for the molecule **133a**, provided the title compound as a white solid.

Reaction time : 30 min + 6 h



Yield : 90%

Mp : 273-274 ^{0}C

IR (KBr) : ν 2924, 1641, 1595 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.26 (s, 3H), 2.43 (s, 3H), 7.29 (d, 2H, *J* = 8.0 Hz), 7.48-7.56 (m, 3H), 7.58 (d, 2H, *J* = 8.0 Hz), 8.27-8.36 (m, 2H), 12.86 (b s, 1H)

^{13}C NMR (100 MHz) : δ 12.92, 21.48, 118.76, 127.61, 128.87, 128.90, 129.19, 131.60, 132.42, 135.95, 139.14, 152.99, 161.20, 166.23

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

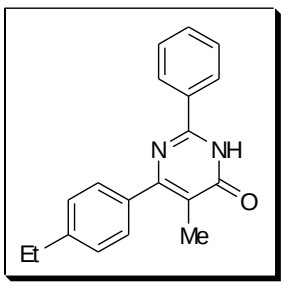
Anal calc'd for $C_{18}H_{16}N_2O$: C, 78.24; H, 5.84; N, 10.14

Found : C, 78.16; H, 5.91; N, 10.07

6-(4-Ethylphenyl)-5-methyl-2-phenylpyrimidin-4(3*H*)-one (133j)

This compound was obtained as a white solid *via* the reaction of methyl 3-acetoxy-3-(4-ethylphenyl)-2-methylene propanoate (**94o**) with DABCO and subsequent treatment of the resulting salt with benzamidine hydrochloride, following a similar procedure described for the molecule **133a**.

Reaction time : 30 min + 6 h



Yield : 76%

Mp : 267-269 ^{0}C

IR (KBr) : ν 2928, 1641, 1597 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.29 (t, 3H, *J* = 7.6 Hz), 2.27 (s, 3H), 2.73 (q, 2H, *J* = 7.6 Hz), 7.32 (d, 2H, *J* = 8.0 Hz), 7.48-7.57 (m, 3H),

7.61 (d, 2H, *J* = 8.0 Hz), 8.26-8.32 (m, 2H), 12.69 (b s, 1H)

^{13}C NMR (100 MHz) : δ 12.93, 15.57, 28.85, 118.78, 127.61, 128.73, 128.86, 129.27, 131.59, 132.43, 136.16, 145.43, 152.99, 161.20, 166.24

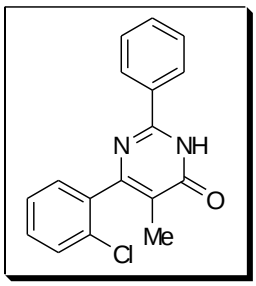
LCMS (m/z) : 291 $(M+H)^+$

Anal calc'd for $C_{19}H_{18}N_2O$: C, 78.59; H, 6.25; N, 9.65

Found : C, 78.69; H, 6.21; N, 9.58

6-(2-Chlorophenyl)-5-methyl-2-phenylpyrimidin-4(3*H*)-one (133k)

Reaction of methyl 3-acetoxy-3-(2-chlorophenyl)-2-methylenepropanoate **(94p)** with DABCO and then treatment of the resulting salt with benzamidine hydrochloride, following a similar procedure described for the molecule **133a**, provided the title compound as a white solid.



Reaction time : 30 min + 6 h

Yield : 80%

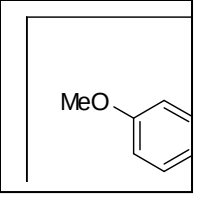
Mp : 247-249 ^{0}C

IR (KBr) : ν 2920, 1651, 1601 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.02 (s, 3H), 7.35-7.45 (m, 3H), 7.46-7.58 (m, 4H), 8.23-8.32 (m, 2H), 13.06 (b s, 1H)

^{13}C NMR (100 MHz) : δ 12.12, 121.30, 126.96, 127.75, 128.91, 129.87, 129.92, 130.07, 131.73, 132.25, 132.49, 137.85, 153.72, 160.12, 165.64

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

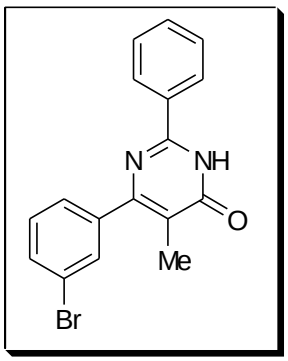


Anal calc'd for $C_{17}H_{13}ClN_2O$: C, 68.81; H, 4.42; N, 9.44

Found : C, 68.72; H, 4.51; N, 9.36

6-(3-Bromophenyl)-5-methyl-2-phenylpyrimidin-4(3*H*)-one (133l)

This compound was obtained as a white solid *via* the treatment of the salt (generated from methyl 3-acetoxy-3-(3-bromophenyl)-2-methylene propanoate (**94q**) and DABCO) with benzamidine hydrochloride, following a similar procedure described for the molecule **133a**.



Reaction time : 30 min + 6 h

Yield : 73%

Mp : 210-212 ^{0}C

IR (KBr) : ν 2914, 1658, 1597 cm^{-1}

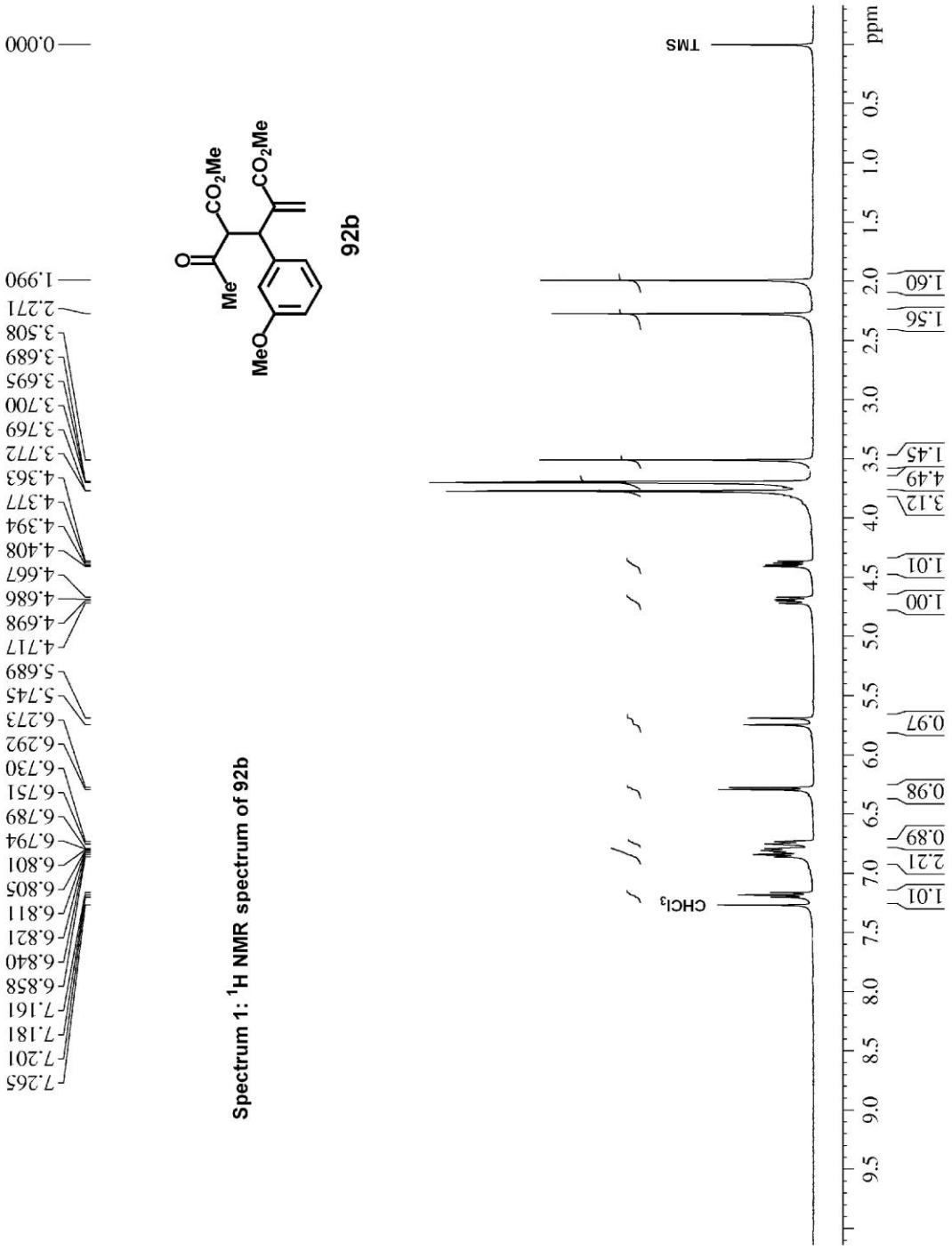
^{1}H NMR (400 MHz) : δ 2.24 (s, 3H), 7.33-7.40 (m, 1H), 7.50-7.63 (m, 5H), 7.83 (s, 1H), 8.23-8.32 (m, 2H), 12.60 (b s, 1H)

^{13}C NMR (100 MHz) : δ 12.77, 119.55, 122.43, 127.67, 127.79, 128.94, 129.74, 131.84, 132.05, 132.14, 140.76, 153.46, 159.69, 166.12

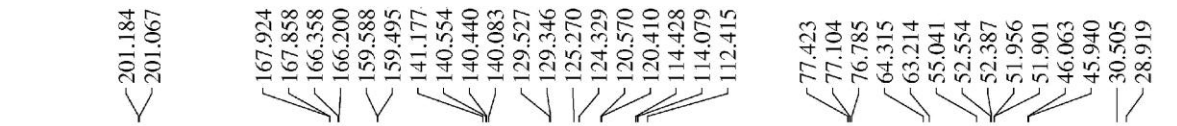
LCMS (m/z) : 341 $(M+H)^+$, 343 $(M+2+H)^+$

Anal calc'd for $C_{17}H_{13}BrN_2O$: C, 59.84; H, 3.84; N, 8.21

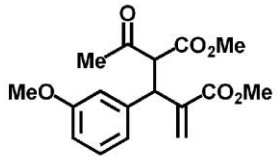
Found : C, 59.76; H, 3.89; N, 8.32



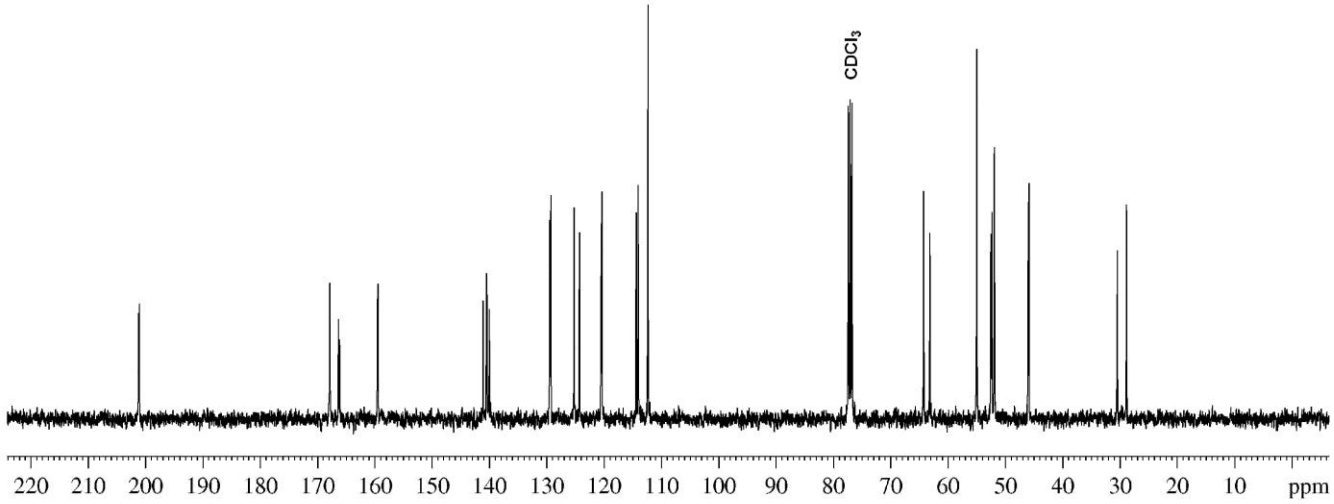
Spectrum 1: ^{1}H NMR spectrum of 92b

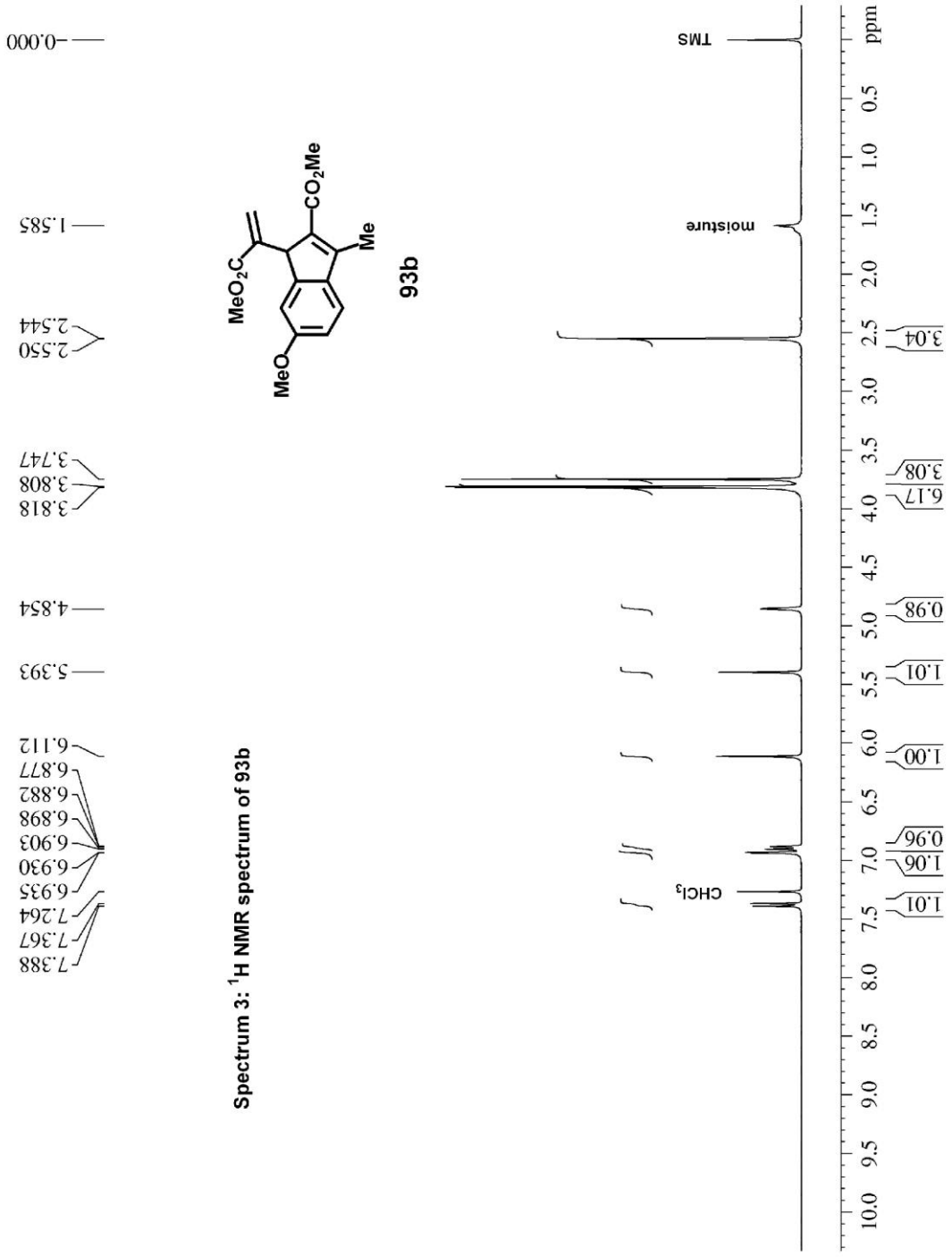


Spectrum 2: ^{13}C NMR spectrum of 92b

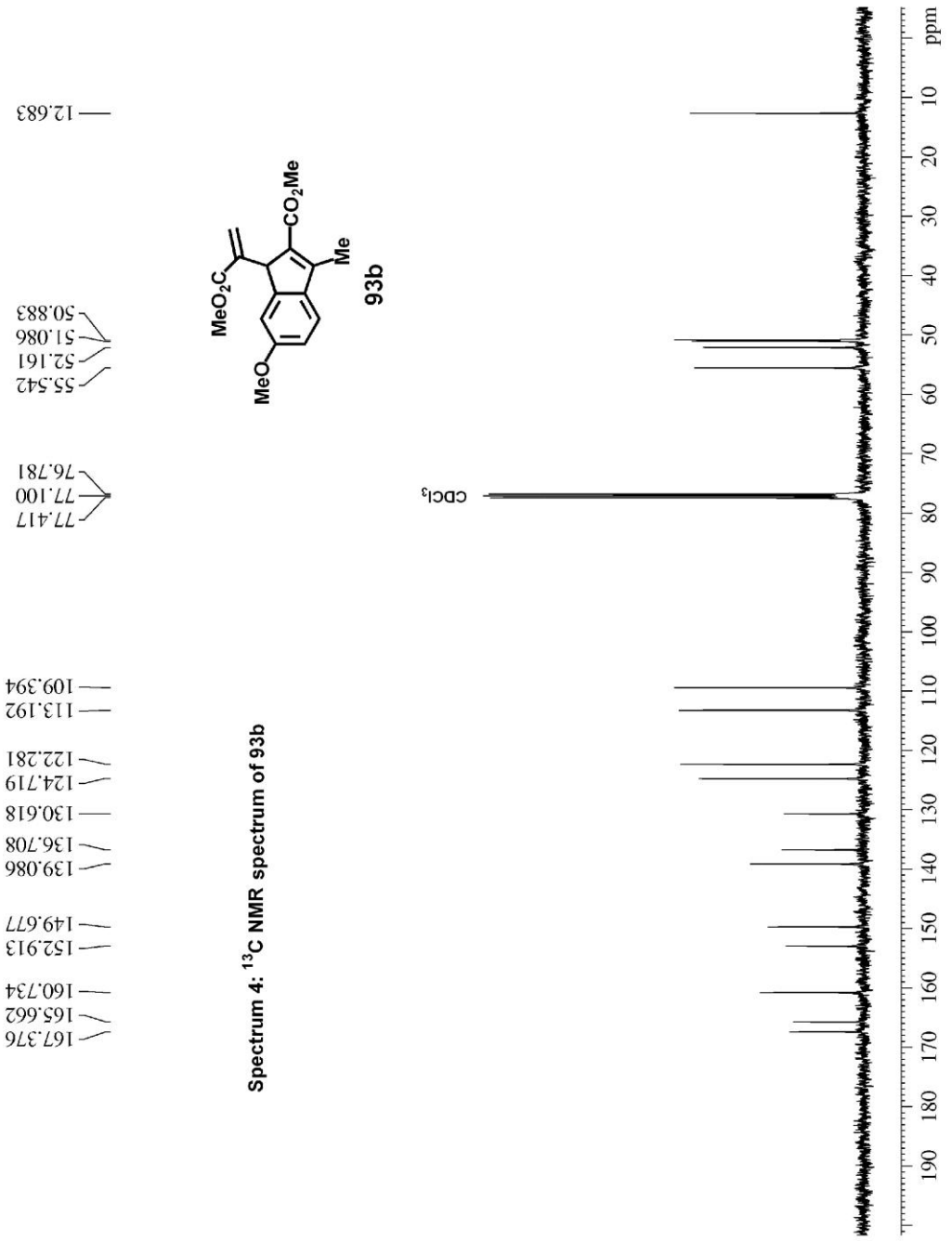


92b



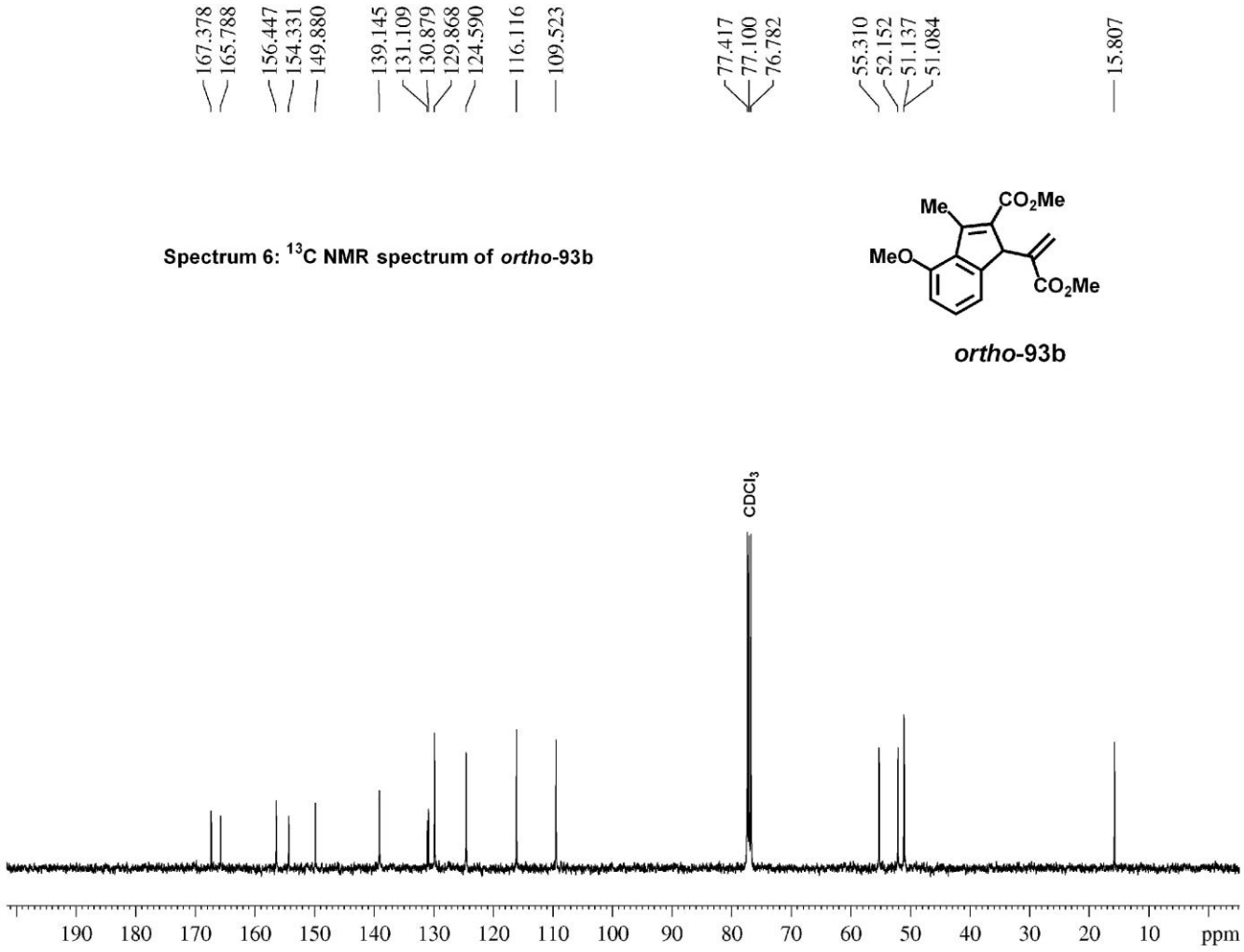


Spectrum 3: ^{1}H NMR spectrum of 93b



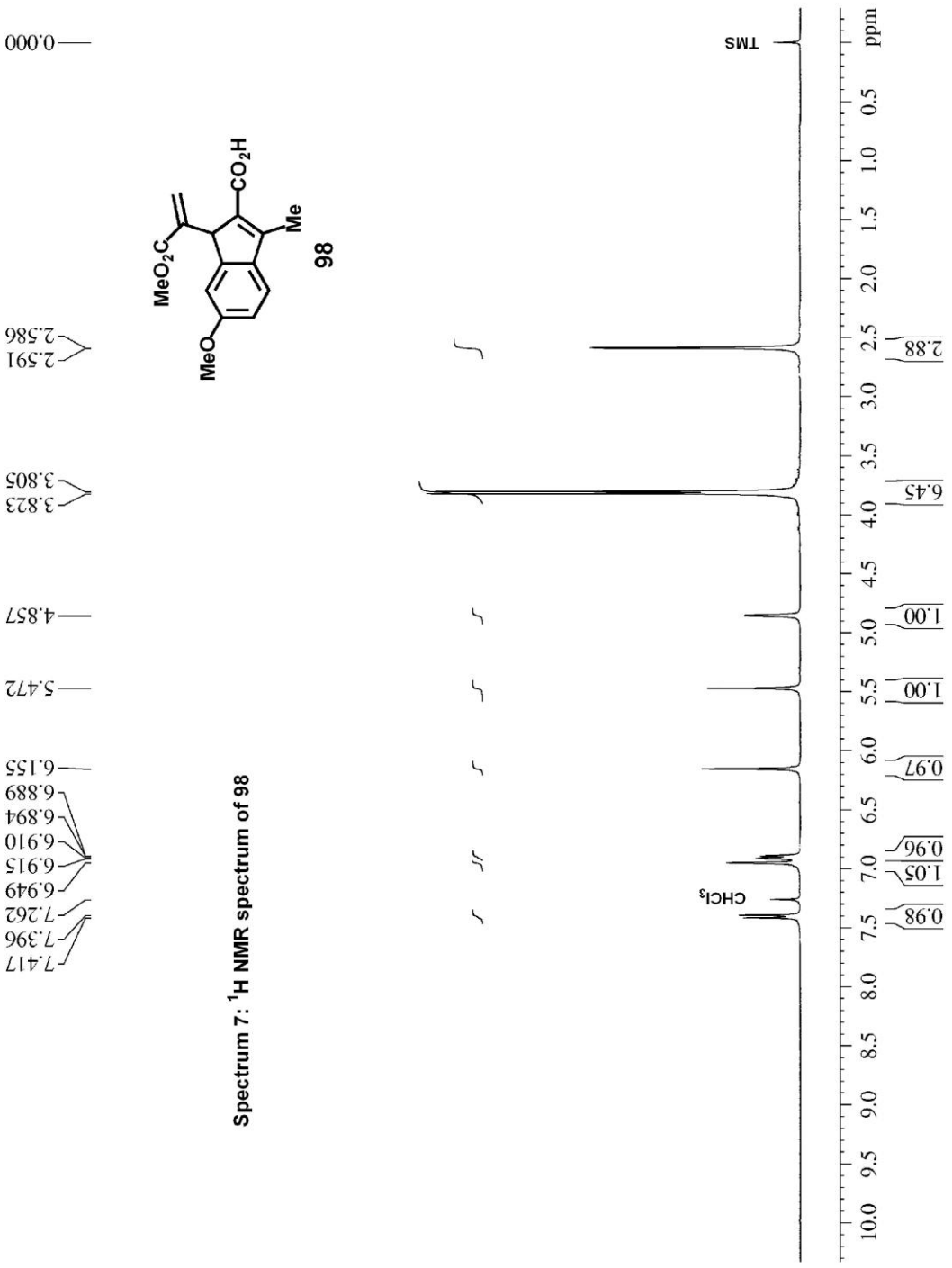
Spectrum 4: ^{13}C NMR spectrum of 93b

Spectrum 5: ^{1}H NMR spectrum of *ortho*-93b

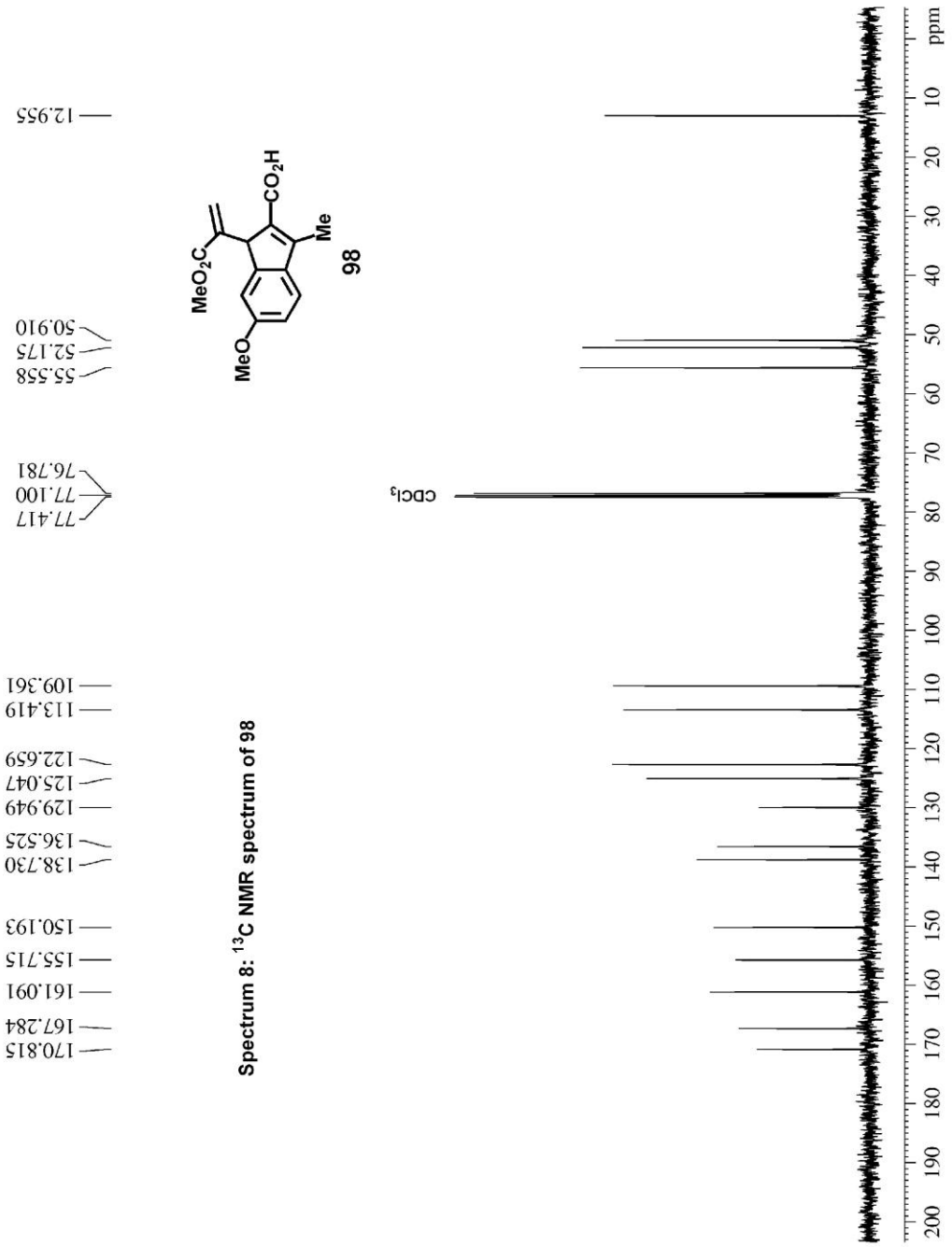


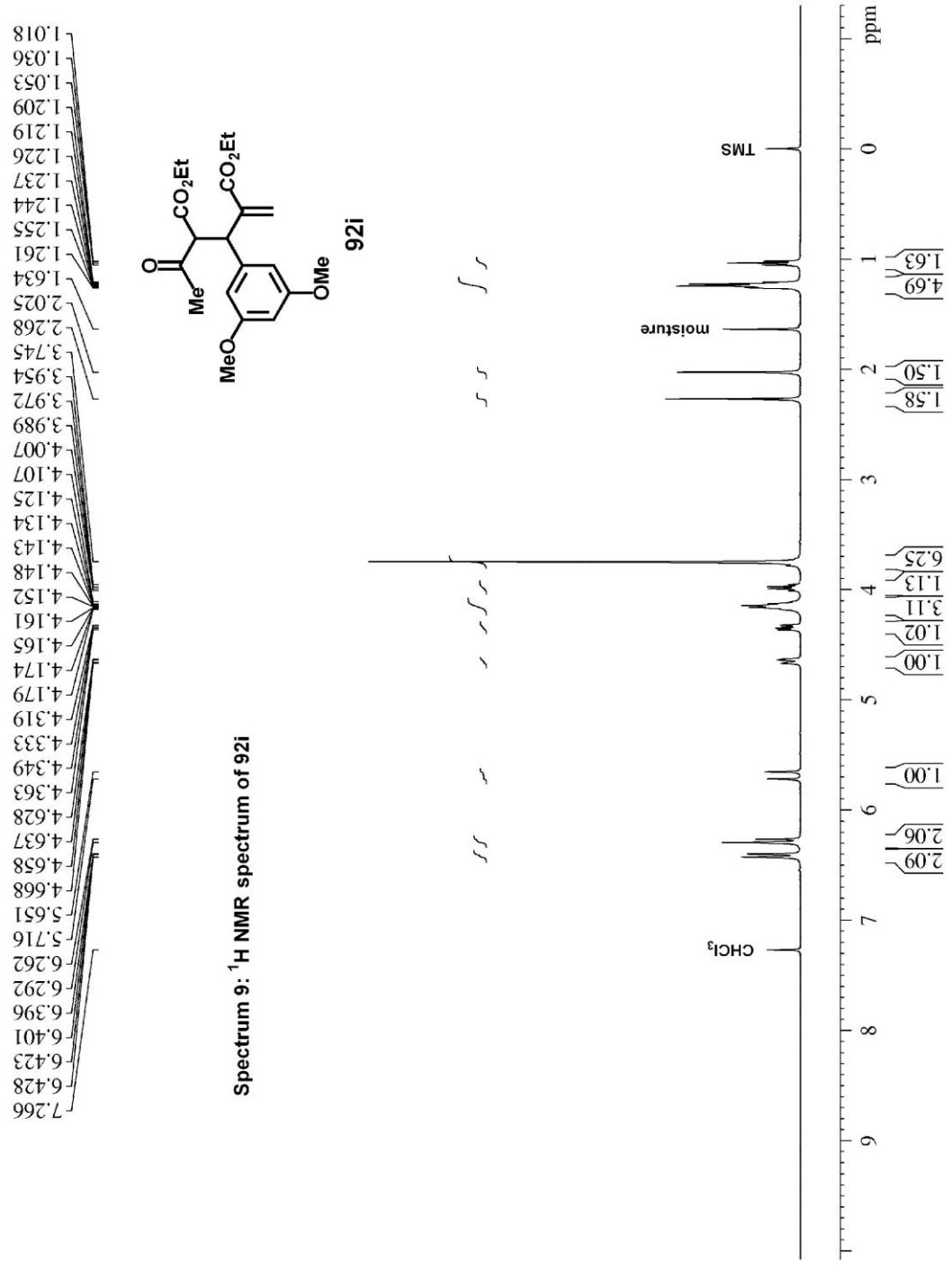
Spectrum 6: ^{13}C NMR spectrum of *ortho*-93b

***ortho*-93b**

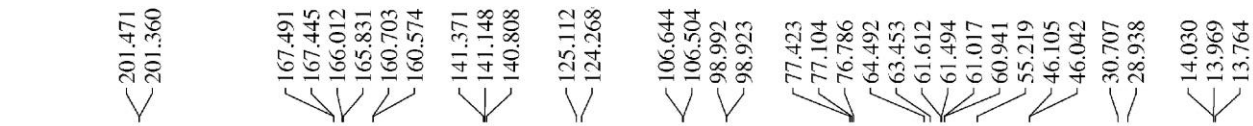


Spectrum 7: ^{1}H NMR spectrum of 98

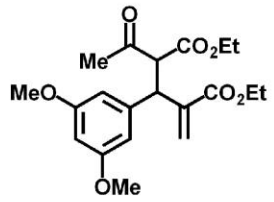

Spectrum 8: ^{13}C NMR spectrum of 98
98
MeO
MeO2C
CO2H
Me
CDCl3
ppm
12.955
50.910
52.175
55.558
76.781
77.100
77.417
109.361
113.419
122.659
125.047
129.949
136.525
138.730
150.193
155.715
161.091
167.284
170.815



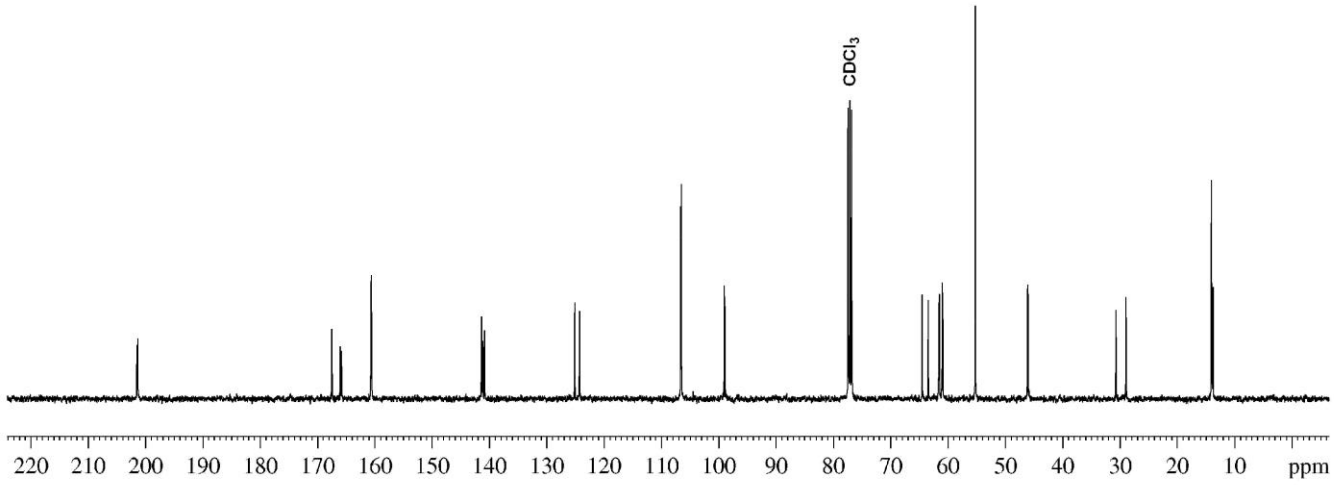
Spectrum 9: ^{1}H NMR spectrum of 92i

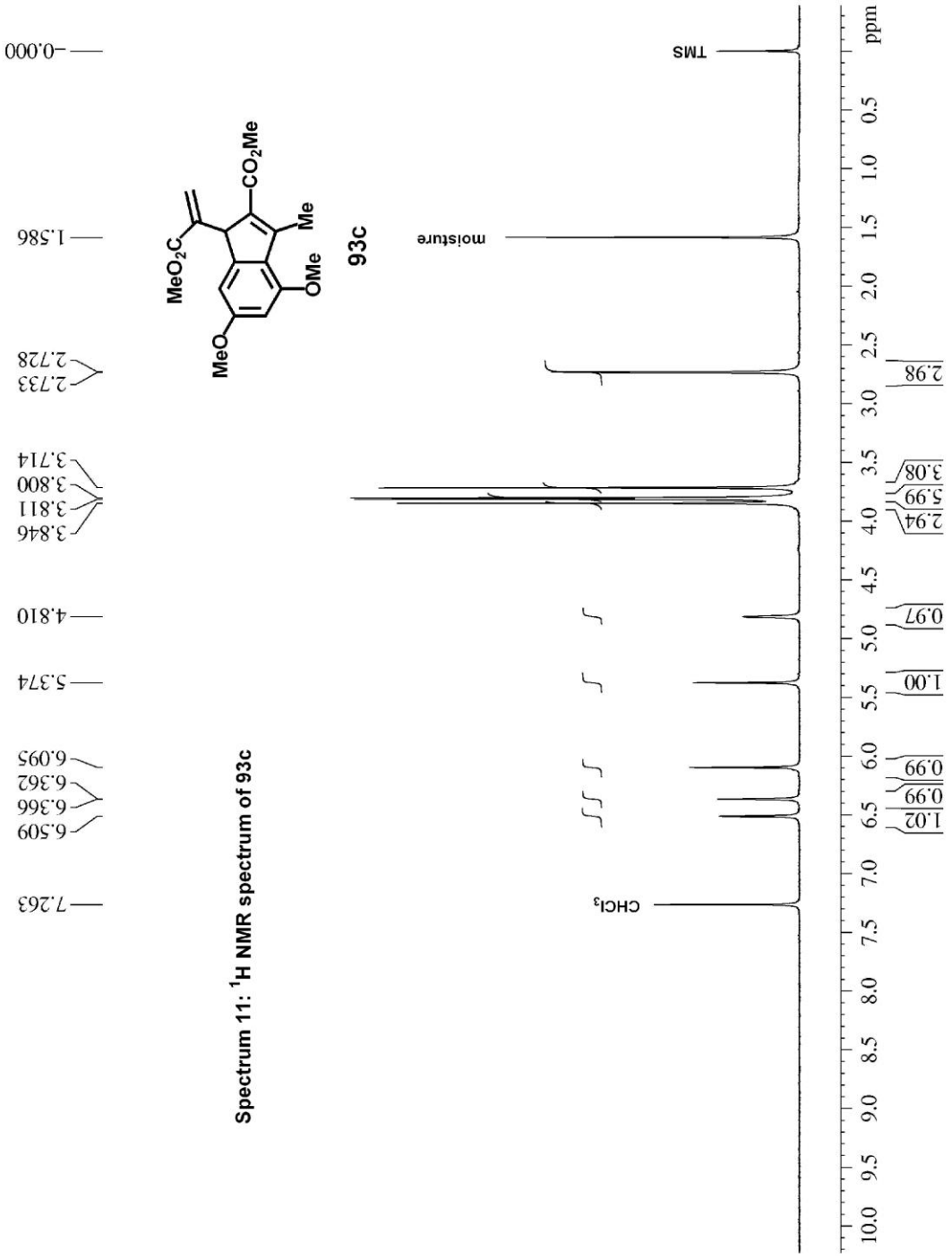


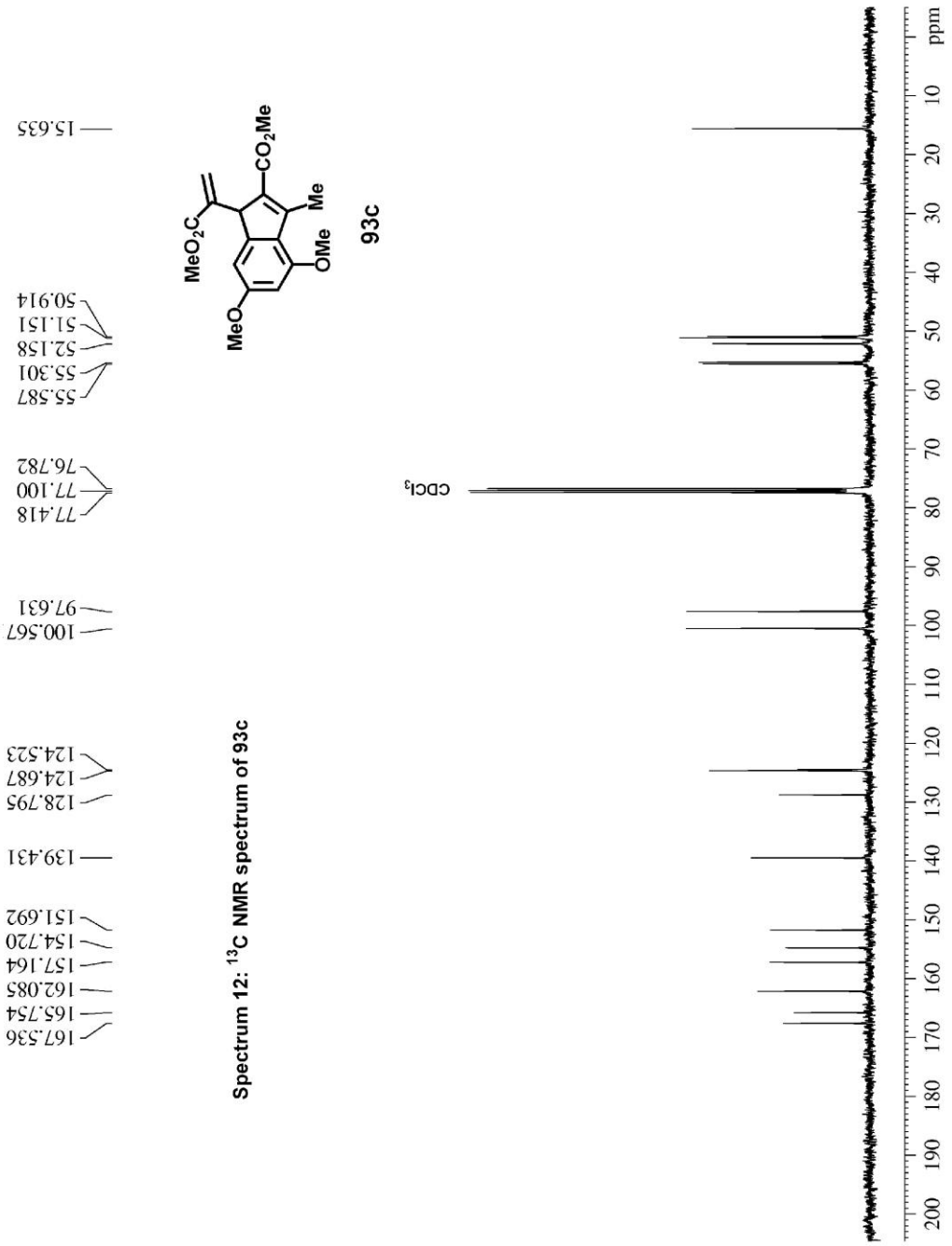
Spectrum 10: ^{13}C NMR spectrum of 92i



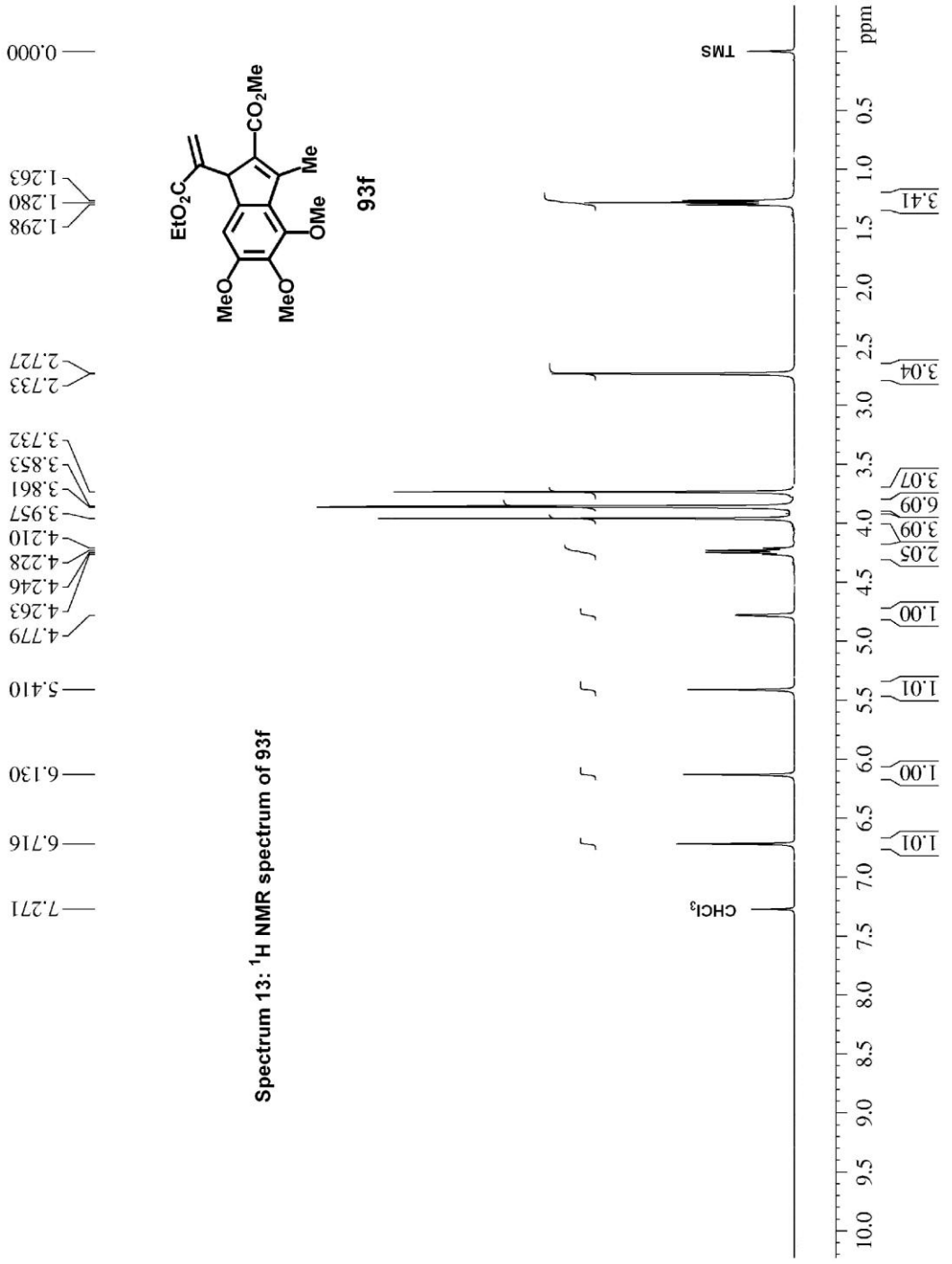
92i




Spectrum 11: ^{1}H NMR spectrum of 93c
93c
MeO$_2$C
CO$_2$Me
Me
OMe
MeO
TMS
moisture
CHCl$_3$
ppm
0.000
1.586
2.728
2.733
3.714
3.800
3.811
3.846
4.810
5.374
6.095
6.362
6.366
6.509
7.263
2.98
3.08
5.99
2.94
0.97
1.00
0.99
0.99
1.02

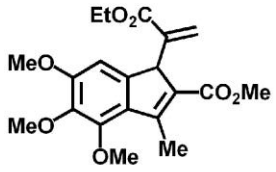


Spectrum 12: ^{13}C NMR spectrum of 93c

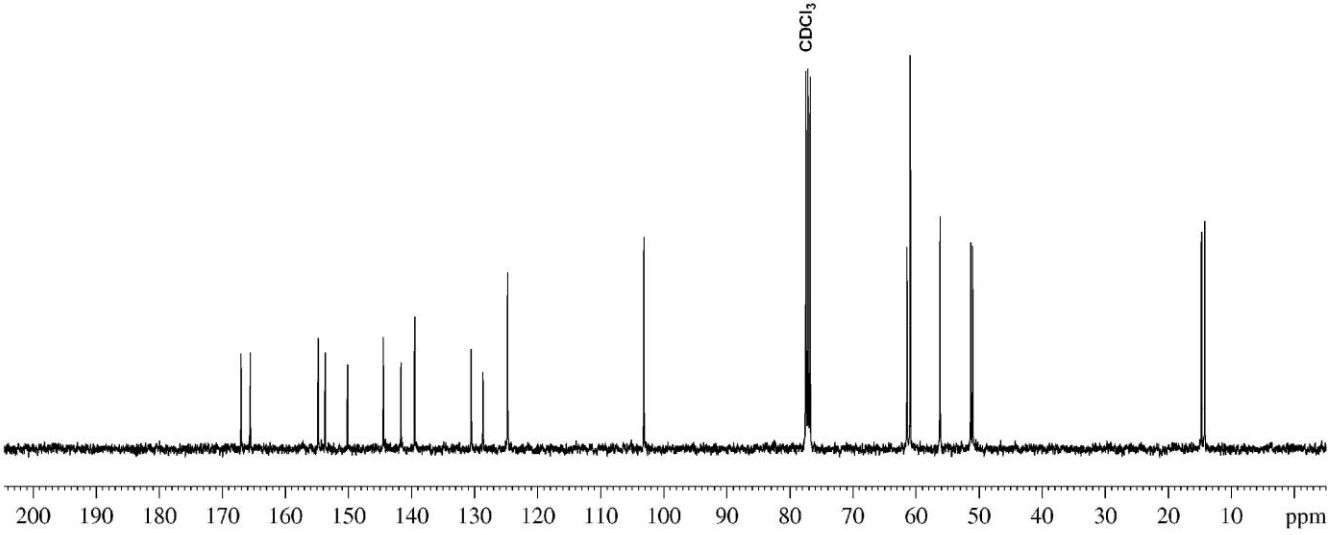

93f
Spectrum 13: ^{1}H NMR spectrum of 93f
TMS
CHCl$_3$
ppm
0.000
1.263
1.280
1.298
2.727
2.733
3.732
3.853
3.861
3.957
4.210
4.228
4.246
4.263
4.779
5.410
6.130
6.716
7.271
3.41
3.04
3.07
6.09
3.09
2.05
1.00
1.01
1.00
1.01

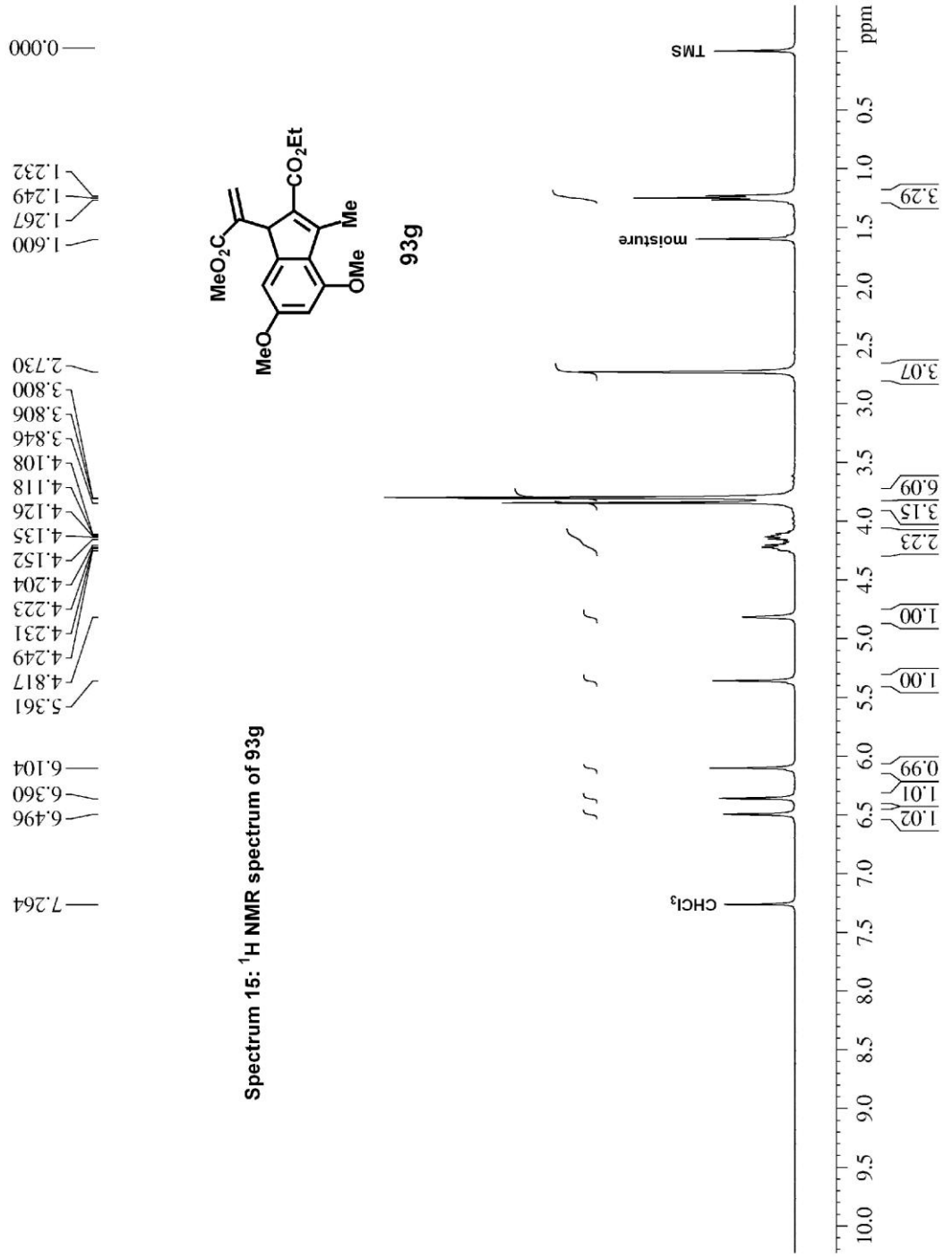
166.984
165.544
154.760
153.659
150.110
144.467
141.617
139.468
130.519
128.655
124.716
103.108
77.418
77.100
76.782
61.436
60.895
56.147
51.304
50.970
14.708
14.167

Spectrum 14: ^{13}C NMR spectrum of 93f

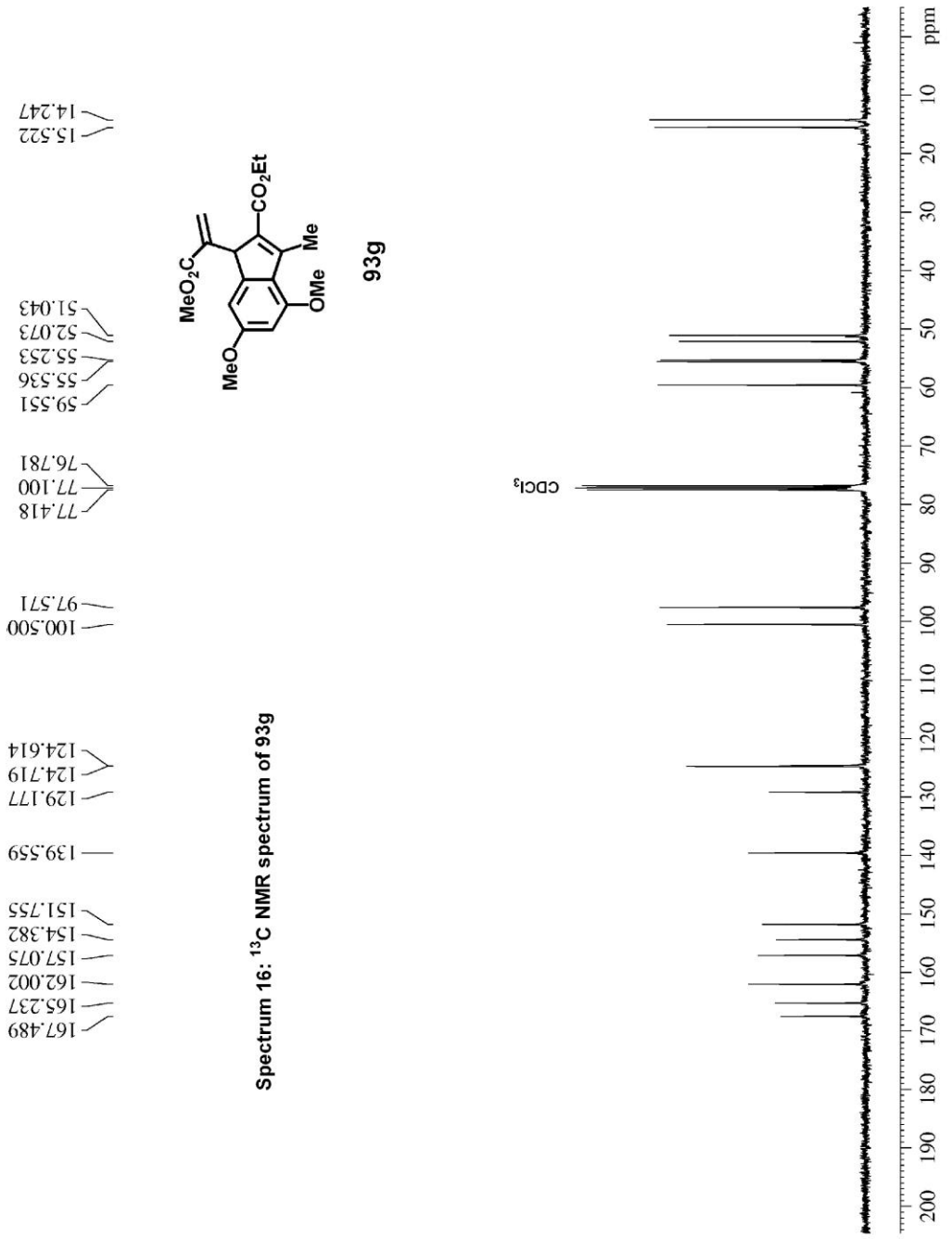


93f

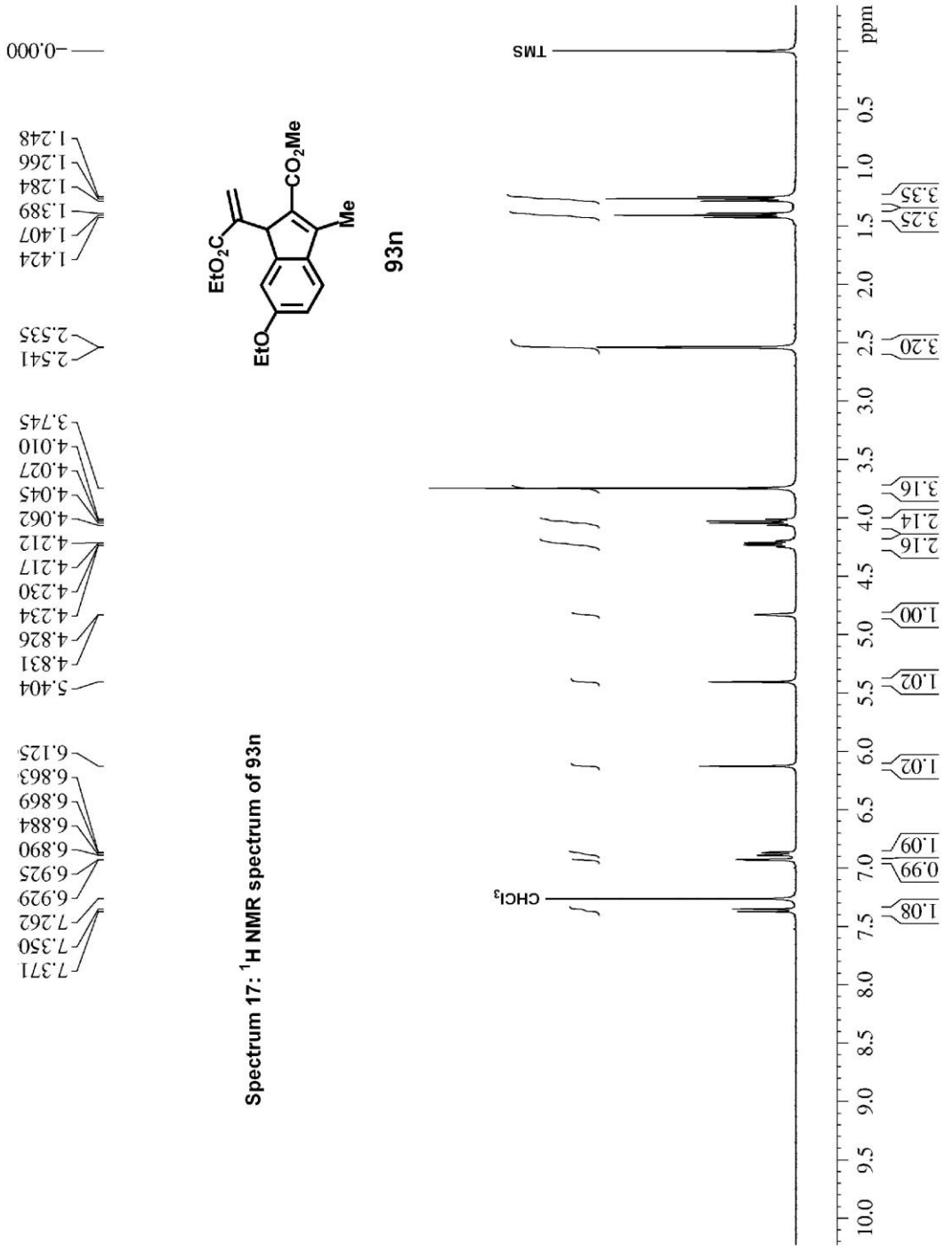


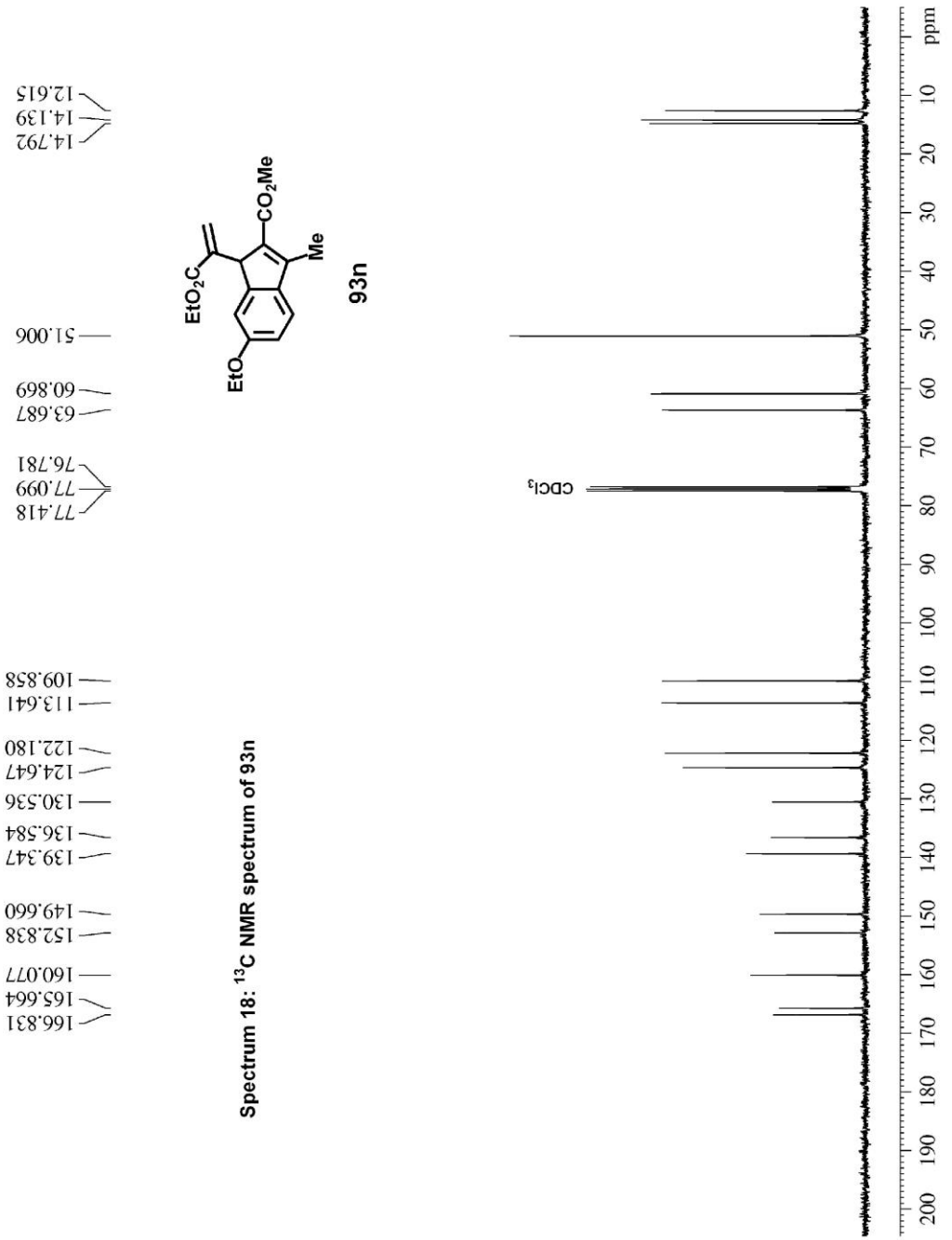


Spectrum 15: ^{1}H NMR spectrum of 93g

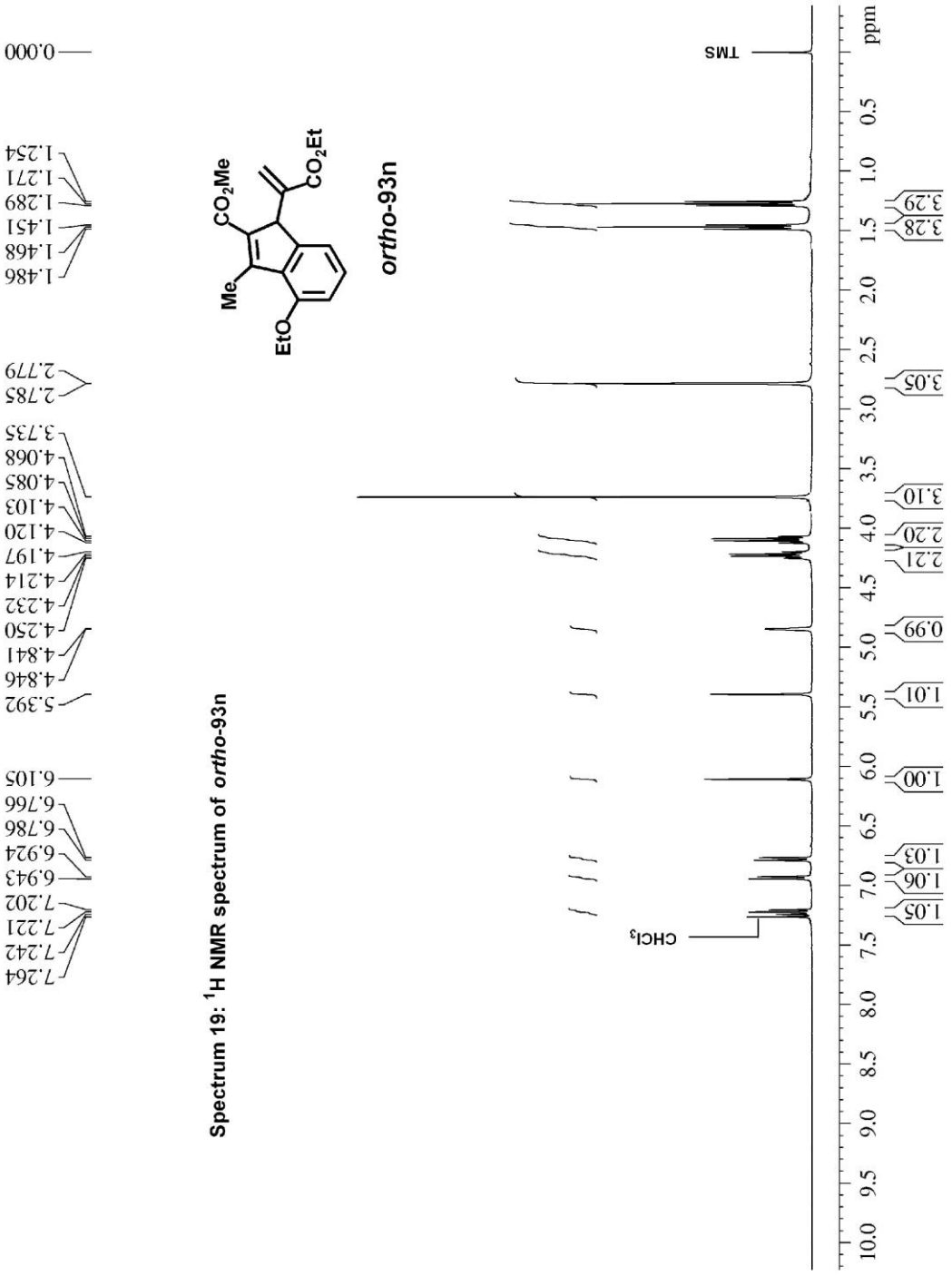


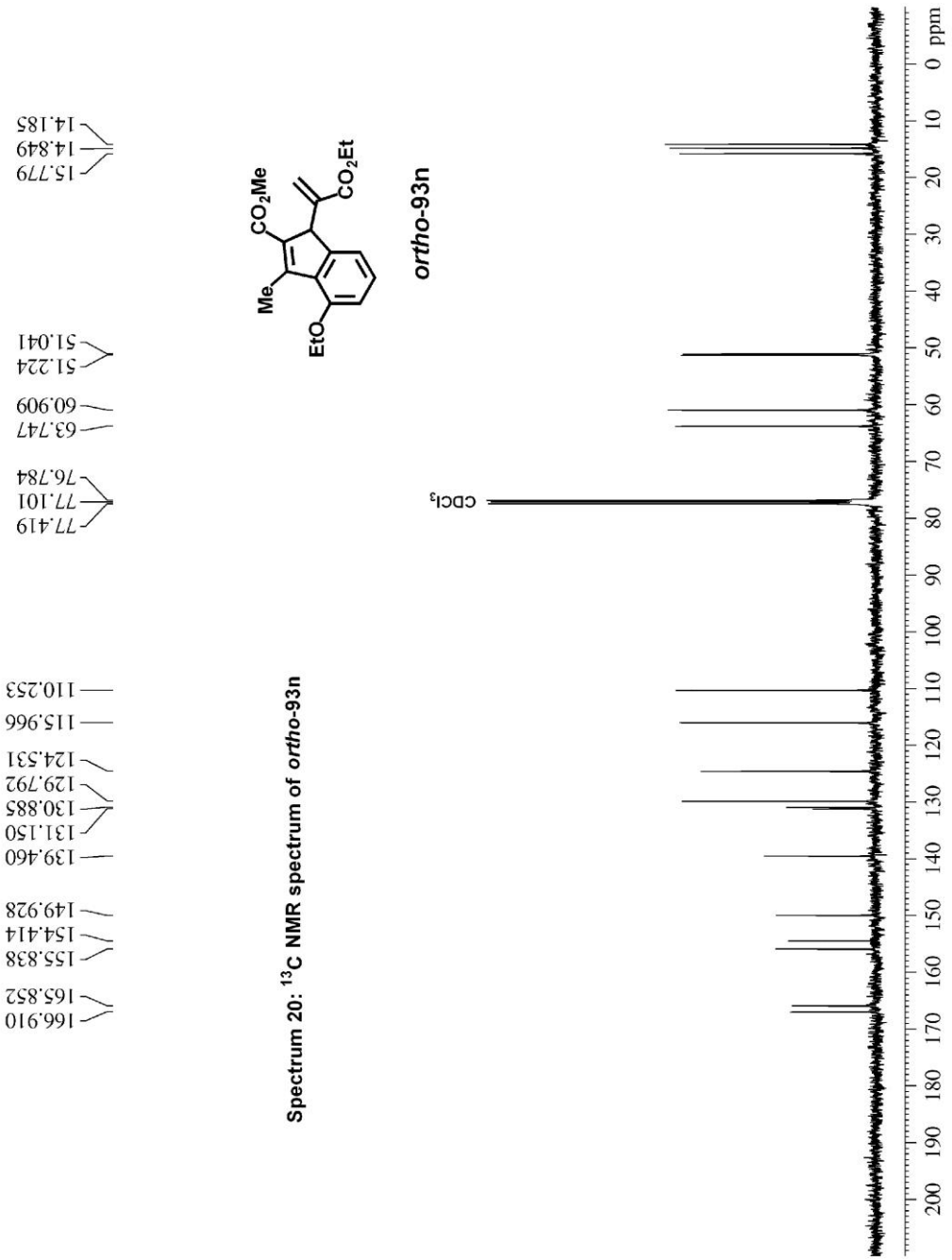
Spectrum 16: ^{13}C NMR spectrum of 93g

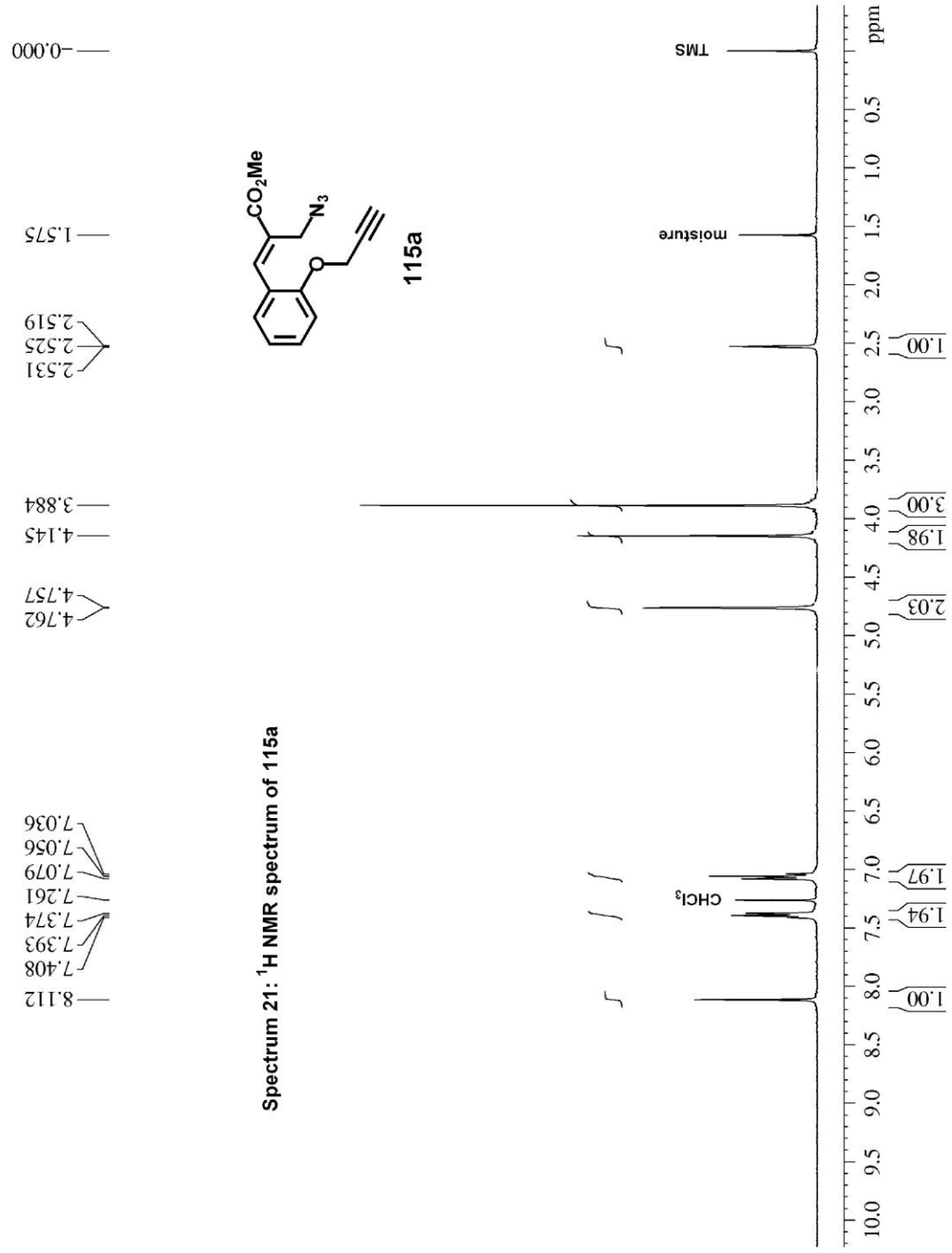

93n
Spectrum 17: ^{1}H NMR spectrum of 93n
TMS
CHCl3
ppm
0.000
1.248
1.266
1.284
1.389
1.407
1.424
2.535
2.541
3.745
4.010
4.027
4.045
4.062
4.212
4.217
4.230
4.234
4.826
4.831
5.404
6.125
6.863
6.869
6.884
6.890
6.925
6.929
7.262
7.350
7.371
1.08
0.99
1.09
1.02
1.02
1.00
2.16
2.14
3.16
3.20
3.25
3.35

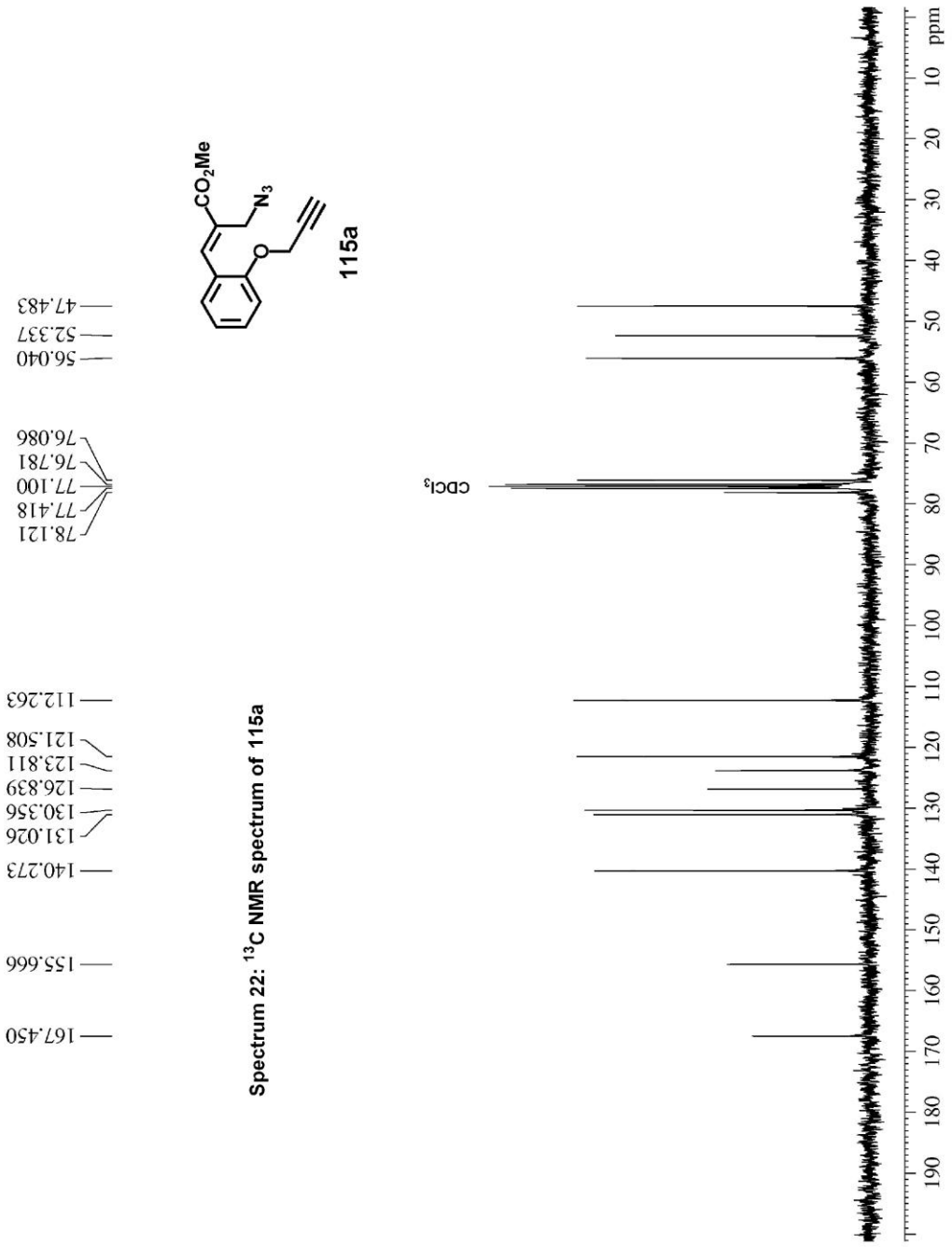


Spectrum 18: ^{13}C NMR spectrum of 93n

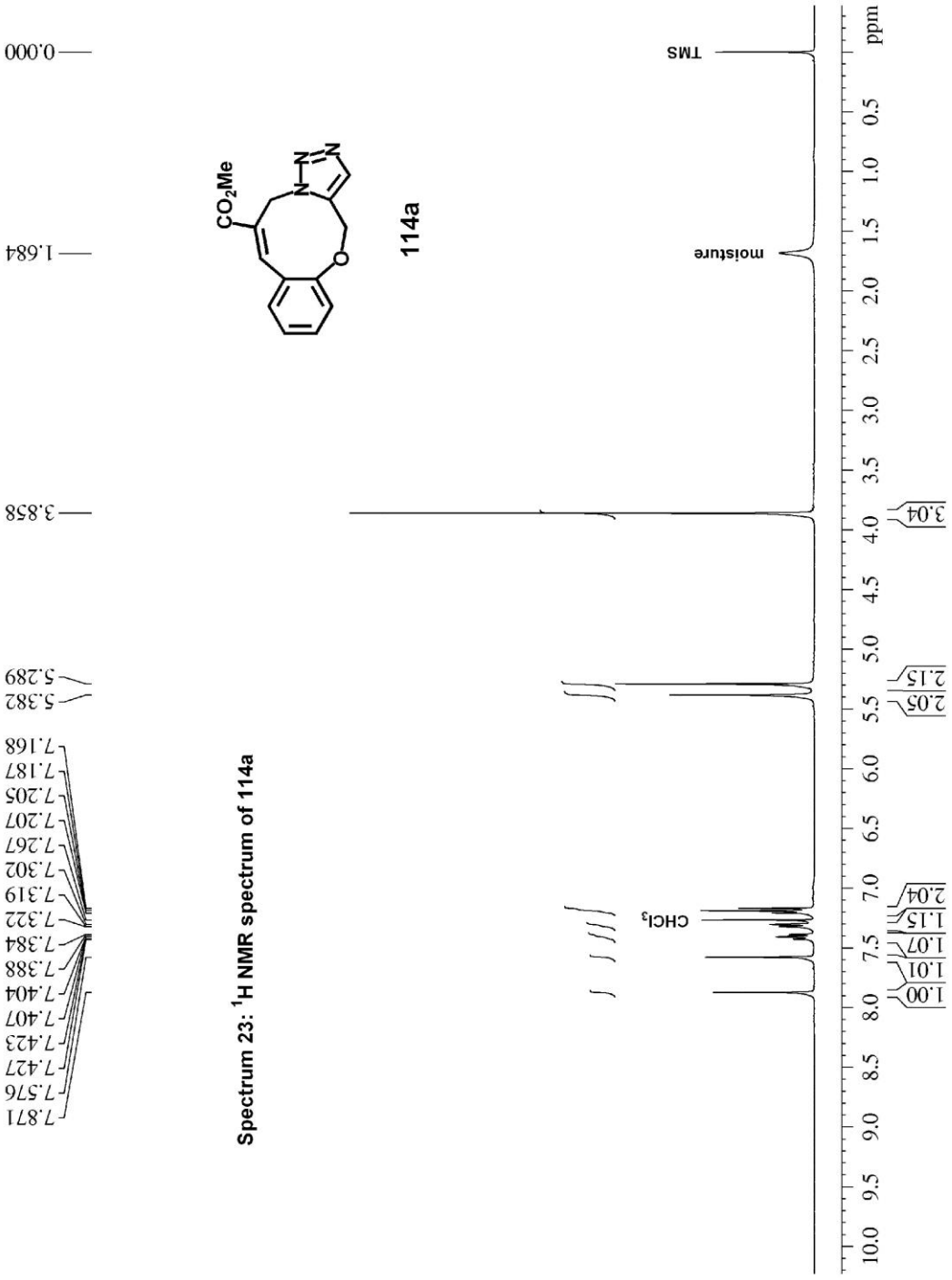

0.000
1.254
1.271
1.289
1.451
1.468
1.486
2.779
2.785
3.735
4.068
4.085
4.103
4.120
4.197
4.214
4.232
4.250
4.841
4.846
5.392
6.105
6.766
6.786
6.924
6.943
7.202
7.221
7.242
7.264
Me
CO2Me
CO2Et
EtO
ortho-93n
Spectrum 19: 1H NMR spectrum of ortho-93n
TMS
CHCl3
1.05
1.06
1.03
1.00
1.01
0.99
2.21
2.20
3.10
3.05
3.28
3.29
ppm


Spectrum 20: ^{13}C NMR spectrum of *ortho*-93n
ortho-93n
CO2Me
CO2Et
Me
EtO
CDCl3
ppm
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
14.185
14.849
15.779
51.041
51.224
60.909
63.747
76.784
77.101
77.419
110.253
115.966
124.531
129.792
130.885
131.150
139.460
149.928
154.414
155.838
165.852
166.910

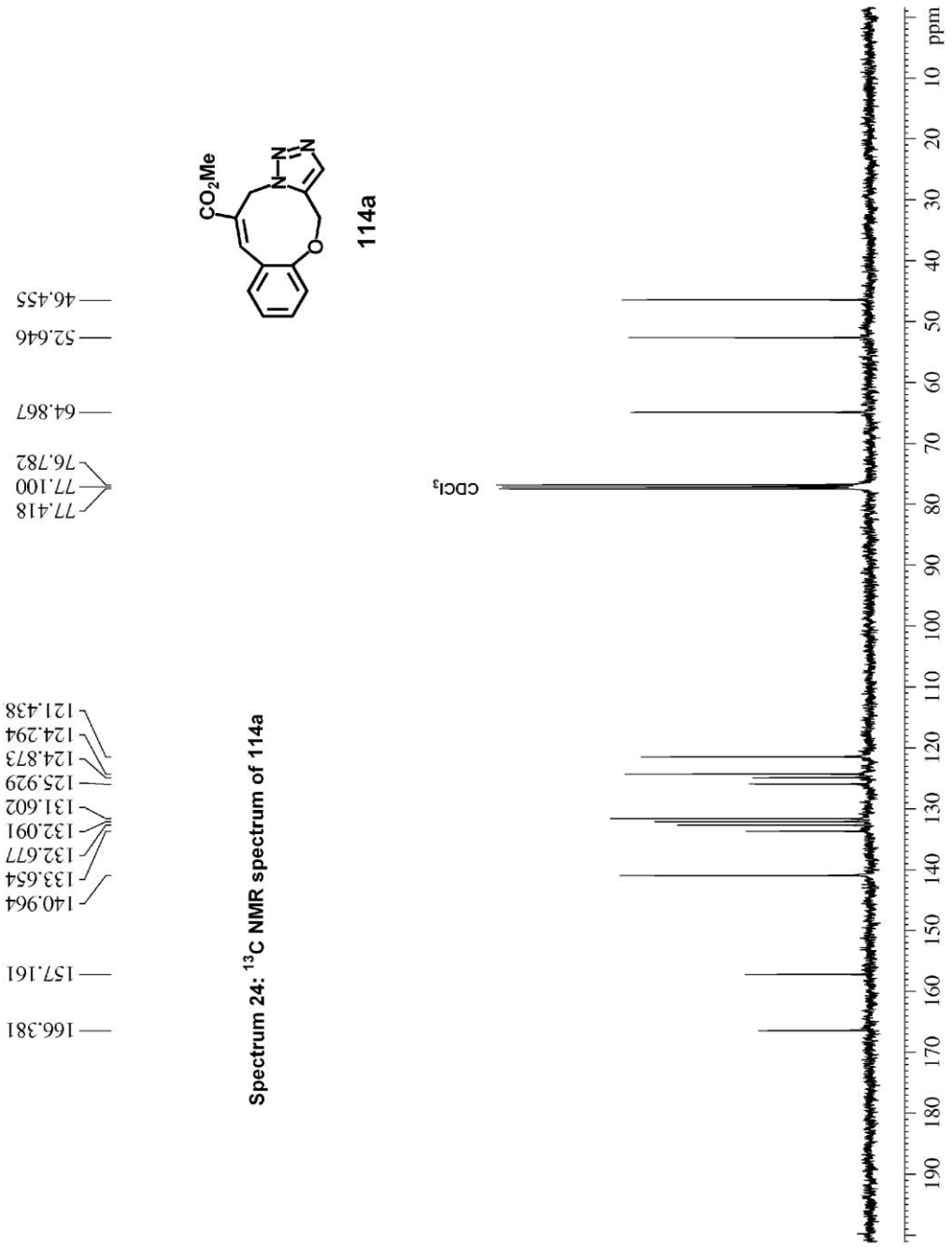

Spectrum 21: ^{1}H NMR spectrum of 115a
115a
CO_2Me
N_3
TMS
moisture
$CHCl_3$
ppm
0.000
1.575
2.519
2.525
2.531
3.884
4.145
4.757
4.762
7.036
7.056
7.079
7.261
7.374
7.393
7.408
8.112
1.00
1.94
1.97
1.98
3.00
2.03
1.00

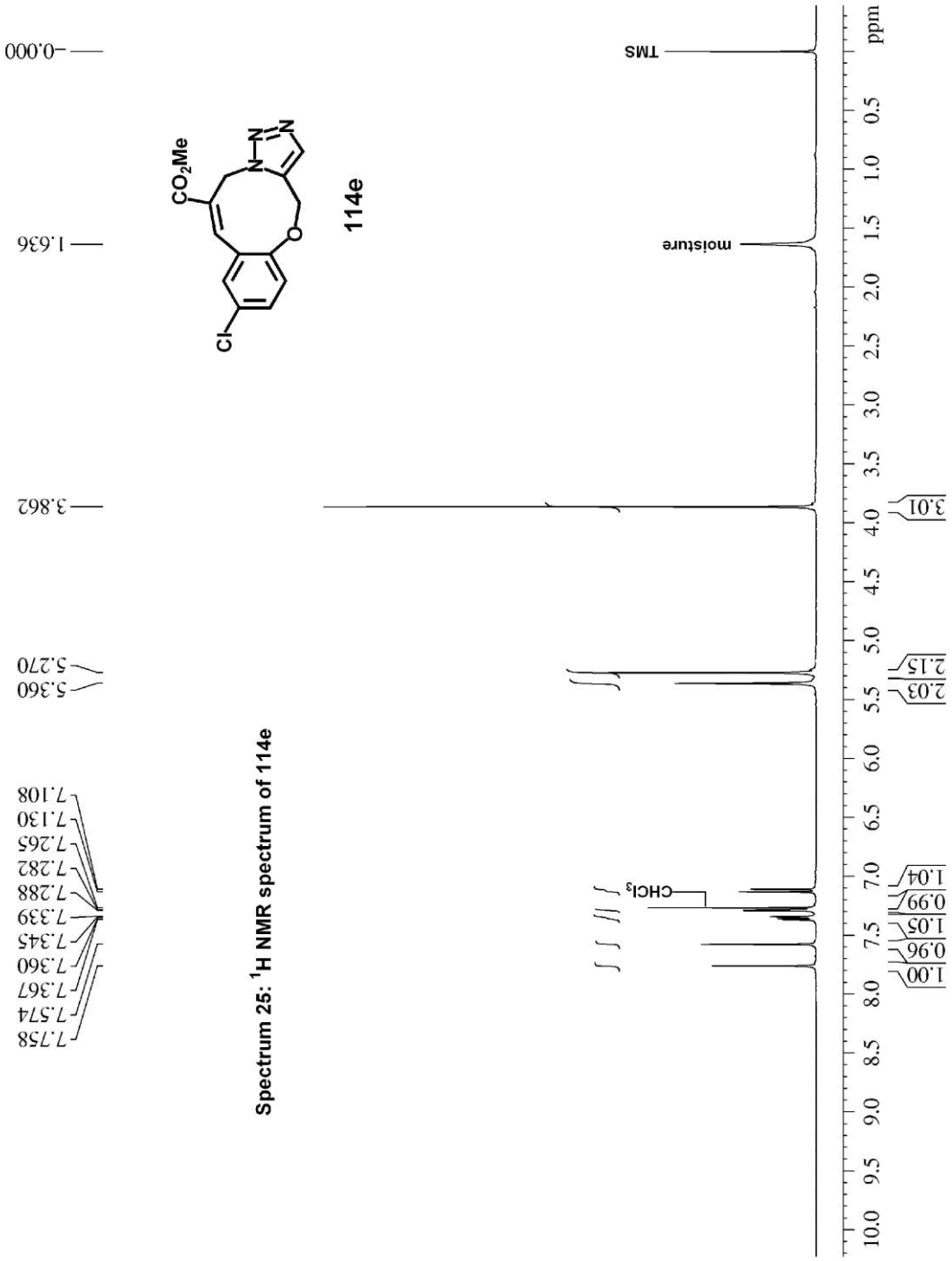


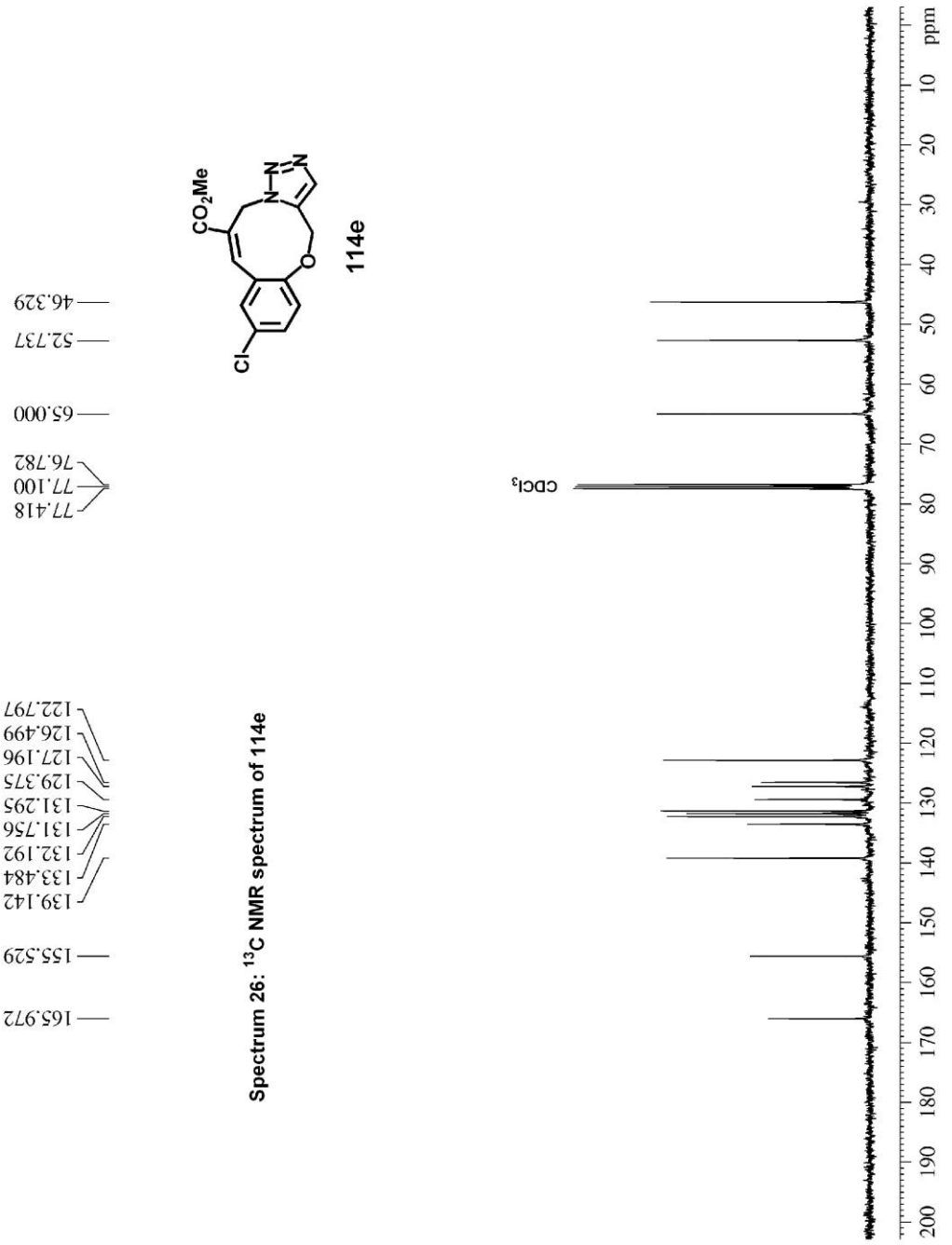
Spectrum 22: ^{13}C NMR spectrum of 115a



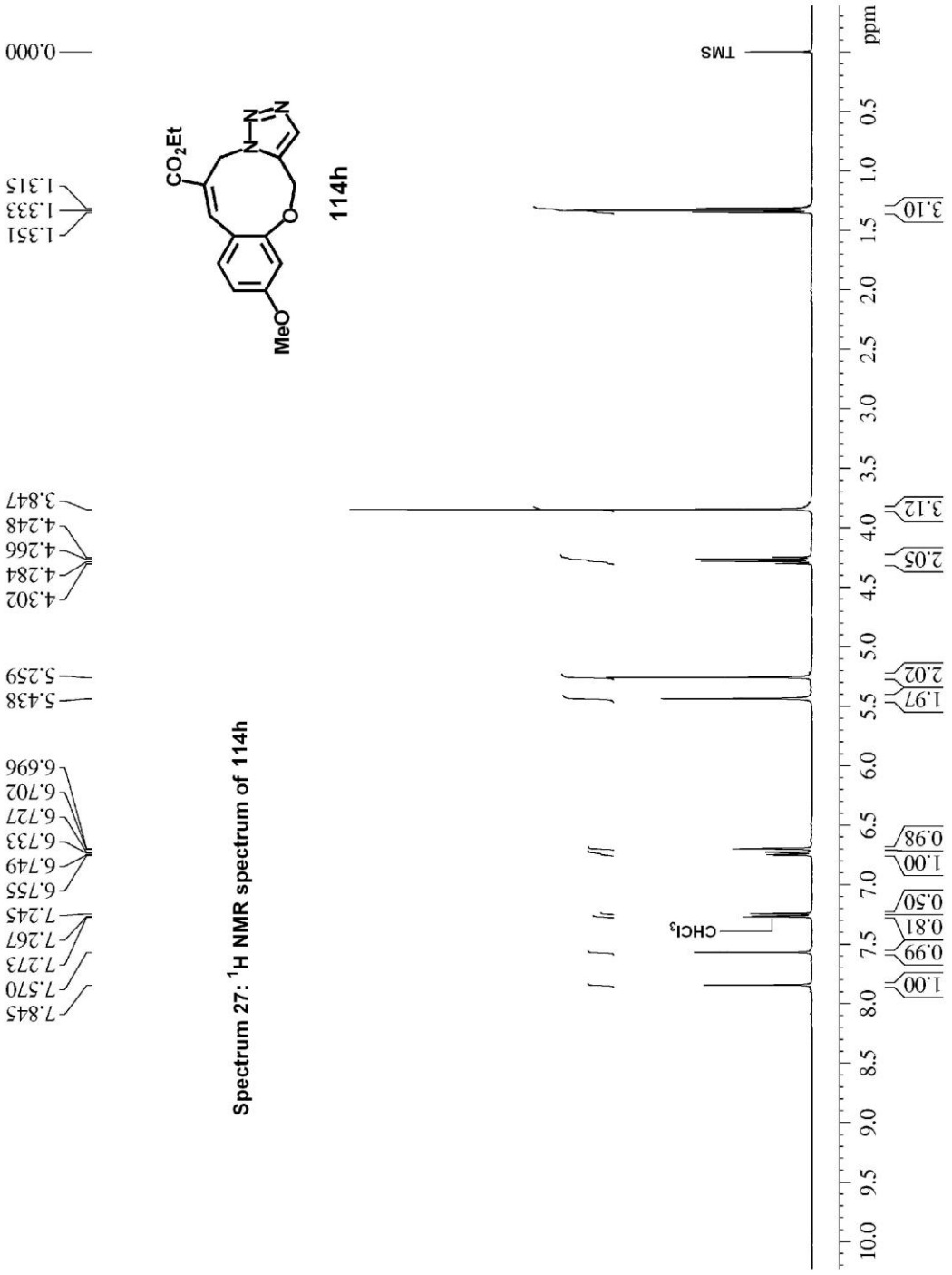
Spectrum 23: ^{1}H NMR spectrum of 114a


CO2Me
114a
Spectrum 24: 13C NMR spectrum of 114a
CDCl3
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
46.455
52.646
64.867
76.782
77.100
77.418
121.438
124.294
124.873
125.929
131.602
132.091
132.677
133.654
140.964
157.161
166.381

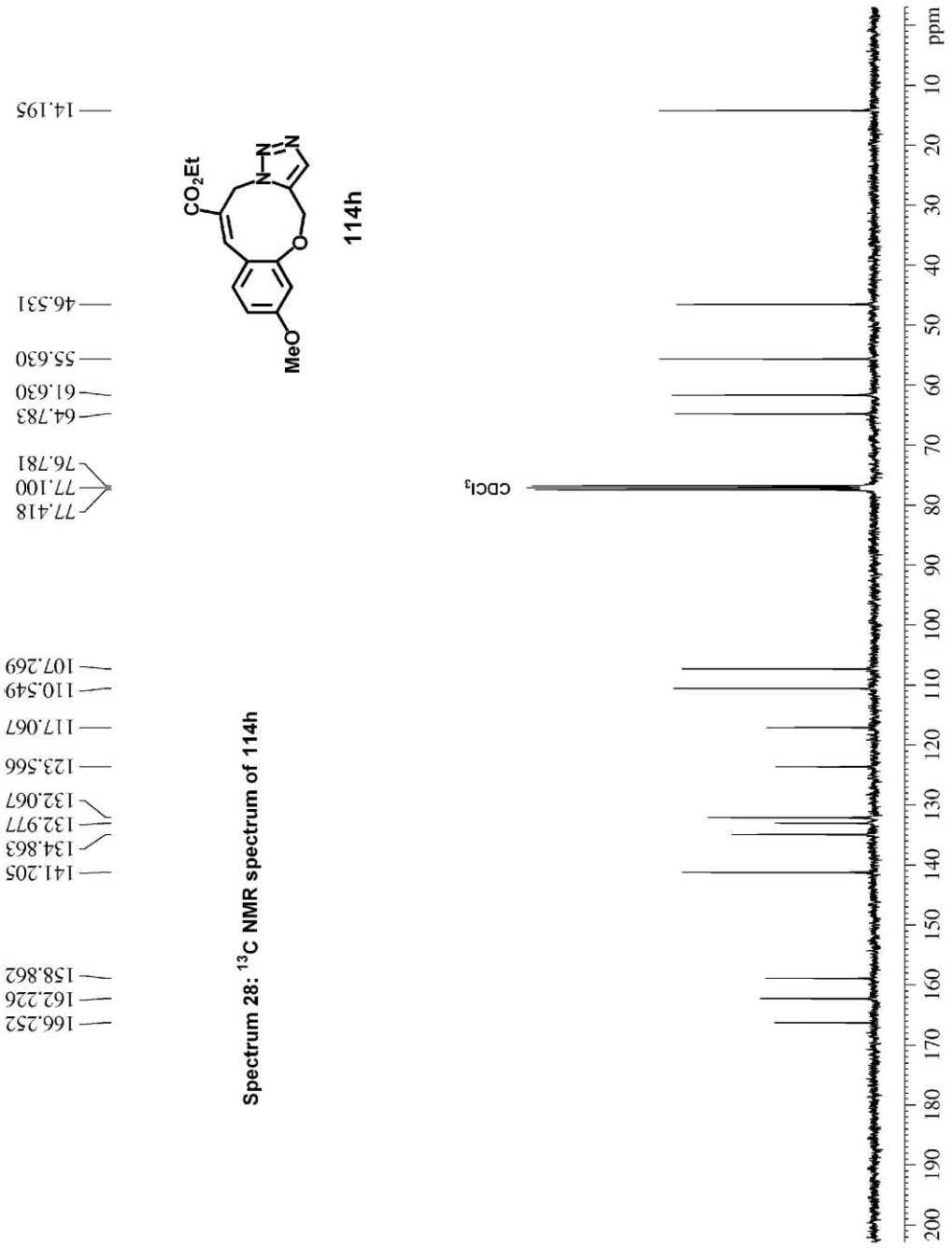

114e
Spectrum 25: ^{1}H NMR spectrum of 114e
TMS
moisture
CHCl3
ppm
0.000
1.636
3.862
5.270
5.360
7.108
7.130
7.265
7.282
7.288
7.339
7.345
7.360
7.367
7.574
7.758
1.00
0.96
1.05
0.99
1.04
2.03
2.15
3.01



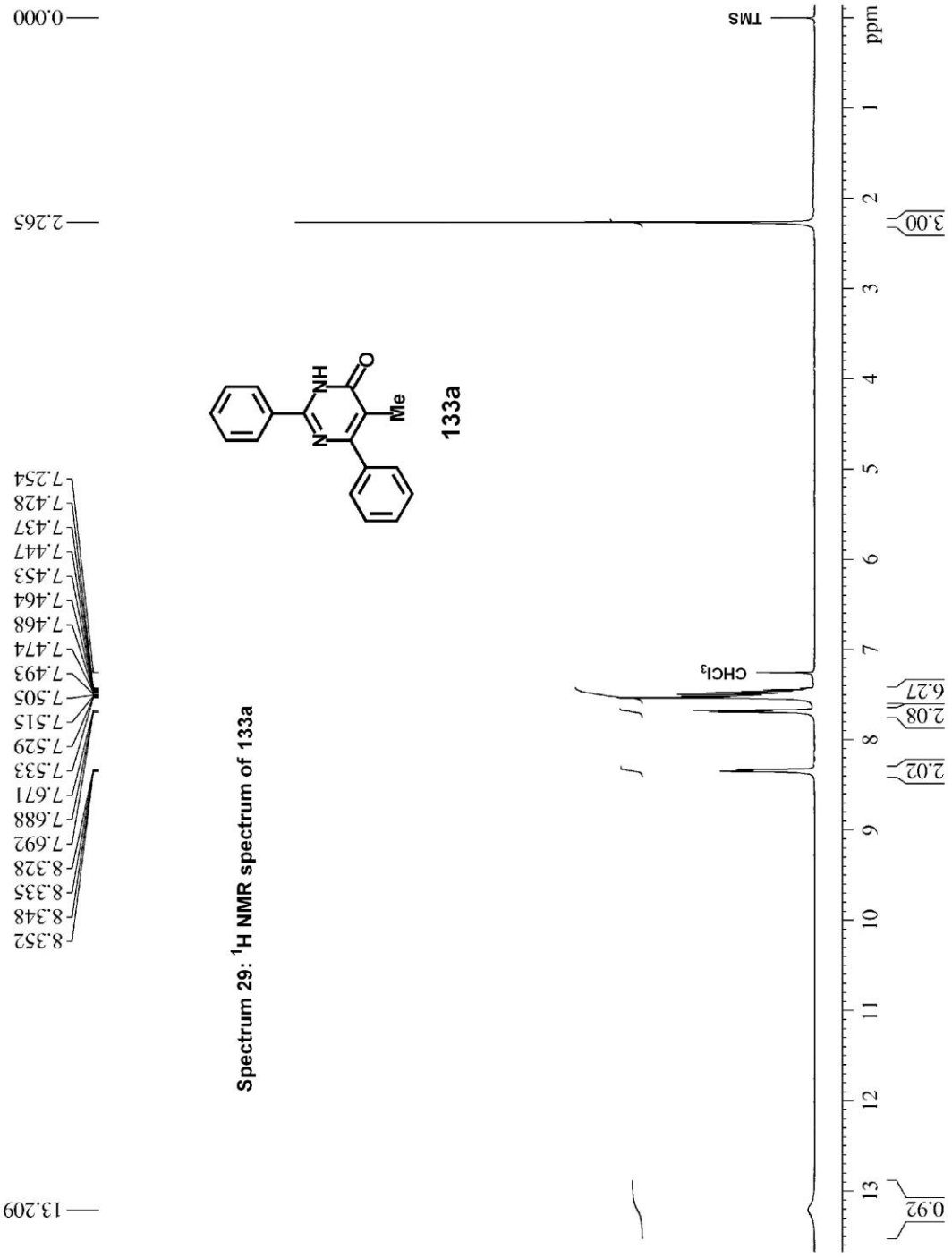
Spectrum 26: ^{13}C NMR spectrum of 114e



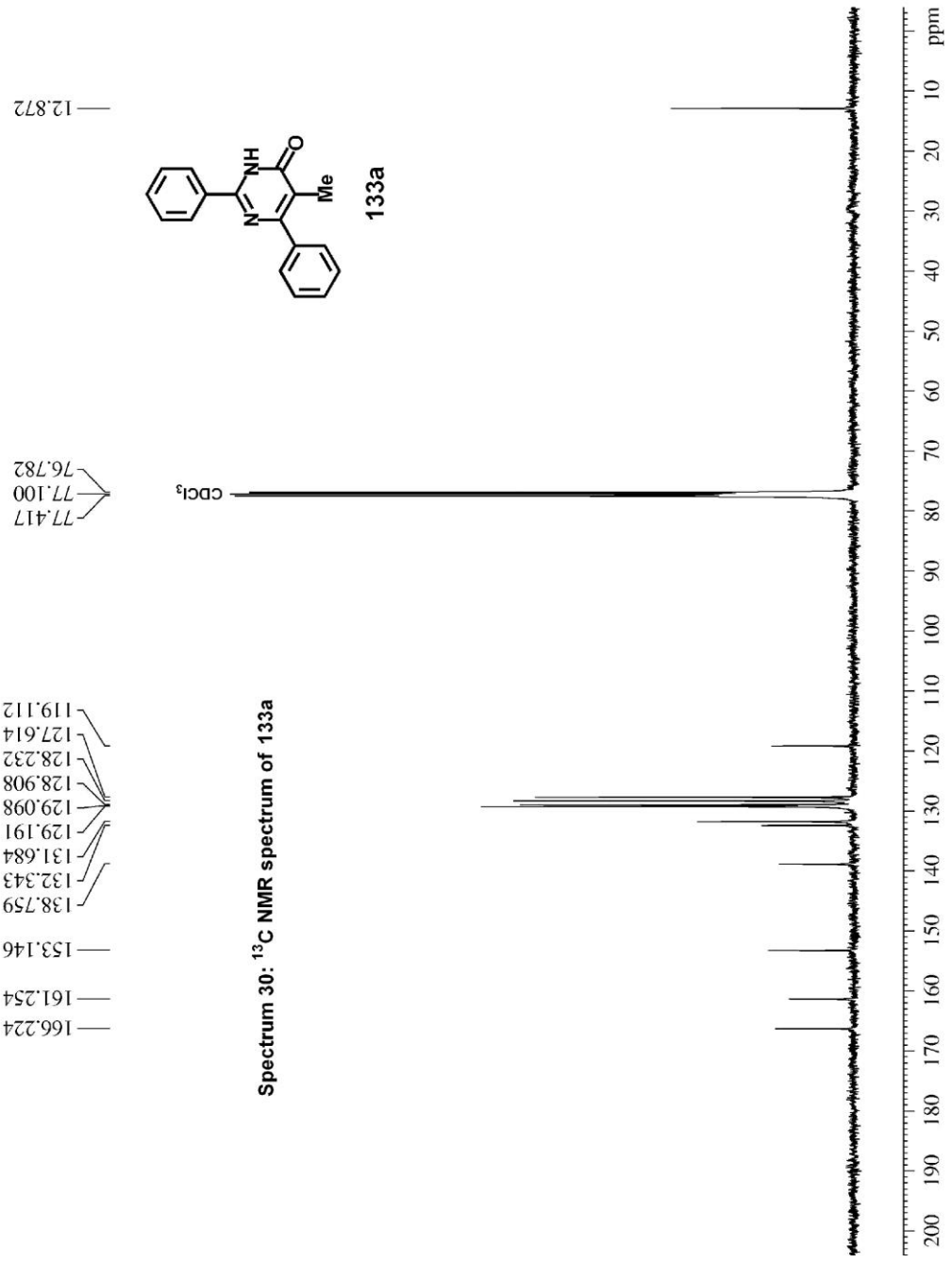
Spectrum 27: ^{1}H NMR spectrum of 114h

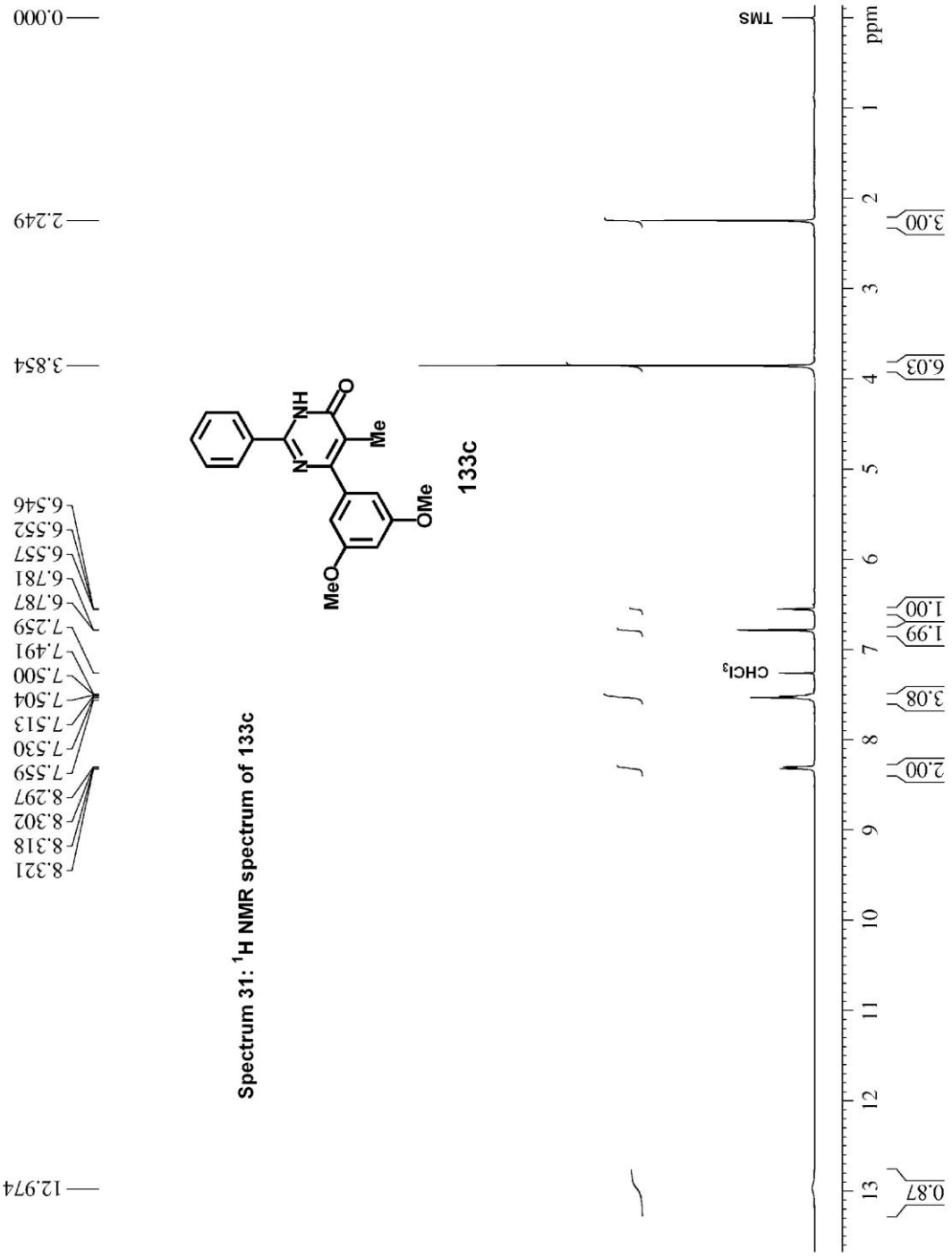


Spectrum 28: ^{13}C NMR spectrum of 114h

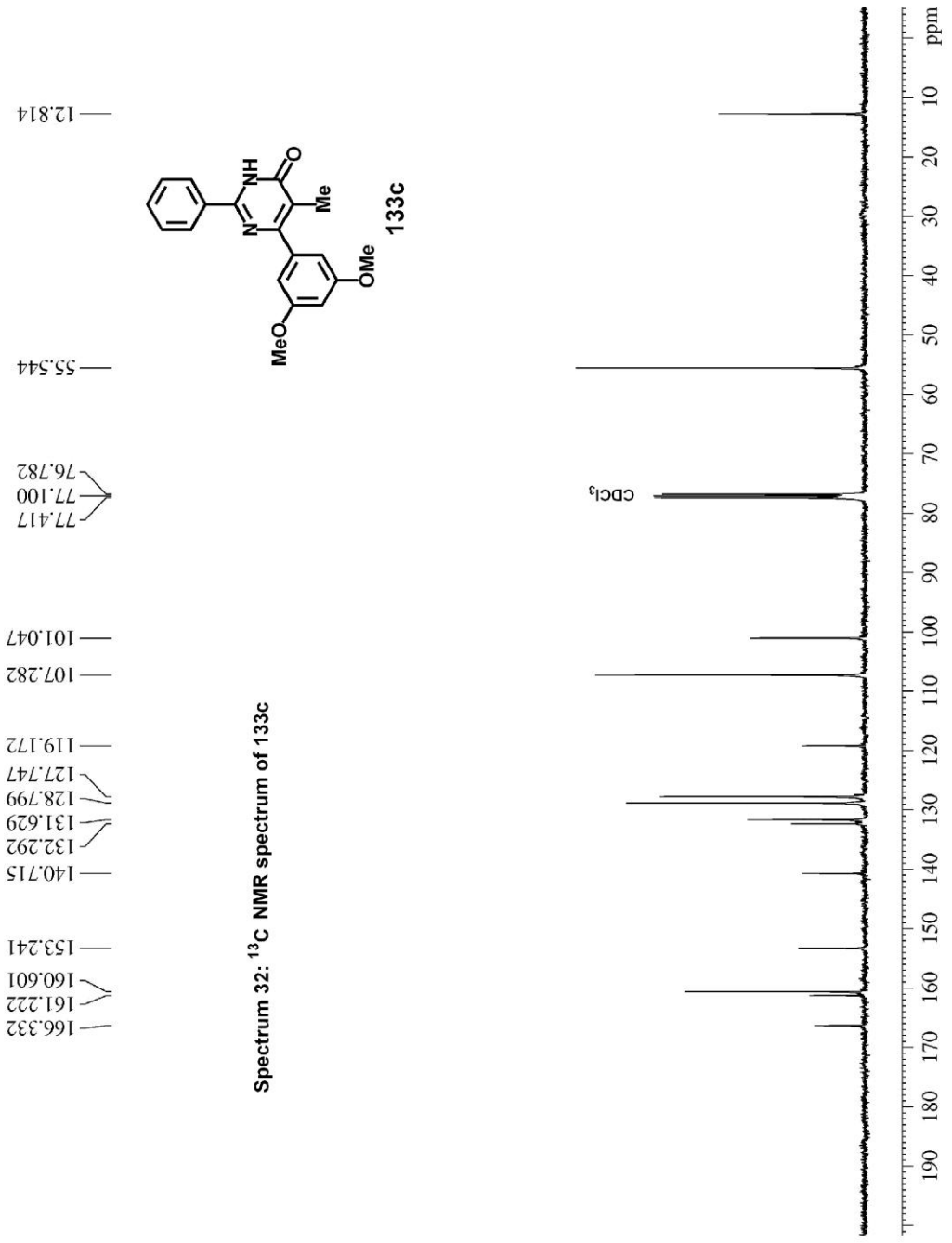


Spectrum 29: ^{1}H NMR spectrum of 133a

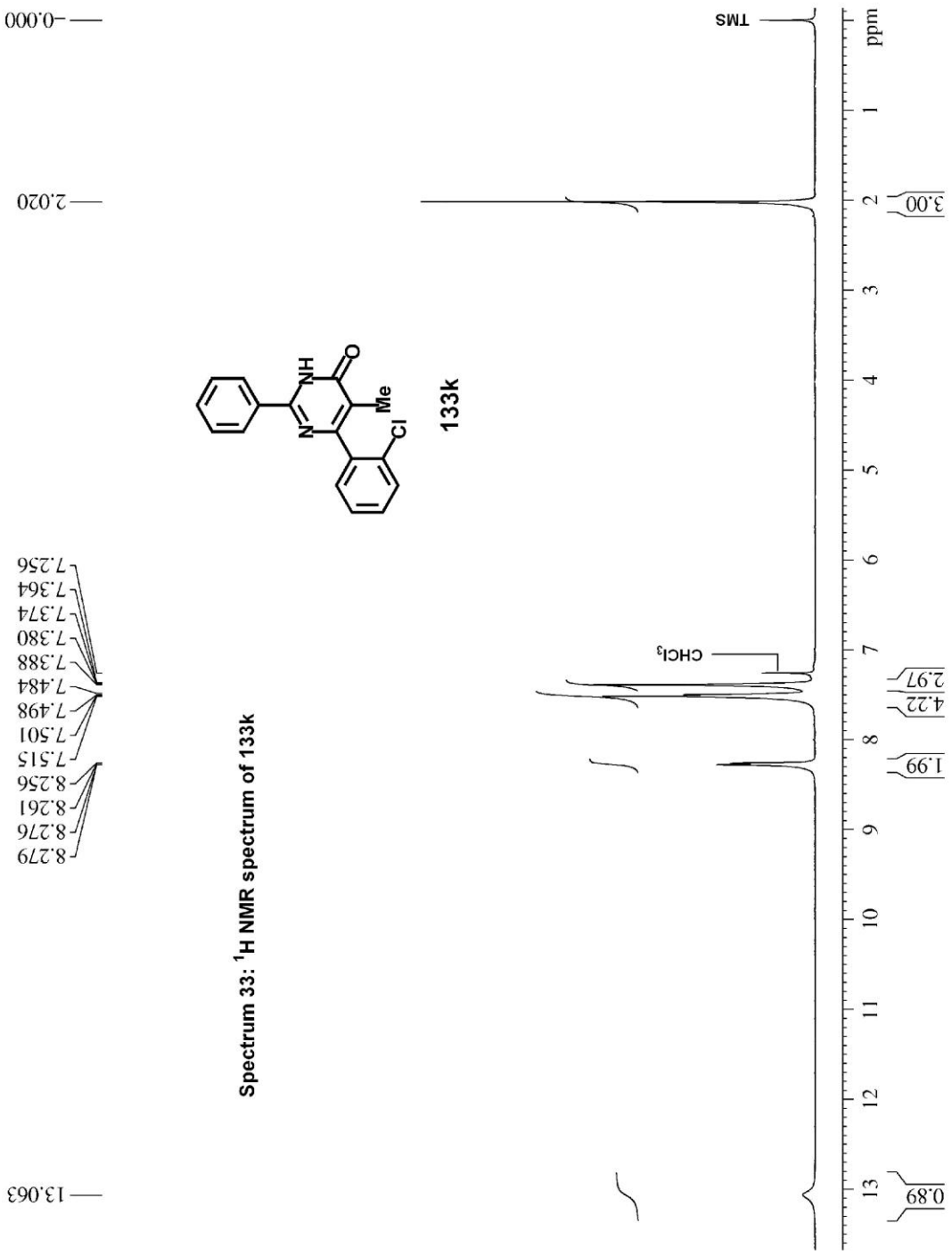

Spectrum 30: ^{13}C NMR spectrum of 133a
133a
NH
O
N
Me
CDCl3
12.872
76.782
77.100
77.417
119.112
127.614
128.232
128.908
129.098
129.191
131.684
132.343
138.759
153.146
161.254
166.224
ppm



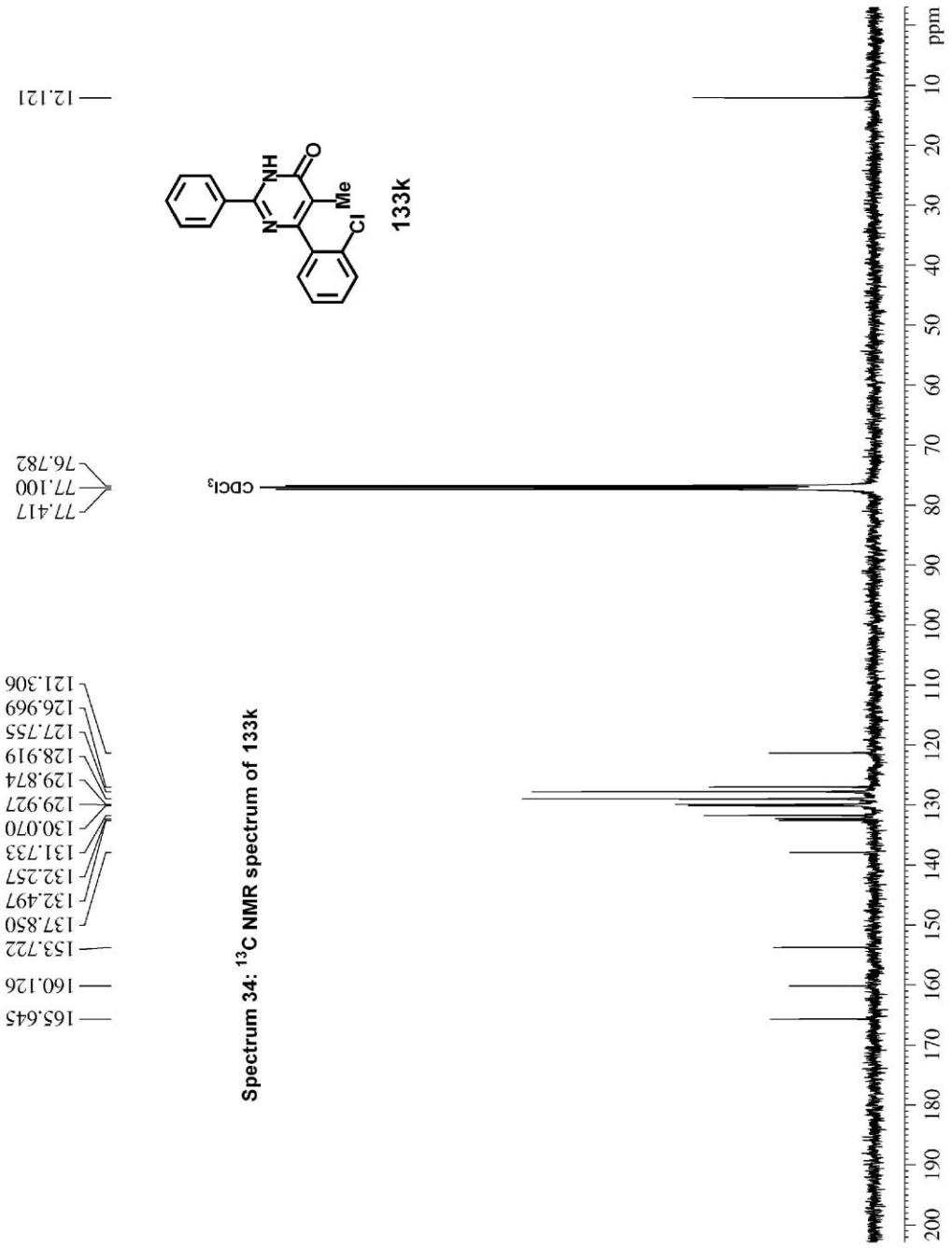
Spectrum 31: ^{1}H NMR spectrum of 133c



Spectrum 32: ^{13}C NMR spectrum of 133c



Spectrum 33: ^{1}H NMR spectrum of 133k



Spectrum 34: ^{13}C NMR spectrum of 133k

APPENDIX

(X-RAY CRYSTALLOGRAPHIC DATA)

Table I. Atomic coordinates ($x10^4$) and equivalent isotropic displacement parameters (A^2x10^3) for **93b**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	x	y	z	U (eq)
C(1)	9523(2)	9348(2)	3562(2)	43(1)
C(2)	7871(2)	9703(2)	4750(2)	48(1)
C(3)	7202(2)	11230(2)	4894(2)	51(1)
C(4)	8179(2)	13582(2)	3507(2)	62(1)
C(5)	9442(3)	14021(2)	2434(2)	66(1)
C(6)	10846(2)	12911(2)	1689(2)	57(1)
C(7)	11001(2)	11350(2)	1979(2)	50(1)
C(8)	9718(2)	10928(2)	3044(2)	44(1)
C(9)	8313(2)	12019(2)	3822(2)	49(1)
C(10)	9614(2)	8795(2)	2350(2)	42(1)
C(11)	8302(2)	9093(2)	2037(2)	59(1)
C(12)	11321(2)	7933(2)	1469(2)	45(1)
C(13)	12943(2)	6687(2)	-526(2)	71(1)
C(14)	7180(2)	8498(2)	5684(2)	54(1)
C(15)	7705(3)	5761(2)	6291(2)	77(1)
C(16)	5645(2)	12050(3)	5973(2)	73(1)
C(17)	13546(3)	12389(3)	-57(2)	85(1)
O(1)	12564(1)	7640(2)	1693(1)	64(1)
O(2)	11340(2)	7495(2)	407(1)	62(1)
O(3)	5862(2)	8715(2)	6634(2)	79(1)
O(4)	8211(2)	7056(2)	5377(1)	64(1)
O(5)	12037(2)	13474(2)	675(2)	78(1)

Table II. Atomic coordinates ($x10^4$) and equivalent isotropic displacement parameters (A^2x10^3) for ***ortho*-93b**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	x	y	z	U (eq)
C(1)	1815(2)	6460(2)	7486(1)	41(1)
C(2)	2010(2)	4891(2)	6891(2)	44(1)
C(3)	2339(2)	4734(2)	5707(2)	42(1)
C(4)	2825(2)	6654(2)	4386(2)	48(1)
C(5)	2885(2)	8142(2)	4407(2)	60(1)
C(6)	2543(2)	9137(2)	5426(2)	64(1)

Atom	x	y	z	U (eq)
C(7)	2162(2)	8703(2)	6466(2)	53(1)
C(8)	2135(2)	7231(2)	6467(1)	42(1)
C(9)	2458(2)	6198(2)	5439(1)	41(1)
C(10)	2991(2)	7477(2)	9065(1)	42(1)
C(11)	4417(2)	7315(2)	9762(2)	56(1)
C(12)	2438(2)	8723(2)	9780(2)	47(1)
C(13)	3084(3)	10834(2)	11940(2)	69(1)
C(14)	1766(2)	3675(2)	7502(2)	53(1)
C(15)	676(3)	2826(3)	9028(3)	95(1)
C(16)	2494(2)	3324(2)	4748(2)	58(1)
C(17)	3561(3)	6080(3)	2361(2)	81(1)
O(1)	1185(2)	8954(2)	9187(1)	72(1)
O(2)	3472(1)	9550(1)	11173(1)	64(1)
O(3)	2187(2)	2541(2)	7266(2)	81(1)
O(4)	1012(2)	3987(1)	8414(1)	66(1)
O(5)	3124(2)	5597(2)	3403(1)	63(1)

Table III. Atomic coordinates ($x10^4$) and equivalent isotropic displacement parameters (A^2x10^3) for **98**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	x	y	z	U (eq)
C(1)	1938(3)	8855(2)	3480(2)	32(1)
C(2)	1762(3)	7566(3)	4926(3)	35(1)
C(3)	2051(3)	7821(3)	6040(3)	36(1)
C(4)	2880(3)	10050(3)	6134(3)	42(1)
C(5)	3165(3)	11460(3)	5295(3)	45(1)
C(6)	3095(3)	12098(3)	3793(3)	41(1)
C(7)	2714(3)	11332(3)	3090(3)	38(1)
C(8)	2402(3)	9927(3)	3940(2)	33(1)
C(9)	2480(3)	9279(3)	5440(3)	34(1)
C(10)	3235(3)	8269(3)	2410(3)	37(1)
C(11)	4574(4)	6981(3)	2792(3)	59(1)
C(12)	2978(4)	9211(3)	834(3)	54(1)
C(13)	1359(5)	11622(4)	-917(3)	94(1)
C(14)	1096(3)	6356(3)	5013(3)	40(1)
C(15)	1951(4)	6887(3)	7641(3)	50(1)
C(16)	3183(4)	14294(3)	1576(3)	74(1)
O(1)	3790(3)	8802(3)	-124(2)	111(1)
O(2)	1731(3)	10596(2)	577(2)	57(1)
O(3)	949(2)	5242(2)	6200(2)	53(1)
O(4)	681(2)	6527(2)	3792(2)	48(1)
O(5)	3427(2)	13499(2)	3090(2)	59(1)

Table IV. Atomic coordinates ($x10^4$) and equivalent isotropic displacement parameters (A^2x10^3) for **93c**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	x	y	z	U (eq)
C(1)	3966(1)	6585(2)	-376(1)	33(1)
C(2)	4691(1)	7458(2)	-228(1)	37(1)
C(3)	5345(1)	7219(2)	464(1)	37(1)
C(4)	5551(1)	5570(2)	1536(1)	38(1)
C(5)	5174(1)	4595(2)	1731(1)	38(1)
C(6)	4366(1)	4207(2)	1230(1)	35(1)
C(7)	3918(1)	4796(2)	529(1)	33(1)
C(8)	4306(1)	5783(2)	343(1)	31(1)
C(9)	5114(1)	6192(2)	832(1)	33(1)
C(10)	3210(1)	7416(2)	-563(1)	34(1)
C(11)	3236(1)	8676(2)	-302(1)	50(1)
C(12)	2424(1)	6684(2)	-1041(1)	41(1)
C(13)	990(1)	6836(3)	-1658(1)	83(1)
C(14)	4688(1)	8343(2)	-788(1)	43(1)
C(15)	3951(1)	9003(3)	-2045(1)	74(1)
C(16)	6183(1)	7815(2)	811(1)	54(1)
C(17)	6844(1)	5175(3)	2649(1)	72(1)
C(18)	3311(1)	2595(2)	987(1)	57(1)
O(1)	2363(1)	5507(2)	-1268(1)	68(1)
O(2)	1781(1)	7457(2)	-1195(1)	61(1)
O(3)	5238(1)	9080(2)	-704(1)	67(1)
O(4)	3985(1)	8232(1)	-1446(1)	53(1)
O(5)	6341(1)	5987(2)	1996(1)	55(1)
O(6)	4073(1)	3217(1)	1496(1)	47(1)

Table V. Atomic coordinates ($x10^4$) and equivalent isotropic displacement parameters (A^2x10^3) for **93h**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	x	y	z	U (eq)
C(1)	8383(3)	9077(2)	-251(2)	46(1)
C(2)	7470(3)	9819(2)	-274(3)	47(1)
C(3)	7900(3)	10251(2)	670(3)	48(1)
C(4)	9975(4)	10017(2)	2470(3)	55(1)
C(5)	11114(4)	9508(3)	2947(3)	61(1)
C(6)	11462(4)	8857(2)	2366(3)	58(1)
C(7)	10631(3)	8669(2)	1318(3)	54(1)
C(8)	9477(3)	9161(2)	862(3)	45(1)
C(9)	9143(3)	9838(2)	1398(3)	48(1)

Atom	x	y	z	U (eq)
C(10)	7595(3)	8263(2)	-390(2)	45(1)
C(11)	6537(4)	8131(2)	-18(3)	67(1)
C(12)	8125(4)	7603(2)	-953(3)	54(1)
C(13)	7628(5)	6345(3)	-1946(4)	98(2)
C(14)	6296(4)	10020(2)	-1249(3)	54(1)
C(15)	5190(4)	9650(3)	-3109(3)	78(1)
C(16)	5328(4)	8989(3)	-3883(3)	99(2)
C(17)	7305(4)	11035(2)	950(3)	74(1)
C(18)	10559(5)	11320(3)	3353(4)	94(2)
C(19)	11544(5)	9185(4)	4802(3)	116(2)
C(20)	13145(4)	7818(3)	2351(4)	88(1)
O(1)	9285(3)	7593(2)	-1039(2)	77(1)
O(2)	7196(3)	7012(2)	-1369(2)	78(1)
O(3)	5422(3)	10545(2)	-1310(2)	77(1)
O(4)	6301(2)	9528(2)	-2090(2)	64(1)
O(5)	9601(3)	10640(2)	3044(2)	74(1)
O(6)	11929(3)	9665(2)	4014(2)	80(1)
O(7)	12646(3)	8434(2)	2924(2)	80(1)

Table VI. Atomic coordinates ($x10^4$) and equivalent isotropic displacement parameters (A^2x10^3) for **93k**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	x	y	z	U (eq)
C(1)	3057(4)	4187(2)	2118(1)	46(1)
C(2)	5113(4)	4090(2)	1537(1)	46(1)
C(3)	5810(4)	5407(2)	1290(1)	47(1)
C(4)	4365(4)	7952(2)	1648(2)	58(1)
C(5)	2832(5)	8701(2)	2118(2)	63(1)
C(6)	1280(4)	8010(2)	2639(2)	56(1)
C(7)	1232(4)	6530(2)	2688(1)	48(1)
C(8)	2781(3)	5782(2)	2210(1)	44(1)
C(9)	4378(4)	6465(2)	1701(1)	47(1)
C(10)	3239(4)	3404(2)	2962(1)	46(1)
C(11)	1706(5)	2413(3)	3161(2)	68(1)
C(12)	5228(4)	3810(2)	3573(2)	52(1)
C(13)	7123(6)	3464(4)	4934(2)	95(1)
C(14)	5872(4)	2690(2)	1250(2)	53(1)
C(15)	8762(5)	1327(3)	614(2)	85(1)
C(16)	7655(4)	5823(3)	688(2)	61(1)
C(17)	-1847(4)	8295(3)	3600(2)	66(1)
C(18)	-3055(6)	9520(3)	4019(3)	103(1)
O(1)	6692(3)	4669(2)	3427(1)	85(1)

Atom	x	y	z	U (eq)
O(2)	5212(4)	3137(2)	4324(1)	78(1)
O(3)	4700(4)	1614(2)	1272(2)	90(1)
O(4)	7967(3)	2683(2)	928(1)	71(1)
O(5)	-111(3)	8896(2)	3092(1)	77(1)

Table VII. Atomic coordinates ($x10^4$) and equivalent isotropic displacement parameters (A^2x10^3) for ***ortho*-93k**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	x	y	z	U (eq)
C(1)	1919(3)	2969(3)	2183(1)	46(1)
C(2)	28(3)	3818(3)	2506(1)	46(1)
C(3)	-779(3)	2606(3)	3070(1)	47(1)
C(4)	381(3)	-802(3)	3714(1)	54(1)
C(5)	1849(3)	-2241(3)	3695(2)	66(1)
C(6)	3458(3)	-2013(3)	3194(2)	68(1)
C(7)	3651(3)	-369(3)	2700(1)	58(1)
C(8)	2172(3)	1070(3)	2706(1)	46(1)
C(9)	538(3)	869(3)	3205(1)	46(1)
C(10)	1875(3)	2994(2)	1205(1)	43(1)
C(11)	264(3)	3105(3)	748(1)	55(1)
C(12)	3794(3)	2781(3)	798(1)	51(1)
C(13)	5478(4)	2501(4)	-498(2)	86(1)
C(14)	-810(3)	5728(3)	2227(1)	53(1)
C(15)	-320(4)	8526(3)	1422(2)	68(1)
C(16)	-2690(3)	2872(3)	3507(2)	65(1)
C(17)	-1508(4)	-2630(3)	4678(2)	68(1)
C(18)	-3359(3)	-2379(4)	5150(2)	75(1)
O(1)	5310(2)	2668(3)	1178(1)	79(1)
O(2)	3672(2)	2717(2)	-49(1)	75(1)
O(3)	-2336(2)	6451(2)	2446(1)	84(1)
O(4)	349(2)	6627(2)	1689(1)	59(1)
O(5)	-1233(2)	-923(2)	4198(1)	66(1)

Table VIII. Atomic coordinates ($x10^4$) and equivalent isotropic displacement parameters (A^2x10^3) for **114a**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	x	y	z	U (eq)
C(1)	8635(1)	6694(1)	2098(1)	22(1)
C(2)	7427(1)	8073(1)	1081(1)	22(1)

Atom	x	y	z	U (eq)
C(3)	7431(1)	9470(1)	1299(1)	20(1)
C(4)	6949(1)	10491(1)	682(1)	24(1)
C(5)	8624(1)	9354(1)	3273(1)	19(1)
C(6)	9464(1)	9274(1)	3433(1)	18(1)
C(7)	9806(1)	8184(1)	3386(1)	21(1)
C(8)	9408(1)	6901(1)	3064(1)	22(1)
C(9)	9823(1)	5837(1)	3727(1)	29(1)
C(10)	9468(1)	4621(1)	3451(1)	34(1)
C(11)	8693(1)	4438(1)	2495(1)	33(1)
C(12)	8275(1)	5470(1)	1809(1)	28(1)
C(13)	9948(1)	10501(1)	3774(1)	20(1)
C(14)	11098(1)	11632(1)	4038(1)	32(1)
N(1)	7198(1)	11569(1)	1295(1)	24(1)
N(2)	7824(1)	11265(1)	2269(1)	21(1)
N(3)	7969(1)	9992(1)	2278(1)	18(1)
O(1)	8263(1)	7727(1)	1408(1)	22(1)
O(2)	9747(1)	11452(1)	4029(1)	28(1)
O(3)	10632(1)	10444(1)	3768(1)	29(1)

Table IX. Atomic coordinates ($x10^4$) and equivalent isotropic displacement parameters (A^2x10^3) for **133e**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	x	y	z	U (eq)
C(1)	3308(2)	5328(2)	8374(1)	18(1)
C(2)	6593(2)	3711(2)	8962(1)	19(1)
C(3)	7847(2)	3022(2)	8209(1)	18(1)
C(4)	6710(2)	3617(2)	7601(1)	17(1)
C(5)	840(2)	6533(2)	8477(1)	19(1)
C(6)	-140(3)	7239(2)	7829(1)	22(1)
C(7)	-2431(3)	8354(2)	7898(1)	26(1)
C(8)	-3780(3)	8767(2)	8617(1)	28(1)
C(9)	-2831(3)	8070(2)	9261(1)	27(1)
C(10)	-531(3)	6968(2)	9197(1)	23(1)
C(11)	10277(2)	1690(2)	8173(1)	21(1)
C(12)	7818(2)	3175(2)	6787(1)	18(1)
C(13)	9918(2)	3308(2)	6518(1)	19(1)
C(14)	10807(2)	3045(2)	5746(1)	20(1)
C(15)	9655(2)	2651(2)	5226(1)	19(1)
C(16)	7565(2)	2527(2)	5489(1)	18(1)
C(17)	6661(2)	2782(2)	6267(1)	18(1)
C(18)	6978(2)	2171(2)	4215(1)	19(1)
C(19)	5202(2)	1889(2)	3844(1)	23(1)

Atom	x	y	z	U (eq)
N(1)	4416(2)	4713(2)	7689(1)	18(1)
N(2)	4338(2)	4902(2)	9001(1)	20(1)
O(1)	7424(2)	3310(2)	9558(1)	25(1)
O(2)	6262(2)	2187(2)	5029(1)	21(1)

Table X. Atomic coordinates ($x10^4$) and equivalent isotropic displacement parameters (A^2x10^3) for **133f**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	x	y	z	U (eq)
C(1)	5011(1)	8923(2)	1610(1)	14(1)
C(2)	6311(1)	10035(2)	848(1)	15(1)
C(3)	7253(1)	10169(2)	1441(1)	15(1)
C(4)	6988(1)	9611(2)	2066(1)	15(1)
C(5)	3797(1)	8234(2)	1691(1)	16(1)
C(6)	3659(2)	7481(2)	2324(1)	19(1)
C(7)	2561(2)	6773(2)	2422(1)	22(1)
C(8)	1571(2)	6822(2)	1894(1)	21(1)
C(9)	1694(2)	7597(2)	1269(1)	22(1)
C(10)	2799(1)	8292(2)	1161(1)	19(1)
C(11)	8426(1)	10976(2)	1318(1)	18(1)
C(12)	7912(1)	9566(2)	2708(1)	15(1)
C(13)	9072(1)	8923(2)	2698(1)	17(1)
C(14)	9911(1)	8838(2)	3304(1)	19(1)
C(15)	9608(2)	9406(2)	3919(1)	20(1)
C(16)	8448(2)	10051(2)	3934(1)	18(1)
C(17)	7589(1)	10118(2)	3334(1)	17(1)
C(18)	7085(1)	11240(2)	4641(1)	21(1)
C(19)	7142(2)	11807(2)	5387(1)	23(1)
C(20)	5941(2)	12568(3)	5510(1)	32(1)
N(1)	5856(1)	9034(2)	2157(1)	15(1)
N(2)	5217(1)	9382(2)	969(1)	15(1)
O(1)	6445(1)	10453(2)	252(1)	20(1)
O(2)	8251(1)	10584(2)	4572(1)	25(1)

REFERENCES

(1) Mahrwald, R. *Chem Rev*. **1999**, *99*, 1095.

(2) Reymond, S.; Cossy, J. *Chem. Rev*. **2008**, *108*, 5359.

(3) Poon, T.; Mundy, B. P.; Shattuck, T. W. *J. Chem. Educ.* **2002**, *79*, 264.

(4) Mikami, K.; Shimizu, M. *Chem. Rev*. **1992**, *92*, 1021.

(5) Walborsky, H. M. *Acc. Chem. Res*. **1990**, *23*, 286.

(6) Monfette, S.; Fogg, D. E. *Chem. Rev.* **2009,** *109*, 3783.

(7) Maryanoff, B. E.; Reitz, A. B. *Chem. Rev*. **1989**, *89*, 863.

(8) Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev*. **2000**, *100*, 3009.

(9) Poulsen, T. B.; Jorgensen, K. A. *Chem. Rev*. **2008**, *108*, 2903.

(10) Aktoudianakis, E.; Chan, E.; Edward, A. R.; Jarosz, I.; Lee, V.; Mui, L.; Thatipamala, S. S.; Dicks, A. P. *J. Chem. Educ.* **2008**, *85*, 55.

(11) Baylis, A. B.; Hillman, M. E. D. German patent 2155113, **1972**, *Chem. Abstr*. **1972**, *77*, 34174q.

(12) Hillman, M. E. D.; Baylis, A. B. U. S. Patent 3, 743, 669. **1973**.

(13) Rauhut, M. M.; Currier, H. American Cyanamide Co. U. S. Patent, **1963**, 3074999. *Chem. Abstr*. **1963**, *58*, 11224a.

(14) a) Morita, K.; Suzuki, Z.; Hirose, H. *Bull. Chem. Soc. Jpn.* **1968**, *41*, 2815.
b) Morita, K.; Kobayashi, T. *Bull. Chem. Soc. Jpn.* **1969**, *42*, 2732.

(15) Basavaiah, D.; Reddy, B. S.; Badsara, S. S. *Chem. Rev*. **2010**, *110*, 5447.

(16) Declerck, V.; Martinez, J.; Lamaty, F. *Chem. Rev*. **2009**, *109*, 1.

(17) Singh, V.; Batra, S. *Tetrahedron* **2008**, *64*, 4511.

(18) Basavaiah, D.; Rao, A. J.; Satyanarayana, T. *Chem. Rev*. **2003**, *103*, 811.

(19) Ciganek, E. *Organic Reactions*; Paquette, L. A., Ed; New York: Wiley, **1997**, vol. *51*, p 201.

(20) Basavaiah, D.; Rao, P. D.; Hyma, R. S. *Tetrahedron* **1996**, *52*, 8001.

(21) Drewes, S. E.; Roos, G. H. P. *Tetrahedron* **1988**, *44*, 4653.

(22) Basavaiah, D.; Veeraraghavaiah, G. *Chem. Soc. Rev*. **2012**, *41*, 68.

(23) Basavaiah, D.; Rao, K. V.; Reddy, R. J. *Chem. Soc. Rev*. **2007**, *36*, 1581.

(24) Masson, G.; Housseman, C.; Zhu, J. *Angew. Chem., Int. Ed.* **2007**, *46*, 4614.

(25) Shi, Y-L.; Shi, M. *Eur. J. Org. Chem*. **2007**, 2905.

(26) Shi, Y-L.; Shi, M. *Org. Biomol. Chem.* **2007**, *5*, 1499.

(27) Timmons, C.; Kattuboina, A.; Banerjee, S.; Li, G. *Tetrahedron* **2006**, *62*, 7151.

(28) Redondo, M. C.; Ribagorda, M.; Carreno, M. C. *Org. Lett.* **2010**, *12*, 568.

(29) Basavaiah, D.; Roy, S.; Das, U. *Tetrahedron* **2010**, *66*, 5612.

(30) Karthikeyan, K.; Saranya, N.; Kalaivani, A.; Perumal, P. T. *Synlett* **2010**, 2751.

(31) Abaee, M. S.; Mojtahedi, M. M.; Pasha, G. F.; Akbarzadeh, E.; Shockravi, A.; Mesbah, A. W.; Massa, W., *Org. Lett.* **2011**, *13*, 5282.

(32) Krafft, M. E.; Campbell, M. J.; Kerrigan, S.; Cran, J. W. *Tetrahedron Lett.* **2011**, 5*2*, 1090.

(33) Yadav, L. D. S.; Srivastava, V. P.; Patel, R. *Synlett* **2010**, 1047.

(34) Das, B.; Damodar, K.; Chowdhury, N.; Saritha, D.; Ravikanth, B.; Krishnaiah, M. *Tetrahedron* **2008**, *64*, 9396.

(35) Al-Awadi, N. A.; Ibrahim, M. R.; Abdelhamid, I. A.; Elnagdi, M. H. *Tetrahedron* **2008**, *64*, 8202.

(36) Dordonne, S.; Crousse, B.; Bonnet-Delpon, D.; Legros, J. *Chem. Commun.* **2011**, 5855.

(37) Guerra, K. P.; Afonso, C. A. M. *Tetrahedron* **2011**, *67*, 2562.

(38) You, J.; Xu, J.; Verkade, J. G. *Angew. Chem., Int. Ed.* **2003**, *42*, 5054.

(39) Kuan, H-H.; Reddy, R. J.; Chen, K. *Tetrahedron* **2010**, *66*, 9875.

(40) He, L.; Jian, T-Y.; Ye, S. *J. Org. Chem.* **2007**, *72*, 7466.

(41) Duggan, A. R.; Kaye, P. T. *J. Chem. Res.* **2007**, 148.

(42) He, K.; Zhou, Z. H.; Tang, H. Y.; Zhao, G. F.; Tang, C. C. *Chin. Chem. Lett*. **2005**, *16*, 1427.

(43) He, K.; Zhou, Z.; Zhao, G.; Tang, C. *Heteroat. Chem.* **2006**, *17*, 317.

(44) Marcucci, E.; Martelli, G.; Orena, M.; Rinaldi, S. *Monatsh. Chem.* **2007**, *138*, 27.

(45) Alcaide, B.; Almendros, P.; Aragoncillo, C.; Rodriguez-Acebes, R. *J. Org. Chem*. **2004**, *69*, 826.

(46) Pan, J-F.; Chen, K. *Tetrahedron Lett.* **2004**, *45*, 2541.

(47) Lu, A.; Xu, X.; Gao, P.; Zhou, Z.; Song, H.; Tang. C. *Tetrahedron*: *Asymmetry* **2008**, *19*, 1886.

(48) Guan, X-Y.; Wei, Y.; Shi, M. *Chem. Eur. J.* **2010**, *16*, 13617.

(49) Shah, J.; Yacob, Z.; Bunge, A.; Liebscher, J. *Synlett* **2010**, 2079.

(50) Zhong, F.; Wang, Y.; Han, X.; Huang, K-W.; Lu, Y. *Org. Lett.* **2011**, *13*, 1310.

(51) Takizawa, S.; Kiriyama, K.; Ieki, K.; Sasai, H. *Chem. Commun.* **2011**, 9227.

(52) Guan, X-Y.; Wei, Y.; Shi, M. *Eur. J. Org. Chem.* ***2010***, 4098.

(53) Yuan, K.; Song, H-L.; Hu, Y.; Wu, X-Y. *Tetrahedron* **2009**, *65*, 8185.

(54) Gong, J-J.; Yuan, K.; Wu, X-Y. *Tetrahedron: Asymmetry* **2009**, *20*, 2117.

(55) Nakayama, Y.; Gotanda, T.; Ito, K., *Tetrahedron Lett.* **2011**, *52*, 6234.

(56) Kar, A.; Argade, N. P. *Synthesis* **2005**, 1234.

(57) Hoffmann, H. M. R.; Rabe, J. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 795.

(58) Sugahara, T.; Ogasawara, K. *Synlett* **1999**, 419.

(59) Chapuis, C.; Buchi, G. H.; Wuest, H. *Helv. Chim. Acta* **2005**, *88*, 3069.

(60) Lei, X.; Porco Jr., J. A. *J. Am. Chem. Soc.* **2006**, *128*, 14790.

(61) Akiyama, H.; Fujimoto, T.; Ohshima, K.; Hoshino, K.; Yamamoto, I.; Iriye, R. *Org. Lett.* **1999**, *1*, 427.

(62) Shigetomi, K.; Kishimoto, T.; Shoji, K.; Ubukata, M. *Tetrahedron: Asymmetry* **2008**, *19*, 1444.

(63) de Carvalho e Silveira, G. P.; Coelho, F. *Tetrahedron Lett.* **2005**, *46*, 6477.

(64) Rosini, G.; Borzatta, V.; Paolucci, C.; Righi, P. *Green Chem.* **2008**, *10*, 1146.

(65) Kamal, A.; Krishnaji, T.; Reddy, P. V. *Tetrahedron Lett*. **2007**, *48*, 7232.

(66) Basavaiah, D.; Satyanarayana, T. *Tetrahedron Lett.* **2002**, *43*, 4301.

(67) Chen, C-Y.; Chang, M-Y.; Hsu, R-T.; Chen, S-T.; Chang, N-C. *Tetrahedron Lett*. **2003**, *44*, 8627.

(68) Clive, D. L. J.; Li, Z.; Yu, M. *J. Org. Chem.* **2007**, *72*, 5608.

(69) Feltrin, M. P.; Almeida, W. P. *Synth. Commun.* **2003**, *33*, 1141.

(70) Basavaiah, D.; Pandiaraju, S.; Sarma, P. K. S. *Tetrahedron Lett.* **1994**, *35*, 4227.

(71) Basavaiah, D.; Reddy, R. M. *Tetrahedron Lett.* **2001**, *42*, 3025.

(72) Gowrisankar, S.; Kim, K. H.; Kim, J. N. *Bull. Korean Chem. Soc*. **2008**, *29*, 2537.

(73) Basavaiah, D.; Aravindu, K.; Kumar, K. S.; Reddy, K. R. *Eur. J. Org. Chem.* **2010**, 1843.

(74) Gowrisankar, S.; Lee, K. Y.; Lee, C. G.; Kim, J. N. *Tetrahedron Lett.* **2004**, *45*, 6141.

(75) Du, Y.; Feng, J.; Lu, X. *Org. Lett.* **2005**, *7*, 1987.

(76) Tan, B.; Candeias, N. R.; Barbas, C. F., III. *J. Am. Chem. Soc.* **2011**, *133*, 4672.

(77) Deng, H-P.; Wei, Y.; Shi, M. *Org. Lett.* **2011**, *13*, 3348

(78) Shanbhag, P.; Nareddy, P. R.; Dadwal, M.; Mobin, S. M.; Namboothiri, I. N. N. *Org. Biomol. Chem*. **2010**, *8*, 4867.

(79) Reddy, Y. S.; Kadigachalam, P.; Basak, R. K.; Pal, A. P. J.; Vankar, Y. D. *Tetrahedron Lett.* **2012**, *53*, 132.

(80) Aggarwal, V. K.; Patin, A.; Tisserand, S. *Org. Lett.* **2005**, *7*, 2555.

(81) Basavaiah, D.; Kumaragurubaran, N. *Tetrahedron Lett.* **2001**, *42*, 477.

(82) Basavaiah, D.; Bakthadoss, M.; Pandiaraju, S. *Chem. Commun.* **1998**, 1639.

(83) Basavaiah, D.; Satyanarayana, T. *Org. Lett.* **2001**, *3*, 3619.

(84) Zulykama, Y.; Perumal, P. T. *Tetrahedron Lett.* **2009**, *50*, 3892.

(85) Zhong, W.; Zhao, Y.; Su, W. *Tetrahedron* **2008**, *64*, 5491.

(86) Pirovani, R. V.; Ferreira, B. R. V.; Coelho, F. *Synlett* **2009**, 2333.

(87) Weichert, A.; Hoffmann, H. M. R. *J. Org. Chem.* **1991**, *56*, 4098.

(88) Mehta, G.; Bhat, B. A.; Kumara, T. H. S. *Tetrahedron Lett.* **2009**, *50*, 6597.

(89) Basavaiah, D.; Sharada, D. S.; Veerendhar, A. *Tetrahedron Lett*. **2004**, *45*, 3081.

(90) Selvakumar, N.; Kumar, P. K.; Reddy, K. C. S.; Chary, B. C. *Tetrahedron Lett.* **2007**, *48*, 2021.

(91) Cho, J-H.; Ko, S. Y.; Oh, E.; Park, J. C.; Yoo, J. U. *Helv. Chim. Acta* **2002**, *85*, 3994.

(92) Paioti, P. H. S.; Coelho, F. *Tetrahedron Lett*. **2011**, *52*, 6180.

(93) Basavaiah, D.; Rao, A. J. *Chem. Commun.* **2003**, 604.

(94) Virieux, D.; Guillouzic, A-F.; Cristau, H-J. *Tetrahedron* **2006**, *62*, 3710.

(95) Reddy, C. R.; Reddy, M. D.; Srikanth, B.; Prasad, K. R. *Org. Biomol. Chem*. **2011**, *9*, 6027.

(96) Singh, V.; Batra, S. *Eur. J. Org. Chem.* **2007**, 2970.

(97) Lee, K. Y.; Lee, Y. J.; Kim, J. N. *Bull. Korean Chem. Soc.* **2007**, *28*, 143.

(98) Bakthadoss, M.; Sivakumar, N.; Sivakumar, G.; Murugan, G. *Tetrahedron Lett*. **2008**, *49*, 820.

(99) Basavaiah, D.; Satyanarayana, T. *Chem. Commun.* **2004**, 32.

(100) Basavaiah, D.; Devendar, B.; Lenin, D. V.; Satyanarayana, T. *Synlett* **2009**, 411.

(101) Garrido, N. M.; Garcia, M.; Diez, D.; Sanchez, M. R.; Sanz, F.; Urones, J. G. *Org. Lett.* **2008**, *10*, 1687.

(102) Kim, S. H.; Kim, K. H.; Kim, H. S.; Kim, J. N. *Tetrahedron Lett.* **2008**, *49*, 1948.

(103) Gowrisankar, S.; Lee, H. S.; Kim, J. M.; Kim, J. N. *Tetrahedron Lett*. **2008**, *49*, 1670.

(104) Lee, H. S.; Kim, K. H.; Kim, Y. M.; Kim, J. N. *Bull. Korean Chem. Soc*. **2010**, *31*, 1761.

(105) Basavaiah, D.; Reddy, K. R. *Tetrahedron* **2010**, *66*, 1215.

(106) Basavaiah, D.; Reddy, R. J. *Org. Biomol. Chem*. **2008**, *6*, 1034.

(107) Basavaiah, D.; Devendar, B.; Aravindu, K.; Veerendhar, A. *Chem. Eur. J.* **2010**, *16*, 2031.

(108) Just, M. J.; Tekkam, S.; Alam, M. A.; Jonnalagadda, S. C.; Johnson, J. L.; Mereddy, V. R. *Tetrahedron Lett*. **2011**, *52*, 5349.

(109) Yadav, L. D. S.; Srivastava, V. P.; Patel, R. *Tetrahedron Lett*. **2009**, *50*, 1423.

(110) Saito, S.; Sato, Y.; Ohwada, T.; Shudo, K. *J. Am. Chem. Soc.* **1994**, *116*, 2312.

(111) Kurouchi, H.; Sugimoto, H.; Otani, Y.; Ohwada, T. *J. Am. Chem. Soc.* **2010**, *132*, 807.

(112) Nakamura, S.; Sugimoto, H.; Ohwada, T. *J. Org. Chem.* **2008**, *73*, 4219.

(113) Basavaiah, D.; Reddy, R. M.; *Indian J. Chem.* **2001**, *40B*, 985.

(114) Basavaiah, D.; Pandiaraju, S.; Padmaja, K. *Synlett* **1996**, 393.

(115) Alvarez, R.; Velazquez, S.; San-Felix, A.; Aquaro, S.; De Clercq, E.; Perno, C-F.; Karlsson, A.; Balzarini, J.; Camarasa, M. J. *J. Med. Chem.* **1994**, *37*, 4185.

(116) Buckle, D. R.; Outred, D. J.; Rockell, C. J. M.; Smith, H.; Spicer, B. A. *J. Med. Chem*. **1983**, *26*, 251.

(117) Kume, M.; Kubota, T. K.; Kimura, Y.; Nakashimizu, H.; Motokawa, K. *Chem. Pharm. Bull.* **1993**, *41*, 758.

(118) Genin, M. J.; Allwine, D. A.; Anderson, D. J.; Barbachyn, M. R.; Emmert, D. E.; Garmon, S. A; Graber, D. R.; Grega, K. C.; Hester, J. B.; Hutchinson, D. K.; Morris, J.; Reischer, R. J.; Ford, C. W.; Zurenko, G. E.; Hamel, J. C.; Schaadt, R. D.; Stapert, D.; Yagi, B. H. *J. Med. Chem.* **2000**, *43*, 953.

(119) Brockunier, L. L.; Parmee, E. R.; Ok, H. O.; Candelore, M. R.; Cascieri, M. A.; Colwell, L. F., Jr.; Deng, L.; Feeney, W. P.; Forrest, M. J.; Hom, G. J.; MacIntyre, D. E.; Tota, L.; Wyvratt, M. J.; Fisher, M. H.; Weber, A. E. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 2111.

(120) Oliva, A. I.; Christmann, U.; Font, D.; Cuevas, F.; Ballester, P.; Buschmann, H.; Torrens, A.; Yenes, S.; Pericas, M. A. *Org. Lett.* **2008**, *10*, 1617.

(121) Chandrasekhar, S.; Seenaiah, M.; Kumar, A.; Reddy, C. R.; Mamidyala, S. K.; Kumar, C. G.; Balasubramanian, S. *Tetrahedron Lett*. **2011**, *52*, 806.

(122) Hotha, S.; Anegundi, R. I.; Natu, A. A. *Tetrahedron Lett*. **2005**, *46*, 4585.

(123) Declerck, V.; Toupet, L.; Martinez, J.; Lamaty, F. *J. Org. Chem.* **2009**, *74*, 2004.

(124) Sreedhar, B.; Reddy, P. S.; Kumar, N. S. *Tetrahedron Lett.* **2006**, *47*, 3055.

(125) Chandrasekhar, S.; Basu, D.; Rambabu, Ch. *Tetrahedron Lett.* **2006**, *47*, 3059.

(126) Ko, S. H.; Lee, K-J. *J. Heterocycl. Chem.* **2004**, *41*, 613.

(127) Song, Y. S.; Lee, K-J. *J. Heterocycl. Chem.* **2006**, *43*, 1721.

(128) Feng, J.; Zhang, Z.; Wallace, M. B.; Stafford, J. A.; Kaldor, S. W.; Kassel, D. B.; Navre, M.; Shi, L.; Skene, R. J.; Asakawa, T.; Takeuchi, K.; Xu, R.; Webb, D. R.; Gwaltney, S. L. II. *J. Med. Chem.* **2007**, *50*, 2297.

(129) Mai, A.; Artico, M.; Sbardella, G.; Massa, S.; Loi, A. G.; Tramontano, E.; Scano, P.; Colla, P. L. *J. Med. Chem.* **1995**, *38*, 3258.

(130) Hodgetts, K. J.; Yoon, T.; Huang, J.; Gulianello, M.; Kieltyka, A.; Primus, R.; Brodbeck, R.; De Lombaert, S.; Doller, D. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 2497.

(131) Wierenga, W.; Skulnick, H. I.; Stringfellow, D. A.; Weed, S. D.; Renis, H. E.; Eidson, E. E. *J. Med. Chem.* **1980**, *23*, 237.

(132) Rahier, N. J.; Cheng, K.; Gao, R.; Eisenhauer, B. M.; Hecht, S. M. *Org. Lett.* **2005**, *7*, 835.

(133) Guo, C. *Tetrahedron Lett.* **2010**, *51*, 548.

(134) Sheibani, H.; Seifi, M.; Bazgir, A. *Synth. Commun.* **2009**, *39*, 1055.

(135) Basavaiah, D.; Satyanarayana, T. *Tetrahedron Lett.* **2002**, *43*, 4301.

(136) Kim, J. M.; Kim, S. H.; Kim, J. N. *Bull. Korean Chem. Soc.* **2007**, *28*, 2505.

(137) Pathak, R.; Batra, S. *Tetrahedron* **2007**, *63*, 9448.

(138) Nag, S.; Madapa, S.; Batra, S. *Synthesis* **2008**, 101.

(139) Basavaiah, D.; Kumaragurubaran, N.; Sharada, D. S.; Reddy, R. M. *Tetrahedron* **2001**, *57*, 8167.

(140) Basavaiah, D.; Kumaragurubaran, N.; Sharada, D. S. *Tetrahedron Lett.* **2001**, *42*, 85.

LIST OF PUBLICATIONS

1. Recent contributions from the Baylis-Hillman reaction to organic chemistry

   D. Basavaiah, ***B. Sekhara Reddy***, S. Singh Badsara *Chem. Rev.* **2010,** *110,* 5447.

2. Chiral diamides as efficient catalytic precursors for the borane-mediated asymmetric reduction of prochiral ketones

   D. Basavaiah, K. Venkateswara Rao, ***B. Sekhara Reddy*** *Tetrahedron*:*Asymmetry* **2007**, *18*, 968.

3. (5*S*)-1-Aza-2-imino-3-oxa-4,4-diphenylbicyclo(3.3.0)octane: a novel chiral catalytic source containing the *N-(C=NH)-O* moiety for the borane-mediated asymmetric reduction of prochiral ketones

   D. Basavaiah, K. Venkateswara Rao, ***B. Sekhara Reddy*** *Tetrahedron*:*Asymmetry* **2007**, *18*, 963.

4. (2*S*)-2-Anilinomethylpyrrolidine: an efficient in situ recyclable chiral catalytic source for the borane-mediated asymmetric reduction of prochiral ketones in refluxing toluene

   D. Basavaiah, K. Venkateswara Rao, ***B. Sekhara Reddy*** *Tetrahedron*:*Asymmetry* **2006**, *17*, 1041.

5. (5*S*)-1,3-Diaza-2-imino-3-phenylbicyclo(3.3.0)octane: first example of guanidine based in situ recyclable chiral catalytic source for borane-mediated asymmetric reduction of prochiral ketones

   D. Basavaiah, K. Venkateswara Rao, ***B. Sekhara Reddy*** *Tetrahedron*:*Asymmetry* **2006**, *17*, 1036.

SYNOPSIS OF THE THESIS ENTITLED

APPLICATION OF BAYLIS-HILLMAN ACETATES: STUDIES TOWARDS DEVELOPMENT OF STRATEGIES FOR SYNTHESIS OF SUBSTITUTED INDENES, [1,2,3]-TRIAZOLO-[1,4]-BENZOXAZONINES AND PYRIMIDIN-4(3*H*)-ONES

TO BE SUBMITTED FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY

BY

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Construction of C-C bonds is the fundamental reaction in organic chemistry. Functional groups play a crucial role in organic synthesis as it depends mostly on the functional group transformations. Therefore it will be interesting and challenging to develop reactions which should involve C-C bond formation leading to the production of densely functionalized molecules. Baylis-Hillman reaction is one such reaction developed in recent years.[1-9] It is a three component C-C bond forming reaction and provides diverse classes of densely functionalized molecules *via* the coupling of α-position of activated alkene with electrophile in the presence of a catalyst. Our research group has been working for last 28 years on various aspects of Baylis-Hillman reaction with main aim of developing this reaction as a powerful synthetic tool in organic chemistry.

This thesis deals with the applications of the Baylis-Hillman adducts in synthesis of carbocyclic and heterocyclic molecules and is divided into three chapters 1) Introduction 2) Objectives, Results & Discussion and 3) Experimental. The first chapter, *i.e.* Introduction describes a brief account of literature on the development of the reaction and on the applications of the Baylis-Hillman adducts for synthesis of various valuable carbocyclic and heterocyclic compounds with an emphasis on recent developments.

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

1) To use the Baylis-Hillman adducts as probes in understanding the chemoselectivity in the intramolecular Friedel-Crafts reaction of substrates containing keto and ester functionalities in a similar environment and subsequently use this chemoselective cyclization methodology in developing a facile protocol for synthesis of functionalized indene derivatives.
2) To use the Baylis-Hillman acetates for construction of [1,2,3]-triazolo-[1,4]-benzoxazonine system employing Huisgen reaction (Click reaction) for construction of 9-membered ring.
3) To develop a simple methodology for synthesis of 2,5,6-trisubstituted pyrimidin-4(3*H*)-one derivatives from Baylis-Hillman acetates.

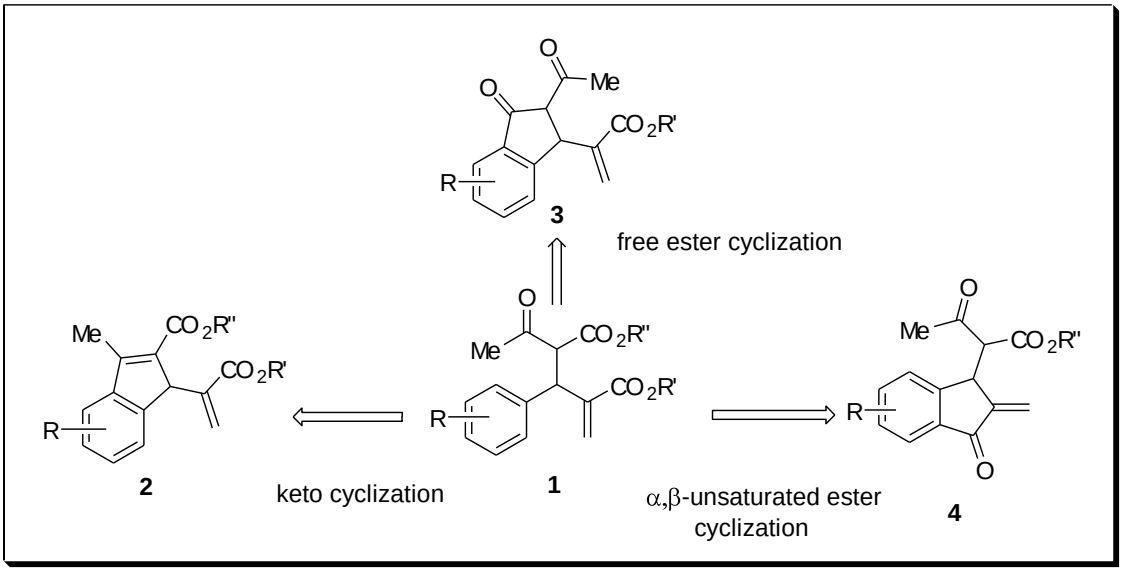
Towards developing the Baylis-Hillman adducts as probes in understanding the chemoselectivity in the intramolecular Friedel-Crafts reaction of substrates containing keto and ester functionalities: Development of a facile methodology for synthesis of functionalized indene derivatives

Intramolecular Friedel-Crafts reaction is an important and useful reaction for obtaining various classes of both carbocyclic and heterocyclic molecules. In these reactions, usually the functional groups such as ketones, esters/acids/acid chlorides and nitriles are used for intramolecular Friedel-Crafts reaction with aromatic ring. It will be highly interesting to examine the competition for cyclization between nitrile and ester, nitrile and keto, ester and keto groups with aromatic ring in a substrate containing such two or three groups in a similar environment.

In this direction we have selected alkyl 4-alkoxycarbonyl-3-aryl-2-methylene-5-oxohexanoate derivatives (**1**) containing one keto group and two ester groups in similar

environment, for intramolecular Friedel-Crafts cyclization with aromatic ring. In principle there are three possible cyclizations in this case to produce three types of compounds **2**, **3** & **4** (Scheme 1).

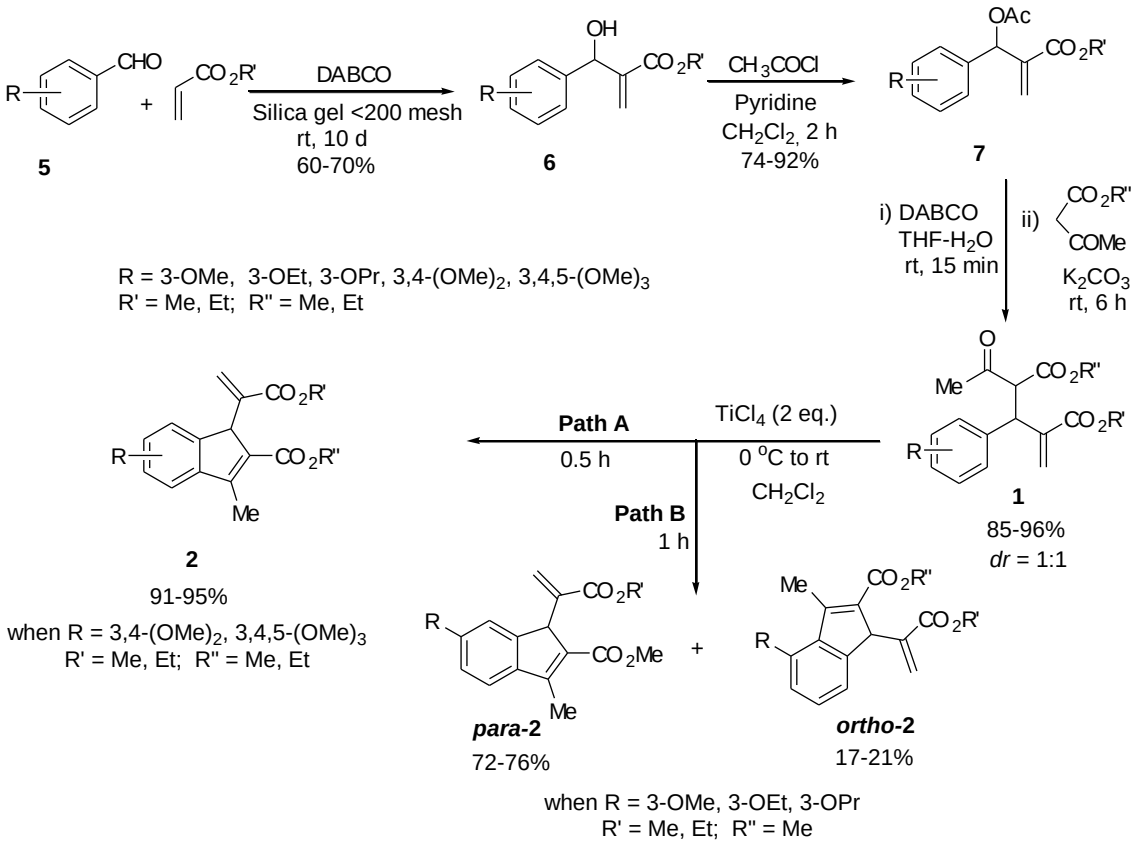
Scheme 1



When we examined the intramolecular Friedel-Crafts cyclization of substrate containing unsubstituted aromatic ring (**1**, R = H, R' = R" = Me) the expected ring formation did not occur under various conditions. At this stage it occurred to us that the substrate containing electron donating group on the aromatic ring may facilitate the intramolecular Friedel-Crafts cyclization. Accordingly such a compound (**1**, R = 3-OMe, R' = R" = Me) was prepared and subjected for intramolecular Friedel-Crafts cyclization. In this direction the best results were obtained when the substrate was treated with $TiCl_4$ at room temperature (addition at 0 ^oC) thus providing the desired indene (**2**) in 96% (*para* cyclized product 76% and *ortho* cyclized product 20%) yield. The generality of this strategy was demonstrated by selecting various acetates of the

BH-alcohols derived from aromatic aldehydes having appropriate electron donating groups on the aromatic ring (Scheme 2). The resulting indenes were obtained in excellent yields (Scheme 2, Path A & B). In some cases we have also obtained the *ortho*-directed Friedel-Crafts cyclized products (Scheme 2, Path B).

Scheme 2

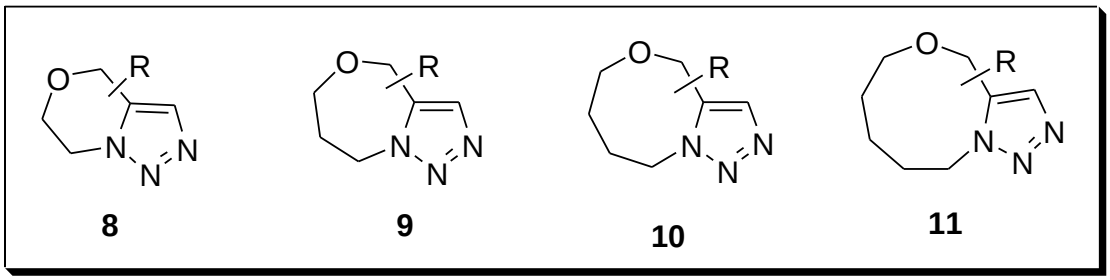


From these studies it is clear that ketone takes part exclusively in the Friedel-Crafts cyclization in preference over ester function even in the presence of two ester functionalities.

Development of a simple protocol for synthesis of [1,2,3]-triazolo-[1,4]-benzoxazonine derivatives from the Baylis-Hillman acetates

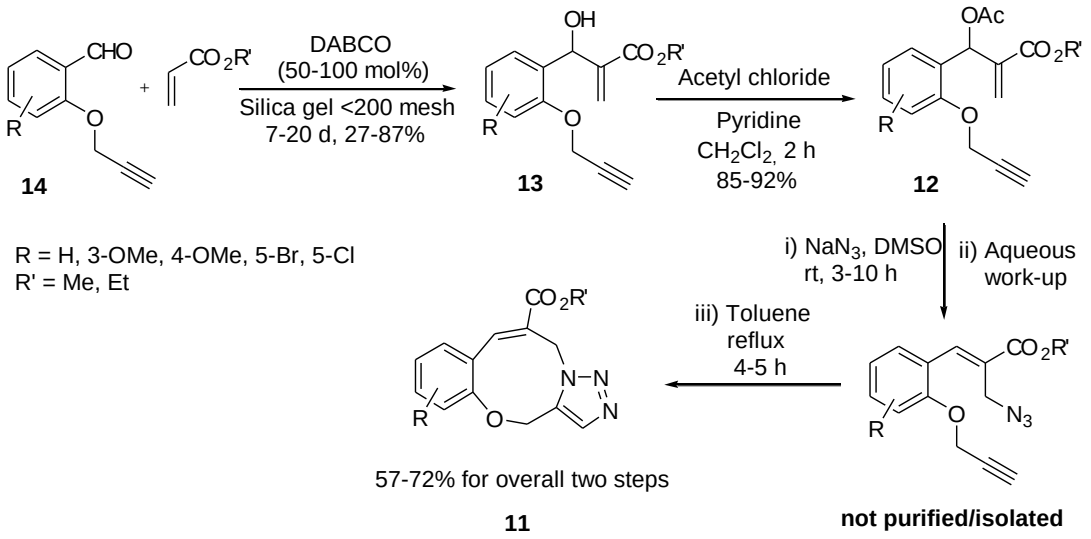
[1,2,3]-Triazole framework has attracted attention of synthetic chemists in recent years as this skeleton is present in many bioactive molecules. Therefore there has been increasing interest in the synthesis of [1,4]-oxazo cyclic systems containing 6/7/8-membered cyclic systems (**8, 9, 10**) (Figure 1) fused with [1,2,3]-triazole framework. However there is not much literature available for synthesis of [1,2,3]-triazolo-[1,4]-oxazonine (**11**) systems.

Figure 1



We have developed a simple methodology for synthesis of [1,2,3]-triazolo-[1,4]-benzoxazonine derivatives (**11**) starting from Baylis-Hillman acetates (**12**). The strategy involves the preparation of azido-alkynes by treatment of Baylis-Hillman acetates with sodium azide. The resulting azido-alkynes obtained (after aqueous work-up) were successfully transformed into [1,4]-benzoxazonine ring fused with triazole derivatives (**11**) in moderate to high yields by heating in toluene under reflux (Scheme 3).

Scheme 3

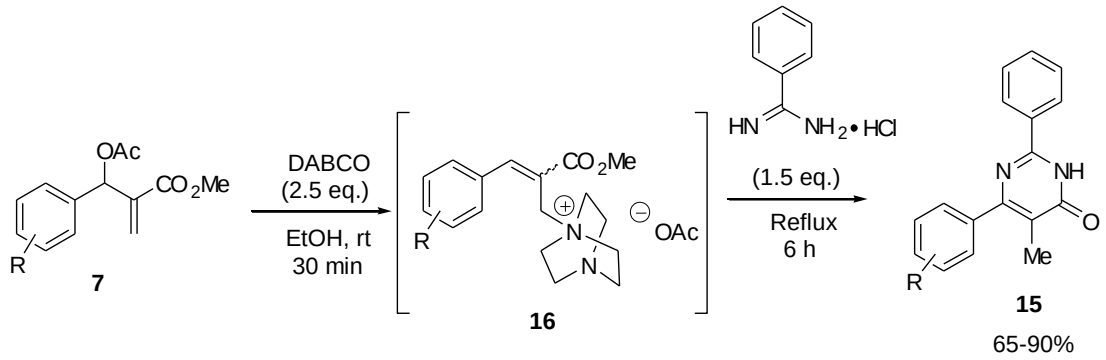


Development of a simple methodology for synthesis of tri-substituted pyrimidin-4(3*H*)-one derivatives from Baylis-Hillman acetates

Pyrimidin-4(3*H*)-one skeleton is yet an important framework present in various pharmacologically active compounds. Due to their remarkable biological activities there has been increasing interest in the synthesis of pyrimidin-4(3*H*)-one derivatives. It is interesting to note that there is no report on the synthesis of 2,5,6-trisubstituted pyrimidin-4(3*H*)-one derivatives using Baylis-Hillman acetates.

We have therefore undertaken this task and developed a facile methodology for synthesis of pyrimidin-4(3*H*)-one derivatives (**15**) from Baylis-Hillman acetates (**7**) in one-pot operation according to Scheme 4. Treatment of the *in situ* generated quaternary salt (**16**), obtained *via* the reaction of Baylis-Hillman acetates (**7**) with DABCO, with benzamidine hydrochloride in refluxing ethanol produced pyrimidin-4(3*H*)-one derivatives (**15**) in high yields.

Scheme 4



R = H, 3-OMe, 3,5-$(OMe)_2$, 3,4,5-$(OMe)_3$, 3-OEt, 3-OPr,
4-OMe, 3,4-$(OMe)_2$, 4-Me, 4-Et, 2-Cl, 3-Br

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

References

(1) Basavaiah, D.; Veeraraghavaiah, G. *Chem. Soc. Rev*. **2012**, *41*, 68.

(2) Basavaiah, D.; Reddy, B.S.; Badsara, S. S., *Chem. Rev*. **2010**, *110*, 5447.

(3) Declerck, V.; Martinez, J.; Lamaty, F. *Chem. Rev*. **2009**, *109*, 1.

(4) Singh, V.; Batra, S. *Tetrahedron* **2008**, *64*, 4511.

(5) Basavaiah, D.; Rao, K. V.; Reddy, R. J.; *Chem. Soc. Rev*. **2007**, *36*, 1581.

(6) Basavaiah, D.; Rao, A. J.; Satyanarayana, T. *Chem. Rev*. **2003**, *103*, 811.

(7) Ciganek, E. *Organic Reactions*; Paquette, L. A., Ed; New York: Wiley, **1997**, vol. *51*, p 201.

(8) Basavaiah, D.; Rao, P. D.; Hyma, R. S. *Tetrahedron* **1996**, *52*, 8001.

(9) Drewes, S. E.; Roos, G. H. P. *Tetrahedron* **1988**, *44*, 4653.