DEVELOPMENT OF NEW SYNTHETIC METHODOLOGIES USING THE BAYLIS-HILLMAN CHEMISTRY

A THESIS SUBMITTED FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

BY

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Dedicated to beloved

Parents, Sisters and Brother

CONTENTS

STATEMENT

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

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

HYDERABAD

AUGUST 2000

M. BAKTHADOSS

CERTIFICATE

Certified that the work embodied in this thesis entitled "DEVELOPMENT OF NEW SYNTHETIC METHODOLOGIES USING THE BAYLIS-HILLMAN CHEMISTRY" has been carried out by **Mr. M. BAKTHADOSS,** under my supervision and the same has not been submitted elsewhere for a degree

Aug. 11, 2000

Professor D. BASAVAIAH

(Thesis Supervisor)

DEAN

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ABBREVIATIONS

Ac	acetyl
BINAP	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
Bn	benzyl
bp	boiling point
i-Bu	isobutyl
n-Bu or Bu^n	n-butyl
t-Bu or Bu^t	*tert*-butyl
cat.	catalyst
CSA	camphorsulfonic acid
cy	cyclo
DABCO	1,4-diazabicyclo[2.2.2]octane
DBU	l,8-diazabicyclo[5.4.0]undec-7-ene
de	diastereomeric excess
DIBAL-H	diisobutylaluminium hydride
DMAP	dimethylaminopyridine
DMF	N,N-dimethyl formamide
dppe	l,2-bis(diphenylphosphino)ethane
ee	ennatiomeric excess
Et	ethyl
evk	ethyl vinyl ketone
n-Hex	n-hexyl
HMPA	hexamethylphosphoramide
HRP	horse radish peroxidase

3-HQ	3-hydroxyquinuclidine
IPA	isopropyl alcohol
LDA	lithium diisopropylamide
Me	methyl
mp	melting point
Ms	mesyl
mvk	methyl vinyl ketone
NBS	N-bromosuccinimide
NMO	N-methylmorpholine oxide
Ph	phenyl
PLAP	pig liver acetone powder
i-Pr or Pr^i	isopropyl
PCC	pyridinium chlorochromate
PPA	poly phosphoric acid
PTC	phase transfer catalyst
py	pyridine
TBAF	tetrabutylammonium fluoride
TBDMS	/-butyldimethylsilyl
TFAA	trifluroacetic anhydride
THF	tetrahydrofuran
TMSOTf	trimethylsilyl trifluromethanesulfonate
p-TsOH	*p*-toluenesulfonic acid

ABSTRACT

During the last two decades there has been a virtual explosion in the discovery of new reactions, reagents and methodologies in organic chemistry, which has been a major source for developments and success in the present day organic synthesis. Baylis-Hillman reaction is one such new reaction, which has seen enormous growth in recent years. This is basically a three component reaction involving activated alkene, carbon electrophile and a tertiary amine catalyst leading to the formation of carbon-carbon bond between the a-position of activated alkenes and carbon electrophiles thus providing densely functionalized molecules.

Our research group has been actively involved for the last 15 years in the development of the Baylis-Hillman reaction as one of the potential sources for stereoselective processes, and in fact has contributed significantly to this effect.

This thesis deals with Baylis-Hillman chemistry with a view to develop novel synthetic methods and utilize these methods for synthesis of natural products and biologically active molecules. This thesis consists of three chapters 1) Introduction, 2) Objectives, Results and Discussion and 3) Experimental. The first chapter *i.e.* introduction provides a summary of recent developments in the Baylis-Hillman chemistry.

The second chapter deals with the objectives, results and discussion. The Baylis-Hillman reaction provides an important class of multifunctional molecules, which have been successfully utilized in several stereoselective transformations. With a view to

expand the scope of the applications of Baylis-Hillman chemistry, we have carried out the thesis work with following objectives.

1). Development of a new general protocol for the synthesis of (*E*)-3-arylidene / alkylidenechroman-4-one, an important structural unit present in several biologically active molecules.

2). Application of this methodology for the synthesis of representative biologically active molecules such as bonducellin monomethyl ether, eucomin dimethyl ether, autumnalin trimethyl ether and (*E*)-3-(4-methoxybenzylidene)-6-methoxychroman-4-one, an antifungal agent.

3). Transformation of Baylis-Hillman adducts into indene and indane derivatives *via* the intramolecular Friedel-Crafts reaction.

4). Synthesis of *dl* and *meso*-bis allyl ethers *via* tandem construction of carbon-carbon and carbon-oxygen bonds using the Baylis-Hillman chemistry.

5). Diastereoselective synthesis of chiral allylamines *via* the treatment of methyl (2Z)-3-aryl-2-(bromomethyl)prop-2-enoates with (S)-l-phenylethylamine in the presence of DABCO

Development of novel protocol for synthesis of (*E*)-3-arylidene / alkylidenechroman-4-ones

The (*E*)-3-benzylidenechroman-4-one moiety occupies a special place in the field of heterocycles, as this skeleton is an integral part of many natural products and biologically active molecules, such as bonducellin **(51),** eucomin (52), autumnalin (53)

and punctatin (54). Therefore, the development of simple, general and new protocol for the synthesis of (*E*)-3-benzylidenechroman-4-one skeleton is of considerable importance today in synthetic organic chemistry The classical and most of the literature methods for the synthesis of (*E*)-3-benzylidenechroman-4-one moiety involve the initial synthesis of chroman-4-one skeleton, followed by the construction of the benzylidene moiety *via* acid or base catalyzed aldol condensation with aryl aldehydes. However, to the best of our knowledge, there is no report in the literature for the synthesis of (*E*)-3-benzylidenechroman-4-one moiety involving the initial preparation of benzylidene moiety and then construction of the chroman-4-one ring system. Therefore, we have undertaken this research program to develop a new protocol for the synthesis of (*E*)-3-benzylidene/alkylidenechroman-4-ones using methyl 3-hydroxy-2-methylenealkanoates (57a-j), the Baylis-Hillman adducts derived from methyl acrylate. Thus, we have developed a simple methodology for the synthesis of (*E*)-3-alkylidene / arylidenechroman-4-ones (Schemes 32, 33, 34 and 35). In this sequence, the key step is the intramolecular Friedel-Crafts reaction of 2-phenoxymethylalk-2-enoic acids (60a-b, 60g-j) *via* the treatment of corresponding acid chlorides **(61a-b, 61g-j)** with $AlCl_3$ to provide the desired chroman-4-ones **(62a-b, 62g-j)** However, when we extend this methodology for compounds 60c-e (R = 4-methylphenyl, 4-ethylphenyl, 4-isopropylphenyl) the desired 3-arylidenechroman-4-ones **(62c-e)** (R = 4-methylphenyl, 4-ethylphenyl, 4-isopropylphenyl) were not obtained, instead 3-(4-alkylphenyl)methyl-4-chromones **(63-65)** were obtained (Scheme 36). Since this methodology does not provide a general synthesis of 3-arylidenechroman-4-ones, we looked for an alternative

method for this purpose. During our studies in this direction we have found that trifluoroacetic anhydride (TFFA) works better for the intramolecular Friedel-Crafts reaction of the 2-phenoxymethylalk-2-enoic acids **(60a-f** and **60i)** to provide desired 3-arylidenechroman-4-ones **(62a-f** and **62i)** (eq. 33 & 34). We have also noticed that the substrates **(60c-e)** (R = 4-methylphenyl, 4-ethylphenyl, 4-isopropylphenyl) which provided 3-(4-alkylphenyl)methyl-4-chromones **(63-65)** *via* intramolecular Friedel-Crafts reaction of the corresponding acid chlorides in the presence of $AlCl_3$, now provided the desired 3-arylidenechroman-4-ones **(62c-e)** (R= 4-methylphenyl, 4-ethylphenyl, 4-isopropylphenyl).

Synthesis of natural products and biologically active molecules

To prove the efficacy of this new protocol, we have synthesized bonducellin mono methyl ether **(62k),** eucomin dimethyl ether **(62l)**, autumnalin trimethyl ether **(62m)** and (*E*)-3-(4-methoxybenzylidene)-6-methoxychroman-4-ones (56), an antifungal agent, by selecting the appropriate Baylis-Hillman adducts and phenolic derivatives.

Synthesis of indene derivatives *via* intramolecular Friedel-Crafts reaction of the Baylis-Hillman adducts

During our studies, aimed at the synthesis of indene derivatives *via* intramolecular Friedel-Crafts reaction of the Baylis-Hillman adducts, we noticed that alkyl 3-(3,4-dialkoxyphenyl)-3-hydroxy-2-methylenealkanoates, the Baylis-Hillman adducts **(71a-e)** obtained from 3,4-dialkoxybenzaldehydes, underwent intramolecular Friedel-Crafts

reaction under the influence of P_2O_5 to provide the substituted indene derivatives **(72a-e)** (Scheme 47, 48 and 49) We have also observed that the **Baylis-Hillman** adducts **(71f-i)** having two different substituents at 3 and 4 positions in the **phenyl ring,** on similar treatment with P2O5 provided regiomeric indene derivatives **(72f-i and 75a-d).** However, subsequent hydrogenation provided the desired indane derivatives **(76a-d)** (Scheme 51 and 52).

Tandem construction of carbon-carbon and carbon-oxygen bonds in the Baylis-Hillman chemistry: Synthesis of functionalized *dl* and *meso* bis allyl ethers

The mechanism of the Baylis-Hillman reaction is believed to proceed through first Michael type addition of DABCO to the activated alkene resulting in the formation of zwitterionic enolate. This enolate adds to aldehydes to generate zwitterionic species B which undergoes proton migration and subsequent elimination of the catalyst provided the desired highly functionalized molecules. It occurred to us that if we can use the oxygen anion (B in Scheme 1) in further controlled reaction with the product there will also be the formation of C-0 bond in the Baylis-Hillman conditions leading to the generation of an interesting class of molecules with more functionalities. During our studies in this direction, we have obtained a very fascinating result when we carried out the Baylis-Hillman coupling of acrylonitrile with aryl aldehydes for longer reaction time *i.e.* eight days, thus providing bis-(l-aryl-2-cyano)prop-2-en-l-yl ethers **(77a-f) in** 6-8 % isolated yields as racemic mixtures (eq 39 and 40). The *dl* stereochemistry of the

compounds 77a and **77b** (R= phenyl, 2-methylphenyl) was confirmed by single crystal X-ray data. We have also examined all these molecules on HPLC using chiral column, chiralcel OD which showed two peaks with equal intensities (in each case) corresponding to both (R, R) and (S, S)-enantiomers thus further confirming *dl* nature of all these molecules. However, when we have extended this reaction for 1-naphthaldehyde, *meso* bis allyl ether (77g) was isolated in 7 % yield (eq. 42). The *meso* stereochemistry was confirmed by single crystal X-ray crystallography. Also HPLC analysis of this ether (77g) on chiralcel OD column showed one peak, presumably confirming the *meso* nature of the molecule. Though the yields of bis allyl ethers are not high in this methodology it is still of interest due to simultaneous formation of carbon-carbon and carbon-oxygen bonds and also due to the high stereochemical purity of the molecules isolated.

Diastereoselective synthesis of chiral ally la mines *via* the treatment of methyl (2Z)-3-aryl-2-(bromomethyl)prop-2-enoates with (S)-1-phenyl-ethylamine in the presence of DABCO

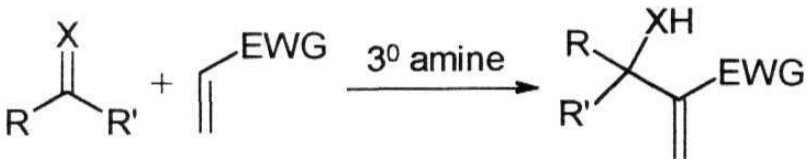
With a view to achieve synthesis of chiral allylamines (**81a-f** and **82a-f)** *via* S_N2' reaction, we have treated various allyl bromide–DABCO salts (**80a-d, 80g-h)** with (S)-1-phenylethylamine. **The** reaction proceeds through S_N2' fashion with 40-58 % diastereoselectivity (Scheme 58, 59 and 60). The absolute configuration of the newly formed stereogenic center of the major isomer has been found to be (R) (as shown in **81a)** as evidenced by single crystal X-ray data of major isomer **(81a)** (R = phenyl)

(Scheme 58). Fortunately, both the major **(81a-f) and minor (82a-f)** diastereomers have been separated by column chromatography in all the cases.

The third chapter deals with the experimental procedures **in detail,** IR, ^{1}H NMR, ^{13}C NMR, mass spectral data, X-ray crystallographic data, microanalyses and physical constants (bp, mp and optical rotations).

INTRODUCTION

During the last two decades there has been a virtual explosion in the discovery of reactions, reagents and methodologies in organic chemistry, which have in fact been the major source for the developments and success of the present day organic synthesis. Baylis-Hillman reaction is one such new reaction which has seen enormous growth in recent years.[6-8] This is basically a three component reaction involving activated alkene, carbon electrophile and a tertiary amine catalyst leading to the formation of carbon-carbon bond between the a-position of activated alkene and carbon electrophile thus providing densely functionallized molecule (eq. 1).



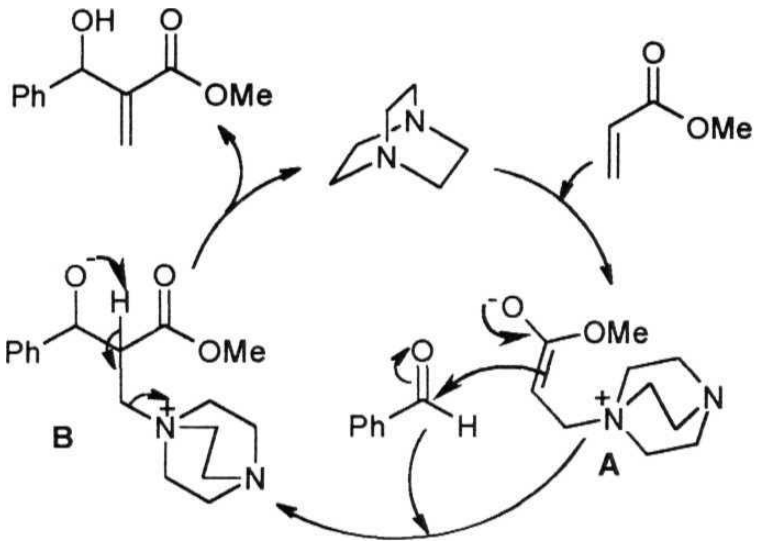
(eq. 1)

X= O, NR_2 ; EWG= electron withdrawing group

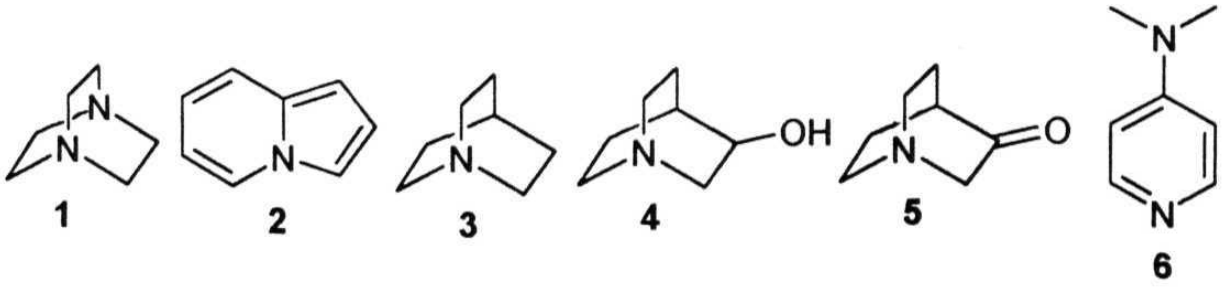
The possible mechanism of this reaction is described in Scheme 1, taking the reaction between methyl acrylate and benzaldehyde under the catalytic influence of DABCO as a model case. The reaction proceeds through first Michael type addition of tertiary amine to activated alkene resulting in the formation of zwitterionic enolate (A). This enolate adds to the aldehyde to generate zwitterionic species (B) which undergoes proton migration and subsequent elimination of the catalyst leads to the formation of highly functionalized molecules (Scheme 1). During the last 15 years there has been

tremendous development of this fascinating reaction as evidenced by three major reviews[6-8] and large number of publications. As the thesis deals with the developments

Scheme 1

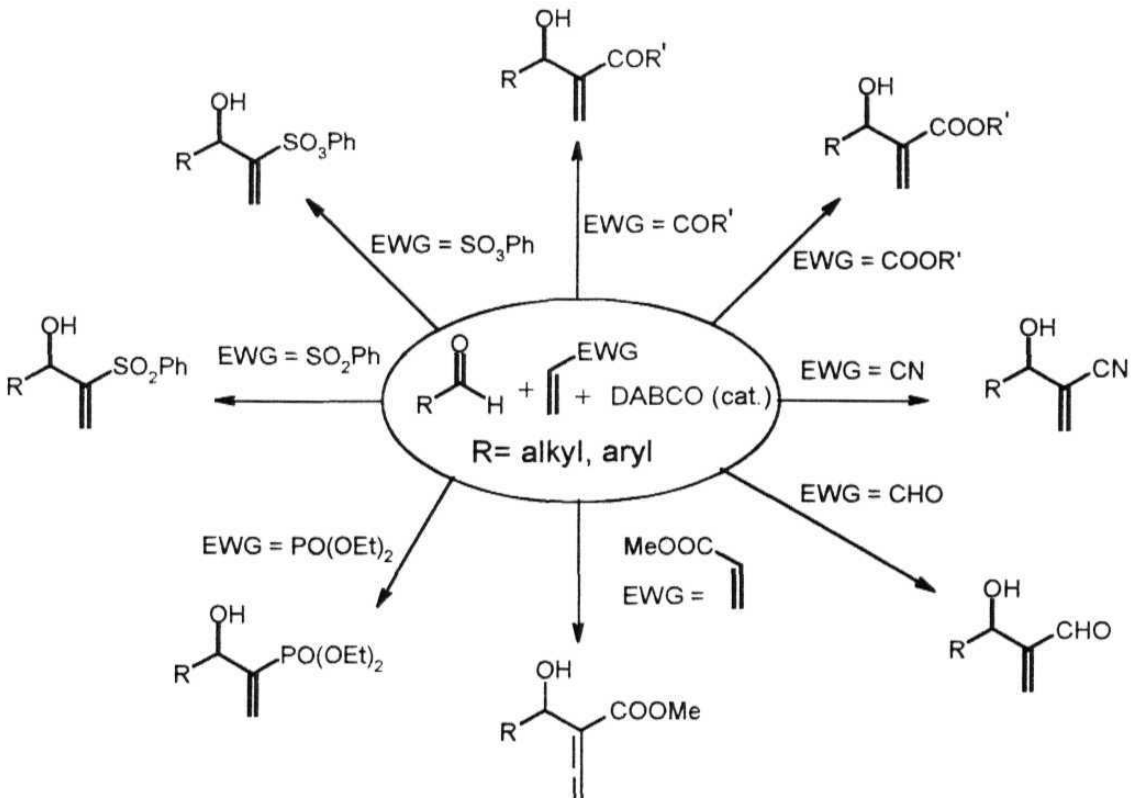


of new synthetic methods using the Baylis-Hillman adducts, very important and recent developments in the reaction have been described in the following. A variety of tertiary amines such as DABCO (1), pyrrocoline (2), quinuclidine (3), 3-hydroxyquinuclidine (4), 3-quinuclidinone (5) and 4-DMAP (6) have been employed as catalysts in the Baylis-Hillman reaction.[6-9] However, DABCO remains to be the catalyst of choice for organic chemists.

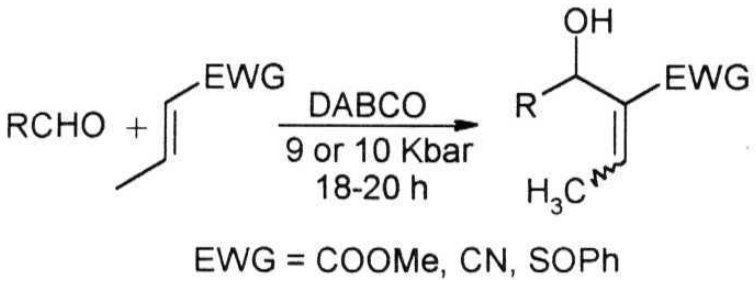


A number of activated alkenes such as a, β-unsaturated nitriles, ' ketones, esters,[14-16] sulfones,[17] sulfonates,[18] phosphonates,[19] allenic esters,[20,21] and acrolein[22-24] have been successfully employed in this fascinating reaction to provide highly functionalized molecules (Scheme 2).

Scheme 2



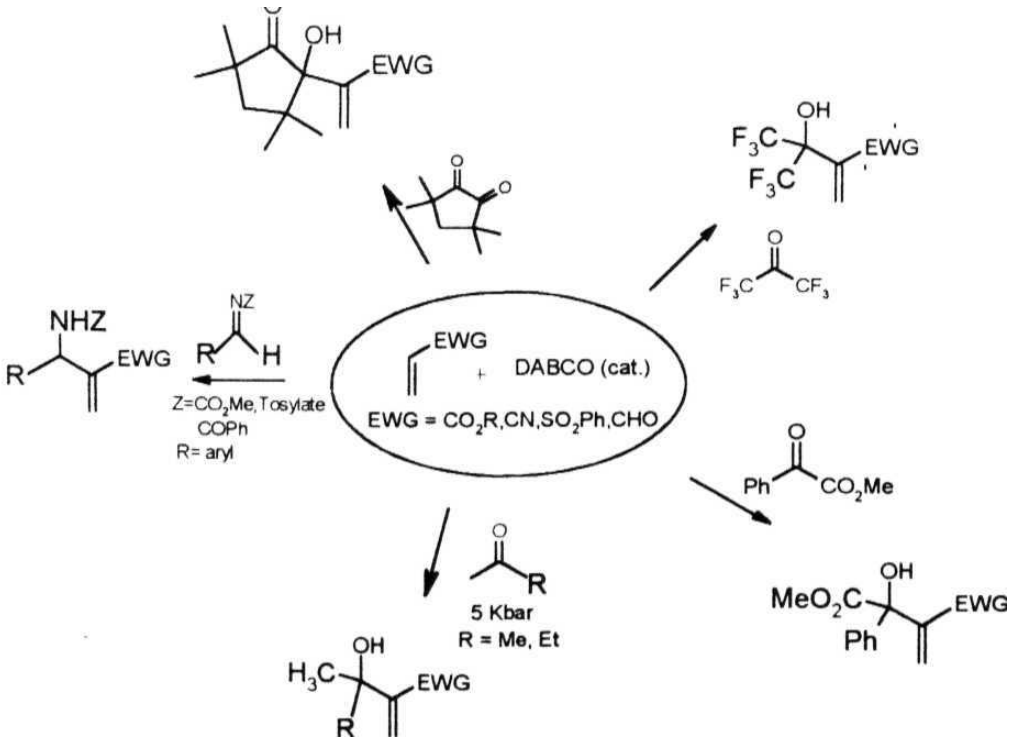
However, the substituted activated alkenes such as methyl crotonate, crotononitrile and phenyl vinyl sulfoxide which are less reactive, require high pressure[25,26] to undergo Baylis-Hillman reaction with electrophiles (eq. 2).



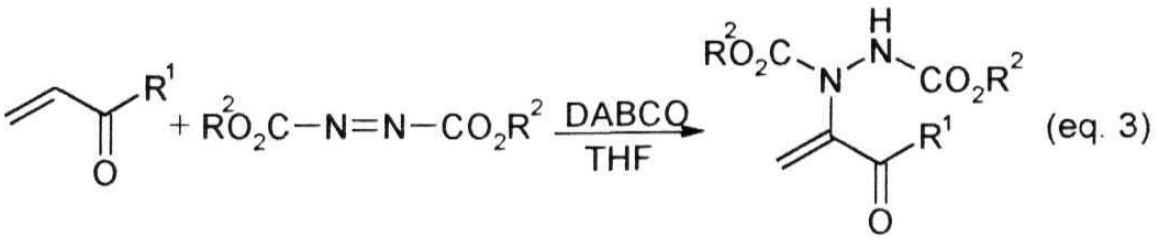
(eq. 2)

Though aldehydes have been the most commonly used electrophiles in this reaction other electrophiles such as a-keto esters,[27,29] aldimines,[30-32] flurinated ketones[33] and non-enolizable ketones[23] etc., have also been successfully employed in this reaction (Scheme 3). Unactivated ketones such as acetone, 2-butanone do not react with activated alkene at atmospheric pressure, however they have been brought into the scope of the reaction at high pressure (Scheme 3).[22,25]

Scheme 3



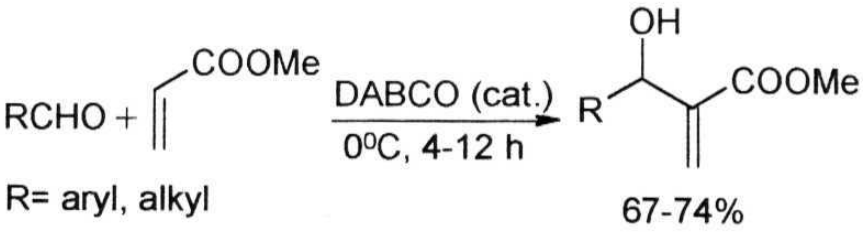
Very recently dialkyl azodicarboxylates were employed as a electrophile in the Baylis-Hillman reaction (eq. 3) by **Kamimura** and coworkers.[34]



(eq. 3)

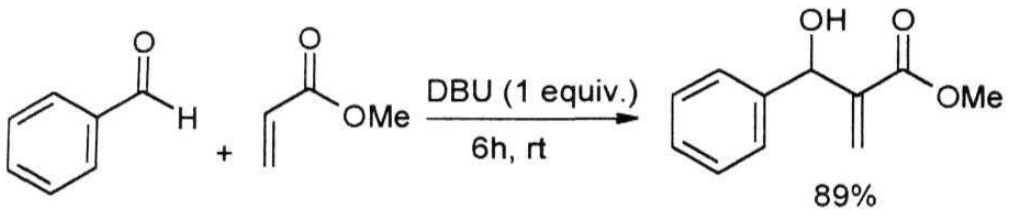
R^1= Me, Et, n-hexyl, n-heptyl, cinnamyl; R^2= Et, *t*-Bu

Baylis-Hillman reaction is normally a slow process requiring few days to few weeks for completion depending upon the activated alkene and electrophile Organic chemists made several efforts to circumvent this problem, thus different reaction conditions such as high pressure,[22,25] microwave irradiation[35] employing additives such as lithium perchlorate[36] and lanthanum triflates[37,38] along with DABCO, have been developed to accelerate the Baylis-Hillman reaction. Leahy and co-workers have found that the reaction is rapid at 0° C (eq. 4).[39]



(eq. 4)

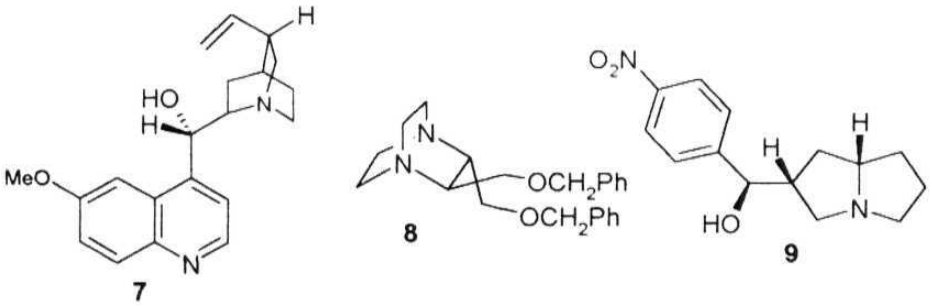
Recently, Aggarwal and Merau have observed that DBU provides much faster reaction rate than that of DABCO and 3-hydroxyquinuclidine (eq. 5).[40]



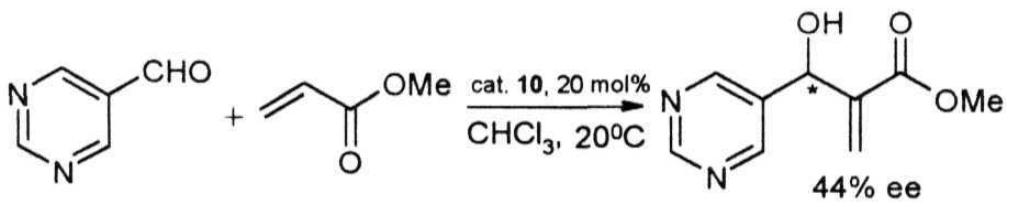
(eq. 5)

Asymmetric Baylis-Hillman reaction

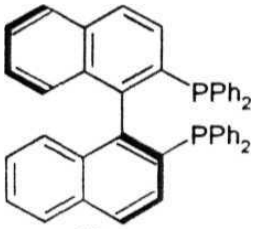
Efforts have been made to develop the asymmetric version of the Baylis-Hillman reaction using chiral source either in catalyst, electrophile or in an activated alkene. Various bicyclic chiral amine catalysts such as quinidine (7),[41] 2,3-disubstituted DABCO (8) and pyrrolizidine (9) have been used with limited to moderate success (up to 67% ee).



Soai *et al.* have used (S)-BINAP (10) as a catalyst for the coupling between the 5-pyrimidinecarboxaldehyde and methyl acrylate to produce the desired Baylis-Hillman adduct in 44% ee (eq. 6).[44]

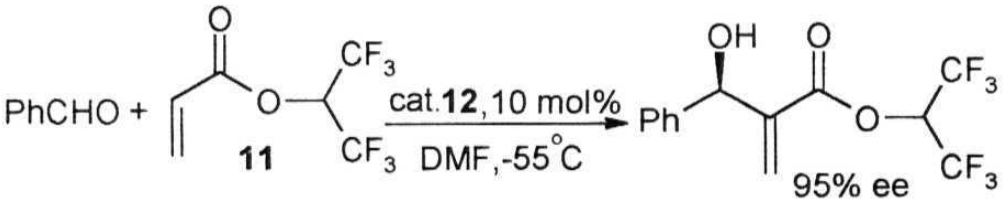


(eq. 6)

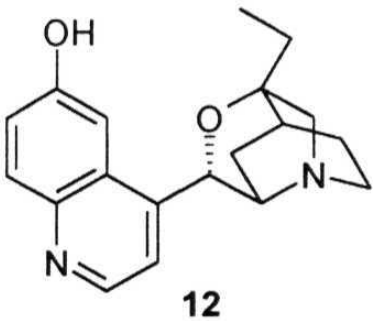


10

Recently, Hatakeyama and coworkers have reported high levels (95% ee) of asymmetric induction in the Baylis-Hillman reaction between 1,1,1,3,3,3-hexafluoroprop-2-yl acrylate (11) and benzaldehyde using (3R, 8R, 9S)-10,11-dihydro-3,9-epoxy-6'-hydroxycinconane (12) as a catalyst (eq. 7).[45]



(eq. 7)



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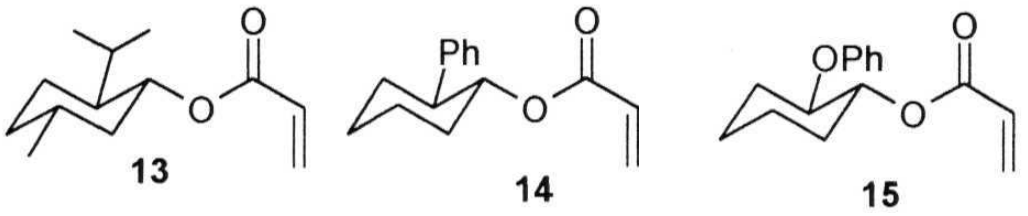
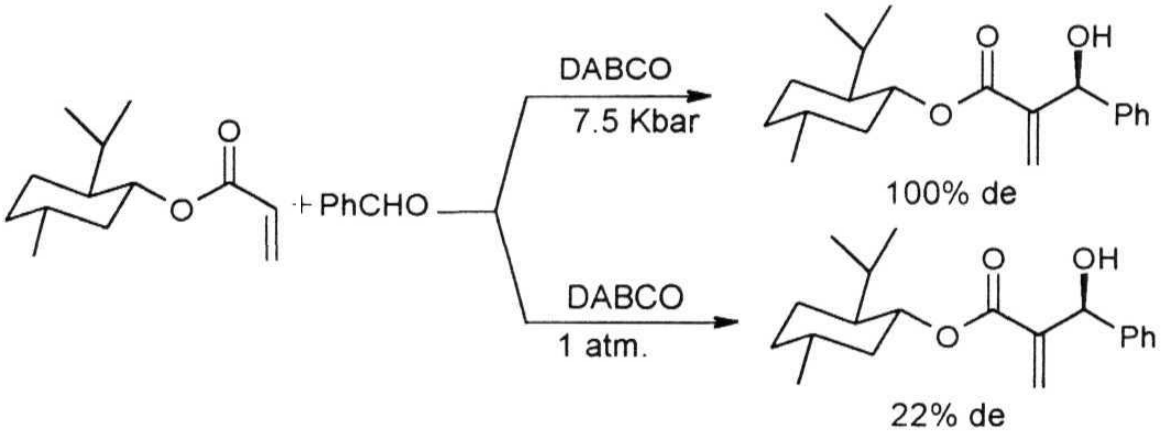
Several chiral acrylates like 13, 14, and 15 derived from various chiral auxiliaries such as (l)-menthol, (lR,2S)-2-phenylcyclohexan-l-ol, (1R,2R)-2-phenoxycyclohexan-1-ol were used as activated alkenes in the Baylis-Hillman reaction but with limited

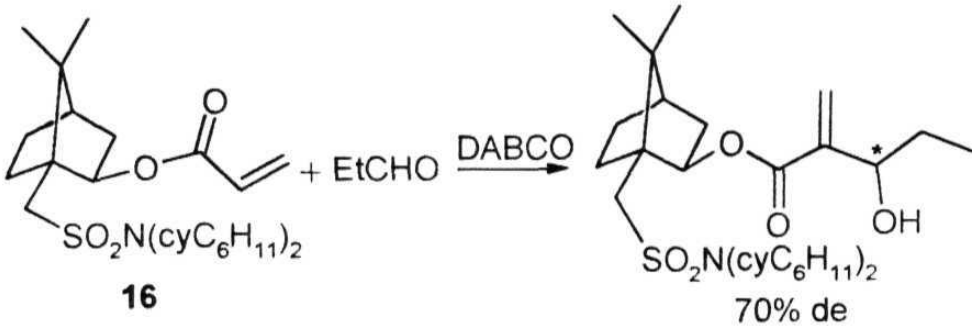
success. The effect of pressure on the asymmetric induction has been observed, thus the Baylis-Hillman reaction between menthyl acrylate and benzaldehyde catalyzed by DABCO at atmospheric pressure resulted in 22% de of the product, where as similar reaction provided 100% de at 7.5 K bar pressure (Scheme 4).



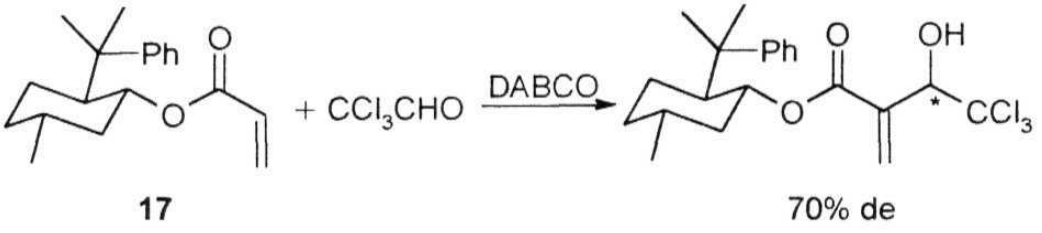
Scheme 4



The chiral acrylates 16 and 17 derived respectively from Oppolzer's chiral auxiliary and 8-phenylmenthol offer better diastereoselectivities (up to 70%) in the Baylis-Hillman reaction (eq. 8& 9).[50,51]



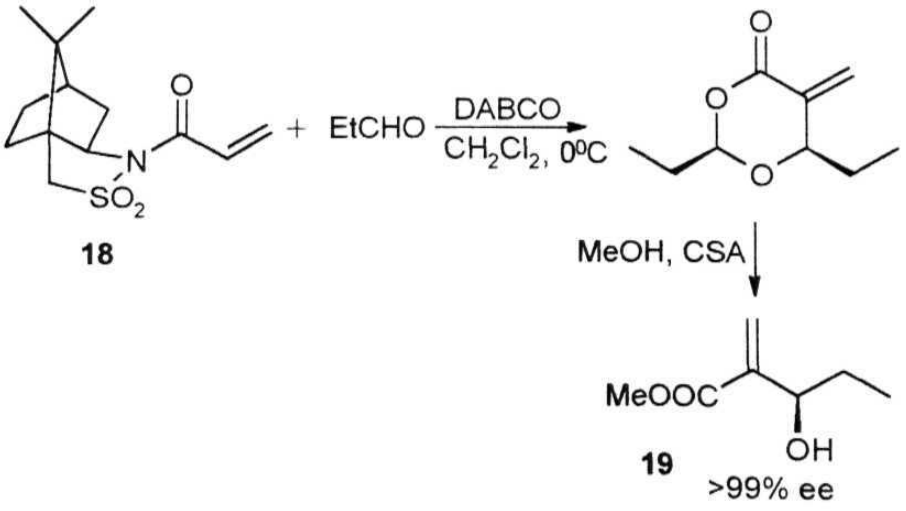
(eq. 8)



(eq. 9)

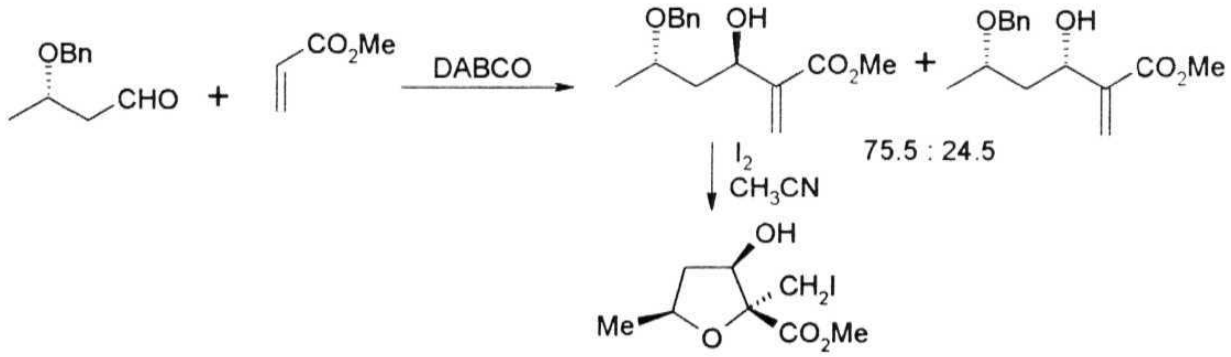
Very recently chiral acrylamide (18) derived from Oppolzer's sultam has been employed as an activated alkene in the Baylis-Hillman reaction to provide the desired Baylis-Hillman adduct (19) in 99% ee (Scheme 5).[52,53]

Scheme 5

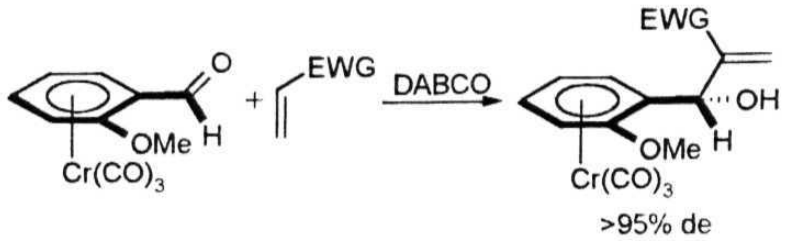


Considerable efforts have been made to achieve asymmetric Baylis-Hillman reaction using various chiral electrophiles. Thus, the Baylis-Hillman reaction of various chiral aldehydes with methyl acrylate and methyl vinyl ketone under the catalytic influence of DABCO has been studied to understand the levels of diastereoselectivity. For example, (S)-O-(methoxymethyl)lactaldehyde reacts with both methyl acrylate and methyl vinyl ketone in the presence of DABCO or 3-hydroxyquinuclidine (3-HQ) to afford the desired adducts as mixtures of *syn* and *anti* diastereomers in ≈ 30:70 ratio.[54] The reaction between (3S)-3-(benzyloxy)butanal and methyl acrylate in the presence of DABCO provided the required adducts as a mixtures *of anti* and *syn* diastereomers from which major anti isomer was seperated and converted into an interesting tetrahydrofuran derivatives (Scheme 6).[55]

Scheme 6



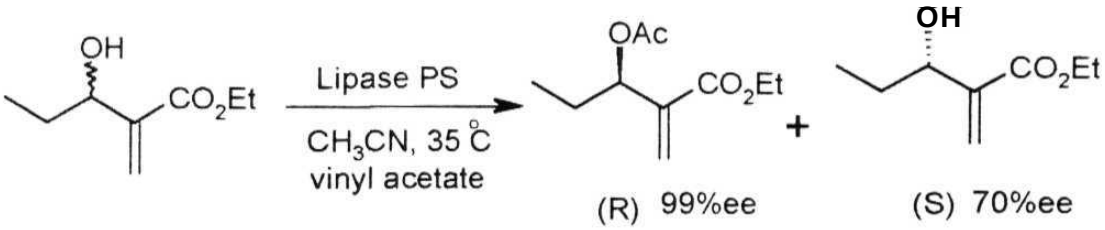
Kundig *et al.* have achieved 95% diastereoselectivity when they employed *ort ho* substituted benzaldehyde tricarbonylchromium complex as a chiral electrophile for coupling with methyl acrylate in the presence of DABCO (eq. 10).[56,57]



(eq. 10)

EWG = COOMe, CN

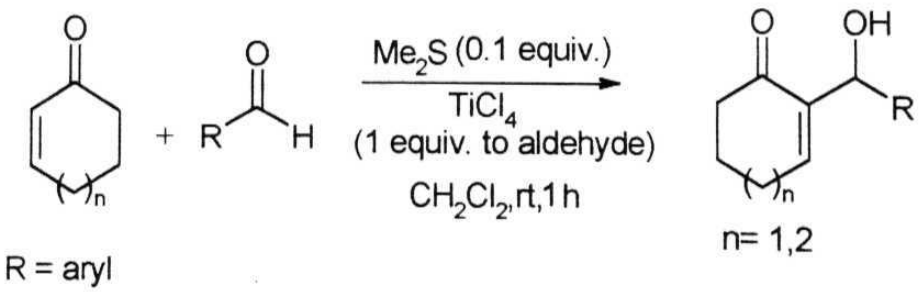
Optically active Baylis-Hillman adducts were also obtained *via* chemicoenzymatic methods Thus biocatalysts such as *Pseudomonas* AK lipase,[59] pig liver acetone powder (PLAP)[59] and horseradish peroxidase (HRP) were used for resolution of Baylis-Hillman adducts.[60] Very recently Tsuboi *et al* reported lipase PS as a biocatalyst for resolution of Baylis-Hillman adducts (eq. 11).[61]



(eq. 11)

Chalcogeno-Baylis-Hillman reaction

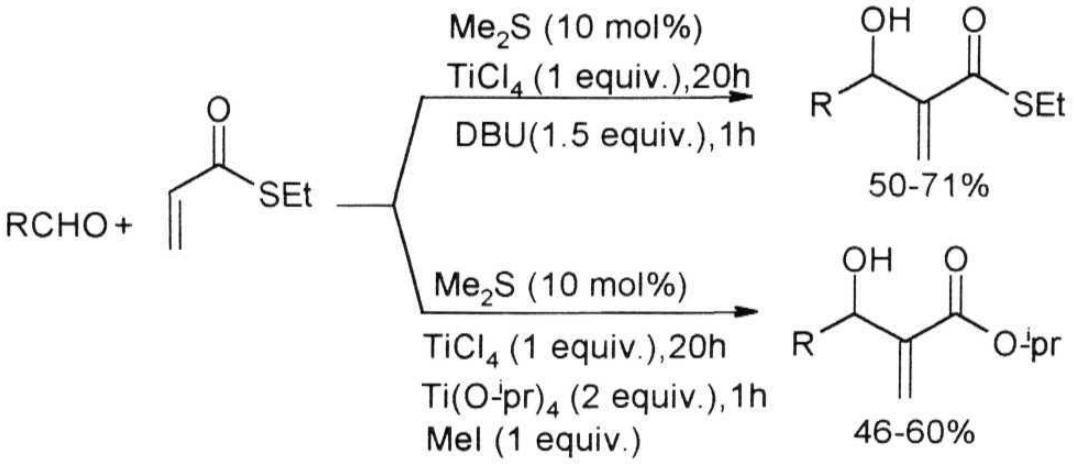
Kataoka *et al* demonstrated the application of sulfides and selenides as catalysts in the presence of $TiCl_4$ in performing the Baylis-Hillman reaction (eq. 12).[62,63]



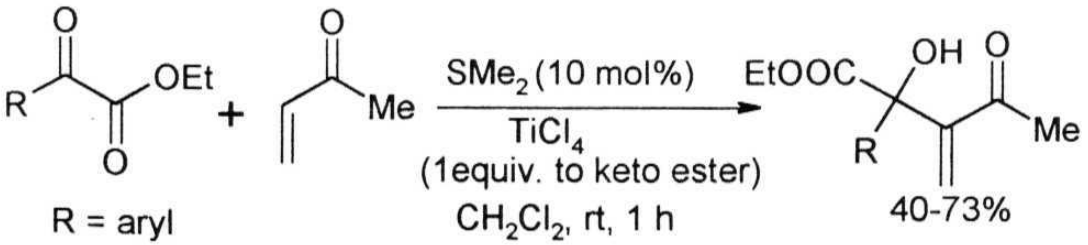
(eq. 12)

Similarly reaction of aldehydes with α,β-unsaturated thio ester using a catalytic amount of Me_2S in the presence of $TiCl_4$ followed by treatment with $Ti(O\text{-}^iPr)_4$ or DBU provided the corresponding α-methyl ene-β-hydroxy esters or thio esters[64] in moderate to good yields (Scheme 7).

Scheme 7

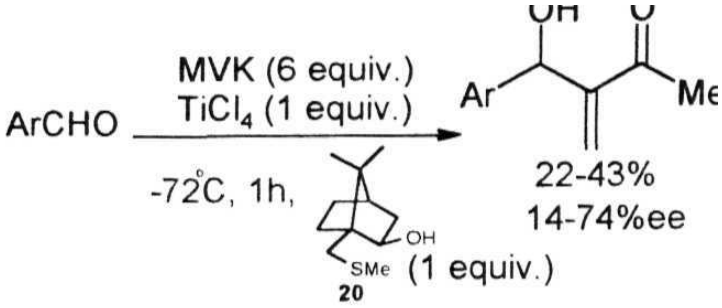


In our laboratory, we have demonstrated the application of α-keto esters as electrophiles in the chalcogeno-Baylis-Hillman reaction (eq. 13).[65]



(eq. 13)

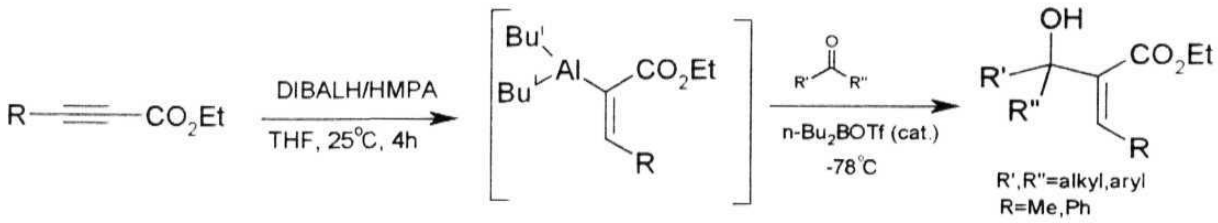
The chiral version of chalcogeno Baylis-Hillman reaction[66] (eq. 14) using chiral sulfur compound (20) has been very recently reported.



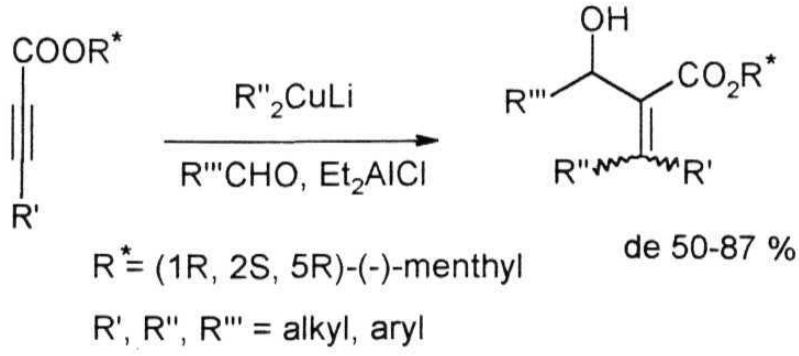
(eq. 14)

Recently Li and coworkers have utilized vinyl aluminium reagents to synthesize Baylis-Hillman type adducts (Scheme 8).[67]

Scheme 8

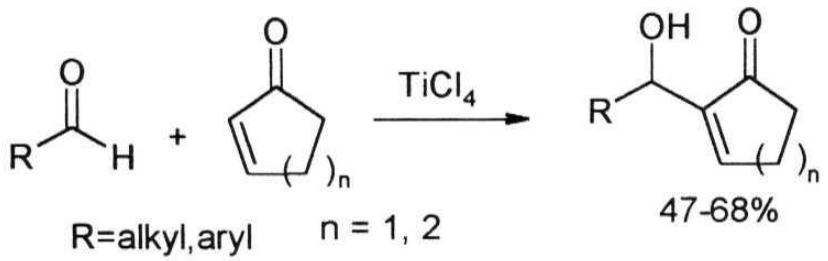


Optically active Baylis-Hillman type adducts with β-subtitution[68] have been prepared using menthyl phenylpropiolate with aldehydes according to the equation 15.



(eq. 15)

Very recently, $TiCl_4$ mediated Baylis-Hillman reaction between aldehydes and α,β-unsaturated alkenones was reported by Li and coworkers (eq. 16).[69,70]



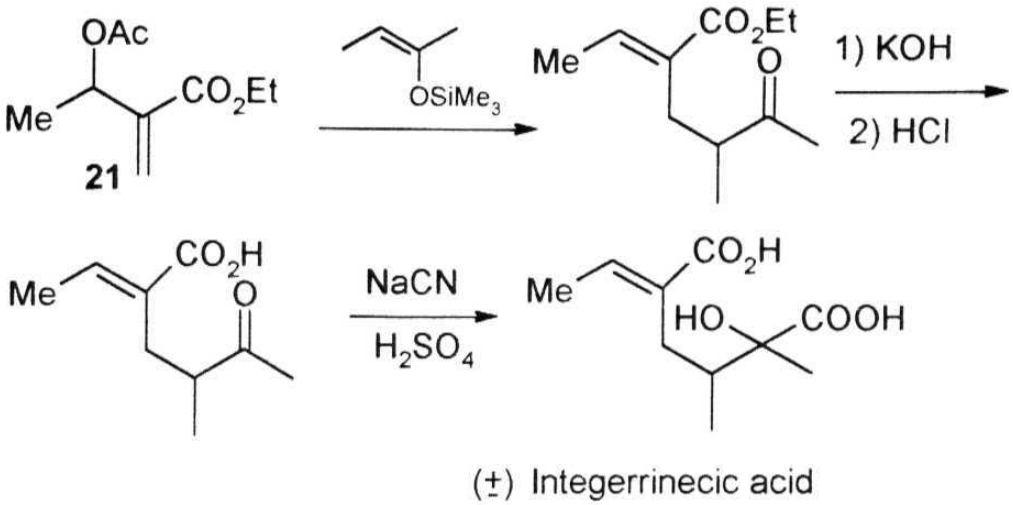
(eq. 16)

Applications of the Baylis-Hillman adducts

Baylis-Hillman adducts have been successfully employed in a variety of organic reactions involving high levels of stereochemical control. In fact, these developments have made the Baylis-Hillman adducts as one of the potential sources for stereoselective processes particularly for construction of stereoselective trisubstituted carbon-carbon double bonds. Some of these methodologies have also been successfully applied in the synthesis of various biologically active molecules. Interesting and recent developments in the application of the Baylis-Hillman adducts are presented in this section.

Drewes *et al.* reported the synthesis of racemic integerrinecic acid utilizing methyl 3-acetoxy-2-methylenebutanoate (21), derived from the corresponding Baylis-Hillman adducts according to Scheme 9.[71]

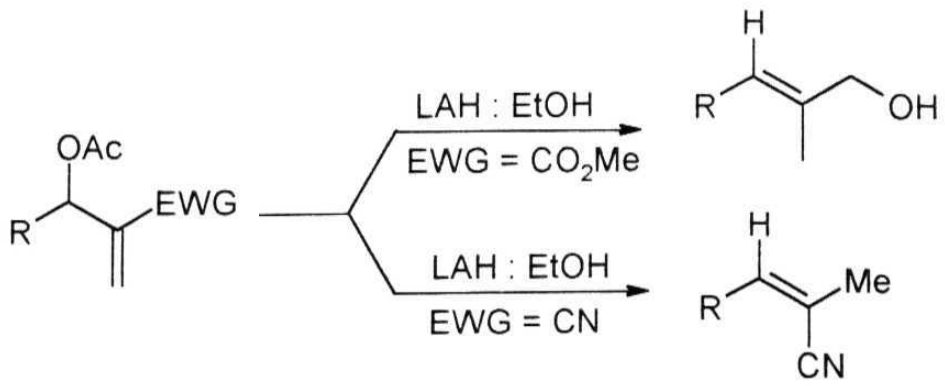
Scheme 9

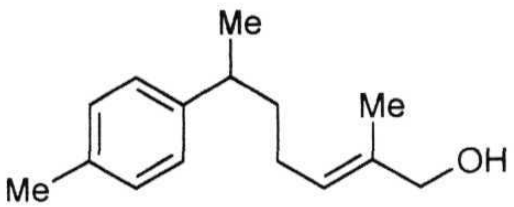


(±) Integerrinecic acid

Stereoselective synthesis of (2*E*)-2-methylalk-2-en-1-ols and (2Z)-2-methylalk-2-enenitriles has been developed *via* the treatment *of* 3-acetoxy-2-methylenealkanoates and 3-acetoxy-2-methylenealkanenitriles respectively with LAH:EtOH (Scheme 10). The efficacy of this methodology has been demonstrated by synthesis of (*E*)-nuciferol (22) a biologically active terpene molecule and a compound (23), a precursor for (Z)-nuciferol.[72]

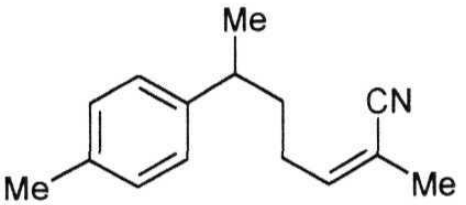
Scheme 10





(±)(*E*)-Nuciferol

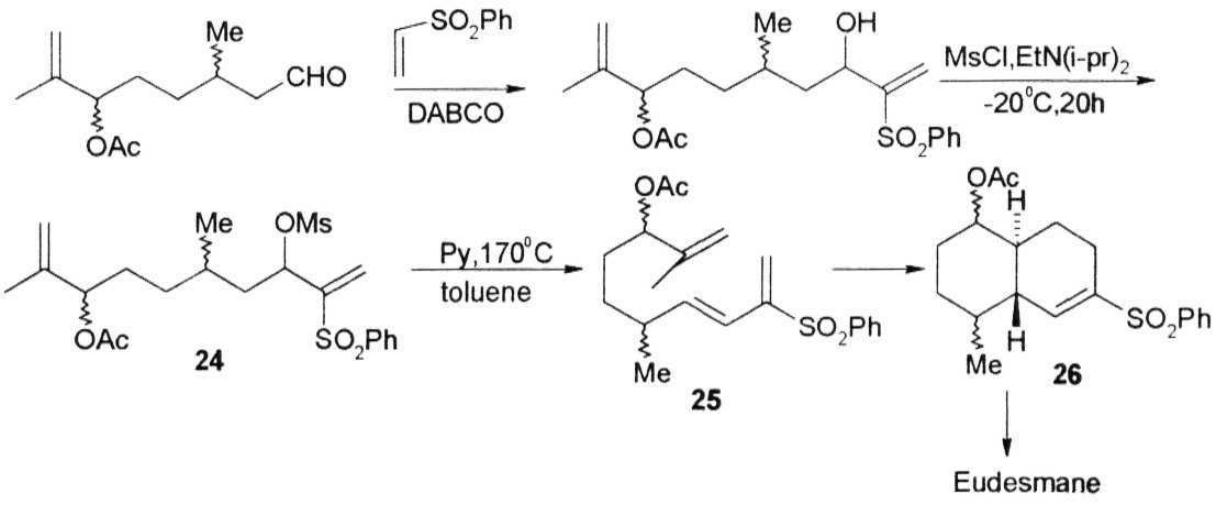
22



23

An elegant synthesis of eudesmane precursor (26)[73] has been described *via* an inverse electron demand intramolecular [4+2] cycloaddition reaction of the triene (25) generated *in situ* from the mesylate (24) of the Baylis-Hillman adduct (Scheme 11).

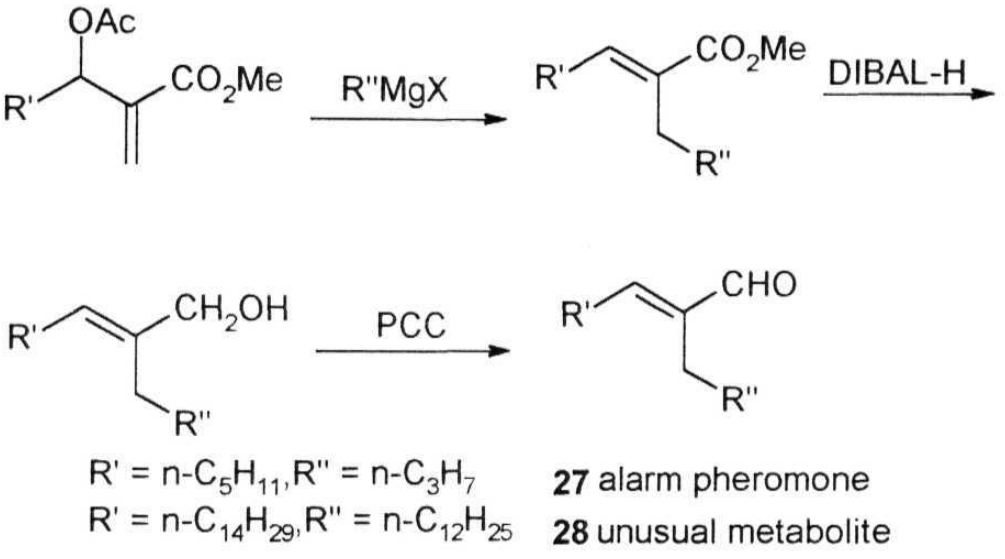
Scheme 11



Our research group has developed a stereoselective synthesis of trisubstituted alkene *via* the treatment of 3-acetoxy-2-methylenealkanoates with Grignard reagents. This methodology has been successfully employed for the synthesis of (2*E*)-2-butyloct-2-enal (27) an alarm pheromone (a component of the African weaver ant) and (2*E*)-2-

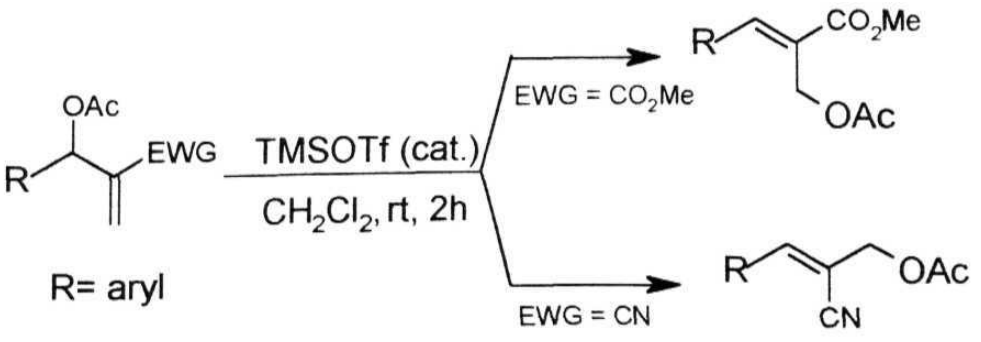
tridecylheptadec-2-enal (28) an unusual metabolite from the red alga *laurencia* species (*Laurencia undulata* and *Laurencia papillosa*) (scheme 12).[74]

Scheme 12

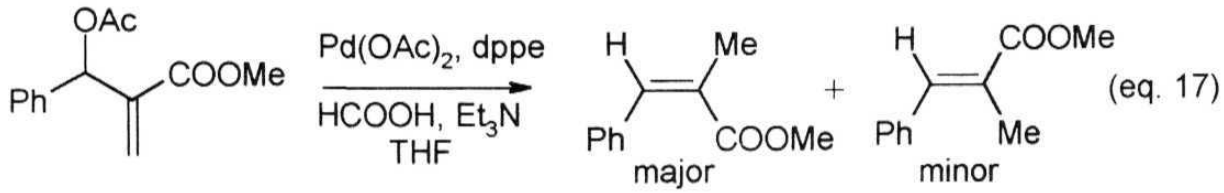


3-Acetoxy-2-methylenealkanoates and 3-acetoxy-2-methylenealkanenitriles have been stereoselectively transformed into methyl (2*E*)-2-acetoxymethylalk-2-enoates and *(2E)*~ 2-acetoxymethylalk-2-enenitriles respectively under the catalytic influence of TMSOTf (Scheme 13).[75]

Scheme 13



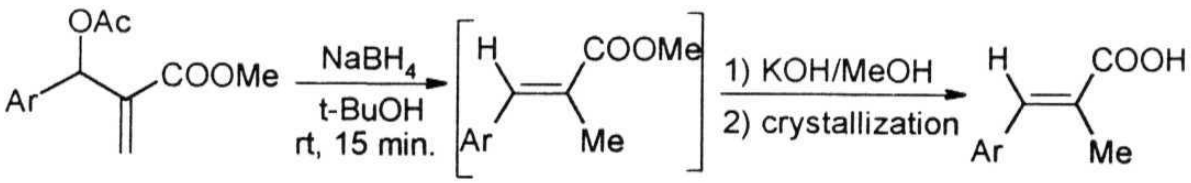
Recently, Pachamuthu and Vankar[76] have utilized methyl 3-acetoxy-2-methylene-3-phenylpropanoate for the synthesis of methyl (Z)-a-methylcinnamate according to equation 17.

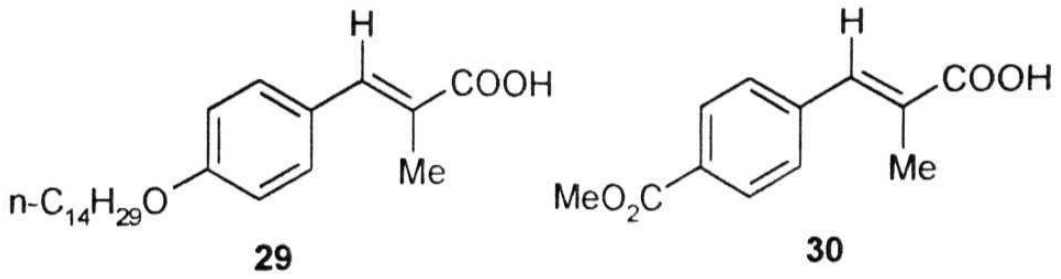


(eq. 17)

Our research group has recently reported an efficient synthesis of (*E*)-α-methylcinnamic acids using the acetates of the Baylis-Hillman adducts (Scheme 14).[77] The efficacy of this methodology has been demonstrated by synthesis of (2*E*)-2-methyl-3-(4-myristyloxyphenyl)prop-2-enoic acid (29), a good hypolipidemic agent and (2*E*)-2-methyl-3-(4-carbomethoxyphenyl)prop-2-enoic acid (30) a valuable synthon for the synthesis of serine protease inhibitor.

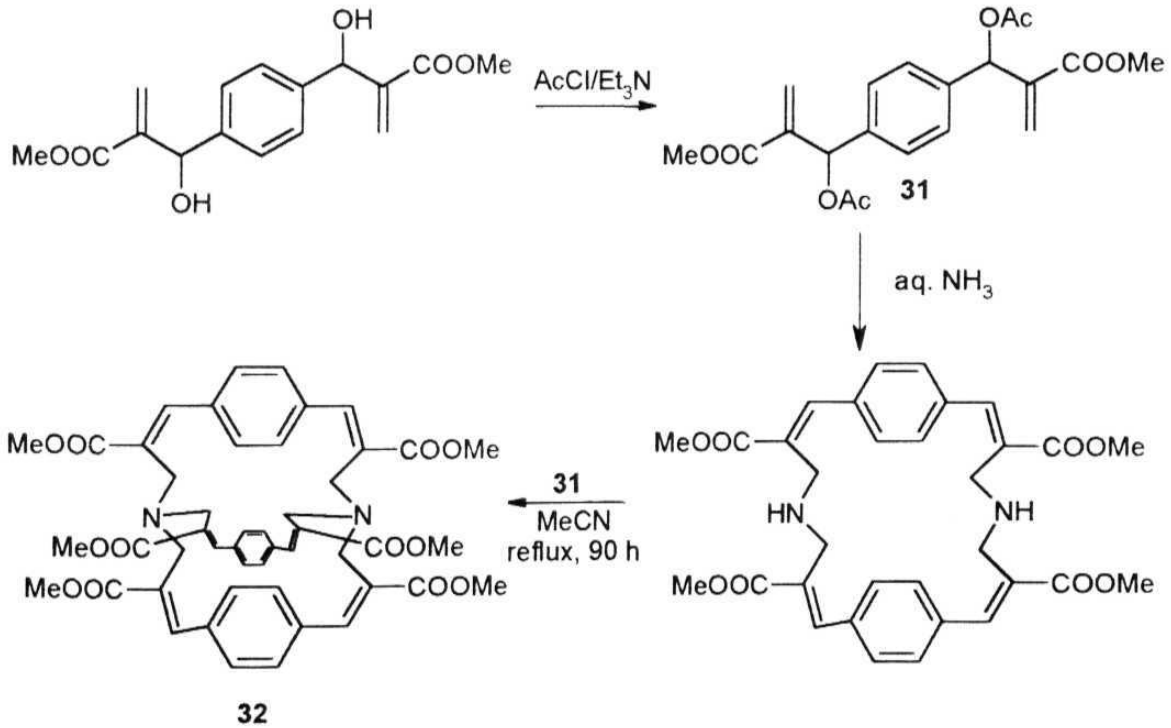
Scheme 14





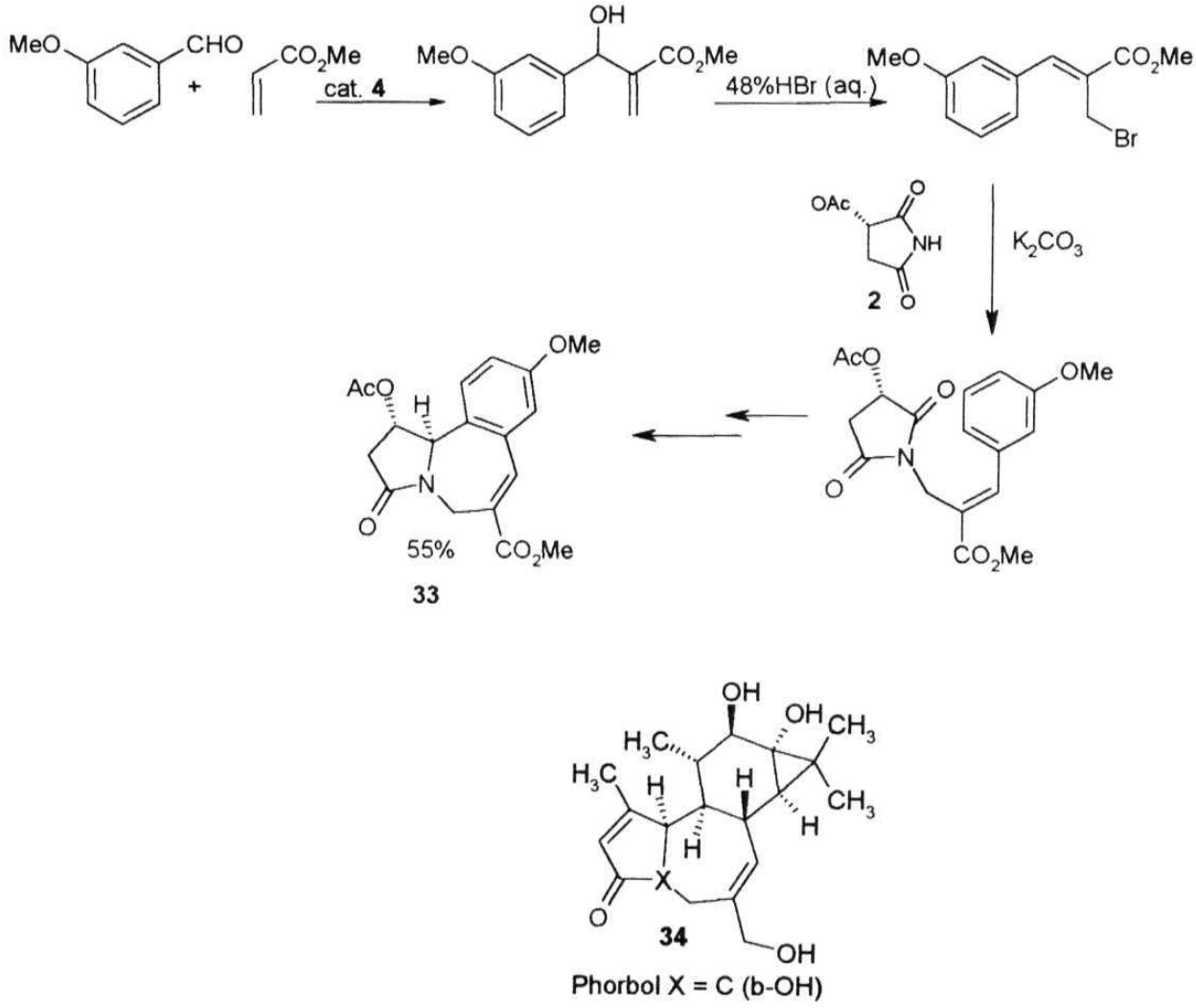
Bauchat and Foucaud have synthesized diaza macrocycle (32) using the diacetate of the Baylis-Hillman adduct 31 according to Scheme 15.

Scheme 15



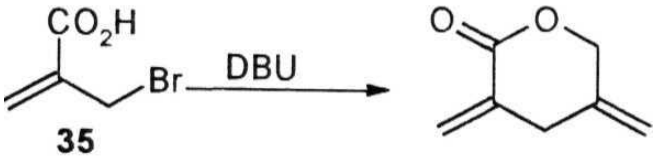
Marson *et al.* reported a convergent stereocontrolled construction of 5-6-7 tricyclic aza analogues (33) of phorbol (34) employing the Baylis-Hillman adducts according to Scheme 16.[79]

Scheme 16

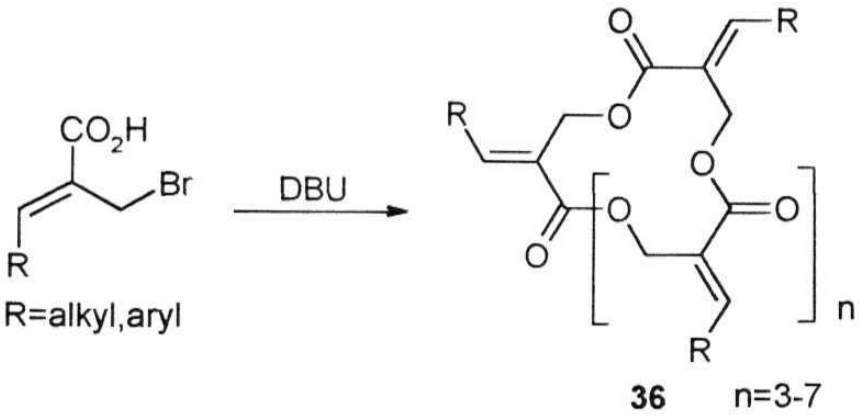


Recently, Blechert and coworkers[80] converted the α-bromomethylacrylic acid (35) into 2,4-dimethylene-5-valerolactone *via* the treatment with DBU (eq. 18). Similar reaction

of β-subtituted α-bromomethylacrylic acids with DBU results in the formation of mixture of macrolactones (36) (eq. 19).



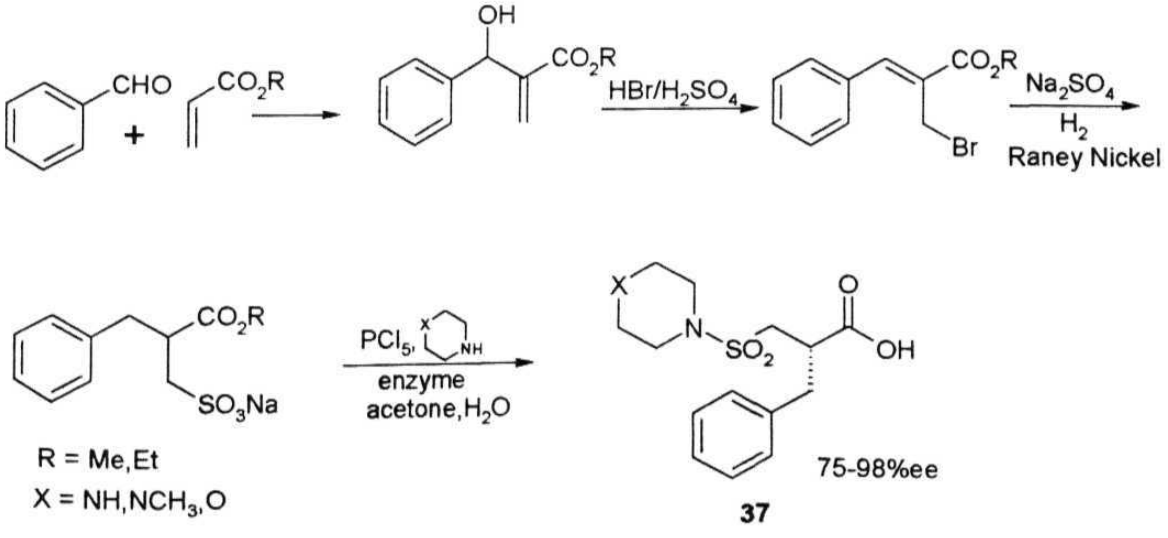
(eq. 18)

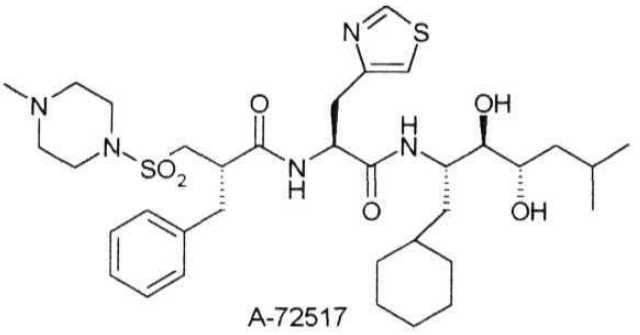


(eq. 19)

Mazdiyansi and coworkers[81] have synthesized a key intermediate (37) for the synthesis of a renin inhibitor (38) from the Baylis-Hillman adducts (Scheme 17).

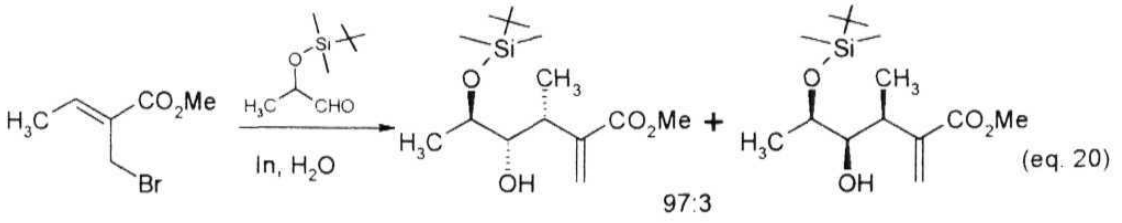
Scheme 17



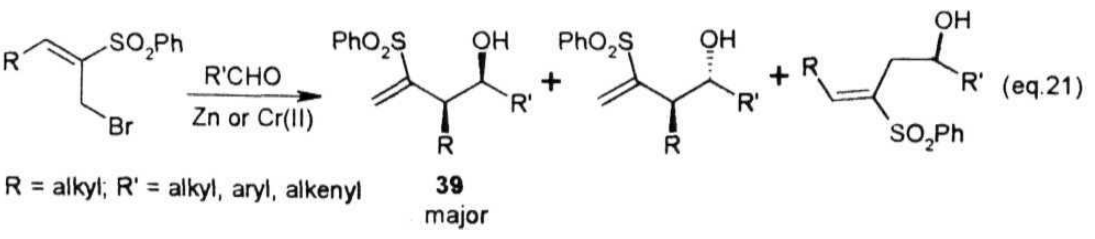


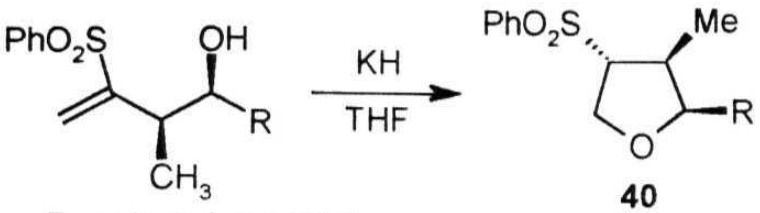
38

Isaac and Paquette[82] have reported indium promoted addition of methyl (Z)-2-(bromomethyl)but-2-enoate to α-(*t*-butyldimethylsiloxy)aldehydes leading to the formation of products with high levels of 3,4-*syn* and *4,5-anti* diastereoselectivity (eq. 20).



Zinc and chromium (II) mediated diastereoselective allylation of aldehydes using allyl bromides derived from the Baylis-Hillman adducts provided the *syn* molecules (39) predominantly (eq. 21).[83] After the separation, the *syn*-hydroxy sulphones were transformed into diastereomerically pure 2,3,4-trisubstituted tetrahydrofurans (40) *via* the treatment with KH (eq. 22).

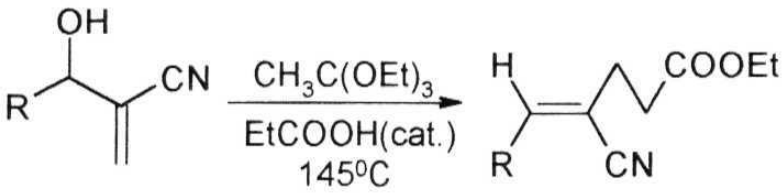




R = phenyl, n-pentyl

(eq. 22)

Our research group has successfully transformed the Baylis-Hillman adducts *i.e.* 3-hydroxy-2-methylenealkanenitriles into (4*Z*)-4-cyanoalk-4-enoates (eq. 23) *via* Johnson-Claisen rearrangement.[84]

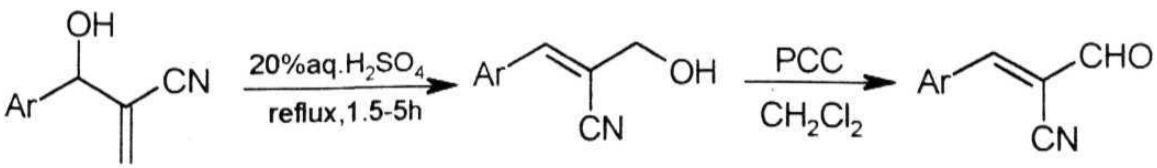


R = alkyl, aryl

(eq. 23)

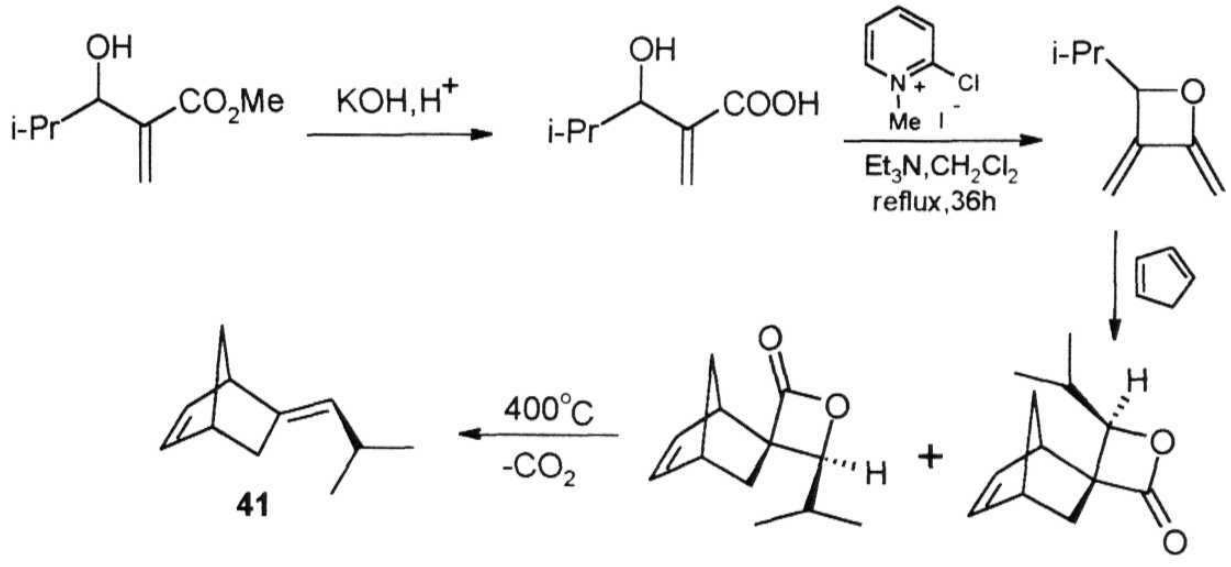
Aqueous sulfuric acid mediated transformation of 3-aryl-3-hydroxy-2-methylenepropanenitriles into (*E*)-α-cyanocinnamyl alcohols and subsequent oxidation with PCC leading to the formation of stereoselectively pure (*E*)-α-cyanocinnamic aldehydes have been described by our research group (Scheme 18).[85]

Scheme 18

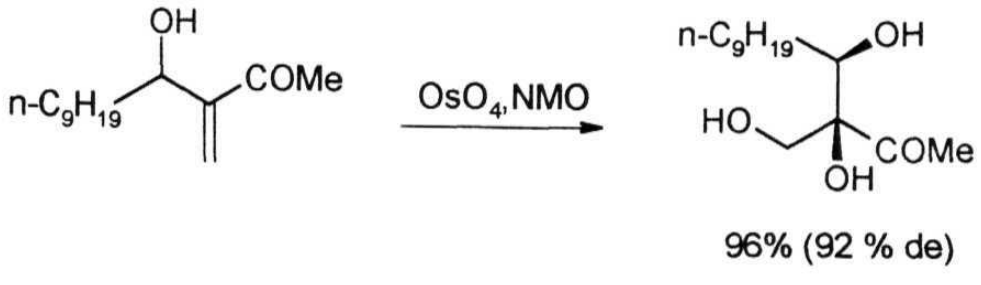


Adam *et al.* have developed a simple synthesis of cycloalkene (41) utilizing the Baylis-Hillman adduct methyl 3-hydroxy-4-methyl-2-methylenepentanoate according to Scheme 19.[86]

Scheme 19



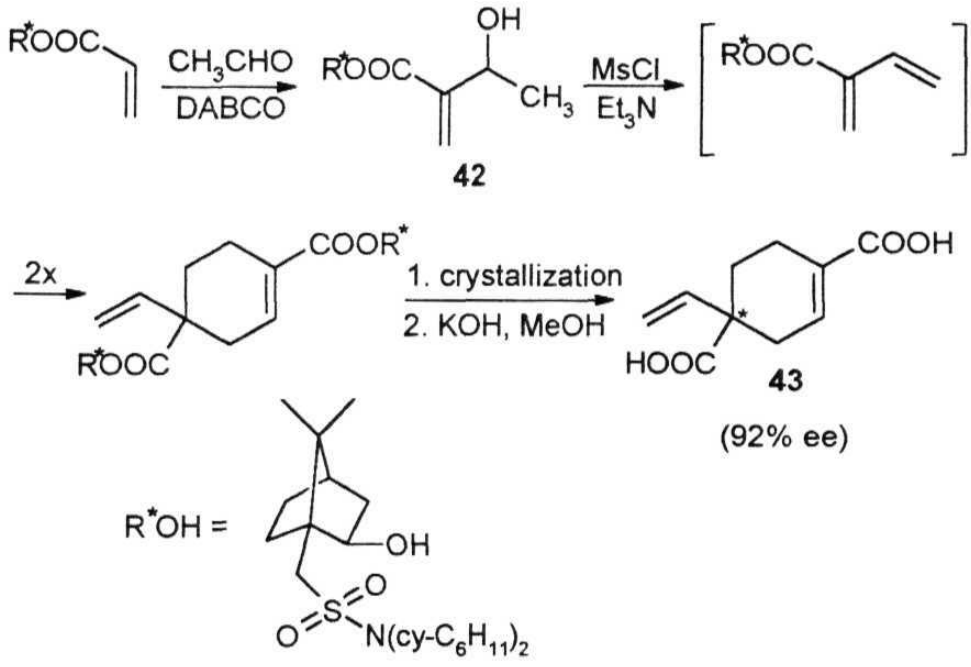
High diastereoselective dihydroxylation of the Baylis-Hillman adducts has been successfully carried out using OsO_4 (eq. 24).[87]



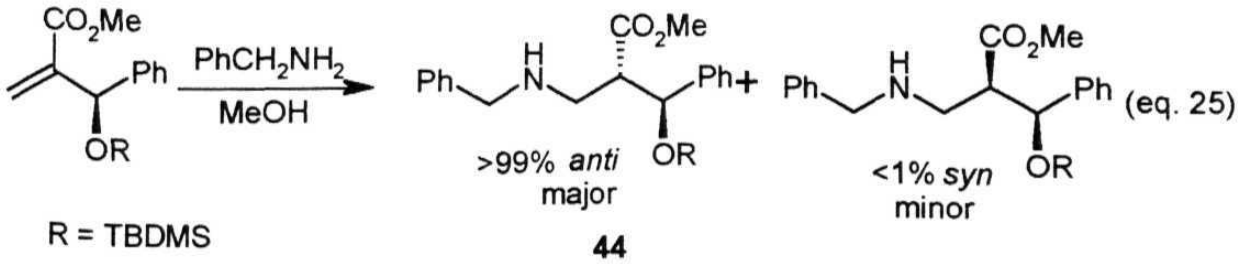
(eq. 24)

First asymmetric synthesis of mikanecic acid (43), an interesting terpene dicarboxylic acid possessing chiral quarternary vinyl centre has been reported from our laboratory *via* Diels-Alder type self dimerization of the diene derived from the Baylis-Hillman adducts (42) (Scheme 20).[88]

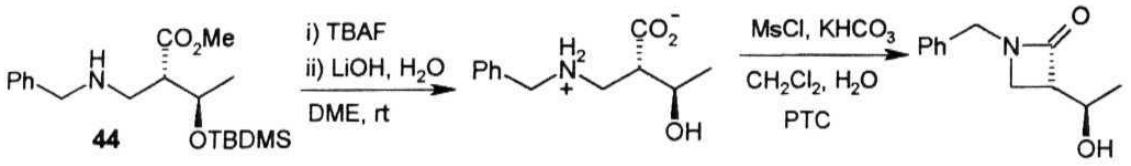
Scheme 20



Perlmutter and Tabone have described a highly *anti* diastereoselective Michael addition of benzylamine to O-protected Baylis-Hillman adduct (eq. 25).[89,90] The *anti* isomer (44) was converted into β-lactam derivative (Scheme 21).

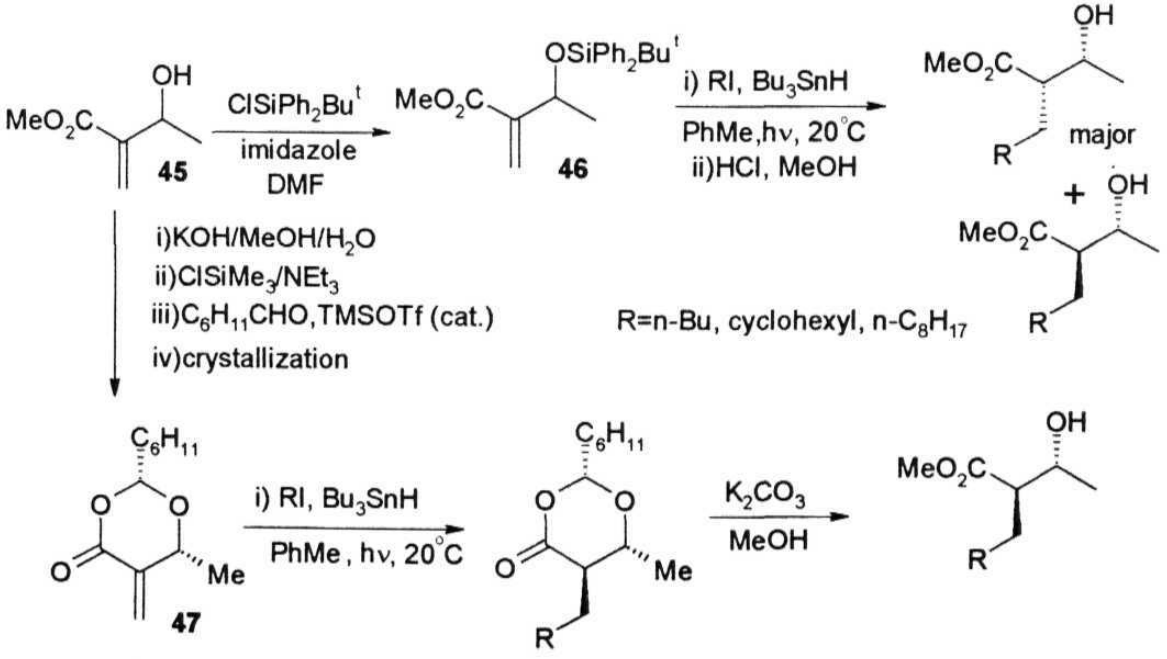


Scheme 21

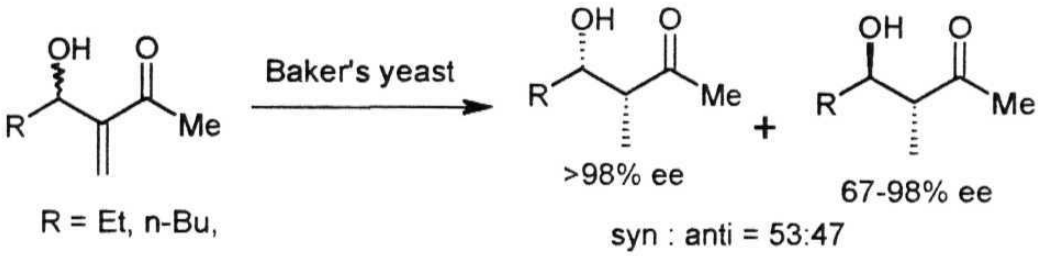


Giese *et al.*[91,92] have reported a highly diastereoselective addition of alkyl radicals to the silyl ether (46) derived from the Baylis-Hillman adduct (45) leading to the formation of *erythro* compounds as a major product. They have also reported a similar alkyl radicals addition to 1,3-dioxane derivative (47) derived from the same Baylis-Hillman adduct to provide *threo* products exclusively (Scheme 22).

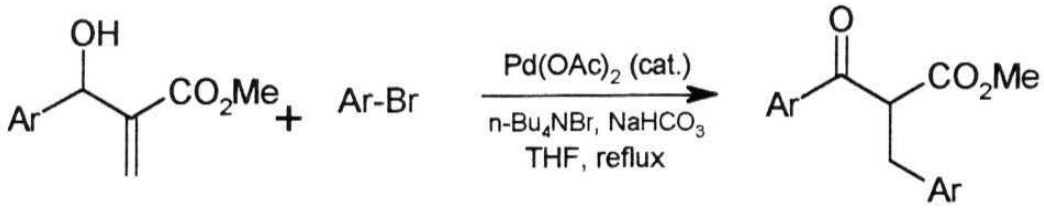
Scheme 22



Utaka *et al.* have described the Baker's Yeast mediated reduction of the Baylis-Hillman adducts which gave *syn* product in 98% enantiomeric excess and *anti* isomers in 67-98% enantiomeric excess (eq. 26).[93]

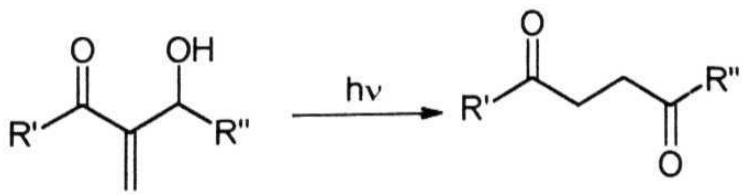


Recently, our research group has reported a simple synthesis of methyl 2-arylmethyl-3-oxoalkanoates *via* the arylation of the Baylis-Hillman adducts *i.e.* methyl 3-hydroxy-2-methylenealkanoates with aryl bromides under the catalytic influence of $Pd(OAc)_2$ (eq. 27).[94]



(eq. 27)

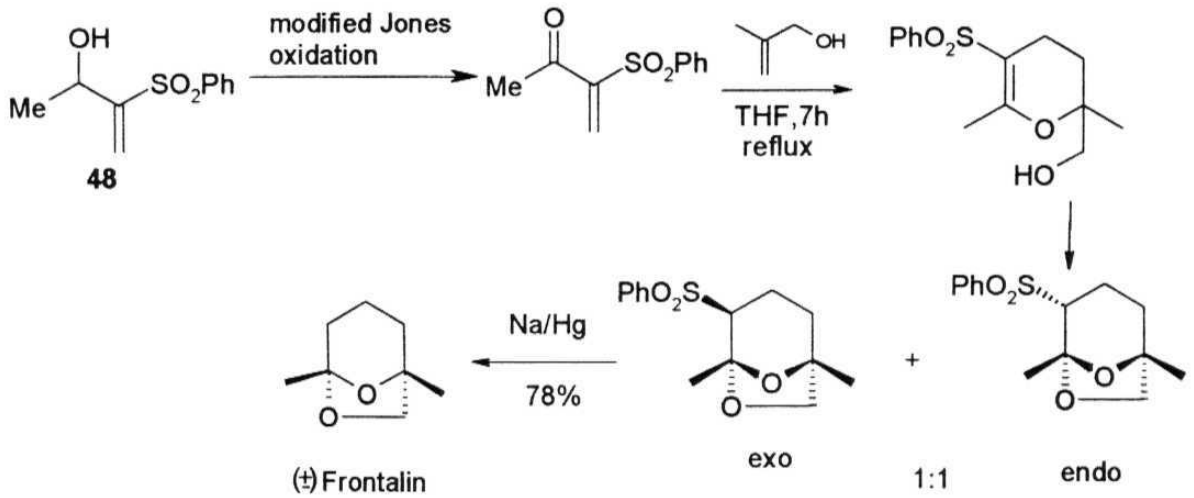
Recently, Mikami *et al.* have reported a novel photochemical carbon skeletal rearrangement of the Baylis-Hillman adducts leading to the formation of 1,4-dicarbonyl compounds (eq. 28).[95]



(eq. 28)

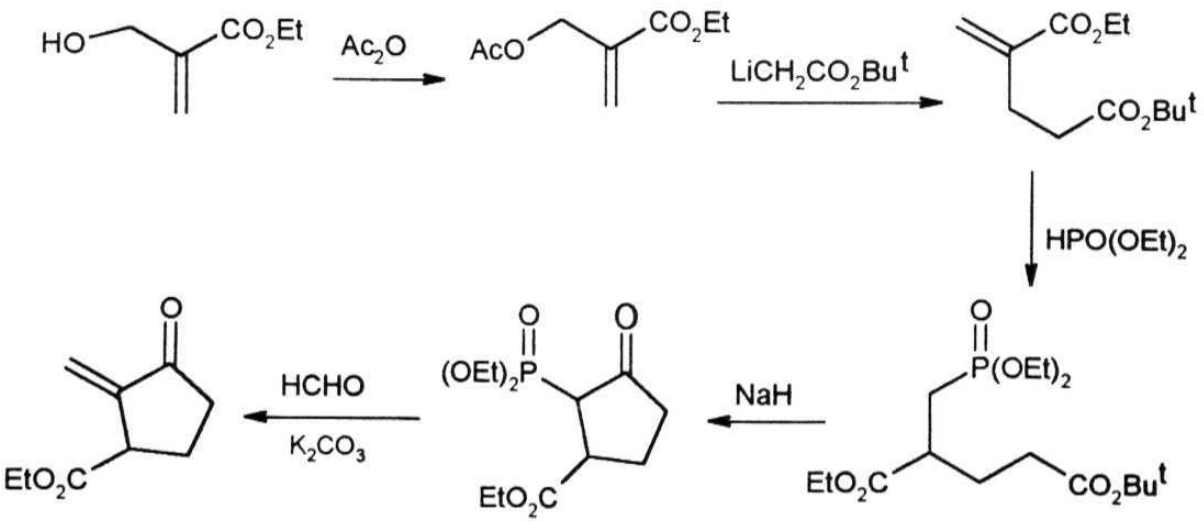
Hoffmann and Weichert[96] have reported simple synthesis of frontalin from the Baylis-Hillman adduct (48), derived from phenyl vinyl sulfone, following the reaction sequence as described in Scheme 23.

Scheme 23



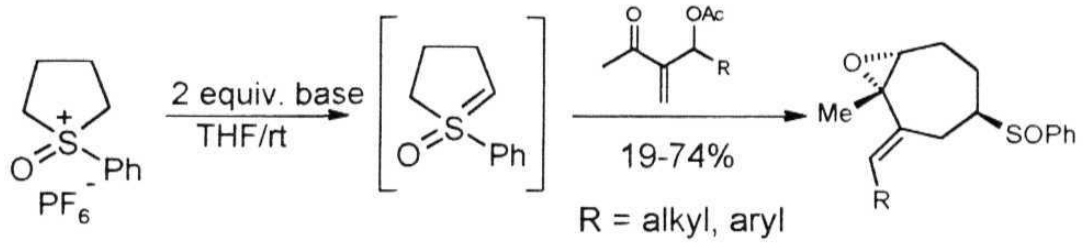
Ethyl 2-(hydroxymethyl)prop-2-enoate, derived from ethyl acrylate, was successfully converted into (±) sarkomycin,[97] an antitumor agent according to Scheme 24.

Scheme 24



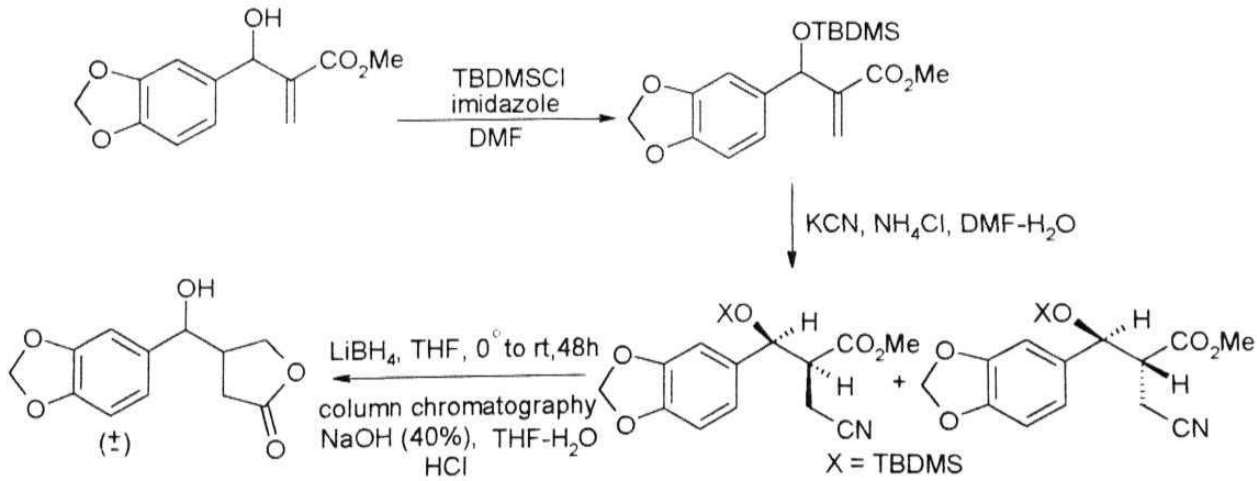
Recently, acetates of the Baylis-Hillman adducts have been successfully converted into cycloheptene oxide derivatives *via* the reaction with cyclic oxosulfonium ylide which is believed to proceed *via* tandem Michael-type addition and intramolecular Corey-Chaykovsky reaction[98] according to Scheme 25.

Scheme 25



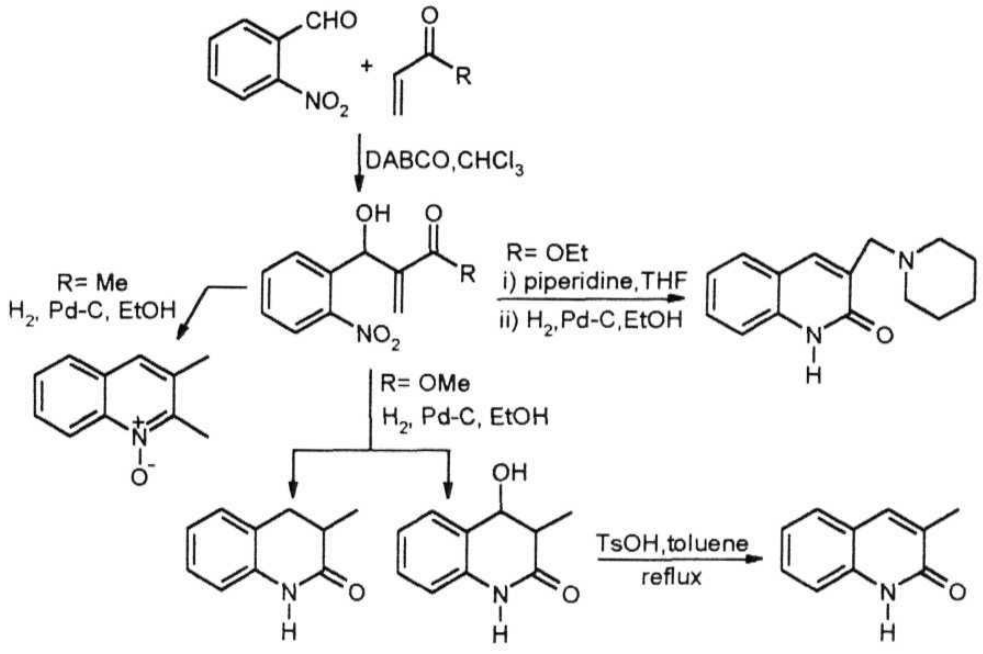
Almeida and Coelho[99] have successfully transformed the Baylis-Hillman adduct, derived from piperonal, into an interesting lignan derivative (Scheme 26).

Scheme 26



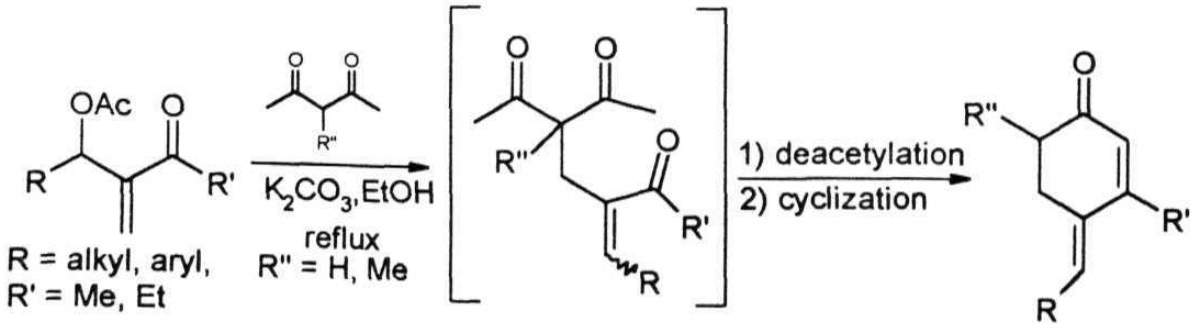
An interesting synthesis of quinoline derivatives has been reported by Kaye *et al.* starting from the Baylis-Hillman adducts derived from o-nitrobenzaldehyde (Scheme 27).[100]

Scheme 27



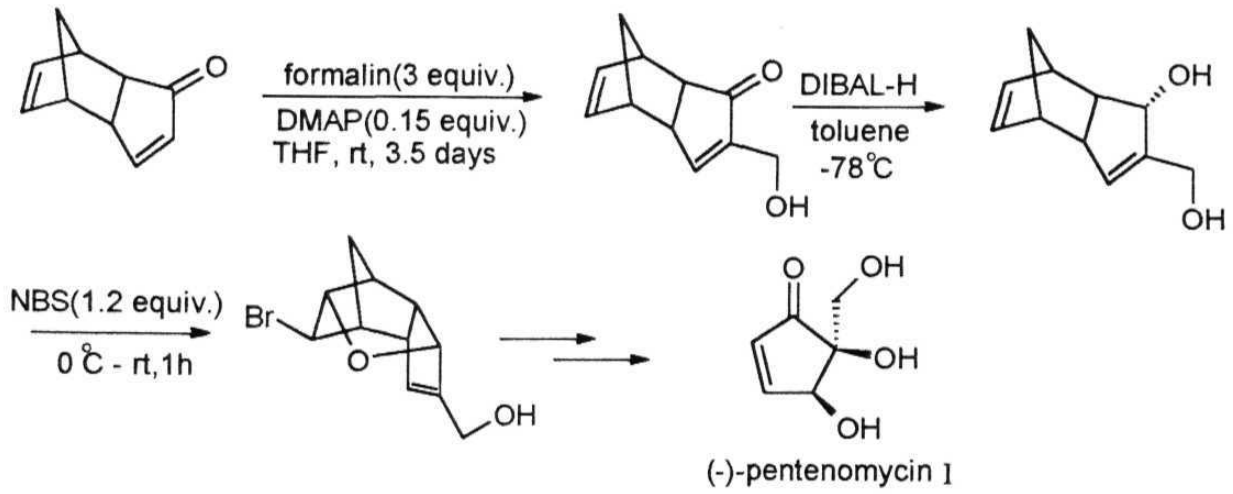
Amri and Chamakh[101] have successfully transformed the acetates of the Baylis-Hillman adducts obtained from alkyl vinyl ketones into 4-alkylidenecyclohex-2-en-l-ones, an important class of synthons (Scheme 28).

Scheme 28



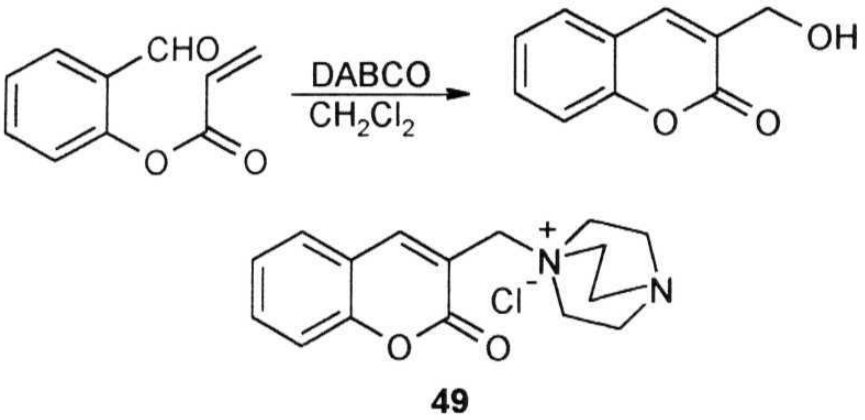
Recently, Ogasawara and Sugahara[102] have reported a new route for the synthesis of cyclopentenoid antibiotic (-) pentenomycin I involving the Baylis-Hillman reaction as one of the key steps (Scheme 29).

Scheme 29



Intramolecular Baylis-Hillman Reaction

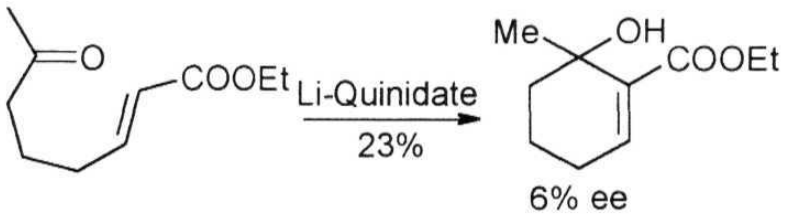
Though there has been considerable development in the Baylis-Hillman chemistry, no significant progress is made in the aspect of intramolecular Baylis-Hillman reaction. Drewes *et al.* have carried out an intramolecular Baylis-Hillman reaction of 2-acrylyloxybenzaldehyde with DABCO in dichloromethane and obtained the desired 3-hydroxymethylcoumarin in only 10% yield (eq. 29), but the major product in this reaction was a quaternary ammonium salt (49).



(eq. 29)

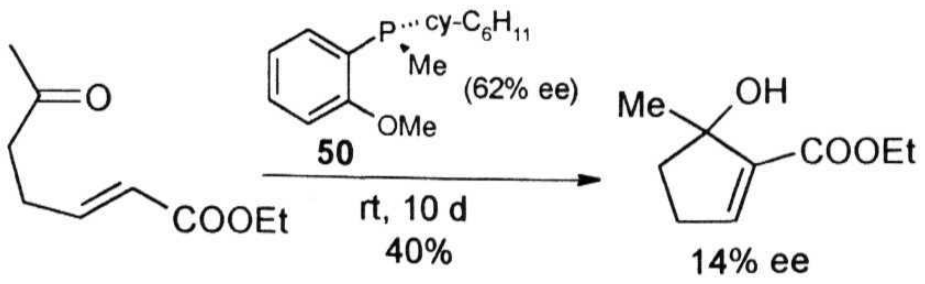
49

Roth and coworkers[104] have reported intramolecular Baylis-Hillman reaction of ethyl (2*E*)-7-oxooct-2-enoate *via* treatment with lithium salt *of* quinidine to provide the desired adduct in 23 % yield with 6% enantioselectivity (eq. 30).



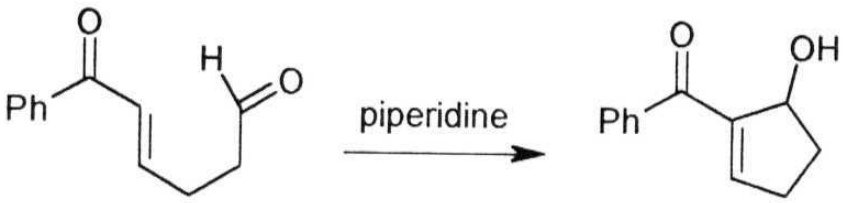
(eq. 30)

The chiral phosphine (50) has also been utilized as a catalyst for enantioselective intramolecular Baylis-Hillman reaction of ethyl (2*E*)-6-oxohept-2-enoate (eq. 31). However, enantioselectivity in this reaction was found to be poor.[104]



(eq. 31)

Recently, an intramolecular Baylis-Hillman cyclization of (4*E*)-6-phenyl-6-oxohex-4-enal with catalytic amount of a secondary amine leading to the formation of the desired cyclic allylic alcohol has been reported (eq 32).[105,106]



(eq. 32)

Objectives, Results and Discussion

From the preceding section it is quite clear that the Baylis-Hillman reaction has been and continues to be an important carbon-carbon bond forming reaction providing an unique class of highly functionalized molecules which have been used in a variety of stereoselective transformations.[6-8] Our research group has been actively involved for the last 15 years in the development of Baylis-Hillman reaction as one of the potential sources for stereoselective processes and in fact has contributed significantly to this effect. This thesis describes our studies in this direction with the following main objectives.

Objectives

1). Development of a new general protocol for the synthesis of (*E*)-3-arylidene / alkylidenechroman-4-one an important structural unit present in several biologically active molecules.

2). Application of this methodology for the synthesis of representative biologically active molecules such as bonducellin monomethyl ether, eucomin dimethyl ether, autumnalin trimethyl ether and (*E*)-3-(4-methoxybenzylidene)-6-methoxychroman-4-one, an antifungal agent.

3). Transformation of Baylis-Hillman adducts into indene and indane derivatives *via* the intramolecular Friedel-Crafts reaction.

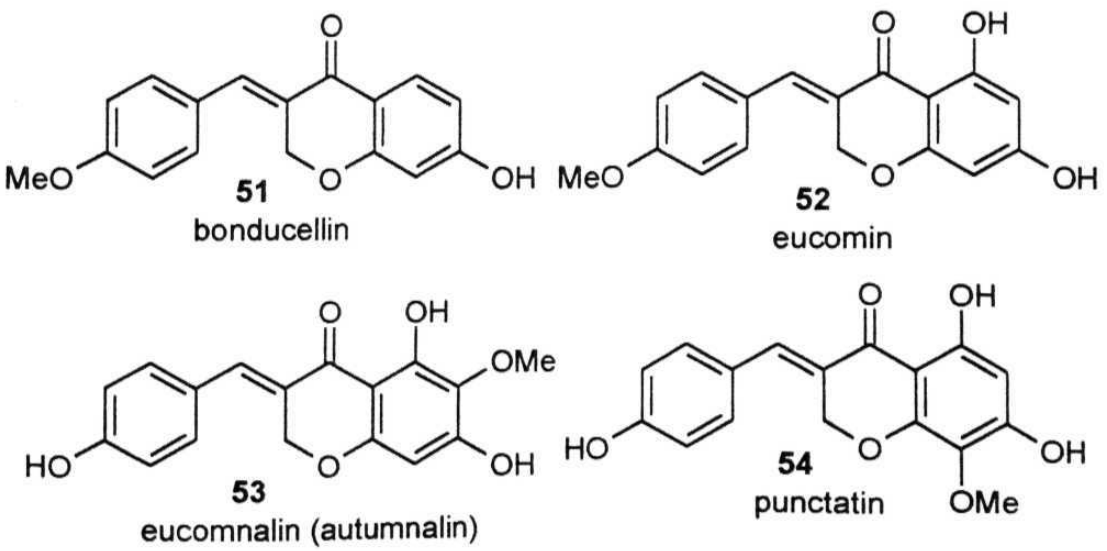
4). Synthesis of *dl* and *meso* allyl ethers *via* tandem construction of carbon-carbon and carbon-oxygen bonds using the Baylis-Hillman chemistry.

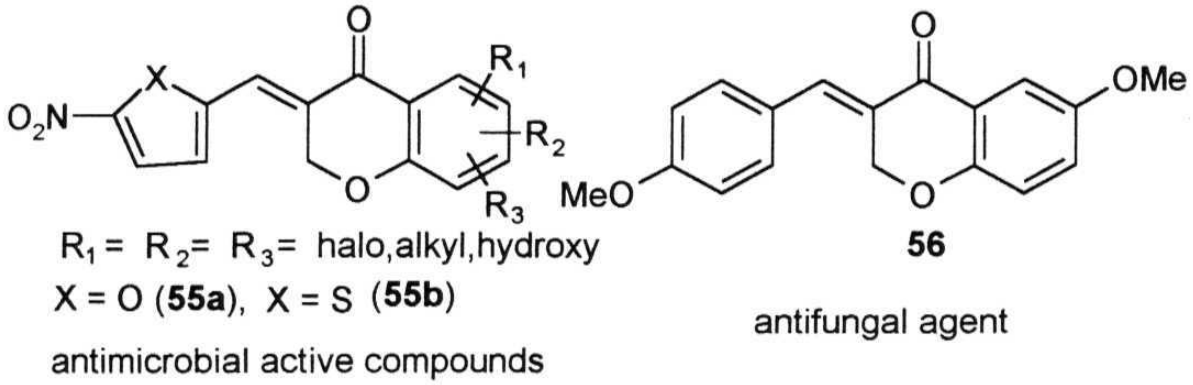
5). Diastereoselective synthesis of chiral ally] amines *via* the treatment of methyl **(2*Z*)-3-aryl-2-(bromomethyl)prop-2-enoates** with (S)-l-phenylethylamine in the presence of DABCO.

Results and Discussion

Development of novel protocol for synthesis of (*E*)-3-arylidene / alkylidenechroman-4-ones

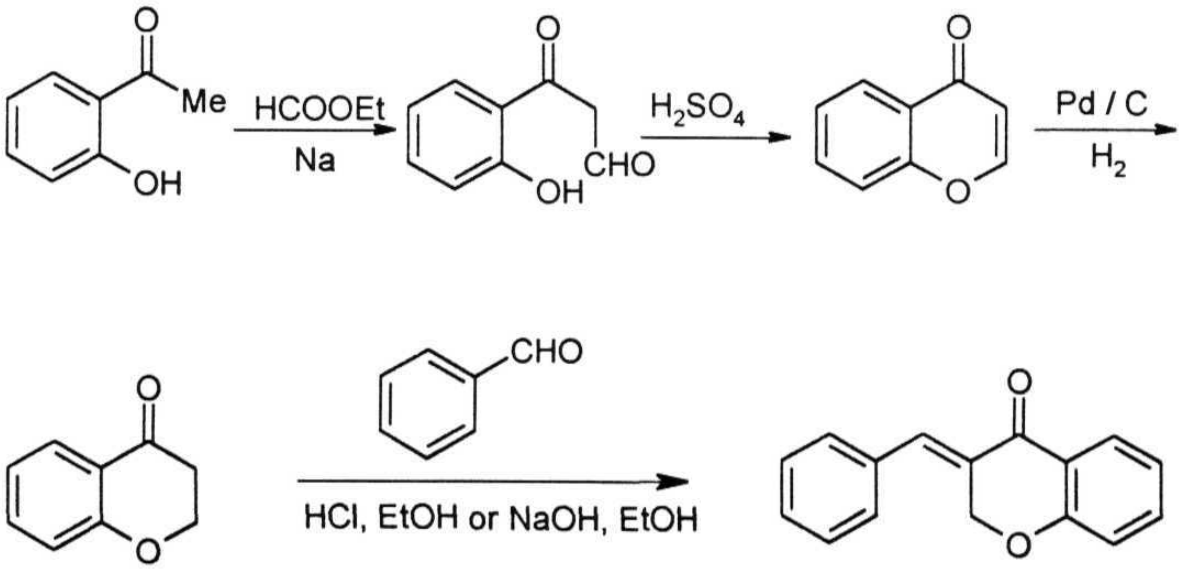
The (*E*)-3-benzylidenechroman-4-one moiety occupies a special place in the field of heterocycles, as this skeleton is an integral part of many natural products and biologically active molecules,[107-109] such as, bonducellin **(51)**,[110-111] eucomin (52),[112] autumnalin **(53)**,[113] punctatin **(54)**,[113] antimicrobial compounds (55a and **55b)**[114] and (*E*)-3-(4-methoxybenzylidene)-6-methoxychroman-4-one an antifungal agent (56)[109] *etc*. Therefore the development of simple general and new protocol for the synthesis of (*E*)-3-benzylidenechroman-4-one skeleton is of considerable importance today in synthetic organic chemistry.



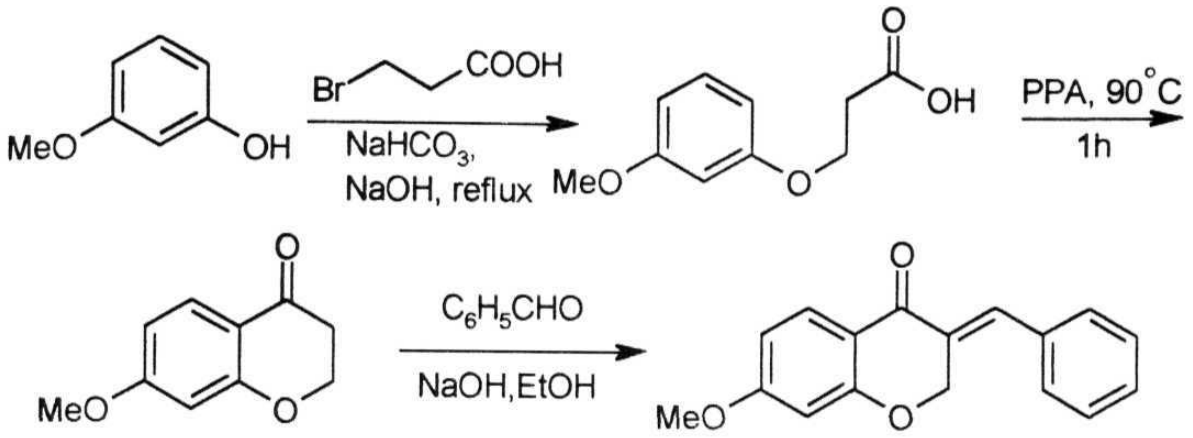


The classical and most of the literature methods for the synthesis of (*E*)-3-benzylidenechroman-4-one moiety involve the initial synthesis of chroman-4-one skeleton, followed by the construction of the benzylidene moiety *via* acid or base catalyzed aldol condensation with aryl aldehydes.[107-108] Some of the important methods reported in the literature are described below (Scheme 30 & 31).[109,115,116]

Scheme 30



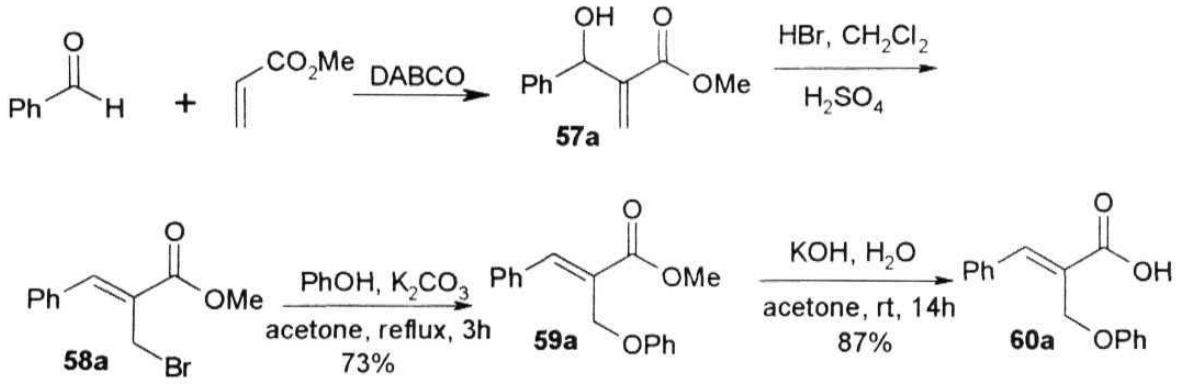
Scheme 31



However, to the best of our knowledge, there is no report in the literature for the synthesis of (*E*)-3-benzylidenechroman-4-one moiety involving the initial preparation of benzylidene moiety and then the construction of the chroman-4-one ring system. Therefore, we have undertaken this research program to develop a new protocol for the synthesis of (*E*)-3-benzylidenechroman-4-ones using methyl 3-aryl-3-hydroxy-2-methylenepropanoates (57) the Baylis-Hillman adducts derived from methyl acrylate. First, we have planned the synthesis of (2*E*)-2-(phenoxymethyl)-3-phenylprop-2-enoic acid **(60a)** according to Scheme 32. The desired methyl 3-hydroxy-2-methylene-3-phenylpropanoate (57a) was obtained *via* the reaction of methyl acrylate with benzaldehyde under the catalytic influence of DABCO. The allyl alcohol (57a) was converted into methyl (2Z)-2-(bromomethyl)-3-phenylprop-2-enoate **(58a)** by treating with 48% HBr in the presence of conc. H_2SO_4 according to the known procedure.[117] Allyl bromide **58a** was then treated with phenol in the presence of K_2CO_3 to give the desired methyl (2*E*)-2-(phenoxymethyl)-3-phenylprop-2-enoate **(59a)** in 73% yield

which was hydrolyzed with KOH/ water / acetone to provide corresponding *(2E)-2-*(phenoxymethyl)-3-phenylprop-2-enoic acid (60a) in 87 % yield (Scheme 32). The structures of these molecules 58a, 59a and 60a were confirmed by IR, H and C NMR spectral analysis. The (Z)-stereochemistry of the compound 58a and (*E*)-stereochemistry of the compounds 59a and 60a were assigned on the basis of H NMR spectral analyses.

Scheme 32

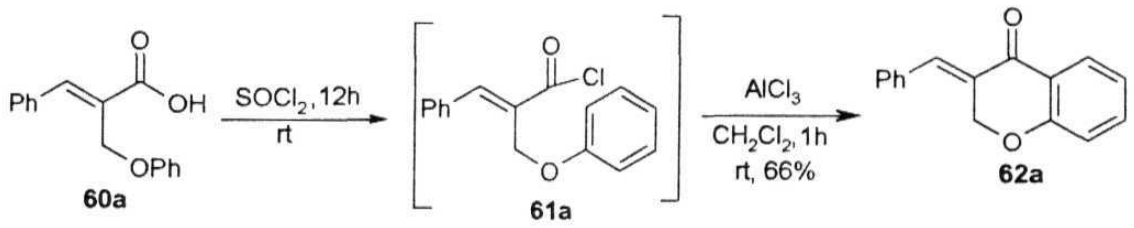


At this stage we planned to transform (2*E*)-2-(phenoxymethyl)-3-phenylprop-2-enoic acid (60a) into the desired (*E*)-3-benzylidenechroman-4-one (62a) *via* an intra-molecular Friedel-Crafts reaction of the corresponding acid chloride (61a). Thus the required acid chloride was prepared by treating the acid (60a) with $SOCl_2$ and the acid

It is well documented in the literature that in the ^1H NMR spectrum, the chemical shifts of the vinylic β-protons *cis* to the ketone, ester, and acid carbonyl groups and that of the corresponding vinylic *trans* β-protons are well differentiated and vinylic *cis* p-protons appear downfield in comparison with that of *trans* β-protons.[118,119] The (Z)-stercochemistry of the allyl bromides (58) was assigned on the basis of the chemical shift values of the β-vinylic protons *i.e.* 8 7.78-7.91 (when R = Ar) and δ 6.97 (when R = alkyl). The (*E*)-stereochemistry of these molecules 59, 60, was assigned on the basis of the chemical shift values of the p-vinylic protons, *i.e.* δ 8.02 - 8 25 (when R = Ar) and δ 6.93-7.11 (when R =alkyl) .[117-122]

chloride as such (without purification) was treated with $AlCl_3$ to provide the desired **(*E*)-3-benzylidenechroman-4-one (62a)** in 66 % yield (Scheme 33). Structure of this molecule was established by IR, ^1H & ^{13}C NMR (Fig 1), mass spectral data and elemental analysis. The (*E*)-stereochemistry was assigned on the basis of ^1H NMR spectral analysis.[$]

Scheme 33

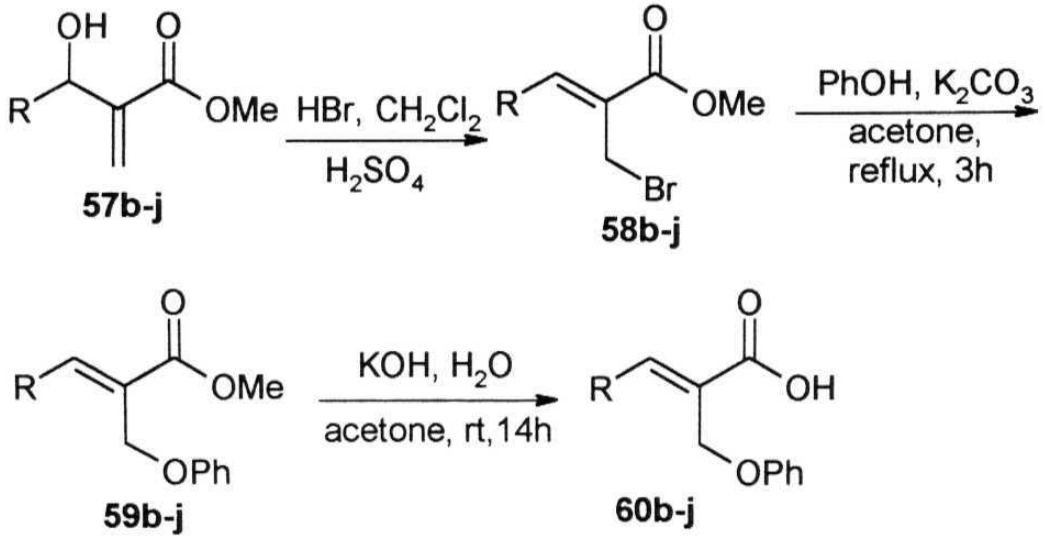


Encouraged by this result, we have prepared a representative class of (2*E*)-2-phenoxymethylalk-2-enoic acids according to Scheme 34 with an aim of converting them into desired chroman-4-ones *via* the intramolecular Friedel-Crafts reaction of the corresponding acid chlorides (Table 1). Intramolecular Friedel-Crafts reaction of the acids **60b, 60g-j**[Φ] *via* the treatment of the corresponding acid chlorides **(61b, 61g-j)** with $AlCl_3$ provided the desired (*E*)-chroman-4-ones **(62b, 62g-j)**[Φ] (Scheme 35, Table 2).[$]

[$] It is well established that the ^1H NMR spectrum of 3-benzylidenechroman-4-ones the vinylic proton *cis* to the carbonyl group appears at ≈ 6. 7.7, while the corresponding *trans* β-proton appears at ≈ 8 6.7.[112 123] In the case of compounds, **62a-h**, **62k-m** and **56** the vinylic β-protons appear at ≈ 8 7.81-7.96. Hence (*E*)-stereochemistry was assigned to the compounds **62a-h, 62k-m** and **56.** In the case of butylidene and pentylidenechroman-4-ones **62i** & **62j** (R = n-Pr, n-Bu) the vinylic β-proton appears at ≈ 8 7.04. Therefore (*E*)-stereochemistry was assigned to them.

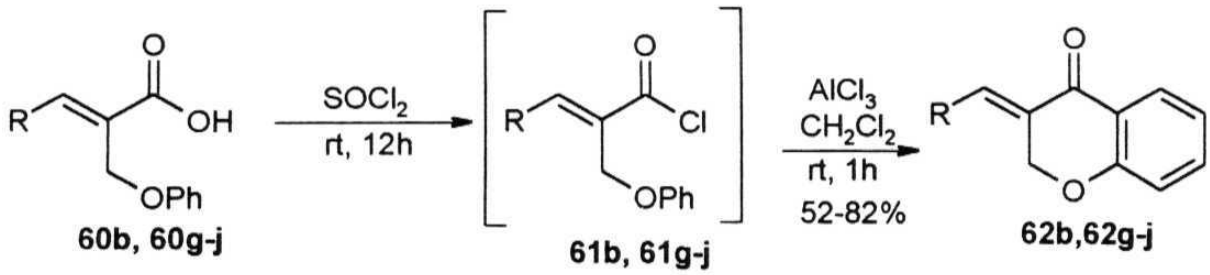
[Φ] For continuity and easy understanding the (*E*)-alkenoic esters, acids and chroman-4-ones obtained from **58a-j** were numbered as **59a-j. 60a-j** and **62a-j** respectively.

Scheme 34



R = 2-methylphenyl, 4-methylphenyl, 4-ethylphenyl, 4-isopropylphenyl, 4-methoxyphenyl, 2-chlorophenyl, 4-chlorophenyl, n-propyl, n-butyl

Scheme **35**



R = 2-methylphenyl, 2-chlorophenyl, 4-chlorophenyl, n-propyl, n-butyl

However, when we extended similar procedure for the substrates (60c-e) the desired corresponding 3-arylidenechroman-4-ones were not obtained, instead, 3-(4-alkyl-phenyl)methyl-4-chromones (63-65) were obtained (Scheme 36 & Table 3). The structure of these molecules were established by IR, ^1H (Fig 2 for compound 63) & ^{13}C NMR (Fig 3 for compound 63), mass spectral and elemental analyses.

Table 1: Synthesis of (2*E*)-2-(phenoxymethyl)-3-aryl/alkylprop-2-enoic acids* (57→58→59→60)

Allyl alcohol	R	(Z)- Allyl bromide[a,i]	Yield[c] (%)	(*E*)-Alkenoic ester[d,e]	Yield[f] (%)	(*E*)-Alkenoic acid[g,h]	Yield[i] (%)
57a	Phenyl	58a	**91**	59a	**73**	60a	**87**
57b	**2-methylphenyl**	58b	**90**	59b	**87**	60b	**93**
57c	**4-methylphenyl**	58c	92	59c	**75**	60c	**83**
57d	**4-ethylphenyl**	**58d**	**90**	59d	**90**	**60(1**	**92**
57c	**4-isopropylphenyl**	58c	**74**	59c	**71**	**60e**	**84**
57f	**4-methoxyphenyl**	58f	**75**	**59f**	**77**	60f	**90**
57g	2-chlorophenyl	**58g**	**80**	**59g**	**73**	**60g**	**94**
57h	4-chlorophenyl	**58h**	**79**	**59h**	**76**	**60h**	**91**
57i	n-propyl	**58i**	**62**	**59i**	**65**	**60i**	**78**
57j	n-butyl	**58j**	**76**		**56**	60j	61

a) The (*Z*)-stereochemistry for the compounds 58 and (*E*)-stereochemistry for the compounds 59, 60 were assigned on the basis 'H NMR spectral analysis.[#]

b) All the compounds were obtained as colorless liquids except 58f (obtained as a solid) and were characterized by IR. ^{1}H NMR. and ^{13}CNMR spectral data.

c) Isolated yields of the pure products after column chromatography (silica gel 2% EtOAc in hexanes)

d) All reactions were carried out in 10 mM scale of allyl bromides with phenol (10 mM) in the presence of K_2CO_3 (10 mM) in acetone at reflux temperature for 3 h. Compound 58i & **58** j gave ~ 15% of a side product, presumably S_N2' products.

e) The compounds 59a-b. 59d. 59g, 59i-j were obtained as colorless viscous liquids and the compounds 59c. **59e. 59f. 59h** were obtained as colorless solids. All these molecules gave satisfactory IR, ^{1}H NMR and ^{13}C NMR spectral analyses.

f) Isolated yields of the pure products after column chromatography (silica gel, 3 % EtOAc in hexanes).

g) Hydrolysis of these esters was carried out on 5 mM scale of the esters with aq. KOH-acetone at room temperature.

h) All the compounds were obtained as colorless solids and were characterized by IR, ^{1}H NMR and ^{13}C NMR spectral data.

1) Isolated yields of pure acids after crystallization (10% EtOAc in hexanes).

Table 2: Synthesis of 3-arylidene or alkylidenechroman-4-ones *via* an intra-molecular Friedel-Crafts reaction of the acid chlorides with $AlCl_3$[a-c]

(*E*)-Alkenoic acid	R	Chroman-4-one	Yield (%)
60a	phenyl	**62a**	66
60b	2-methylphenyl	**62b**	53
60g	2-chlorophenyl	**62g**	82
60h	4-chlorophenyl	**62h**	64
60i	n-propyl	**62i**	56
60j	n-butyl	**62j**	63

a) All the acid chlorides were prepared from lmM scale of the acid and subsequently were treated with $AlCl_3$ (1mM) in CH_2Cl_2 at room temperature for 1h.

b) All the products gave satisfactory IR, ^1H NMR, ^{13}C NMR and elemental analyses.

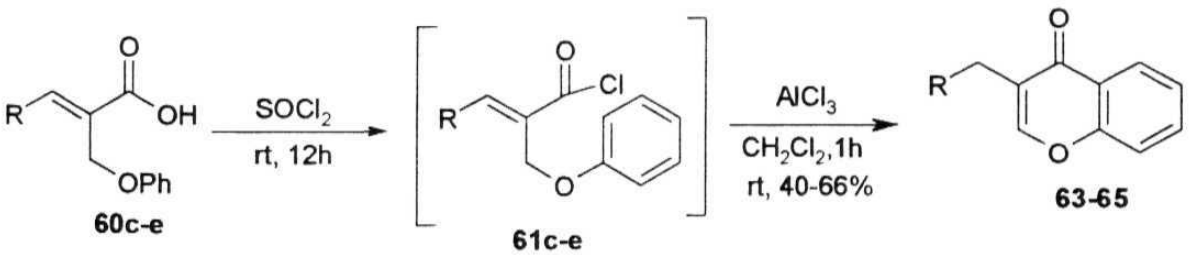
c) The products **62a-b, 62g-h** were obtained as pale yellow crystalline solids and the products **62i-j** obtained as colorless viscous liquids.

d) (*E*)-Stereochemistry was assigned for these molecules on the basis of their ^1H NMR Spectral analyses.[$]

e) Yields of the pure products obtained after column chromatography (silica gel, 3% EtOAc in hexanes) followed by crystallization from EtOAc-hexanes (2:98) in the case of **62a-b, 62g-h** and after column chromatography (silica gel, 3% EtOAc in hexanes) in the case of **62i-j.**

The exact mechanism of these two different results [formation of **(*E*)-3-benzylidine-**chroman-4-ones and 3-(4-alkylphenyl)methyl-4-chromones] is not clear to us. When similar sequence of reaction was extended to the molecule 60f the reaction was not clean and desired product was not obtained This may be due to the cleavage of OMe group with $AlCl_3$ and there by giving several unidentified products (Scheme 37).

Scheme 36



R = 4-methylphenyl, 4-ethylphenyl, 4-isopropylphenyl

Scheme 37

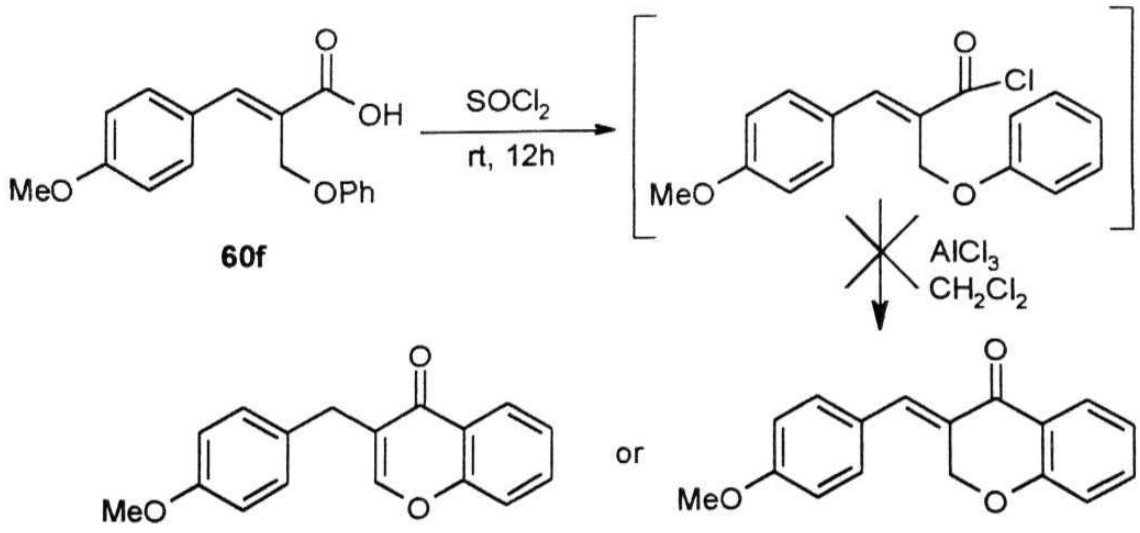


Table 3: Synthesis of 3-(4-alkylphenyl)methyl-4-chromones *via* an intramolecular Friedel-Crafts reaction of the acid chlorides with $AlCl_3$[a,b]

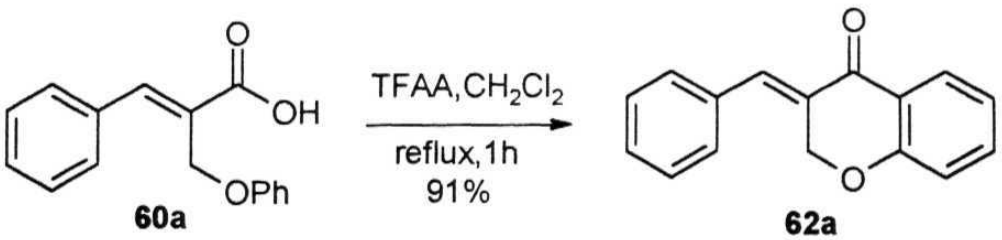
(*E*)-Alkenoic acid	R	4-Chromone	Yield[c] (%)
60c	4-methylphenyl	**63**	66
60d	4-ethylphenyl	**64**	40
60e	4-isopropylphenyl	**65**	48
60f	4-methoxyphenyl	Reaction is not clean	

a) Intramolecular Friedel-Crafts reaction of the acid chlorides obtained from the corresponding acids (1mM) was carried out with $AlCl_3$ (1mM) at room temperature in CH_2Cl_2 for 1h.

b) All the products were obtained as pale yellow crystalline solids and gave satisfactory IR, ^1H NMR and ^{13}C NMR, mass spectral and elemental analyses.

c) Yields of the pure chromones obtained by column chromatography (silica gel, 3 % EtOAc in hexanes) followed by crystallization (2% EtOAc in hexanes).

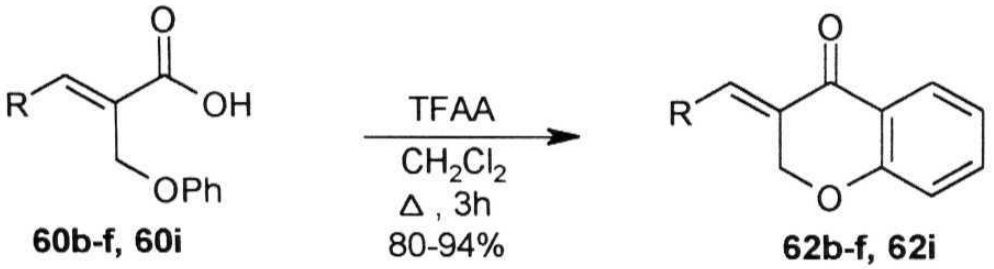
Since this methodology of preparing chroman-4-ones *via* an intramolecular Friedel-Crafts reaction of the corresponding acid chlorides did not provide a general synthesis of arylidene / alkylidenechroman-4-ones, we looked for an alternative method for this purpose. In this direction we have selected trifluoroacetic anhydride (TFAA) as a reagent for effecting intramolecular Friedel-Crafts reaction of the acids (60). First, we have selected (2*E*)-2-(phenoxymethyl)-3-phenylprop-2-enoic acid **(60a)** as a substrate for the treatment with TFAA under various conditions. The best results were obtained when (2*E*)-2-(phenoxymethyl)-3-phenylprop-2-enoic acid (1 mM) was treated with TFAA (1 mM) in CH_2Cl_2 at reflux temperature for 1 hour, thus providing the desired (*E*)-3-benzylidenechroman-4-one **(62a)** in 91% yield (eq. 33). The structure of this molecule was confirmed by IR, ^1H and ^{13}CNMR spectral analysis. Also, this molecule is identical with (*E*)-3-benzylidenechroman-4-one which was prepared *via* the acid chloride according to Scheme 33. Then, we have extended the same methodology for the substrates **60b-f, 60i** which provided the desired 3-arylidenechroman-4-ones **62b-f,** 62i in good yields (eq. 34, Table 4)°. The acids **(60c-e)** which provided 3-(4-alkyl-phenyl)methyl-4-chromones (63-65) (instead of (*E*)-3-arylidenechroman-4-ones) *via* an



(eq. 33)

Φ For continuity and easy understanding the (*E*)-alkenoic esters, acids and chroman-4-ones obtained from 58a-j were numbered as 59a-j, 60a-j and 62a-j respectively.

intramolecular Friedel-Crafts reaction of the corresponding acid chlorides with $AlCl_3$ (Scheme 36), now on treatment with TFAA provided desired (*E*)-3-arylidenechroman-4-ones (62c-e) in excellent yields. These results indicate that the intramolecular Friedel-Crafts reaction of the acid using TFAA as a reagent is far superior method than the intramolecular Friedel-Crafts reaction of the corresponding acid chloride using $AlCl_3$ as reagent.



60b-f, 60i **62b-f, 62i** **(eq. 34)**

R = 2-methylphenyl, 4-methylphenyl, 4-ethylphenyl, 4-isopropylphenyl, 4-methoxyphenyl, n-propyl

Thus, we have developed a new protocol for the synthesis of 3-arylidene / alkyl-idenchroman-4-ones using the Baylis-Hillman adducts. To prove the efficacy of this methodology, we have undertaken first the synthesis of bonducellin monomethyl ether.

Synthesis of bonducellin monomethyl ether

Bonducellin **(51)**[110,111] is a natural product isolated from two natural sources. Purushothaman *et al*[110] have isolated bonducellin as a minor constituent from *Caesalpinia bonducella*, a medicinal plant. Mcpherson *et al*[111] have isolated fairly good amounts of bonducellin from *Caesalpinia pulcherrima*.

Table 4: Synthesis of (*E*) 3-arylidene / alkylidenechroman-4-ones *via* an intra-molecular Friedel-Crafts reaction of the acids with TFAA[a, b]

(*E*)-Alkenoic acid	R	Chroman-4-one[c]	Yield[d]
60a	phenyl	**62a**	91
60b	2-methylphenyl	**62b**	90
60c	4-methylphenyl	62c	94
60d	4-ethylphenyl	**62d**	93
60e	4-isopropylphenyl	**62e**	91
60f	4-methoxyphenyl	**62f**	92
60i	n-propyl	**62i**	80

a) All the reactions were carried out on 1 mM scale of the acid **(60a-f, i)** with TFAA (1 mM) in CH_2Cl_2 at reflux temperature for 1h.

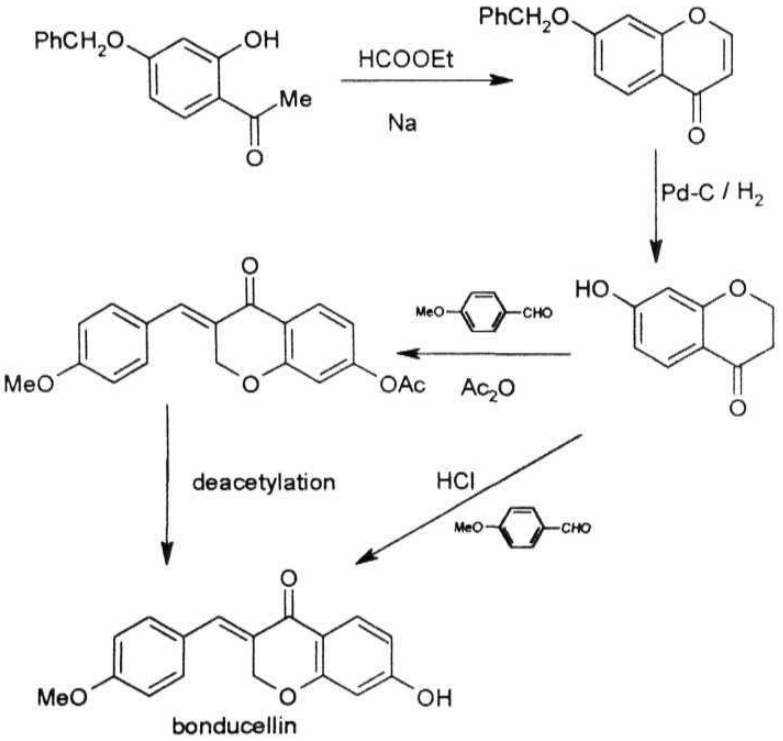
b) All the products gave satisfactory IR, ^{1}H NMR, ^{13}C NMR, mass spectral data and elemental analyses.

c) (*E*)-Stereochemistry of these molecules were assigned on the basis of their ^{1}H NMR spectral analyses.

d) Isolated yields of the pure products **(62a-f)** obtained after crystallization from EtOAc:hexanes (2:98) or column chromatography **(62i)** (silica gel, 3% EtOAc **in** hexanes).

Though the molecule is interesting, only a few methods have been reported for its synthesis in the literature.[124,125] A representative [124] synthesis of bonducellin has been described in Scheme 38. This synthetic sequence describes the construction of chroman-4-one moiety first followed by the introduction of the arylidene group *via* aldol reaction with 4-methoxybenzaldehyde.

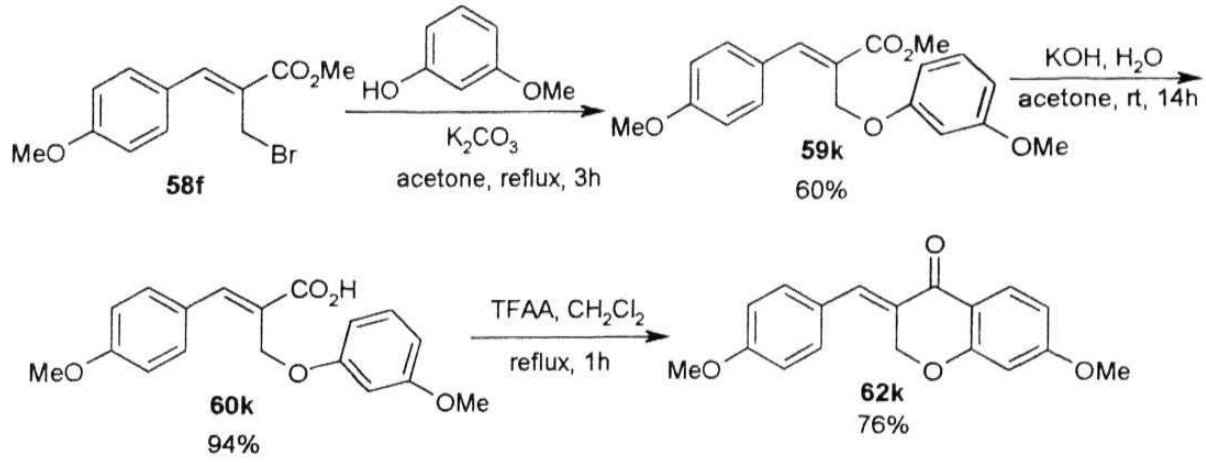
Scheme 38



We have planned the synthesis of bonducellin monomethyl ether according to Scheme 39 based on the new protocol developed by us. Thus, methyl (2*Z*)-2-(bromomethyl)-3-(4-methoxyphenyl)prop-2-enoate (58f) was converted into methyl (2*E*)-2-(3-methoxyphenoxy)methyl-3-(4-methoxyphenyl)prop-2-enoate (**59k**)[@] by the treatment with 3-methoxyphenol in the presence of K_2CO_3. This ester was then hydrolyzed using KOH,

water / acetone solvent system to provide the desired (2*E*)-2-(3-methoxyphenoxy)-methyl-3-(4-methoxyphenyl)prop-2-enoic acid (**60k**)[@] in 94 % yield Subsequent treatment of the acid (60k) with TFAA provided the desired bonducellin monomethyl ether (**62k**)[@] in 76 % yield (Scheme 39). The structure of this molecule was established by IR, ^{1}H (Fig 4) & ^{13}CNMR (Fig 5), mass spectral data and elemental analysis.

Scheme 39

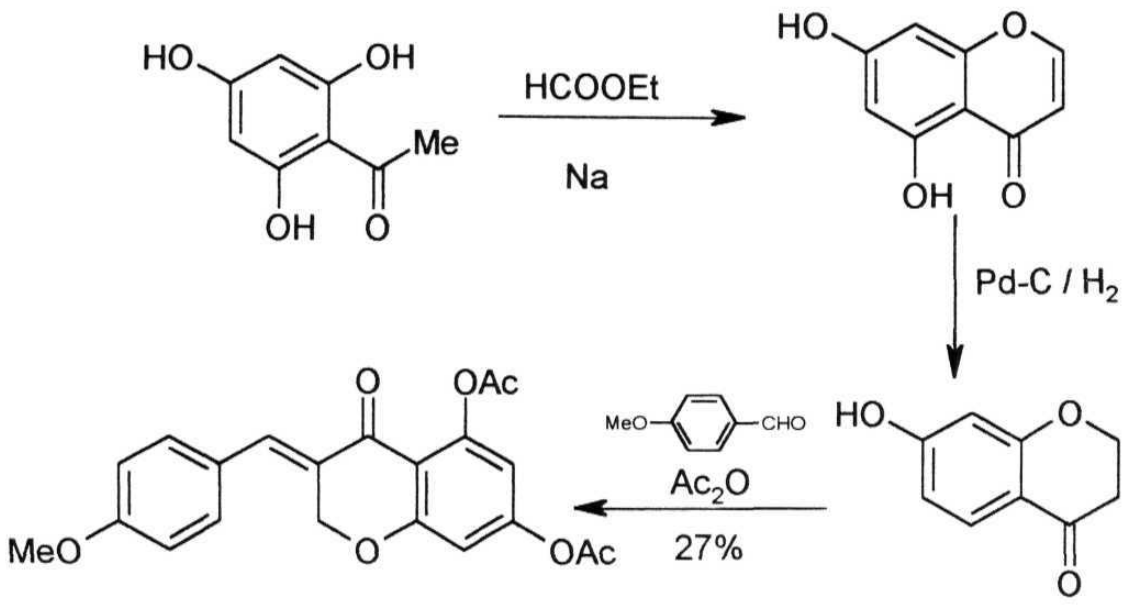


Synthesis of eucomin dimethyl ether

Bohler and Tamm have first isolated eucomin (52)[112] from the bulbs of *eucomis bicolor* BAK (*Liliaceae*). Farkas *et al.*[126-128] have reported the synthesis of eucomin diacetate *via* the aldol reaction of 5,7-dihydroxychroman-4-one[129] with *p*-anisaldehyde in the presence of acetic anhydride under the reflux condition in 27% yield (Scheme 40).

[@] For easy understanding and continuity, methyl (2*E*)-2-(3-methoxyphenoxy)methyl-3-(4-methoxyphenyl)prop-2-enoate, the corresponding acid and the chroman-4-one were numbered as 59k, 60k and 62k respectively.

Scheme 40

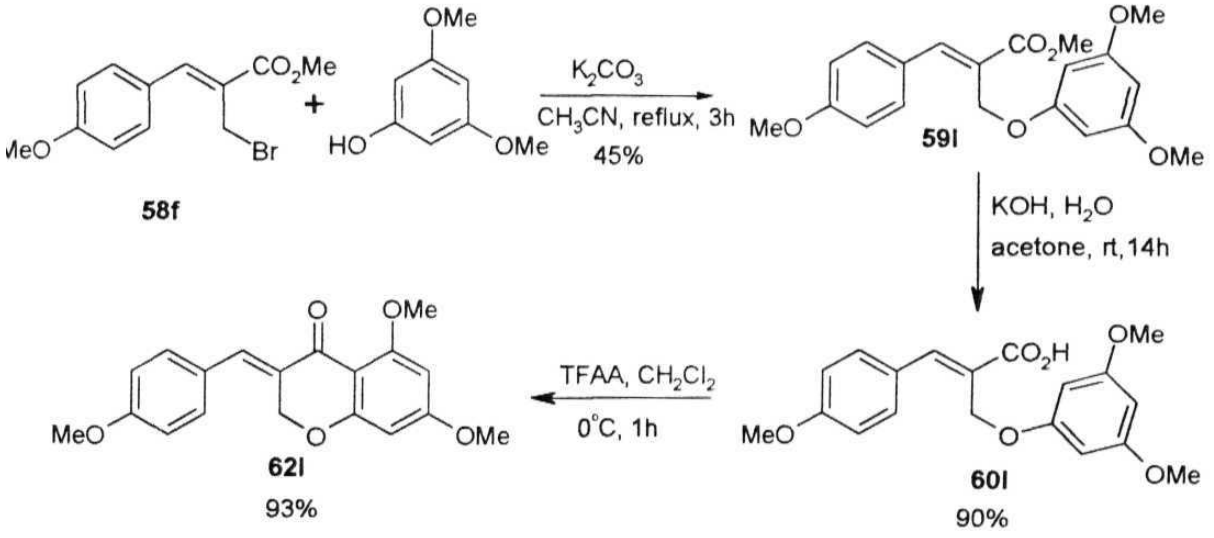


Since eucomin is an interesting molecule, we have undertaken the synthesis of eucomin dimethyl ether according to Scheme 41. Methyl (2Z)-2-(bromomethyl)-3-(4-methoxyphenyl)prop-2-enoate **(58f)** was treated with 3,5-dimethoxyphenol in the presence of K_2CO_3 to afford methyl (2*E*)-2-(3,5-dimethoxyphenoxy)methyl-3-(4-methoxyphenyl)prop-2-enoate **(59l)**[ϖ] in 45% yield. This ester was hydrolyzed with KOH in water-acetone solvent system to provide the corresponding (2*E*)-2-(3,5-dimethoxyphenoxy)methyl-3-(4-methoxyphenyl)prop-2-enoic acid **(60l)**[ϖ] in 90% yield. Subsequent intramolecular Friedel-Crafts reaction of the acid **(60l)** *via* treatment of TFAA under reflux condition in dichloromethane as a solvent provided the desired

For the easy understanding and continuity, methyl **(2*E*)-2-(3,5-dimethoxyphenoxy)methyl-3-(4-methoxyphenyl)prop-2-enoate**, corresponding acid and the **chroman-4-one** were numbered as **59l** and **60l** and **62l** respectively.

eucomin dimethyl ether **(62l)**[m] only in 33% yield. However, the yield has gone up to 93% when we carried out the reaction at 0°C for 1 hour. This methodology represents a simple convenient synthesis of eucomin dimethyl ether with excellent yield. The structure of this molecule was established by IR, ^{1}H (Fig 6) & ^{13}CNMR, mass spectral data and elemental analysis.

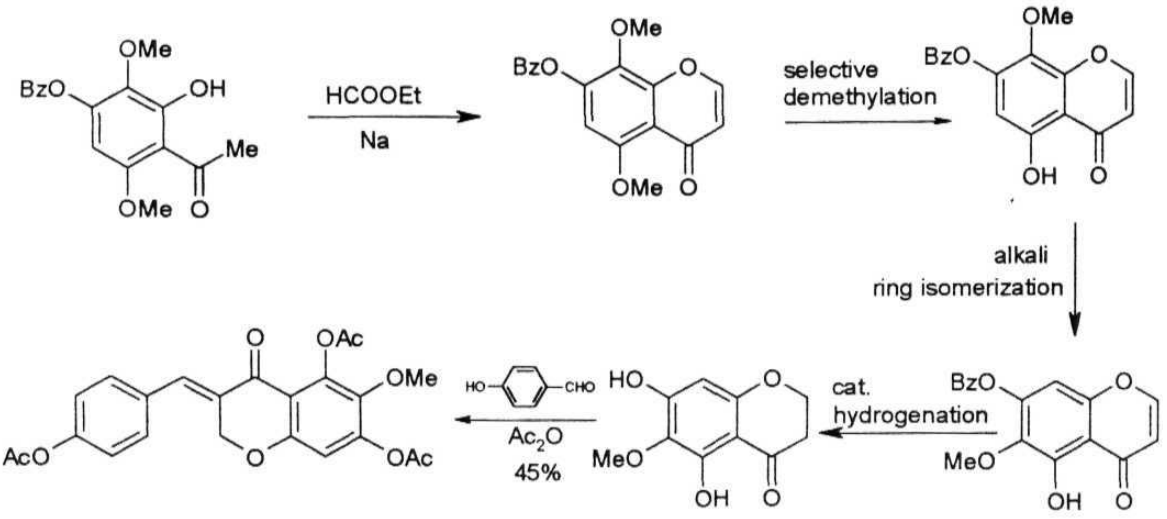
Scheme **41**



Synthesis of eucomnalin (or autumnalin) trim ethyl ether

Autumnalin[113] (later named as Eucomnalin) (53) was first isolated by Sidwell & Tamm from the bulbs of *eucomis autumnalis* GRAEB *{Liliaceae).* Literature survey indicates that only a few methods are known for the synthesis of the above mentioned molecule,[107,127] and a representative method for the synthesis of eucomnalin triacetate is described in Scheme 42.[127] Due to the interesting structural features of this molecule, it

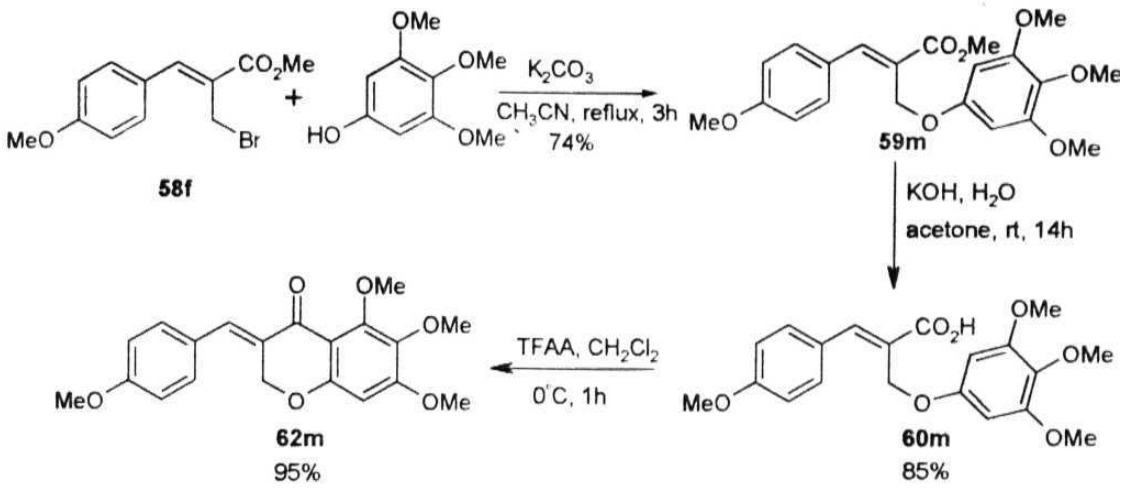
Scheme 42



has attracted our attention and therefore we have planned the synthesis of autumnalin (eucomnalin) trimethyl ether according to Scheme 43. Methyl (2Z)-2-(bromomethyl)-3-(4-methoxyphenyl)prop-2-enoate (58f) was successfully transformed into methyl (2*E*)-3-(4-methoxyphenyl)-2-(3,4,5-trimethoxyphenoxy)methylprop-2-enoate (**59m**)[] *via* the treatment with 3,4,5-trimethoxyphenol in the presence of K_2CO_3. Subsequent hydrolysis using KOH in water-acetone solvent system afforded (2*E*)-3-(4-methoxyphenyl)-2-(3,4,5-trimethoxyphenoxy)methylprop-2-enoic acid (**60m**)[] in 85 % yield. Treatment of the acid (60m) with TFAA for 1h at 0°C provided the desired title compound (**62m**)[] in 95 % yield (Scheme 43). The structure of this molecule was established by IR, ^{1}H& ^{13}CNMR (Fig 7), mass spectral data and elemental analysis.

] For the easy understanding and continuity, methyl (2*E*)-3-(4-methoxyphenyl)-2-(3,4,5-trimethoxyphenoxy)methylprop-2-enoate, corresponding acid and the chroman-4-one were numbered as 59 **m**, 60 **m** and 62m respectively.

Scheme 43

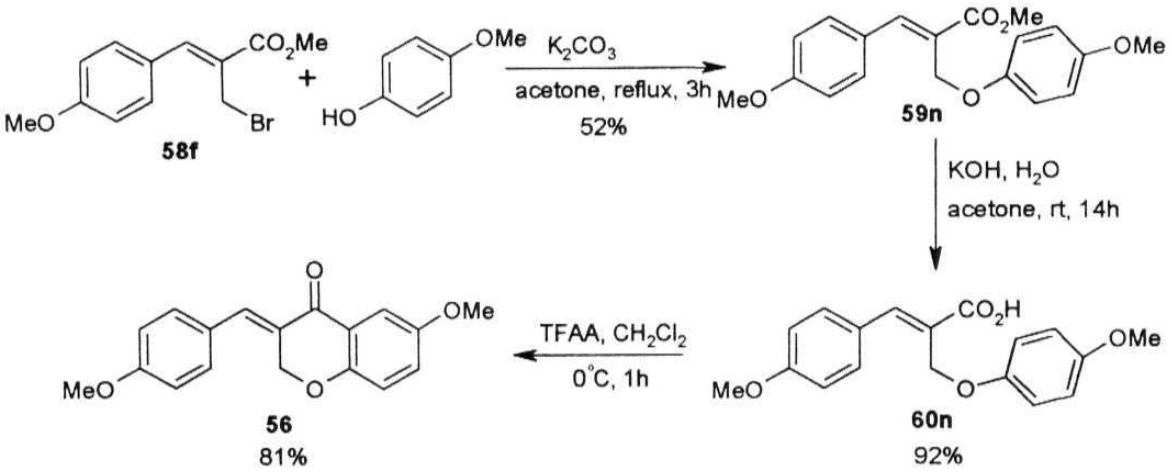


In literature, several biologically active molecules having 3-benzylidenechroman-4-one skeleton have been reported. For example compounds **55a** and **55b**[114] are known to possess antimicrobial activity. Recently Al Nakib[109] *et al* have reported the anti fungal activity of 3-(4-methoxybenzylidene)-6-methoxychroman-4-one (56) against *Cryptococus neoformans* and *Torulopsis* With a view to further expand the scope and demonstrate the efficacy of our new methodology we have successfully synthesized 3-(4-methoxybenzylidene)-6-methoxychroman-4-one (56) in excellent yield according to Scheme 44. The allyl bromide **(58f)** was transformed into the methyl (2*E*)-2-(4-methoxyphenoxy)methyl-3-(4-methoxyphenyl)prop-2-enoate **(59n)**[σ] *via* the treatment with 4-methoxyphenol. Subsequent hydrolysis followed by the treatment of the resulting acid **(60n)**[σ] with TFAA furnished the desired (*E*)-3-(4-methoxybenzylidene)-

For the easy understanding and continuity, methyl (2*E*)-2-(4-methoxyphenoxy)methyl-3-(4-methoxyphenyl)prop-2-enoate and the corresponding acid were numbered as 59 n and 60 n respectively.

6-methoxychroman-4-one (56) (Scheme 44). The structure of this molecule (56) was confirmed by IR, ^{1}H& ^{13}CNMR (Fig 8), mass spectral data and elemental analysis.

Scheme 44



Thus, our new protocol has been successfully used for the synthesis of bonducellin monomethyl ether (62k), eucomin dimethyl ether (**62l**), autumnalin trimethyl ether (62m) and (*E*)-3-(4-methoxybenzylidene)-6-methoxychroman-4-one (56) an antifungal agent in excellent yields (Table 5). These applications clearly demonstrate the importance of the Baylis-Hillman adducts in synthesizing natural and biologically active molecules.

Table 5: Synthesis of monomethyl ether of bonducellin, dimethyl ether of eucomin, trim ethyl ether of autumnalin and antifungal agent (59k-n→60k-n→62k-m, 56)[a]

(*E*)-Alkenoic ester[b,c]	Yield[d]	(*E*)-Alkenoic acid[c,f]	Yield[g]	(*E*)-Arylidene-chroman-4-one [h]	Yield[j]
59k	**60**	**60k**	94	**62k**	76
591	45	**60l**	90	**62l**	93
59m	74	**60m**	85	**62m**	95
59n	52	**60n**	92	**56**	81

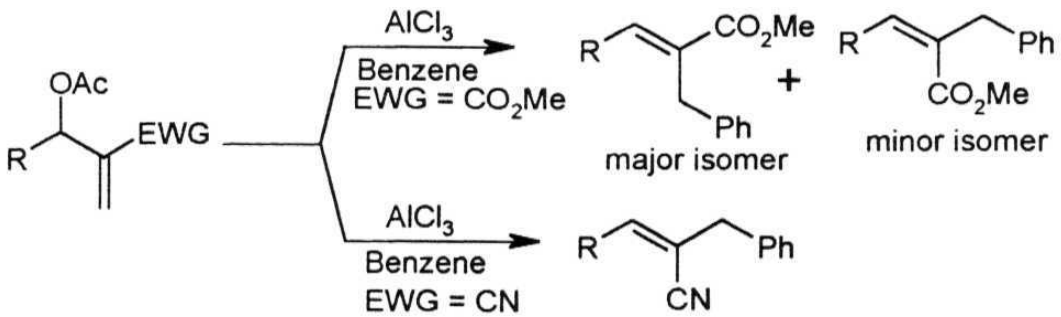
a) The (*E*)-stereochemistry was assigned on the basis of ^{1}H NMR spectral analysis.[$]
b) All the reactions were carried out on 10 mM scale of allyl bromide with 10 mM of substituted phenol in the presence of 10mM of K_2CO_3 at reflux temperature.
c) All the products gave satisfactory IR, ^{1}H NMR, ^{13}C NMR spectral data.
d) Isolated yields of the pure products after careful column chromatography (silica gel, 3% EtOAc in hexanes) based on allyl bromides
e) All the reactions were carried out in 5 mM scale of the ester with aqueous KOH-acetone at room temperature.
f) All the products gave satisfactory IR, ^{1}H NMR, ^{13}C NMR spectral data.
g) Isolated yields of the pure acids **(60k-n)** after crystallization based on esters.
h) All reactions were carried out on 1 mM scale of the acid **(60k-n)** with TFAA (1 mM) in CH_2Cl_2 at reflux temperature or at 0°C for 1h.
i) All the products gave satisfactory IR, ^{1}H NMR, ^{13}C NMR, mass spectral data and elemental analyses.
j) Yields of the pure chroman-4-ones, obtained after crystallization **(62k** & **56)** from EtOAc-hexanes (2:98) or column chromatography (silica gel, 20 % EtOAc in hexanes) followed by crystallization (**62l-m**) from EtOAc-hexanes (15:85) based on acid.

[$] It is well established that the ^{1}H NMR spectrum of 3-benzylidenechroman-4-ones the vinylic proton *cis* to the carbonyl group appears at ≈ 5. 7.7, while the corresponding *trans* β-proton appears at ≈ 8 6.7.[112,123] In the case of compounds, **62a-h, 62k-m** and 56 the vinylic p-protons appear at ≈ δ 7.81-7.96. Hence (*E*)-stereochemistry was assigned to the compounds **62a-h, 62k-m** and **56.** In the case of butylidene and pentylidenechroman-4-ones **62i** & **62j** (R = n-Pr, n-Bu) the vinylic β-proton appears at ≈ δ 7.04. Therefore (*E*)-stereochemistry was assigned to them.

Synthesis of indene and indane derivatives *via* intramolecular Friedel-Crafts reaction of the Baylis-Hillman adducts

Friedel Crafts reaction is one of the most useful reactions in organic chemistry whose applications in academic as well as in industrial fields have been well documented.[130-132] Recently, our research group has utilized 3-acetoxy-2-methylenealkanenitriles and methyl 3-acetoxy-2-methylenealkanoates as stereodefined β-electrophiles for the Friedel-Crafts reaction with benzene in the presence of $AlCl_3$ thus providing a general synthesis of (2Z)-2-benzylalk-2-enenitriles and (2*E*)-2-benzylalk-2-enoates (major) respectively (Scheme 45).[133] However, when this methodology was extended for intramolecular Friedel-Crafts reaction of methyl 3-acetoxy-2-methylene-3-phenylpropanoate with $AlCl_3$ in the absence of benzene the expected indene derivative was not formed, instead methyl (2Z)-2-(chloromethyl)-3-phenylprop-2-enoate (66) was obtained in good yield (Scheme 46).[133]

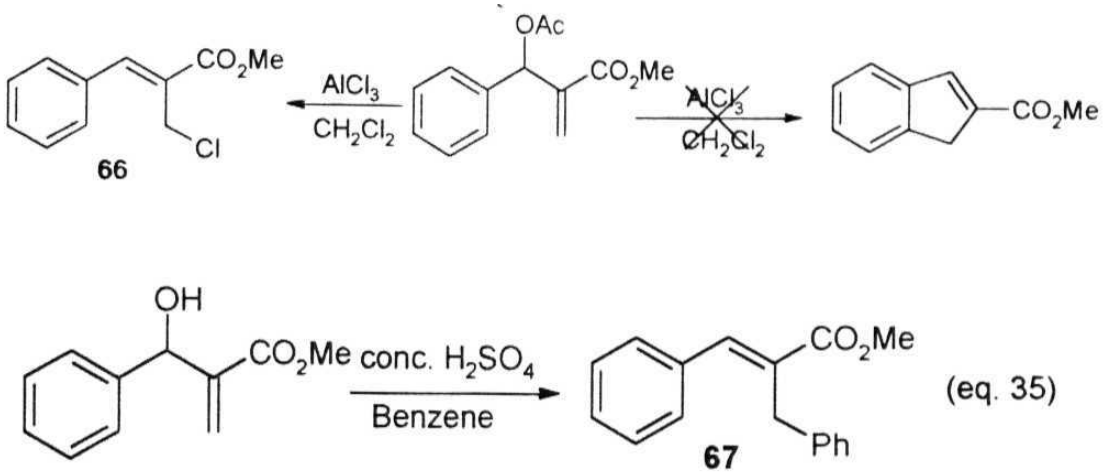
Scheme 45



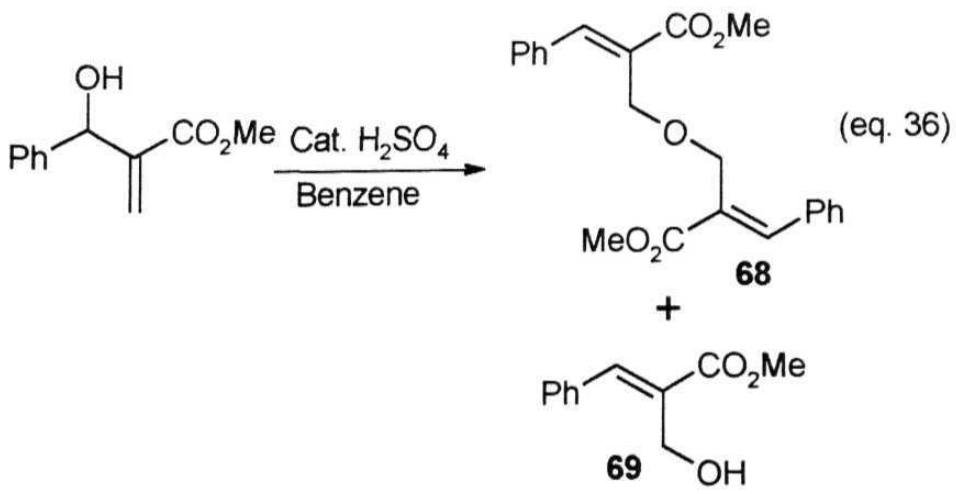
With view to avoid the application of $AlCl_3$ in the Friedel Crafts reaction, we have generated the carbocation by directly treating methyl 3-hydroxy-2-methylene-3-phenylpropanoate with catalytic amount of conc. H2SO4 in benzene thus providing a simple

procedure for preparation of methyl (2*E*)-2-benzyl-3-phenylprop-2-enoate **(67)** (eq. 35).[134]

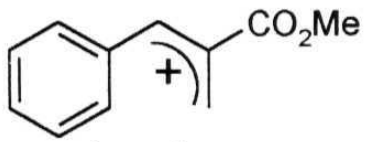
Scheme 46



However, attempts to extend this strategy to the intramolecular Friedel-Crafts reaction of methyl 3-hydroxy-2-methylene-3-phenylpropanoate *via* the generation of carbocation with a catalytic amount of H_2SO_4 in the absence of benzene, did not result in the formation of desired indene derivative. Instead, we have obtained bis allyl ethers (68) and rearranged alcohol (69) with some other unidentified products (eq. 36).



The failure of this intramolecular Friedel-Crafts reaction may be attributed to the less stabilization of carbocation (70) because of presence of the electron withdrawing (CO_2Me) group.

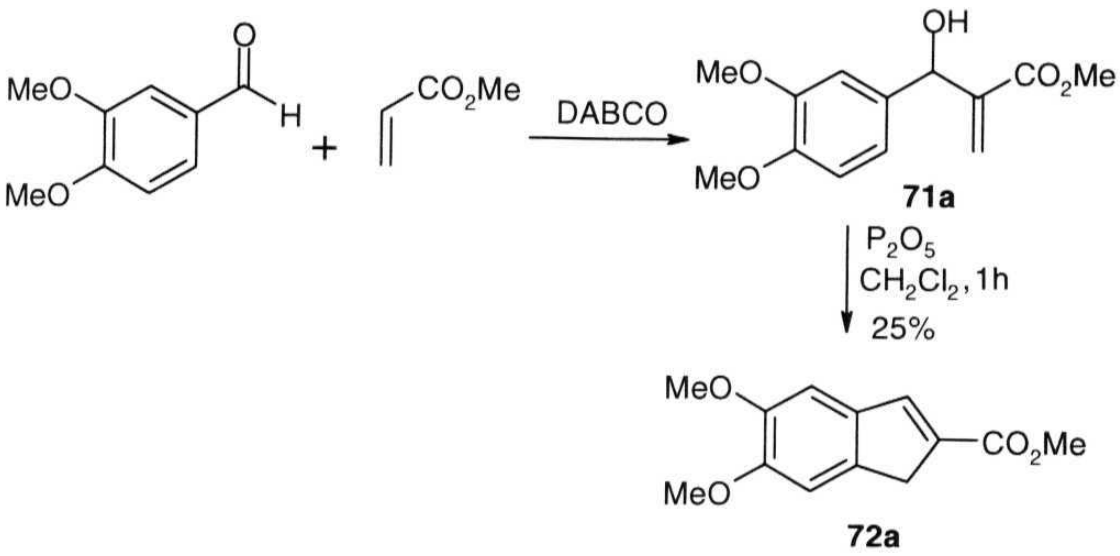


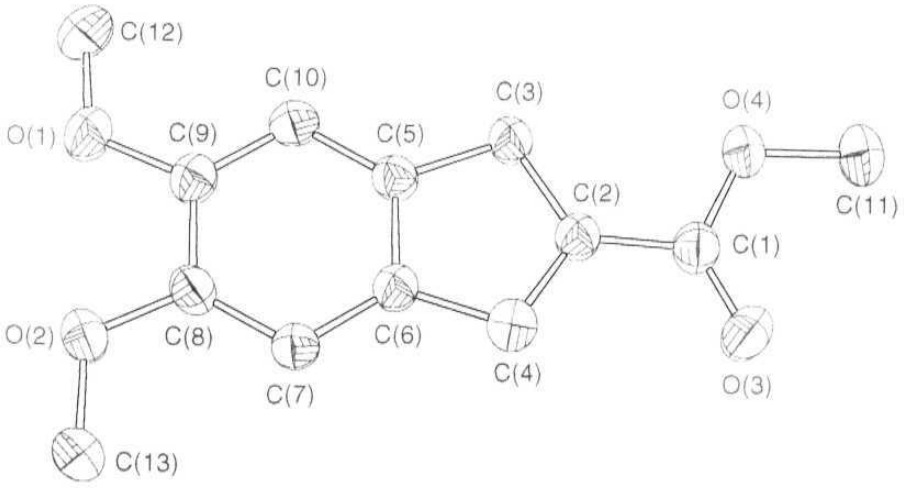
carbocation
70

At this stage, it occurred to us that if there is any group in the aromatic ring, that can stabilize the carbocation, then intramolecular Friedel-Crafts reaction might proceed without any problem. Accordingly, we have selected methyl 3-(3,4-dimethoxyphenyl)-3-hydroxy-2-methylenepropanoate (71a) the Baylis-Hillman adduct, derived from 3,4-dimethoxybenzaldehyde, as a substrate for an intramolecular Friedel-Crafts reaction. However, our attempts to use H_2SO_4 as a catalyst for intramolecular Friedel-Crafts reaction were not successful. With a view to achieve an intramolecular Friedel-Crafts reaction of methyl 3-(3,4-dimethoxyphenyl)-3-hydroxy-2-methylenepropanoate (71a) application of various dehydrating agents were examined. The best results were obtained when the molecule 71a was treated with P2O5 in CH_2Cl_2 at room temperature for 1 hour thus providing the desired indene derivative (72a) in 25% yield (Scheme 47). The structure of this molecule was established by IR, ^1H (Fig 9) & ^{13}C NMR (Fig 10), mass spectral data and elemental analysis. The structure of this molecule was further

confirmed by single crystal X-ray crystallography data (Figure A). The crystal structure data of the compound 72a is summarized in Table I and Table A (Appendix).

Scheme 47





Hydrogen atoms were omitted for clarity

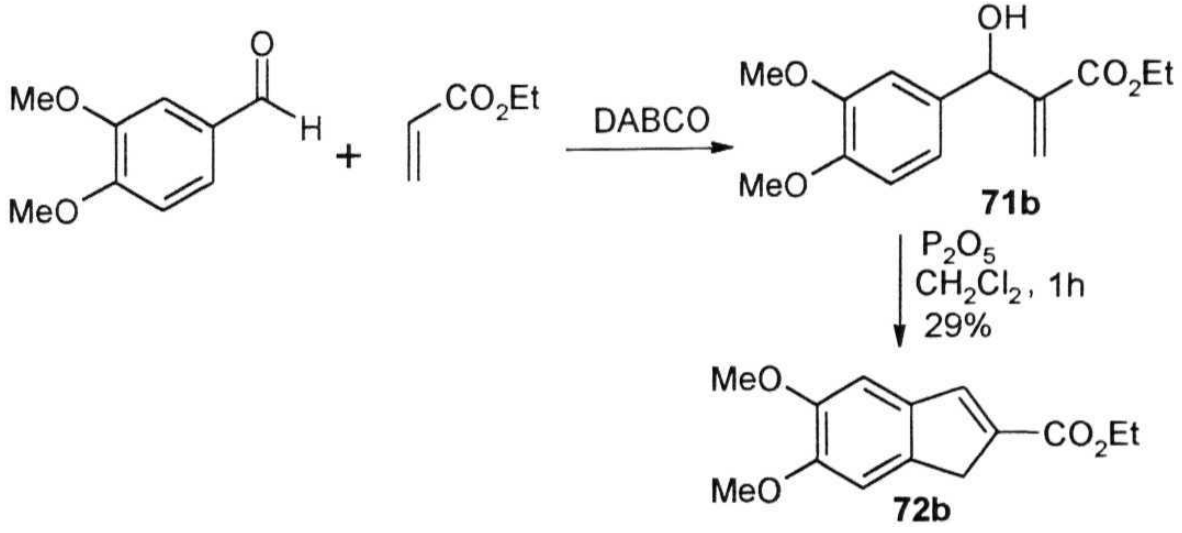
Figure A: Ortep diagram of the molecule 72a

Table I: **Crystal** data and structure refinement for compound 72a

Identification code	72a
Empirical formula	$C_{13}H_{14}O4$
Formula weight	134.24
Temperature	293°(2) K
Wavelength	0.71073 A
Crystal system	Triclinic
Space group	$P\bar{1}$
Unit cell dimensions	a = 6.2653(13) A α = 87.11(5)°
	b = 7.81(2) A β = 86.791(16)°
	c = 12.094(2) A γ = 77.46(5)°
Volume	576.6(15) A^3
Z, Density (calculated)	2, 0.675 Mg/m^3
Absorption coefficient	0.050 mm^{-1}
F(000)	124
Crystal size	0.6 x 0.6 x 0.5 mm
0 range for data collection	1.69 to 27.46°
Index ranges	0 < h < 8, -9 < k < 10, -15< 1 < 15
Reflections collected	2621
Independent reflections	2621 [R(int) = 0.0000]
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2621 / 0 / 157
Goodness-of-fit on F^2	1.047
Final R indices [$I>2\sigma(I)$]	R1 = 0.0568, wR2 = 0.1263
R indices (all data)	R1 =0.0887, wR2 = 0.1418
Largest difference peak and hole	0.437 and -0.444 e. A^{-3}

Though the yield in this reaction is less, this has attracted us because this is the first **report** on the intramolecular Friedel-Crafts reaction of the Baylis-Hillman adducts. We have also examined the application of ethyl 3-(3,4-dimethoxyphenyl)-3-hydroxy-2-methylenepropanoate **(71b)** as substrate for the intramolecular Friedel-Crafts reaction *via* the treatment with P_2O_5. This reaction was also successful and provided the desired indene derivative (72b) though in less yield (31%) (Scheme 48). The structure of this molecule was established by IR, ^1H & ^{13}C NMR, mass spectral data and elemental analysis.

Scheme 48



With a view to have proper understanding of this reaction, we have prepared various Baylis-Hillman adducts **(71c-e,** Table 6) using 3,4-methylenedioxybenzaldehyde (piperonal) as a electrophile. Subsequent treatment with P_2O_5 provided the desired indene derivative **(72c-e)** (Scheme 49, Table 7). The structure of these molecules were established by IR, ^1H & ^{13}C NMR, mass spectral data and elemental analysis.

Table *6:* Synthesis of Baylis-Hillman adducts[a,b]

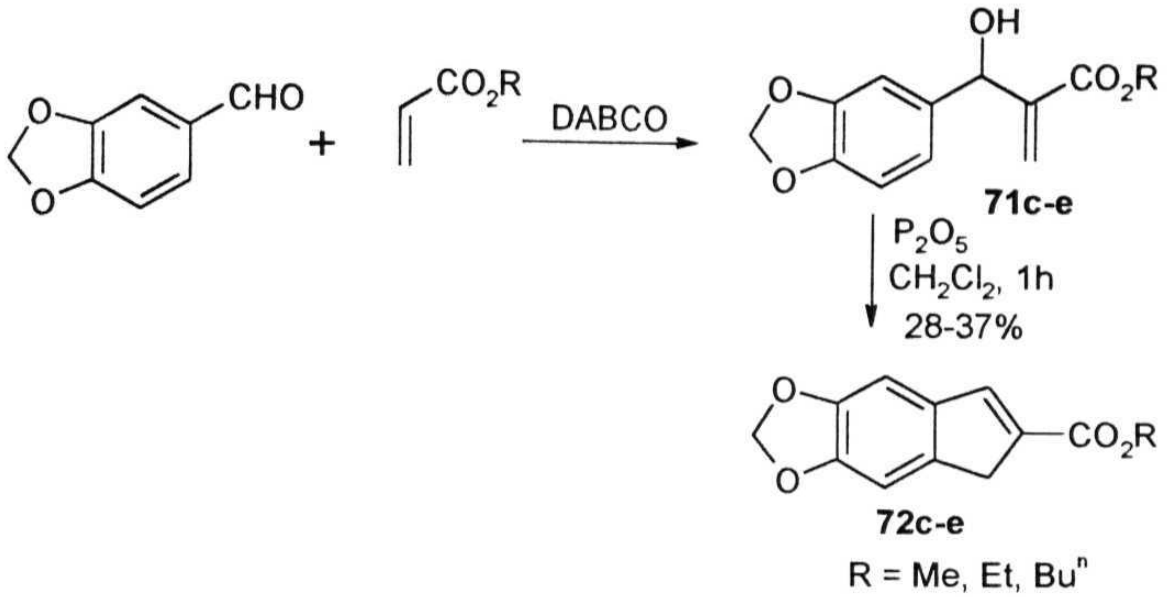
Aldehyde	Acrylate	Time in days	B.H adduct	Yield[c] %
3,4-dimethoxybenzaldehyde	methyl acrylate	40 d	**71a**	40
3,4-dimethoxybenzaldehyde	ethyl acrylate	49 d	**71b**	36
3,4-methylenedioxybenzaldehyde	methyl acrylate	47 d	**71c**	58
3,4-methylenedioxybenzaldehyde	ethyl acrylate	40 d	**71d**	40
3,4-methylenedioxybenzaldehyde	n-butyl acrylate	55 d	**71e**	38
4-ethoxy-3-methoxybenzaldehyde	methyl acrylate	35 d	**71f**	32
4-ethoxy-3-methoxybenzaldehyde	ethyl acrylate	35 d	**71g**	44
3-methoxy-4-n-propoxybenzaldehyde	methyl acrylate	26 d	**71h**	35
3-methoxy-4-n-propoxybenzaldehyde	ethyl acrylate	28 d	**71i**	56

a) All reactions were carried out on 20 mM scale of aldehydes with 30 mM of acrylates in the presence of DABCO (15 mol%) at room temperature.

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

c) Yields of the pure Baylis-Hillman adducts obtained after column chromatography (silica gel, 15% EtOAc in hexanes).

Scheme 49



In order to examine the generality and further expand the scope of the reaction, we have also prepared some more Baylis-Hillman adducts **(71f-i)** according to Scheme 50 Thus, *o*-vanillin was converted into the desired 3-methoxy-4-alkoxybenzaldehydes (73-**74)** in good yields *via* the treatment with alkyl bromides in the presence of K2CO3. The aldehydes **(73-74)** were used as electrophiles for Baylis-Hillman reaction with various acrylates to afford the desired adducts **(71f-i)** for use in intramolecular Friedel-Crafts reaction (Scheme 50, Table 6).

Scheme 50

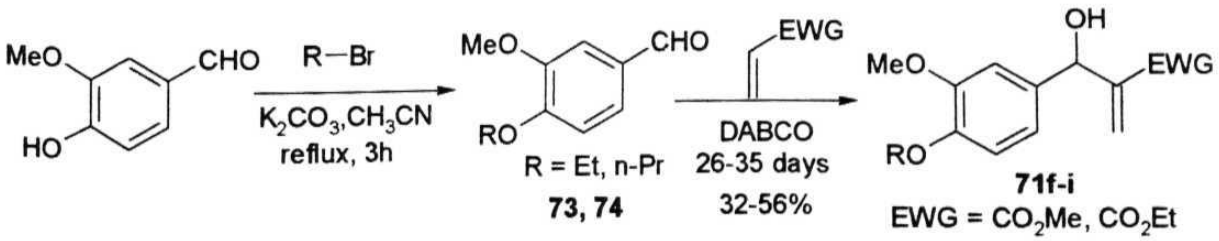
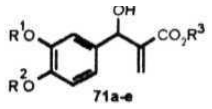


Table 7: Synthesis of indene derivatives[a,b]

 71a-e				72a-e Product	Yield[c] (%)
Substrate	R^1	R^2	R^3		
71a	Me	Me	Me	**72a**[d]	25
71b	Me	Me	Et	**72b**	31
71c	-CH_2-		Me	72c	29
71d	-CH_2-		Et	**72d**	28
71e	-CH_2-		Bu^n	**72e**	37

a) All reactions were carried out on 2 mM scale of the Baylis-Hillman alcohol with P_2O_5 (0.2 g) at room temperature for 1 h.

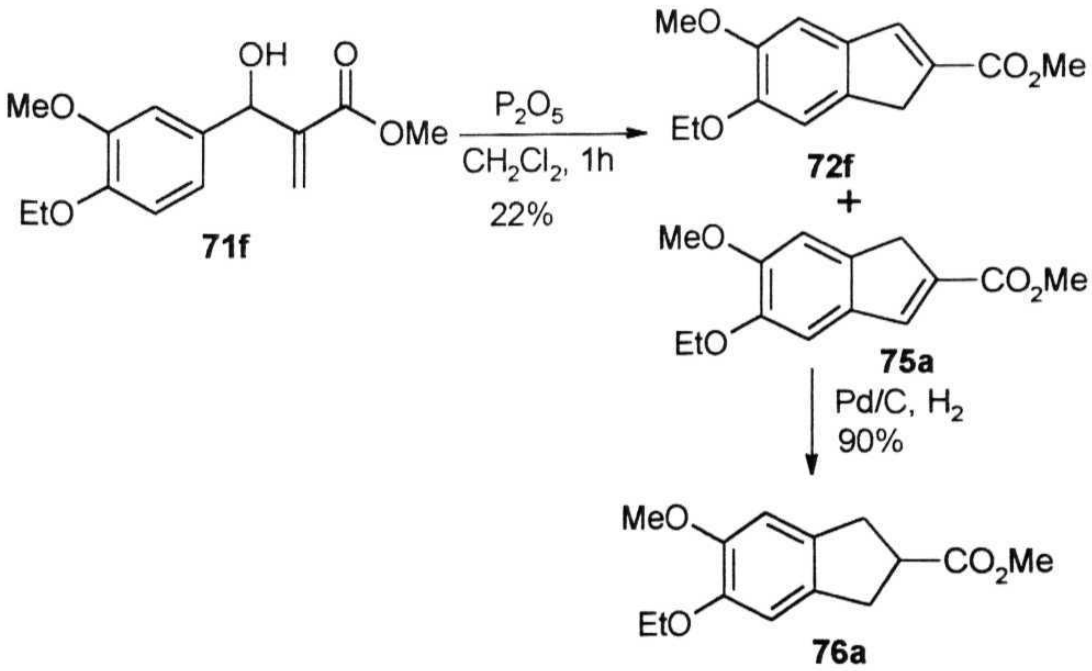
b) All the products were obtained as colorless solids and gave satisfactory IR, ^1H NMR, ^{13}C NMR, mass spectral and elemental analyses.

c) Yields of the pure products obtained after column chromatography (silica gel, 8% EtOAc in hexanes).

d) Structure of the molecule **(72a)** was further confirmed by single crystal X-ray data.

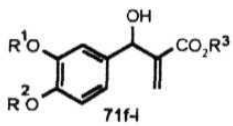
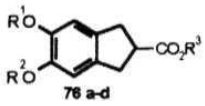
We have first examined the molecule **71** f as a substrate for Fried el-Crafts reaction *via* the treatment with P2O5, which provided the desired indene derivative as a mixture of methyl 5-ethoxy-6-methoxyindene-2-carboxylate **(72f)**[V] and methyl 6-ethoxy-5-methoxyindene-2-carboxylate **(75a)**[V] (regioisomers). However, subsequent hydrogenation of this mixture provided the indane derivative methyl 5-ethoxy-6-methoxyindane-2-carboxylate **(76a)**[V] (Scheme 51, Table 8). The structure of this molecule was established by IR, ^{1}H (Fig 11) & ^{13}C NMR (Fig 12), mass spectral data and elemental analysis. Similar results were obtained with the molecules **(71g-i)** as substrates in the intramolecular Friedel-Crafts reaction, thus providing a simple synthesis of substituted indane derivatives **76b-d**[V] (Scheme 52, Table 8).

Scheme 51



[V] For the easy understanding and continuity, the regioisomers of indenes derived from **71f-i** were numbered as 72f-i and 75a-d and the corresponding indane derivatives were numbered as 76a-d.

Table 8: Synthesis of indane derivatives

 71f-i				Indene[a,b]	Yield[c]	 76 a-d	Yield[f]
Substrate	R^1	R^2	R^3	Product	%	Product[d,e]	(%)
71f	Me	Et	Me	**72f&75a**	**22**	**76a**	**90**
71g	Me	Et	Et	**72g & 75b**	**17**	**76b**	**91**
71h	Me	Pr^n	Me	**72h & 75c**	**20**	**76c**	**96**
71i	Me	Pr^n	Et	**72i & 75d**	**25**	**76d**	**88**

a) All the reactions were carried out on 2 mM scale of the Baylis-Hillman adducts with 0.2 g of P_2O_5 at room temperature for 1 hour.

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

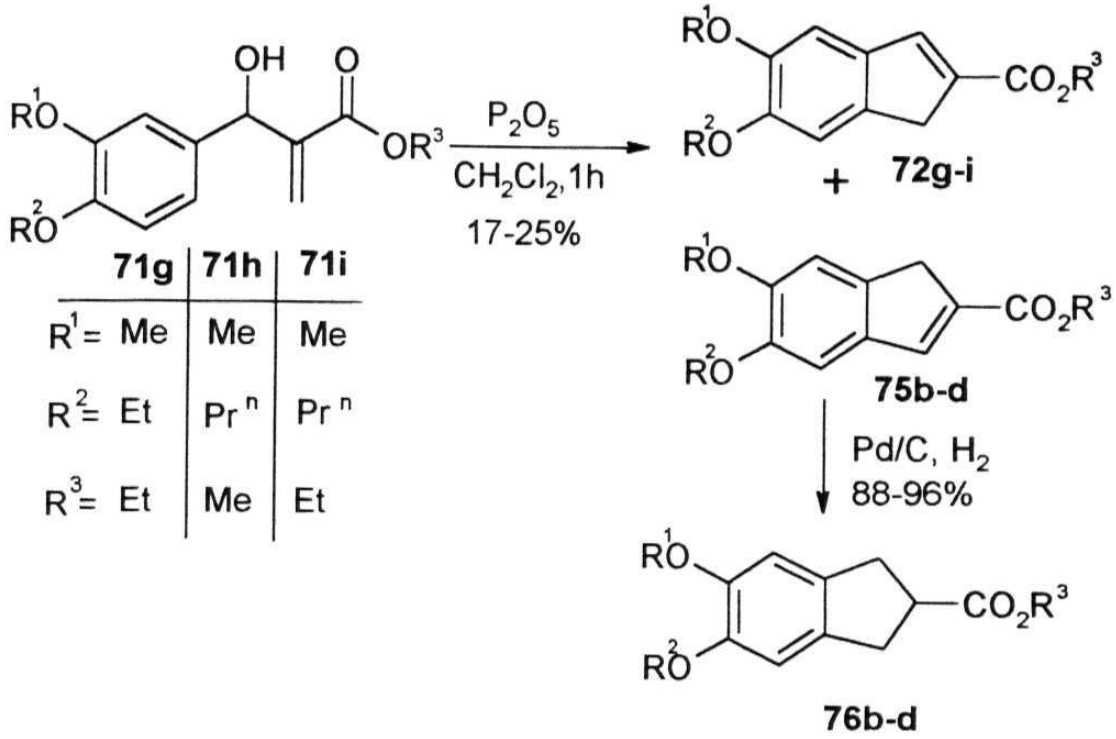
c) Yields of mixture of indene derivatives after column chromatography (silica gel, 8% EtOAc in hexanes).

d) Hydrogenation reactions were carried out on 0.5 mM scale of indene derivatives with 10 % Pd/C as a catalyst.

e) All the **products** obtained as colorless viscous liquids and gave satisfactory IR, ^1H NMR, ^{13}C NMR, mass spectral and elemental analyses.

f) Yields of the pure indane derivatives obtained after column chromatography (silica gel, 8 % EtOAc in hexanes).

Scheme 52

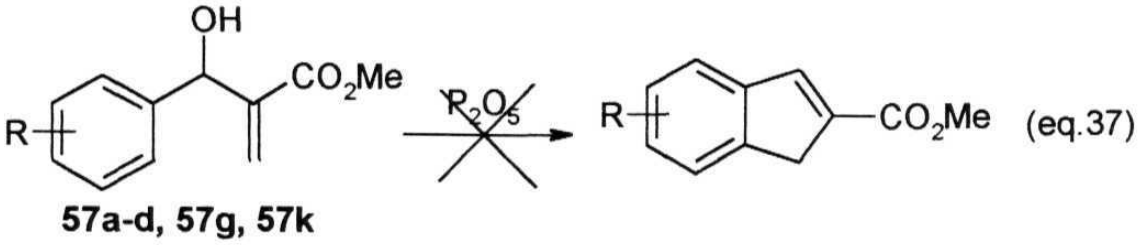


	71g	71h	71i
R^1 =	Me	Me	Me
R^2 =	Et	Pr^n	Pr^n
R^3 =	Et	Me	Et

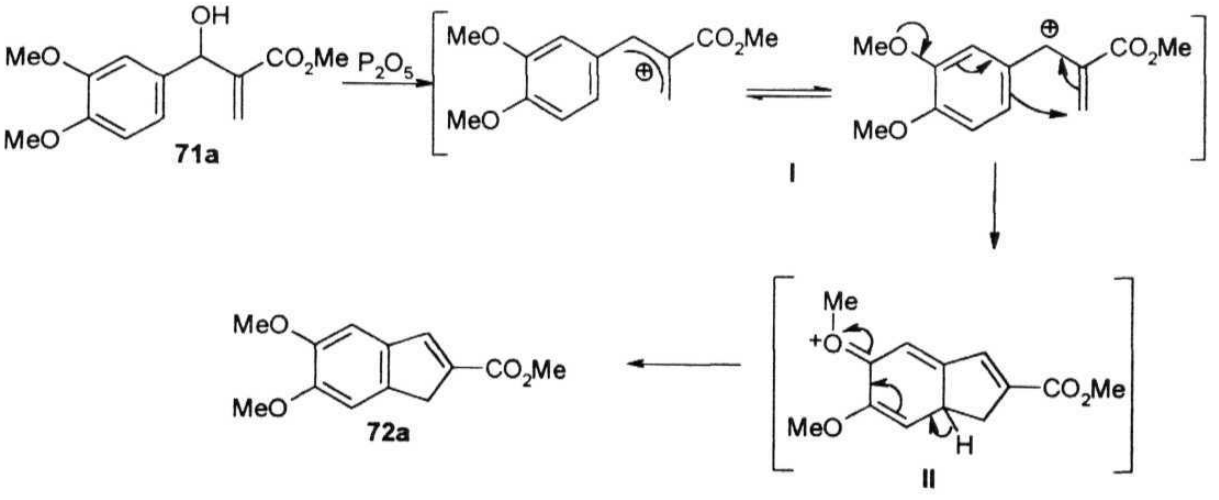
The possible reaction mechanism

With a view to understand the mechanism, we have subjected the Baylis-Hillman adducts (**57a-d,** 57g) for intramolecular Friedel-Crafts reaction *via* the treatment with P_2O_5. These reactions were not clean (eq 37). On the basis of these results the possible mechanism is described in Scheme 53. The reaction may proceed through the carbocation I, followed by carbon-carbon bond formation facilitated by methoxy group at 3^r position of the aromatic ring leading to the formation of the species **II,** subsequent aromatization leads to the formation of an indene product (Scheme 53). We were

surprised to find that the intramolecular Friedel-Crafts reaction of 57k (R= 3-methoxy) did not produce the desired indene.

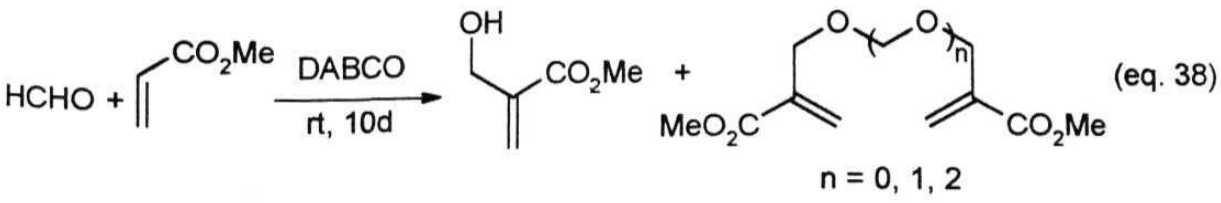


Scheme 53



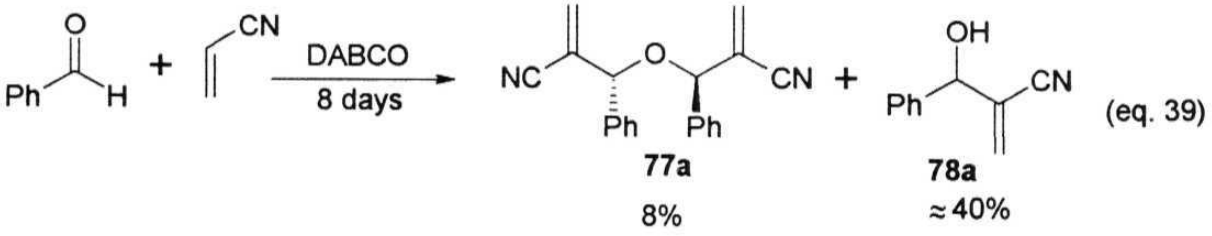
Tandem construction of carbon-carbon and carbon-oxygen bonds in the Baylis-Hillman chemistry: Synthesis of functionalized *dl* and *meso* bis allyl ethers

Designing molecules with symmetry and functionalities and synthesizing them in a meticulous manner has been the source of success and growth for the present day organic synthesis. Stereoselective construction of carbon-carbon bonds and carbon hetero-atom bonds has been and continues to be the most fundamental reaction in organic chemistry and hence represents a forefront of research in synthetic organic chemistry.[135-138] The mechanism of the Baylis-Hillman reaction is believed to proceed through initial Michael type addition of DABCO to the activated alkene followed by the aldol type reaction of the resultant zwitterion enolate with aldehyde to produce the desired multifunctional molecule after elimination of the catalyst DABCO (Scheme 1). It occurred to us that if we can use the oxygen anion (B in Scheme 1) in further controlled reaction with the product there will also be the formation of C-0 bond in the Baylis-Hillman conditions leading to the generation of an interesting class of molecules with more functionalities. A careful literature survey reveals that ethers are formed as side products in the Baylis-Hillman reaction of methyl acrylate and formaldehyde (eq.38).[139,140]



(eq. 38)

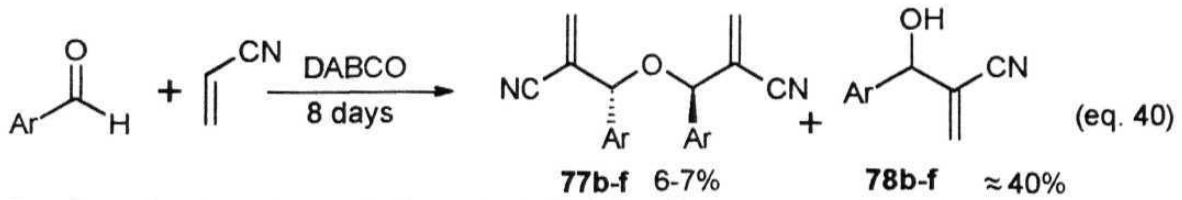
However, to the best of our knowledge there is no report in literature on a similar reaction with other aldehydes leading to the formation of bis allyl ethers. We have therefore undertaken this project of examining the reaction between aryl aldehydes and acrylonitrile under the Baylis-Hillman conditions with a view that bis allyl ethers can be synthesized in one-pot operation and if possible they can be isolated in stereochemically pure form. During our studies in this direction we have carried out number of experiments. We have obtained a very fascinating result when we have carried out the Baylis-Hillman coupling reaction of acrylonitrile with benzaldehyde for longer time *i.e.* eight days at room temperature, thus providing bis(2-cyano-l-phenylprop-2-en-l-yl) ether (77a) in 8 % isolated yield as a racemic mixture (eq. 39) along with the usual Baylis-Hillman adduct (78a) *i.e.* 3-hydroxy-2-methylene-3-phenylpropanenitrile (≈ 40%) and some other unidentified products.



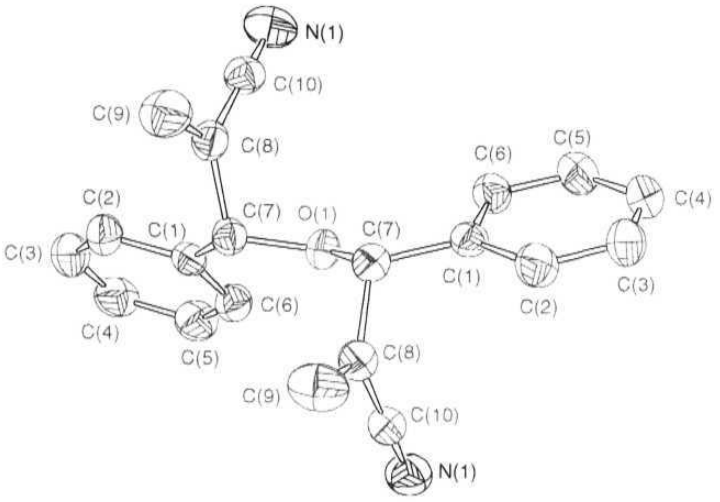
(eq. 39)

The structure of the product (77a) was confirmed by IR, ^{1}H (Fig 13) and ^{13}C NMR (Fig 14) spectral data and elemental analysis. The *dl* nature of the molecule was confirmed by single crystal X-ray data (Figure B). The crystal structure data of the compound 77a is summarized in Table II and Table B (Appendix). HPLC analysis of this molecule

(Fig 15) on chiralcel OD column showed two peaks of equal intensity presumably arising from both the (R,R)- and (S,S)-enantiomers thus conforming the recemic nature of this molecule. This success led us to examine the generality of this reaction. Accordingly, we have carried out the reaction of a variety of aromatic aldehydes with acrylonitrile in the presence of DABCO for longer time *i.e.* 8 days thus leading to the isolation of functionalized *dl*-bis-allyl ethers (77b-f) in 6-7% yields (eq. 40, Table 9)

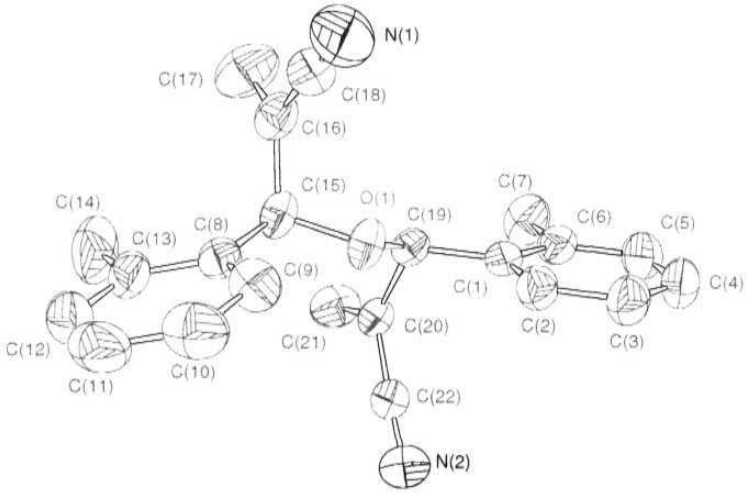


along with the usual Baylis-Hillman adducts (78b-f) (≈ 40%) and some other unidentified products. In fact, we have also examined all these molecules on HPLC using chiral column, chiralcel OD, which showed two peaks of equal intensity (in each case) corresponding to both (R,R)- and (S, S)-enantiomers thus further confirming *dl* nature of these molecules. The structure of the compound 77b was also determined by single crystal X-ray data [Figure C, Table III and Table C (Appendix)]. The formation of bis allyl ethers **77a-f** can be possibly explained according to Scheme 54. This mechanism has been confirmed to some extent by treating the Baylis-Hillman adduct, 3-hydroxy-2-methylene-3-phenylpropanenitrile (78a), with DABCO for 8 days which provided the desired racemic bis allyl ether 77a in 7% yield (eq. 41) along with the starting material (78a) (≈40%) and some unidentified products.



Hydrogen atoms were omitted for clarity

Figure B: Ortep diagram of the molecule 77a



Hydrogen atoms were omitted for clarity

Figure C: Ortep diagram of the molecule 77b

Table II: Crystal data and structure refinement for 77a.

Identification code	77a
Empirical formula	$C_{20} H_{16} N_2 O$
Formula weight	300.34
Temperature	293(2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, C2/c
Unit cell dimensions	a = 21.972(6) A a = 90°
	b = 6.087(3) A P= 117.000(19)°
	c= 13.756(3) A y=90°
Volume	1639.3(10) A^3
Z, Calculated density	8, 1.217 Mg/m^3
Absorption coefficient	0.076 mm^{-1}
F(000)	632
Crystal size	0.60 x 0.60 x 0.28 mm
0 range for data collection	2.08 to 29.98°
Index ranges	$0<h<30$, $0 \le k \le 8$, $-19 \le l \le$
Reflections collected / unique	2424/2375 [R(int) = 0.0175]
Completeness to 26 = 29.98	45.7%
Refinement method	Full-matrix least-squares on F2
Data / restraints / parameters	2375/0/ 105
Goodness-of-fit on F^2	1.088
Final R indices [$I>2\sigma(I)$]	R1 =0.0486, wR2 = 0.1351
R indices (all data)	R1 = 0.0671, wR2 = 0.1573
Largest difference peak and hole	0.15 and -0.25 e. A^{-3}

Table III: Crystal data and structure refinement for 77b.

Identification code	77b
Empirical formula	$C_{28} H_{20} N_2 O$
Formula weight	400.46
Temperature	293(2) K
Wavelength	0.71073 A
Crystal system, space group	Triclinic, P1
Unit cell dimensions	a = 8.1202(17) A a = 68.387(9)°
	b= 11.1234(11) A (3 = 74.405(11)°
	c = 13.5254(14) A 8=76.640(12)°
Volume	1082.0(3) A^3
Z, Calculated density	2, 1.229 Mg/m^3
Absorption coefficient	0.075 mm^{-1}
F(000)	420
Crystal size	0.64 x 0.40 x 0.32 mm
θ range for data collection	1.65 to 24.99°
Index ranges	0<h<9,-12<k< 13,-14<1< 16
Reflections collected / unique	3805 / 3805 [R(int) = 0.0000]
Completeness to 2θ = 24.99	99.9%
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3805/0/280
Goodness-of-fit on F^2	0.859
Final R indices [I>2σ(I)]	R1 = 0.0378, wR2 = 0.1040
R indices (all data)	R1 = 0.0651, wR2 = 0.1414
Largest difference peak and hole	0.12 and -0.14 e $Å^{-3}$

Table 9: Synthesis of functionalized *dl* and *meso* bis allyl ethers[a, b]

Aldehyde **Ar =**	Product	Yield[c] %	mp (° C)
phenyl	**77a**[d] *(dl)*	8	92
2-methylphenyl	**77b**[d] *(dl)*	7	109-110
4-methylphenyl	**77c** *(dl)*	7	96-97
4-ethylphenyl	**77d** *(dl)*	6	103
4-isopropylphenyl	**77e** *(dl)*	7	132
2,4-dichlorophenyl	**77f** *(dl)*	6	149-150
naphth-1-yl	**77g**[d] *(meso)*	7	141-142

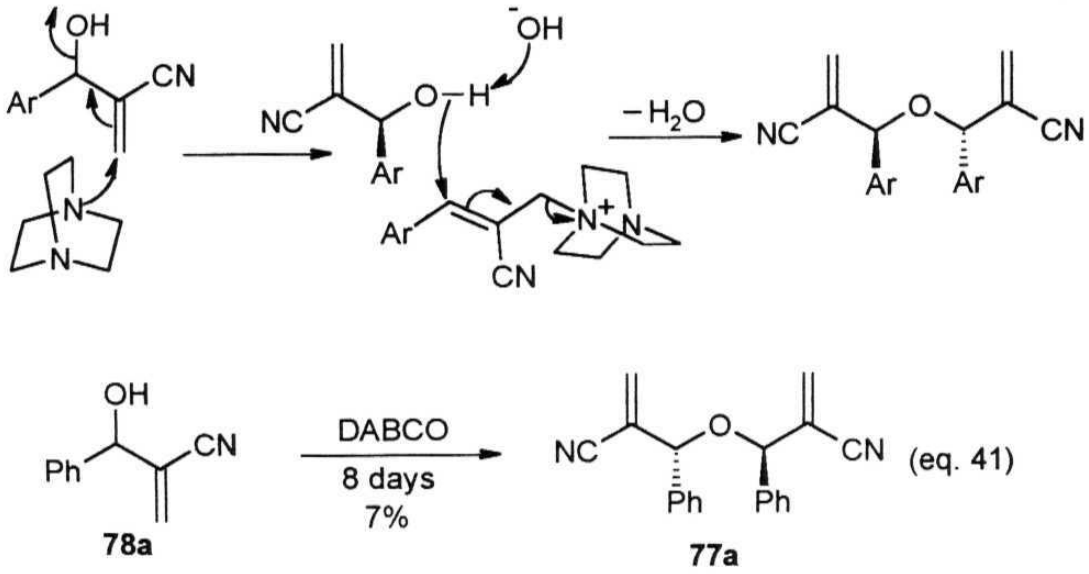
a) All the reactions were carried out on 20 mM scale of the aldehyde with 30 mM of acrylonitrile and 15 mol% of DABCO at room temperature for 8 days.

b) All products gave satisfactory IR, ^{1}H NMR (200 MHz), ^{13}C NMR (50 M Hz), and elemental analyses.

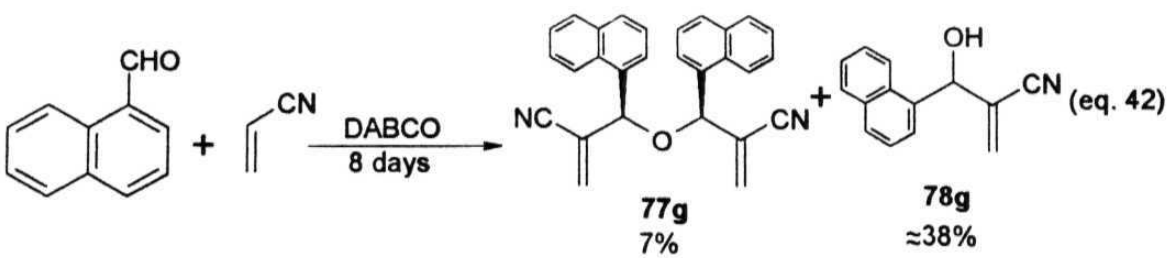
c) Yields of pure products obtained after column chromatography (silica gel, 5% EtOAc in hexanes).

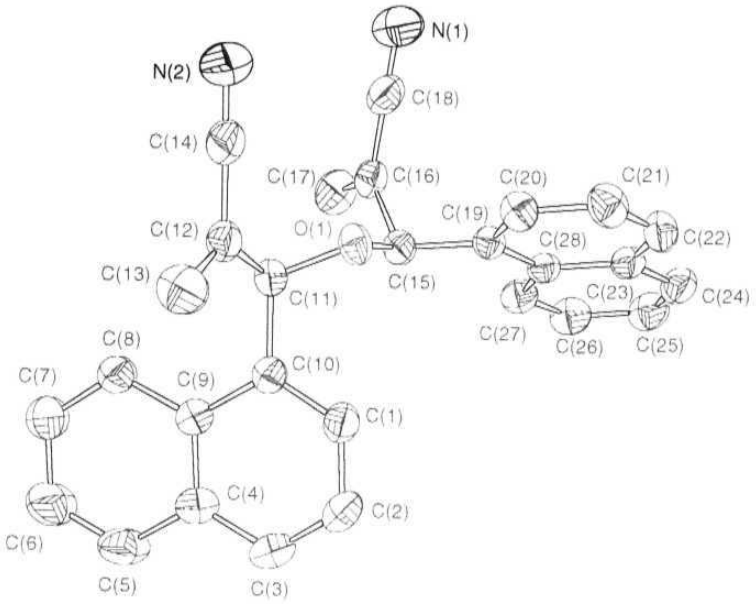
d) Structure of these molecule (77a, 77b and 77g) were determined by single crystal X-ray data.

Scheme 54



However, when we have extended this reaction to 1-naphthaldehyde, surprisingly *meso* bis allyl ether (77g) was isolated in 7% yield (eq. 42) along with the usual Baylis-Hillman adduct (≈ 38%) and some other unidentified products. The structure of the product (77g) was confirmed by IR, ^{1}H (Fig 16) and ^{13}C NMR (Fig 17) spectral data and elemental analysis. The stereochemistry was established by single crystal X-ray data (Figure D). The crystal structure data of the compound 77g is summarized in Table IV and Table D (Appendix). HPLC analysis of this molecule 77g (Fig 18) on chiralcel OD column showed a single peak thus presumably confirming the *meso* nature of the molecule.

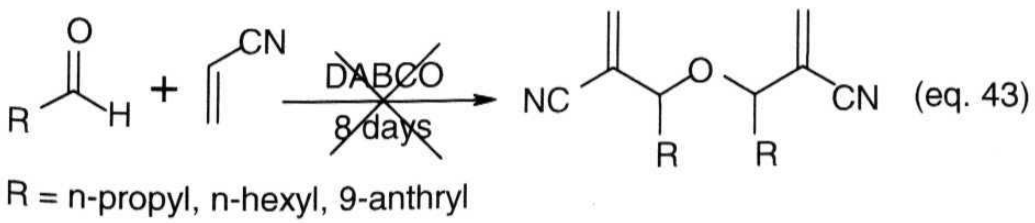




Hydrogen atoms were omitted for clarity

Figure D: Ortep diagram of the molecule 77g

However, our attempts to use 9-anthraldehyde, propionaldehyde and hexanal for similar coupling reaction with acrylonitrile in the presence of DABCO were unsuccessful (eq. 43). Since the yields of the bis allyl products are very low we are not able to comment anything about the stereochemical course of the reaction.



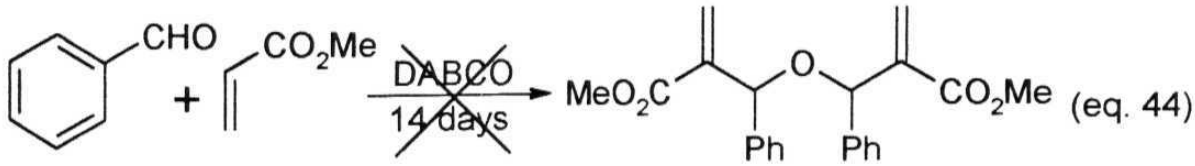
R = n-propyl, n-hexyl, 9-anthryl

Table IV. Crystal data and structure refinement for 77g

Identification code	**77g**
Empirical formula	$C_{22}H_{20}N_2O$
Formula weight	328.40
Temperature	293(2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, $P2_1/n$
Unit cell dimensions	a = 8.469(3) A α = 90°
	b= 12.300(7) A (3 =95.92(3)°
	c= 18.024(9) A γ = 90°
Volume	1867.6(15) A^3
Z, Calculated density	4, 1.168 Mg/m^3
Absorption coefficient	0.072 mm^{-1}
F(000)	696
Crystal size	0.63 x 0.63 x 0.63 mm
6 range for data collection	2.01 to 24.98°
Index ranges	0 < **h** < **10,** 0 < **k** < **14,** -21 < **1** < **21**
Reflections collected	3506
Independent reflections	3278 [R(int) = 0.0583]
Refinement method	Full-matrix least-squares on F
Data / restraints / parameters	3278/0/228
Goodness-of-fit on F^2	1.056
Final R indices [I>2σ(I)]	R1 = 0.0388, wR2 =0.0955
R indices (all data)	R1 =0.0688, wR2 = 0.1159
Largest difference peak and hole	0.113 and -0.149 e. A^{-3}

Diastereoselective synthesis of chiral allyl amines *via* the treatment of (S)-1-phenylethylamine with methyl (2Z)-3-aryI-2-(bromomethyl) prop-2-enoate in the presence of DABCO

Though the yields are not high, the reaction discussed in the previous section *i.e.* preparation of bis allyl ethers is of interest due to simultaneous formation of carbon-carbon and carbon-oxygen bonds and also due to the high stereochemical purity of the molecules isolated. We therefore felt that it will be interesting to examine the similar reaction of aldehydes with methyl acrylates with a view to isolate the similar *dl* or *meso* allyl ethers Accordingly we have treated methyl acrylate with benzaldehyde under the influence of DABCO for extended reaction time (eq 44), unfortunately the required bis allyl ether was not formed.



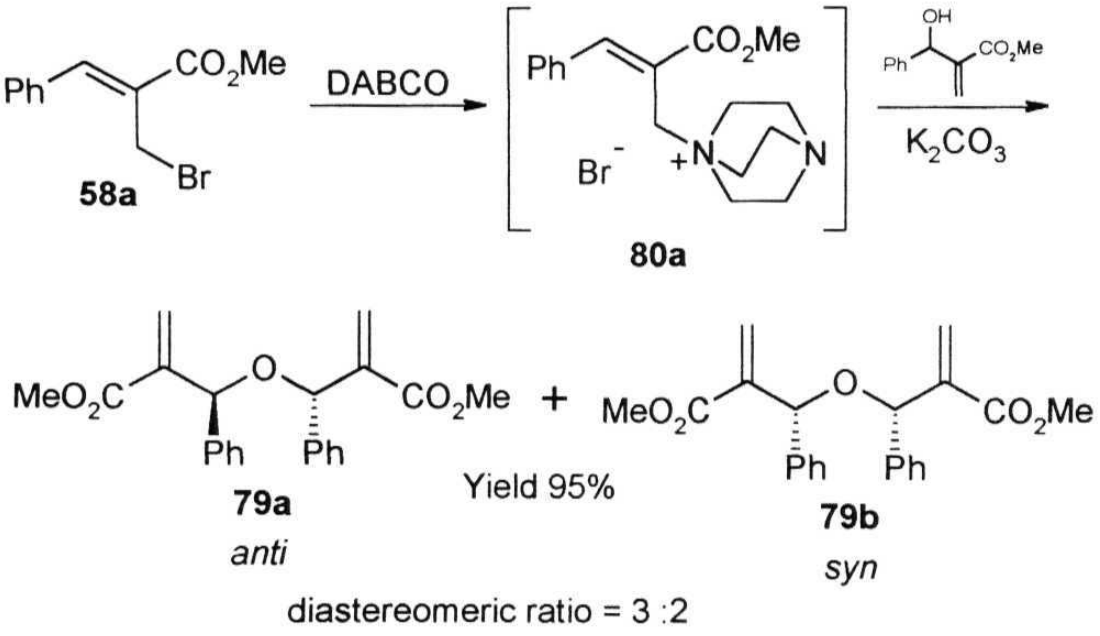
(eq. 44)

79

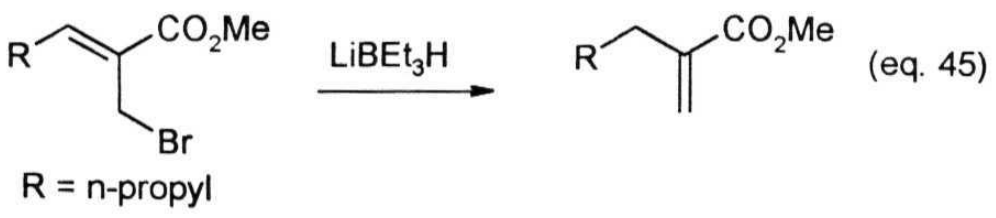
At this stage it occurred to us that treatment of methyl (2Z)-2-(bromomethyl)-3-phenylprop-2-enoate (58a) with DABCO can generate the corresponding salt (80a) which might react with methyl 3-hydroxy-2-methylene-3-phenylpropanoate to provide the expected bis allyl ethers. Accordingly, we have generated the allylbromide–DABCO salt by treating the methyl (2Z)-(2-bromomethyl)-3-phenylprop-2-enoate with DABCO. Subsequent treatment with methyl 3-hydroxy-2-methylene-3-

phenylpropanoate, (57a) (the Baylis Hillman adduct) in the presence of K_2CO_3 provided the desired bis allyl ether (79a & 79b) in excellent yield. However the diastereoselectivity is very poor (≈20%) (Scheme 55). No attempt was made to assign the stereochemistry to major and minor isomers because of low diasteroselectivity in the reaction. This reaction indicates that it is basically a S_N2' reaction.

Scheme 55

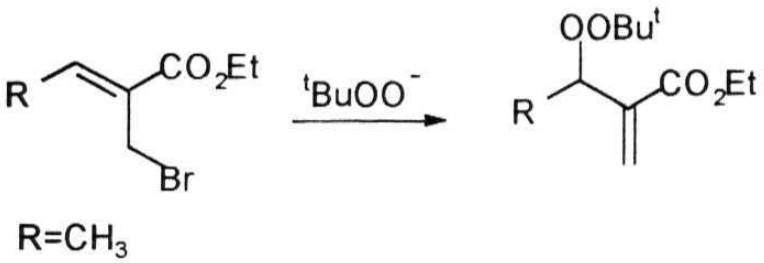


There are some reports in the literature on the addition of various nucleophiles to the allyl bromides (58) in S_N2' fashion. Hoffmann and Rabe have reported[141] the addition of $LiBEt_3H$ to the allyl bromide to furnish a-substituted acrylate (eq. 45).



8)

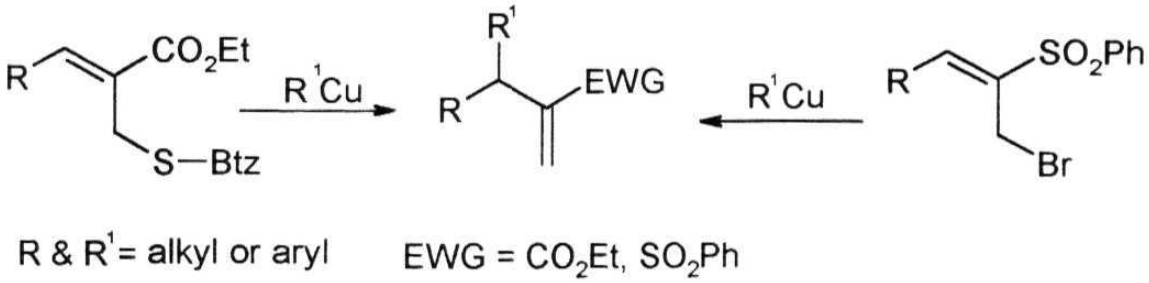
Maillard[142] and coworkers reported the addition of t-butyl peroxide to the allyl bromide in the presence of polyethylene oxide 400 which provided the corresponding allyl t-butyl peroxide in 45% yield (eq 46)



(eq. 46)

The allyl sulfides and allyl bromides derived from Baylis-Hillman adducts react with cuprates in S_N2' fashion to provide the desired 2-substituted acrylate derivatives (Scheme 56).[143,144]

Scheme 56



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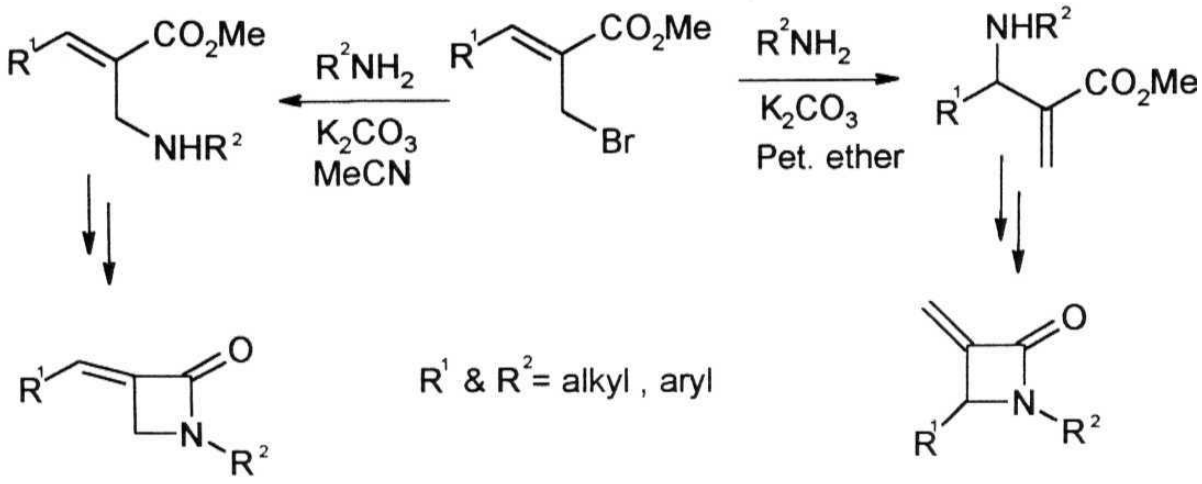
Recently, Hoffmann and Buchholz have reported nucleophilic addition of primary amines to the allyl bromides. The reactions were found to be solvent dependant. The S_N2 product was formed with high regioselectivity when acetonitrile was used as a solvent where as S_N2' product was formed when petroleum ether was used as a solvent

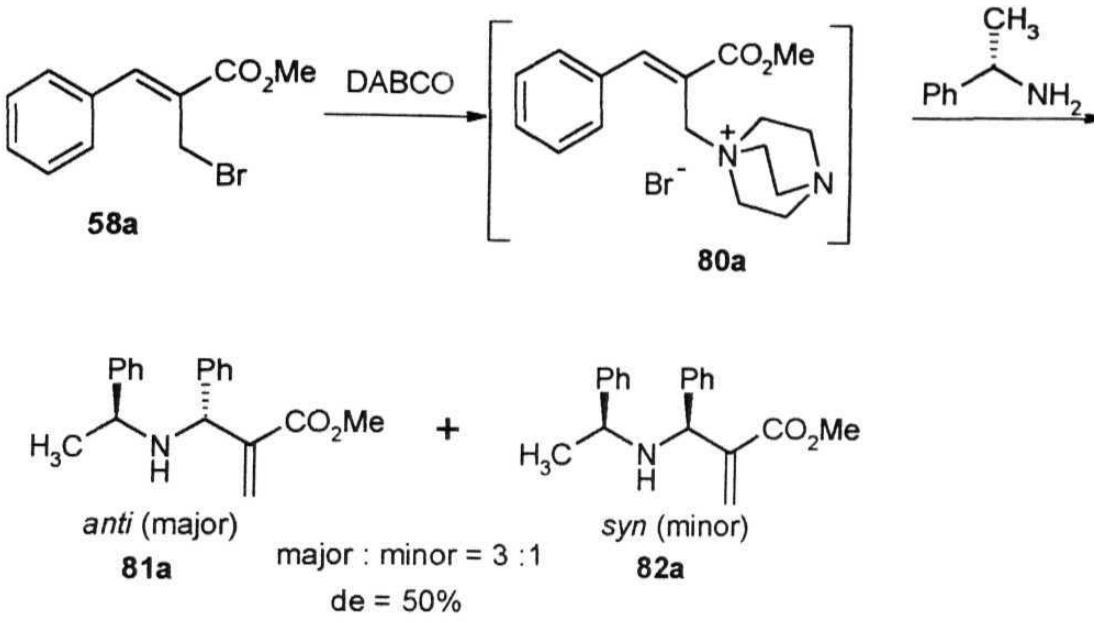
in the reaction. Both the S_N2 and S_N2' products were subsequently transformed into the corresponding β-lactams according to Scheme 57.

Scheme 57



It occurred to us that there is a possibility of chiral induction in the reaction of allyl bromide–DABCO salt (80a) with chiral secondary amine, so that diastereomerically pure or enriched allyl amine can be formed. Accordingly, we have first selected a-methylbenzylamine as a chiral secondary amine for nucleophilic addition reaction to allyl bromide in the presence of DABCO. Thus, the treatment of bromide-DABCO salt (80a) with (S)-l-phenylethylamine at room temperature for 1hour in methylene chloride as solvent provided the desired allyl amine as a mixture of diastereomers (81a and 82a) (Scheme 58). In the ^1H NMR spectrum of the crude product the olefinic proton *cis* to the ester group showed two singlets (due to diastereomers) in the ratio of 75:25 thus indicating that the reaction is 50% diastereoselective.

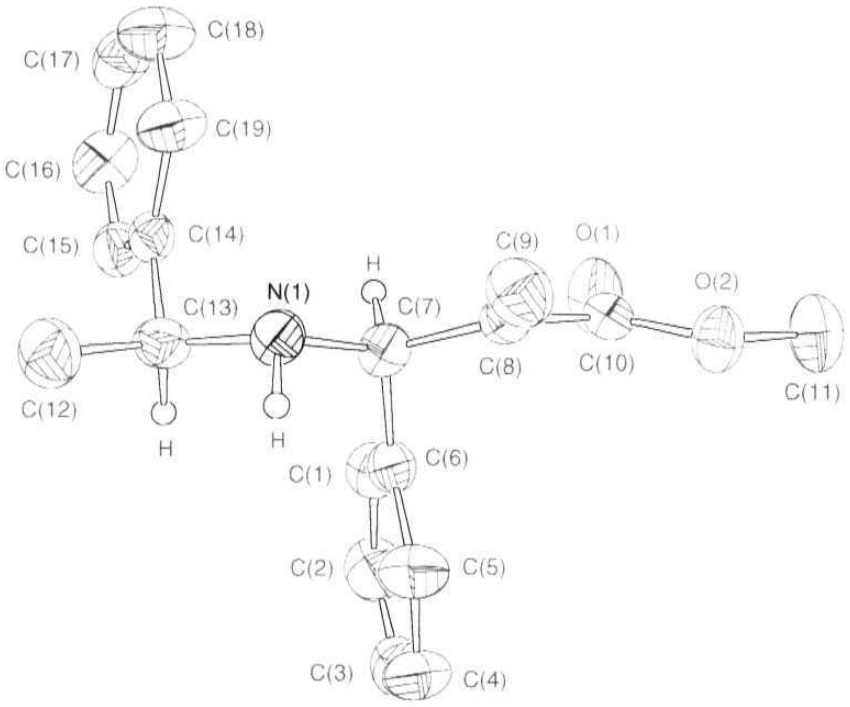
Scheme 58



It is interesting to note that both the diastereomers were separated by column chromatography. Both the major **81a**© and minor **82a**© isomers gave satisfactory IR, ^{1}H (Fig 19 and 20) and ^{13}C NMR (Fig 21 and 22) spectral data. We have further confirmed the structure of the major isomer by mass spectral and elemental analysis. It is very pleasant to notice that the major diastereomer (81a) is a solid and was obtained as single crystals. The stereochemical assignment of the major isomer was made on the basis of single crystal X-ray data (Figure E). The crystal structure data of the compound 81a is summarized in Table V and Table E (Appendix). The absolute configuration of the newly formed stereogenic center of the major isomer has been

© For easy understanding the major isomer 81a is referred to as *anti* isomer and the minor isomer 82a is referred to as *syn* isomer.

found to be *(R)* as shown in **81a.** Next we have examined the reaction of methyl (2Z)-2-(bromomethyl)-3-(2-methylphenyl)prop-2-enoate **(58b)** with (S)-l-phenylethylamine. This reaction is 58% diastereoselective as evidenced by integration of the diastereomeric olefinic protons *cis* to the ester group in the ^{1}H NMR spectrum of the crude product (thus providing *anti* **81b** and *syn* **82b** in the ratio of 79:21) (Scheme 59).



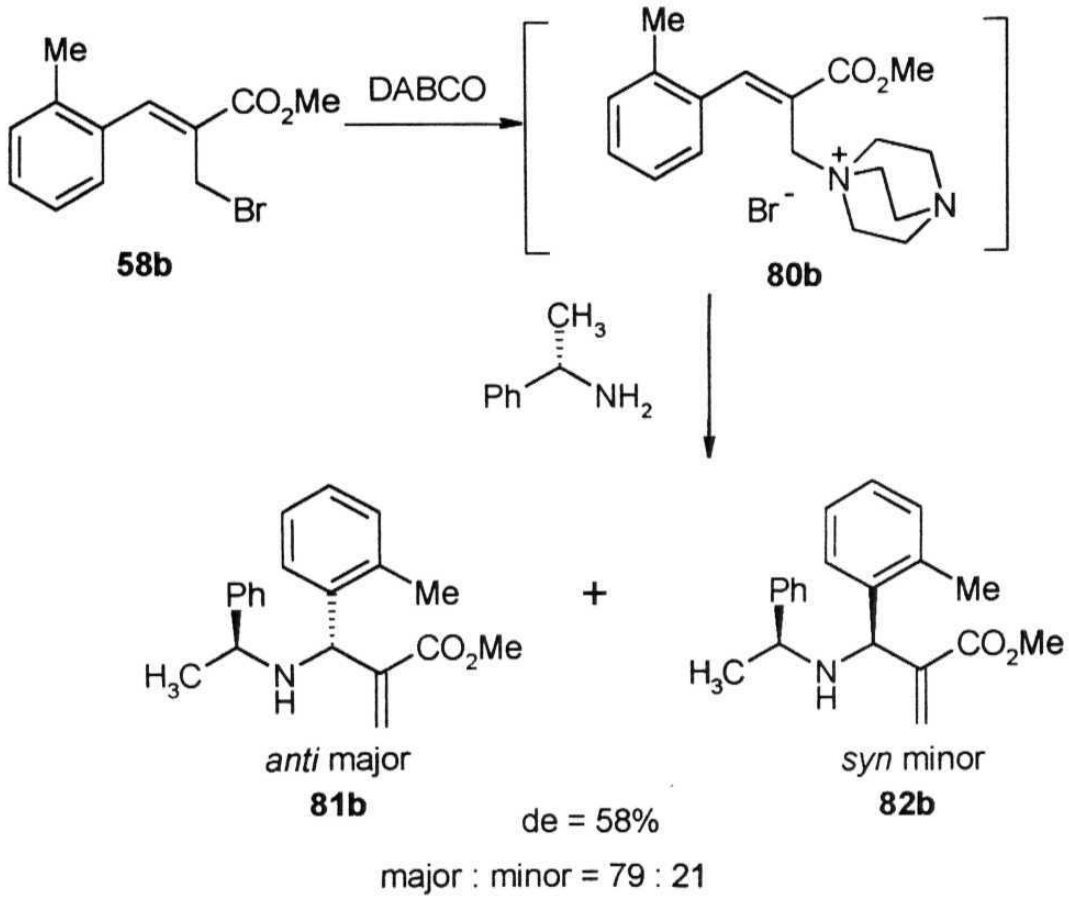
Hydrogen atoms were omitted (except nitrogen attached hydrogen and hydrogens present in the asymmetric center) for clarity.

Figure E: Ortep diagram of the molecule 81a

Table V. Crystal data and structure refinement for 81a

Identification code	**81a**
Empirical formula	$C_{19} H_{21} N O_2$
Formula weight	294.86
Temperature	293(2) K
Wavelength	0.71073 A
Crystal system, space group	Orthorhombic, P2,2]2]
Unit cell dimensions	a = 6.639(3) A a = 90°
	b= 13.2464(14) A (3 = 90°
	c= 19.199(2) A γ = 90°
Volume	1688.4(8) A^3
Z, Calculated density	4, 1.160 Mg/m^3
Absorption coefficient	0.075 mm^{-1}
F(000)	630
Crystal size	0.52 x 0.45 x 0.45 mm
6 range for data collection	1.87 to 24.94°
Index ranges	0 < h < 7 , 0 < k < 15, 0 < 1 < 22
Reflections collected / unique	1724/ 1724 [R(int) = 0.0000]
Completeness to 2θ = 24.94	100.0%
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1724/1/205
Goodness-of-fit on F^2	0.639
Final R indices [I>2σ (I)]	R1 =0.0429, wR2 = 0.1319
R indices (all data)	R1 = 0.1028, wR2 = 0.2154
Absolute structure parameter	-8(5)
Largest difference peak and hole	0.195 and -0.237 e. A'^3

Scheme 59

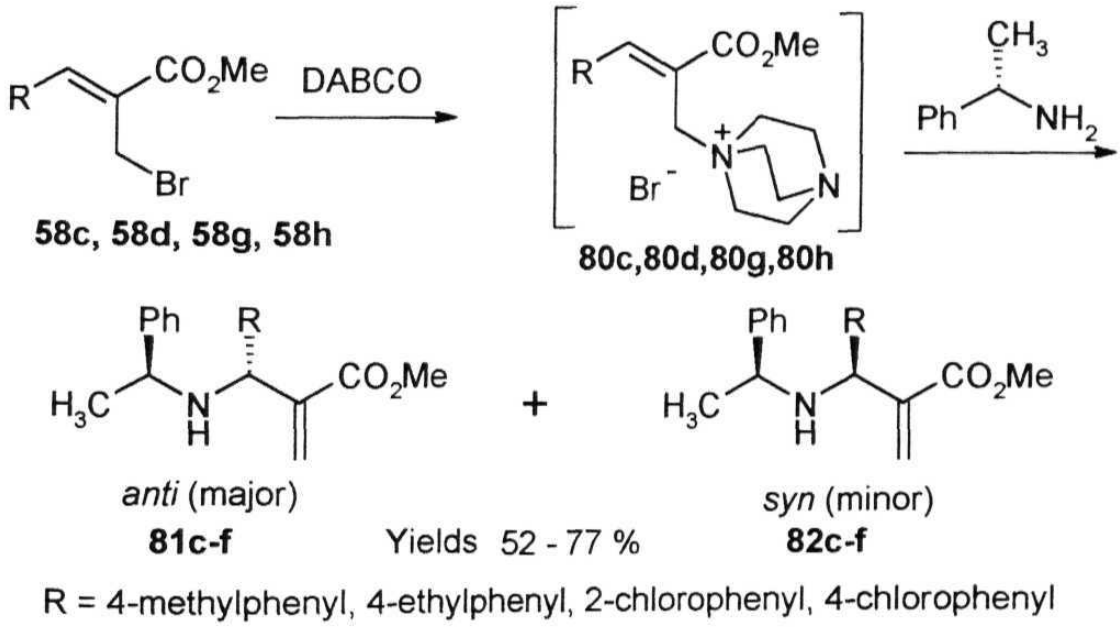


Encouraged by these results we have transformed representative allyl bromides (58c, **58d,** 58g, 58h)® derived from Baylis-Hillman adducts, into the desired allyl amine products (81c-f, **82c-f)**© in good yields (Scheme 60, Table 10) *via* the treatment of corresponding allyl bromide–DABCO salts with (S)-l-phenylethylamine at room temperature for 1 hour in methylene chloride as a solvent. The diastereoselectivity in

© For easy understanding and continuity the major isomers and minor isomers obtained in the reaction of the corresponding allyl bromides 58b-d, **58g-h** with (S)-l-phenylethylamine in the presence of DABCO were numbered as 81b-f and 82b-f respectively.

these reactions ranges from 40-53% Fortunately both the major and minor isomers have been separated by column chromatography in all the cases. In analogy with **81a** and **82a** all the other major isomers **81b-f** and minor isomers **82b-f** were assigned *anti* and *syn* stereochemistry respectively as indicated in the Scheme 59 and 60.

Scheme 60



Thus, we have successfully developed a simple method for the diastereoselective synthesis of optically active allyl amines *via* the reaction of allyl bromides–DABCO salts with (S)-l-phenylethylamine. These studies clearly demonstrate the importance of allyl bromides derived from Baylis-Hillman adducts in diastereoselective organic synthesis.

Table 10: **Diastereoselective** addition of chiral amine to **olefins**[a, b]

Allyl bromide	R	de (%)	Compound (major)[c,d]	Yield[e] (%)	Compound (minor)[c]	Yield[e] (%)
58a	phenyl	50	**81a**[f]	50	82a	17
58b	2-methylphenyl	58	81b	47	82b	15
58c	4-methylphenyl	40	81c	36	82c	16
58d	4-ethylphenyl	42	81d	41	82d	22
58g	2-chlorophenyl	42	81e	56	82e	21
58h	4-chlorophenyl	53	81f	54	82f	16

a) The diastereomeric excess of the compounds (**81a-f** & 82a-f) was determined by ^{1}H NMR spectral analysis. In the ^{1}H NMR spectrum of the crude product(s), the olefinic proton (*cis* to ester group) shows two singlets (due to diastereomers), thus the diastereomeric excess was determined by the integration ratio of these two singlets.

b) All the reactions were carried out on 2 mM scale of the allyl bromide with 2 mM of DABCO at room temperature for lh and the resulting salt was subsequently treated with (S)-l-phenylethylamine (2 mM) at room temperature for lh.

c) All the allyl amines were obtained as colorless viscous liquids except molecule 81a (which was obtained as a solid). All the products gave satisfactory IR, ^{1}H NMR (200 MHz), ^{13}C NMR (50 MHz).

d) All the major *(anti)* isomers were further characterized by mass spectral and elemental analyses.

e) Yields of pure allyl amines obtained after careful column chromatography (silica gel, 8 % EtOAc in hexanes).

f) Structure of the molecule was determined by single crystal X-ray data.

CONCLUSIONS

All the objectives mentioned in the beginning of the chapter have been achieved with considerable success. We have successfully developed a new protocol for the synthesis of (*E*)-3-benzylidenechroman-4-ones in four step sequence from the Baylis-Hillman adducts. The efficacy of this methodology has been successfully demonstrated by synthesis of bonducellin monomethyl ether, eucomin dimethyl ether, autumnalin trimethyl ether and (*E*)-3-(4-methoxybenzylidene)-6-methoxychroman-4-one an antifungal agent. We have successfully transformed for the first time the Baylis-Hillman adducts into indene and indane derivatives *via* the intramolecular Friedel-Crafts reaction using P_2O_5. We have also synthesized *dl* and *meso* bis allyl ethers *via* tandem construction of carbon-carbon and carbon oxygen-bonds by utilizing the Baylis-Hillman Chemistry. Finally we have also successfully carried out diastereoselective addition of (S)-l-phenylethylamine to methyl (2Z)-3-aryl-2-(bromomethyl)prop-2-enoates in the presence of DABCO thus providing a simple method for synthesis of the chiral allyl amines.

EXPERIMENTAL

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

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

Elemental Analysis. Elemental analyses were performed on a Perkin-Elmer 240c-CHN analyzer.

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

Nuclear Magnetic Resonance Spectra: Proton magnetic resonance spectra and carbon-13 magnetic resonance spectra were recorded on BRUKER-AC-200 spectrometer. ^1H NMR (200 MHz) spectra for all the samples were measured in chloroform-d with TMS (8 = 0 ppm) as internal standard. ^{13}C NMR (50 MHz) spectra for all the samples were measured in chloroform-d with its middle peak of the triplet (δ = 77.10 ppm) as internal standard. Spectral assignments are as follows: (1) Chemical shifts on the δ scale, (2) Standard abbreviation for multiplicity, *i.e.* s = singlet, d = doublet, t = triplet, **q** = quartet, **sept** = **septet,** m = multiplet, **dd** = **doublet of doublet, dt = doublet of triplet, br =**

broad, (3) Number of hydrogens integrated for the signal, (4) coupling constant J in Hertz.

Mass Spectral Analysis: Mass spectra were recorded on Hewlett Packard (model HP 5989A) or Finnigon MAT (1020C) mass spectrometer.

Optical Rotations: Optical rotations were measured on Jasco DIP 370 Digital polarimeter at the wavelength of the sodium D-line (589 nm) and at ambient temperatures.

Chromatography: Analytical thin layer chromatography (TLC) was performed on glass plates (7x2 cm) coated with Acme's silica gel G or GF 254 (250 mμ) containing 13% calcium Sulfate as binder. The spots were visualized by short exposure to iodine vapor or uv light. Column chromatography was carried out using Acme's silica gel (100-200 mesh). High pressure liquid chromatography (HPLC) analysis was carried out on Shimadzu LC-10AD Chromatopac equipped with SPD-10A UV-VIS detector using HPLC grade solvents.

X-ray **Crystallography**

The X-ray diffraction measurement were carried out at 293 K on an automated Enraf-Nonious MACH 3 diffractometer using graphite monochromated, Mo-Kα (λ =0.71073 A°) radiation with CAD4 software. The single crystal was fixed to a capillary head by an appropriate fixing material. Primary unit cell constants were determined with a set of 25 narrow frame scans. Intensity data were collected by the ω scan mode. Stability of the crystal during the measurement was monitored by measuring the intensity of the

standard reflections after every one and half hour intervals. No appreciable variation of the crystal was detected. The data were reduced using XT AL program. No absorption correction was applied. The structure was solved by direct methods and refined by full-matrix least-squares using the SHELXS-86 and SHELXL-93 program packages respectively.

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

Methyl 3-hydroxy-2-methylene-3-phenylpropanoate (57a):

A mixture of benzaldehyde (50 mM, 5.306 g), methyl acrylate (75 mM, 6.456 g) and DABCO (7.5 mM, 0.841 g) was kept at room temperature for 7 days The reaction mixture was diluted with ether (60 mL) and washed successively with 2N HC1 solution, water and aqueous $NaHCO_3$ solution. Organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and residue thus obtained was distilled under reduced pressure to afford the alcohol **57a** as a colorless liquid in 84% (8.064 g) yield.

bp : 122-125^0 C / 2.7 mm

IR (neat) : 3449, 1720, 1630 cm^{-1}

^{1}H NMR : 5 3.12 (b, 1H), 3.70 (s, 3H), 5.55 (s, 1H), 5.83 (s, lH),6.32(s, 1H), 7.21-7.45 (m, 5H)

^{13}C NMR : 6 51.68, 72.71, 125.56, 126.59, 127.61, 128.23, 141.40, 142.20, 166.58

Methyl 3-hydroxy-2-methylene-3-(2-methylphenyl)propanoate (57b):

This compound was prepared from 2-tolualdehyde, methyl acrylate and DABCO (cat.) following a similar procedure described for the molecule **57a,** as a colorless liquid.

Reaction time : 8 days

Yield : 80%

bp : 134-136^{0}C/4.2 mm

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

^{1}H NMR 5 2.32 (s, 3H), 2.71 (b, 1H), 3.76 (s, 3H), 5.61 (d, 1H, J=2.2 Hz), 5.81 (s, 1H), 6.32 (s, 1H), 7.10-7.31 (m, 3H), 7.38-7.45 (m, 1H)

^{13}C NMR :5 18.99,51.88,69.15, 125.90, 126.10, 126.35, 127.74, 130.41, 135.68, 138.96, 141.98, 167.04

Methyl 3-hydroxy-2-methylene-3-(4-methylphenyl)propanoate (57c):

This compound was prepared from 4-tolualdehyde, methyl acrylate and DABCO (cat.) following a similar procedure described for the molecule 57a, as a colorless liquid.

Reaction time : 8 days

Yield : 79%

bp : 140-143^{0}C/5.2 mm

LR(neat) : 3341, 1716, 1631 cm^{-1}

^{1}H NMR : 8 2.33 (s, 3H), 2.71 (br, 1H), 3.71 (s, 3H), 5.53 (s, 1H), 5.84 (s, 1H), 6.32 (s, 1H), 7.14 (d, 2H, J= 7.8 Hz), 7 26 (d, 2H, J= 7.8 Hz)

^{13}C NMR : δ 20.91, 51.63, 72.51, 125.28, 126.50, 128.89, 137.21, 138.40, 142.20, 166.57

Methyl 3-(4-ethylphenyl)-3-hydroxy-2-methylenepropanoate (57d):

This compound was prepared from 4-ethylbenzaldehyde, methyl acrylate and DABCO (cat.) following a similar procedure described for the molecule 57a, as a colorless liquid.

Reaction time : 7 days

Yield : 82%

bp : 148-150^{0}C/4 mm

IR (neat) : 3466, 1722, 1630 cm^{-1}

^{1}H NMR : 6 1.23 (t, 3H, J= 7.7 Hz), 2.64 (q, 2H, J= 7.78 Hz), 2.98 (b, 1H), 3.72 (s, 3H), 5.54 (s, 1H), 5.86 (s, 1H), 6.33 (s, 1H), 7.19 (d, 2H, J=7.7 Hz), 7.29 (d, 2H,J=7.7 Hz)

^{13}C NMR :6 15.24, 28.35, 51.57, 72.53, 125.18, 126.59, 127.67, 138.73, 142.37, 143.55, 166.58

Methyl 3-hydroxy-3-(4-isopropylphenyl)-2-methylenepropanoate (57e):

This compound was obtained as a colorless liquid *via* the reaction between 4-isopropyl benzaldehyde and methyl acrylate in the presence of catalytic amount of DABCO following a similar procedure described for the molecule 57a.

Reaction time : 6 days

Yield : 84%

bp : 165-167^{0}C/4.5 mm

IR (neat) : 3466, 1722, 1630 cm^{-1}

^{1}H NMR : 8 1.22 (d, 6H, J = 6.8 Hz), 2.88 (m, 1H), 3.00 (b, 1H), 3.70 (s, 3H), 5.53 (s, 1H), 5.84 (s, 1H), 6.32 (s, 1H), 7.19 (d, 2H, J= 7.6 Hz), 7.28 (d, 2H, J= 7.6 Hz)

^{13}C NMR : 5 23.87, 33.72, 51.73, 72.73, 125.46, 126.37, 126.61, 138.81, 142.29, 148.31, 166.69

Methyl **3-hydroxy-3-(4-methoxyphenyl)-2-methylenepropanoate (57f):**

This compound was obtained as a crystalline solid *via* the reaction between 4-methoxybenzaldehyde and methyl acrylate in the presence of DABCO (cat.) following a similar procedure described for the molecule 57a {after column chromatography (silica gel, 10% EtOAc in hexanes)}.

Reaction time : 10 days

Yield : 68%

mp : 61°C

IR (KBr) : 3447, 1718, 1620 cm^{-1}

^{1}H NMR : 5 3.07 (d, 1H, J = 4.0 Hz), 3.70 (s, 3H), 3.78 (s, 3H), 5.51 (d, 1H, J = 4.0 Hz), 5.85 (s, 1H), 6.31 (s, 1H), 6.85 (d 2H, J=8.4 Hz), 7.27 (d, 2H, J = 8.4 Hz)

^{13}C NMR : 5 51.74, 55.15, 72.42, 113.77, 125.18, 127.92,133.64, 142.43, 159.17, 166.70

Methyl 3-(2-chlorophenyl)-3-hydroxy-2-methylenepropanoate (57g):

This compound was obtained as **a** colorless liquid ***via*** **the reaction between 2-chlorobenzaldehyde and** methyl acrylate in the presence **of DABCO (cat.) following a** similar procedure described for the molecule 57a.

Yield : 85%

bp : 116-117^{0}C/0.4 mm

IR (neat) : 3447, 1722, 1631 cm^{-1}

^{1}H NMR : 6 3.40 (d, 1H, J = 3.2 Hz), 3.77 (s, 3H), 5.58 (s, 1H), 5.97 (d, 1H, J = 3.2 Hz), 6.33 (s, 1H), 7.19-7.42 (m, 3H), 7.54 (dd, 1H, J =7.0 and 1.8 Hz)

^{13}C NMR : 6 51.95, 69.05, 126.71, 126.92, 128.13, 128.90, 129.38, 132.80, 138.47, 140.85, 166.85

Methyl 3-(4-chlorophenyl)-3-hydroxy-2-methylenepropanoate (57h):

This compound was obtained as a colorless liquid *via* the reaction between 4-chlorobenzaldehyde and methyl acrylate in the presence of DABCO (cat.) following a similar procedure described for the molecule **57a.**

Reaction time : 6 days

Yield : 85%

bp : 121-123^{0}C/0.6 mm

IR (neat) : 3476, 1716, 1630 cm^{-1}

^{1}H NMR 5 3.11 (br, 1H), 3.72 (s, 3H), 5.52 (s, 1H), 5.83 (s, 1H), 6.33 (s, 1H), 7.30 (m, 4H)

^{13}C NMR : 5 51.88, 72.13, 125.94, 128.03, 128.43, 133.41, 139.93, 141.79, 166.48

Methyl 3-hydroxy-2-methylenehexanaote (57i):

This compound was prepared from butyraldehyde, methyl acrylate and DABCO (cat.) following a similar procedure described for the molecule 57a, (after column chromatography, silica gel, 10% EtOAc in hexanes) as a colorless liquid.

Reaction time : 7 days

Yield : 61%

IR (neat) : 3445, 1718, 1631 cm^{-1}

^{1}H NMR : 5 0.92 (t, 3H, J = 7.4 Hz), 1.20-1.72 (m, 4H), 2,7 (br, 1H), 3.76 (s, 3H), 4.39 (t, 1H, J = 6.7 Hz), 5.78 (s, 1H), 6.21 (s, 1H)

^{13}C NMR : 5 13.66, 18.81.38.38, 51.62, 70.74, 124.47, 142.90, 166.94.

Methyl 3-hydroxy-2-methyleneheptanoate (57j):

This compound was prepared from velaraldehyde and methyl acrylate in the presence of catalytic amount of DABCO following a similar procedure described for the molecule 57a, (after column chromatography, silica gel, 10% EtOAc/ hexanes) as a colorless liquid.

Reaction time : 7 days

Yield : 63%

IR (neat) : 3447, 1718, 1630 cm^{-1}

^{1}H NMR : 5 0.85 (t, 3H, J = 6.4 Hz), 1.15-1.76 (m, 6H), 2,90 (b, 1H), 3.72 (s, 3H), 4.35 (m, 1H), 5.76 (s, 1H), 6.16 (s, 1H)

^{13}C NMR : 8 13.82, 22.39, 27.84, 35.98, 51.64, 71.19, 124.48, 142.95, 166.98

Methyl (2Z)-2-(bromomethyl)-3-phenylprop-2-enoate (58a):

This compound was prepared according to the literature procedure.[117]

To a stirred solution of methyl 3-hydroxy-2-methylene-3-phenylpropanoate (57a) (10 mM, 1.92 g) in dichloromethane (15 mL) was added hydrobromic acid (48%, 3.3 mL) followed by a drop wise addition of concentrated sulfuric acid (2.9 mL) at 0°C. After stirring overnight at room temperature the reaction mixture was poured into ice cold water and then extracted with ether (3×15 mL). The combined organic layer was dried over anhydrous Na_2SO_4 and solvent was evaporated. The crude product thus obtained, was purified by column chromatography (silica gel, 2% EtOAc in hexanes) to provide **58a** in 91% (2.32 g) yield, as a colorless oil.

IR (neat) : 1716, 1626 cm^{-1}

^{1}H NMR : 8 3.85 (s, 3H), 4.36 (s, 2H), 7.32-7.61 (m, 5H), 7.79 (s, 1H)

^{13}C NMR : δ 26.59, 52.24, 128.75, 129.49, 134.14, 142.71, 166.36

Methyl (2Z)-2-(bromomethyl)-3-(2-methylphenyl)prop-2-enoate (58b):

This was prepared *via* the treatment of methyl 3-hydroxy-2-methylene-3-(2-methyl-phenyl)propanoate (57b) with 48% HBr and sulfuric acid following the similar procedure described for the molecule 58a as a colorless liquid.

Yield : 90%

IR (neat) : 1720, 1628 cm^{-1}

^{1}H NMR : 5 2.31 (s, 3H), 3.90 (s, 3H), 4.29 (s, 2H), 7.22-7.36 (m, 3H), 7.51-7.59 (m, 1H), 7.91 (s, 1H)

^{13}C NMR : 5 19.82, 26.50, 52.33, 126.06, 127.93, 129.33, 129.58, 130.32, 133.56, 137.24, 142.07, 166.40

Methyl (2Z)–2-(bromomethyl)-3-(4-methylphenyl)prop-2-enoate(58c):

This was prepared by the reaction of methyl 3-hydroxy-2-methylene-3-(4-methyl-phenyl)propanoate (57c) with 48% HBr and concentrated sulfuric acid following a similar procedure described for the molecule 58a, as a colorless oil.

Yield : 92%

IR (neat) : 1716, 1626 cm^{-1}

^{1}H NMR : 5 2.39 (s, 3H), 3.86 (s, 3H), 4.41 (s, 2H), 7.27 (d, 2H, J = 8.0 Hz) 7.48 (d, 2H, J = 8.0 Hz), 7.79(s, 1H)

^{13}C NMR : 6 21.31, 26.92, 52.22, 127.70, 129.54, 129.76, 131.35, 139.97, 142.96, 166.61

Methyl (2Z)-2-(bromomethyl)-3-(4-ethylphenyl)prop-2-enoate (58d):

This was prepared by the treatment of methyl 3-hydroxy-2-methylene-3-(4-ethylphenyl)propanoate (57d) with HBr (48%) and H2SO4 following similar procedure described for the molecule 58a, as a colorless oil.

Yield : 90%

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

^{1}H NMR : 5 1.26 (t, 3H, J = 7.8 Hz), 2.70 (q, 2H, J = 7.8 Hz), 3.88 (s, 3H), 4.43 (s, 2H), 7.30 (d, 2H, J = 8.0 Hz), 7.52 (d, 2H, J = 8.0 Hz), 7.81 (s, 1H)

^{13}C NMR :8 15.16,26.99,28.72,52.27, 127.78, 128 40, 129.93, 131.64, 143.03, 146.29, 166.69

Methyl (2Z)-2-(bromomethyl)-3-(4-isopopylphenyl)prop-2-enoate (58e):

This was prepared by treating methyl 3-hydroxy-2-methylene-3-(4-isopropylphenyl)propanoate (57e) with 48% HBr in the presence of conc. sulfuric acid following similar procedure described for the molecule 58a, as a colorless oil.

Yield : 74%

IR (neat) : 1718, 1624 cm^{-1}

^{1}H NMR : δ 1.28, (d, 6H, J = 7.0 Hz), 2.96 (sep, 1H, J = 7.0 Hz), 3.88 (s, 3H), 4.44 (s, 2H), 7.33 (d, 2H, J = 8.1 Hz), 7.54 (d, 2H, J = 8.1 Hz), 7.82 (s, 1H)

^{13}C NMR : 8 23.68, 27.04, 33.99, 52.27, 126.97, 127.69, 129.97, 131.73, 142.99,

150.85, 166.66

Methyl **(2Z)-2-(bromomethyl)-3-(4-methoxyphenyl)prop-2-enoate** (58f):

This was prepared by treating methyl 3-hydroxy-2-methylene-3-(4-methoxyphenyl)propanoate (57f) with HBr (48%) in the presence of conc. H_2SO_4 following similar procedure described for the molecule 58a, as a colorless solid.

Yield : 75%

mp : 63-65°C

IR (KBr) : 1707, 1621 cm^{-1}

^1H NMR : 5 3.86 (s, 3H), 3.87 (s, 3H), 4.45 (s, 2H), 6.98 (d, 2H, J = 6.8Hz), 7.58 (d, 2H, J = 6.8Hz), 7.78 (s, 1H)

^{13}C NMR : 6 27.52, 52.32, 55.37, 114.45, 126.17, 126.74, 131.98, 142.91, 160.88, 166.90

Methyl **(2Z)-2-(bromomethyl)-3-(2-chlorophenyl)prop-2-enoate** (58g):

This compound was obtained by the reaction of methyl 3-(2-chlorophenyl)-3-hydroxy-2-methylenepropanoate (57g) with 48% HBr in the presence of conc. sulfuric acid following the similar procedure described for the molecule 58a, as a colorless viscous liquid.

Yield : 80%

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

^1H NMR : 8 3.90 (s, 3H), 4.27 (s, 2H), 7.34-7.48 (m, 3H), 7.71 (m,lH), 7.92 (s,lH)

^{13}C NMR : δ 26.12, 52.50, 127.00, 129.57, 129.83, 130.56, 132.90, 134.49, 139.45, 166.00

Methyl (2Z)-2-(bromomethyl)-3-(4-chlorophenyl)prop-2-enoate (58h):

This compound was obtained by treating methyl 3-(4-chlorophenyl)-3-hydroxy-2-methylenepropanoate **(57h)** with 48% HBr in the presence of conc. sulfuric acid following the similar procedure described for the molecule **58a,** as a colorless liquid

Yield : 79%

IR (neat) : 1718, 1628 cm^{-1}

^1H NMR : δ 3.87 (s, 3H), 4.34 (s, 2H), 7.37-7.61 (m, 4H), 7.75 (s, 1H)

^{13}C NMR : δ 26.16, 52.39, 129.08, 129.19, 130.84, 132.57, 135.63, 141.29, 166.16

Methyl (2Z)-2-(bromomethyl)hex-2-enoate (58i):

This was prepared by treatment of methyl 3-hydroxy-2-methylenehexanoate **(57i)** with 48% HBr and conc. sulfuric acid following the similar procedure described for the molecule **58a,** as colorless liquid.

Yield : 62%

IR (neat) : 1720, 1641 cm^{-1}

^1H NMR : 8 0.97 (t, 3H, J = 7.6Hz), 1.54 (m, 2H), 2.27 (m, 2H), 3.79

(s, 3H), 4.22 (s, 2H), 6.97 (t, 1H, J = 7.4 Hz)

^{13}C NMR : 5 13.81, 21.42, 24.19, 30.77, 52.00, 129.38, 148.20, 166.01

Methyl (2Z)-2-(bromomethyl)hept-2-enoate (58j):

This was prepared by the reaction of methyl 3-hydroxy-2-methyleneheptanaote (57j) with 48 % HBr in the presence of con. suifliric acid following the similar procedure described for the molecule 58a, as a colorless liquid.

Yield : 76%

IR (neat) : 1720, 1641 cm^{-1}

^{1}H NMR : 5 0.91 (t, J = 7.2 Hz), 1.25-1.60 (m, 4H), 2.28 (m, 2H), 3.78 (s, 3H), 4.22 (s, 2H), 6.97 (t, 1H, J = 7.6 Hz)

^{13}C NMR :5 13.71,22.37,24.17,28.49,30.20,51.94, 129.15, 148.38, 165.93

Methyl (2*E*)-2-(phenoxymethyl)-3-phenylprop-2-enoate (59a):

A mixture of methyl (2Z)-2-(bromomethyl)-3-phenylprop-2-enoate (10 mM, 2.55 g) and anhydrous K_2CO_3 (10 mM, 1.38 g), phenol (10 mM, 0.94 g) in acetone (10 mL) was refluxed with stirring for 3 hours. Then the reaction mixture was cooled to room temperature and acetone was removed under reduced pressure. The residue was diluted with water (25 mL), and extracted with ether (3 x 25 mL). The combined organic layer was dried over anhydrous Na_2SO_4 and solvent was evaporated. Purification of

crude product thus obtained, by column chromatography (silica gel, 3% EtOAc in hexanes) provided product **59a** in 73% (1.956 g) yield, as a colorless oil.

IR (neat) : 1716, 1635 cm^{1}

^{1}H NMR : 6 3.83 (s, 3H), 4.82 (s, 2H), 6.92-7.06 (m, 3H), 7.23-7.55 (m, 7H), 8.05 (s, 1H)

^{13}C NMR : 6 52.17, 62.72, 114.99, 121.09, 127.33, 128.65, 129.44, 129.54, 129.71, 134.39, 145.49, 158.48, 167.53

Methyl (2*E*)-3-(2-methylphenyl)-2-(phenoxymethyl)prop-2-enoate (59b):

This compound obtained as a colorless liquid *via* the reaction of methyl (2Z)-2-(bromomethyl)-3-(2-methylphenyl)prop-2-enoate **(58b)** with phenol in the presence of K_2CO_3 following a similar procedure described for the molecule **59a**

Yield : 87%

IR (neat) : 1720, 1625 cm^{-1}

^{1}H NMR : 8 2.34, (s, 3H), 3.87 (s, 2H), 4.75 (s, 2H), 6.83-7.45 (m, 9H), 8.13 (s, 1H)

^{13}C NMR : δ 19.59, 51.85, 62.76, 114.78, 120.73, 125.70, 128.02, 128.78, 128.06, 129.80, 133.45, 136.84, 143.84, 158.30, 167.16

Methyl *(2E)*-3-(4-methylphenyl)-2-(phenoxymethyl)prop-2-enoate (59c):

This was prepared by the treatment of methyl (2Z)-2-(bromomethyl)-3-(4-methylphenyl)prop-2-enoate **(58c)** with phenol in the presence of K2CO3 following a similar procedure described for the molecule 59a, as a colorless solid.

Yield : 75%

mp : 72-73°C

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

^{1}H NMR : 5 2.34 (s, 3H), 3.83 (s, 3H), 4.82 (s, 2H), 6.95-7.46 (m, 9H), 8.02 (s, 1H)

^{13}C NMR : 521.35, 52.18, 62.91, 115.11, 121.12, 126.48, 129.49, 129.93, 131.70, 140.01, 145.71, 158.63, 167.78

Methyl (2*E*)-3-(4-ethylphenyl)-2-(phenoxymethyl)prop-2-enoate (59d):

This was obtained *via* treatment of methyl (2Z)-2-(bromomethyl)-3-(4-ethylphenyl) prop-2-enoate **(58d)** with phenol in the presence of K_2CO_3 following similar procedure described for the molecule 59a, as a colorless liquid.

Yield : 90%

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

^{1}H NMR : δ 1.23 (t, 3H, J = 7.7 Hz), 2.66 (q, 2H, J = 7.7 Hz), 3.85 (s, 3H), 4.85 (s, 2H), 6.95-7.49 (m, 9H), 8.05 (s, 1H)

^{13}C NMR : S 15.15,28.66, 52.09,62.85, 115.04, 121.05, 126.42, 128.22,

129.42, 129.98, 131.87, 145.65, 146.20, 158.58, 167.71

Methyl (2*E*)-3-(4-isopropylphenyl)-2-(phenoxymethyl)prop-2-enoate (59e):

This was obtained *via* the reaction of methyl (2Z)-2-(bromomethyl)-3-(4-isopopylphenyl)prop-2-enoate (58e) with phenol in the presence of K_2CO_3 following the similar procedure described for the molecule 59a, as a colorless crystalline solid.

Yield : 71%

mp :71~73°C

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

^1H NMR : 5 1.25 (d, 6H, J = 6.8 Hz), 2.91 (sept. 1H, J = 6.8 Hz), 3.85 (s, 3H), 4.86 (s, 2H), 6.94-7.49 (m, 9H), 8.05 (s, 1H)

^{13}C NMR : δ 23.83, 34.10, 52.32, 62.91, 115.13, 121.16, 126.40, 126.97, 129.56, 130.15, 132.08, 145.89, 150.98, 158.66, 167.93

Methyl (2*E*)-3-(4-methoxyphenyl)-2-(phenoxymethyl)prop-2-enoate (59f):

This was obtained *via* treatment of methyl (2Z)-2-(bromomethyl)-3-(4-methoxyphenyl) prop-2-enoate **(58f)** with phenol in the presence of K_2CO_3 following similar procedure described for the molecule 59a, as a colorless crystalline solid.

Yield : 77%

mp : 76-77°C

IR(KBr) :1701,1622 cm^{-1}

^{1}H NMR : 6 3.81 (s, 3H), 3.84 (s, 3H), 4.86 (s, 2H), 6.88 (d, 2H, J = 8.7 Hz), 6.94-7.44 (m, 5H), 7.48 (d, 2H, J = 8.7 Hz), 8.02 (s, 1H)

^{13}C NMR : 5 52.13, 55.24, 62.84, 114.23, 115.01, 121.08, 124.79, 126.99, 129.49, 131.85, 145.57, 158.55, 160.94, 167.90

Methyl (2*E*)-3-(2-chlorophenyl)-2-(phenoxymethyl)prop-2-enoate (59g):

This was prepared by reaction of methyl (2Z)-2-(bromomethyl)-3-(2-chlorophenyl) prop-2-enoate **(58g)** with phenol in the presence of K2CO3 following similar procedure described for the molecule 59a, as a colorless viscous liquid.

Yield : 73%

IR (neat) : 1720, 1639 cm^{-1}

^{1}H NMR : 5 3.88 (s, 3H), 4.74 (s, 2H), 6.91-7.61 (m, 9H), 8.16 (s, 1H)

^{13}C NMR : 5 52.32, 63.10, 115.10, 121.24, 126.92, 129.46, 129.60, 130.54, 130.73, 133.17, 134.45, 141.86, 158.51, 167.04

Methyl (2*E*)-3-(4-chlorophenyl)-2-(phenoxymethyl)prop-2-enoate (59h):

This was obtained *via* treatment of methyl (2Z)-2-(bromomethyl)-3-(4-chlorophenyl) prop-2-enoate **(58h)** with phenol in the presence of K_2CO_3 following similar procedure described for the molecule 59a, as a colorless crystalline solid.

Yield : 76%

mp : 77-79°C

IR(KBr) : 1705, 1620 cm^{1}

^{1}H **NMR** : 8 3.84 (s, 3H), 4.79 (s, 2H), 6.93-7.51 (m, 9H), 7.97 (s, 1H)

^{13}C **NMR** : 8 52.35, 62.69, 115.12, 121.39, 128.01, 129.03, 129.60, 131.15, 132.95, 135.83, 144.16, 158.44, 167.36

Methyl (2*E*)-2-(phenoxymethyl)hex-2-enoate (59i):

This was obtained as a colorless liquid *via* the reaction between methyl (2Z)-2-(bromomethyl)hex-2-enoate **(58i)** and phenol in the presence of K2CO3 following similar procedure described for the molecule **59a,** as a colorless liquid.

Yield : 65%

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

^{1}H NMR : δ 0.94 (t, 3H, J = 7.6 Hz), 1.51 (m, 2H), 2.30 (m, 2H), 3.77, (s, 3H), 4.75 (s, 2H), 6.84-7.05 (m, 3H), 7.12 (t, 1H, J = 7.4Hz), 7.22-7.39 (m, 2H)

^{13}C NMR : 8 13.68, 21.82, 30 76, 51.72, 61.88, 114.89, 120.88, 127.98, 129.30, 149.32, 158.79, 167.02.

Methyl (2*E*)-2-(phenoxymethyl)hept-2-enoate (59j):

This was obtained *via* the reaction of methyl (2Z)-2-(bromomethyl)hept-2-enoate **(58j)** with phenol in the presence of K_2CO_3 following similar procedure described for the molecule **59a,** as a colorless liquid

no

Yield : 56%

IR (neat) : 1720, 1651 cm^{-1}

^1H NMR : 5 0.91 (t, 3H, J = 6.8 Hz), 1.26-1.55 (m, 4H), 2.36 (m, 2H), 3.78 (s, 3H), 4.77 (s, 2H), 6.91-7.02 (m, 3H), 7.14 (t, 1H, J = 8.8 Hz), 7.30 (m, 2H)

^{13}C NMR : 6 13.79, 22.39, 28.63, 30.76, 51.86, 62.00, 115.01, 120.98, 127.86, 129.41, 149.75, 158.89, 167.16

(2*E*)-2-(Phenoxymethyl)-3-phenylprop-2-enoic acid (60a):

To a stirred solution of methyl (2*E*)-2-(phenoxymethyl)-3-phenylprop-2-enoate (5 mM, 1.34 g) in acetone (4 mL) was added aqueous KOH (1 g in 10 mL water) at room temperature. After 14h, the reaction mixture was diluted with cold con. HC1 (5 mL) and extracted with ether (3×10 mL). The combined organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and crude product thus obtained was purified by crystallization (5% EtOAc in hexanes) to afford **60a** in 87% (1.105 g) yield, as **a** colorless crystalline solid.

mp : 87-88°C

IR (KBr) : 3300-2500, 1685, 1620 cm^{-1}

^1H NMR : 8 4.85 (s, 2H), 6.94-7.08 (m, 3H), 7.23-7.62 (m, 7H), 8.17 (s, 1H), 10.52 (b, 1H)

^{13}C NMR :562.56, 115.20, 121.32, 126.78,128.86, 129.58,130.10,134.31,

147.81, 158.59, **172.92**

(2*E*)-3-(2-Methylphenyl)-2-(phenoxymethyl)prop-2-enoic acid (60b):

This was prepared by the treatment of methyl (2*E*)-3-(2-methylphenyl)-2-(phenoxymethyl)prop-2-enoate (59b) with KOH in acetone/water following similar procedure described for the molecule **60a,** as a colorless crystalline solid.

Yield : 93%

mp : 125-127°C

IR (KBr) : 3400-2500, 1682, 1623 cm^{-1}

^{1}H NMR : 8 2.34 (s, 3H), 4.75 (s, 2H), 6.86-7.52 (m, 9H), 8.25 (s, 1H)

^{13}C NMR :5 19.98, 62.74, 115.14, 121.18, 126.19, 127.58, 129.27, 129.48, 129.80, 130.27, 133.52, 137.48, 146.45, 158.58, 172.94

(2*E*)-3-(4-Methylphenyl)-2-(phenoxymethyl)prop-2-enoic acid (60c):

This was prepared by hydrolysis of (2*E*)-3-(4-methylphenyl)-2-(phenoxymethyl)prop-2-enoate (59c) with KOH in acetone/water following similar procedure described for the molecule **60a,** as a colorless crystalline solid.

Yield : 83%

mp : 198-199°C

IR (KBr) : 3400-2500, 1674, 1619 cm^{-1}

^{1}H NMR : δ 2.35 (s, 3H), 4.84 (s, 2H), 6.84-7.53 (m, 9H), 8.12 (s, 1H)

^{13}C NMR : 5 21.50, 62.74, 115.25, 121.30, 125.67, 129.62, 130.28, 131.58, 140.62, 147.85, 158.65, 171.89

(2*E*)-3-(4-Ethylphenyl)-2-(phenoxymethyl)prop-2-enoic acid (60d):

This compound was obtained by the treatment of methyl (2*E*)-3-(4-ethylphenyl)-2-(phenoxymethyl)prop-2-enoate (59d) with KOH in acetone / water following similar procedure described for the molecule 60a, as a colorless crystalline solid.

Yield : 92%

mp : 127-129°C

IR (KBr) : 3400-2600, 1689, 1620 cm^{-1}

^{1}H NMR : 8 1.15 (t, 3H, J = 7.6 Hz), 2.58 (q, 2H, J=7.6 Hz), 4.78 (s, 2H), 6.82-7.49 (m, 9H), 8.08 (s, 1H)

^{13}C NMR : 8 15.23, 28.82, 62.59, 115.17, 121.24, 125.71, 128.42, 129.57, 130.41, 131.73, 146.86, 148.00, 158.63, 173.25

(2*E*)-3-(4-Isopropylphenyl)-2-(phenoxymethyl)prop-2-enoic acid (60e):

Methyl (2*E*)-3 -(4-isopropylphenyl)-2-(phenoxymethyl)prop-2-enoate (59e) was hydrolyzed using KOH in water/acetone following similar procedure described for the molecule 60a, to afford 60e as a colorless crystalline solid.

Yield : 84%

mp : 260-262°C

IR (KBr) : 3300-2550, 1687, 1620 cm^{1}

^{1}H NMR : 6 1.15 (d, 6H, J = 7.0 Hz), 2.82 (sep, 1H, J = 7.0 Hz), 4.77 (s, 2H), 6.81-7.48 (m,9H), 8.07 (s, 1H)

^{13}C NMR : 6 23.72, 34.05, 62.48, 115.05, 121.15, 125.51, 126.96,129.51 130.38, 131.76, 147.91, 151.38, 158.52, 172.76

(2*E*)-3-(4-Methoxyphenyl)-2-(phenoxymethyl)prop-2-enoic acid (60f):

Hydrolysis of methyl (2*E*)-3-(4-methoxyphenyl)-2-(phenoxymethyl)prop-2-enoate (59f) with KOH in water / acetone following similar procedure described for the molecule **60a,** provided **60f** as a white crystalline solid.

Yield : 90%

mp : 200-202°C

IR (KBr) : 3450-2600,1670, 1621 cm^{1}

^{1}H NMR : 8 3.82 (s, 3H), 4.87 (s, 2H), 6.82-7.42 (m, 7H),7.52 (d, 2H, **J** = 8.6 Hz) 8.13 (s, **1H)**

(2*E*)-3-(2-Chlorophenyl)-2-(phenoxymethyl)prop-2-enoic acid (60g):

This was obtained by hydrolysis of methyl (2*E*)-3-(2-chlorophenyl)-2-(phenoxymethyl)prop-2-enoate (59g) using KOH in acetone / water following similar procedure described for the molecule **60a,** as a colorless crystalline solid.

Yield : 94%

mp . 142-143°C

IR (KBr) : 3300-2500, 1693, 1626 cm^{-1}

^1H NMR : 5 4.77 (s, 2H), 6.89-7.72 (m 9H), 8.30 (s, 1H)

^{13}C NMR : 6 62.80, 115.17,121.39, 127.05, 128.77, 129.56, 129.74, 130.90, 132.96, 134.71, 144.14, 158.49, 172.21.

(2*E*)-3-(4-Chlorophenyl)-2-(phenoxymethyl)prop-2-enoic acid (60h):

This was obtained by hydrolysis of methyl (2*E*)-3-(4-chlorophenyl)-2-(phenoxymethyl) prop-2-enoate **(59h)** using KOH in water / acetone following similar procedure described for the molecule 60a, as a colorless crystalline solid.

Yield :91%

mp : 177-179°C

IR (KBr) : 3150-2500, 1687, 1620 cm^{-1}

^1H NMR : 5 4.80 (s, 2H), 6.84-7.55 (m, 9H), 8.09 (s, 1H), 9.00 (b, 1H)

^{13}C NMR : 5 62.41, 115.17, 121.53, 127.24, 129.21, 129.68, 131.42, 132.72, 136.41, 146.42, 158.41, 172.30

(2*E*)-2-(Phenoxymethyl)hex-2-enoic acid (60i):

This was obtained by hydrolysis of methyl (2*E*)-2-(phenoxymethyl)hex-2-enoate (59i) with KOH in acetone/water following similar procedure described for the molecule **60a,** as a colorless crystalline solid.

ns

Yield : 78%

mp : 79-80°C

IR (KBr) : 3350-2600, 1687, 1643 cm^{-1}

^{1}H NMR : 6 0.92 (t, 3H, J =7.0 Hz), 1.49 (m, 2H), 2.31 (m, 2H), 4.73 (s, 2H), 6.85-7.00 (m, 3H), 7.20-7.41 (m, 3H), 10.86 (b, 1H)

^{13}C NMR :6 13.78, 21.79, 31.09, 61.53, 114.96, 121.05, 127.55, 129.42, 152.33, 158.75, 172.44

(2*E*)-2-(Phenoxymethyl)hept-2-enoic acid (60j):

This was obtained by hydrolysis of methyl (2*E*)-2-(phenoxymethyl)hept-2-enoate **(60j)** using KOH in acetone / water following similar procedure described for the molecule 60a, as a colorless crystalline solid.

Yield : 61%

mp : 82-84°C

IR (KBr) : 3360-2500, 1689, 1643 cm^{-1}

^{1}H NMR : 8 0.90 (t, 3H, J = 7.0 Hz), 1.23-1.56 (m, 4H), 2.35 (m, 2H), 4.75 (s, 2H), 6.90-7.01 (m, 3H), 7.21-7.36 (m, 3H)

^{13}C NMR : δ 13.83, 22.45, 28.95, 30.67, 61.64, 115.06, 121.12, 127.40, 129.49,152.65, 158.82, 172.43

(*E*)-3-Benzylidenechroman-4-one (62a): (Prepared *via* acid chloride)

To (2*E*)-2-(phenoxymethyl)-3-phenylprop-2-enoic acid (lmM, 0.254 g) was added $SOCl_2$ (1 mL) and stirred for 12 hours at room temperature. Excess $SOCl_2$ was removed under reduced pressure and the reaction mixture was diluted with dichloromethane (5 mL). To this solution freshly sublimed $AlCl_3$ granules (1 mM, 0.133 g) were added at room temperature. After stirring 1 hour, the reaction mixture was diluted with dil HC1 (5 mL, 0.2 N) and extracted with ether (3×10 mL). The combined organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and the crude product thus obtained was purified by column chromatography (silica gel, 3% EtOAc in hexanes) followed by crystallization (2% EtOAc in hexanes) to provide **62a** in 66 % (0.156 g) yield as a pale yellow crystalline solid.

mp : 110-111°C (Lit[145] 110-112°C)

IR(KBr) : 1668,1601cm^{-1}

^{1}H NMR : 5 5.35 (d, 2H, J = 1.6 Hz), 6.95-7.60(m, 8H), 7.88(s, 1H), 8.03 (d, 1H, J = 7.8Hz)

^{13}C NMR : 5 67.63, 117.93, 121.91, 122.06, 127.96, 128.74, 129.46,129.99 130.97, 134.43, 135.85, 137.44, 161.17, 182.17.

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

Analysis calcd. for $C_{16}H_{12}O_2$: C, 81.34; H, 5.12

Found :C, 81.45; H, 5.12

(*E*)-3-(2-Methylbenzylidene)chroman-4-one (62b):

This was obtained by the treatment of the acid chloride, prepared from (2*E*)-3-(2-methylphenyl)-2-(phenoxymethyl)prop-2-enoic acid **(60b),** with $AlCl_3$ following similar procedure described for the molecule 62a, as a pale yellow crystalline solid.

Yield : 53%

mp : 72-73°C

IR(KBr) : 1674, 1606 cm^{-1}

^1H NMR : δ 2.36 (s, 3H), 5.19 (d, 2H, J = 1.5 Hz), 6.92-7.56 (m, 7H), 7.96 (s, 1H), 8.04 (d, 1H, J =7.8 Hz)

^{13}C NMR : 8 19.88, 67.58, 117.88, 121.78, 122.06, 125.67, 127.87, 128.83, 129.36, 130.45, 131.21, 133.35, 135.76, 136.57, 137.97, 161.24, 182.27

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

Analysis calcd. for $C_{17}H_{14}O_2$: C, 81.58; H, 5.64

Found :C, 81.35; H, 5.66

(*E*)-3-(2-Chlorobenzylidene)chroman-4-one (62g)

This compound was obtained by treating the acid chloride, prepared from (2*E*)-3-(2-chlorophenyl)-2-(phenoxymethyl)prop-2-enoic acid **(60g),** with $AlCl_3$ following similar procedure described for the molecule **62a,** as a pale yellow crystalline solid.

Yield : 82%

mp : 97-98°C

IR(KBr) : 1670, 1604 cm^{-1}

^1H NMR : 5 5.19 (d, 2H, J = 1.6 Hz), 6.96-7.57 (m, 7H), 7.96 (s, 1H), 8.05 (d, 1H, J = 7.8 Hz).

^{13}C NMR : 6 67.48, 117.94, 121.93, 126.62, 127.92, 130.01, 130.28, 130.46, 132.46, 132.84, 134.29, 134.88, 135.95, 161.26, 181.88.

MS (m/z) : 270 (M^+)

Analysis calcd. for $C_{16}H_{11}O_2Cl$: C, 70.99; H, 4.10

Found : C, 70.75; H, 4.08

(*E*)-3-(4-Chlorobenzylidene)chroman-4-one (62h):

This compound was prepared by treating the acid chloride, obtained from (2*E*)-3-(4-chlorophenyl)-2-(phenoxymethyl)prop-2-enoic acid **(60h),** with $AlCl_3$ following similar procedure described for the molecule **62a,** as a pale yellow crystalline solid.

Yield : 64%

mp : 166-167°C (lit 167-169°C)[109]

IR(KBr) . 1672, 1606 cm^{-1}

^1H NMR : 5 5.29 (d, 2H, J = 1.6 Hz), 6.93-7.15 (m, 2H), 7.23 (d, 2H, J = 8.3 Hz), 7.34-7.51 (m 3H), 7.79 (s, 1H), 8.01 (dd, 1H, J = 7.8 and 1.6 Hz)

^{13}C NMR :567.53, 117.99, 122.08, 128.03, **129.12, 131.23, 131.53, 132.91, 135.65, 136.01, 161.19,181.93**

MS (m/z) : 270 (M^+)

Analysis calcd. for $C_{16}H_{11}O_2Cl$: C, 70.99; H, 4.10

Found :C, 71.31; H, 4.10

(*E*)-3-Butylidenechroman-4-one (62i):

This compound was obtained *via* the treatment of the acid chloride prepared from (2*E*)-2-(phenoxymethyl)hex-2-enoic acid (60i) with $AlCl_3$ following similar procedure described for the molecule 62a, as a colorless viscous liquid.

Yield : 56%

IR (neat) : 1682, 1604 cm^{-1}

^1H NMR : 5 0.97 (t, 3H, J = 7.0Hz), 1.56 (m, 2H), 2.22 (m, 2H), 5.04 (s, 2H), 6.86-7.03 (m, 3H), 7.42-7.53 (m, 1H), 7.99 (dd, 1H, J = 6.0 and 1.6 Hz).

^{13}C NMR :5 13.82,22.00,29.96,66.91, 117.92, 121.79,122.24, 128.08, 131.18, 135.58, 140.79, 161.70, 181.98

Analysis calcd. for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98

Found : C, 77.48, H, 6.95

(*E*)-3-Pentylidenechroman-4-one (62j):

This compound was prepared by treating the acid chloride, obtained from (2*E*)-2-(phenoxymethyl)hept-2-enoic acid **(60j)** with $AlCl_3$ following similar procedure described for the molecule **62a,** as a colorless liquid.

Yield : 63%

IR (neat) : 1682, 1630 cm^{-1}

^1H NMR : 8 0.92 (t, 3H, J = 7.1 Hz), 1.27-1.61 (m, 4H), 2.25 (m, 2H), 5.03 (s, 2H), 6.83-7.12 (m, 3H), 7.45 (t, 1H, J = 9.0 Hz),7.98 (d, 1H, J = 7.7 Hz)

^{13}C NMR :5 13.69,22.28,27.52,30.64,66.69, 117.75, 121.60, 122.01, 127.86, 130.77, 135.42, 140.92, 161.49, 181.77

MS (m/z) : 202 (M^+)

Analysis calcd. for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46

Found : C, 77.58; H, 7.47

3-(4-Methylphenyl)methyI-4-chromone(63):

This compound was obtained in the reaction of the acid chloride generated from **(2*E*)-3-**(4-methylphenyl)-2-(phenoxymethyl)prop-2-enoic **acid (60c) with $AlCl_3$ following** similar procedure described for the molecule **62a,** as a pale yellow crystalline solid (The desired (*E*)-3-(4-methylbenzylidene)chroman-4-one **was not** obtained).

Yield : 66%

mp : 89-91°C (Lit[146] 90-91°C)

IR(KBr) : 1645, 1610 cm^{-1}

^1H **NMR** : 8 2.31 (s, 3H), 3.77 (s, 2H), 7.05-7.68 (m, 8H), 8.22 (dd, 1H, J = 7.6 & 1.8 Hz).

^{13}C **NMR** : 8 20.99, 31.25, **117.99, 123.94, 124** 86, 125.99, 128.93, 129.30, 133.31, 135.59, 135.99, 153.04, 156.47, 177.36.

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

Analysis calcd. for $C_{17}H_{14}O_2$: C, 81.58; H, 5.64

Found :C, 81.71; H, 5.64

3-(4-Ethylphenyl)methyl-4-chromone (64):

This compound was obtained in the reaction of acid chloride prepared from (2*E*)-3-(4-ethylphenyl)-2-(phenoxymethyl)prop-2-enoic acid (**60d**), with $AlCl_3$ following similar procedure described for the molecule **62a,** as a pale yellow crystalline solid. The desired (*E*)-3-(4-ethylbenzylidene)chroman-4-one was not obtained.

Yield : 40%

mp : 42-43°C

IR(KBr) : 1643, 1612 cm^1

^1H NMR : 8 1.22 (t, 3H,J = 7.6 Hz), 2.62 (q, 2H, J = 7.6 Hz), 3.79 (s, 2H), 7.06-7.71 (m, 8H), 8.23 (d, 1H, J = 7.5 Hz).

^{13}C NMR : 8 15.54,28.43,31.23, 117.95, 123.86, 124.82, 125.90, 128.06,

128.95, 133.30, 135.77, 142.35, 153.04, 156.39, 177.35.

MS (m/z) : 264 (M^+)

Analysis calcd. for $C_{18}H_{16}O_2$: C, 81.79; H, 6.10

Found :C, 81.55; H, 6.13

3-(4-IsopropyIphenyl)methyl-4-chromone (65):

This compound was obtained in the reaction of acid chloride prepared from (2*E*)-3-(4-isopropylphenyl)-2-(phenoxymethyl)prop-2-enoic acid **(60e)** with $AlCl_3$ following similar procedure described for the molecule **62a,** as a pale yellow crystalline solid. The desired (*E*)-3-(4-isopropylbenzylidene)chroman-4-one was not obtained.

Yield : 48%

mp : 67°C

IR(KBr) : 1641, 1609 cm^1

^1H NMR : 5 1.15 (d, 6H, J = 6.8 Hz), 2.80 (sept. 1H, J = 6.8 Hz), 3.71 (s, 2H), 7.07-7.34 (m, 6H), 7.50-7.62 (m, 2H), 8.16 (d, 1H, J = 6.6 Hz)

^{13}C NMR : 5 23.92, 31.17, 33.65, 117.91, 123.91, 124.78, 125.91, 126.58, 128.91, 133.23, 135.92, 146.97, 153.00, 156.41, 177.26.

MS (m/z) : 278 (M^+)

Analysis calcd. for $C_{19}H_{18}O_2$: C, 81.99; H, 6.52

Found : C, 82.35; H, 6.55

Synthesis of arylidcne/alkylidene chroman-4-ones using TFAA as a reagent for intramolecular Friedel-Crafts reaction of the (2*E*)-2-(phenoxymethyl)-3-alk-2-enoic acids (60a-f and 60i)

(*E*)-3-Benzylidenechroman-4-one (62a):

To a stirred solution of (2*E*)-2-(phenoxymethyl)-3-phenylprop-2-enoic acid **(60a)** (1 mM, 0.254 g) in anhydrous dichloromethane was added trifluoroacetic anhydride (1 mM, 0.210 g) and heated under reflux for 1 hour. The reaction mixture was diluted with water (3 mL) and extracted with ether (3×10 mL). The combined organic layer was dried over anhydrous Na_2SO_4 Solvent was evaporated and the crude solid thus obtained was crystallized (2% EtOAc in hexanes) to provide **62a** as a pale yellow crystalline solid in 91% (0.214 g) yield Spectral data are identical with that of product prepared *via* the treatment of (2*E*)-2-(phenoxymethyl)-3-phenylprop-2-enoyl chloride with $AlCl_3$.

(*E*)-3-(2-Methylbenzylidene)chroman-4-one (62b):

This was obtained *via* the treatment of (2*E*)-3-(2-methylphenyl)-2-(phenoxymethyl)prop-2-enoic acid **(60b)** with TFAA following similar procedure described for the molecule **62a,** as pale yellow crystalline solid in 90 % yield.

Spectral data are identical with that of product prepared *via* the treatment of (2*E*)-2-(phenoxymethyl)-3-(2-methylphenyl)prop-2-enoyl chloride with $AlCl_3$.

(*E*)-3-(4-Methylbenzylidene)chroman-4-one (62c):

This was obtained *via* intramolecular Friedel-Crafts reaction of (2*E*)-3-(4-methylphenyl)-2-(phenoxymethyl)prop-2-enoic acid **(60c)** with TFFA following similar procedure described for the molecule **62a,** as pale yellow crystalline solid.

Yield : 94%

mp : 117-118°C (Lit[146] mp 118-119°C)

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

^1H NMR : 8 2.40 (s, 3H), 5.36 (d, 2H, J = 1.1 Hz), 6.91-7.58 (m, 7H), 7.86 (s, 1H), 8.02 (dd, 1H, J = 7.8 and 1.8 Hz)

^{13}C NMR : δ 21.45, 67.72, 117.87, 121.83, 122.08, 127.91, 129.48, 130.15, 131.59, 135.73, 137.52, 139.91, 161.08, 182.16

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

Analysis calcd. for $C_{17}H_{14}O_2$: C, 81.58; H, 5.64

Found :C, 81.75; H, 5.63

(*E*)-3-(4-Ethylbenzylidene)chroman-4-one (62d):

This was obtained by treatment of (2*E*)-3-(4-ethylphenyl)-2-(phenoxymethyl)prop-2-enoicacid **(60d)** with TFAA following similar **procedure described for the molecule 62a,** as pale yellow crystalline solid.

Yield : 93%

mp : 77-79°C

IR(KBr) : **1664,** 1597 cm^{1}

^{1}H NMR : **8 1.26 (t,** 3H, **J** = 7.4 Hz), 2 70 **(q, 2H, J =** *1A* Hz), **5.37** (s, **2H),** 6 90-7.59 (m, **7H),** 7.86 (s, 1H), 8.02 **(d, 1H, J** = 7.8 Hz)

^{13}C NMR : 6 15.20,28.75, 67.73, 117.84, 121.78, 122.12, 127.89, 128.25 130.22, 131.87, 135.65, 137.43, 146.12, 161.11, 182.07

MS (m/z) : 264 (M^{+})

Analysis calcd. for $C_{18}H_{16}O_{2}$: C, 81.79; H, 6 10

Found :C, 81.50; H, 6.12

(*E*)-3-(4-Isopropylbenzylidene)chroman-4-one (62e):

This was obtained *via* the intramolecular Friedel-Crafts cyclization of (2*E*)-3-(4-isopropylphenyl)-2-(phenoxymethyl)prop-2-enoic acid **(60e)** using TFAA following similar procedure described for the molecule **62a,** as a pale yellow crystalline solid.

Yield : 91%

mp : 90-91°C

IR(KBr) ; 1668, 1602 cm^{-1}

^{1}H NMR : δ 1.28 (d, 3H, J = 7.2 Hz), 2.96 (sept. 1H J = 7.2 Hz), 5.37 (d, 2H, J = 1.8 Hz), 6.91-7.52 (m, 7H), 7,86 (s, **1H),** 8.02 **(dd,** 1H, **J = 7.8 Hz and** 1.6 Hz)

^{13}C NMR : **6** 23.80, 34.11, 67.78, 117.90, 121.86, 122.17, 126.90, 127.97,

130.32, 132.05, 135.74, 137.55, 150.80, 161.17, 182.23

MS (m/z) : 278 (M^+)

Analysis calcd. for $C_{19}H_{18}O_2$: C, 81.99; H, 6.52

Found :C, 81.85; H, 6.51

(*E*)-3-(4-Methoxybenzylidene)chroman-4-one (62f):

This was obtained *via* intramolecular Friedel-Crafts cyclization of (2*E*)-3-(4-methoxyphenyl)-2-(phenoxymethyl)prop-2-enoic acid **(60f)** using TFAA following similar procedure described for the molecule **62a,** as a pale yellow crystalline solid.

Yield : 92%

mp : 131-133°C (lit 133-134 °C)[146]

IR(KBr) : 1666, 1602 cm^{-1}

^1H NMR : 5 3.85 (s 3H), 5.37 (d, 2H, J = 1.8 Hz), 6.91-7.51 (m, 7H) 7.83 (s, 1H), 8.01 (d, 1H, J = 7.7 Hz)

^{13}C NMR : δ 55.33, 67.77, 114.29, 117.78, 121.75, 122.14, 127.03, 127.83, 128.92, 132.01, 135.54, 137.10, 160.75, 160.97, 181.94

MS (m/z) : 266 (M^+)

Analysis calcd for $C_{17}H_{14}O_3$: C, 76.68; H, 5.30

Found : c, 76.90; H, 5.27

(*E*)-3-Butylidenechroman-4-one (62i):

This compound was obtained *via* the treatment of (2*E*)-2-(phenoxymethyl)hex-2-enoic acid **(60i)** with TFAA following similar procedure described for the molecule **62a,** as a viscous liquid in 80% yield.

Spectral data are identical with that of product prepared *via* the treatment of (2*E*)-2-(phenoxymethyl)hex-2-enoyl chloride with $AlCl_3$.

Methyl (2*E*)-2-(3-methoxyphenoxy)methyl-3-(4-methoxyphenyl)prop-2-enoate (59k):

This was obtained *via* treatment of methyl (2Z)-2-(bromomethyl)-3-(4-methoxyphenyl) prop-2-enoate **(58f)** with 3-methoxyphenol in the presence of K_2CO_3 following similar procedure described for the molecule 59a, as a colorless viscous liquid.

Yield : 60%

IR (neat) : 1712, 1621 cm^{-1}

^1H NMR : 5 3.77 (s, 3H), 3.79 (s, 3H), 3.81 (s, 3H), 4.82 (s, 2H), 6.50-6.62 (m,3H) (m, 3H), 6.87 (d, 2H, J = 8.6 Hz), 7.14-7.22 (m, 1H (m,lH), 7.44 (d, 2H, J = 8.6 Hz), 7.99 (s, 1H)

^{13}C NMR : 5 52.02, 55.13, 62.86, 101.39, 106.80, 106.99, 114.19, 124.67, 126.90, 129.85, 131.80, 145.46, 159.75, 160.86, 160.92, 169.77

(2*E*)-2-(3-Methoxyphenoxy)methyl-3-(4-methoxyphenyl)prop-2-enoic acid (60k):

This was obtained by hydrolysis of methyl (2*E*)-2-(3-methoxyphenoxy)methyl-3-(4-methoxyphenyl)prop-2-enoate (59k) with KOH in acetone / water following similar procedure described for the molecule **60a,** as a colorless crystalline solid.

Yield : 94%

mp : 128-130°C

IR (KBr) : 3400-2600, 1676, 1620 cm^{-1}

^1H NMR : 8 3.79 (s, 3H), 3.80 (s, 3H), 4.85 (s, 2H), 6.51-6.62 (m, 3H), 6.90 (d, 2H, J= 8.7Hz), 7.15-7.28 (m, 1H), 7.50 (d, 2H, J =8.7 Hz), 8.10 (s, 1H)

^{13}C NMR : δ 55.37, 62.70, 101.60, 107.16, 114.44, 123.99, 126.89, 130.00, 132.35, 147.75, 159.86, 160.99, 161.42, 173.14

(*E*)-3-(4-Methoxybenzylidene)-7-methoxychroman-4-one (62k):

(Bonducellin monomethyl ether)

This compound was obtained by the reaction of (2*E*)-2-(3-methoxyphenoxy)methyl-3-(4-methoxyphenyl)prop-2-enoic acid (60k) with TFAA following similar procedure described for the molecule **62a,** as a pale yellow crystalline solid.

Yield : 76%

mp : 127-129°C (Lit[146] 129-130°C)

IR (KBr) : 1666, 1602 cm^{-1}

^1H NMR : δ 3.85 (s, 3H), 3.86 (s, 3H), 5.37 (s, 2H), 6.38-6.43 (m, 1H), 6.58-

6.68 (m, 1Hz), 6.96 (d, 2H, J = 8 5 Hz), 7.21-7.36 (m, 2H), 7.81 (s, lH),6.96(d, 1H, J = 8.7 Hz)

^{13}C NMR : 6 55.43, 55.65, 68.10, 100.85, 110 33, 114.30, 115.93, 127.28, 128.98, 129.71, 131 94, 136.55, 16063, 162.99, 165.97, 180.97

MS (m/z) : 296 (M^+)

Analysis calcd. for $C_{18}H_{16}O_4$: C, 72 96; H, 5.44

Found :C, 72.75; H, 5.41

Methyl (2*E*)-2-(3,5-dimethoxyphenoxy)methyl-3-(4-methoxyphenyl)prop-2-enoate (591):

This was obtained *via* treatment of methyl (2*Z*)-2-(bromomethyl)-3-(4-methoxyphenyl) prop-2-enoate (**58f**) with 3,5-dimethoxyphenol in the presence of K_2CO_3 in acetonitrile as a solvent following similar procedure described for the molecule **59a,** as a colorless liquid

Yield : 45%

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

^{1}H NMR : 6 3.77 (s, 6H), 3.81 (s, 3H), 3.83 (s, 3H), 4.81 (s, 2H), 6.12-6.22 (m, 3H), 6.89 (d, 2H, J = 8.7 Hz), 7.44 (d, 2H, J = 8.7 Hz), 8.00 (s, 1H).

^{13}C NMR : 8 52.14, 55.26, 62.87, 93.46, 93.73, 114.24, 124.49, 126.89, 131.85, 145.65, 160.38, 160.95, 161.51, 167.84

(2*E*)-2-(3,5-Dimethoxyphenoxy)methyl-3-(4-methoxyphenyl)prop-2-enoic acid 60l):

This was obtained *via* the hydrolysis of methyl (2*E*)-2-(3,5-dimethoxyphenoxy)methyl-3-(4-methoxyphenyl)prop-2-enoate (**59l**) with KOH in acetone / water following similar procedure described for the molecule **60a,** as a colorless crystalline solid.

Yield : 90%

mp : 126-128°C

IR (KBr) : 3400-2600, 1668, 1602 cm^{-1}

^1H NMR : 5 3.77 (s,6H), 3.82 (s, 3H), 4.83 (s, 2H), 6.10-6.23 (m, 3H), 6.91 (d, 2H, J = 8.7 Hz), 7.49 (d, 2H, J = 8.7 Hz), 8.11 (s, 1H).

^{13}C NMR : δ 55.35, 62.59, 93.69, 93.84, 114.40, 123.69, 126.76, 132.33, 147.83, 160.40, 161.37,161.56 173.10.

(*E*)-3-(4-Methoxybenzylidene)-5,7-dimethoxychroman-4-one (621):

(Eucomin dimethyl ether)

To a stirred solution of (2*E*)-2-(3,5-dimethoxyphenoxy)methyl-3-(4-methoxyphenyl)-prop-2-enoic acid **(601)** (1 mM, 0.344 g) in dry dichloromethane was added trifluoroacetic anhydride (1 mM, 0 210 g) at 0°C temperature. After stirring 1 hour at 0°C the reaction mixture was diluted with water (3 ml) and extracted with ether (3×10 mL). The combined organic layer was dried over anhydrous Na_2SO_4 Solvent was evaporated and the crude product thus obtained was purified by column chromatography (silica gel, 20% EtOAc in hexanes) followed by crystallization (15%

EtOAc in hexanes) to provide **62l** as a pale yellow crystalline solid in 93% yield (0.303 **g)**

mp : 139-140°C (Lit[112] 141-144° C)

TR(KBr) : 1666, 1612 cm^{1}

^{1}H NMR 6 3.82 (s, 3H), 3 84 (s, 3H), 3.90 (s, 3H), 5.23 (d, 2H, J = 1.7 Hz), 6.06 (d, 1H, J = 2 8 Hz), 6.1 l(d, 1H, J = 2.8 Hz) 6.94 (d, 2H, 8.6), 7.23 (d, 2H, J = 8.6 Hz), 7.76 (s, 1H)

^{13}C NMR : 5 55.41, 55.61, 56.21, 67.69, 93.09, 114.21, 127.56 130.25, 131.72, 135.67, 160.41, 162.89, 164.64, 165.75, 179.58

MS (m/z) : 326 (M^{+})

Analysis calcd. for $C_{19}H_{18}O_5$: C, 69.93, H, 5.56

Found : C, 69.95; **H,** 5.54

Methyl (2*E*)-3-(4-methoxyphenyl)-2-(3,4,5-trimethoxyphenoxy)methylprop-2-enoate (59m):

This was obtained by the treatment of methyl (2Z)-2-(bromomethyl)-3-(4-methoxyphenyl)prop-2-enoate **(58f)** with 3,4,5-trimethoxyphenol in the presence of K_2CO_3 in acetonitrile as a solvent following similar procedure described for the molecule **59a,** as a colorless liquid.

Yield : 74%

IR (neat) : 1712, 1604 cm^{-1}

^{1}H NMR : 5 3.81 (s, 3H), 3.83 (s, 6H), 3.84 (s, 3H), 3.89 (s, 3H), 4.84 (s, 2H) 6.25 (s, 2H), 6.92 (d, 2H, J = 8.6 Hz), 7.48 (d, 2H, J = 8.6 Hz), 8.00 (s, 1H).

^{13}C NMR : 5 52.13, 55.28, 56.04,60.90,63.19,92.88, 114.29, 124.66, 126.92 131.90, 132.01, 145.49, 153.73, 155.10, 161.04, 167.87

(2*E*)-3-(4-Methoxyphenyl)-2-(3,4,5-trimethoxyphenoxy)methylprop-2-enoic acid (60m):

This was obtained *via* the hydrolysis of methyl (2*E*)-3-(4-methoxyphenyl)-2-(3,4,5-trimethoxyphenoxy)methylprop-2-enoate **(59m)** with KOH in water / acetone following similar procedure described for the molecule **60a,** as a colorless crystalline solid.

Yield : 85%

mp : 159-160°C

IR (KBr) : 3300-2600, 1672, 1602 cm^{-1}

^{1}H NMR : 6 3.81 (s, 3H), 3.84 (s, 6H), 3.94 (s, 3H), 4.86 (s, 2H), 6.26 (s, 2H), 6.94 (d, 2H, J = 8.6 Hz), 7.53(d, 2H, J = 8.6 Hz), 8.12 (s, 1H)

^{13}C NMR : 6 55.41, 56.20, 61.01, 62.98, 93.21, 114.48, 123.94, 126.85, 132.35, 133.00, 147.65, 153.85, 155.13, 161.49, 172.79

(*E*)-3-(4-Methoxybenzylidene)-5,6,7-trimethoxychroman-4-one (62m):

(Autumnalin monomethyl ether)

This **compound** was obtained by the reaction of (2*E*)-3-(4-methoxyphenyl)-2-(3,4,5-trimethoxyphenoxy)methylprop-2-enoic acid (60m) with TFAA following similar procedure described **for** the molecule **62l**, as a pale yellow **crystalline** solid.

Yield : 95%

mp : 116-118°C (Lit[113] 115-117°C)

IR(KBr) : 1672, 1601 cm^{-1}

^1H NMR : 6 3.84 (s, 3H), 3.86 (s, 3H), 3.89 (s, 3H), 3.99 (s, 3H), 5.25 (s, 2H), 6.26 (s, 1H), 6.96 (d, 2H, J = 8.5 Hz), 7.25 (d, 2H, J = 8.5 Hz), 7.80 (s, 1H)

^{13}C NMR : 8 55.40, 56.12, 61.28, 61.62, 67.71,96.24, 110.77, 114.29, 127.41, 129.95, 131.77, 136.08, 138.03, 154.88, 159.24, 159.38, 160.59, 179.53

MS (m/z) : 356 (M^+)

Analysis calcd. for $C_{20}H_{20}O_6$: C, 67.41; H, 5.66

Found : C, 67.61; H, 5.68

Methyl (2*E*)-2-(4-methoxyphenoxy)methyl-3-(4-methoxyphenyl)prop-2-enoate (59n):

This was obtained *via* treatment of methyl (2Z)-2-(bromomethyl)-3-(4-methoxyphenyl) prop-2-enoate **(58f)** with 4-methoxyphenol in the presence of K2CO3 following similar procedure described for the molecule 59a, as a colorless liquid.

Yield : 52%

IR (neat) : 1714, 1632. cm"[1]

^{1}H NMR : 5 3.79 (s, 3H), 3.82 (s, 3H), 3.84 (s, 3H), 4.81 (s, 2H), 6.75-7.00 (m, 6H), 7.49 (d, 2H, J = 8.6 Hz), 8.00 (s, 1H).

^{13}C NMR : 6 52.11, 55.32, 55.76,63.80, 114.29, 114.80, 116.27, 125.25, 127.18, 131.91, 145.34, 152.81, 154.34, 161.01, 168.01

(2*E*)-3-(4-Methoxyphenyl)-2-(4-methoxyphenoxy)methylprop-2-enoic acid (60n):

This was obtained by hydrolysis of methyl (2*E*)-2-(4-methoxyphenoxy)methyl-3-(4-methoxyphenyl)prop-2-enoate (59n) with KOH in acetone / water following similar procedure described for the molecule 60a, as a colorless crystalline solid.

Yield : 92%

mp : 182-185°C

IR (KBr) : 3440-2500, 1668, 1602 cm^{-1}

^{1}H NMR : 5 3 78 (s, 3H), 3.82 (s, 3H), 4.82 (s, 2H), 6 83-6.98 (m, 6H), 7.52 (d, 2H, J = 8.6 Hz), 8.09 (s, 1H)

(*E*)-3-(4-Methoxybenzylidene)-6-methoxychroman-4-one (56):

(An antifungal agent)

This compound was obtained by treating (2*E*)-2-(4-methoxyphenoxy)methyl-3-(4-methoxyphenyl)prop-2-enoic acid **(60n)** with TFAA following similar procedure described for the molecule **62a,** as a pale yellow crystalline solid.

Yield : 81%

mp : 132-134°C (Lit[109] 132-133°C)

IR (KBr) : 1670, 1599 cm^{-1}

^1H NMR : 6 3.84 (s, 3H), 3.86 (s, 3H), 5.33 (d, 2H, J = 1.5 Hz), 6.88-7.35 (m, 6H), 7.44 (d, 1H, J = 2.8 Hz), 7.83 (s, 1H)

^{13}C NMR : 8 55.34,55.80,67.79, 108.47, 114.28, 119.06, 122.14, 124.68, 127.11, 129.08, 131.99, 137.11, 154.49, 155.65, 160.73, 181.96

MS (m/z) : 296 (M^+)

Analysis calcd for $C_{18}H_{16}O_4$: C, 72.96; H, 5.44

Found :C, 73.10, H, 5.46

Methyl 3-(3,4-dimethoxyphenyl)-3-hydroxy-2-methylenepropanoate (71a):

A mixture of 3,4-dimethoxybenzaldehyde (20 mM, 3.323 g) with methyl acrylate (30 mM, 2.582 g) and DABCO (3 mM, 0.336 g) was kept at room temperature for 40 days. The reaction mixture was diluted with ether (30 mL) and washed successively with 2N HC1 solution, water and aqueous $NaHCO_3$ solution. Organic layer was dried over

anhydrous Na_2SO_4. Solvent was evaporated and residue thus obtained was purified by column chromatography (silica gel, 15%EtOAc in hexanes) afford the alcohol **71a** as a colorless liquid in 40% (2.40 g) yield.

IR (neat) .3497, 1718 cm^{-1}

^1H NMR : 6 2.98 (d, 1H, J = 5.7 Hz), 3.73 (s, 3H), 3.87 (s, 6H), 5.52 (d, 1H, J = 5.7 Hz), 5.83 (s, 1H), 6.32 (s, 1H), 6.75-6.96 (m, 3H)

^{13}C NMR : **5 51.85, 55.84, 72.78,** 109.96, 111.03, 118.98, 125.52, 133.99, 142.25, 148.65, 148.98, 166.78

Ethyl 3-(3,4-dimethoxyphenyl)-3-hydroxy-2-methylenepropanoate (71b):

This compound was obtained as a colorless viscous liquid *via* the treatment of 3,4-dimethoxybenzaldehyde with ethyl acrylate in the presence of DABCO (cat.) following similar procedure described for the molecule **71** a.

Reaction time : 49 days

Yield : 36%

IR (neat) : 3503, 1712, 1625 cm^{-1}

^1H NMR : 8 1.25 (t, 3H, J = 6.9 Hz), 3.01 (d, 1H, J = 4.8 Hz), 3 87 (s, 3H), **4.18** (q, 2H, J = 6.9 Hz), 5.52 (d, 1H, J = 4.8 Hz), 5.81 (d, 1H, J = **12** Hz), 6.32 (s, 1H), 6 80-6.97 (m, 3H)

^{13}C NMR : 5 13.95, 55.77, 60.74, 72.71, 109.97, 110.98, 118.97, 125.11, 134.10, 142.51, 148.55, 148.90, 166.29

Methyl 3-hydroxy-3-(3,4-methylenedioxyphenyl)-2-methylenepropanoate (71c):

This compound was obtained as a colorless viscous liquid *via* the treatment of piperonal with methyl acrylate in the presence of DABCO (cat) following similar procedure described for the molecule **71a.**

Reaction time : 47days

Yield : 58%

IR (neat) : 3449, 1707, 1628 cm^{-1}

^{1}H NMR : 6 2.93 (b, 1H), 3.72 (s, 3H), 5.48 (s, 1H), 5.85 (s, 1H), 5.94 (s, 2H), 6.32 (s, 1H), 6.68-6 88 (m, 3H).

^{13}C NMR : 6 51.86, 72.73, 101.02, 107.24, 108.06, 120.23, 125.51, 135.47, 142.21, 147.17, 147.73, 166.69.

Ethyl 3-hydroxy-3-(3,4-methylenedioxyphenyI)-2-methyIenepropanoate (71 d):

This compound was obtained as a colorless viscous liquid *via* the treatment of piperonal with ethyl acrylate in the presence of DABCO (cat.) following similar procedure described for the molecule **71a.**

Reaction time : 40 days

Yield : 40%

IR (neat) : 3447, 1712, 1630 cm^{-1}

^{1}H NMR : 8 1.25 (t, 3H, J = 8.8 Hz), 2.90 (b, 1H), 4.17 (q, 2H, J = 8.8 Hz), 5.47 (s, 1H) 5.82 (d, 1H, J = 0.58), 5.93 (s, 2H), 6.31 (s, 1H), 6.70-6.89 (m,

3H)

^{13}C NMR : δ 14.00, 60.84, 72.72, 100.99, 107.24, 108.00, 120.22, 125.21, 135.55, 142.42, 147.09, 147.65, 166.22

Butyl 3-hydroxy-3-(3,4-methylenedioxyphenyl)-2-methylenepropanoate (71e):

This was obtained as a colorless viscous liquid *via* the treatment of piperonal with n-butyl acrylate in the presence of cat. amount of DABCO following similar procedure described for the molecule **71a**

Reaction time : 55 days

Yield : 38%

IR (neat) : 3485, 1712, 1630 cm^{-1}

^{1}H NMR : 5 0.94 (t, 3H, J = 8.0 Hz), 1.22-1.73 (m, 4H), 2.93 (d, 1H, J = 5.0 Hz), 4.11 (t, 2H, J = 8.0 Hz), 5.49 (d, 1H, J = 5.0 Hz), 5.84 (d, 1H, J = 1.8 Hz), 5.97 (s, 2H), 6.32 (s, 1H), 6.74-6.86 (m, 3H).

^{13}C NMR : 6 13.54, 19.02, 30.46, 64.58, 72.32, 100.95, 107.34, 107.88, 120.33, 124.77, 135.73, 142.66, 147.02, 147.58, 166.19

Methyl 5,6-dimethoxyindene-2-carboxylate (72a):

To a stirred solution of methyl 3-(3,4-dimethoxyphenyl)-3-hydroxy-2-methylene-propanoate (71a) (2 mM, 0.504 g) in dichloromethane was added P_2O_5 (0.20 g) at room temperature. After 1h the reaction mixture was diluted with water (1 mL) and extracted

with ether (3×10 mL). The combined organic layer was dried over anhydrous Na_2SO_4 and solvent was evaporated. The crude product obtained was purified by column chromatography (silica gel, 8% EtOAc in hexanes) to afford indene **72a** in 25% (0.117 g) yield, as a colorless crystalline solid.

Yield : 25%

mp : 107°C

IR (KBr) : 1697, 1608 cm^{-1}

^1H NMR : 5 3.62 (d, 2H, J = 1.5 Hz), 3 82 (s, 3H), 3.92 (s, 3H), 3.93 (s, 1H), 7.02 (s,lH), 7.06 (s, 1H), 7.64 (s, 1H)

^{13}C NMR : 5 38.39, 51.42, 56.16, 106.18, 107.74, 135.42, 138.37, 141.42, 148.85, 149.92, 165.00

MS (m/z) : 234 (M^+)

Analysis calcd. for $C_{13}H_{14}O_4$: C, 66.66; H, 6.02

Found : C, 66.92, H, 6.04

Ethyl 5,6-dimethoxyindene-2-carboxylate (72b):

This compound obtained as a colorless crystalline solid *via* treatment of ethy 3-(3,4-dimethoxyphenyl)-3-hydroxy-2-methylenepropanoate **71b** with P_2O_5 following similar procedure described for the molecule 72a.

Yield :31%

mp : 89-91°C

IR (KBr) : 1703, 1608 cm^{-1}

^1H NMR : 6 1.35 (t, 3H, J = 7.1 Hz), 3.63 (s, 2H), 3.91 (s, 3H), 3.93 (s, 3H), 4.29 (q, 2H, J = 7.1 Hz), 7.03 (s, 1H), 7.06 (s, 1H) 7.65 (s, 1H)

^{13}C NMR : 5 14.26, 38.21, 55.98, 59.97, 106.01, 107.60, 135.26, 135.72, 138.19, 140.94, 148.67, 149.69, 164.70

MS (m/z) : 248 (M^+)

Analysis calcd. for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50

Found : C, 67.90; H, 6.48

Methyl 5,6-methylenedioxyindene-2-carboxylate (72c):

This was obtained as a colorless crystalline solid *via* treatment of methyl 3-hydroxy-3-(3,4-methylenedioxyphenyl)-2-methylenepropanoate **(71c)** with P2O5 following similar procedure described for the molecule 72a, as a crystalline solid.

Yield : 29%

mp : 162-165°C

IR(KBr) :1689,1620 cm^{-1}

^1H NMR : 8 3.59 (d, 2H, J = 1.3 Hz), 3.82 (s, 3H), 5.99 (s, 2H), 6.95 (s, 1H), 6.98 (s,1H),7.62(s, 1H)

^{13}C NMR : δ 38.36, 51.47, 101.39, 103.54, 105.44, 135.80, 136.51, 139.92, 141.21, 147.30, 148.46, 165.20

MS (m/z) : 218 (M^+)

Analysis calcd. for $C_{12}H_{10}O_4$: C, 66.05; H, 4.62

Found c, 65 75; H, **4.61**

Ethyl 5,6-methylenedioxyindene-2-carboxylate (72d):

This was obtained as a colorless crystalline solid *via* treatment of ethyl 3-hydroxy-3-(3,4-methylenedioxyphenyl)-2-methylenepropanoate (**71d**) with P_2O_5 following similar procedure described for the molecule 72a.

Yield : 28%

mp : 97-98°C

IR(KBr) : 1693, 1619 cm^{-1}

^1H NMR : 5 1.34 (t, 3H, J = 6.7 Hz), 3.59 (s, 2H), 4.28 (q, 2H, J = 6.7 Hz), 5.99 (s, 2H), 6.95 (s, 1H), 6.98 (s, 1H) 7.62 (s, 1H)

^{13}C NMR : 6 14.37, 38.23, 60.13, 101.30, 103.37, 105.29, 136.15, 136.45, 139.78, 140.81, 147.16, 148.27, 164.65

MS (m/z) : 232 (M^+)

Analysis calcd. for $C_{13}H_{12}O_4$: C, 67.23; H, 5.21

Found : C, 66.98; H, 5.22

Butyl 5,6-methylenedioxyindene-2-carboxylate (72e):

This was obtained as a colorless crystalline solid *via* treatment of butyl 3-(3,4-methylenedioxyphenyl)-3-hydroxy-2-methylenepropanoate (71e) with P_2O_5 following similar procedure described for the molecule 72a.

Yield : 37%

mp : 83-84°C

IR(KBr) : 1691, 1620 cm^{-1}

^1H NMR :6 0.97(t, 3H, J = 7.1 Hz), 1 38-1.54 (m, 2H), 1.64-1.80 (m, 2H), 3.59 (s, 2H), 4.22 (t, 2H, J = 6.6 Hz), 5.99 (s, 1H), 6.95 (s, 1H), 6.98 (s, 1H), 7.62 (s, 1H)

^{13}C NMR : 5 13.69, 19.24, 30.84, 38.20, 64.02, 101.26, 103.32, 105.25, 136.14, 136.43, 139.74, 140.73, 147.13, 148.24, 164.68

MS (m/z) : 260 (M^+)

Analysis calcd. for $C_{15}H_{16}O_4$: C, 69.22; H, 6.20

Found :C, 69.25; H, 6.17

4-Ethoxy-3-methoxybenzaldehyde (73):

To a stirred mixture of *o*-vanil in (10 mM, 1.521 g) and anhydrous K_2CO_3 (10 mM, 1.38 g) in acetonitrile (15 mL) ethyl bromide was added (10 mM, 1.09 g) and this suspension was refluxed for 3 hours. The reaction mixture was cooled to room temperature and acetonitrile was removed under reduced pressure. Then the residue was diluted

with water (25 mL), then extracted with ether (3x25 mL) The combined organic layer was dried over anhydrous Na_2SO_4 and solvent was evaporated. Purification of crude product thus obtained by column chromatography (silicagel, 15% EtOAc in hexanes) provided 72a in 83 % (1 50 g) yield as a colorless solid.

mp : 50-52°C

IR (KBr) :1682 cm^{-1}

^{1}H NMR : 5 1.50 (t, 3H, J = 6.8 Hz), 3.93 (s, 3H), 4.19 (q, 2H, J = 6.8 Hz), 6.96 (d, 2H, J = 7.8 Hz), 7.41-7.55 (m, 2H) 9.84 (s, 1H)

^{13}C NMR :S 14.44, 55.88, 64.52, 109.54, 111.46, 126.37, 129.97, 149.81, 153.92, 190.51

3-Methoxy-4-propoxybenzaldehyde (74):

This compound was obtained by treating o-vanilin with n-propyl bromide in the presence of K2CO3 following similar procedure described for the molecule 73, as a colorless crystalline solid.

Yield : 73%

mp : 59-60°C

IR(KBr) :1682 cm^{-1}

^{1}H NMR : 8 1.06 (t, 3H, J = 7.70 Hz), 1.91 (m, 2H), 3.93 (s, 3H), 4.07, (t, 2H, J = 6.8 Hz), 6.96 (d, 1H, J = 7.9 Hz), 7.41-7.51 (m, 2H), 9.84 (s, 1H)

^{13}C NMR : δ 10.17, 22.14, 55.80, 70.39, 109.31, 111.37, 126.45, 129.76,

149.72, 154.05, 190.57

Methyl 3-(4-ethoxy-3-methoxyphenyl)-3-hydroxy-2-methylenepropanoate (71f):

This compound was prepared from 4-ethoxy-3-methoxybezaldehyde, methyl acrylate and DABCO (cat) following similar procedure described for the molecule **71a,** as a colorless viscous liquid.

Reaction time: 35 days

Yield : 32%

IR (neat) : 3508, 1703, 1622 cm^{-1}

^{1}H NMR : 8 1.45 (t, 3H, J =6 8 Hz), 2.93 (d, 1H, J = 5.6 Hz), 3.73 (s, 3H), 3 87 (s, 3H), 4.09 (q, 2H, J = 6.8 Hz), 5.52 (d, JH, J = 5.6 Hz), 5.82 (s,lH), 6.32 (s, 1H), 6.80-6.98 (m, 3H).

^{13}C NMR :5 14.67,51.72, 55.76,64.24,72.53, 110.23, 112.43, 118.94, 125.25, 133.94, 142.27, 147.83, 149.16, 166.69

Ethyl 3-(4-ethoxy-3-methoxyphenyl)-3-hydroxy-2-methylenepropanoate (71 g):

This compound was prepared from 4-ethoxy-3-methoxybezaldehyde, ethyl acrylate and DABCO (cat) following similar procedure described for the molecule **71a,** as **a** colorless viscous liquid.

Reaction time : 35 days

Yield : 44%

IR (neat) : 3506, 1718 cm^{-1}

^1H NMR : 6 1.24 (t, 3H, J = 7.5 Hz), 1.44 (t, 3H, J = 7.0 Hz), 3.03 (d, 1H, J = 5.0 Hz), 3.86 (s, 3H), 4.06-4.29 (m, 4H), 5.51 (d, 1H, J = 5.0 Hz), 5.80 (s, 1H), 6 31 (s, 1H), 6.76-6.92 (m, 3H)

^{13}C NMR :6 13.92, 14.66,55.74,60.72,64.20,72.60, 110.15, 112.32, 118.95, 125.05, 133.99, 142 48, 147.75, 149 07, 166.29

Methyl 3-hydroxy-3-(3-methoxy-4-propoxyphenyl)-2-methylenepropanoate (71 h):

This compound was prepared from 3-methoxy-4-propoxybezaldehyde, methyl acrylate and DABCO (cat.) following similar procedure described for the molecule 71a, as a colorless viscous liquid.

Reaction time : 26 days

Yield : 35%

IR (neat) : 3450, 1718,1635 cm^{-1}

^1H NMR :5 1.02 (t, 3H, J = 7.5Hz), 1.84 (m, 2H), 2.99 (d, 1H, J = 5.0 Hz), 3.72 (s, 3H), 3.85 (s, 3H), 3.95 (t, 2H, J = 6.7 Hz), 5.52 (d, 1H, J = 5.0 Hz), 5.82 (s, 1H), 6.31 (s, 3H), 6.83-6.91 (m, 3H)

^{13}C NMR :5 10.26,22.34,51.67,55.82,70.42,72.43, 110.49, 112.68, 119.00, 125.15, 133.96, 142.30, 148.07, 149.23, 166.66

Ethyl 3-hydroxy-3-(3-methoxy-4-propoxyphenyl)-2-methylenepropanoate(71i):

This compound was prepared from 3-methoxy-4-propoxybezaldehyde, ethyl acrylate and DABCO (cat) following similar procedure described for the molecule **71a,** as a colorless viscous liquid.

Reaction time : 28 days

Yield : 56%

IR (neat) : 3493, 1718, 1630 cm^{-1}

^{1}H NMR : 8 1.03 (t, 3H, J = 7.7 Hz), 1.25 (t, 3H, J = 6.8 Hz), 1.85 (m, 2H), 3.02 (b, 1H), 3.86 (s, 3H), 3.96 (t, 2H, J = 6.8 Hz), 4.16 (q, 2H, J = 6.8 Hz), 5.52 (s, 1H), 5.80 (d, 1H, J = 1.8 Hz), 6.32 (s, 1H), 6.84-6.93 (m, 3H)

^{13}C NMR :8 10.29, 13.92,22.37,55.84,60.70, 70.43,72.63, 110.43, 112.64, 119.00, 125.01, 134.02, 142.51, 148.06, 149.24, 166.28.

Reaction of methyl 3-(4-ethoxy-3-methoxyphenyl)-3-hydroxy-2-methylenepropanoate with P_2O_5: Preparation of methyl 5-ethoxy-6-methoxyindene-2-carboxylate (72f) and methyl 6-ethoxy-5-methoxyindene-2-carboxylate (75a): (Regio isomers of indene)

Treatment of methyl 3-(4-ethoxy-3-methoxyphenyl)-3-hydroxy-2-methylenepropanoate **(71f)** with P_2O_5 following similar procedure described for the molecule **72a** provided regio isomers of indene in ≈ 70:30 ratio (as evidenced by ^{1}H NMR & ^{13}CNMR spectral analyses) as a colorless solid.

Yield : 22%

mp : 96-99°C

IR (KBr) : 1699,1608 cm^{-1}

^1H NMR : δ 1.49 (t, 3H, J = 6 7 Hz), 3.61 (s, 2H), 3.82 (s, 3H), 3 90 & 3.92 (2s, 3H), 4.15 (q, 2H J = 6.7 Hz), 7.03 (s, 1H), 7.06 (s, 1H), 7.644 (s,lH)

^{13}C NMR :6 14.71, 38.23, 51.28, 56.08, 64.54, 106.35. 107.66, 107.87, 108.99, 135.21, 138.25, 141.37. 147.96. 149.02, 149.13. 150.18. 165.21

The underlined chemical shift values arise from minor isomer

Reaction of ethyl 3-(4-ethoxy-3-methoxyphenyl)-3-hydroxy-2-methylenepropanoate with P_2O_5: Preparation of ethyl 5-ethoxy-6-methoxyindene-2-carboxyIate (72g) **and ethyl 6-ethoxy-5-methoxyindene-2-carboxylate (75b):**

Treatment of ethyl 3-(4-ethoxy-3-methoxyphenyl)-3-hydroxy-2-methylenepropanoate **(71g)** with P_2O_5 following similar procedure described for the molecule **72a** provided regio isomers of indene in ≈ 80:20 ratio (as evidenced by ^1H NMR & ^{13}CNMR spectral analyses) as a colorless solid.

Yield : 17%

mp : 89-92°C

IR (KBr) : 1693, 1608 cm^{-1}

^1H NMR : 6 1.35 (t, 3H, J = 7.4 Hz), 1.49 (m, 3H), 3.61 (s, 2H), 3.90 & 3.91(2s, 3H), 4.10-4.33 (m, 4H), 7.02 (s, 1H), 7.06 (s, 1H), 7.65 (s, 1H)

^{13}C NMR : δ 14.36, 14.76, 38.26, 56.11, 60.09, 64.54, 106.27, 107.57, 107.84, 108.96, 135.29, 135.71, 138.25, 14115. 147.91, 148.97, 149.04, 150.07, 164.89

The underlined chemical shift values arise from minor isomer.

Reaction of methyl 3-hydroxy-3-(3-methoxy-4-propoxyphenyl)-2-methylenepropanoate with P_2O_5: Preparation of methyl 6-methoxy-5-propoxyindene-2-carboxylate (72h) and methyl 5-methoxy-6-propoxyindene-2-carboxylate (75c):

Treatment of methyl 3-hydroxy-3-(3-methoxy-4-propoxyphenyl)-2-methylenepropanoate **(71h)** with P_2O_5 following similar procedure described for the molecule 72a provided a regio isomers of indene (as evidenced by ^1H NMR & ^{13}CNMR spectral analyses) as a colorless solid in ≈ 95:5 ratio.

Yield : 20%

mp : 79-81°C

IR(KBr) : 1697, 1610 cm^1

^1H NMR : 6 1.05 (t, 3H, J = 7.0 Hz), 1.80-2.01 (m, 2H), 3.61 (s, 2H), 3.82 (s, 3H), 3.89 & 191 (2s, 3H), 3.98-4.10 (m,2H), 7.03 (s,lH), 7.06 (s,lH), 7.65 (s, 1H)

^{13}C NMR ; 5 10.36, 22.48, 38.24, 51.29, 56.21, 70.76, 106.65, 107.98. 108.10, 109.28, 135.23, 138.33, 141.39, 149.18, 148.28, 149.46, 150.36, 165.23

The underlined chemical shift values arise from minor isomer.

Reaction of ethyl 3-hydroxy-3-(3-methoxy-4-propoxyphenyl)-2-methylenepropanoate with P_2O_5: Preparation of ethyl 6-methoxy-5-propoxyindene-2-carboxylate (72i) and ethyl 5-methoxy-6-propoxyindene-2-carboxylate (75d):

Treatment of ethyl 3-hydroxy-3-(3-methoxy-4-propoxyphenyl)-2-methylenepropanoate **(71i)** with P_2O_5 following similar procedure described for the molecule **72a** provided regio isomers of indene in ≈ 72:28 ratio (as evidenced by ^1H NMR & ^{13}CNMR spectral analyses) as a colorless solid.

Yield : 25%

mp : 89-92°C

IR(KBr) : 1689, 1609 cm^{-1}

^1H NMR :8 1.05 (t, 3H, J = 7.2 Hz), 1.35 (m,3H), 1.80-2.02 (m, 2HX 3.60 & 162 (2s, 2H), 3.89 (s, 3H), 4.02 (t, 2H, J = 7.0 Hz), 4.28 (q, 2H, J = 6.7 Hz), 7.03 (s,lH), 7.05 (s,1H), 7.64 (s, 1H)

^{13}C NMR : δ 10.37, 14.34, 22.50, 38.22, 56.16, 60.02, 70.72, 106.61, 107.94, 10810. 109.28, 135.32, 135.67, 138.31, 141.12, 149.15, 148.25, 149.39, 150.30, 164.81

The underlined chemical shift values arise from minor isomer.

Methyl 5-ethoxy-6-methoxyindane-2-carboxylate (76a):

The mixture of regioisomers of indene *i.e.* methyl 5-ethoxy-6-methoxyindene-2-carboxylate **(72f)** and methyl 6-ethoxy-5-methoxyindene-2-carboxylate **(75a)** was

dissolved (0.5 mM, 0.124 g) in ethyl acetate and subjected to hydrogenation using 10% Pd/C (5 mg) as a catalyst for 4 hours. The catalyst was filtered off, solvent was evaporated and the product was purified on column chromatography (silica gel, 8% EtOAc in hexanes) as a viscous liquid.

Yield : 90% (0.112 g)

IR (neat) : 1734, 1610 cm^{-1}

^1H NMR : 8 1.43 (t, 3H, J = 6.8 Hz) 3.06-3.44 (m, 5H), 3.71 (s, 3H), 3.83 (s, 3H), 4.05 (q, 2H, J = 6.8 Hz), 6.73 (s, 2H)

^{13}C NMR :5 14.87,36.16,43.87,51.82,56.18,64.66, 108.08, 109.48, 133.16, 133.25, 147.69, 148.83, 175.78

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

Analysis calcd. for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25

Found : C, 67.36; H, 7.24

Ethyl 5-ethoxy-6-methoxyindane-2-carboxylate (76b):

This was obtained *via* catalytic hydrogenation of ethyl 5-ethoxy-6-methoxyindene-2-carboxylate (72g) and ethyl 6-ethoxy-5-methoxyindene-2-carboxylate (75b) following similar procedure described for the molecule 76a, as a colorless liquid.

Yield : 91%

IR (neat) : 1732, 1610 cm^{-1}

^1H NMR : 8 1.27 (t, 3H, J = 6.8 Hz), 1.43 (t, 3H, J = 6.8 Hz), 3.12-3.42 (m, 5H),

3.83 **(s, 3H), 4.05 (q, 2H, J** = 6.8 **Hz), 4.17 (q, 2H, J =6.8 Hz), 6.73 (s, 2H)**

^{13}C NMR **:6 14.23, 14.85, 36 15, 43.99, 56.14, 60.53, 64 61,** 108.03, 109.42, 133.20, 133.29, 147.62, 148.75, 175.32

MS (m/z) : 264 (M^+)

Analysis calcd. for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63

Found : C, 67.90, **H,** 7.64

Meyhyl 6-methoxy-5-propoxyindane-2-carboxylate (76c):

This was obtained *via* catalytic hydrogenation of methyl 6-methoxy-5-propoxyindene-2-carboxylate **(72h)** and methyl 5-methoxy-6-propoxyindene-2-carboxylate (75c) following similar procedure described for the molecule **76a,** as a colorless viscous liquid.

Yield : 96%

IR (neat) : 1736, 1610 cm^{-1}

^{1}H NMR :S 1.03 (t, 3H, J = 6.9 Hz), 1.85 (m, 2H), 3.13-3.41 (m, 5H), 3.72(s, 3H), 3.83 (s, 3H), 3.94 (t, 2H, J = 6.8 Hz), 6.75 (s, 2H)

^{13}C NMR : 5 10.44, 22.60, 36.17, 43.91, 51.82, 56.34, 71.02, 108.46, 109.86, 133.29, 148.05, 149.02, 175.80

MS (m/z) : 264 (M^+)

Analysis calcd. for C15H20 O_4 : C, 68.16; H, 7.63

Found : C, 68.29; H, 7.61

Ethyl 6-methoxy-5-propoxyindane-2-carboxylate (76d):

This was obtained *via* catalytic hydrogenation of ethyl 6-methoxy-5-propoxyindene-2-carboxylate (72i) and ethyl 5-methoxy-6-propoxyindene-2-carboxylate (75d) following similar procedure described for the molecule 76a, as a colorless viscous liquid.

Yield : 88%

IR (neat) : 1732, 1610 cm^{-1}

^1H NMR :5 1.02(t, 3H,J = 7.6 Hz), 1.27 (t, 3H, J = 7.6 Hz), 1.85 (m, 2H), 3.02-3.42 (m, 5H), 3.82 (s, 3H), 3.93 (t, 2H, J = 6.8 Hz), 4.17 (q, 2H, J = 6.8 Hz), 6.70 (s, 2H)

^{13}C NMR : 8 10.40, 14.22, 22.54, 36.13, 44.00, 56.26, 60.52, 70.92, 108.33, 109.72, 133.29, 147.93, 148.90, 175.31

MS (m/z) : 278 (M^+)

Analysis calcd. for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97

Found : C, 69.30; H, 7.99

Reaction of aromatic aldehyde and acrylonitrile in the presence of DABCO for 8 days

A mixture of benzaldehyde (20 mM, 2.122 g), acrylonitrile (30 mM, 1.591 g) and DABCO (15 mol%, 3 mM, 0.336 g,) was kept at room temperature for 8 days. The

reaction mixture was diluted with ether (30 mL) and washed with water. Aqueous layer was extracted with ether (3x20 mL) Combined organic layer was dried over anhydrous Na_2SO_4 and solvent was evaporated. A careful column chromatography of the residue (silica gel, ethyl acetate:hexanes 5:95) provided,

i) the most non polar molecule as a viscous liquid which on crystallization from 10% EtOAc in hexanes to provide the desired *dl*-bis allyl ether **77a** as colorless crystals.

ii) the usual Baylis-Hillman adduct **78a,** and

iii) some other unidentified products.

rf/-Bis(2-cyano-l-phenylprop-2-en-l-yI) ether (77a):

Yield : 8% (0.246 g)

mp : 92°C

IR (KBr) : 2229, 1620, 1602 cm^{-1}

^1H NMR : 6 4.80 (s, 2H), 5.94 (s, 2H), 6.01 (s, 2H), 7.28-7.51 (m, 10H)

^{13}C NMR : 6 78.15, 116.62, 124.44, 127.52, 129.08, 129.43, 130.76, 135.68

Analysis calcd. for $C_{20}H_{16}N_2O$: C, 79.98; H, 5.37; N, 9.33

Found : C, 79.76; H, 5.39; N, 9.29

3-Hydroxy-2-methylene-3-phenylpropanenitrile (Side product) (78a):

Yield : 40%

bp : 126-129^{0}C/2.1 mm

IR (neat) : 3466, 2227, 1624 cm^{-1}

^{1}H NMR : 6 2.52 (b, 1H), 5.27 (s, 1H), 6.01 (s, 1H), 6.09 (s, 1H), 7.38 (s, 5H)

^{13}C NMR : 5 73.90, 116.95, 126.27, 126.46, 128.75, 129.91, 139.23

Reaction between 2-methylbenzaldehyde and acrylonitrile in the presence of DABCO for 8 days:

This reaction was carried out following the similar procedure described for the reaction between benzaldehyde and acrylonitrile. The reaction provided *dl*-bis[2-cyano-1-(2-methylphenyl)prop-2-en-l-yl] ether (77b) in 7% yield as a crystalline solid (directly from column chromatography) along with usual Baylis-Hillman adduct 3-hydroxy-2-methylene-3-(2-methylphenyl)propanenitrile (side product) (78b) in 38% yield and some unidentified products.

***dl*-Bis[2-cyano-1-(2-methylphenyl)prop-2-en-1-yl] ether (77b):**

mp : 109-110°C

IR (KBr) :2227, 1620 cm^{-1}

^{1}H NMR . 5 2 02 (s, 6H), 5.00 (s, 2H), 5.86 (d, 2H, J = 1 5 Hz), 6 00 (s, 2H), 7.14-7.46 (m,8H)

^{13}C NMR : 6 18.72, 74.57, 116.84, 124.03, 126.97, 127.90, 129.28, 130.51, **131.12,** 133.30, 136.86

MS (m/z) : 328 (M^+)

Analysis calcd for $C_{22}H_{20}N_2O$: C, 80.46; H, 6.14; N, 8.53

Found : c, 80.38; H, 6.12; N, 8.56.

3-Hydroxy-2-methylene-3-(2-methylphenyl)propanenitrile (Side product) (78b):

bp : 136-137^0 C/2.4 mm

IR (neat) : 3429, 2229, 1622 cm^{-1}

^1H NMR : 6 2.33 (s, 3H), 2.75 (b, 1H), 5.48 (s, 1H), 5.98 (s, 1H), 6.02 (s, 1H), 7.20 (m, 3H), 7.38 (m, 1H)

^{13}C NMR :6 18.80,70.20, 117.02, 125.15, 126.15, 126.29, 128.38, 130.35, 130.54, 135.39, 136.79

Reaction between 4-methylbenzaldehyde and acrylonitrile in the presence of DABCO for 8 days:

This reaction was carried out following the similar procedure described for the reaction between benzaldehyde and acrylonitrile. The reaction provided *dl*-bis[2-cyano-1-(4-methylphenyl)prop-2-en-l-yl] ether (77c) in 7% yield as a crystalline solid (directly from column chromatography) along with usual Baylis-Hillman adduct (3-hydroxy-2-

methylene-3-(4-methylphenyl)propanenitrile (Side product) (78c) in 39% yield and some unidentified products.

***dl*-Bis[2-cyano-1-(4-methylphenyl)prop-2-en-1-yl] ether (77c):**

mp : 96-97°C

IR(KBr) : 2231, 1620cm^{-1}

^{1}H NMR : 5 2.39 (s, 6H), 4.76 (s, 2H), 5.94 (d, 2H, J = 1.4 Hz), 5.99 (d, 2H, J = 1.4 Hz), 7.18-7.33 (m, 8H)

^{13}C NMR : 5 21.22, 77.76, 116 84, 124.76, 127.61, 129.81, 130.42, 132.70

MS (m/z) : 328 (M^{+})

Analysis calcd. for $C_{22}H_{20}N_2O$: C, 80.46; H, 6.14; N, 8.53

Found : C, 80.60; H, 6.11; N, 8.58

3-Hydroxy-2-methylene-3-(4-methylphenyl)propanenitrile (Side product) (78c):

bp : 132-134^{0}C/1.5 mm

IR (neat) : 3450, 2229, 1616 cm^{-1}

^{1}H NMR : 5 2.30 (br, 1H), 2.36 (s, 3H), 5.25 (s, 1H), 6.02 (s, 1H), 6.10 (s, 1H), 7 22 (d, 2H, J = 7.2 Hz), 7.27 (d, 2H, J = 7.2 Hz)

^{13}C NMR : 5 21.03, 73.68, 117.01, 126 40, 129.39, 129.62, 136 26, 138.51

Reaction between 4-ethylbenzaldehyde and acrylonitrile in the presence of DABCO for 8 days:

This reaction was performed following similar procedure described for the reaction between benzaldehyde and acrylonitrile The reaction afforded *dl*-bis[2-cyano-1-(4-ethylphenyl)prop-2-en-]-yl] ether (77d) in 6% yield as a crystalline solid (directly from column chromatography) along with usual Baylis-Hillman adduct (3-hydroxy-3-(4-ethylphenyl)-2-methylenepropanenitrile (side product) **(78d)** in 40% yield and some unidentified products.

***dl*-Bis[2-cyano-1-(4-ethylphenyl)prop-2-en-1-yl] ether** (77d):

mp : 103°C

IR(KBr) :2226, 1620 cm^{-1}

^1H NMR : 6 1.27 (t, 6H, J = 7.6 Hz), 2.69 (q, 4H, J = 7.6 Hz), 4.78 (s, 2H), 5.94 (s, 2H), 5.99 (s, 2H), 7.18-7.31, (m, 8H)

^{13}C NMR : 15.31,28.64,77.81, 116.93, 124.87, 127.72, 128.65, 130.43, 132.96, 145.71

MS (m/z) : 356 (M^+)

Analysis calcd. for $C_{24}H_{24}N_2O$: C, 80.87; H, 6.79; N, 7.86

Found : C, 81.20; H, 6.78; N, 7.82

3-Hydroxy-3-(4-ethylphenyl)-2-methylenepropanenitrile (Side product) (78d):

bp : 145-146^{0}C/2 mm

IR (neat) : 3447, 2229, 1616 cm^{-1}

^{1}H NMR : 6 1.24 (t, 3H, J = 7.8 Hz), 2.14 (br, 1H), 2.67 (q, 2H, J = 7.8 Hz), 5.27 (s, 1H), 6.03 (s, 1H), 6.11 (s, 1H), 7.28 (m, 4H)

^{13}C NMR :6 15.19, 28.29, 73.50, 116.95, 126.15, 126.35, 128.04, 129.67, 136.34, 144.61

Reaction between 4-isopropylbenzaldehyde and acrylonitrile in the presence of DABCO for 8 days:

This reaction was performed by the following similar procedure described for the reaction between benzaldehyde and acrylonitrile. The reaction provided *dl*-bis[2-cyano-l-(4-isopropylphenyl)prop-2-en-l-yl] ether (77e) in 7% yield as a crystalline solid (directly from column chromatography) along with usual Baylis-Hillman adduct (3-hydroxy-3-(4-isopropylphenyl)-2-methylenepropanenitrile (side product) **(78e)** in 42% yield and some unidentified products.

***dl*-Bis[2-cyano-1-(4-isopropylphenyl)prop-2-en-1-yl] ether** (77e):

mp ; 132°C

IR (KBr) 2226, 1619 cm^{-1}

^{1}H NMR : 8 1.28 (d, 12H, J = 6.8 Hz), 2.95 (sept, 2H, J = 6.8 Hz), 4.79 (s, 2H),

5.95 (s, 2H), 5.99 (s, 2H), 7.19-7.36 (m, 8H)

^{13}C NMR : 8 23.89, 33.94, 77.79, 116.96, 124.86, 127.22, 127.67, 130.43, 133.08, 150.28

MS(m/z) : 384 (M^+)

Analysis calcd. for $C_{26}H_{28}N_2O$: C, 81.21; H, 7.34; N, 7.29

Found : C, 81.00, H, 7.36; N, 7.25

3-Hydroxy-3-(4-isopropylphenyl)-2-methylenepropanenitrile (Side product) (78e):

bp : 149-150^0 C/1.1 mm

IR (neat) : 3443, 2229, 1616 cm^{-1}

^1H NMR : δ 1.26 (t, 6H, J = 6.8 Hz), 2.38 (br, 1H), 2 93 (sept, 1H, J = 6.8 Hz), 5.26 (s, 1H), 6.02 (s, 1H), 6.11 (s, 1H), 7.28 (m, 4H)

^{13}C NMR : δ 23.83, 33.77, 73.79, 117.08, 126.32, 126.52, 126.85, 129.73, 136.58, 149.53

Reaction between 2,4-dichlorobenzaldehyde and acrylonitrile in the presence of DABCO for 8 days:

This reaction was carried out, following similar procedure described for the reaction between benzaldehyde and acrylonitrile. The reaction provided *dl*-bis[2-cyano-1-(2,4-dichlorophenyl)prop-2-en-l-yl] ether (77f) in 6% yield as a crystalline solid (after column chromatography followed by crystallization from 10% EtOAc in hexanes) along

with usual Baylis-Hillman adduct 3-hydroxy-3-(2,4-dichlorophenylphenyl)-2-methylenepropanenitrile (Side product) (78f) in 37% yield and some unidentified products.

***dl*-Bis[2-cyano-1-(2,4-dichlorophenyl)prop-2-en-1-yl] ether** (77f):

mp : 149-150°C

IR(KBr) :2226, 1622, cm^{-1}

^{1}H NMR : 6 5.33 (s, 2H), 5.95 (s, 2H), 6.07 (s, 2H), 7.32-7.74 (m, 6H)

^{13}C NMR : 5 75.17, 115.95, 122.38, 128.51, 129.68, 129.85, 132.01, 132.39, 134.30, 136.27

Analysis calcd. for $C_{20}H_{12}N_2OCl_4$: C, 54.83; H, 2.76; N, 6.39

Found : C, 54.99; H, 2.74; N, 6.41

3-Hydroxy-3-(2,4-dichlorophenyl)-2-methylenepropanenitrile (Side product) (78f):

IR (neat) : 3499, 2235, 1585 cm^{-1}

^{1}H NMR : 5 2.67 (br, 1H), 5.73(s, 1H), 6.08 (s, 2H), 7.26-7.70 (m, 3H)

^{13}C NMR : 5 70.06, 116.50, 124.45, 127.94, 128.99, 129.53, 131.60, 133.21, 155.27

Reaction between 1-naphthaldehyde and acrylonitrile in the presence of DABCO for 8 days:

This reaction was carried out following the similar procedure described for the reaction between benzaldehyde and acrylonitrile The reaction provided *meso*-bis[2-cyano-1-(naphth-1-yl)prop-2-en-1-yl] ether (77 *g)* in 7% yield as a crystalline solid (directly from column chromatography) along with usual Baylis-Hillman adduct 3-hydroxy-2-methylene-3-(naphth-l-yl)propanenitrile (Side product) (78g) in 38% yield and some unidentified products.

***meso*-Bis[2-cyano-1-(naphth-1-yl)prop-2-en-1-yl] ether** (77g):

mp : 141-142°C

lR(KBr) :2227,1620 cm^{-1}

^{1}H NMR : 8 5.40 (s, 2H), 5,87 (s, 2H), 6.00 (s, 2H), 7.35-7.60 (m, 8H), 7.80-8.05 (m, 6H)

^{13}C NMR : δ 76.81, 116.80, 123.48, 124.05, 125.30, 126.22, 126.76, 127.79, 129.08, 130.49, 130.84, 131.51, 134.17

MS (m/z) : 400 (M^{+})

Analysis calcd. for $C_{28}H_{20}N_2O$: C, 83.98; H, 5.03; N, 6.99

Found : C, 8422; H, 5 02; N, 7.00

3-Hydroxy-2-methylene-3-(naphth-1-yl)propanenitrile (Side product) (78g):

IR (neat) : 3429, 2227, 1512 cm^{-1}

^1H NMR : 6 2.57 (br, 1H), 6.00 (s, 1H), 6.09 (d, 1H, J = 7.47), 7.45-8.06 (m, 7H)

^{13}C NMR : 5 71.06, 117.16, 123.11, 125.05, 125.30, 125.61, 125.89, 126.51, 128.95, 129.54, 130.44, 130.90, 133.91, 134.41

3-Hydroxy-2-methylene-3-phenylpropanenitrile (78a):

A mixture of benzaldehyde (50 mM, 5.306 g), acrylonitrile (75 mM, 3.979 g) and DABCO (7.5 mM, 0.841 g) was kept at room temperature for 40 h. The reaction mixture was diluted with ether (60 mL) and washed successively with 2N HC1 solution, water and aqueous $NaHCO_3$ solution. Organic layer was dried over anhydrous Na_2SO_4, solvent was evaporated and residue thus obtained was distilled under reduced pressure to afford the alcohol (77a) as a colorless liquid in 80% (6.36 g) yield. Spectral data are identical with that of side product obtained *via* the treatment of benzaldehyde with acrylonitrile in the presence of DABCO for 8 days.

Bis|2-carbomethoxy-l-phenyl prop-2-en-1-yl| ether (79):

To a stirred solution of methyl (2Z)-2-(bromomethyl)-3-phenylprop-2-enoate (58a) (2 mM, 0.510 g) in acetonitrile (5 mL) was added DABCO (2 mM, 0 224 g) at room temperature. After 1h, methyl 3-hydroxy-2-methylene-3-phenylpropanoare (57a) (2 mM, 0.38 g) and K_2CO_3 (2 mM, 0.276 g) were added and refluxed for lh. The reaction

mixture was cooled to room temperature and acetonitrile was **removed under** reduced **pressure. Then** the crude mixture was diluted with water (2 mL) and extracted with ether (3x10 mL). The combined organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and the crude product thus obtained was purified by column chromatography (silica gel, 8% EtOAc in hexanes) to provide bis **allyl** ether as a mixture of diastereomers **(79a** and **79b)** as a colorless viscous liquid.

Yield : 95% (0.348 g)

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

^1H NMR : 8 158 & 3.65 (2s, 6H), 5.17 & 5.28 (2s, 2H), 6.04 & 6.10 (2s, 2H), 6.30 & 6.38 (2s, 2H), 7.25 & 7.30 (2s, 10H)

^{13}C NMR : δ 51.58. 51.72. 76.47. 76.59, 76.84, 124.79, 125.39, 127.70, 127.85, 127.99, 128.26. 139.05. 139.73, 140.79. 141.54, 16602. 166.11

The diastereoselectivity is 20%. The underlined chemical shift values refer to the minor diastereomer.

Reaction of methyl (2Z)-2-(bromomethyl)-3-phenylprop-2-enoate (58a) with (S)-l-phenylethylamine in the presence of DABCO:

To a stirred solution of methyl (2Z)-2-(bromomethyl)-3-phenylprop-2-enoate **(58a)** (2 mM, 0.510 g) in dichloromethane (5 mL) was added DABCO (2 mM, 0.224 g) at room temperature. After 1h, (S)-l-phenylethylamine (2 mM, 0.242 g) was added and stirring continued for an additional lh. Then the reaction mixture was diluted with water (2

mL) and extracted with ether (3×10 mL). The combined organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and the crude product thus obtained was subjected to column chromatography (silica gel, 8% EtOAc in hexanes) to provide both major (colorless crystalline solid) and minor (colorless liquid) diastereomeric products in pure form.

de : 50% (^1H NMR of the crude product shows two singlets at 5 6.25 and 6.41 for diastereomeric olefinic protons *cis* to the ester group in 3:1 ratio indicating that the reaction is 50% diastereoselective).

Methyl **(3R)-2-methylene-3-[(S)-1-phenylethylamino]-3-phenylpropanoate** (81a): (Major isomer)

Yield : 50% (0.293 g) (colorless crystalline solid)

$[\alpha]_D^{25}$: -120.36 (c 1.35, MeOH)

mp : 68°C

IR (KBr) : 3314, 1716, 1626 cm^{-1}

^1H NMR :5 1.32 (d, 3H, J = 6 6 Hz), 1.73 (b, 1H), 3.63 (m, 4H), 4.48 (s, 1H), 5.79 (s, 1H), 6.25 (s, 1H), 7.15-7.45 (m, 10H)

^{13}C NMR : 5 24.60, 51.67, 55.15, 60.09, 125.26, 126.85, 126.96, 127.21, 127.84, 128.40, 141.54, 143 15, 145.28, 166.92

MS (m/z) : 280 $(M-CH_3)^+$

Analysis calcd. for $C_{19}H_{21}NO_2$: C, 77.26; H, 7.17; N, 4.74

Found :C, 77.42; H, 7.19; N, 4.73

Methyl (3S)-2-methylene-3-[(S)-1-phenylethylamino]-3-phenylpropanoate (82a):

(Minor isomer)

Yield : 17% (0.103 g) (colorless liquid)

$[\alpha]_D^{25}$: +58.48 (c 1.25, MeOH)

IR (neat) : 3339, 1718, 1626 cm^{-1}

^1H NMR 6 1.37(d,3H,J = 6.5 Hz), 1.67 (b, 1H), 3.64 (s, 3H), 3.77(q, 1H, J = 6.5 Hz), 4.44 (s, 1H), 5.90 (s, 1H), 6.41 (s, 1H), 7.12-7.45 (m, 10H)

^{13}C NMR : 5 24.43, 51.55, 55.46, 60.77, 125.91, 126.75, 127.02, 127.21, 128.30, 128.50, 141.42, 142.22, 145.65, 166.87

Reaction of methyl (2*Z*)-2-(bromomethyl)-3-(2-methylphenyl)prop-2-enoate with (S)-l-phenylethylamine in the presence of DABCO

This reaction was carried out following similar procedure described for the reaction between **58a** with (S)-l-phenylethylamine. Both major and minor isomers are separated by column chromatography (silica gel, 8% EtOAc in hexanes).

de 58% (^1H NMR of the crude product shows two singlets at 6 6.23 and 6.46 for the diastereomeric olefinic protons *cis* to the ester group in the ratio of 79:21).

Methyl (3R)-2-methylene-3-[(S)-1-phenylethylamino]-3-(2-methylphenyl)propanoate (81b): (Major isomer)

Yield : 47% (colorless liquid)

$[\alpha]_D^{25}$: -60.47 (c 2.30, MeOH)

IR (neat) : 3333, 1722, 1628 cm^{-1}

^1H NMR : 5 1.33 (d, 3H, J = 6.6 Hz), 1.86 (b, 1H), 2.05 (s, 3H), 3.50-3.74 (m, 4H), 4.74 (s,1H), 5.54 (s,1H), 6.22, (s,1H), 7.08-7.44 (m, 9H)

^{13}C NMR : 5 19.07, 24.57, 51.72, 55.36, 55.61, 125.85, 126.02, 126.78, 126.87, 126.94, 128.30, 130.51, 136.74, 138.95, 142.64, 145.17, 167.29

MS (m/z) : 294 $(M-CH_3)^+$

Analysis calcd. for $C_{20}H_{23}NO_2$ C, 77.64; H, 7.49; N, 4.53

Found C, 77.37; H, 7.52; N, 4.54

Methyl (3S)-2-methylene-3-[(S)-l-phenylethylamino]-3-(2-methylphenyl)propanoate (82b): (Minor isomer)

Yield : 15% (colorless liquid)

$[\alpha]_D^{25}$: +90.67 (c 0.81, MeOH)

IR (neat) : 3339,1722, 1628 cm^{-1}

^1H NMR : 5 1.39 (d, 3H, J = 6.7 Hz), 1.67 (s, 1H), 2.02 (s, 3H), 3.64 (s, 3H), 3.73 (q, 1H, J = 6.7 Hz), 4.77 (s, 1H), 6.05 (s, 1H), 6.46, (s, 1H),

7.03-7.45 (m, 9H)

^{13}C NMR : 8 18.92, 23.63, 51.70, 55 61, 55.68, 125.13, 126 01, 126 84, 126.94, 127.14, 128.50, 130.51, 136.25, 139.78, 141.44, 145.58, 167.17

Reaction of methyl (2*Z*)-2-(bromomethyl)-3-(4-methylphenyl)prop-2-enoate with (S)-1-phenylethylamine in the presence of DABCO

This reaction was carried out following the similar procedure described for the reaction between **58a** and (S)-1-phenylethylamine Both major and minor isomers are separated by column chromatography (silica gel, 8% EtOAc in hexanes).

de : 40% (^1H NMR of the crude product shows two singlets at δ 6.21 and 6.37 for the diastereomeric olefinic protons *cis* to the ester group in the ratio of 7:3).

Methyl (3R)-2-methylene-3-[(S)-1-phenylethylamino]-3-(4-methylphenyl)propanoate (81c): (Major isomer)

Yield : 36% (colorless liquid)

$[\alpha]_D^{25}$: -116.61 (c 0.88, MeOH)

IR (neat) : 3339, 1724, 1628 cm^{-1}

^1H NMR :5 1.30 (d, 3H, J= 6.7 Hz), 1.73 (s, 1H), 2.33 (s, 3H), 3.55-3.72 (m, 4H), 4.44 (s, 1H), 5.78 (d,lH, J = 1.5 Hz), 6.22, (s, 1H), 7.02-7.45 (m, 9H)

^{13}C NMR : 5 21.14, 24.61, 51.63, 55.12, 59.81, 125.00, 126.87, 127.74, 128.39, 129.11, 136.75, 138.51, 143.33, 145.36, 167.00

MS (m/z) : 294 $(M\text{-}CH_3)^+$

Analysis calcd. for $C_{20}H_{23}NO_2$ C, 77.64; H, 7.49; N, 4.53

Found C, 77.95; H, 7.45; N, 4.55

Methyl (3S)-2-methylene-3-[(S)-1-phenylethylamino]-3-(4-methylphenyl)propanoate (82c): (Minor isomer)

Yield : 16% (colorless liquid)

$[\alpha]_D^{25}$: +69.72 (c 0.90, MeOH)

IR (neat) : 3341, 1722, 1626 cm^{-1}

^1H NMR : 5 1.35 (d, 3H, J = 6.7 Hz), 1.70 (b, 1H), 2.30 (s, 3H), 3.63 (s, 3H), 3.75 (q, 1H, J = 6.7 Hz), 4.41 (s, 1H), 5.89 (s, 1H), 6.38, (d,lH, J = 1.22 Hz), 7.06-7.39 (m, 9H)

^{13}C NMR : 5 21.10, 24.50, 51.63, 55.38, 60.38, 125.81, 126.74, 126.99, 127.10, 128.52, 129.07, 136.63, 139.20, 141.33, 145.68, 166.93

Reaction of methyl (2Z)-2-(bromomethyI)-3-(4-ethylphenyI)prop-2-enoate with (S)-1-phenylethylamine in the presence of DABCO

This reaction was performed following the similar procedure described for the reaction

between 58a and (S)-1-phenylethylamine Both major and minor isomers are separated by column chromatography (silica gel, 8% EtOAc in hexanes).

de : 42% (^{1}H NMR of the crude product shows two singlets at 6 6.21 and 6.37 for the diastereomeric olefinic protons *cis* to the ester group in the ratio of 71:29).

Methyl (3R)-3-(4-ethylphenyl)-2-methylene-3-[(S)-1-phenylethylamino]propanoate (81d): (Major isomer)

Yield : 41% (colorless liquid)

$[\alpha]_D^{25}$:-118.67 (c 1.81, MeOH)

IR (neat) : 3337, 1722, 1628 cm^{-1}

^{1}H NMR : 6 1.25 (t, 3H, J = 7.6 Hz), 1.32 (d, 3H, J = 6.7 Hz), 1.68 (b, 1H), 2.65 (q, 1H, J =7.6 Hz), 3.64 (m, 4H), 4.46 (s, 1H), 5.79 (s, 1H), 6.23, (s, 1H), 7.11-7.40 (m,9H)

^{13}C NMR .6 15.43,24.58,28.51, 51.66, 55.06, 59.80, 125.10, 126.86, 127.73, 127.85, 128.38, 130.46, 138.63, 143.05, 143.22, 145.33, 167.00

MS (m/z) : 308 $(M-CH_3)^+$

Analysis calcd. for $C_{21}H_{25}NO_2$: C, 77.99, H, 7.79; N, 4.33

Found :C, 78.25; H, 7.84; N, 4.33

Methyl (3S)-3-(4-ethylphenyl)-2-methylene-3-[(S)-1-phenylethylamino]propanoate (82d): (Minor isomer)

Yield : 22% (colorless liquid)

$[\alpha]_D^{25}$: +75.83 (c 1.22, MeOH)

IR (neat) : 3341, 1720, 1626 cm^{-1}

H NMR :5 1.19(t,3H,J = 7.5 Hz), 1.34 (d, 3H, J = 6.6 Hz), 1.98 (b, 1H), 2.59 (q, 2H, J = 7.5 Hz), 3.61 (s, 3H), 3.75 (q, 1H, J = 6.6 Hz), 4.41 (s, 1H), 5.89 (s, 1H), 6.37, (s, 1H), 7.07-7.36 (m, 9H)

^{13}C NMR : 5 15.45, 24.46, 28.43, 51.55, 55.29, 60.30, 125.81, 126.65, 126.90, 127.04, 127.76, 128.44, 139.30, 141.12, 142.87, 145.54, 166.84

Reaction of methyl (2Z)-2-(bromomethyI)-3-(2-chIorophenyl)prop-2-enoate with (S)-l-phenylethylamine in the presence of DABCO

This reaction was carried out following the similar procedure described for the reaction between **58a** and (S)-l-phenylethylamine. Both major and minor isomers are separated by column chromatography (silica gel, 8% EtOAc in hexanes).

de : 42%. (The ^1H NMR of the crude product shows two singlets at 5 6.26 and 6.41 for the diastereomeric olefinic protons *cis* to the ester group in the ratio of 71:29).

Methyl (3R)-3-(2-chlorophenyl)-2-methylene-3-[(S)-1-phenylethylamino]propanoate (81 e): (Major isomer)

Yield : 56% (colorless liquid)

$[\alpha]_D^{25}$:-33.47 (c 1.16, MeOH)

IR (neat) : 3339, 1722, 1630 cm^{-1}

^1H NMR : 6 1.33 (d, 3H, J = 6.2 Hz), 1.98 (b, 1H), 3.58-3.80 (s, 4H), 4.95 (s, 1H), 5.62, (s, 1H), 6.26 (s, 1H), 7.12-7.59 (m, 9H)

^{13}C NMR : 8 24.36, 51.67, 55.73, 57.01, 126.52, 126 78, 126.87, 126.97, 128.28, 129.00, 129.82, 134.17, 138.81, 141.55, 144.96, 166.82

MS (m/z) : 314 $(M-CH_3)^+$, 316 $(M-CH_3+2)^+$

Analysis calcd. for C19H20N O_2Cl : C, 69.19; H, 6.11; N, 4.24

Found : C, 69.50; H, 6.15; N, 4.23

Methyl **(3S)-3-(2-chlorophenyl)-2-methylene-3-[(S)-1-phenylethylamino]propan**oate (82e): (Minor isomer)

Yield : 21% (colorless liquid)

$[\alpha]_D^{25}$: +27.84 (c 0.88, MeOH)

IR (neat) : 3341, 1722, 1628 cm^{-1}

^1H NMR : δ 1.41 (d, 3H, J= 6.6 Hz), 1.89 (b, 1H), 3 69 (s, 3H), 3.79 (q, 1H, J ≈ 6.6 Hz), 5.08 (s, 1H), 5.89 (s, 1H), 6.43 (s, 1H), 7.10-7.50 (m, 9H)

^{13}C NMR : δ 23.41, 51.62, 55.61, 56.82, 126.46, 126.67, 126.91, 128.25, 128.83,

129.54, 133.76, 138.92, 140.68, 145.14, 166.68

Reaction of methyl (2*Z*)-2-(bromomethyl)-3-(4-chlorophenyl)prop-2-enoate with (S)-l-phenylethylamine in the presence of DABCO

This reaction was carried out following the similar procedure described for the reaction between 58a and (S)-l-phenylethylamine. Both major and minor isomers are separated by column chromatography (silica gel, 8%EtOAc in hexanes).

de : 53% (^{1}H NMR of the crude product shows two singlets at 8 6.24 and 6.40 for the diastereomeric olefinic protons *cis* to the ester group in the ratio of 76.5:23.5).

Methyl (3R)-3-(4-chlorophenyl)-2-methylene-3-[(S)-1-phenylethylamino]propanoate (81f): (Major isomer)

Yield : 54% (colorless liquid)

$[\alpha]_D^{25}$: -148.70 (c 0.96, MeOH)

IR (neat) : 3337, 1722, 1628 cm^{-1}

^{1}H NMR :8 1.30 (d, 3H, J = 6.6 Hz), 1.68 (b, 1H), 3.56 (q, 1H, J = 6.6 Hz), 3.62 (s, 3H), 4.43 (s, 1H), 5.80 (s, 1H), 6.25 (s, 1H), 7.12-7.41 (m, 9H)

^{13}C NMR : δ 24.39, 51.55, 55.08, 59.37, 125.27, 126.64, 126.97, 128.41, 129.16, 132.80, 140.09, 142.73, 144.92, 166.47

MS (m/z) : 314 $(M-CH_3)^+$, 316 $(M-CH_3+2)^+$

Analysis calcd for $C_{19}H_{20}NO_2Cl$: c, 69.19, H, 6.11; N, 4.24

Found : C, 69.47, H, 6.12, N, 4.20

Methyl (3S)-3-(4-chlorophenyl)-2-methylene-3-[(S)-1-phenylethylamino]propanoate (82f): (Minor isomer)

Yield : 16% (colorless liquid)

$[\alpha]_D^{25}$: +76.12 (c 1.55, MeOH)

IR (neat) : 3339, 1720, 1626 cm^{-1}

^1H NMR :8 1.29 (d, 3H, J= 6.4 Hz), 1.80 (b, 1H), 3.56 (s, 3H), 3.68(q, 1H, J = 6.4 Hz), 4.29 (s, 1H), 5.78 (s, 1H), 6.33 (s, 1H), 7.08-7.32 (m, 9H)

^{13}C NMR : 5 24.48, 51.57, 55.28, 60.15, 126.44, 126.58, 126.97, 128.29, 128.41, 132.62, 140.53, 140.63, 145.21, 166.46

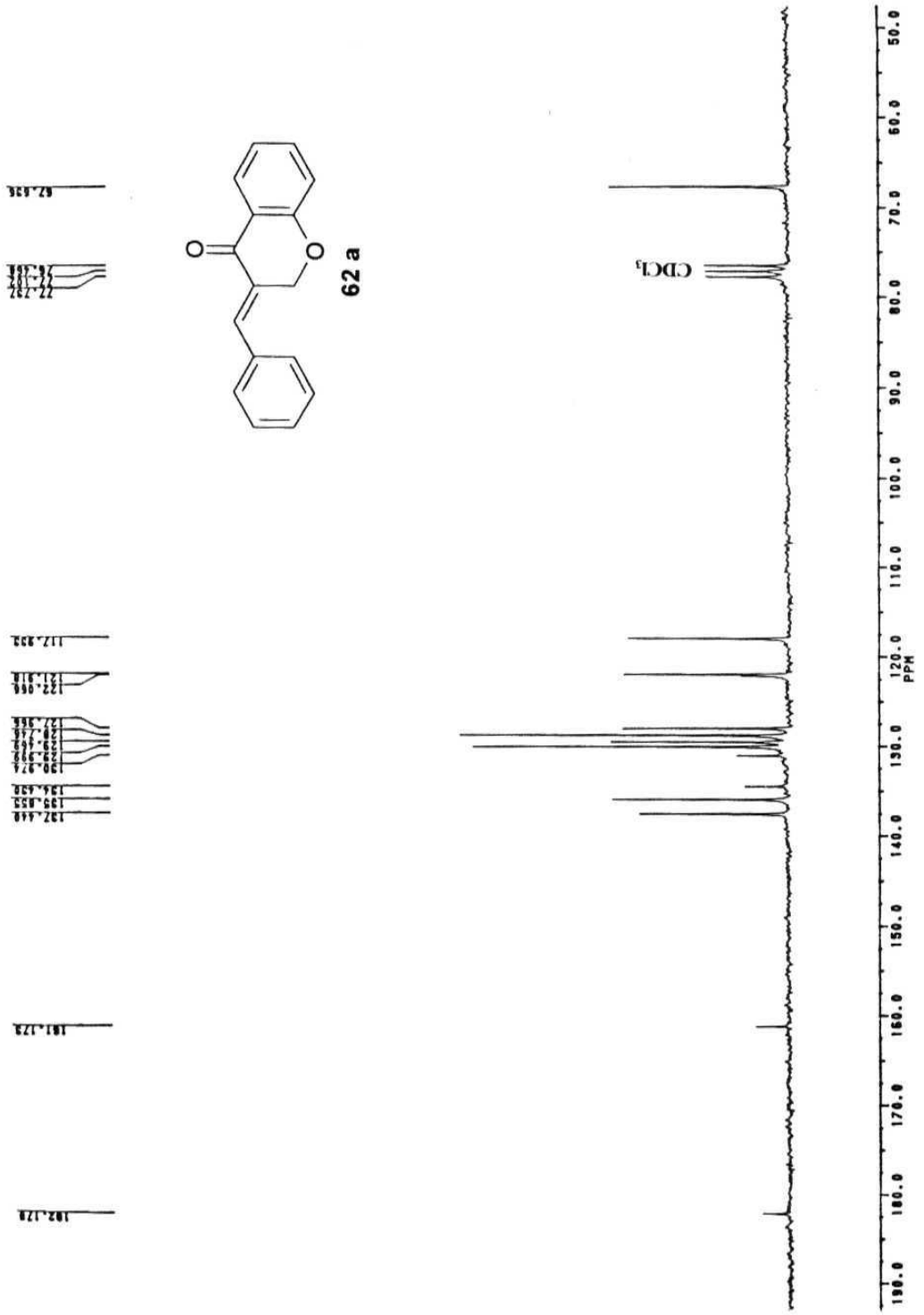


Fig 1: ^{13}C NMR spectrum of **62a**

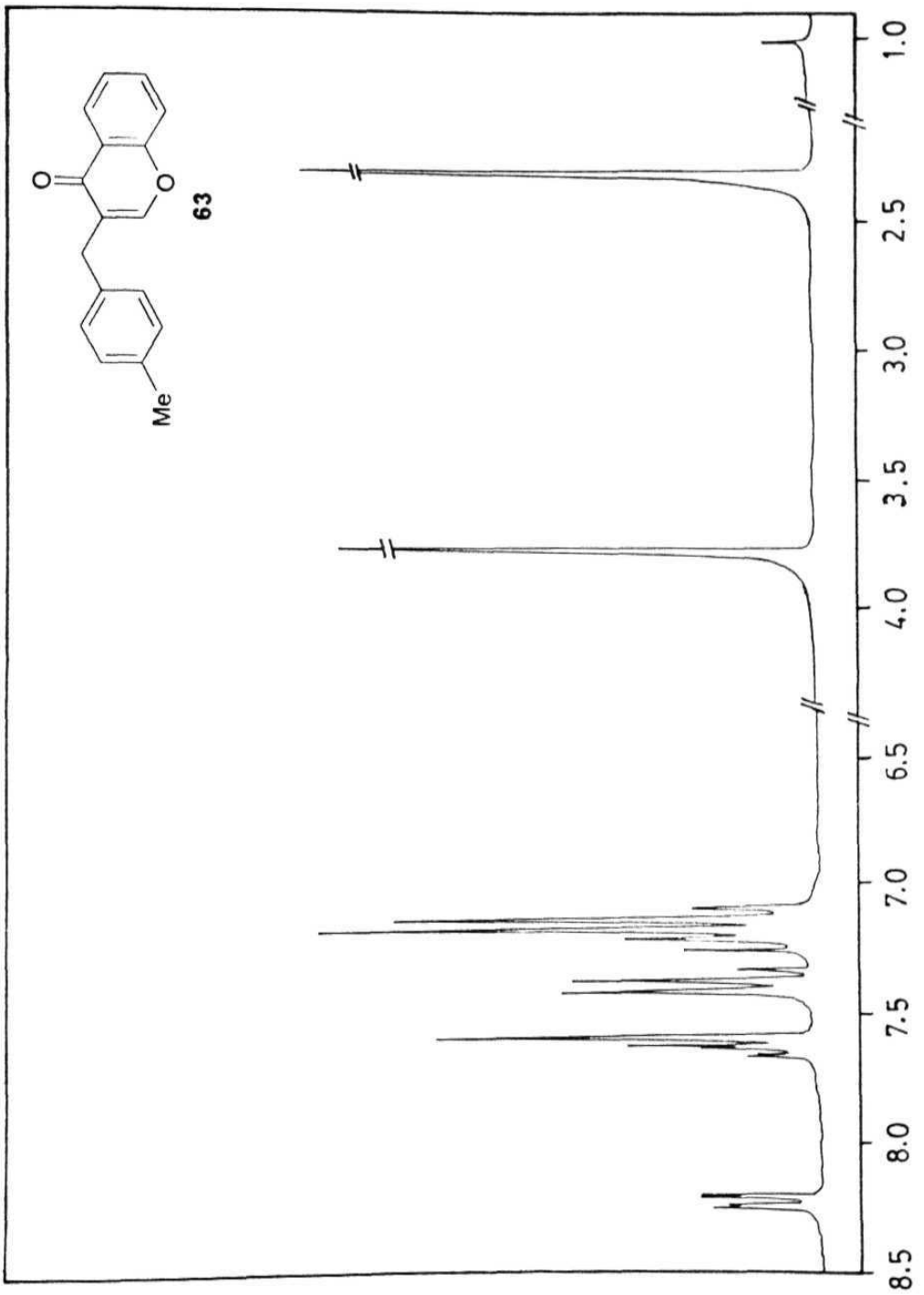


Fig 2: ^{1}H NMR spectrum of **63**

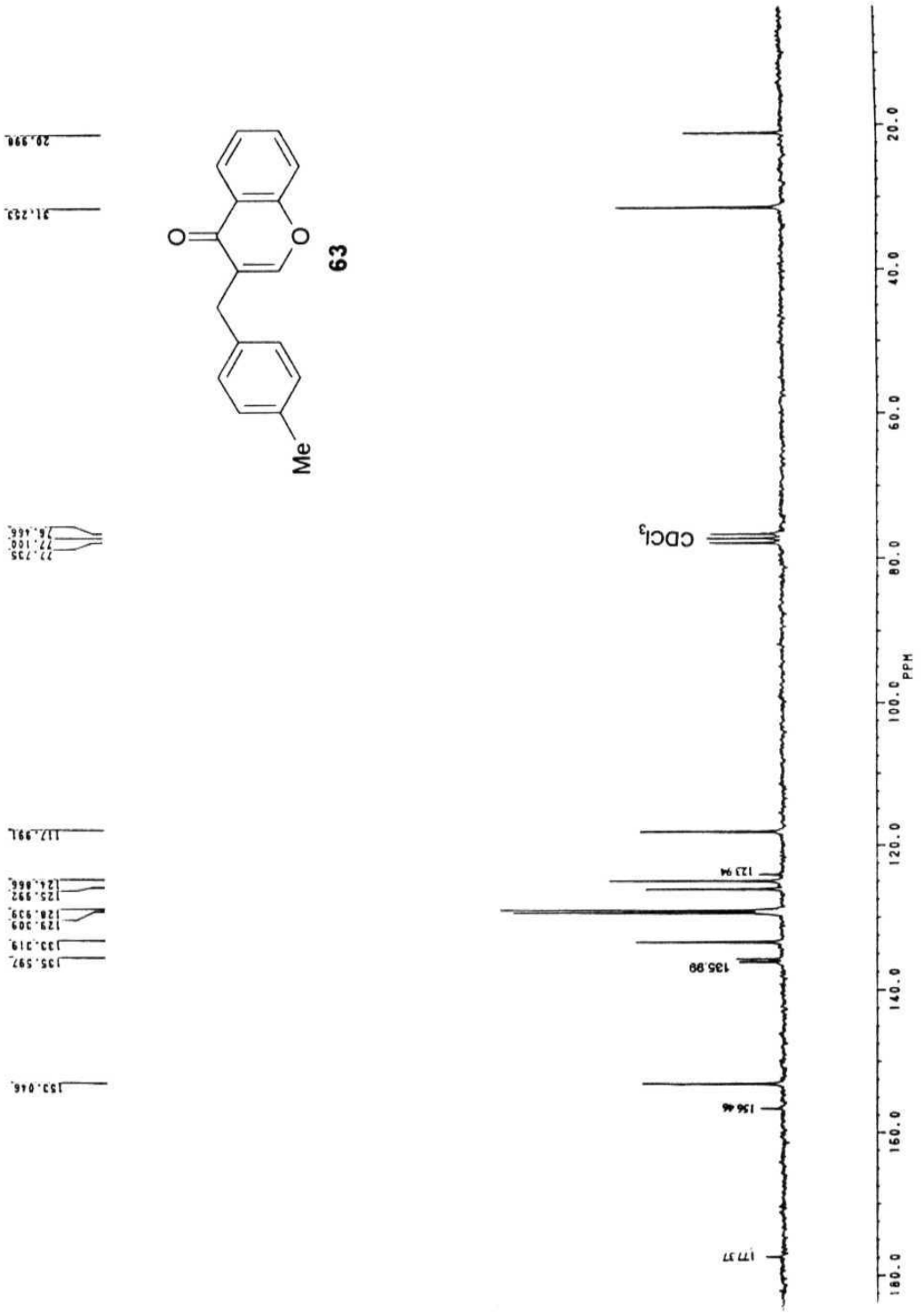


Fig 3: ^{13}C NMR spectrum of **63**

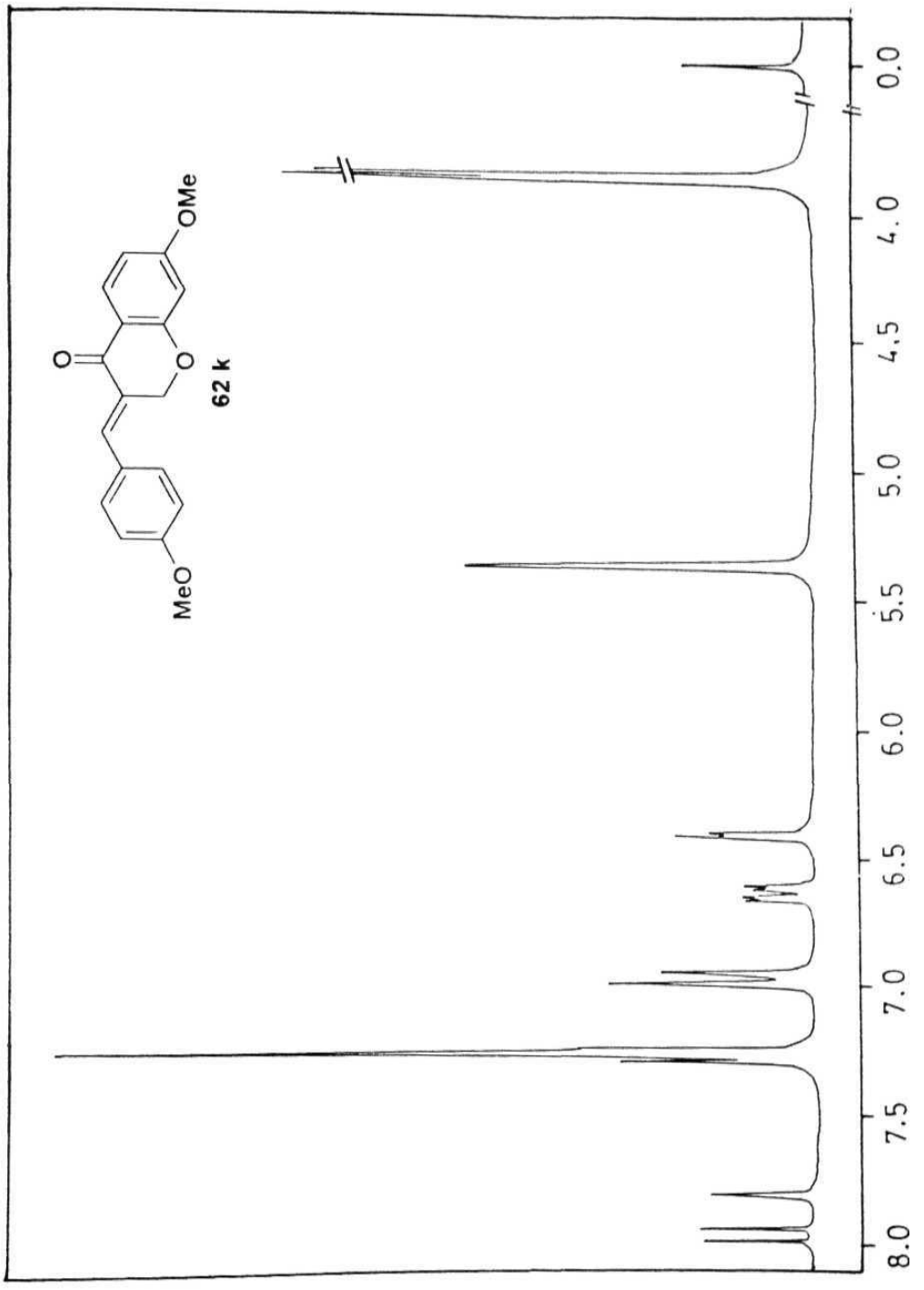


Fig 4: ^{1}H NMR spectrum of **62k**

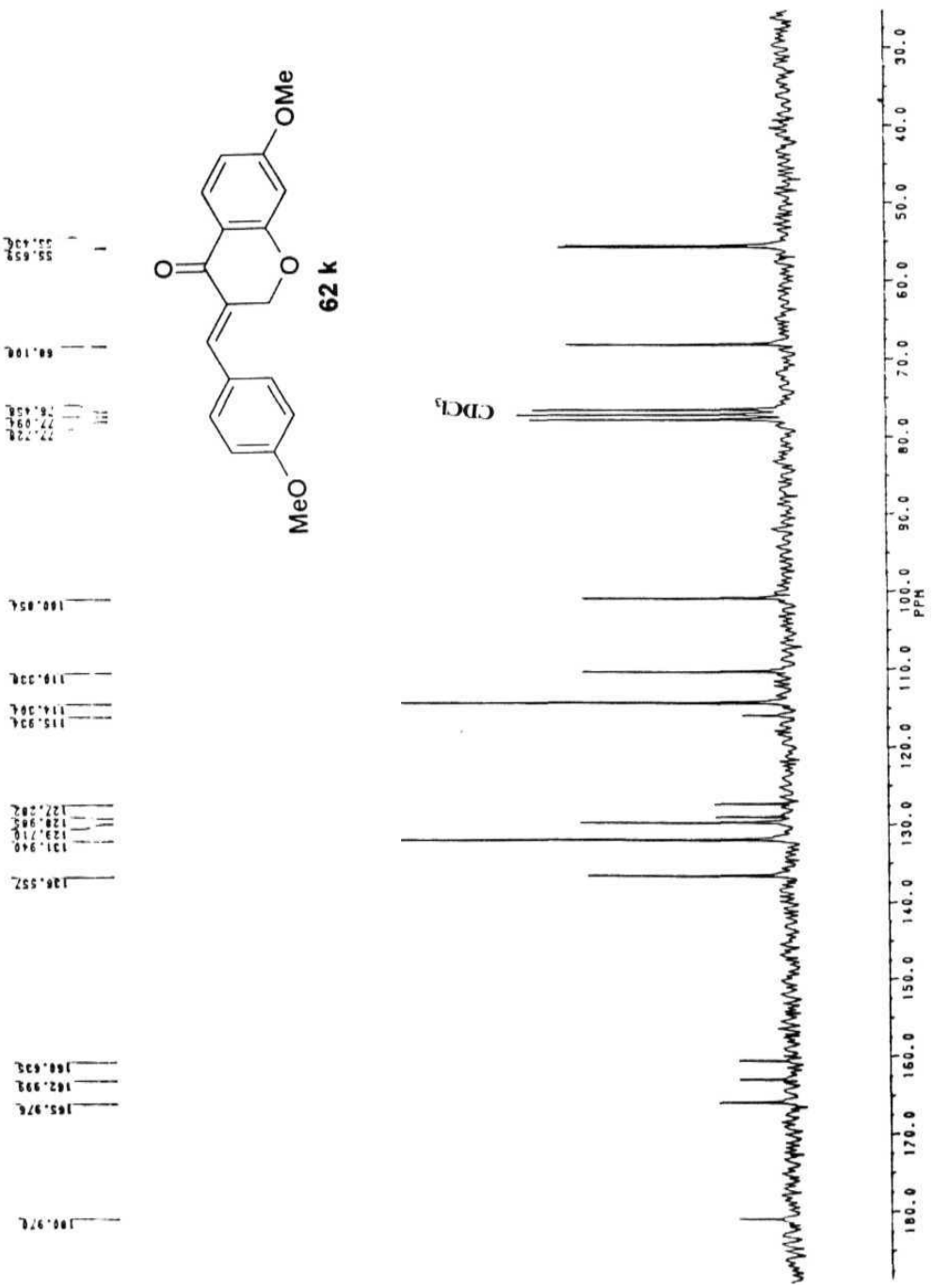


Fig 5: ^{13}C NMR spectrum of **62k**

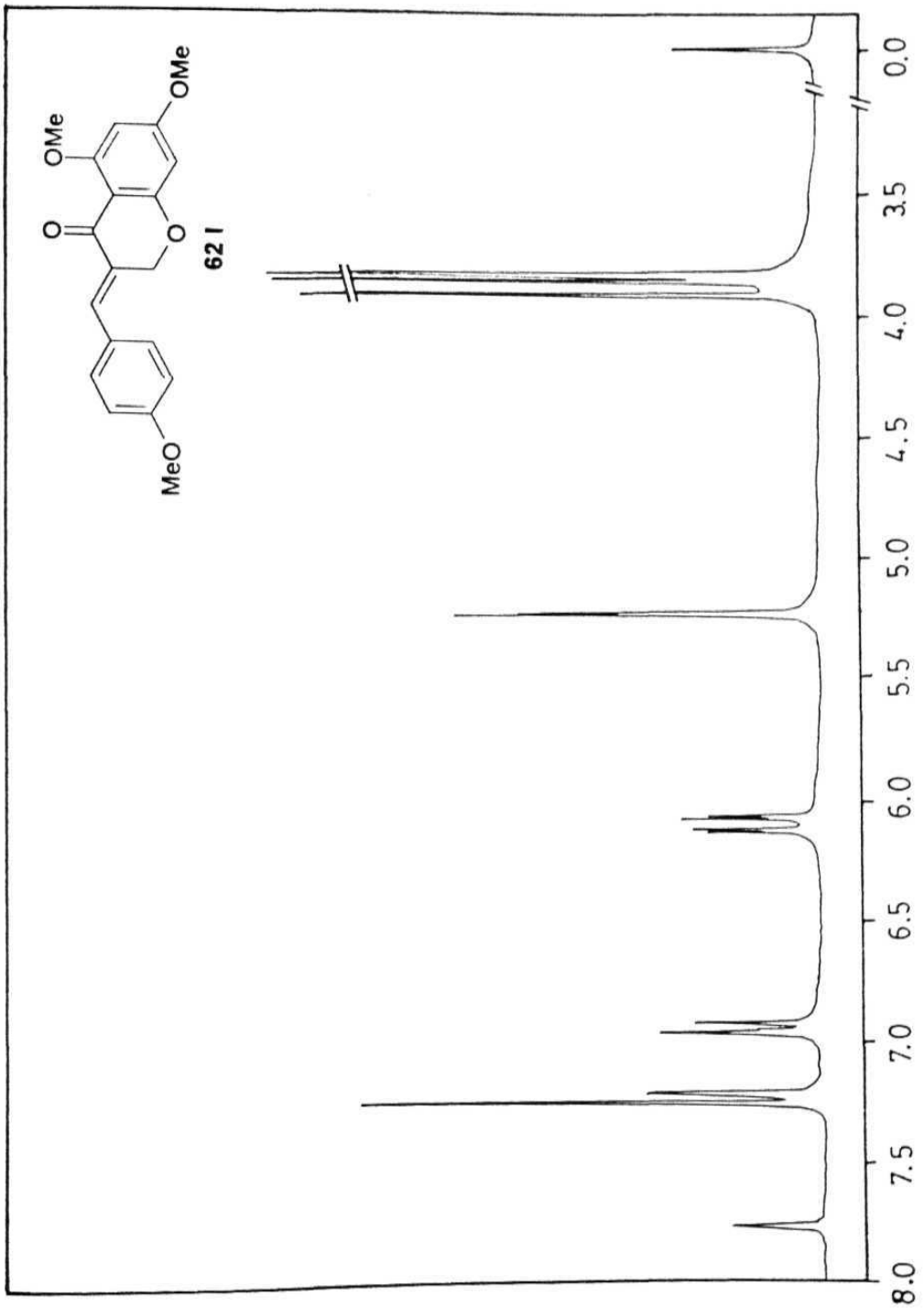


Fig 6: ^{1}H NMR spectrum of **62I**

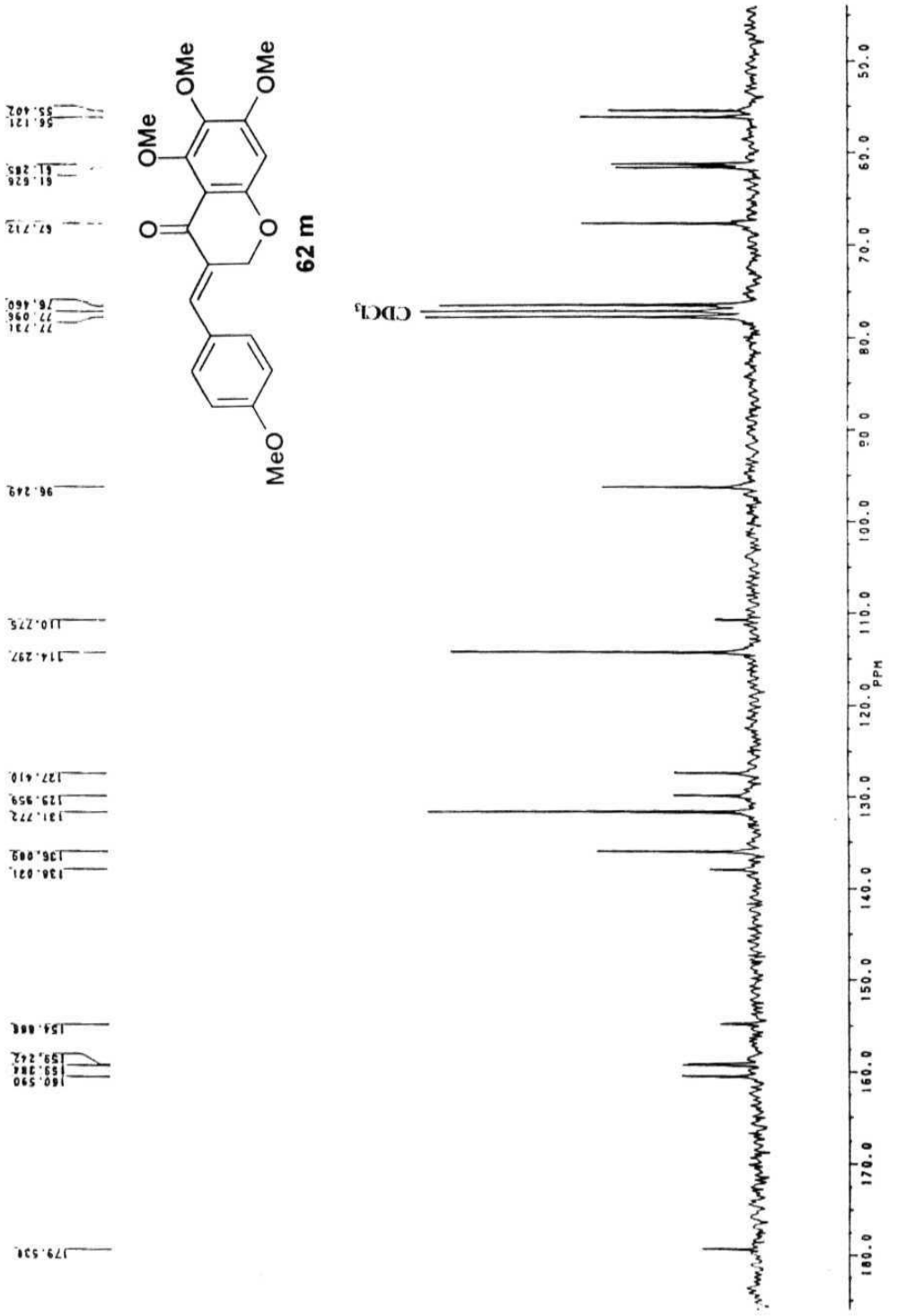


Fig 7: ^{13}C NMR spectrum of **62m**

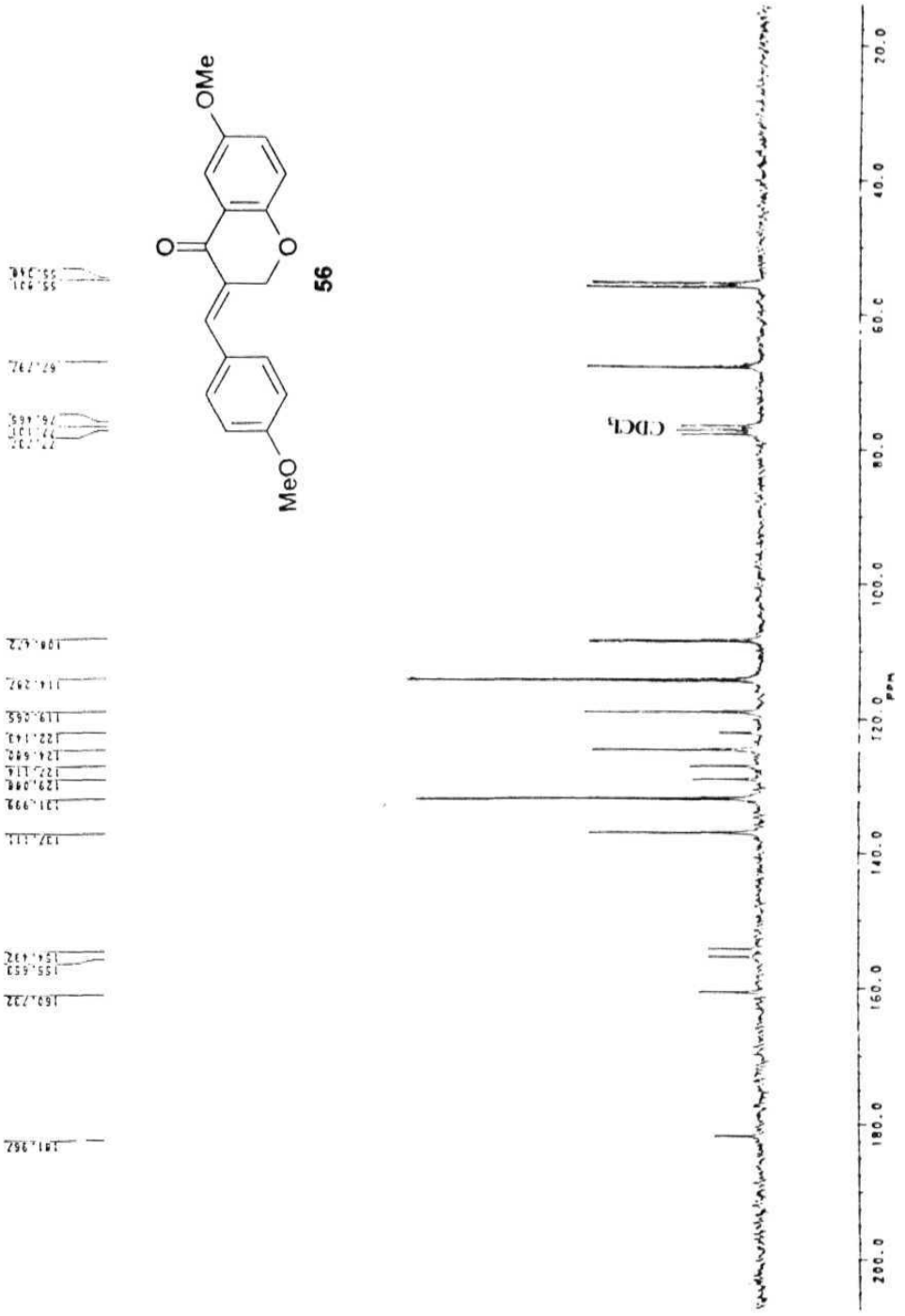


Fig 8: ^{13}C NMR spectrum of **56**

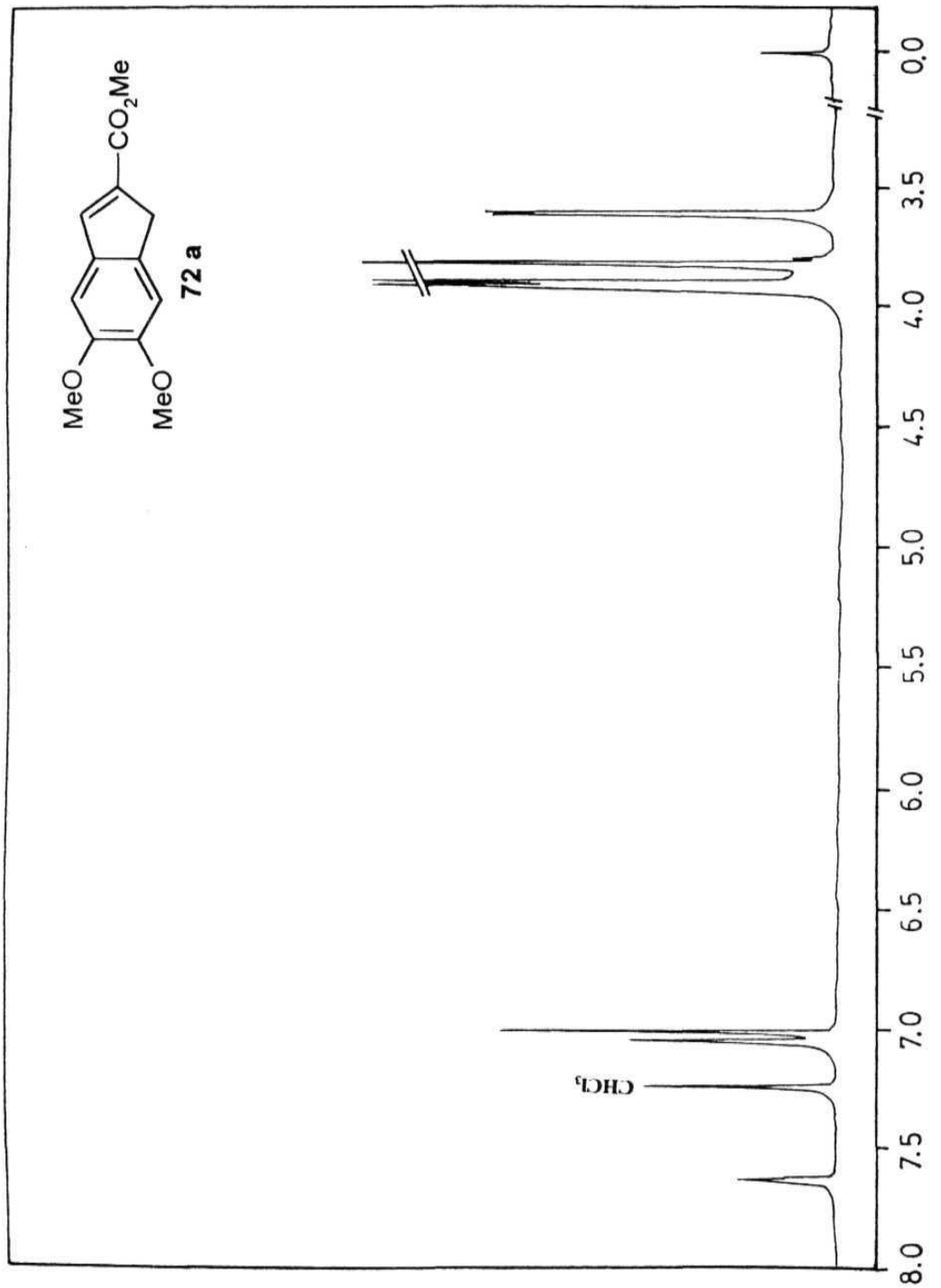


Fig 9: ^{1}H NMR spectrum of **72a**

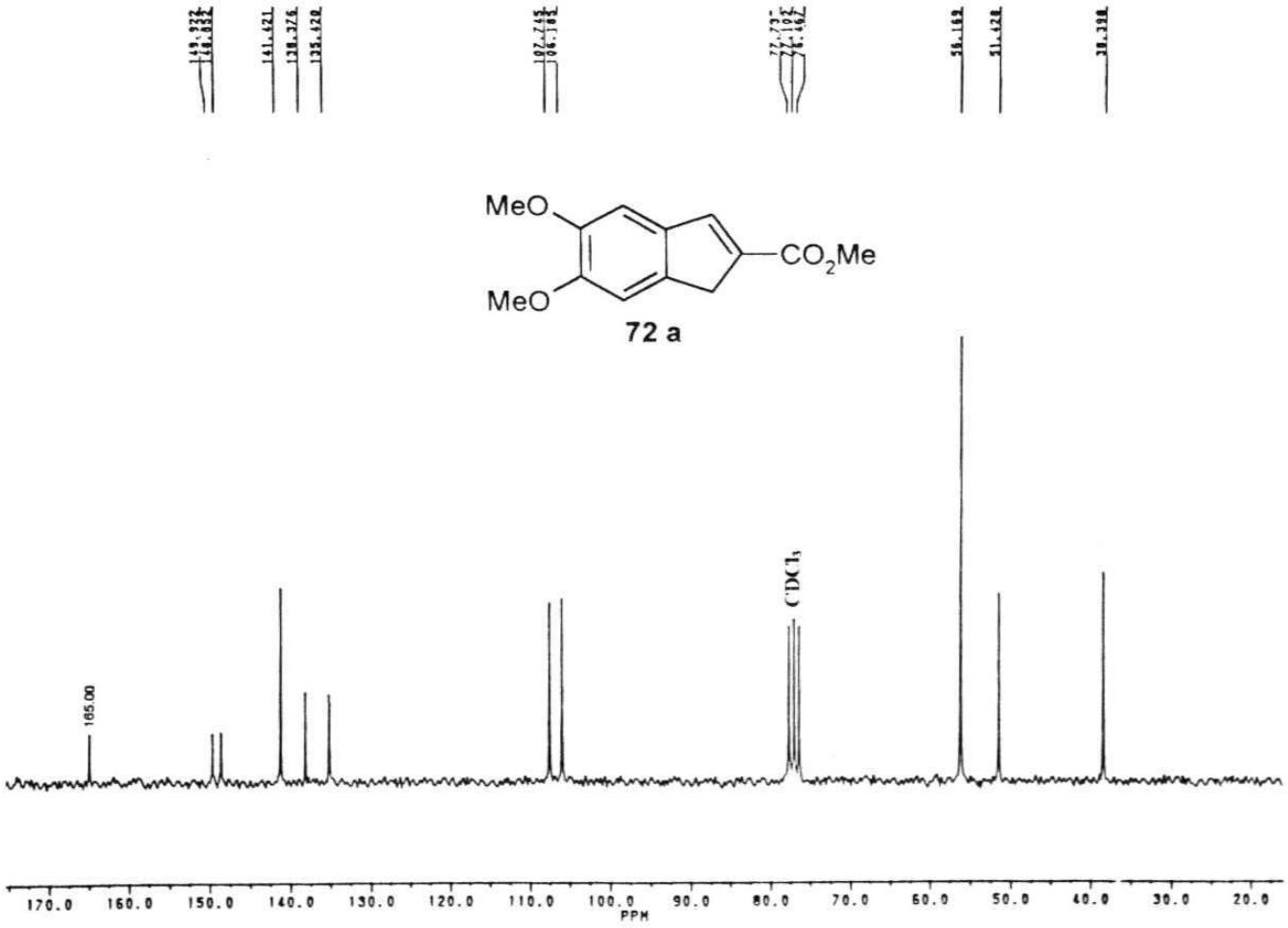


Fig 10: ^{13}C NMR spectrum of **72a**

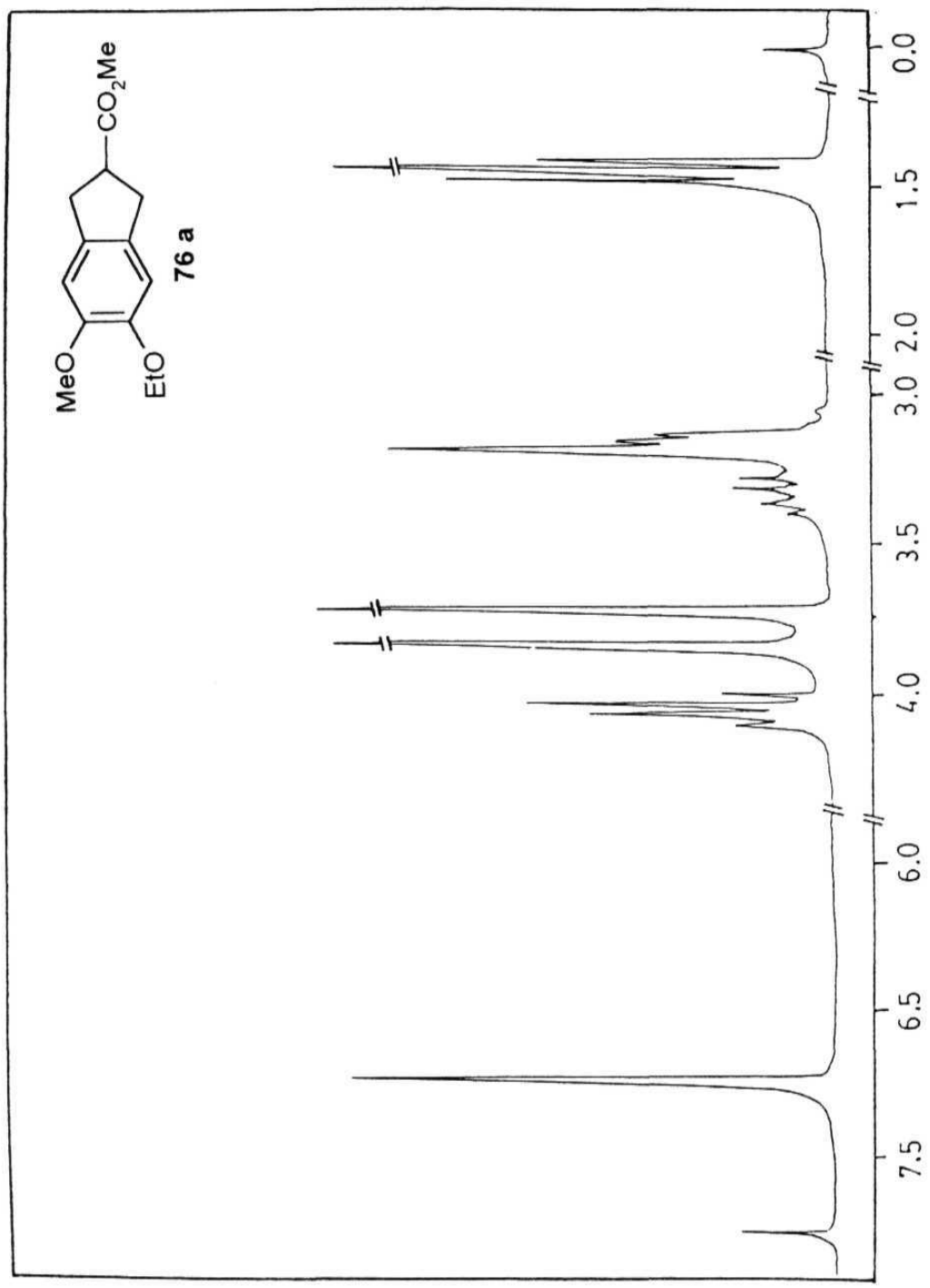


Fig 11: ^{1}H NMR spectrum of **76a**

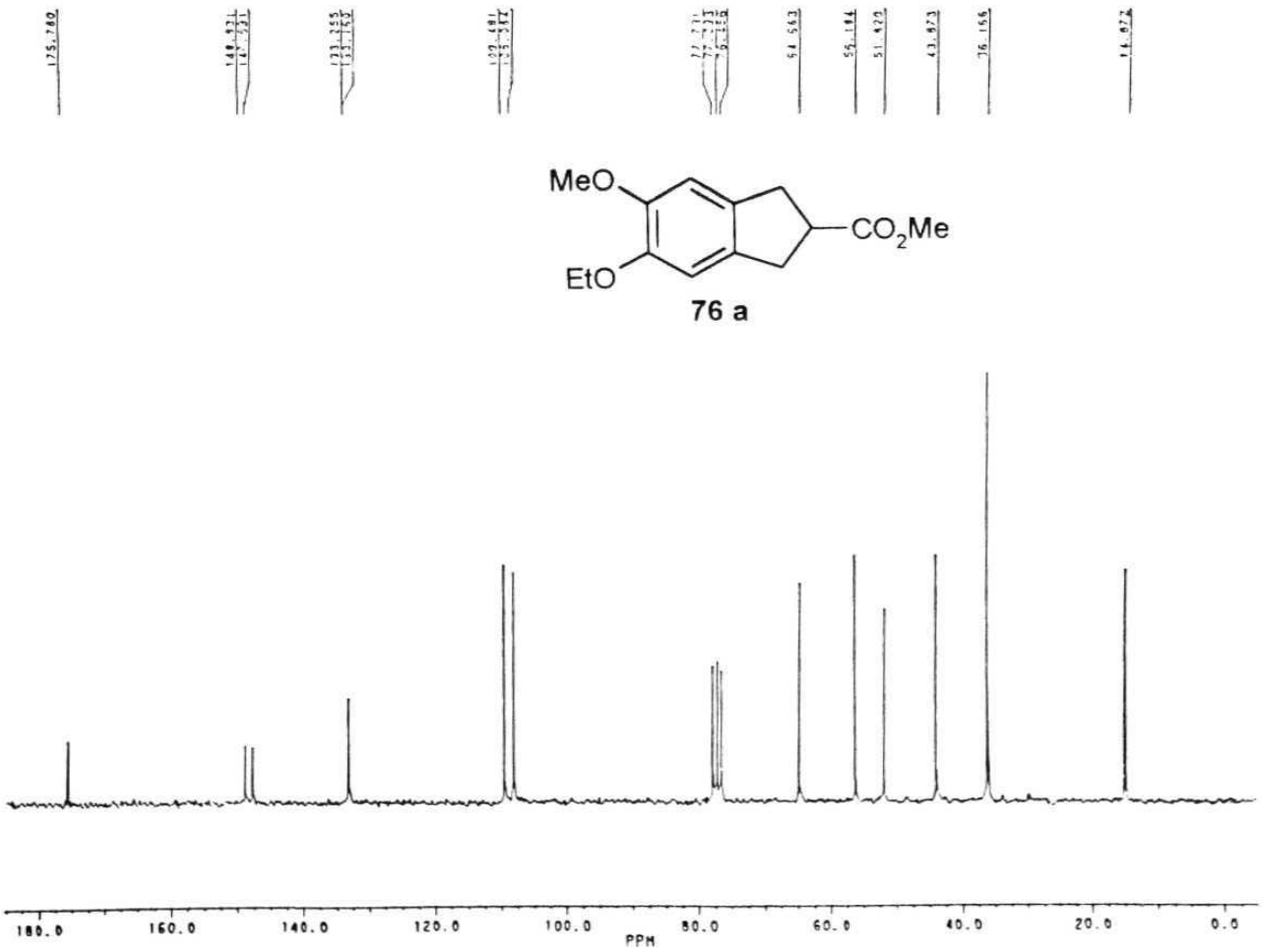


Fig 12: ^{13}C NMR spectrum of 7**6a**

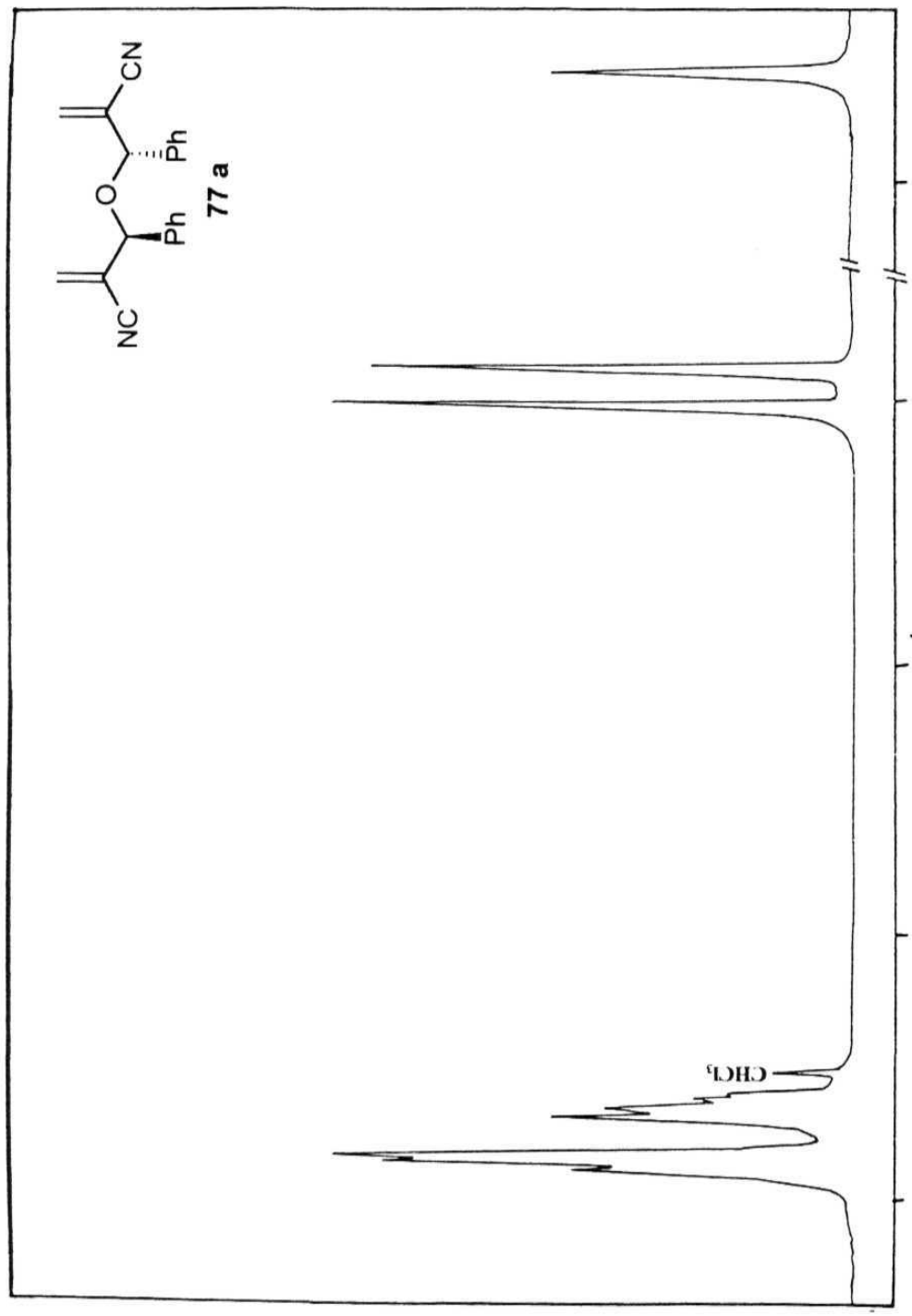


Fig 13: ^{1}H NMR spectrum of **77a**

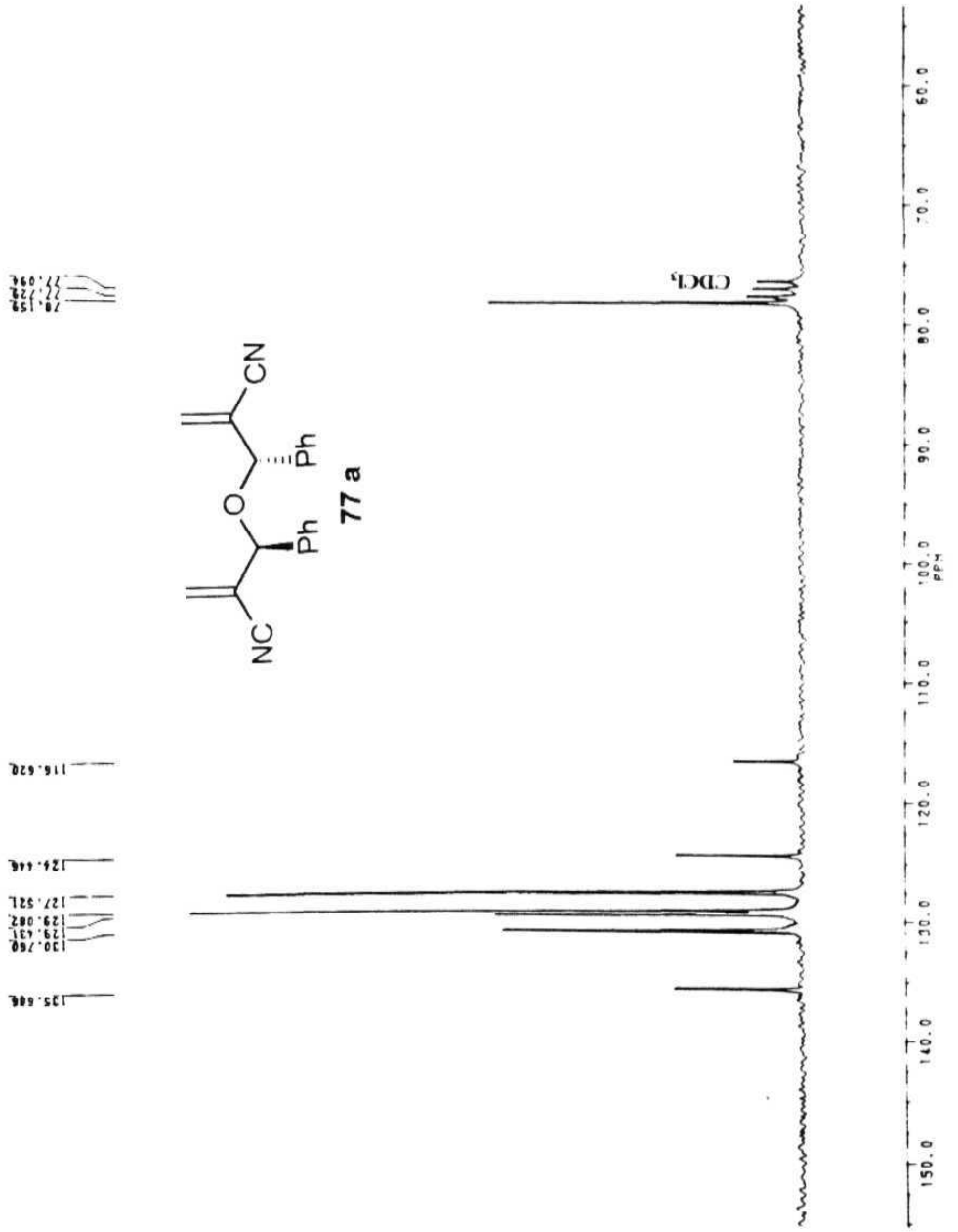


Fig 14: ^{13}C NMR spectrum of **77a**

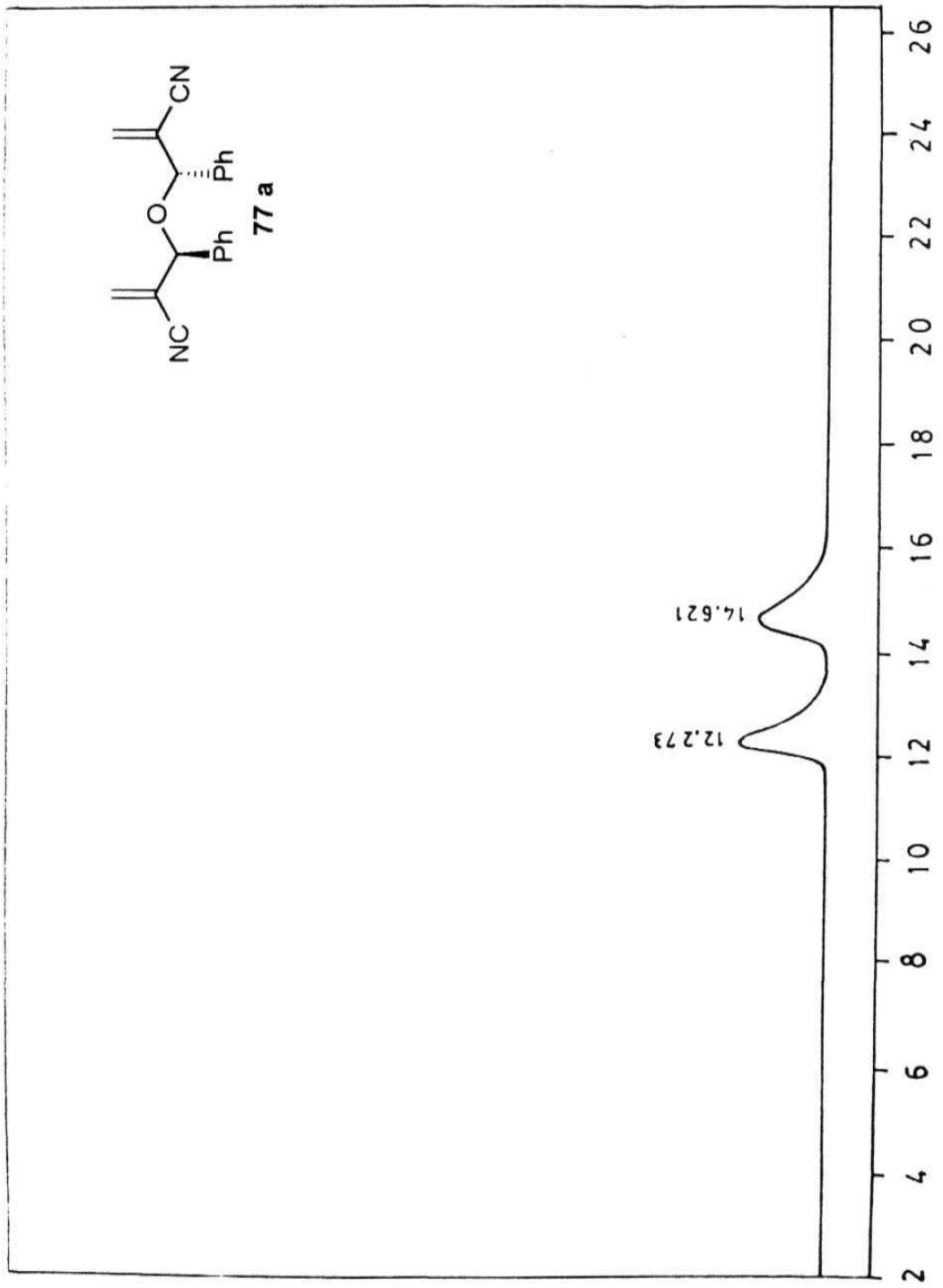


Fig 15: HPLC analysis (Chromatogram of **77a** on CHIRALCEL OD column)

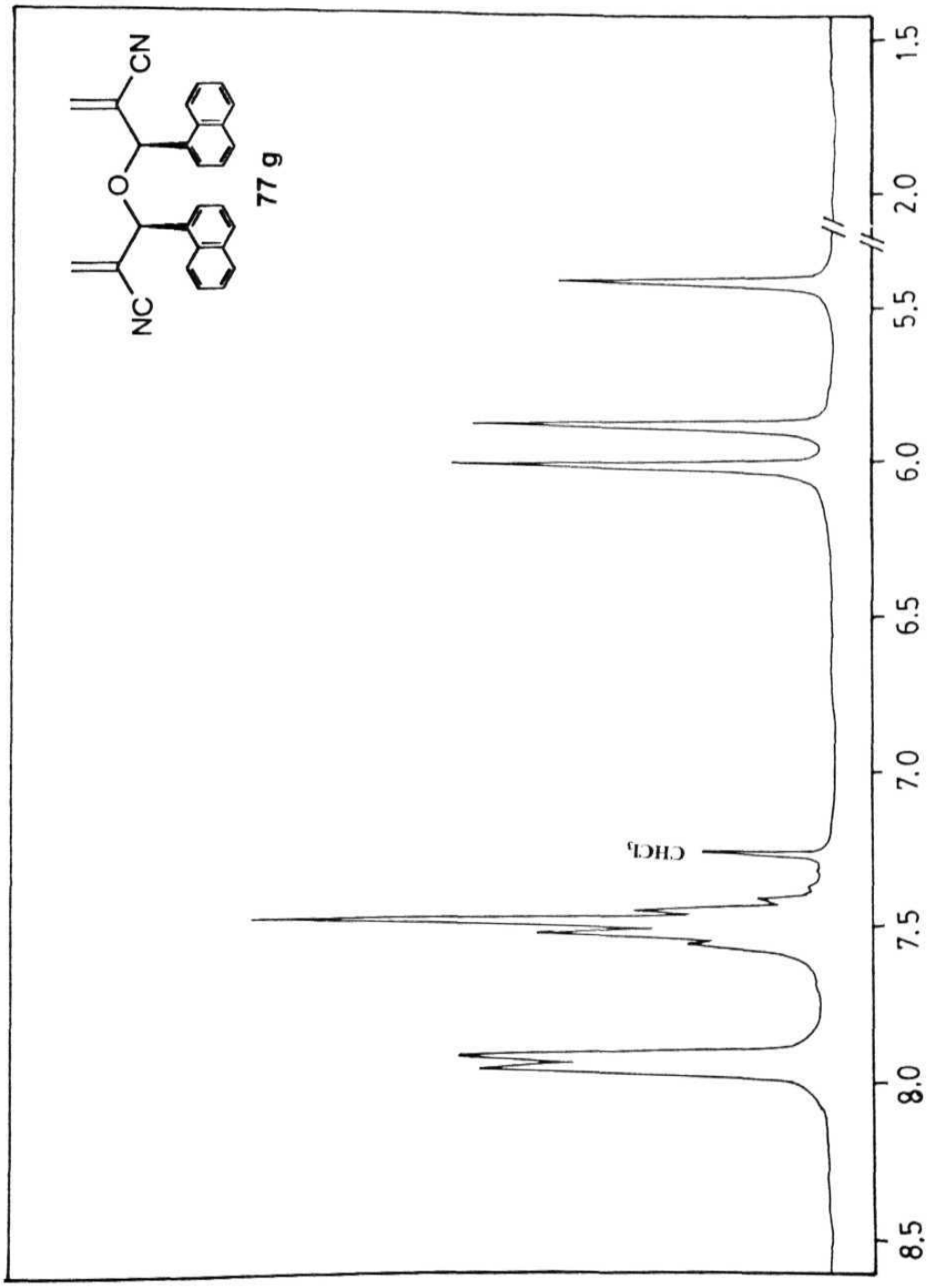


Fig 16: ^{1}H NMR spectrum of **77g**

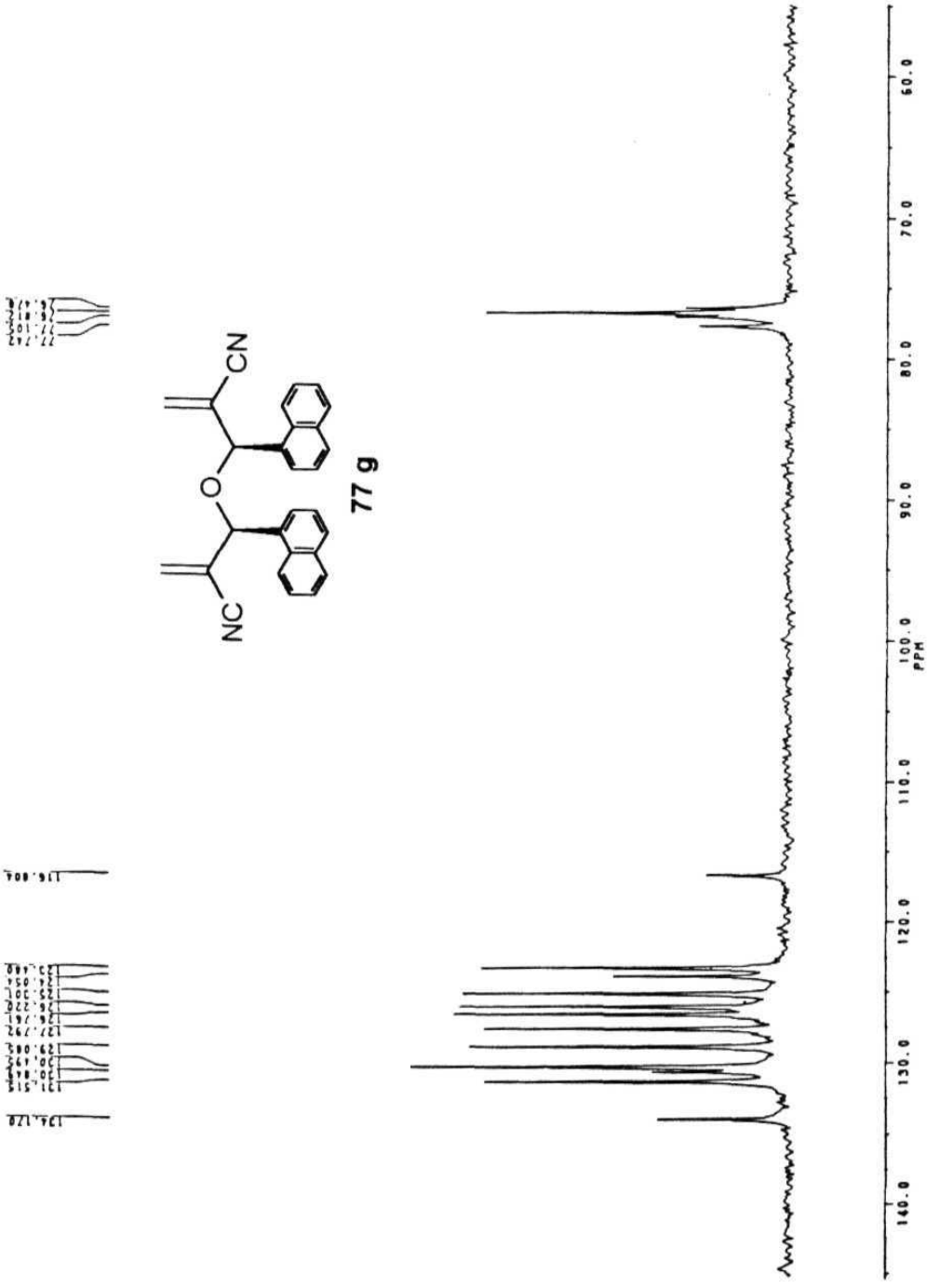


Fig 17: ^{13}C NMR spectrum of **77g**

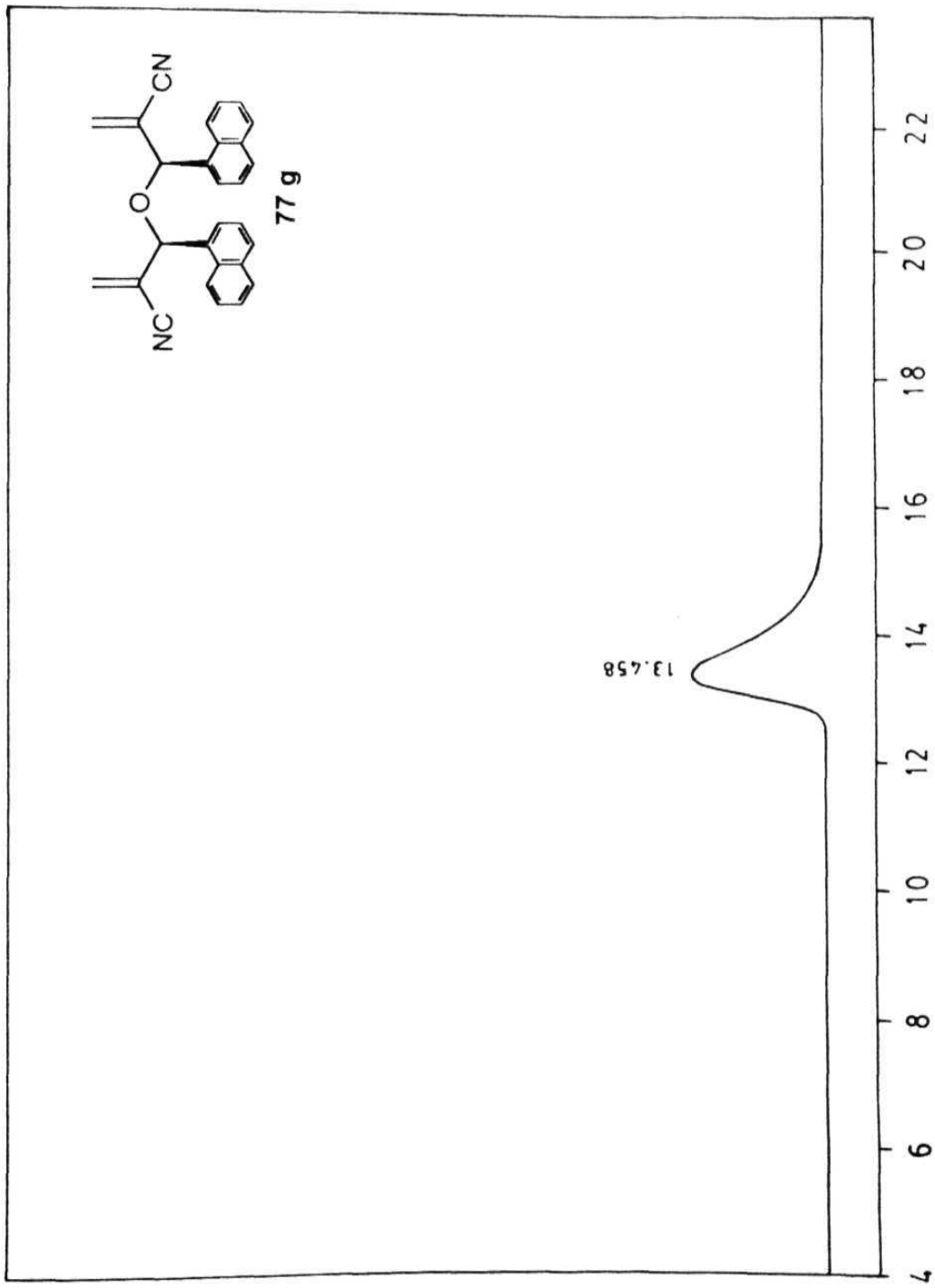


Fig 18: HPLC analysis (Chromatogram of **77g** on CHIRALCEL OD column)

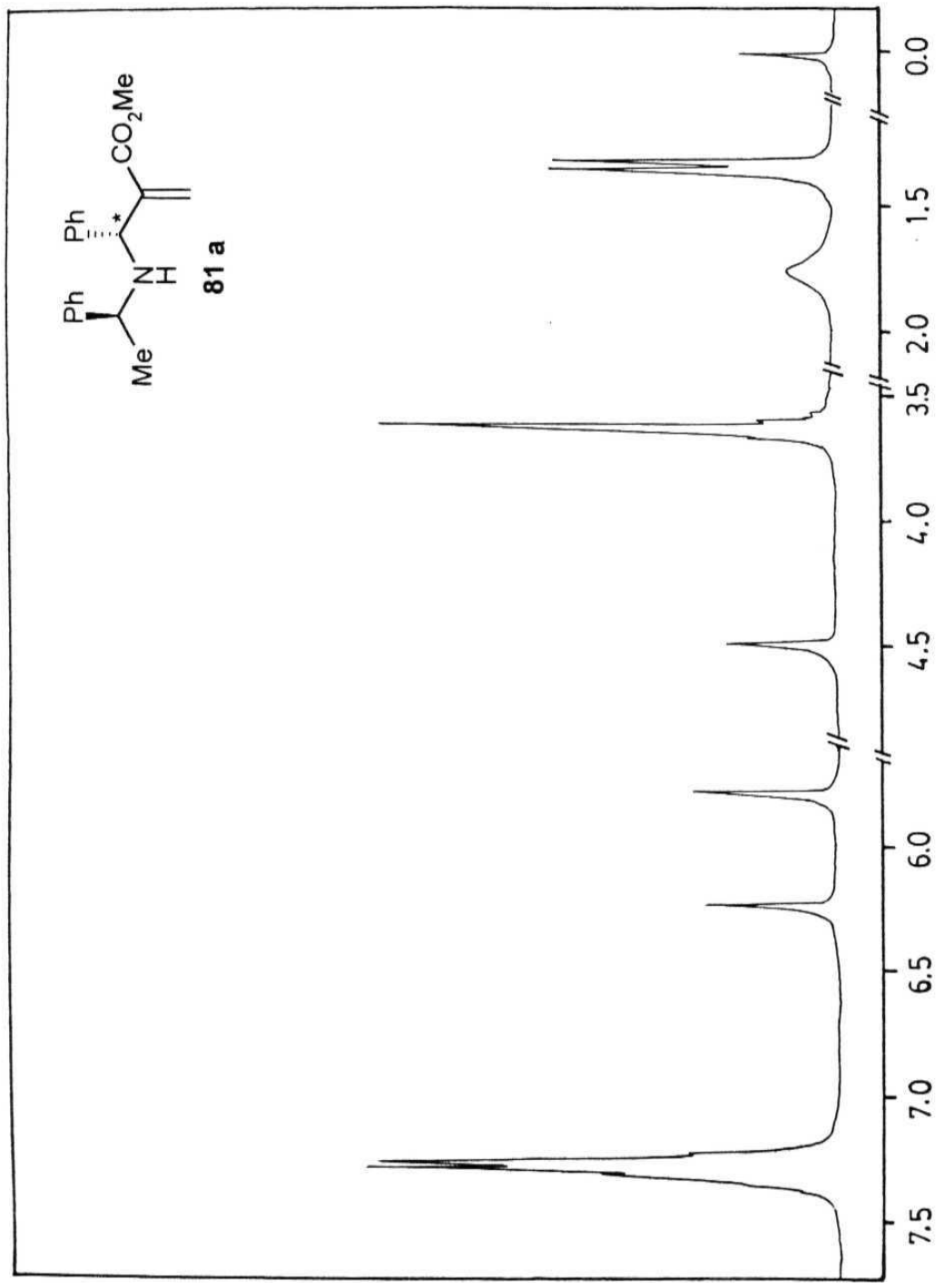


Fig 19: ^{1}H NMR spectrum of **81a**

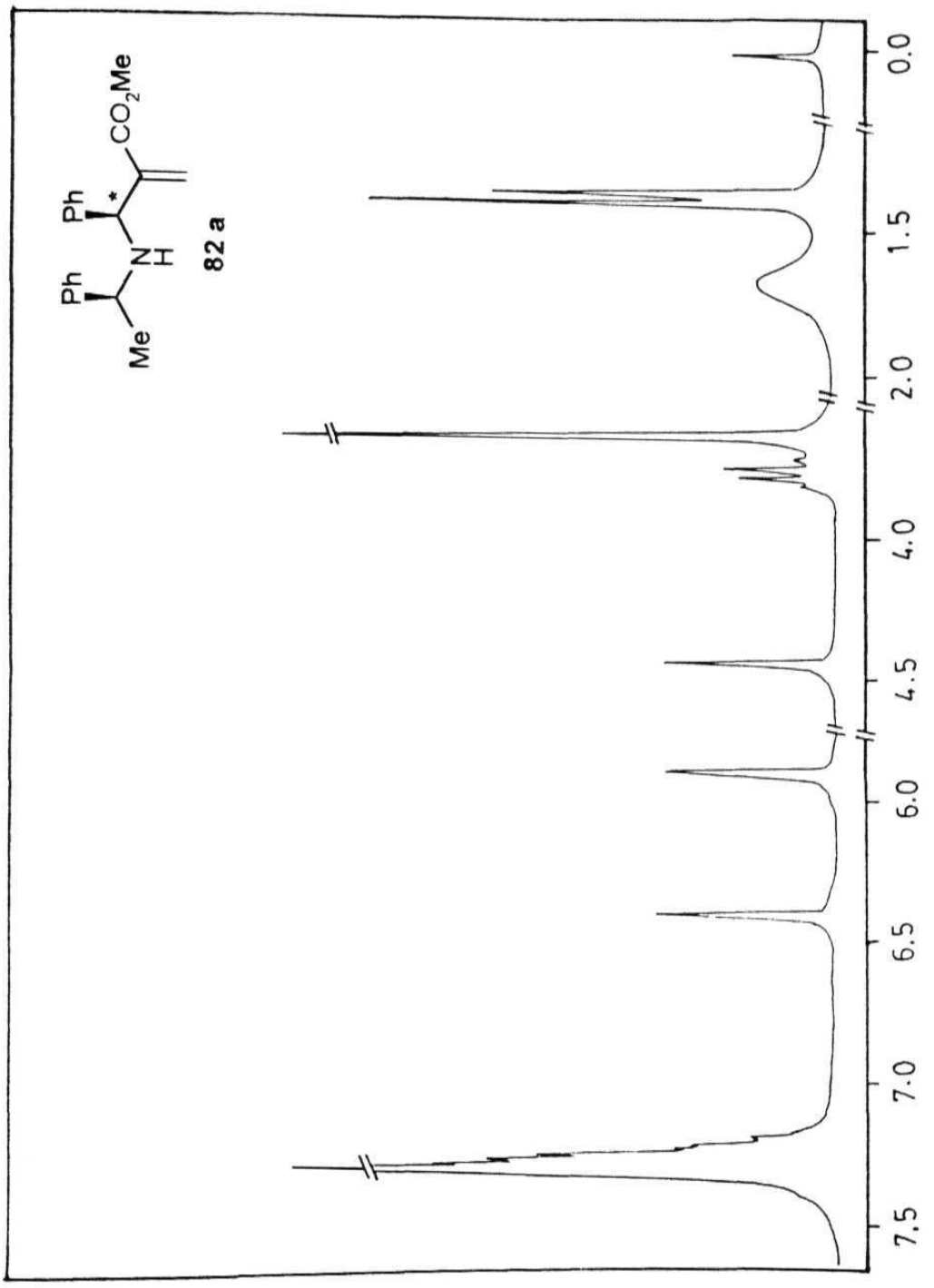


Fig 20: ^{1}H NMR spectrum of **82a**

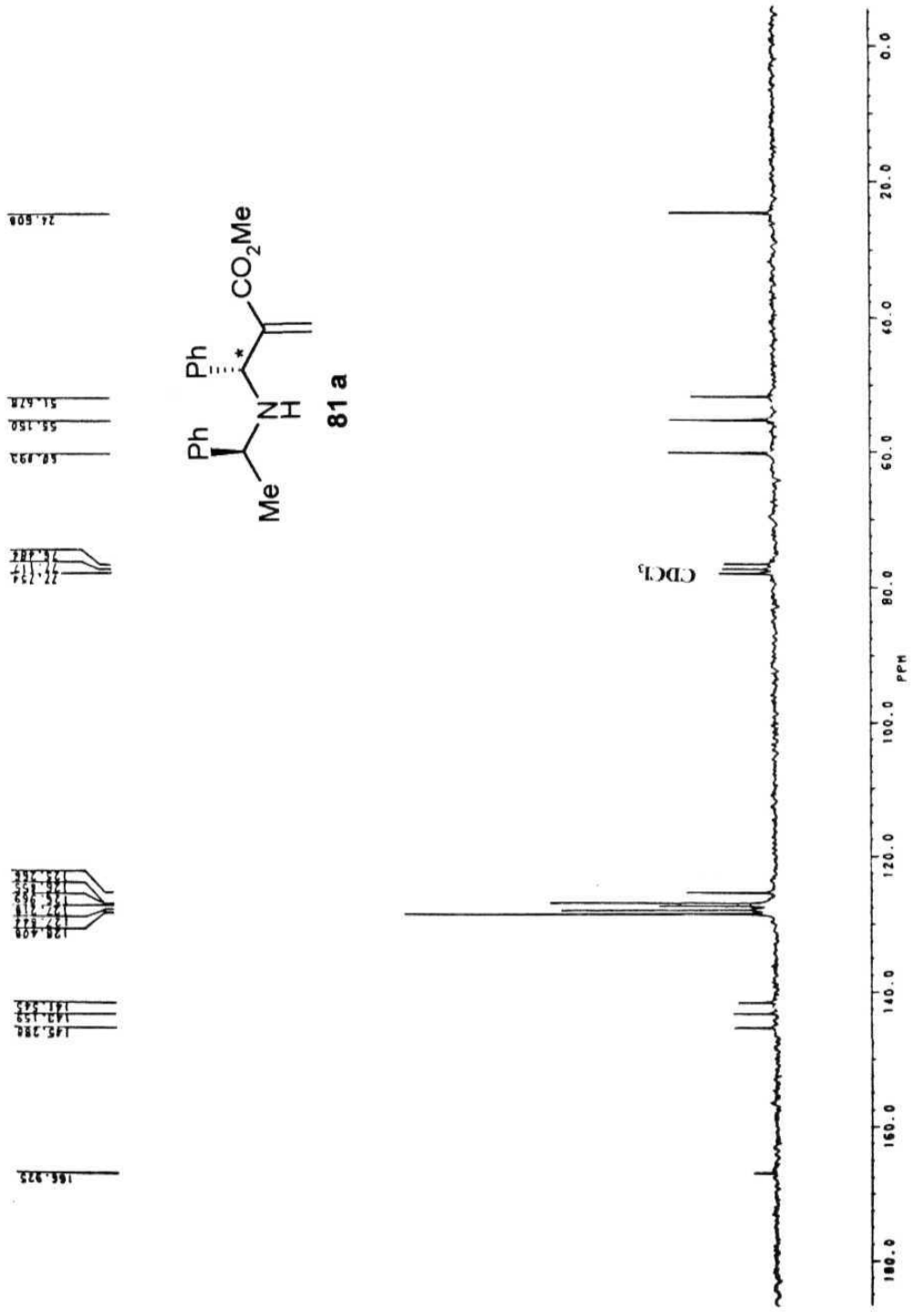


Fig 21: ^{13}C NMR spectrum of **81a**

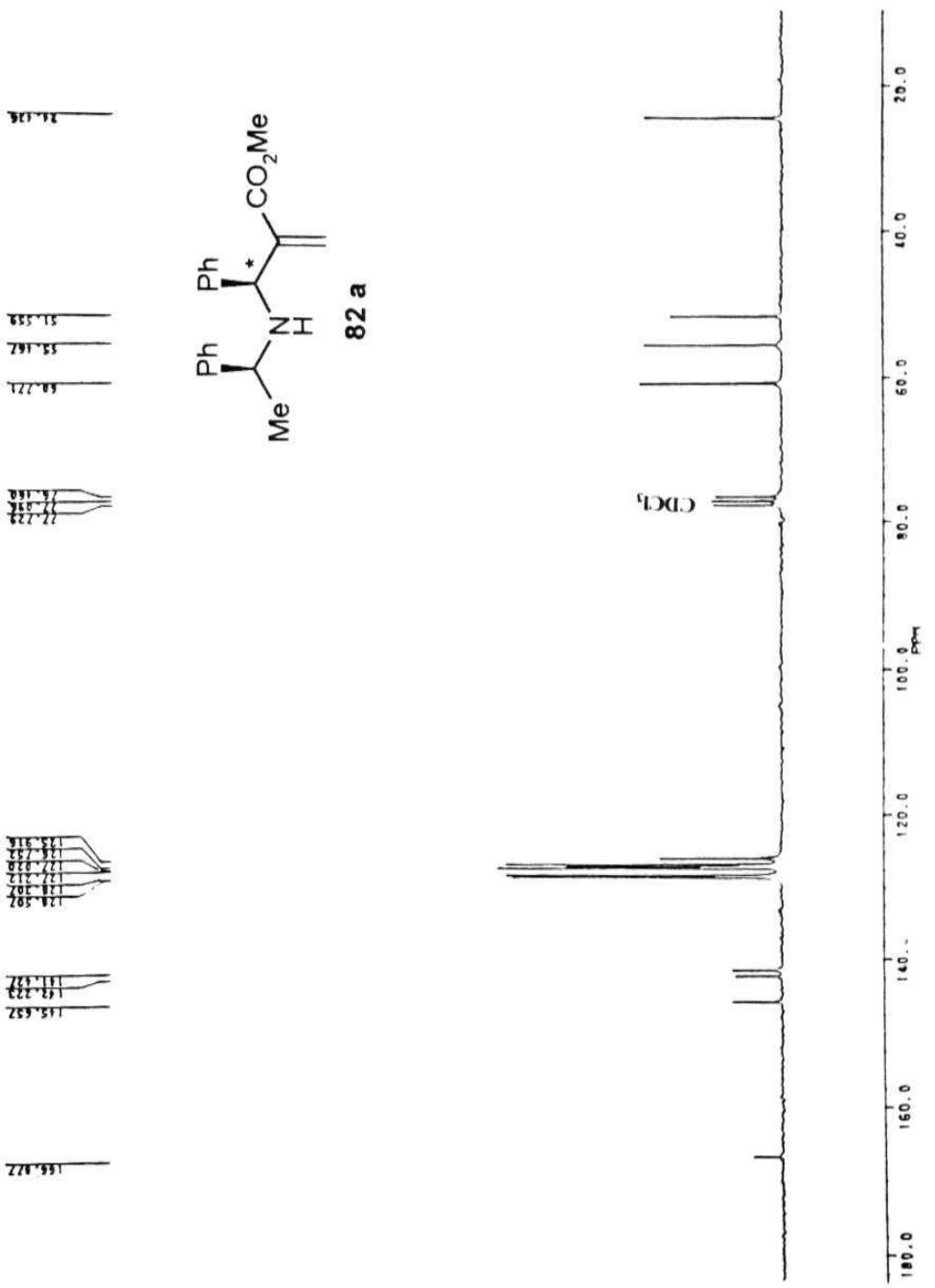


Fig 22: ^{13}C NMR spectrum of **82a**

APPENDIX

(X-Ray Crystallographic Data)

Table A: Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for 72a. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor:

	x	y	z	U(eq)
0(2)	482(3)	5805(3)	1234(1)	57(1)
0(4)	-21(3)	8376(3)	7768(1)	56(1)
0(1)	-3302(3)	7757(3)	1602(2)	60(1)
0(3)	3468(3)	7164(3)	7325(2)	74(1)
C(l)	1609(4)	7643(3)	7063(2)	49(1)
C(2)	851(4)	7514(3)	5958(2)	44(1)
C(3)	-1318(4)	8268(3)	5544(2)	47(1)
C(4)	2190(4)	6607(3)	5143(2)	47(1)
C(5)	-1126(4)	7734(3)	4367(2)	42(1)
C(6)	955(4)	6723(3)	4145(2)	41(1)
C(7)	1578(4)	6023(3)	3112(2)	45(1)
C(8)	85(4)	6384(3)	2289(2)	44(1)
C(9)	-2011(4)	7449(3)	2498(2)	45(1)
C(10)	-2626(4)	8104(3)	3535(2)	48(1)
C(11)	582(5)	8529(5)	8884(2)	72(1)
C(12)	-5315(4)	9007(4)	1715(2)	64(1)
C(13)	2599(4)	4758(4)	975(2)	60(1)

Table B: Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A x 10) for 77a U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
0(1)	5000	9192(2)	2500	**41(1)**
N(l)	4207(1)	8303(2)	-464(1)	65(1)
C(1)	3797(1)	9054(2)	1928(1)	40(1)
C(2)	3129(1)	9735(3)	1274(1)	55(1)
C(3)	2583(1)	8484(3)	1201(1)	64(1)
C(4)	2693(1)	6556(3)	1770(1)	62(1)
C(5)	3354(1)	5870(3)	2424(1)	59(1)
C(6)	3905(1)	7115(2)	2509(1)	48(1)
C(7)	4386(1)	10473(2)	2013(1)	40(1)
C(8)	4289(1)	11305(2)	913(1)	43(1)
C(9)	4264(1)	13404(3)	652(1)	69(1)
C(10)	4243(1)	9641(2)	139(1)	45(1)

Table C: Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for 77b. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
0(1)	1086(2)	8069(1)	4129(1)	44(1)
N(l)	1160(3)	6734(2)	1925(2)	88(1)
N(2)	-2412(3)	6457(3)	4506(2)	93(1)
C(l)	2199(2)	8895(2)	5494(2)	48(1)
C(2)	3029(3)	9311(2)	6069(2)	54(1)
C(3)	3386(2)	8508(2)	7035(2)	52(1)
C(4)	2912(2)	7248(2)	7493(2)	47(1)
C(5)	3180(3)	6426(2)	8532(2)	70(1)
C(6)	2625(4)	5248(3)	8991(2)	86(1)
C(7)	1805(4)	4817(2)	8426(2)	72(1)
C(8)	1552(3)	5568(2)	7418(2)	51(1)
C(9)	2081(2)	6812(2)	6918(2)	41(1)
C(10)	1759(2)	7671(2)	5885(1)	39(1)
C(ll)	941(2)	7222(2)	5224(1)	40(1)
C(12)	-986(2)	7200(2)	5628(2)	45(1)
C(13)	-1937(3)	7534(3)	6458(2)	67(1)

C(14)	-1779(3)	6787(2)	4997(2)	**59(1)**
C(15)	2769(2)	7983(2)	3455(1)	**39(1)**
C(16)	3111(2)	6781(2)	3118(2)	**45(1)**
C(17)	4331(3)	5793(2)	3400(2)	66(1)
C(18)	2018(3)	6751(2)	2457(2)	55(1)
C(19)	2820(2)	9238(2)	2509(1)	**38(1)**
C(20)	1317(2)	10009(2)	2255(2)	47(1)
C(21)	1319(3)	11178(2)	1386(2)	**54(1)**
C(22)	2837(3)	11572(2)	769(2)	53(1)
C(23)	4422(3)	10813(2)	986(2)	45(1)
C(24)	6003(3)	11210(2)	342(2)	57(1)
C(25)	7524(3)	10484(2)	549(2)	62(1)
C(26)	7551(3)	9314(2)	1413(2)	**58(1)**
C(27)	6060(2)	8887(2)	2057(2)	47(1)
C(28)	4435(2)	9627(2)	1866(1)	39(1)

Table D: Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for 77g. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
0(1)	2371(1)	2082(1)	3894(1)	57(1)
N(2)	899(2)	-148(2)	2587(1)	92(1)
N(l)	3698(3)	3514(2)	5612(1)	116(1)
C(l)	4489(2)	1333(1)	3288(1)	48(1)
C(2)	4586(2)	536(1)	3836(1)	57(1)
C(3)	5818(2)	-197(2)	3909(1)	70(1)
C(4)	6970(2)	-146(2)	3428(1)	79(1)
C(5)	6884(2)	634(2)	2881(1)	76(1)
C(6)	5645(2)	1379(1)	2792(1)	60(1)
C(7)	5600(3)	2198(2)	2165(1)	84(1)
C(8)	-18(2)	2538(1)	4418(1)	54(1)
C(9)	308(2)	1716(2)	4941(1)	69(1)
C(10)	-849(3)	1345(2)	5365(1)	86(1)
C(ll)	-2323(3)	1776(2)	5264(2)	97(1)
C(12)	-2670(3)	2577(2)	4746(2)	93(1)
C(13)	-1541(2)	2980(2)	4314(1)	71(1)

C(14)	-1967(3)	3858(2)	3752(2)	112(1)
C(15)	1274(2)	2943(1)	3974(1)	54(1)
C(16)	2140(2)	3900(2)	4340(1)	62(1)
C(17)	2142(4)	4879(2)	4043(2)	105(1)
C(18)	3012(3)	3697(2)	5053(1)	75(1)
C(19)	3115(2)	2118(1)	3216(1)	47(1)
C(20)	1892(2)	1827(1)	2578(1)	48(1)
C(21)	1329(3)	2509(2)	2052(1)	75(1)
C(22)	1311(2)	733(2)	2581(1)	58(1)

Table E: Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for **81a.** U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
0(2)	1803(7)	7406(3)	6444(2)	58(1)
NO)	6499(8)	5376(4)	5168(2)	50(1)
0(1)	635(7)	5983(4)	5971(3)	72(1)
CO)	3466(10)	3888(5)	6265(3)	59(2)
C(2)	3568(14)	3270(6)	6852(4)	76(2)

C(3)	4759(14)	3532(7)	7392(4)	76(2)
C(4)	5936(14)	4385(7)	7361(4)	78(2)
C(5)	5868(12)	4995(6)	6773(3)	67(2)
C(6)	4633(9)	4748(5)	6219(3)	47(1)
C(7)	4613(9)	5403(4)	5562(3)	45(1)
C(8)	3989(8)	6480(5)	5730(3)	43(1)
C(9)	5083(11)	7282(5)	5582(4)	65(2)
C(10)	1968(10)	6582(4)	6055(3)	48(1)
C(U)	-123(12)	7566(5)	6753(4)	72(2)
C(12)	9112(11)	4400(7)	4596(4)	73(2)
C(13)	6978(10)	4383(5)	4878(3)	51(2)
C(14)	5491(9)	4112(4)	4308(3)	45(1)
C(15)	4652(11)	3157(5)	4264(3)	58(2)
C(16)	3377(13)	2901(6)	3728(4)	73(2)
C(17)	2927(12)	3592(6)	3227(4)	71(2)
C(18)	3725(14)	4550(6)	3262(4)	74(2)
C(19)	5001(12)	4792(5)	3803(3)	66(2)

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