Towards the Synthesis of Chromanone and Benzochromanone Frameworks Using the Baylis-Hillman Bromides

A THESIS SUBMITTED FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY

BY

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Dedicated to

Lalithambika

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

OCTOBER 2008 **PANDRANGI ANUPAMA**

CERTIFICATE

Certified that the work embodied in this thesis entitled **"Towards the Synthesis of Chromanone and Benzochromanone Frameworks Using the Baylis-Hillman Bromides"** has been carried out by Miss. P. ANUPAMA, under my supervision and the same has not been submitted elsewhere for a degree.

Professor D. BASAVAIAH

(Thesis Supervisor)

DEAN

SCHOOL OF CHEMISTRY

UNIVERSITY OF HYDERABAD

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Pandrangi Anupama

ABBREVIATIONS

Ac	acetyl
AIBN	azobisisobutyronitrile
aq.	aqueous
BINOL	1,1'-bi-2-naphthol
Bn	benzyl
Bp	boiling point
n-Bu or Bu^n	*n*-butyl
i-Bu or Bu^i	*iso*-butyl
s-Bu or Bu^s	*secondary*-butyl
t-Bu or Bu^t	*teritiary* butyl
cat.	catalyst
mCPBA	*meta*-chlorobenzoic acid
CSA	10-camphorsulfonic acid
cy	cyclo
DABCO	1,4-diazabicyclo(2.2.2)octane
DBU	1,8-diazabicyclo(5.4.0)undec-7-ene
dba	dibenzylidene acetone
DCE	dichloroethane
DCM	dichloromethane
de	diastereomeric excess

DMAP	4-(dimethylamino)pyridine
DMS	dimethyl sulfide
DMSO	dimethyl sulfoxide
DMF	N,N-dimethylformamide
ee	enantiomeric excess
Et	ethyl
EWG	electron withdrawing group
n-Hex	*n*-hexyl
c-Hex	cyclohexyl
3-HQD	3-hydroquinuclidine
Me	methyl
Mp	melting point
MS	molecular sieves
MsCl	mesyl chloride
MVK	methyl vinyl ketone
PCC	pyridinium chlorochromate
Ph	phenyl
PPTS	pyridinium p-toluenesulfonate
Pr	*n*-propyl

i-Pr or Pr^i	*iso*-propyl
py	pyridine
rt	room temperature
TBAB	tetrabutyl ammonium bromide
THF	tetrahydrofuran
TFA	trifluoroacetic acid
TFAA	trifluoroacetic anhydride
TMG	tetramethylguanidine
TMSOTf	trimethylsilyl trifluoromethanesulfonate
Triton B	dimethyl benzyl-acetyl-ammonium hydroxide
TsOH or *p*-TSA	*para*-toluenesulfonic acid

ABSTRACT

Organic chemistry, particularly synthetic organic chemistry, has become one of the most powerful and important branches of science. Construction of carbon-carbon bond indeed occupies the most important place in organic chemistry due to its fundamental role in building and assembling various structural carbon frameworks to provide all kinds of natural and unnatural molecules including the most complex molecules. The evolving trends in organic chemistry particularly in synthetic organic chemistry clearly emphasize the need for discovering novel and efficient carbon-carbon bond forming reactions involving the concepts of selectivity, that is, constructing a carbon-carbon bond at the required place in a substrate which has more than one competing sites for the formation of carbon-carbon bonds. For easy understanding let us consider methyl vinyl ketone (MVK) as a substrate for constructing carbon-carbon bonds. There are five sites where one can construct carbon-carbon bonds and there are methods available in the literature for the construction of C-C bonds at the required places.

Another important requirement in the present day context of organic chemistry is the concept of atom-economy. This concept has gained unique importance and in fact, has become one of the essential requirements for development of any novel C-C bond forming reactions. The Baylis Hillman reaction is one such carbon-carbon bond forming reaction developed in recent years well equipped with the concept of selectivity and atom-economy. Thus this reaction provides the procedure to construct carbon-carbon bonds at α-position of activated alkenes (like methyl vinyl ketone) in atom-economical

fashion and indeed this reaction has become one of the most powerful synthetic tools for construction of carbon-carbon bonds. This thesis deals with the studies towards development of novel methodologies for synthesis of oxygen heterocycles using the Baylis-Hillman adducts and consists of three chapters, that is, 1. Introduction 2. Objectives, Results and Discussion 3. Experimental.

In the first chapter, a brief literature survey on the developments and recent applications of the Baylis-Hillman reaction is described.

The second chapter deals with objectives, results and discussions and describes our studies towards the application of the Baylis-Hillman bromides in synthesis of heterocyclic compounds containing oxygen in the ring with the following main objectives.

Objectives:

1) To develop a novel and facile methodology for the synthesis of tetrahydrodipyrandione derivatives [7,12-bisarylidene-5,14-dioxatricyclo[8.4.0.$0^{4,9}$]tetradeca-1,3,9-triene-8,11-dione] using the Baylis-Hillman bromides as starting materials.

2) To develop a simple methodology for the synthesis of 7:8-benzochroman-4-one frameworks using the Baylis-Hillman bromides as synthons.

3) To develop facile methodology for the synthesis of 5:6-benzochroman-4-one derivatives using the Baylis-Hillman bromides as starting materials.

A facile synthesis of tetrahydrobenzodipyrandiones from the Baylis-Hillman bromides:

Tetrahydrobenzodipyrandione framework has attracted the attention of organic chemists because some of these compounds possess interesting psychotropic, antithrombic and

antihistaminic properties. The medicinal importance of these compounds containing tetrahydrobenzodipyrandione framework has attracted our attention and we have therefore developed a simple methodology for synthesis of these frameworks (**80a-h**) starting from the Baylis-Hillman bromides (**82a-h**) (Schemes 35-38, and 40)

Development of facile synthesis of 7:8-benzochroman-4-one frameworks from Baylis-Hillman bromides:

The 7:8-benzochroman-4-one derivatives occupy an interesting place in the class of oxygen heterocyclic chemistry because of presence of this framework in a number of biologically active natural products. Fascinated by the medicinal importance of these derivatives, we have developed simple methodologies for obtaining 7:8-benzochroman-4-one (**99a-g**) using Baylis-Hillman bromides and 1-naphthol (Schemes 46 and 48).

Novel and facile synthesis of 5:6-benzochroman-4-one frameworks using Baylis-Hillman bromides:

The 5:6-benzochroman-4-one framework is another important skeleton has attracted the attention of organic and medicinal chemists owing to the antimicrobial activity against trichomonads, gram-positive and gram-negative bacteria and fungi. We have therefore developed a facile methodology for obtaining 5:6-benzochroman-4-one frameworks (**108a-e,h**) using the Baylis-Hillman bromides and 2-naphthol (Schemes 53 and 54, Eqs. 30 and 31).

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

LIST OF PUBLICATIONS

(1) A facile synthesis of tetrahydrobenzodipyrandiones from the Baylis-Hillman adducts

D. Basavaiah, and **Pandrangi Anupama** *(to be communicated)*.

(2) Novel and facile synthesis of benzochromanones using Baylis-Hillman adducts

D. Basavaiah, and **Pandrangi Anupama** *(to be communicated)*.

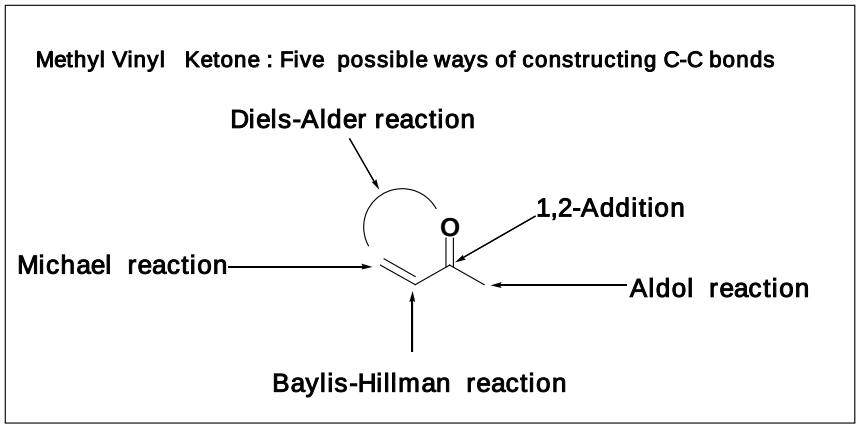
INTRODUCTION

Organic chemistry, particularly synthetic organic chemistry, has become one of the most powerful and important branches of science. Construction of carbon-carbon bond indeed occupies the most important place in organic chemistry due to its fundamental role in building and assembling various structural carbon frameworks to provide all kinds of natural and unnatural molecules including the most complex molecules.[1] The evolving trends in organic chemistry particularly in synthetic organic chemistry[1] clearly emphasize the need for discovering novel and efficient carbon-carbon bond forming reactions involving the concepts of selectivity, that is, constructing a carbon-carbon bond at the required place in a substrate which has more than one competing sites for the formation of carbon-carbon bonds. For easy understanding let us consider methyl vinyl ketone (MVK) as a substrate for constructing carbon-carbon bonds. There are five sites where one can construct carbon-carbon bonds (Fig. 1) and there are methods available in the literature for the construction of C-C bonds at the required places.[2-6]

Another important requirement in the present day context of organic chemistry is the concept of atom-economy. This concept has gained unique importance and in fact, has become one of the essential requirements for development of any novel C-C bond forming reactions. The Baylis Hillman reaction is one such carbon-carbon bond forming reaction developed in recent years well equipped with the concept of selectivity and atom-economy. Thus this reaction provides the procedure to construct carbon-carbon bonds at α-position of activated alkenes (like methyl vinyl ketone) in atom-economical

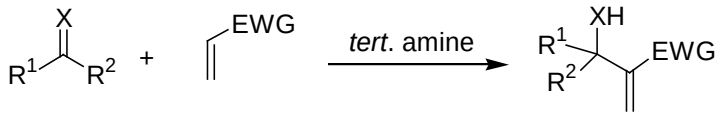
fashion and indeed this reaction has become one of the most powerful synthetic tools for construction of carbon-carbon bonds.

Fig. 1



The Baylis-Hillman reaction

This reaction has its origin to a German patent filed in 1972 by A. B. Baylis and M. E. D. Hillman.[6] This is a three component reaction essentially involving the coupling of α-position of an activated alkene with an electrophile under the influence of a catalyst (or catalytic system) particularly a teritiary amine [most commonly DABCO (**1**)] leading to the formation of densely functionalized molecules in an operationally simple one-pot atom economy procedure (Eq. 1).[7-11]



Eq. 1

R^1 = aryl, alkyl, aralkyl, heteroaryl

R^2 = H, alkyl, COOR

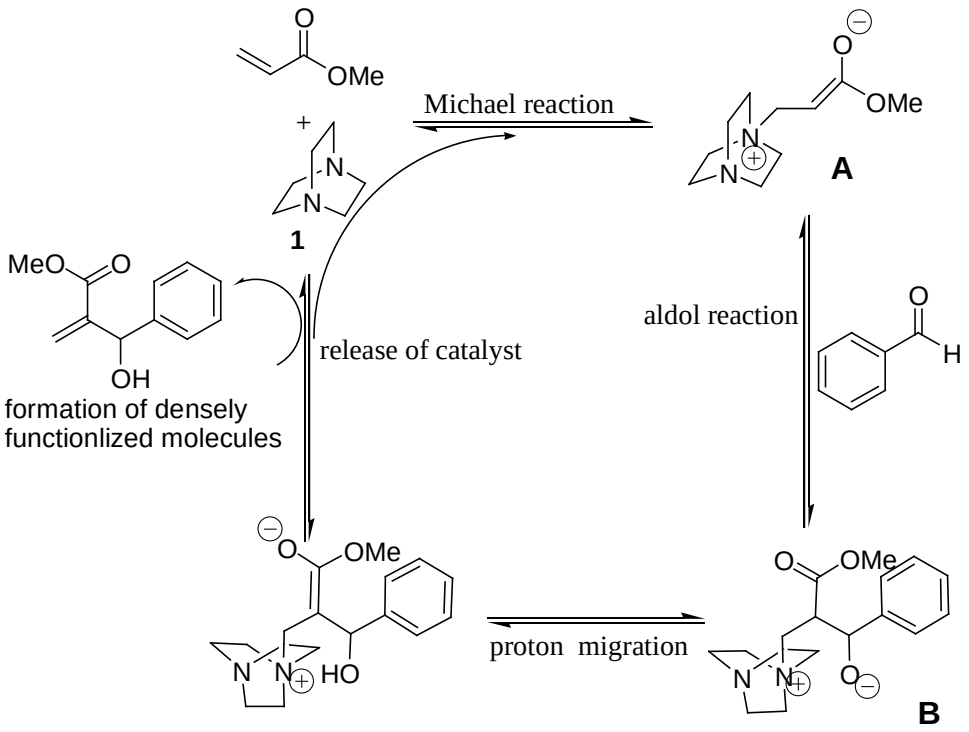
X = O, NCOOR, NTs, NSO_2Ph

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

MECHANISM:

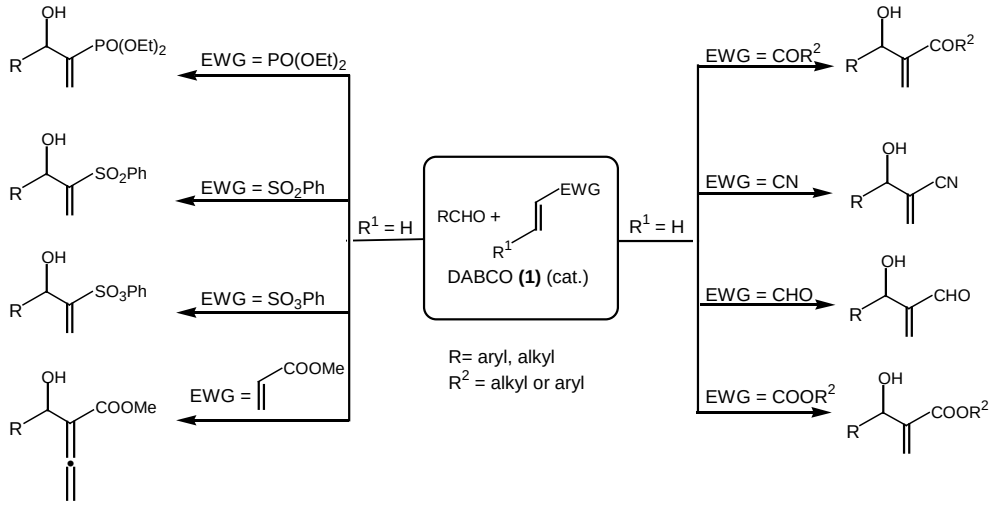
The development of any reaction, in fact, depends on understanding the stepwise process, that is, mechanistic path way(s).[12-20] The exact mechanism of this fascinating reaction is not yet clearly understood due to the large variety of substrates and several classes of catalysts employed in this reaction and also due to the reaction complexities involved. Although exact reaction path way(s), is not yet understood, the widely accepted mechanism of the amine-catalyzed reaction based on the present level of understanding is depicted pictorially in the Scheme 1 taking the reaction between methyl acrylate (as an activated olefin) and benzaldehyde (as an electrophile) under the catalytic influence of DABCO (**1**) (as a catalyst) as a model case.[12-20] This reaction is believed to involve at least four steps 1) the Michael reaction 2) aldol reaction 3) proton migration 4) release of catalyst and formation of densely functionalized molecules. Thus the first step in this catalytic cycle might involve the Michael type nucleophilic addition of the tertiary amine to activated alkene (methyl acrylate) to produce a zwitterionic enolate **A**. This enolate subsequently might add on to the aldehyde (benzaldehyde) leading to the aldol type adduct, that is, zwitterion **B**, which subsequently releases the catalyst after undergoing proton transfer leading to the generation of highly functionalized molecules. These molecules are commonly referred to as the Baylis-Hillman adducts (Scheme 1).

Scheme 1



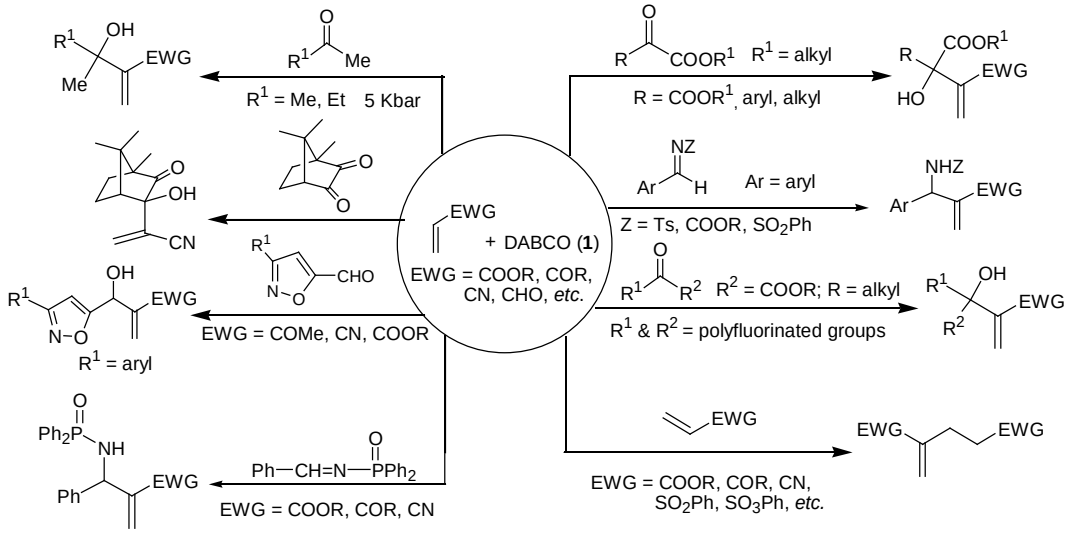
During the past two decades the Baylis-Hillman reaction has grown exponentially and now reached the status of being one of the most important useful carbon-carbon bond forming reactions in organic chemistry as demonstrated by more than 1300 research publications, five major reviews,[7-11] many mini reviews.[21-27] There is a vast literature available now describing the applications of various activated alkenes, electrophiles and catalysts for performing the Baylis-Hillman reactions.[7-11, 21-27] Thus various activated alkenes such as alkyl acrylates, acrylonitrile, alkyl vinyl ketones, acrylamides, vinyl sulfones, vinly sulfonates, vinyl phosphinates, cyclic alkenones, nitroalkenes, β-substituted alkenes *etc.*, have been employed for coupling with several electrophiles.[7-11,27] Selected examples are given in Scheme 2.[7-11]

Scheme 2



Although aldehydes have been the most commonly used electrophiles several other electrophiles such as α-keto esters, fluoro ketones, aldimine derivatives, activated alkenes, *N*-benzylidenediphenylphosphinamide, non-enolizable 1,2-diketones, azodicarboxylates *etc.*, were successfully employed for coupling with various activated alkenes. [7-11,27] Representative examples are given in Scheme 3.[7-11]

Scheme 3



In addition to DABCO several other tertiary amine catalysts such as DBU, DMAP, imidazole, trimethyl amine (aqueous or methanolic solution), quinuclidine, TMG, azoles and triazoles, urotropine *etc*. have been used to catalyze or perform the Baylis-Hillman reaction. Also several non-amine catalysts such as phosphines, chalcogenides in combination with Lewis-acids such as $TiCl_4$, $BF_3.OEt_2$, BBr_3, Lewis acid like $TiCl_4$, and bases like sodium methoxide (methoxide ion) *etc*. have been employed for the coupling of activated alkenes with electrophiles to provide multi-functional molecues. [7-11, 21-27]

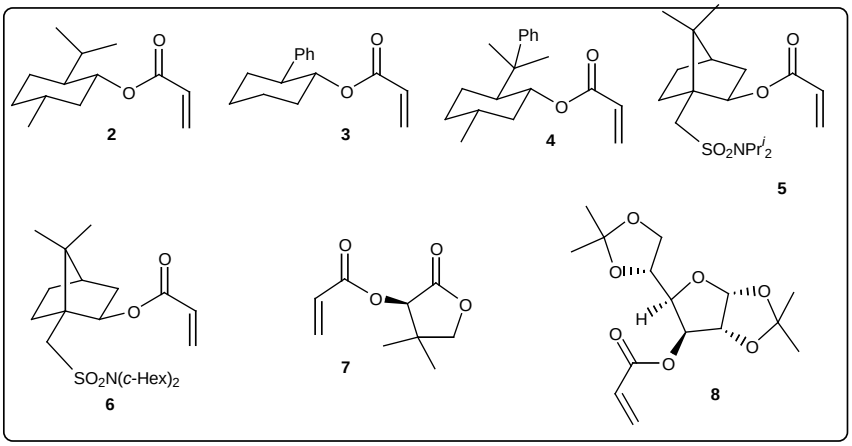
Asymmetric Baylis-Hillman reaction

If the electrophile is prochiral, a chiral center is generated in the product and hence there exists a possibility of developing its asymmetric version. This can in principle be achieved in four different ways 1) using chiral activated alkene 2) chiral electrophile 3) chiral catalyst 4) chiral solvent or additive. Organic chemists have been actively involved in these directions and obtained reasonable success in all these angles. Some of the important recent developments are described in this section.

CHIRAL ACTIVATED ALKENES:

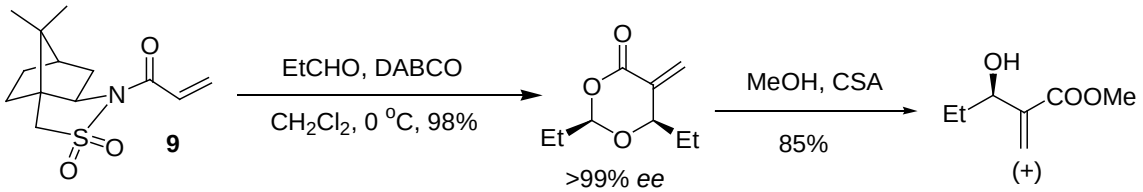
Asymmetric version of the the Baylis-Hillman reaction using chiral activated alkenes has been systematically studied. Thus various chiral acrylates (**2-8**) (Fig. 2)[28-34] derived from various chiral auxiliaries such as cyclohexanol derivatives (**2-4**),[28,29,31] camphor derivatives (**5 & 6**),[28-30] (*R*)–(+)-pentalactone (**7**),[32,33] and sugar derivative (**8**)[34] have been employed in the Baylis-Hillman reaction to provide the resulting adducts in low to moderate diastereoselectivities.

Figure 2

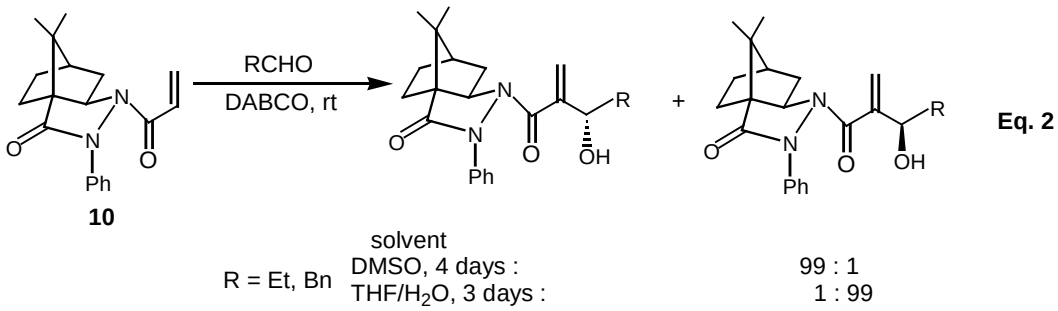


Leahy and coworkers[35] have successfully used enantiopure acrylamide (**9**), derived from (1*S*)-(+)-10-camphorsulphonic acid, as a chiral activated alkene in the Baylis-Hillman reaction with various aldehydes to provide the resulting Baylis-Hillman adducts in high enantioselectivities (> 99% ee). One representative example is shown in Scheme 4.

Scheme 4



Enantiomerically pure acryloylhydrazide (**10**) has been employed for Baylis-Hillman coupling with various aldehydes under the influence of DABCO by Yang and Chen[36] to provide the resulting Baylis-Hillman adducts in very high diastereoselectivities. A remarkable reversal in stereoselectivity has been observed by changing solvent system from DMSO to THF / H_2O. Representative examples are described in Eq. 2.

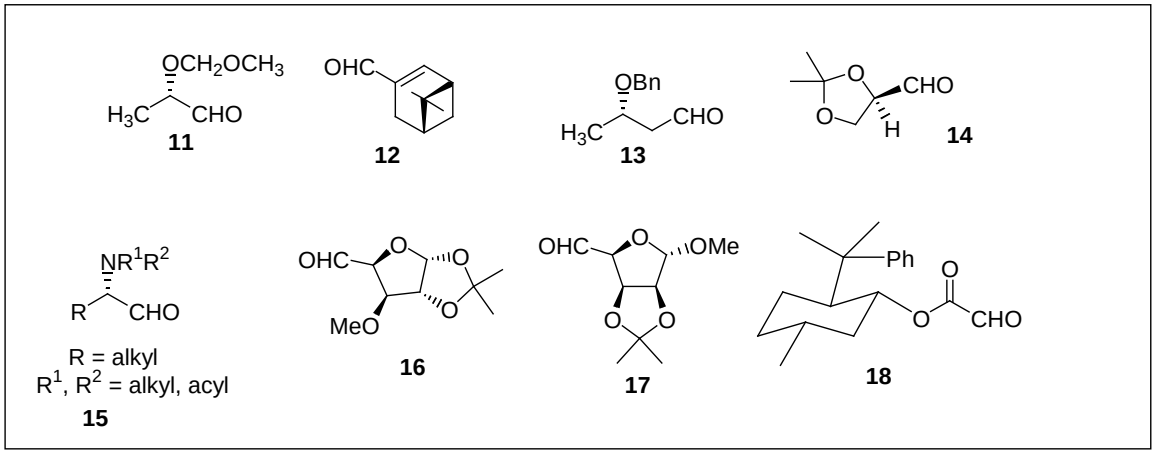


Eq. 2

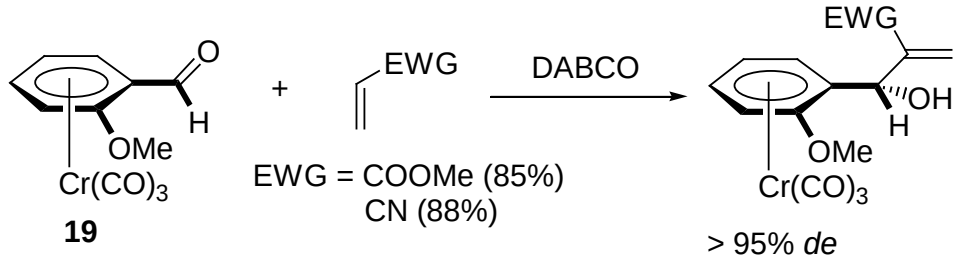
CHIRAL ELECTROPHILES:

Various chiral electrophiles such as (*S*)-*O*-(methoxymethyl)lactaldehyde (**11**),[37] (*R*)-myrtenal (**12**),[31] (*S*)-3-benzyloxybutyraldehyde (**13**),[38] isopropylidene (*R*)-glyceraldehyde (**14**),[31] α-dialkylamino and α-(*N*-acylamino)aldehydes (**15**),[39,40] sugar derived aldehydes (**16 & 17**)[41,42] and 8-phenylmenthylglyoxal (**18**)[43] *etc.*, (Fig. 3), have been successfully used for Baylis-Hillman coupling with various activated alkenes to afford the resulting alcohols with low to high diastereoselectivities.

Figure 3

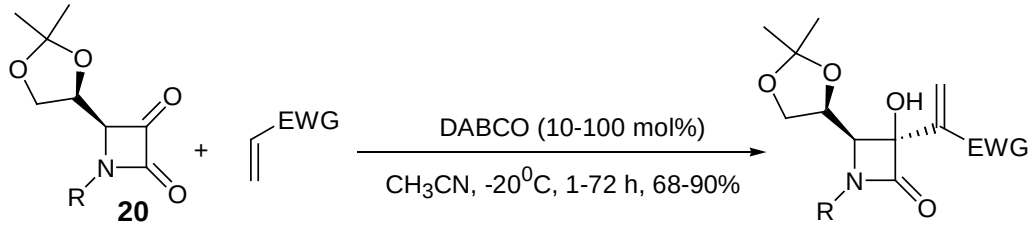


Ortho substituted benzaldehyde tricarbonylchromium complex (**19**) has been employed as an electrophile in the Baylis-Hillman reaction with various activated olefins under the influence of DABCO to afford the desired Baylis-Hillman adducts in >95% *de* by Kundig and coworkers.[44] One representative example is presented in Eq. 3.



Eq. 3

Alcaide and coworkers[45] have successfully employed enantiopure 3-oxo-2-azetidinones (**20)** for Baylis-Hillman coupling with activated alkenes to provide the resulting products in high diastereoselectivities (Eq. 4).



Eq. 4

R = 4-(OMe)C_6H_4, allyl, propargyl
EWG = COMe, COOMe, CN

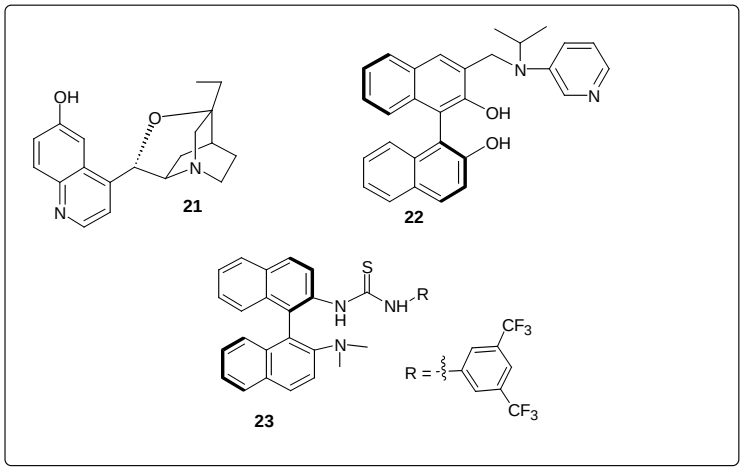
EWG = COMe, COOMe; dr = 100:0
EWG = CN dr = 97:3

CHIRAL CATALYSTS:

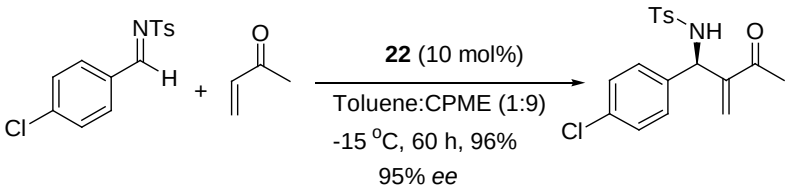
In the case of chiral activated alkenes and electrophiles, the resulting products contain the chiral auxiliary and in order to obtain the required Baylis-Hillman adducts the chiral auxiliary has to be removed. Though the chiral activated alkenes and electrophiles provide the desired Baylis-Hillman adducts (after the removal of chiral auxiliary) with

high enantioselectivities, the actual challenge lies in the development of efficient chiral catalysts for performing the asymmetric Baylis-Hillman reaction.[7-11] Considerable attention has been paid towards developing asymmetric version of Baylis-Hillman reaction using various chiral catalysts. Selected important catalysts (**21**-**23**)[46-48] which gave high enantioselectivities are listed in Fig. 4.

Figure 4



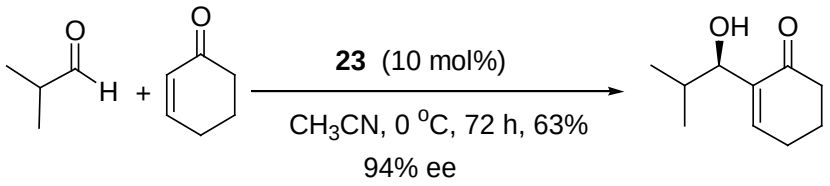
A novel BINOL based bifunctional organocatalyst (**22**) was developed by Sasai and coworkers[47] for high enantioselective Baylis-Hillman reaction of various *N*-tosylimines with MVK. One representative example is described in Eq. 5.



Eq. 5

Recently, Wang and coworkers[48] reported a bifunctional binaphthyl-derived amine thiourea organocatalyst (**23**) to be an efficient catalyst for enantioselective Baylis-Hillman reaction of cyclohex-2-en-1-one with various aldehydes to afford the resulting

adducts in good yields with high enantioselectivites. One representative example is described in Eq. 6.

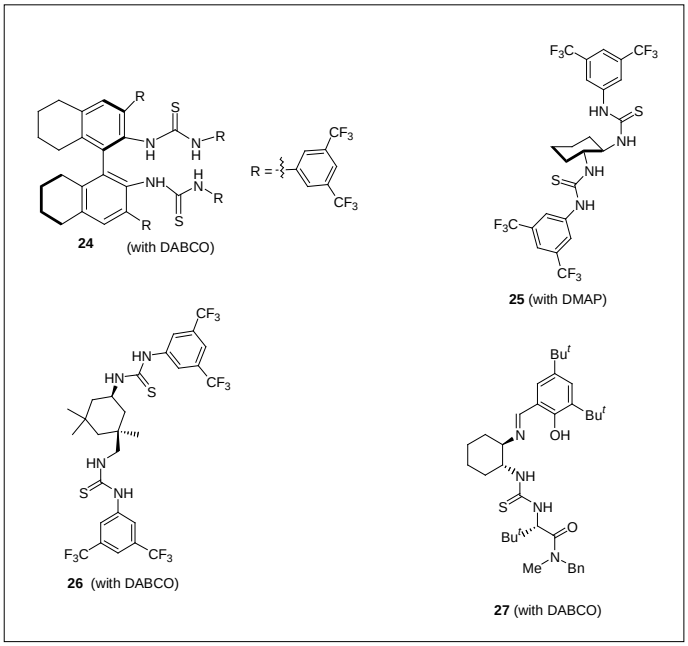


Eq. 6

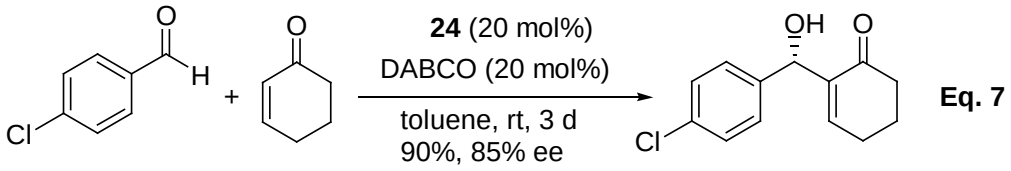
CHIRAL CATALYTIC SOURCES / ADDITIVES

Several chiral catalytic sources / additives, such as, thiourea derivatives (**24-27**)[49-52] were used as chiral additives (along with the catalysts) to perform asymmetric Baylis-Hillman reaction (Fig. 5).

Figure 5



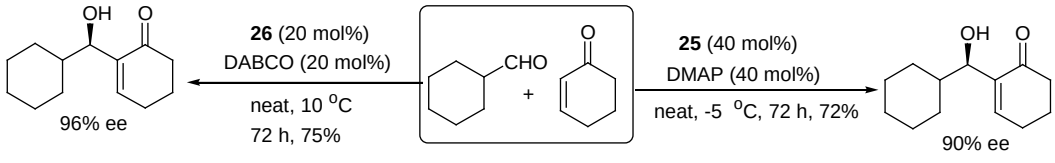
Very recently, Shi and coworkers[49] developed effective asymmetric Baylis-Hillman reaction involving the addition of cyclohex-2-en-1-one or cyclopent-2-en-1-one to aromatic aldehydes catalyzed by bis(thio)urea organocatalyst (**24**) and DABCO. The corresponding adducts were obtained in good to excellent yields and moderate to good enantiomeric excesses up to 88% ee under mild conditions (one example is given in Eq. 7).



Eq. 7

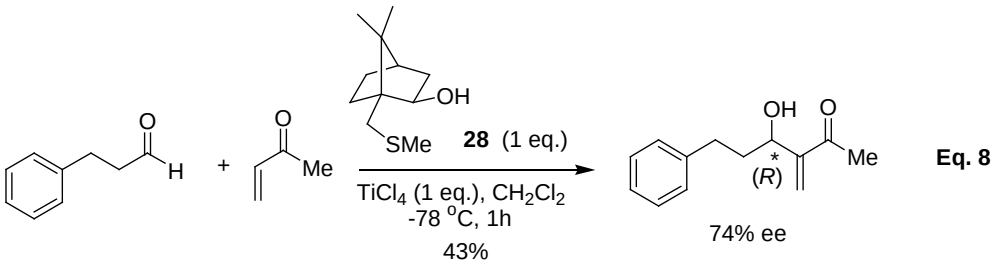
Nagasawa and Berkessel research groups,[50,51] independently designed and synthesized, cyclohexane based thiourea derivatives (**25**) and (**26**) respectively and successfully employed them as efficient co-catalysts for Baylis-Hillman reaction of various aldehydes with cyclohex-2-en-1-one to afford the corresponding allyl alcohols with high enantioselectivities. Representative examples are given in Scheme 5.

Scheme 5



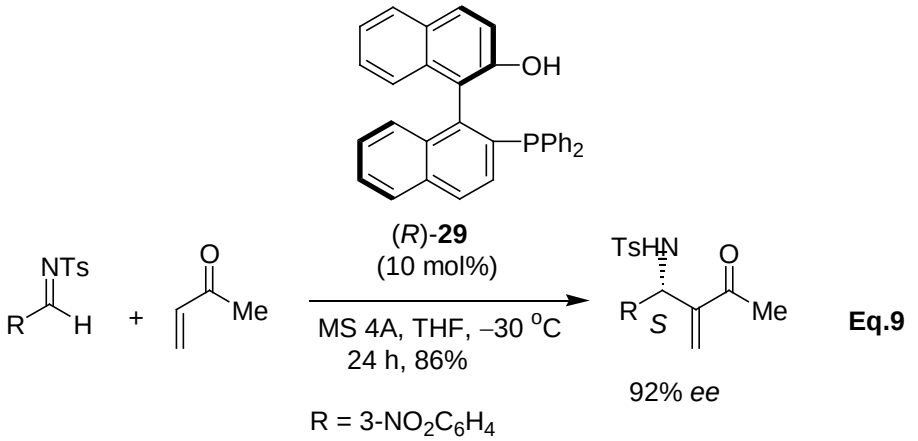
Non-amine catalysts mediated asymmetric Baylis-Hillman Reactions:

Kataoka and co-workers[53] have reported an interesting asymmetric chalcogeno-Baylis-Hillman reaction with enantiopure hydroxy chalcogenides as catalysts. One representative example [reaction between hydrocinnamaldehyde and MVK in the presence of 10-methylthioisoborneol (**28**)] is presented in Eq. 8.



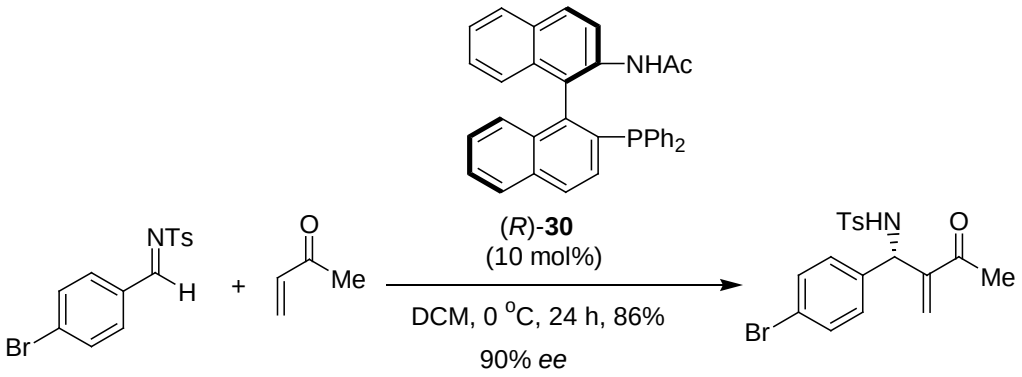
Eq. 8

Shi and Chen[54] have described an interesting asymmetric Baylis-Hillman reaction employing (*R*)-2′-diphenylphosphinyl-[1,1′]-binaphthalenyl-2-ol [(*R*)-**29**] as a chiral phosphine catalyst. Thus, the coupling of *N*-sulfonated imines with methyl vinyl ketone in presence of (*R*)-**29** provided the corresponding Baylis-Hillman adducts in high enantioselectivities. One example is presented in Eq. 9.



Eq.9

Very recently, Shi and coworkers[55] have designed and synthesized new chiral phosphine-amide Lewis base catalyst (**30**) for aza-Baylis-Hillman reaction. Thus, the coupling of *N*-sulfonated imines with methyl vinyl ketone in presence of (*R*)-**30** provided the corresponding Baylis-Hillman adducts in high enantioselectivities. One representative example is presented in Eq. 10.

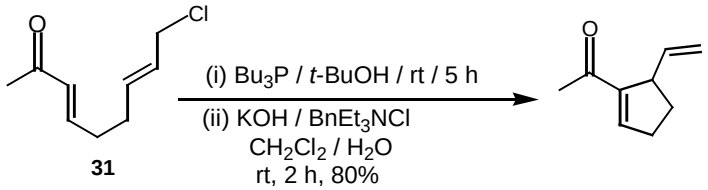


Eq. 10

INTRAMOLECULAR BAYLIS-HILLMAN REACTION:

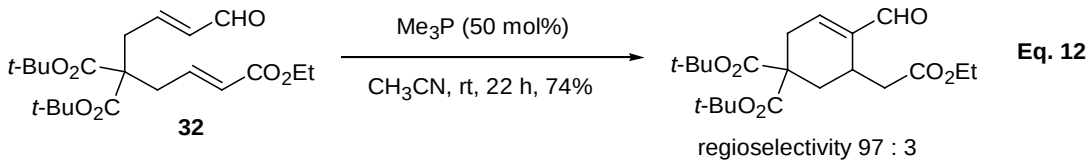
Although the intramolecular Baylis-Hillman reaction did not grow earlier as expected, in recent years this aspect has, indeed, received much attention from the organic chemists. Some of the recent and interesting developments in this direction are presented in this section.[7-11]

Krafft and Haxell described an interesting trialkyl phosphine mediated Baylis-Hillman ring closing reaction of enone-allyl chloride system (**31)** to provide cyclic adducts in good yields. One representative example is presented in Eq. 11.[56]



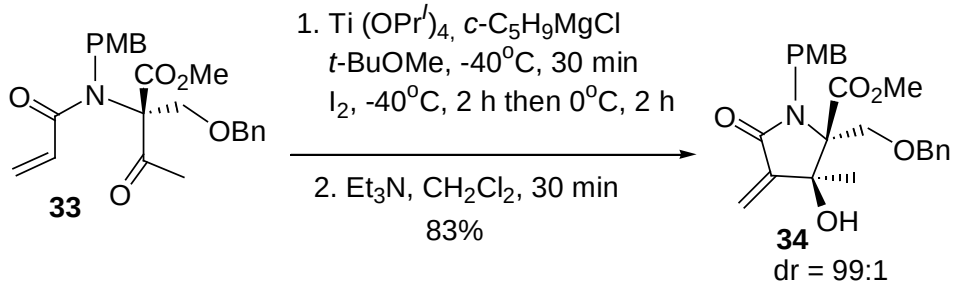
Eq. 11

An intramolecular Baylis-Hillman ring closing reaction of the substrate containing two activated alkenes (**32**) to provide a convenient method for synthesis of functionalized cycloalkene derivatives was described by Roush and coworkers.[57] One representative example is presented in Eq. 12.



Eq. 12

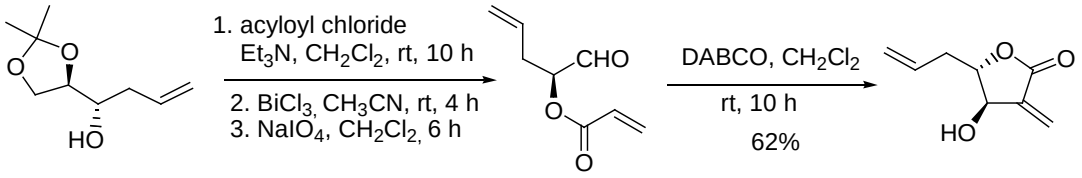
Corey and coworkers[58] during their work on salinosporamide A, has synthesized an important key intermediate (**34**) from the compound (**33**) *via* intramolecular Baylis-Hillman reaction (Eq. 13).



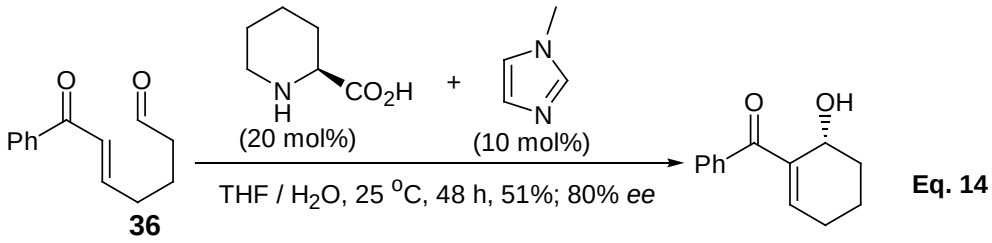
Eq.13

An intramolecular diastereoselective Baylis-Hillman reaction of chiral substrates (**35**) (aldehyde-acrylate system) is reported by Radha Krishana *et.al.,* to afford α-methylene-β-hydroxylactone following the reaction sequence as shown in Scheme 6.[59]

Scheme 6



Miller and coworkers[60] demonstrated, the application of (*S*)-2-pipecolinic acid for promoting asymmetric intramolecular Baylis-Hillman reaction of enone-aldehyde system (**36**) in the presence of *N*-methylimidazole to provide the resulting adduct in good enantioselectivities (Eq. 14).



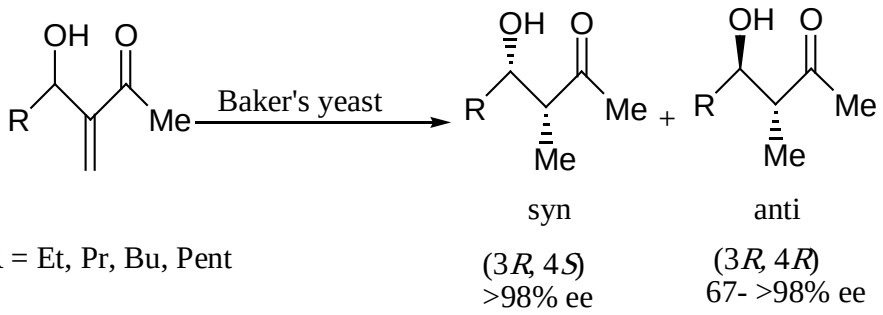
Eq. 14

APPLICATIONS OF THE BAYLIS-HILLMAN ADDUCTS:

The Baylis-Hillman adducts play a key role in organic synthesis due to the presence of multifunctional groups [a minimum of three chemospecific functional groups *i.e*. hydroxy (or amino), alkene and electron withdrawing group] in close proximity and these molecules have been used as substrates in a number of organic transformation methodologies and in the synthesis of various natural products and bioactive molecules. Some of the recent developments involving these strategies / methodologies[7-11] are presented in this section.

The Baylis-Hillman adducts, derived from methyl vinyl ketone as activated alkene and aldehydes as electrophiles, have been resolved into enantiomers *via* the biocatalytic

reduction using Bakers yeast by Utaka and coworkers.[61] Representative examples are presented in Eq. 15.



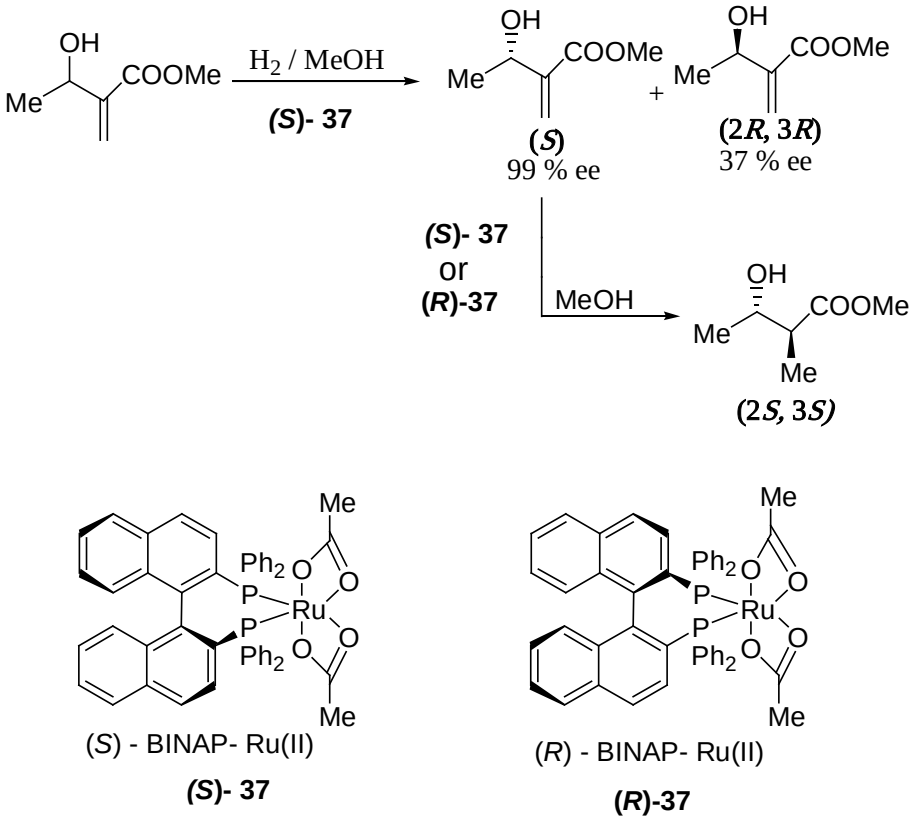
R = Et, Pr, Bu, Pent

Eq.15

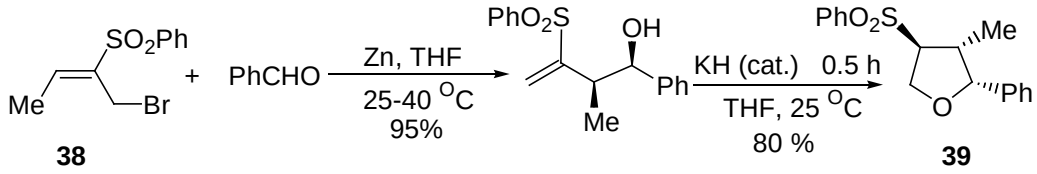
Kinetic resolution of methyl 3-hydroxy-2-methylenebutanoate, the Baylis-Hillman adduct obtained *via* the coupling of acetaldehyde and methyl acrylate, was reported by Noyori and coworkers *via* the catalytic hydrogenation using the chiral catalyst (***R***)-**37** and (***S***)-**37** leading to the formation of the (*S*)-methyl 3-hydroxy-2-methylenebutanoate, in very high enantioselectivities. They have also observed an interesting substrate control in the asymmetric hydrogenation of (*S*)-methyl 3-hydroxy-2-methylenebutanoate. Thus the hydrogenation of this ester using either the catalyst (***R***)-**37** or (***S***)-**37** provided the reduced compound with (2*S*, 3*S*) configuration (Scheme 7).[62]

Normant and coworkers have successfully transformed the Baylis-Hillman bromide *i.e.*, (2*Z*)-1-bromo-2-(phenylsulfonyl)but-2ene (**38**) into diastereomerically pure 2,3,4 trisubstituted tetrahydrofurans (**39**) following the reaction sequence described in Scheme 8.[63]

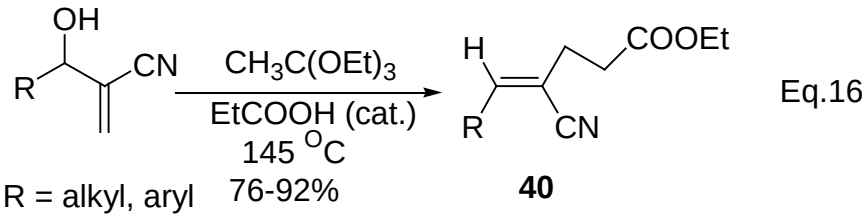
Scheme 7



Scheme 8



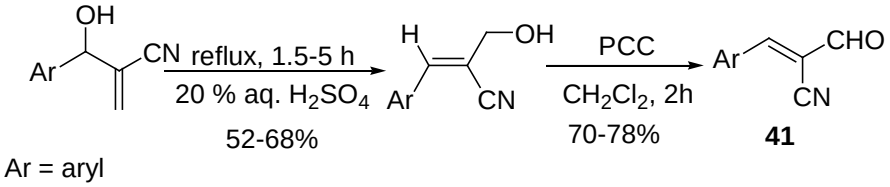
Our research group[64] successfully used the Baylis-Hillman adducts derived from acrylonitrile and aldehydes, as substrates for the Johnson-Claisen rearrangement thus providing a facile methodology for stereoselective synthesis of (4*Z*)-4-cyanoalk-4-enolates (**40**) according to Eq. 16.



Eq.16

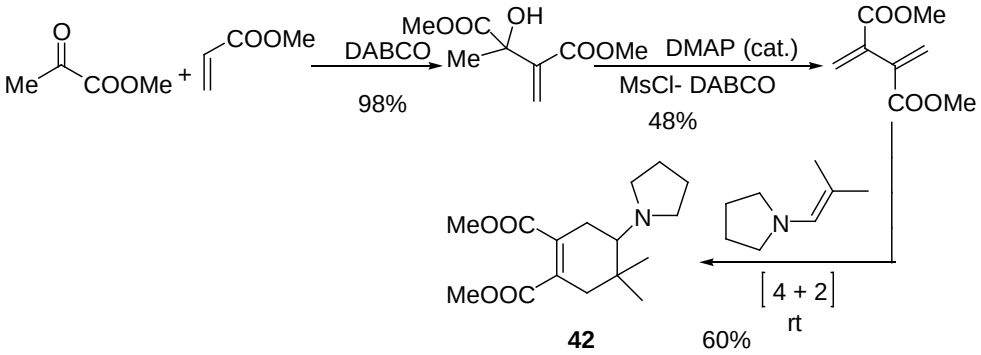
3-Hydroxy-2-methylene-3-arylpropanenitriles have been conveniently isomerized into (*E*)-α-cyanocinnamyl alcohols *via* the treatment 20% aq. sulfuric acid. These primary alcohols have been subsequently oxidized into (*E*)-α-cyanocinnamic aldehydes (**41**) (Scheme 9).[65]

Scheme 9

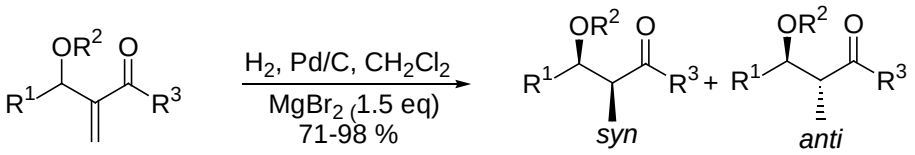


The Baylis-Hillman adduct, derived from methyl acrylate and methyl pyruvate, has been transformed into 2,3-dimethoxycarbonyl-1,3-butadiene by Grundke and Hoffmann.[66] This diene was subsequently converted into an interesting molecule (**42**) *via* the Diels-Alder reaction with pyrrolidinoisobutene (Scheme 10).

Scheme 10



Bouzide and coworkers have described an interesting highly diastereoselective heterogeneous hydrogenation of the Baylis-Hillman adducts with palladium on carbon under the influence of $MgBr_2$ to provide the resulting adducts with *syn* configuration (*syn* aldol products) (Eq. 17).[67]



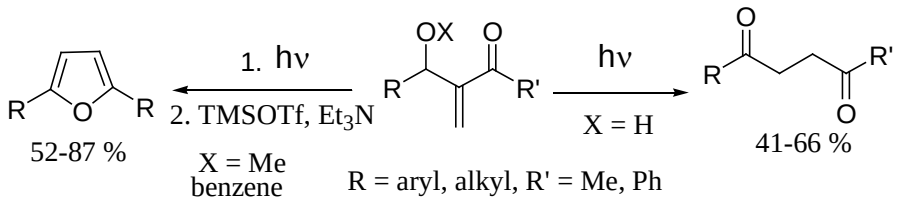
Eq. 17

R^1= Et, *i*-Pr, Ph; R^2= H, Me; R^3= Me, OMe, OEt

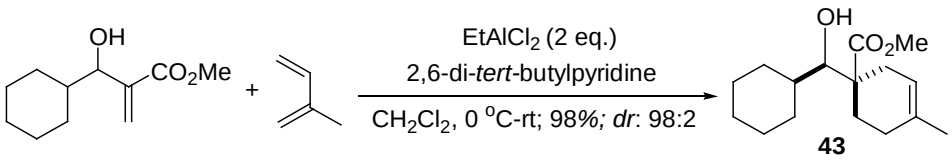
syn/anti--28-81/1

Mikami and coworkers[68,69] have reported an interesting transformation of the Baylis-Hillman adducts, obtained from alkyl vinyl ketones, into 1,4-diketones and substituted furan derivatives under photochemical conditions according to Scheme 11.

Scheme 11



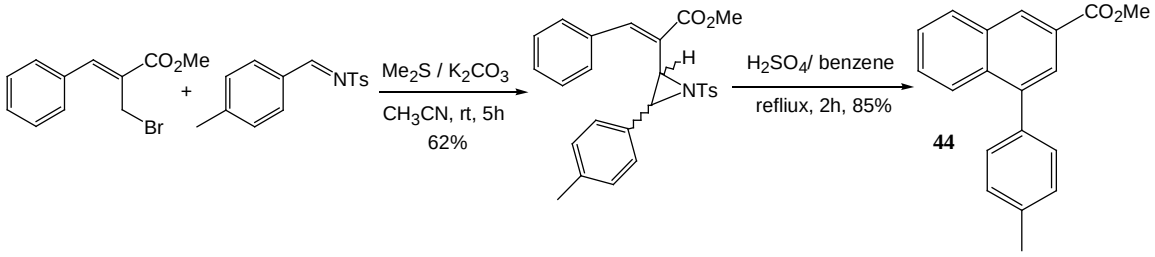
Very recently, Aggarwal *et.al*., successfully used Baylis-Hillman adducts as excellent dienophiles in Diels-Alder reaction with dienes to provide the corresponding adducts (**43**) with complete diastereocontrol.[70] Representative examples are presented in Eq. 18.



Eq. 18

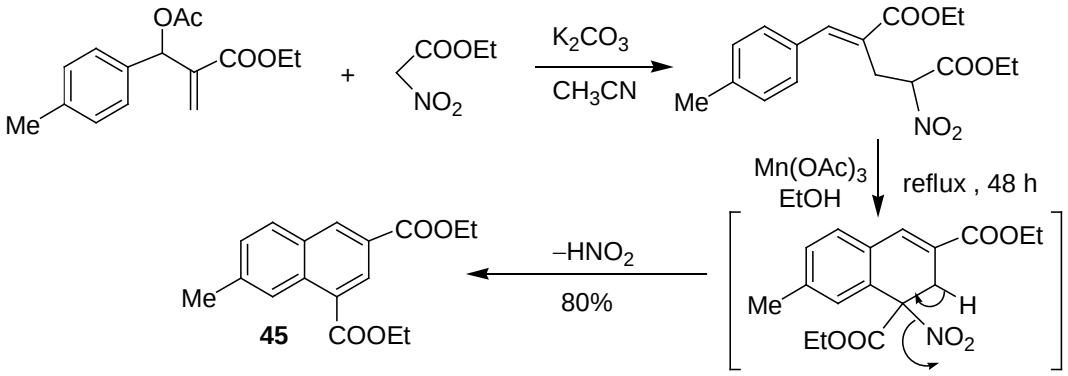
The Baylis-Hillman bromides have been conveniently transformed into *N*-tosylaziridines *via* the dimethyl sulfide mediated reaction with *N*-tosylimine by Kim and coworkers.[71] Subsequently, the resulting aziridines have been converted into 1-arylnaphthalene derivatives (**44**) *via* treatment with H_2SO_4. One representative example is described in Scheme 12.

Scheme 12



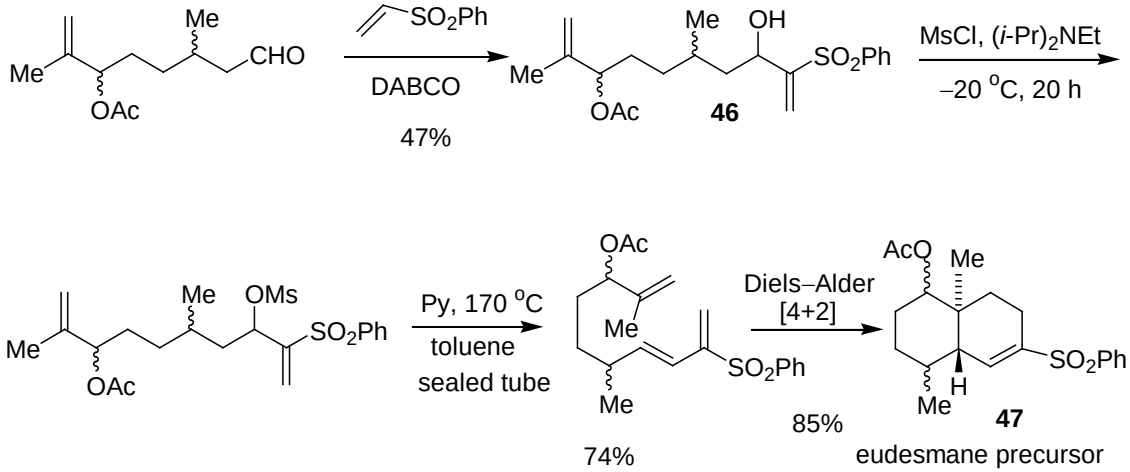
Kim and coworkers[72] have reported an interesting methodology for the synthesis of 1,3-disubstituted naphthalenes (**45**) from the acetates of Baylis-Hillman adducts according to Scheme 13 (One representative example is presented).

Scheme 13

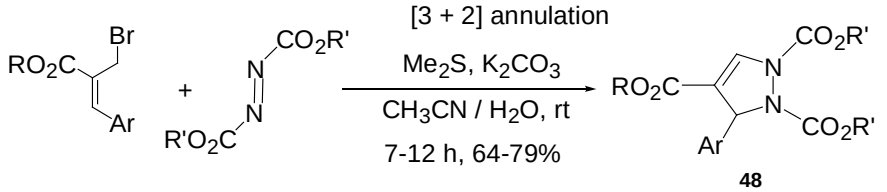


Weichert and Hoffmann have reported an interesting synthesis of the eudesmane (an important natural product) precursor (**47**) using the Baylis-Hillman adduct (**46**) according to Scheme 14.[73]

Scheme 14



Very recently, our research group[74] successfully employed Baylis-Hillman bromides as a valuable source of 1,3-dipoles for cyclo-addition onto dialkyl azodicarboxylates (dipolarophiles) under the influence of dimethyl sulfide and potassium carbonate, to provide functionalized dihydropyrazole derivatives (**48**) in a simple one-pot [3 + 2] annulation strategy (Eq. 19).

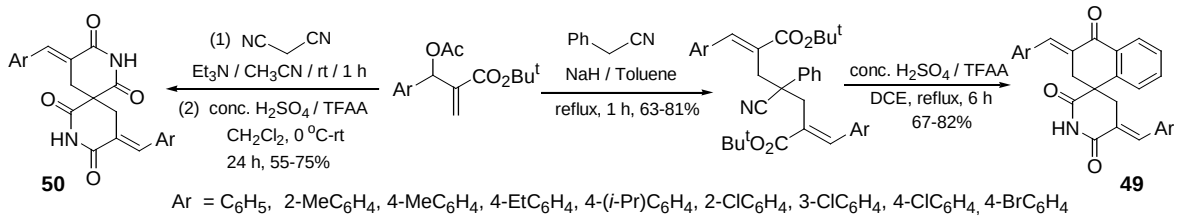


Eq. 19

Ar = C_6H_5, 4-MeC_6H_4, 3-ClC_6H_4, 4-ClC_6H_4, 4-BrC_6H_4
R = Me, Et, Bu, Bu^t; R' = Et, Pr^i

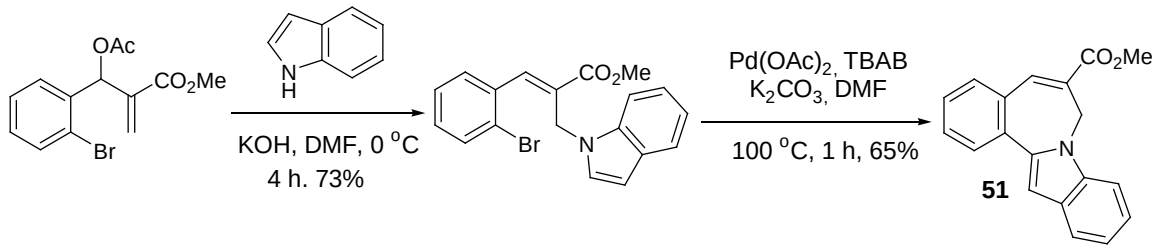
Recently, our research group[75] developed a simple and convenient synthesis of di(*E*)-arylidene-tetralone-spiro-glutarimides (**49**) from the Baylis-Hillman acetates *via* an interesting biscyclization strategy involving the facile C-C and C-N bonds formation following the reaction sequence as described in Scheme 15. Also, one-pot multistep transformation of the Baylis-Hillman acetates into di(*E*)-arylidene-spiro-bisglutarimides (**50**) has been also developed by our research group (Scheme 15).

Scheme 15



Very recently, Kim and coworkers[76] reported an interesting protocol for synthesis of tetra-cyclic indole derivatives (**51**) from the acetates of Baylis-Hillman adducts following the reaction sequence presented in Scheme 16 (One representative example is presented).

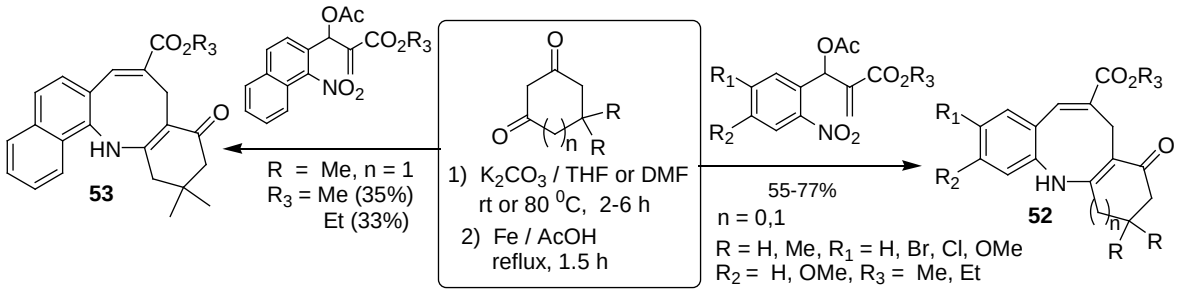
Scheme 16



Recently, our research group[77] has developed a simple, convenient, and one-pot synthesis of functionalized tri / tetracyclic frameworks (**52** & **53**) containing an important azocine

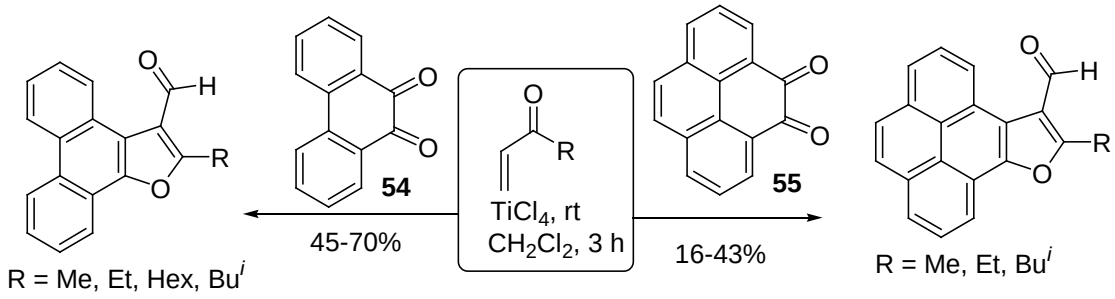
moiety, from the acetates of Baylis-Hillman adducts following the reaction sequence involving alkylation, reduction, and cyclization steps, as described in Scheme 17.

Scheme 17



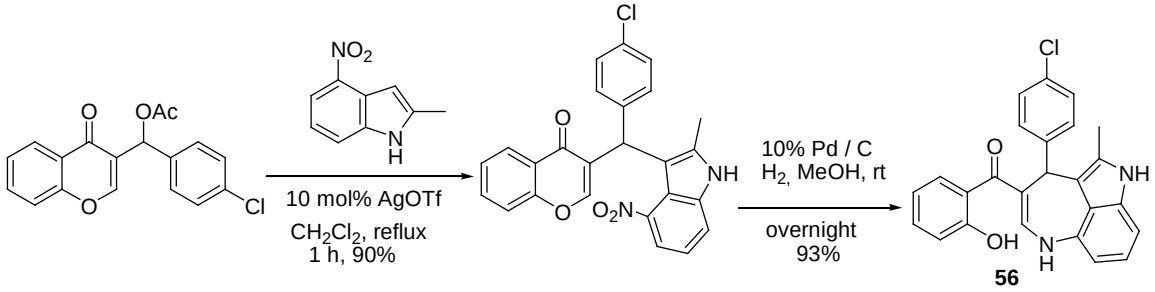
Our research group has meticulously reported a simple synthesis of functionalized fused furans *via* the $TiCl_4$ mediated reaction of alkyl vinyl ketones with aryl 1,2-diones (**54** & **55**) according to the Scheme 18.[78]

Scheme 18

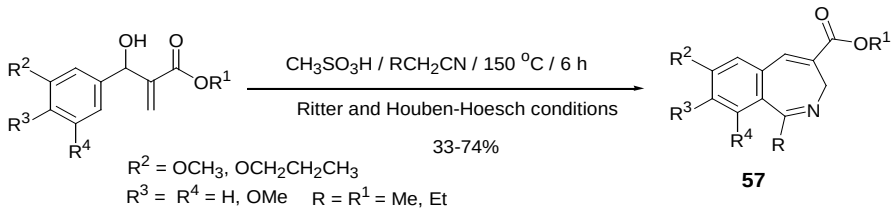


An interesting synthesis of the azepinoindole derivatives (**56**) has been developed by Chen and coworkers[79] *via* the regioselective nucleophilic substitution of acetate of the Baylis-Hillman adducts with indoles under the catalytic influence of AgOTf followed by reductive cyclization. One representative example is presented in Scheme 19.

Scheme 19



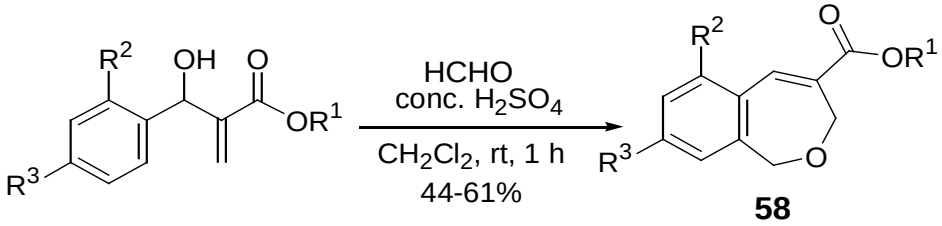
Our research group[80] reported an interesting one-pot transformation of Baylis-Hillman adducts into 2-benzazepines (**57**) *via* novel and tandem construction of C-N and C-C bonds involving simultaneous Ritter and Houben-Hoesch reactions as described in Eq. 20.



R^2 = OCH_3, $OCH_2CH_2CH_3$
R^3 = R^4 = H, OMe R = R^1 = Me, Et
-R^2-R^3- = -OCH_2O-

Eq. 20

Later on, our research group[81] also reported a novel one-pot synthesis of 2-benzoxepines (**58**) *via* the treatment of the Baylis-Hillman adducts with formaldehyde in the presence of conc. H_2SO_4 involving tandem construction of C-O and C-C bonds as described in Eq. 21.

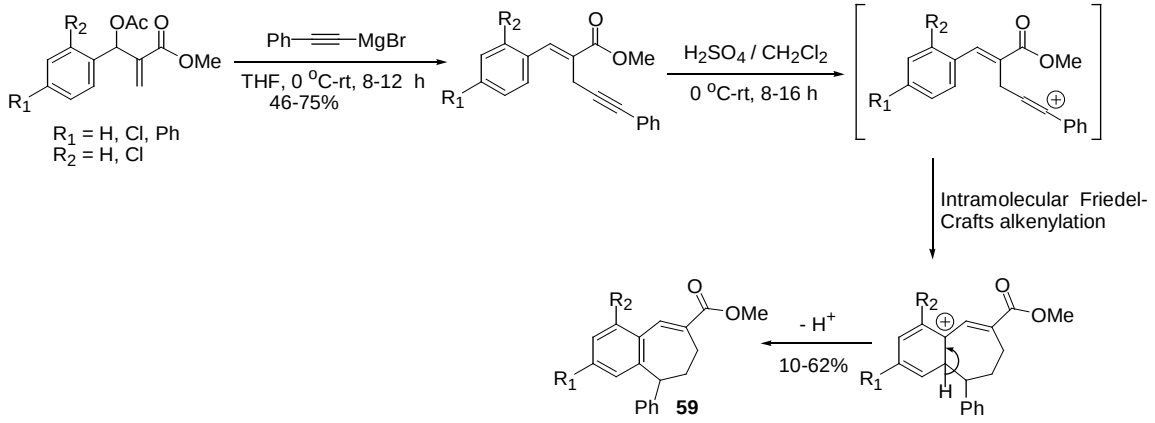


Eq. 21

R^1 = Me, Et; R^2 = H, Me; R^3 = H, Me, Et, Pr^i

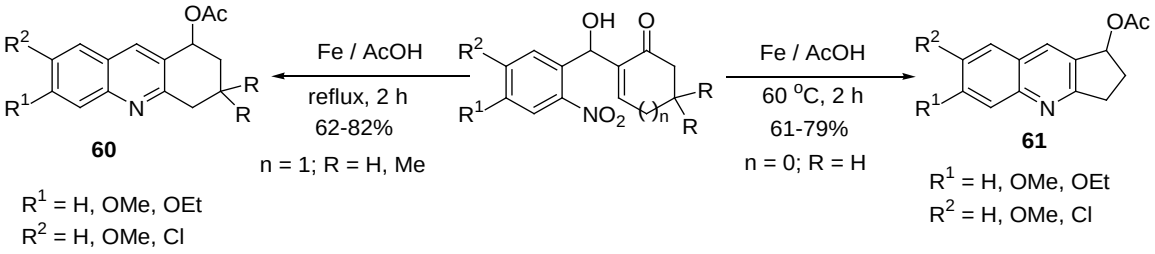
A facile synthesis of 7*H*-benzocycloheptene derivatives (**59**) from acetates of the Baylis-Hillman adducts was developed by Kim and coworkers[82] according to reaction sequence as described in Scheme 20.

Scheme 20

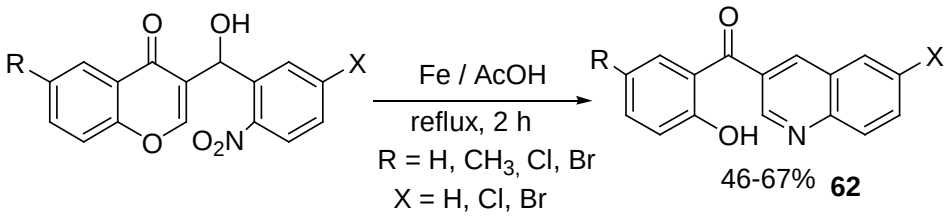


Our research group[83,84] reported an interesting strategy for one-pot synthesis of functionalized 1, 2, 3, 4-tetrahydroacridines (**60**) and cyclopenta[*b*]quinolines (**61**) from the Baylis-Hillman alcohols (Scheme 21).

Scheme 21

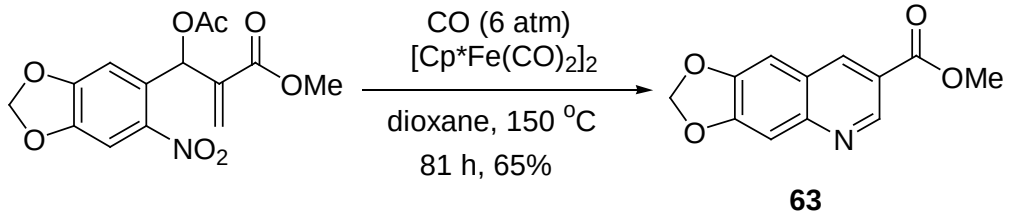


Recently, our research group reported a simple synthesis of 3-benzoylquinolines (**62**) from the Baylis-Hillman alcohols, obtained from various chromones and 2-nitrobenzaldehydes, *via* the treatment with Fe / AcOH in Eq. 22.[85]



Eq. 22

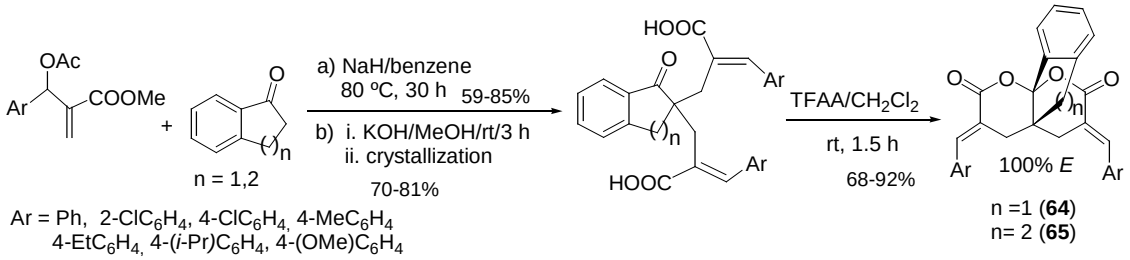
Nicholas and O'Dell have reported the synthesis of 3-substituted quinolines (**63**) *via* transition metal catalyzed reductive cyclization of the acetates of Baylis-Hillman adducts (derived from 2-nitrobenzaldehydes and methyl acrylate). One representative example is shown in Eq. 23.[86]



Eq. 23

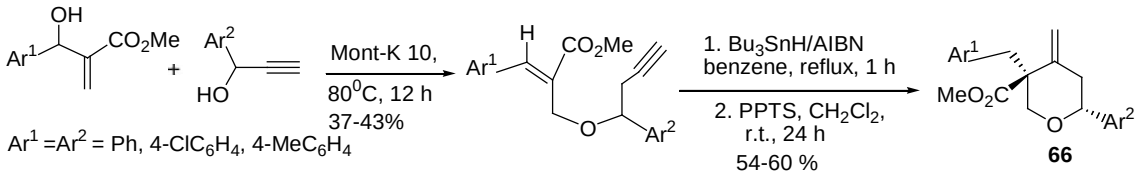
Our research group[87] has developed a simple and convenient three-step synthesis of functionalized [4.4.3] and [4.4.4]propellano-bislactones (**64** & **65**) from the acetates of Baylis-Hillman adducts following the reaction sequence as shown in Scheme 22.

Scheme 22



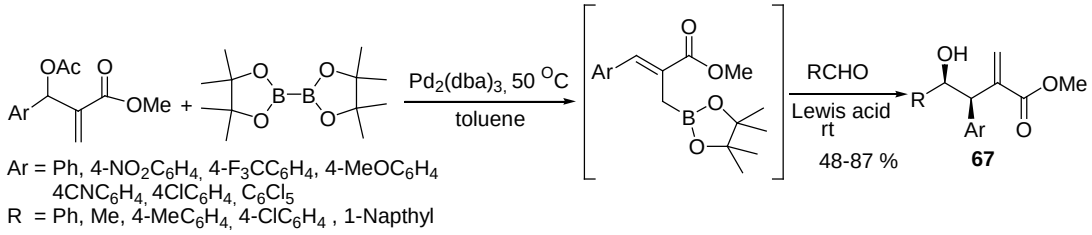
Shanmugam and Rajasingh developed the stereoselective synthesis of poly-substituted functionalized tetrahydropyrans (**66**) from the Baylis-Hillman acetates following the reaction sequence as shown in Scheme 23.[88]

Scheme 23

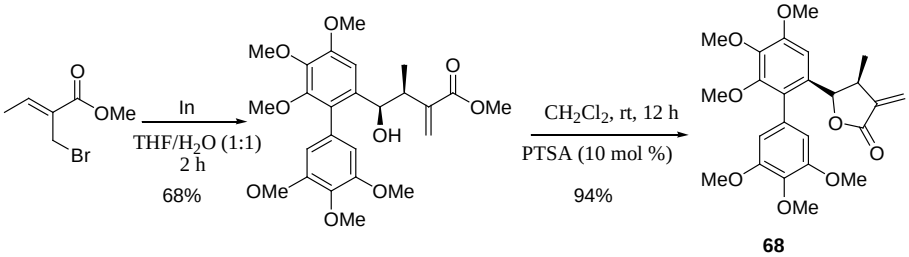


Kabalka and coworkers[89,90] have meticulously transformed the Baylis-Hillman acetates into *syn*-homoallyl alcohols (**67**) following the reaction sequence as shown in Scheme 24. Subsequently Kabalka has also developed a simple synthesis of eupomatilone (**68**) an important natural product starting from the Baylis-Hillman bromide [(2*Z*)-2-(bromomethyl)but-2-enoate] following the reaction sequence as shown in Scheme 25.

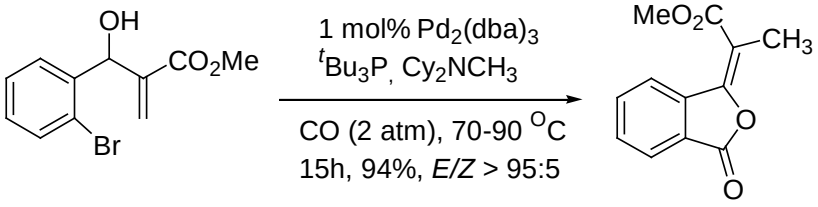
Scheme 24



Scheme 25

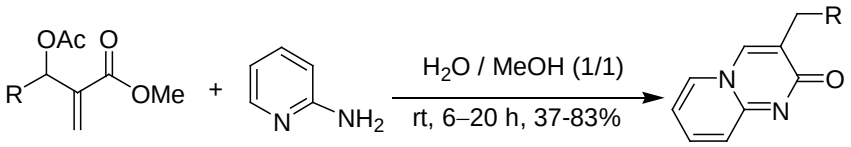


Palladium-mediated carbonylative methodology for the preparation of phthalides has been reported by Coelho and coworkers[91] from the Baylis-Hillman adducts derived from *o*-bromobenzaldehydes. One representative example is presented in Eq. 24.



Eq. 24

A facile one-pot synthetic transformation of the acetates of the Baylis-Hillman adducts into fused pyrimidones *via* the reaction with 2-aminopyridine in environment-friendly aqueous media was reported by our research group (Eq. 25).[92]

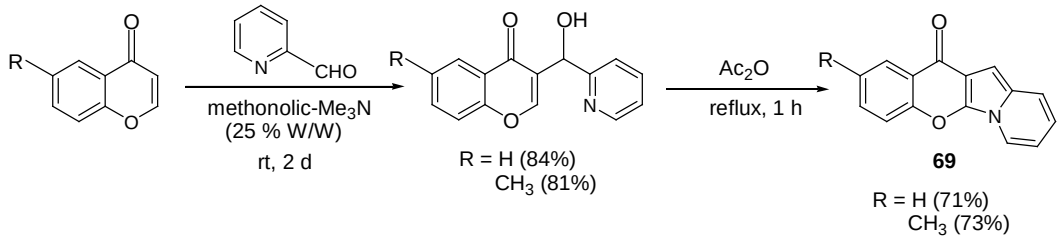


Eq. 25

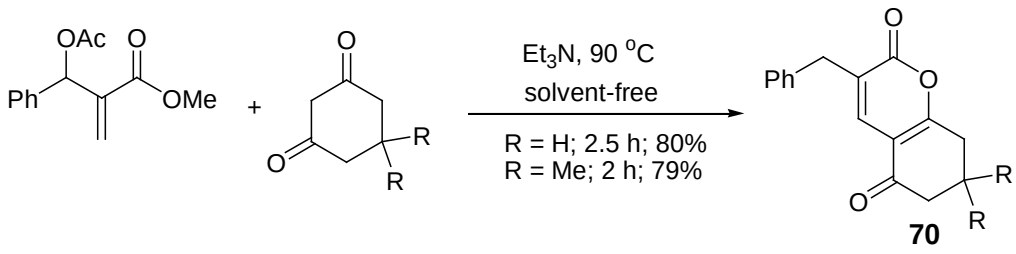
R= Ph, 4-MeC_6H_4, 4-EtC_6H_4, 4-(*i*-Pr)C_6H_4, 2-ClC_6H_4, 4-ClC_6H_4, 3-$MeOC_6H_4$, 4-$MeOC_6H_4$, Pent

Our research group[93] has successfully employed Baylis-Hillman adducts, obtained from chromone derivatives and pyridine-2-carboxaldehyde into tetracyclic indolizine fused chromone systems (**69**). Representative example is presented in Scheme 26.

Scheme 26



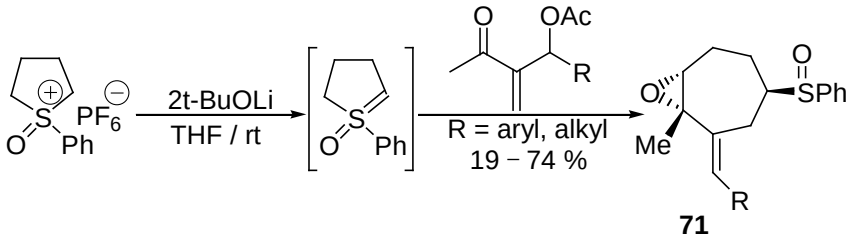
A simple, efficient synthesis of 3-arylmethyl-7,8-dihydro-6*H*-chromene-2,5-dione (**70**) from Baylis-Hillman acetates derived from various aromatic aldehydes and cyclohexane-1,3-dione derivatives under solvent-free conditions is described by Su and coworkers.[94] One example is presented in Eq. 26.



Eq. 26

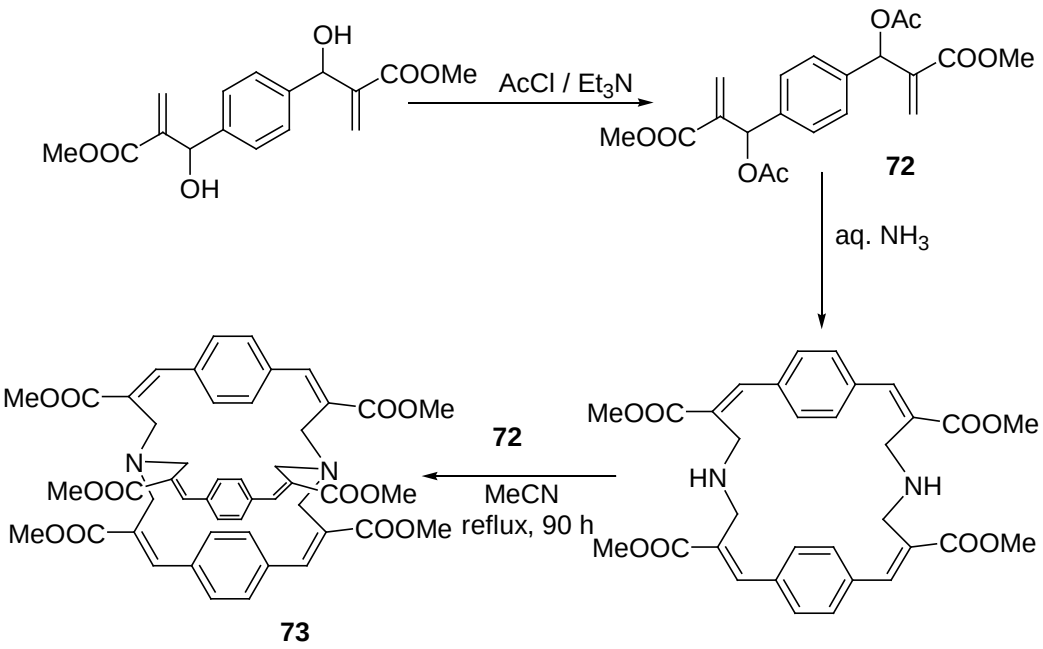
An interesting tandem Michael-intramolecular Corey-Chaovsky reaction of cyclic oxonium ylides with the acetates of the Baylis-Hillman adducts providing the stereoselective synthesis of cycloheptene-oxide derivatives (**71**) was reported by Fujito and coworkers [95] following the reaction sequence as described in Scheme 27.

Scheme 27



Bauchat and Foucaud[96] have reported an interesting synthesis of diazamacrocycle (**73**) from the bis-acetate (**72**) of bis-Baylis-Hillman adduct obtained from methyl acrylate and terphthaldehyde following the reaction sequence as described in the Scheme 28.

Scheme 28


OH
COOMe
AcCl / Et3N
OAc
COOMe
MeOOC
OH
MeOOC
OAc
72
aq. NH3
MeOOC
COOMe
HN
NH
MeOOC
COOMe
72
MeCN
reflux, 90 h
N
N
MeOOC
COOMe
MeOOC
COOMe
73

Objectives, Results and Discussion

From the preceding section it is quite clear that the Baylis-Hillman reaction occupies a special place in organic synthesis because this reaction provides unique class of multifunctional molecules having enormous synthetic potential. These multifunctional molecules have been successfully employed in various organic transformation methodologies and in synthesis of natural products. During the last 24 years, our research group has been actively working on various aspects of this reaction with the main objective of developing this reaction into an important synthetic tool in organic synthesis. This thesis describes our studies towards the application of the Baylis-Hillman bromides in synthesis of heteroocyclic compounds containing oxygen in the ring with the following main objectives.

Objectives:

1) To develop a novel and facile methodology for the synthesis of tetrahydrodipyrandione derivatives [7,12-bisarylidene-5,14-dioxatricyclo[8.4.0.$0^{4,9}$]tetradeca-1,3,9-triene-8,11-dione] using the Baylis-Hillman bromides as starting materials.

2) To develop a simple methodology for the synthesis of 7:8-benzochroman-4-one frameworks using the Baylis-Hillman bromides as synthons.

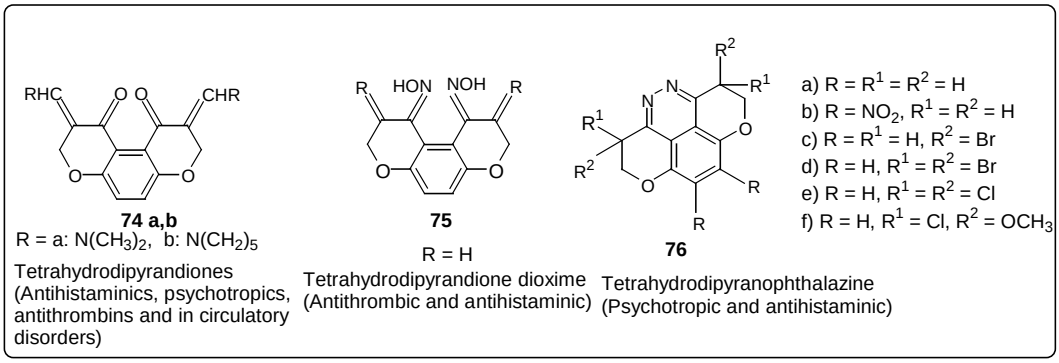
3) To develop facile methodology for the synthesis of 5:6-benzochroman-4-one derivatives using the Baylis-Hillman bromides as starting materials.

Results and Discussion:

Facile synthesis of tetrahydrobenzodipyrandiones from the Baylis-Hillman adducts:

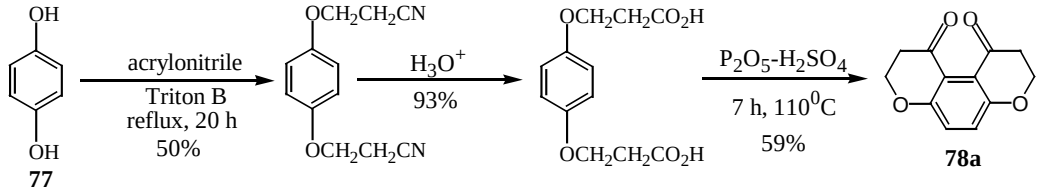
Tetrahydrobenzodipyrandione framework has attracted the attention of organic chemists because some of these compounds [for example (**74-76**) (**Fig 6**)] possess interesting psychotropic, antithrombic and antihistaminic properties.[97-101] Due to the importance of these compounds organic chemists have directed their attention to develop simple methodologies for synthesis of various derivatives of this framework. Some important strategies or methodologies from the literature are presented in this section.

Figure 6



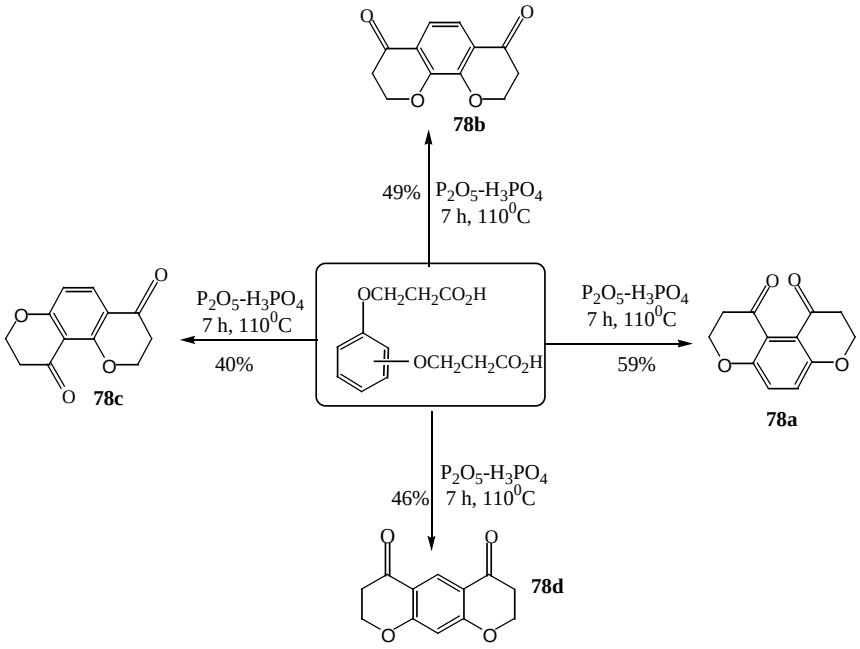
Eiden and Schmiz [97,98] reported the synthesis of tetrahydrobenzodipyrandione derivative (**78a**) starting from 1,4-dihydroxybenzene (**77**) following the reaction sequence as shown in Scheme 29.

Scheme 29



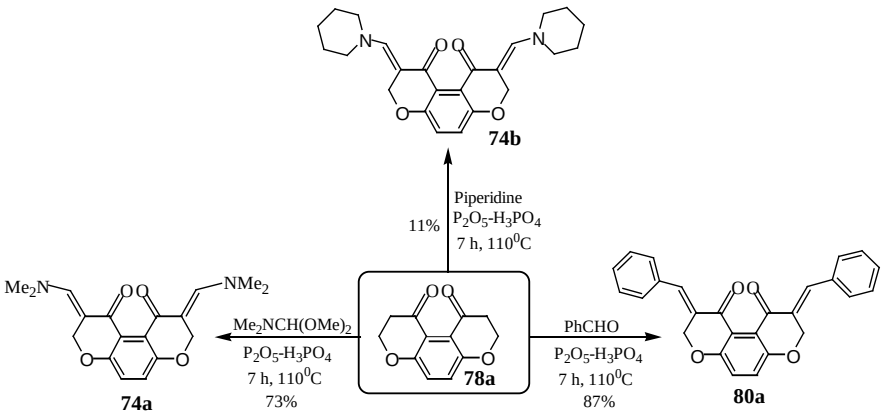
A general synthesis of tetrahydrobenzodipyrandiones **78a-d** *via* the Friedel-Crafts reaction of regiomeric bis(carboxyethoxy)benzenes in the presence of polyphosphoric acid was reported by Eiden and coworkers[97] following the reaction sequence as shown in Scheme 30.

Scheme 30



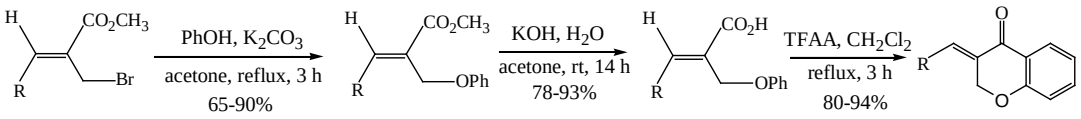
Eiden and Schmiz[97] have reported the synthesis of various tetrahydrobenzodipyrandione derivatives (**74a,b** and **80a**) starting from tetrahydrobenzodipyrandione (**78a**) following the reaction sequence as shown in Scheme 31. It is interesting to note that the compound **80a** was useful as antihistaminics, psychotropics, antithrombins and in circulatory disorders.[97]

Scheme 31



The medicinal importance of these compounds containing tetrahydrobenzodipyrandione framework has attracted our attention and we have therefore focused our studies to develop a simple methodology for synthesis of these frameworks. Our research group has some-time ago reported a simple methodology for the synthesis of *(E)*-3-arylidene chroman-4-one derivatives[102] (**79**) *via* the reaction of the Baylis-Hillman bromides with phenols followed by hydrolysis and then Friedel-Crafts cyclization of the resulting *α*-phenoxymethylcinnamic acid with TFAA (Scheme 32).

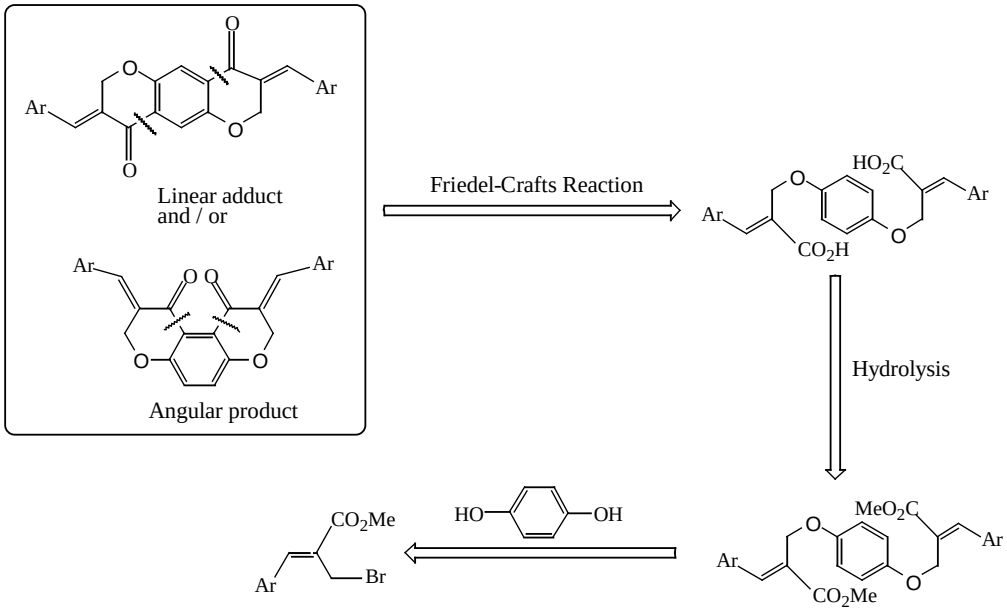
Scheme 32



Based on this methodology it occurred to us that treatment of Baylis-Hillman bromides with 1,4-dihydroxybenzene (**77**) followed by hydrolysis should in principle provide the biscinnamic acid derivatives and subsequent Friedel-Crafts cyclization should provide the

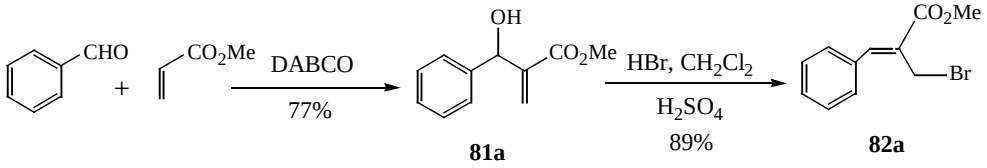
tetrahydrobenzodipyran-1,6-dione derivatives. The retrosynthetic strategy is presented in Scheme 33. The biscinnamic acids in principle can afford two types of products *i.e.*, angularly fused / linearly fused Fiedel Crafts products. We felt that it will be interesting to see the nature of Friedel-Crafts reaction as the resulting products might throw some light on the mechanistic pathway.

Scheme 33



Accordingly we have first selected the Baylis-Hillman bromide, methyl (2*Z*)-2-(bromomethyl)-3-phenylprop-2-enoate (**82a**) as a substrate for our study in this direction. The required allyl bromide (**82a**)[103] was prepared from the Baylis-Hillman alcohol, methyl 3-hydroxy-2-methylene-3-phenylpropanoate (**81a**), which in turn, was obtained *via* the reaction between benzaldehyde and methyl acrylate in the presence of catalytic amount of DABCO (Scheme 34).

Scheme 34

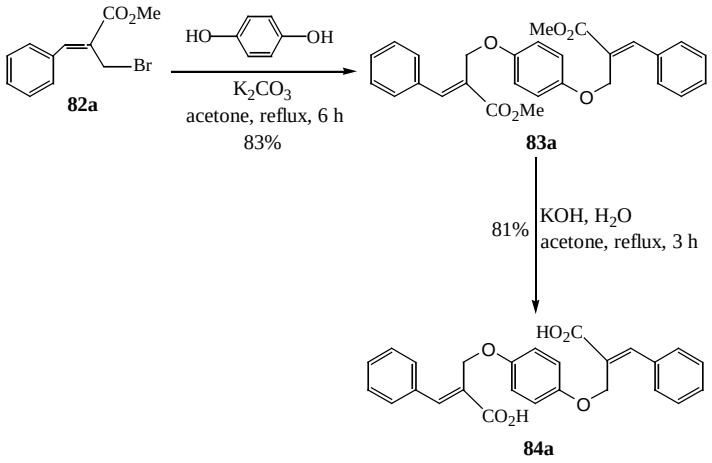


Next we have examined the reaction of the allyl bromide (**82a**) with 1,4-dihydroxy-benzene (**77**) under various conditions. The best result in this direction was obtained when the allyl bromide (**82a**) was treated with 1,4-dihydroxybenzene (**77**) in the presence of K_2CO_3 thus providing the desired biscinnamic ester, 1,4-bis[(2*E*)-2-methoxycarbonyl-3-phenylprop-2-enyloxy]benzene (**83a**)[§] in 83% isolated yield (Scheme 35). The diester was obtained in almost stereochemically pure form with *(E)*-configuration[#]. Structure of this bis ester was confirmed by IR, ^{1}H and ^{13}C NMR spectral data. Subsequent hydrolysis of the biscinnamic ester (**83a**) with KOH / H_2O provided the biscinnamic acid, 1,4-bis[(2*E*)-2-carboxy-3-phenylprop-2-enyloxy]benzene (**84a**) [§] in stereochemically pure (*E*)[#]-form after crystallization. The *(Z)*-stereochemistry of the compound (**82a**) and *(E)*-stereochemistry of the compounds **83a**[§] and **84a** were assigned on the basis of ^{1}H NMR spectral analysis.[#]

[#] It has been reported in literature that in the ^{1}H NMR spectrum, the chemical shifts of the vinylic *β*-protons *cis* to the ketone, ester, and acid carbonyl groups appear downfield in comparison with that of *trans β*-protons.[104,105] The *(Z)*-stereochemistry of the allyl bromides (**82a-h**) was assigned on the basis of the chemical shift values of the *β*-vinylic protons i.e δ 7.66-8.03. The *(E)*-stereochemistry of these molecules **83a-h, 84a-h** was assigned on the basis of the chemical shift values of the *β*-vinylic protons, i.e. δ 7.89-8.22.[103-108]

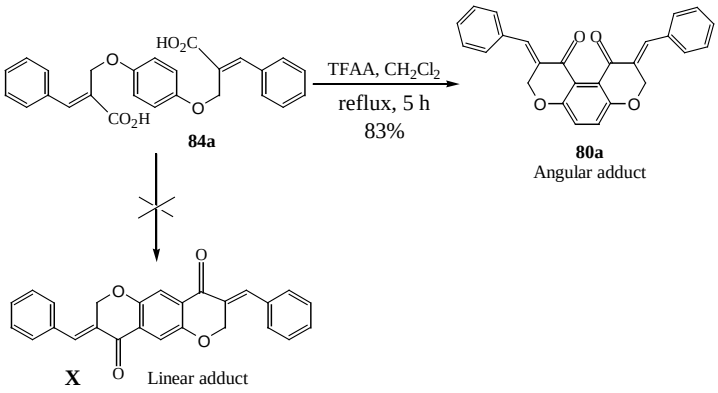
[§]For continuity and easy understanding the (*E*)-alkenoic esters, acids and bischromanones obtained from **82a-h** were numbered as **83a-h, 84a-h** and **80a-h** respectively.

Scheme35



The next task was to transform the biscinnamic acid (**84a**) into the corresponding bischromanone framework. Accordingly we have treated the biscinnamic acid (**84a**) with TFAA (trifluoroacetic anhydride) under different reaction conditions. The best results in this direction were obtained when we have treated the biscinnamic acid (**84a**) with TFAA at 40^0C thus providing the required compound 7,12-bisbenzylidene-5,14-dioxatricyclo[8.4.0.$0^{4,9}$]tetradeca-1,3,9-triene-8,11-dione (**80a**) as a nice light yellow solid (Scheme 36). The structure of this compound was confirmed by IR, ^{1}H NMR$^{\$}$ (spectrum 1), ^{13}C NMR (spectrum 2), mass spectral data (LCMS) and elemental analysis.

Scheme 36



Actually it is not that easy to say the compound obtained is either linear product (**X**) or angular product (**80a**) on the basis of spectral data. Therefore we have obtained single crystals and further confirmed the structure by single crystal X-ray data (ORTEP diagram, Fig. A-1). It is interesting to note that we did not obtain the expected tetrahydrobenzodipyran-4,9-dione (**X**) (linear product) but we obtained sterically hindered tetrahydrobenzodipyran-4,5-dione (**80a**) (angular product). This is, therefore an interesting reaction in the sense that the Friedel-Crafts cyclization provided the more hindered angular product in preference to the less hindered linear product.

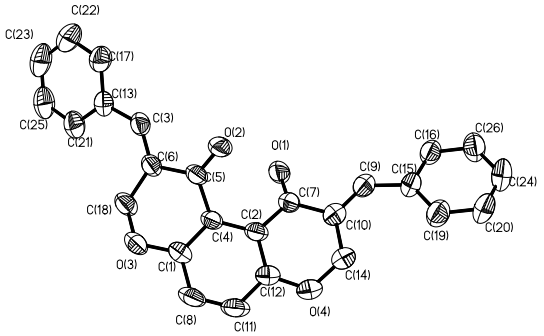


Fig. A1
ORTEP diagram of compound **80a**
(Hydrogen atoms are omitted for clarity)

To understand the generality of this reaction sequence we have next selected methyl (2*Z*)-2-(bromomethyl)-3-(2-methylphenyl)prop-2-enoate (**82b**) as a substrate with a view to understand the effect of ortho substitution on the phenyl ring. The required allyl bromide (**82b**) was prepared from Baylis-Hillman alcohol, 2-methylene-3-hydroxy-3-(2-methylphenyl)propanoate (**81b**). The desired Baylis-Hillman alcohol (**81b**) was obtained

via the DABCO catalyzed reaction between methyl acrylate and 2-methylbenzaldehyde (Scheme 37). The allyl bromide (**82b**) was treated with 1,4-dihydroxybenzene (**77**) following the similar procedure as in the case of (**82a**). Hydrolysis of the resulting bis-cinnamic ester (**83b**) into the corresponding bis-cinnamic acid (**84b**) followed by the subsequent intramolecular Friedel-Crafts reaction provided the expected 7,12-bis(2-methylbenzylidene)-5,14-dioxatricyclo[8.4.0.0^{4,9}]tetradeca-1,3,9-triene-8,11-dione (**80b**)[$] as a yellow solid. The structure of this molecule was confirmed by IR, ^{1}H NMR, ^{13}C NMR, mass spectral data (LCMS) and elemental analysis. The structure of the product was further confirmed by single crystal X-ray data. (For ORTEP diagram, see Fig. A-2).

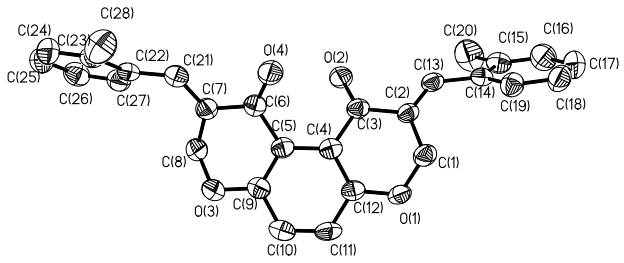
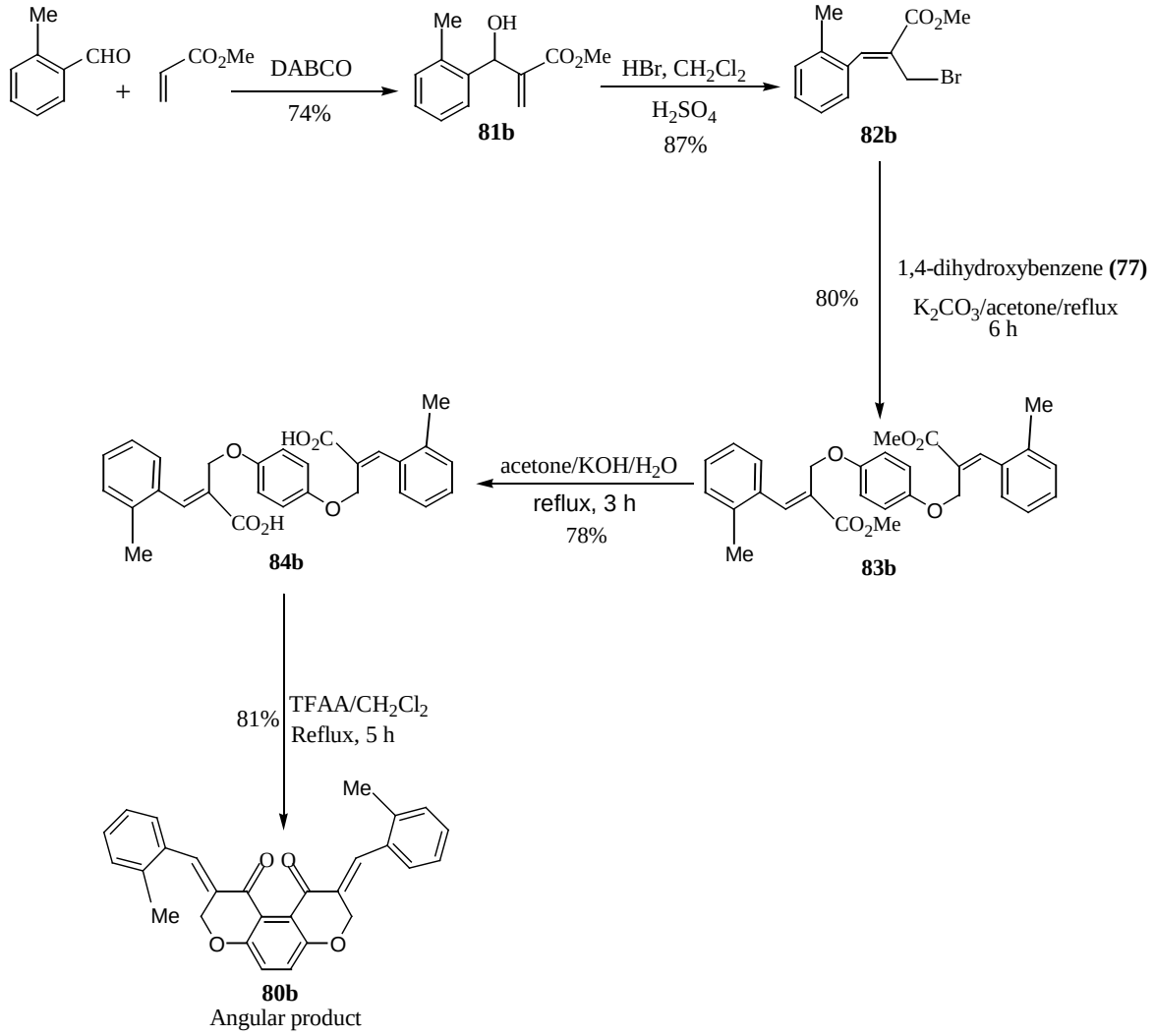


Fig. A2
ORTEP diagram of compound **80b**
(Hydrogen atoms are omitted for clarity)

[$] Stereochemical assignments of the compounds **80a-h** were made on the chemical shift values of the *β*-vinylic proton signals in the ^{1}H NMR spectra of the crude products as well as crystallized products. It is well established in the literature that the ^{1}H NMR spectrum of 3-benzylidenechroman-4-ones the vinylic proton *cis* to the carbonyl group appears at ~ δ 7.7, while the corresponding *trans β*-proton appears at ~ δ 6.7.[109,110] . The *(E)*-stereochemistry of the compounds **80a-h** was assigned on the basis of chemical shift value *of β*-vinylic proton [the *β*-vinylic proton appeared at δ 7.78-8.06 and there was no peak observed ~ δ 6.7 (*Z*-isomer)]. The ^{1}H NMR spectra of the crude as well as crystallized product of compounds **80a-h** indicated the absence of *(Z)*-isomer. The *(E)*-Streochemistry was also confirmed by the single crystal X-ray data analysis for the compounds **80a,b,f**.

Scheme 37



With a view to understand the effect of methoxy group at 2-position of the aryl group, we have extended the strategy to the allyl bromide containing 2-methoxy group. Accordingly we have prepared the required allyl bromide (**82c**) according to the Scheme 38.

Treatment of this allyl bromide (**82c**) with 1,4-dihydroxybenzene (**77**) provided the bis-cinnamic ester (**83c**)[#] Hydrolysis of this ester (**83c**) followed by the treatment of the resulting bis-cinnamic acid (**84c**)[#] with TFAA gave the required 7,12-bis(2-methoxybenzylidene)-5,14-dioxatricyclo[8.4.0.0^{4,9}]tetradeca-1,3,9-triene-8,11dione (**80c**) in 84% isolated[§,$]. The structure of the compound was established by IR, ^{1}H NMR (spectrum # 3), ^{13}C NMR (spectrum # 4) mass spectral data(LCMS), elemental analysis.

[§] For continuity and easy understanding the (*E*)-alkenoic esters, acids and biscnhromanones obtained from **82a-h** were numbered as **83a-h, 84a-h** and **80a-h** respectively.

[#] It has been reported in literature that in the ^{1}H NMR spectrum, the chemical shifts of the vinylic *β*-protons *cis* to the ketone, ester, and acid carbonyl groups appear downfield in comparison with that of *trans β*-protons.[104,105] The *(Z)*-stereochemistry of the allyl bromides (**82a-h**) was assigned on the basis of the chemical shift values of the *β*-vinylic protons i.e δ 7.66-8.03. The *(E)*-stereochemistry of these molecules **83a-h, 84a-h** was assigned on the basis of the chemical shift values of the *β*-vinylic protons, i.e. δ 7.89-8.22.[103-108]

[$] Stereochemical assignments of the compounds **80a-h** were made on the chemical shift values of the *β*-vinylic proton signals in the ^{1}H NMR spectra of the crude products as well as crystallized products. It is well established in the literature that the ^{1}H NMR spectrum of 3-benzylidenechroman-4-ones the vinylic proton *cis* to the carbonyl group appears at ~ δ 7.7, while the corresponding *trans β*-proton appears at ~ δ 6.7.[109,110] . The *(E)*-stereochemistry of the compounds **80a-h** was assigned on the basis of chemical shift value *of β*-vinylic proton [the *β*-vinylic proton appeared at δ 7.78-8.06 and there was no peak observed ~ δ 6.7 (*Z*-isomer)]. The ^{1}H NMR spectra of the crude as well as crystallized product of compounds **80a-h** indicated the absence of *(Z)*-isomer. The *(E)*-Streochemistry was also confirmed by the single crystal X-ray data analysis for the compounds **80a,b,f**.

Scheme 38

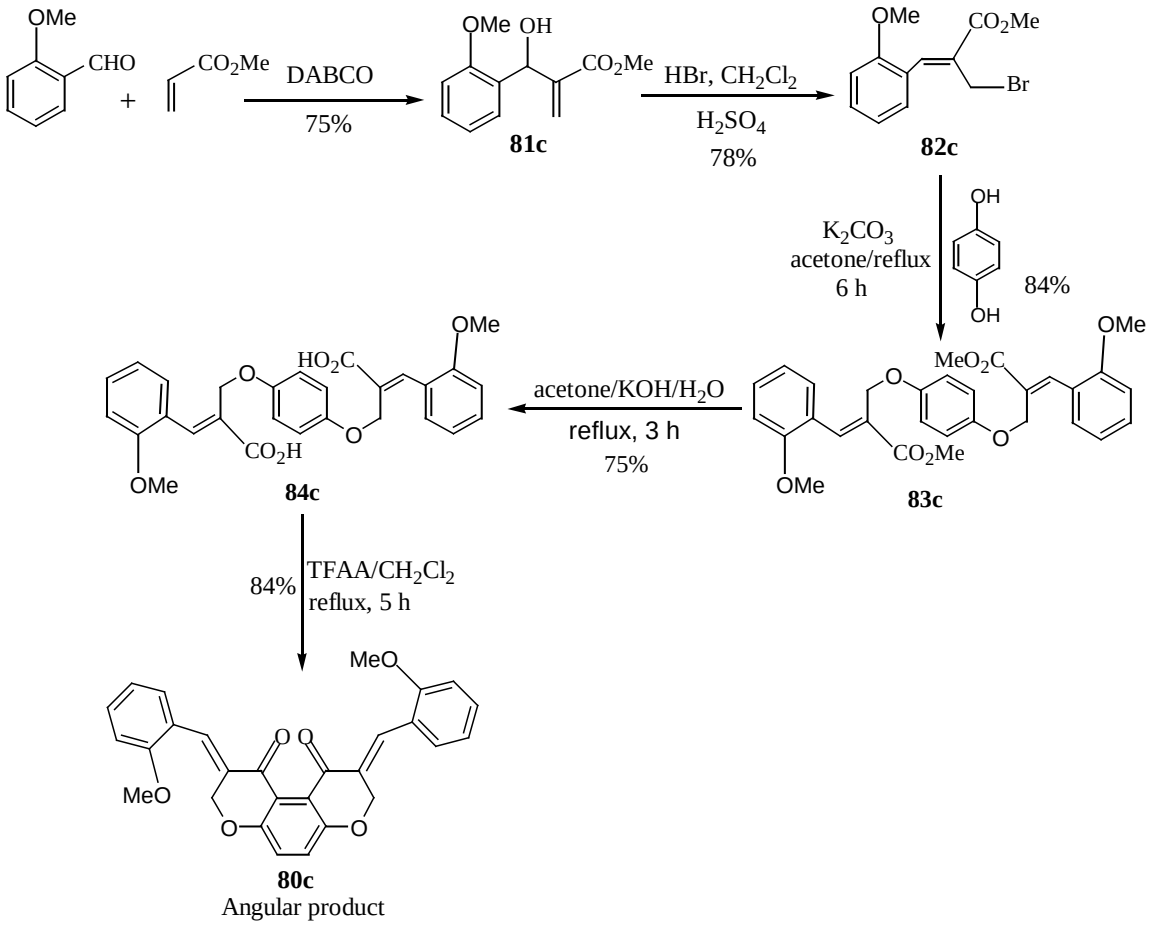

OMe
CHO
+
CO2Me
DABCO
75%
OMe OH
CO2Me
81c
HBr, CH2Cl2
H2SO4
78%
OMe
CO2Me
Br
82c
K2CO3
acetone/reflux
6 h
OH
OH
84%
OMe
MeO2C
O
O
CO2Me
OMe
83c
acetone/KOH/H2O
reflux, 3 h
75%
OMe
HO2C
O
O
CO2H
OMe
84c
84%
TFAA/CH2Cl2
reflux, 5 h
MeO
O
O
MeO
O
O
80c
Angular product

Table 1: Crystal data and structure refinement for 80a

Identification code	: **80a**
Empirical formula	: $C_{26}H_{18}O_4$
Formula Weight	: 394.40
Temperature	: 293(2)K
Wavelength	: 0.71073 A^0
Crstal system, space group	: Triclinic, P-1 (International Table No. 2)
Unit cell dimensions	: a = 7.5944 (7); α = 100.100 (2) deg.
	: b = 8.2188 (8); β = 93.608 (2) deg.
	: c = 16.8142 (16); γ = 111.5050 (10) deg.
Volume	: 951.98 (16) A^3
Z, Calculated density	: 2, 1.376 g/cm^3
Absorption coefficient	: 0.092 mm^{-1}
F(000)	: 412.0
Crystal size	: 0.40 x 0.07 x 0.22 mm
Theta range for data collection	: 1.24 to 26.03 deg.
Limiting indices	: -9 < = h < = 9, -10 < = k < = 10, -20 < = 1 < = 20
Reflections collected / unique	: 9897 / 3722 [R (int) = 0.0262]
Completeness to theta = 26.03	: 99.3%
Absorption correction	: Multi-scan
Max. and min. transmission	: 0.9926 and 0.8432
Refinement method	: Full-matrix least-squares on F^2
Data / restrains / parameters	: 3722 / 0 / 271
Goodness-of-fit on F^2	: 1.023
Final R indices [I>2sigma(I)]	: R1 = 0.0580, wR = 0.1424
R indices (all data)	: R1 = 0.0878, wR2 = 0.1588
Largest diff. peak and hole	: 0.499 and -0.196 e. A^{-3}

Table 2: Crystal data and structure refinement for 80b

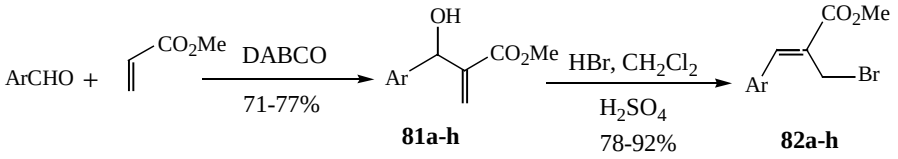
Identification code	: **80b**
Empirical formula	: $C_{28}H_{22}O_4$
Formula Weight	: 426.49
Temperature	: 293(2)K
Wavelength	: 0.71073 A^0
Crstal system, space group	: Orthorhombic, P 21 21 21 (International Table No. 61)
Unit cell dimensions	: a = 7.145 (3); α = 90 deg.
	: b = 11.958 (4); β = 90 deg.
	: c = 25.021 (9); γ = 90 deg.
Volume	: 2137.7 (13) A^3
Z, Calculated density	: 4, 1.325 g/cm^3
Absorption coefficient	: 0.088 mm^{-1}
F(000)	: 904
Crystal size	: 0.40 x 0.07 x 0.22 mm
Theta range for data collection	: 1.63 to 28.32 deg.
Limiting indices	: -9 < = h < = 9, -15 < = k < = 15, -33 < = 1 < = 33
Reflections collected / unique	: 24790 / 2981 [R (int) = 0.0791]
Completeness to theta = 28.32	: 97.8%
Absorption correction	: Multi-scan
Max. and min. transmission	: 0.9965 and 0.9641
Refinement method	: Full-matrix least-squares on F^2
Data / restrains / parameters	: 2981 / 0 / 291
Goodness-of-fit on F^2	: 1.270
Final R indices [I>2sigma(I)]	: R1 = 0.0827, wR = 0.1379
R indices (all data)	: R1 = 0.1212, wR2 = 0.1487
Largest diff. peak and hole	: 0.217 and -0.182 e. A^{-3}

Table 3: Crystal data and structure refinement for 80f

Identification code	: **80f**
Empirical formula	: $C_{26}H_{16}Cl_2O_4$
Formula Weight	: 463.29
Temperature	: 293(2)K
Wavelength	: 0.71073 A^0
Crstal system, space group	: Orthorhombic, P 21 21 21 (International Table No. 61)
Unit cell dimensions	: a = 7.2498 (9); α = 90 deg.
	: b = 12.0230 (15); β = 90 deg.
	: c = 24.351 (3); γ = 90 deg.
Volume	: 2122.5 (5) A^3
Z, Calculated density	: 4, 1.450 g/cm^3
Absorption coefficient	: 0.338 mm^{-1}
F(000)	: 952
Crystal size	: 0.40 x 0.07 x 0.22 mm
Theta range for data collection	: 1.67 to 28.30 deg.
Limiting indices	: -9 < = h < = 9, -15 < = k < = 14, -31 < = 1 < = 26
Reflections collected / unique	: 13361 / 2897 [R (int) = 0.0662]
Completeness to theta = 28.30	: 96.2%
Absorption correction	: Multi-scan
Max. and min. transmission	: 0.9605 and 0.8822
Refinement method	: Full-matrix least-squares on F^2
Data / restrains / parameters	: 2897 / 0 / 289
Goodness-of-fit on F^2	: 1.004
Final R indices [I>2sigma(I)]	: R1 = 0.0606, wR = 0.1076
R indices (all data)	: R1 = 0.1171, wR2 = 0.1239
Largest diff. peak and hole	: 0.199 and -0.185 e. A^{-3}

Next we have directed our attention to understand the generality of this reaction strategy. Accordingly we have prepared a representative class of the Baylis-Hillman adducts (**81d-h**) (Scheme 39, Table 4) *via* the reaction of various aromatic aldehydes and methyl acrylate. These allyl alcohols (**81d-h**) were converted into the corresponding bromides (**82d-h**) *via* the reaction with HBr (Table 5, Scheme 39).

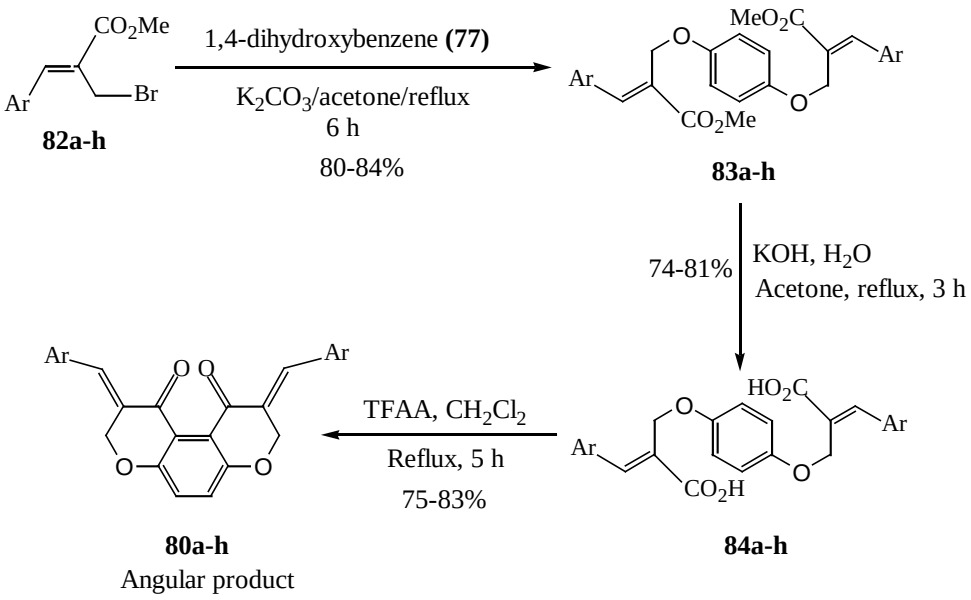
Scheme 39



Ar = Ph, 2-MeC_6H_4, 2-OMeC_6H_4, 4-ClC_6H_4, 4-i-PrC_6H_4, 2-ClC_6H_4, 4-BrC_6H_4, 4-MeC_6H_4

We have next treated these allyl bromides (**82d-h**) with 1,4-dihydroxybenzene (**77**) to give the required biscinnamic ester (**83d-h**) (Scheme 40) which on hydrolysis provided the desired biscinnamic acid (**84d-h**) in excellent yields and with complete *(E)*-selectivity after crystallization (Table 6) . Subsequent treatment with TFAA provided the expected tetrahydrobenzodipyran-4,5-dione derivatives (**80d-h**)[§] in excellent yields (Table 7) . The structure of these compounds were established by IR, ^{1}H NMR (spectrum # 5 and 7 for compounds **80e** and **80g**), ^{13}C NMR (spectrum # 6 and 8 for compounds (**80e** and **80g**) mass spectral data(LCMS), and elemental analysis. The structure and *(E)*-stereochemistry of **80f** was further confirmed by single crystal X-ray data and the ORTEP diagram is presented in Fig. A-3.

Scheme 40



Ar = Ph, 2-MeC_6H_4, 2-$OMeC_6H_4$, 4-ClC_6H_4, 4-i-PrC_6H_4, 2-ClC_6H_4, 4-BrC_6H_4, 4-MeC_6H_4

[$] Stereochemical assignments of the compounds **80a-h** were made on the chemical shift values of the *β*-vinylic proton signals in the ^{1}H NMR spectra of the crude products as well as crystallized products. It is well established in the literature that the ^{1}H NMR spectrum of 3-benzylidenechroman-4-ones the vinylic proton *cis* to the carbonyl group appears at ~ δ 7.7, while the corresponding *trans β*-proton appears at ~ δ 6.7.[109,110] . The *(E)*-stereochemistry of the compounds **80a-h** was assigned on the basis of chemical shift value *of β*-vinylic proton [the *β*-vinylic proton appeared at δ 7.78-8.06 and there was no peak observed ~ δ 6.7 (*Z*-isomer)]. The ^{1}H NMR spectra of the crude as well as crystallized product of compounds **80a-h** indicated the absence of *(Z)*-isomer. The *(E)*-Streochemistry was also confirmed by the single crystal X-ray data analysis for the compounds **80a,b,f**.

[§]For continuity and easy understanding the *(E)*-alkenoic esters, acids and bischromanones obtained from **82a-h** were numbered as **83a-h, 84a-h** and **80a-h** respectively.

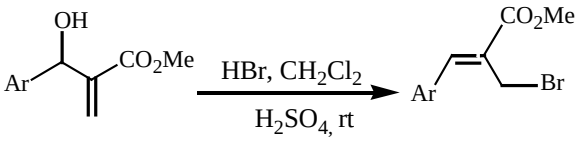
Table 4: Synthesis of Baylis-Hillman alcohols (81a-h)[a,b]

81a-h

S.No	Ar	Time	Baylis-Hillaman adduct	Yield (%)[c]
1	C_6H_5	8d	**81a**	77
2	2-MeC_6H_4	8d	**81b**	74
3	2-MeOC_6H_4	10d	**81c**	75
4	4-ClC_6H_4	8d	**81d**	76
5	4-i-PrC_6H_4	8d	**81e**	72
6	2-ClC_6H_4	8d	**81f**	71
7	4-BrC_6H_4	8d	**81g**	75
8	4-MeC_6H_4	8d	**81h**	72

a) All the reactions were carried out on 200 mmol scale of aldehydes with 300 mmol methyl acrylate 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, 10% EtOAc in hexanes).

Table 5: Synthesis of Baylis-Hillman Bromides[a,c]

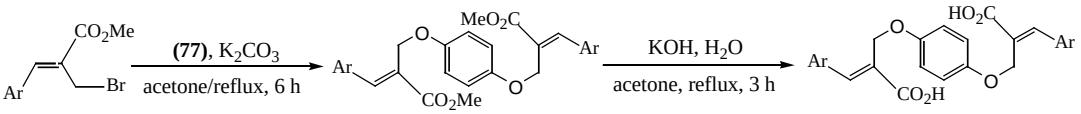


81a-h **82a-h**

S.No	Ar	Time	*(Z)*-Allyl Bromide[b,c]	Yield (%)[d]
1	C_6H_5	12h	**82a**	89
2	2-MeC_6H_4	12h	**82b**	87
3	2-MeOC_6H_4	12h	**82c**	78
4	4-ClC_6H_4	12h	**82d**	79
5	4-i-PrC_6H_4	12h	**82e**	80
6	2-ClC_6H_4	12h	**82f**	82
7	4-BrC_6H_4	12h	**82g**	88
8	4-MeC_6H_4	12h	**82h**	92

a) All the reactions were carried out on 40 mmol scale of the alcohol (**81a-h**) with 48% hydrobromic acid (100 mmol) in presence of sulphuric acid (40 mmol) at rt for 12 hours. b) The products (**82a-h**) were obtained as colourless liquids and were characterized by IR, ^{1}H NMR and ^{13}C NMR spectroscopy. c) (*Z*)-stereochemical assignments were based on the chemical shift values and integration ratios of isomeric olefin proton signals in ^{1}H NMR of the crude products as well as pure products (**82a-h**). (See foot note '#' page no : 37). d) Yields of the pure bromides obtained after silica gel column chromatography (2% EtOAc in hexanes) and are based on the BH-alcohols.

Table 6: Synthesis of 1,4-bis[(2E)-2-carboxy-3-arylprop-2-enyloxy]benzene[a,b] using Baylis-Hillman bromides

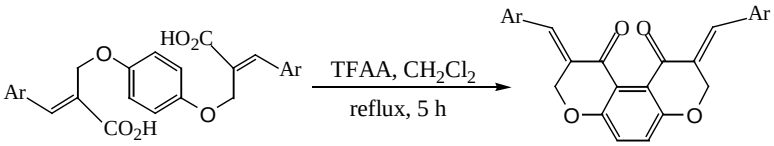


82a-h **83a-h** **84a-h**

Allyl bromide	Ar	Product[c,g]	Yield[d] (%)	Product[e]	Yield (%)[f,g]
82a	C_6H_5	**83a**	83	**84a**	81
82b	2-MeC_6H_4	**83b**	80	**84b**	78
94c	2-MeOC_6H_4	**83c**	84	**84c**	75
82d	4-ClC_6H_4	**83d**	80	**84d**	74
82e	4-i-PrC_6H_4	**83e**	83	**84e**	76
82f	2-ClC_6H_4	**83f**	81	**84f**	78
82g	4-BrC_6H_4	**83g**	82	**84g**	77
82h	4-MeC_6H_4	**83h**	81	**84h**	79

a) All the reactions were carried out in 5 mmol scale of allyl bromides with hydroquinone (2 mmol) in the presence of K_2CO_3 (6 mmol) in acetone at reflux temperature for 6 hours. b) Hydrolysis of these esters were carried out on 1 mmol scale of the esters with aq KOH-acetone at reflux temperature for 3 hours. c) All the compounds **83a-h** were obtained as light brown solids and were characterized by IR, ^{1}H NMR and ^{13}C NMR spectral data. d) Yields are based on 1,4-dihydroxybenzene. e) All the compounds **84a-h** were obtained as white crystalline solids and were characterized by IR, ^{1}H NMR and ^{13}C NMR spectral data. f) Isolated yields of the pure acids (**84a-h**) [after crystallization (Hexane / EtOAc in 2:1 ratio] based on the bis-esters. g) (*E*)-stereochemical assignments were based on the chemical shift values of olefin proton signals in ^{1}H NMR of the crude products as well as pure products (**83 & 84a-h**). See foot note '#' page no : 37).

Table 7: Synthesis of Tetrahydrobenzodipyrandiones [a,b]:



84a-h **80a-h**
Angular product

***E*-Bis cinnamic acid**	**Ar**	**Bischromanone**[b,d]	**Yield %**[c]
84a	C_6H_5	**80a**	83
84b	2-MeC_6H_4	**80b**	81
84c	2-MeOC_6H_4	**80c**	84
84d	4-ClC_6H_4	**80d**	77
84e	4-i-PrC_6H_4	**80e**	75
84f	2-ClC_6H_4	**80f**	80
84g	4-BrC_6H_4	**80g**	82
84h	4-MeC_6H_4	**80h**	83

a) All the reactions were carried out on 0.5 mmol scale of the acid (**84a-h**) with TFAA (0.75 mmol) in CH_2Cl_2 at reflux temperature for 5 hours. b) All the products gave satisfactory IR, ^{1}H NMR, ^{13}C NMR, mass spectral data and elemental analysis. c) Isolated yields of the pure tetrahydrobenzodipyrandiones (**80a-h**) obtained after crystallization [from Hexane / EtOAc (2:1) ratio] and are based on bis-acids . d) *(E)*-stereochemistry was assigned on the basis of ^{1}H NMR spectral analysis. (See foot note '$' page no: 40) and the *(E)*-Streochemistry was also confirmed by the single crystal X-ray data analysis for the compounds **80a,b,f**.

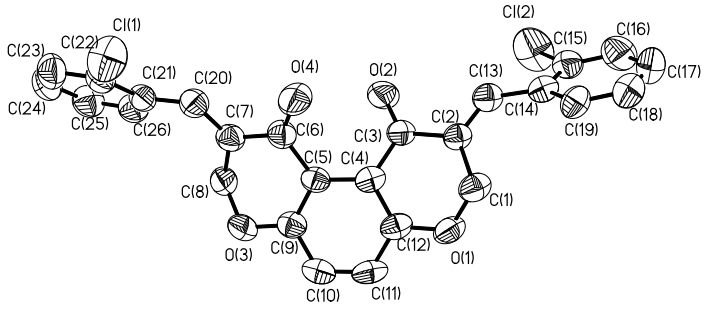
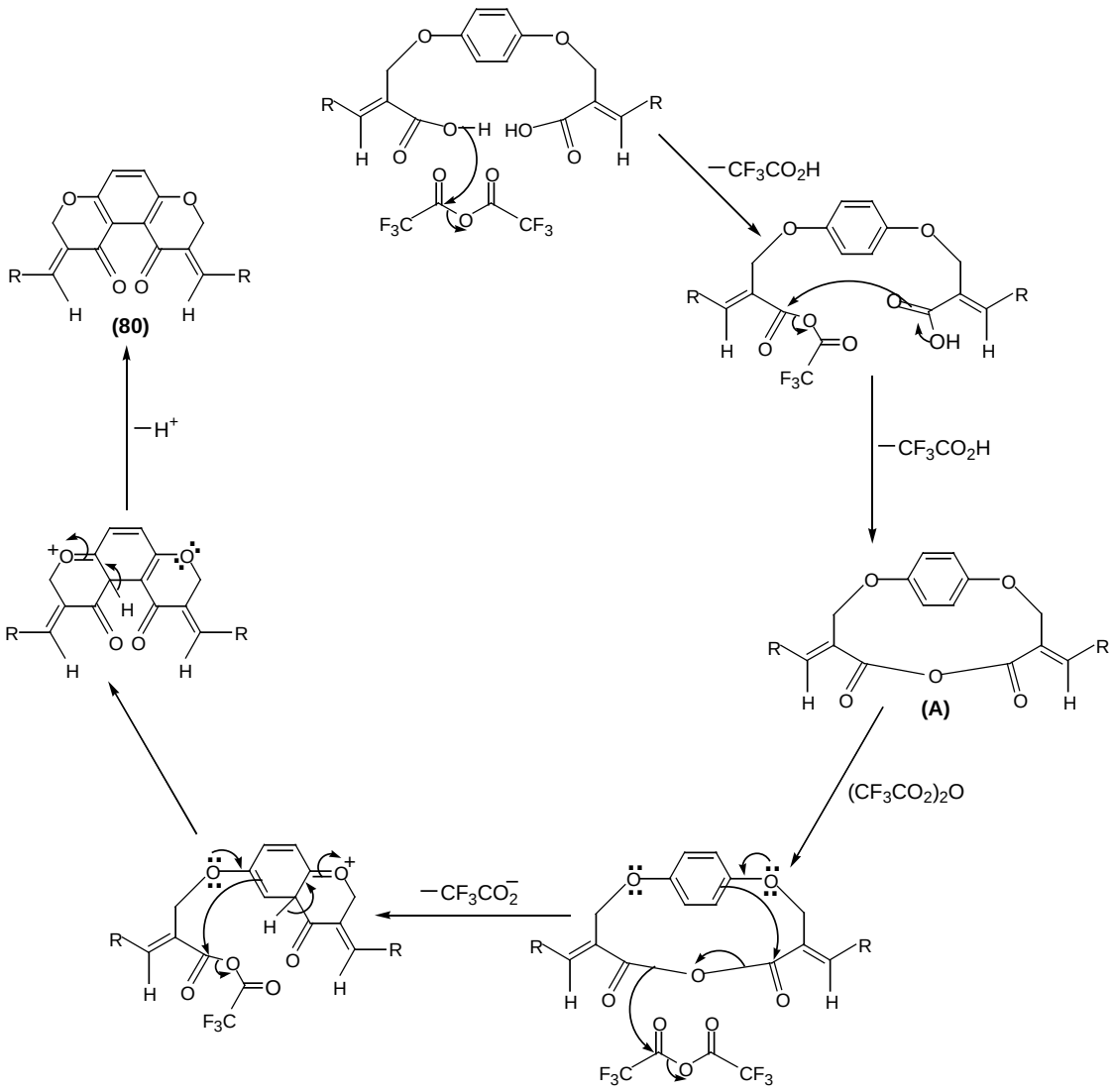


Fig. A3
ORTEP diagram of compound **80f**
(Hydrogen atoms are omitted for clarity)

It is interesting to note that in all these reactions only angular products were obtained and we did not observe any significant amounts of linear adducts. A plausible mechanism for the formation of angular products is presented in Scheme 41. This might be due to the fact that the biscinnamic acid when treated with TFAA first might provide the anhydride **(A)**. Due to the formation of this anhydride framework the resulting Friedel-Crafts reaction exclusively provided the angular product (Scheme 41) due to the proximity effect.

Thus, we have developed a simple and convenient procedure for the synthesis of [7,12-bis(4-arylidene-5,14-dioxatricyclo[8.4.0.0^{4,9}]tetradeca-1,3,9-triene-8,11-dione derivatives thus demonstrating the synthetic application of the Baylis-Hillman adducts in the synthesis of oxygen heterocyclic compounds.

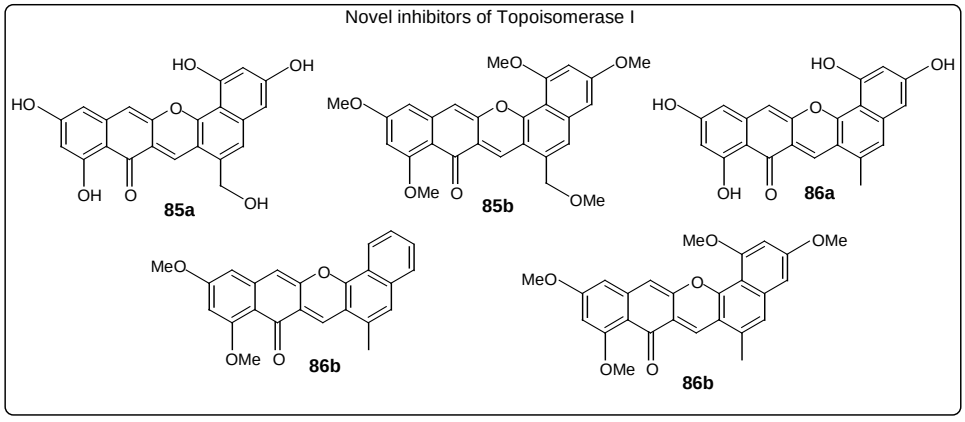
Scheme 41



Development of facile synthesis of 7:8-benzochroman-4-one from Baylis-Hillman adducts:

After successfully developing a simple methodology for obtaining tetrahydrobenzodipyrandiones (**80a-h**) we have next directed our studies towards the synthesis of benzochromanones as these derivatives occupy an interesting place in the oxygen heterocyclic chemistry because of presence of this framework in a number of biologically active natural products.[111-113] Hypoxyxylerone (**85a**), a dibenzoxanthenone isolated from the fungus *Hypoxylon fragiforme* in 1991 by Edwards and coworkers, has been shown to inhibit in vitro topoisomerase I.[114] Also many hypoxyxylerone analogues (**85 & 86**) (Figure 7) were found to possess the activity as Inhibitors of Topoisomerase I[111-113] in *vitro*.

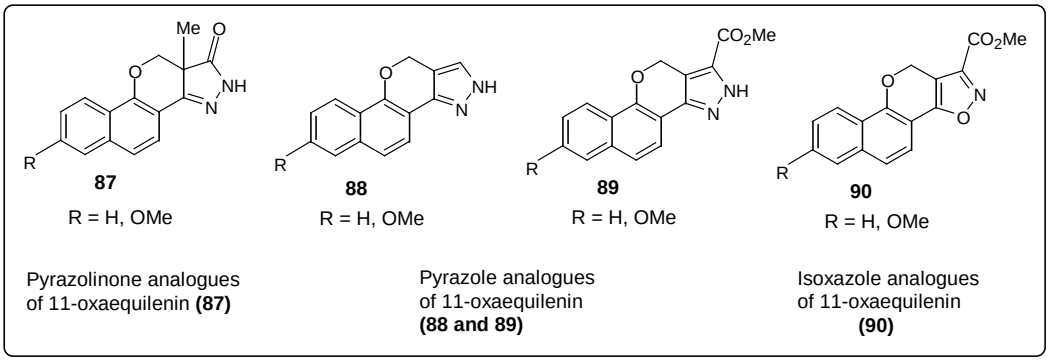
Figure 7



In view of interesting physiological activity[115] exhibited by pyrazole and isoxazole analogues of steroids, synthesis of a few pyrazolinone (**87**), pyrazole (**88 & 89**) and

isoxazole (**90**) (Figure 8) analogues of 11-oxaequilenin[116] 7:8-benzochromanones have been employed as synthons for obtaining these molecules (**87**-**90**).

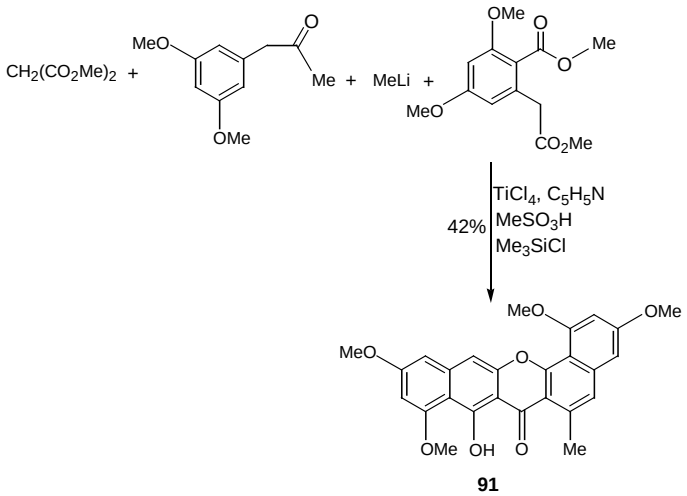
Figure 8



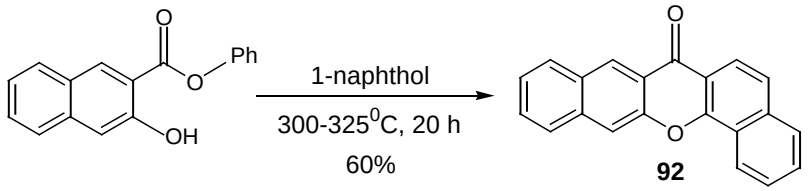
Because of the medicinal importance of these derivatives, development of simple methodologies for obtaining these derivatives has become an attractive endeavour in organic chemistry.

Gimbert and co-workers[111] have reported the synthesis of pentacyclic xanthone (**91**) having 7:8-benzochroman-4-one framework following the reaction sequence as shown in Scheme 42.

Scheme 42



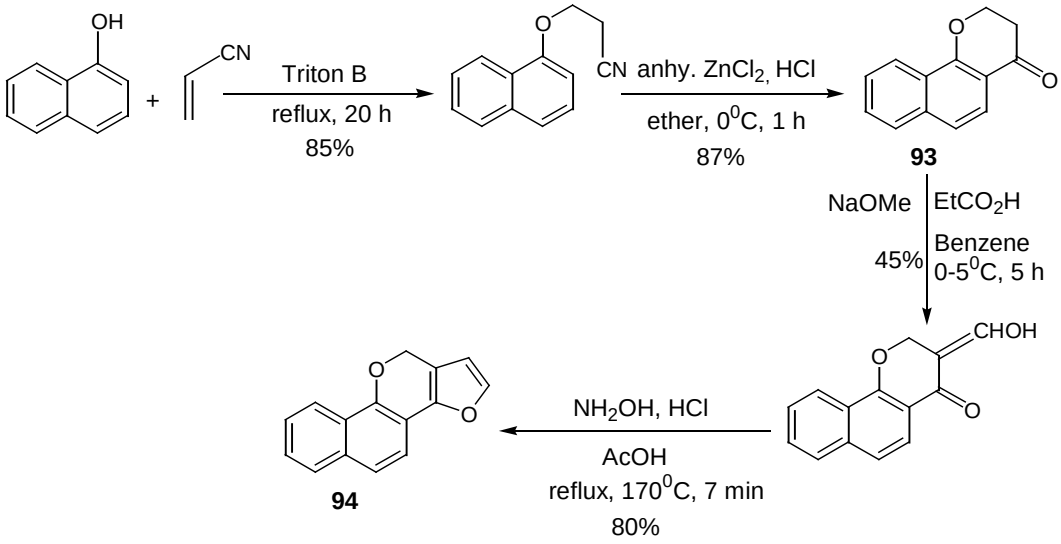
Van Allan and coworkers[116] have reported synthesis of dibenzoxanthenone (92) following the reaction sequence as given in Eq. 27.



Eq. 27

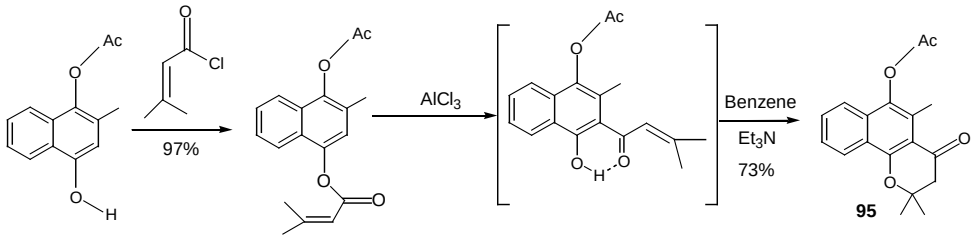
Kasturi[117] and Arunachalam reported synthesis of 2,3-dihydro-4H-naphtho[1,2-b]pyran-4-one (**93**) and benz(h)chromano[3,4-d]isoxazole (**94**) starting from 1-naphthol derivatives following the reaction sequence as shown in Scheme 43 (one example is presented).

Scheme 43

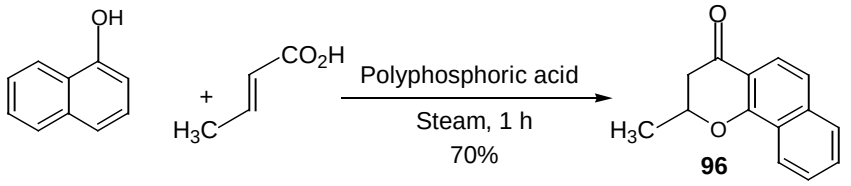


Brucker[118] and Bauld reported synthesis of benzochromanone derivative (**95**) following the reaction sequence as reported in Scheme 44.

Scheme 44



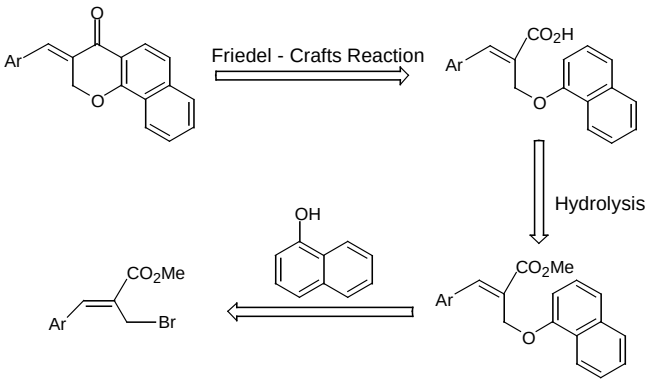
Anjaneyulu and co-workers reported synthesis of benzochromanone derivative (**96**) in good yield by condensing 1-naphthol with crotonic acid in the presence of polyphosphoric acid according to the Eq. 28 (one example is presented).[119]



Eq. 28

Due to the importance of the benzochromanone framework in medicinal chemistry we have undertaken a project of synthesizing these molecules. We felt that Baylis-Hillman bromides could be versatile starting materials for synthesis of 7:8-benzochroman-4-ones. Retrosynthetic strategy is presented in Scheme 45.

Scheme 45



Accordingly we have selected the allyl bromide methyl (2*Z*)-2-(bromomethyl)-3-phenyl prop-2-enoate (**82a**) as a substrate for reaction with 1-naphthol. The best results in this study was obtained when the allyl bromide (**82a**) (2 mmol) was treated with 1-naphthol in the presence K_2CO_3 in acetone under reflux for 6 hours thus providing the desired cinnamic ester (**97a**). Subsequent hydrolysis of the cinnamic ester (**97a**) provided the (2*E*)-2-(1-naphthoxymethyl)-3-phenylprop-2-enoic acid (**98a**) in 86% yield. The transformation of the acid (**98a**) into benzochromanone (**99a**) was effected with TFAA. Thus the treatment of acid (1 mmol) with TFAA (2 mL) for 3 hours provided the desired 7:8-benzochroman-4-one (**99a**)® in 85% isolated yield after purification through column chromatography (Scheme 46) with *(E)*–stereochemistry predominating (*E:Z*= 90:10). The structure of the compound was confirmed by IR, ^{1}H NMR (spectrum 9), ^{13}C NMR (spectrum 10), mass spectral data (LCMS) and elemental analysis. The structure of this molecule was further confirmed by single crystal X-data (ORTEP diagram, Fig. A4) (Table 8).

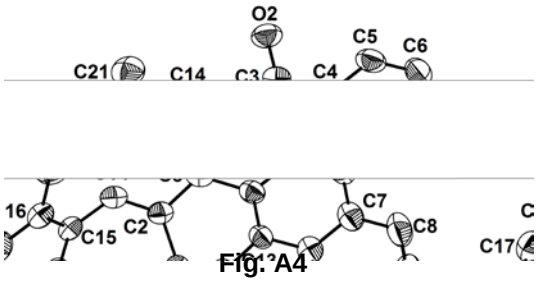
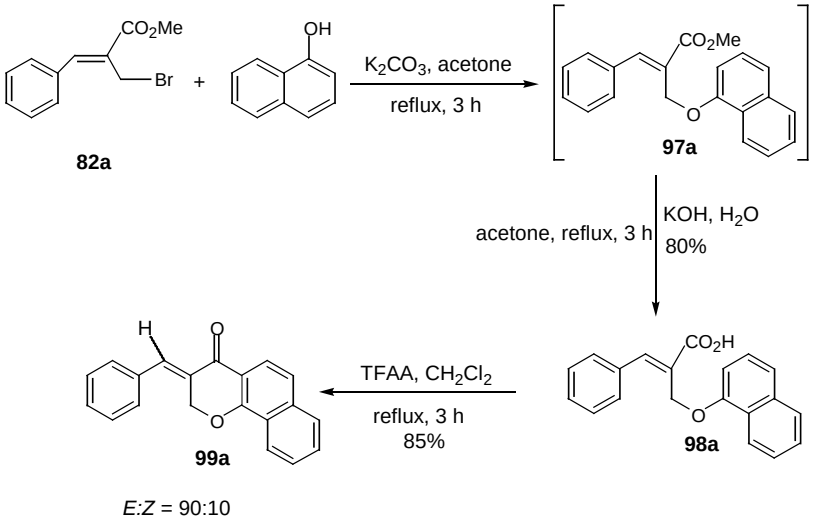


Fig. A4

ORTEP diagram of compound **99b**
(Hydrogen atoms are omitted for clarity)

© It has been reported in literature that in the ^{1}H NMR spectrum, the chemical shifts of the vinylic *β*-protons *cis* to the ketone, ester, and acid carbonyl groups appear downfield in comparison with that of *trans β*-protons.[104,105]. The *(E)*-stereochemistry of these molecules **98a-h** was assigned on the basis of the chemical shift values of the *β*-vinylic protons, i.e. δ 8.00 - 8.36.[103-108]

Scheme 46



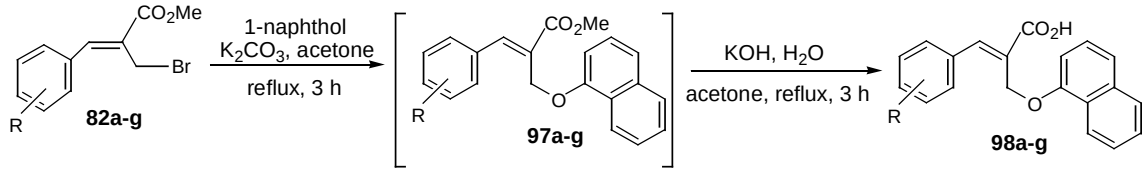
With a view to understand the generality of the reaction strategy we have subjected a number of Baylis-Hillman bromides (**82a-g**) to the reaction with 1-naphthol to provide the cinnamic esters (**97a-g**) which on *in situ* hydrolysis provided the *(E)*-cinnamic acids (**98a-g**) (Table 9). Subsequent Friedel-Craft reaction of these acids afforded the desired benzochromanone derivatives (**99a-g**)[€] in 80-85% yield (Scheme 49, Table 10) with *(E)*-stereochemistry predomination (*E:Z*= 70-98:2-30). The structure of these compounds were established by IR, ^{1}H NMR (spectrum # 11,13, and 15 for compounds **99b, 99c,** and **99e**), ^{13}C NMR (spectrum # 12,14, and 16 for compounds **99b, 99c,** and **99e**), mass spectral data (LCMS), and elemental analysis.

[®] Stereochemical assignments (*E*- and *Z*-stereochemistry) and stereochemical yields (*E* / *Z*) were made on the chemical shift values and integration values of the isomeric *β*-vinylic proton signals in the ^{1}H NMR spectra of the crude products. It is well established in the literature that the ^{1}H NMR spectrum of 3-benzylidenechroman-4-ones the vinylic proton *cis* to the carbonyl group appears at ~ δ 7.7, while the corresponding *trans β*-proton appears at ~ δ 6.7.[109,110] The ^{1}H NMR spectra of the crude as well as crystallized product of compounds **99a-g** indicated the presence of 2-30% minor *(Z)*-isomer. The *E/Z* selectivity was determined by the integration ratio of isomeric *β*-vinylic protons [the *β*-vinylic proton *cis* to carbonyl group (*E*-isomer) appeared at δ 7.81-8.05 with high intensity while same proton *trans* to carbonyl group (*Z*-isomer) appears at δ 6.94-7.15 with low intensity]

Table 8: Crystal data and structure refinement for 99b

Identification code	: **99b**
Empirical formula	: $C_{21}H_{16}O_2$
Formula Weight	: 300.34
Temperature	: 293(2)K
Wavelength	: 0.71073 A^0
Crstal system, space group	: Monoclinic, P2 (1) / n
Unit cell dimensions	: a = 13.5433 (16); α = 90 deg.
	: b = 6.9550 (8); β = 94.034 (2) deg.
	: c = 16.381 (2); γ = 90 deg.
Volume	: 1539.2 (3) $A^{0\,3}$
Z, Calculated density	: 4, 1.296 g/cm^3
Absorption coefficient	: 0.082 mm^{-1}
F(000)	: 632
Crystal size	: 0.72 x 0.40 x 0.10 mm
Theta range for data collection	: 1.89 to 26.02 deg.
Limiting indices	: -16 < = h < = 15, -8 < = k < =8, -20 < = 1 < = 19
Reflections collected / unique	: 9463 / 3025 [R (int) = 0.0321]
Completeness to theta = 26.02	99.8%
Absorption correction	: Empirical
Max. and min. transmission	: 0.9959 and 0.9757
Refinement method	: Full-matrix least-squares on F^2
Data / restrains / parameters	: 3025 / 0 / 209
Goodness-of-fit on F^2	: 1.100
Final R indices [I>2sigma(I)]	: R1 = 0.0671, wR = 0.1421
R indices (all data)	: R1 = 0.0955, wR2 = 0.1554
Largest diff. peak and hole	: 0.173 and -0.174 e. A^{-3}

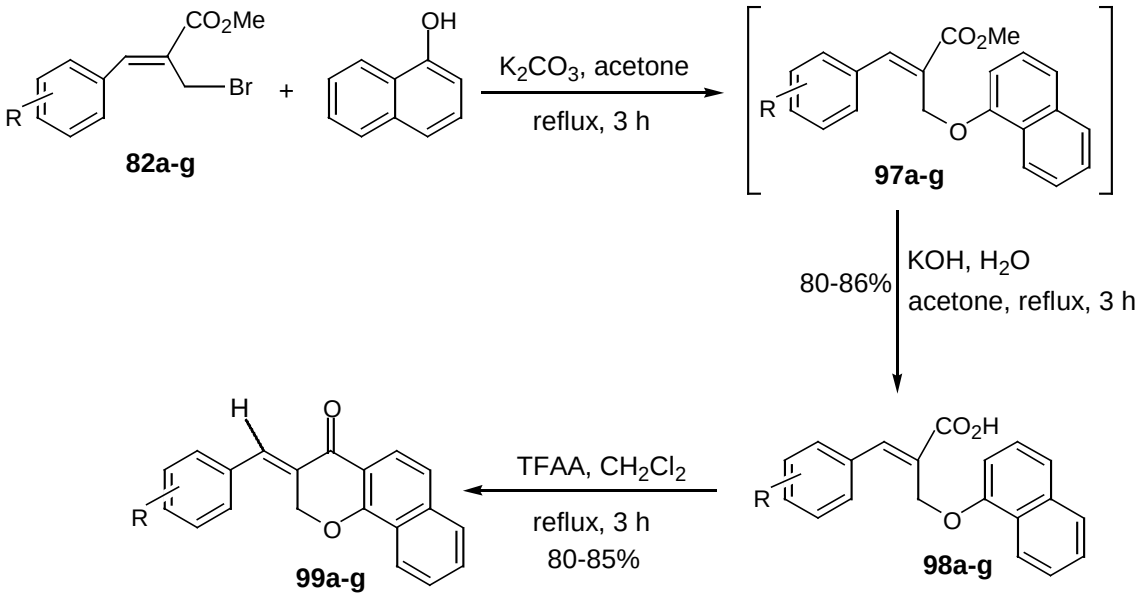
Table 9: Synthesis of (2*E*)-2-(1-naphthoxymethyl)-3-arylprop-2-enoic acids[a,b]



(Z)-Allylbromide	Ar	*(E)*-Alkenoic Acid[c]	Yield %[d]
82a	C_6H_5	**98a**	80
82b	2-MeC_6H_4	**98b**	82
82c	2-MeOC_6H_4	**98c**	84
82d	4-ClC_6H_4	**98d**	81
82e	4-i-PrC_6H_4	**98e**	83
82f	2-ClC_6H_4	**98f**	84
82g	4-BrC_6H_4	**98g**	86

a) All reactions were carried out in 2 mmol scale of allyl bromides (**82a-g**) with 1-naphthol (2.4 mmol) in the presence of K_2CO_3 (4 mmol) in acetone at reflux temperature for 3 hours followed by hydrolysis of the ester using aq. KOH in acetone at reflux temperature for 3 hours without isolation of ester. b) All the compounds were obtained as white crystalline solids and were characterized by IR, ^{1}H NMR and ^{13}C NMR spectral data. c) The (*E*)-stereochemistry for the compounds **98a-g** were assigned on the basis ^{1}H NMR spectral analysis. (See foot note '©' page no : 63) d) Isolated yields of pure acids after crystallization (10% EtOAc in hexanes) based on the allyl bromides.

Scheme 48



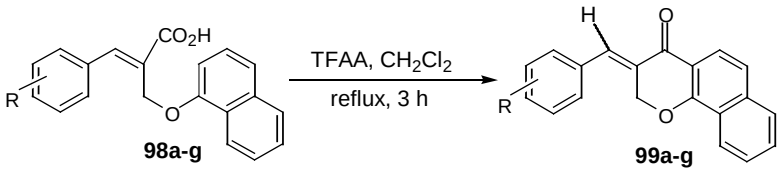
R = H, 2-Me, 2-OMe, 4-Cl, 4-Pr^{i}, 2-Cl, 4-Br

E:Z = 70-98:2-30

[©] It has been reported in literature that in the ^{1}H NMR spectrum, the chemical shifts of the vinylic *β*-protons *cis* to the ketone, ester, and acid carbonyl groups appear downfield in comparison with that of *trans β*-protons.[104,105]. The *(E)*-stereochemistry of these molecules **98a-h** was assigned on the basis of the chemical shift values of the *β*-vinylic protons, i.e. δ 8.00 - 8.36.[103-108]

[€]For continuity and easy understanding the (*E*)-alkenoic esters, acids and biscnhromanones obtained from **82a-g** were numbered as **97a-g, 98a-g** and **99a-g** respectively.

Table 10: Synthesis of 7:8-benzo[h]chroman-4-ones[a-c]

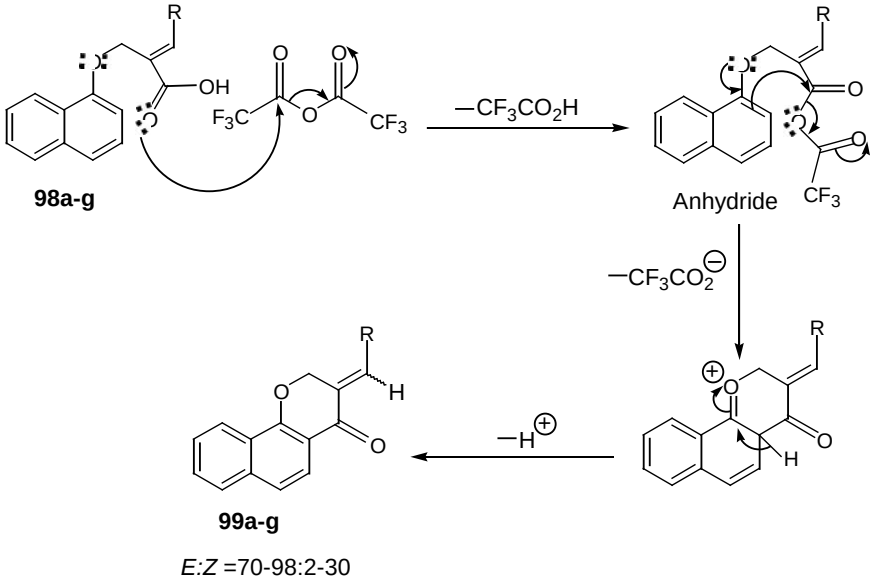


(Z) Allylbromide	Ar	Benzochromanone[c]	*E : Z*[d]	Yield[e] %
98a	C_6H_5	**99a**	90 : 10	85
98b	2-MeC_6H_4	**99b**	90 : 10	80
98c	2-MeOC_6H_4	**99c**	96 : 4	81
98d	4-ClC_6H_4	**99d**	70 : 30	84
98e	4-i-PrC_6H_4	**99e**	98 : 2	82
98f	2-ClC_6H_4	**99f**	90 : 10	83
98g	4-BrC_6H_4	**99g**	97 : 3	85

a) All the reactions were carried out on 1 mmol scale of the acid (**98a-g**) with TFAA (3 mmol) in CH_2Cl_2 at reflux temperature for 3 hours. b) All the products gave satisfactory IR, ^{1}H NMR, ^{13}C NMR, mass spectral data and elemental analysis. c) The products **99a-g** were obtained as pale yellow crystalline solids. d) ^{1}H NMR spectra of the crude products indicated the presence of 2-30% minor *(Z)*-isomer along with the major *(E)*-isomer. (See foot note '®' in page no: 60) e) Yields of the pure products obtained after crystallization from EtoAc-hexanes (2:1 ratio).

A possible mechanism for the intramolecular Friedel-Crafts reaction is presented in Scheme 49. Thus, we have developed a new protocol for the synthesis of 7:8-benzochroman-4-ones using the Baylis-Hillman adducts.

Scheme 49



Novel and facile synthesis of 5:6-benzochroman-4-ones using Baylis-Hillman bromides:

We have next directed our studies towards developing a simple synthesis of 5:6-benzochroman-4-ones as these derivatives have become increasingly important in recent years owing to the antimicrobial activity against trichomonads, gram-positive and gram-negative bacteria and fungi[120] (Figure 9). Several pyrazole and isoxazole analogues of steroid (**101**-**102**) (Figure 10) (which were synthesized from the corresponding 5:6-benzochromanones) were found to exhibit interesting physiological activity.[121,122]

Figure 9

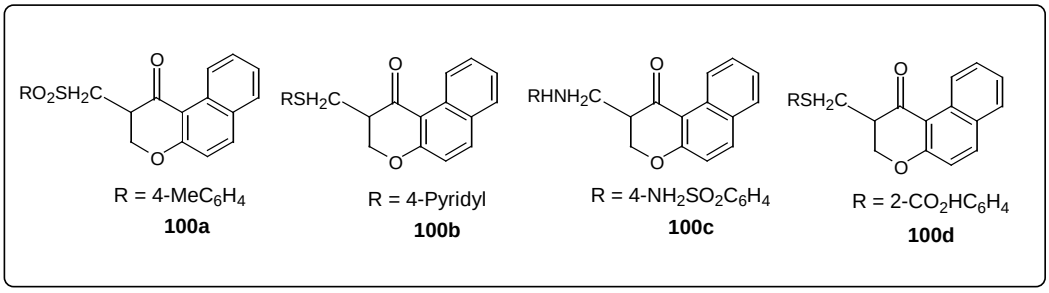
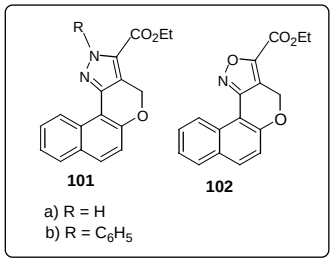
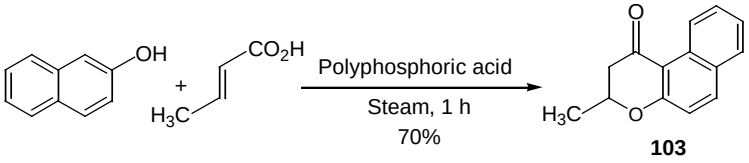


Figure 10



Due to the medicinal and pharmaceutical importance of this framework, there has been increasing interest in developing simple methodology for obtaining these derivatives. Representative literature methods are presented in this section. Anjaneyulu[119] and co-

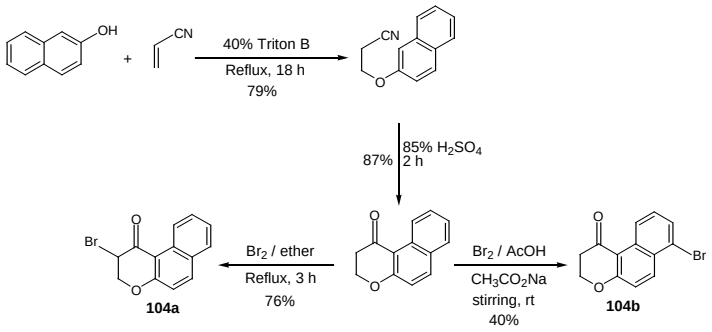
workers have reported synthesis of benzochromanone (**103**) *via* the reaction of 2-naphthol with crotonic acid in the presence of polyphosphoric acid according to Equation 29.



Eq. 29

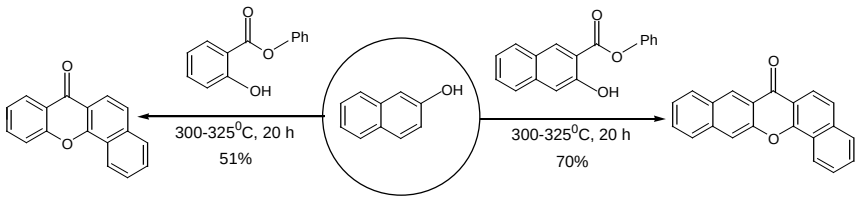
Bachman and Levine[123] reported synthesis of 2-bromo-1-benzo(f)chromanone (**104a**) and 7-bromo-1-benzo(f)chromanone (**104b**) according to the reaction sequence as shown in Scheme 49.

Scheme 49



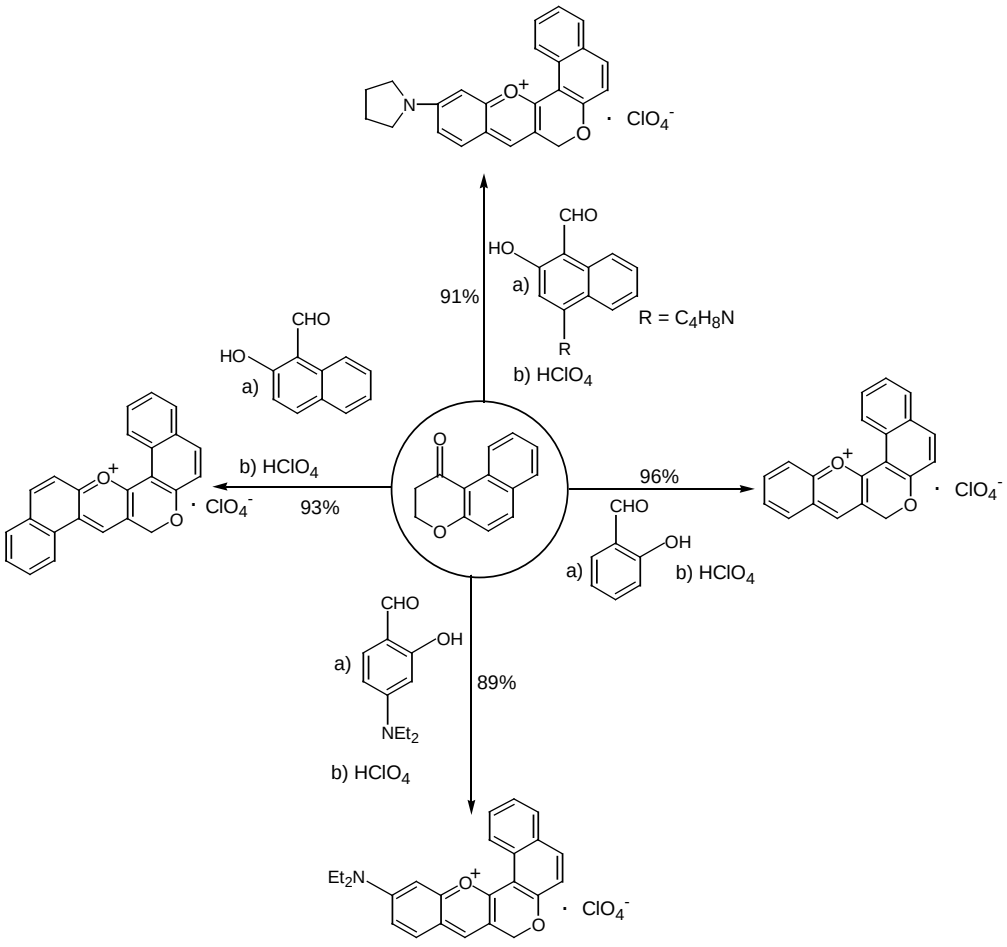
Synthesis of benzoxanthenone and dibenzoxanthenone derivatives (**105a & 105b**) have been reported by Van Allan and coworkers[116] following the reaction sequence as described in the Scheme 50.

Scheme 50



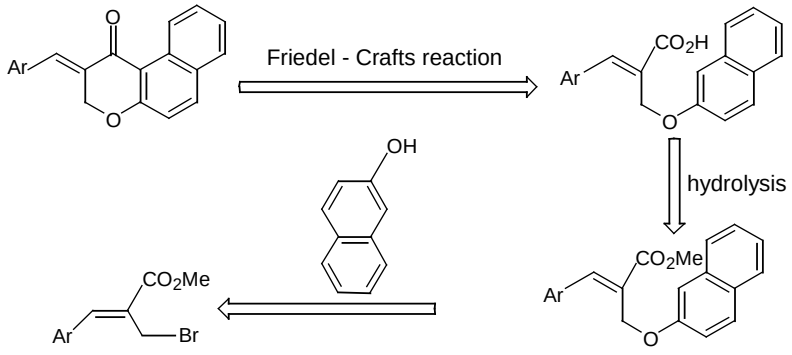
Czemy and co-workers[124] have reported the synthesis of benzopyrylium salts from 5:6-benzochroman-4-one as shown below (Scheme 51).

Scheme 51



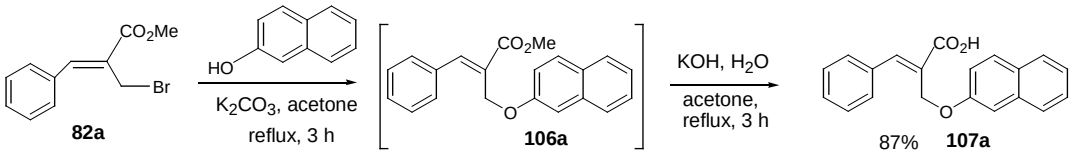
In view of the importance of benzochromanones, we have undertaken this project to synthesize 5:6-benzochroman-4-ones using the Baylis-Hillman adducts according to the retrosynthetic strategy as indicated in Scheme 52.

Scheme 52



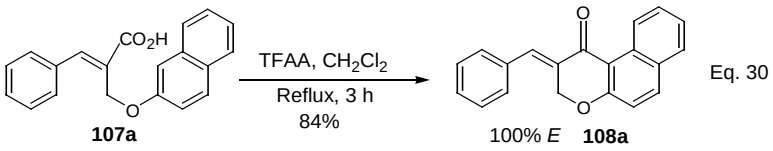
We have here also selected the allyl bromides methyl (2*Z)*-2-(bromomethyl)-3-phenyl prop-2-enoate (**82a**) for treatment with 2-naphthol in the presence of K_2CO_3 to afford the cinnamic ester. The resulting crude cinnamic ester (**106a**) as such was hydrolyzed with aq. KOH in acetone to provide the required (2*E*)-2-(naphthoxymethyl)-3-phenylprop-2-enoic acid (**107a**) in 87% isolated yield (Scheme 53). The *(E)*-stereochemistry of this compound (**107a**) was established by ^{1}H NMR spectral analysis[£].

Scheme 53



Next we planned to transform (2*E*)-2-(2-naphthoxymethyl)-3-phenylprop-2-enoic acid (**107a**) into the desired 5:6-benzochroman-4-one (**108a**) *via* an intramolecular Friedel-Crafts reaction (Scheme 55). We have selected TFAA as a reagent for effecting intramolecular Friedel-Crafts reaction of the acid (**107a**). The best results were obtained

when (2*E*)-2-(2-naphthoxymethyl)-3-phenylprop-2-enoic acid **107a** (1 mmol) was treated with TFAA (3 mL) in CH_2Cl_2 at reflux temperature for 3 hours, thus providing the desired 5:6-benzochroman-4-one (**108a**) in 84% yield (Eq. 30).



Eq. 30

The structure of this molecule was confirmed by IR, ^{1}H NMR (spectrum 17) & ^{13}C NMR (spectrum 18) spectral analysis. The structure of the molecule was also confirmed by single crystal X-ray data (ORTEP diagram, Fig. A5, Table 11).

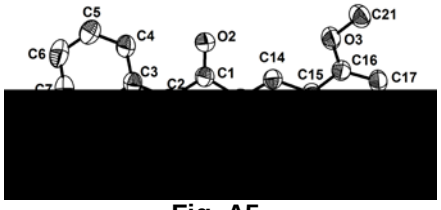


Fig. A5
ORTEP diagram of compound **108c**
(Hydrogen atoms are omitted for clarity)

[£] It has been reported in literature that in the ^{1}H NMR spectrum, the chemical shifts of the vinylic *β*-protons *cis* to the ketone, ester, and acid carbonyl groups appear downfield in comparison with that of *trans β*-protons.[104,105] The *(E)*-stereochemistry of these molecules **107a-e,h** was assigned on the basis of the chemical shift values of the *β*-vinylic protons, i.e. δ 7.68- 8.17.[103-108]

[¢] The *E/Z* selectivity was determined by the integration ratio of isomeric *β*-vinylic proton signals in ^{1}H NMR spectra of the crude as well as crystallized products. It is well documented in the literature that in the ^{1}H NMR spectrum of 3-benzylidenechroman-4-ones the vinylic proton *cis* to the carbonyl group appears at ~ δ 7.7, while the corresponding *trans β*-proton appears at ~ δ 6.7.[109,110] . In the case of compound **108b-e,h,** the ^{1}H NMR spectra of the crude as well as crystallized products, the *β*-vinylic proton *cis* to carbonyl group (*E*-isomer) appeared at δ 7.81-8.05 with high intensity while the same proton *trans* to carbonyl group (*Z*-isomer) appeared at δ 6.83-7.18 with low intensity. The compounds 108 b-e,h were obtained as a mixturte of *(E)* and *(Z)* isomers (E/Z = 90-98: 2-10) In the case of compound **108a** 100% *(E)*-selectivity was determined by the absence of *(Z)*-olefinic proton signal in ^{1}H NMR spectrum of crude as well as pure product. [In the ^{1}H NMR of the crude as well as crystallized product, the *β*-vinylic proton signal appeared

at δ 7.91 (i.e. *(E)*-olefinic proton) and there was no peak observed in the range δ 6.83-7.18 (i.e *(Z)*-olefinic proton)].

Encouraged by this fascinating result we have extended this strategy to a representative classes of the Baylis-Hillman bromides (**82a-e,h**). Thus the treatment of allyl bromides (**82a-e,h**) with 2-naphthol under the influence of K_2CO_3 followed by hydrolysis of the resulting cinnamic esters (**106a-e,h**) provided the desired cinnamic acids (**107a-e,h**) in 81-87% isolated yields. Structures of all these acids were confirmed by IR, ^{1}H NMR, ^{13}C NMR spectral analysis. All these results are presented in Scheme 54 and Table 12. Subsequent intramolecular Friedel-Crafts reaction of the cinnamic acid with TFAA provided the desired benzochromanones (**108a-e,h**)[¢] in 80-84% isolated yields (Eq. 31) with *(E)*-stereochemistry predominating (*E:Z* =90-100:0-10) (Table 13).

Scheme 54

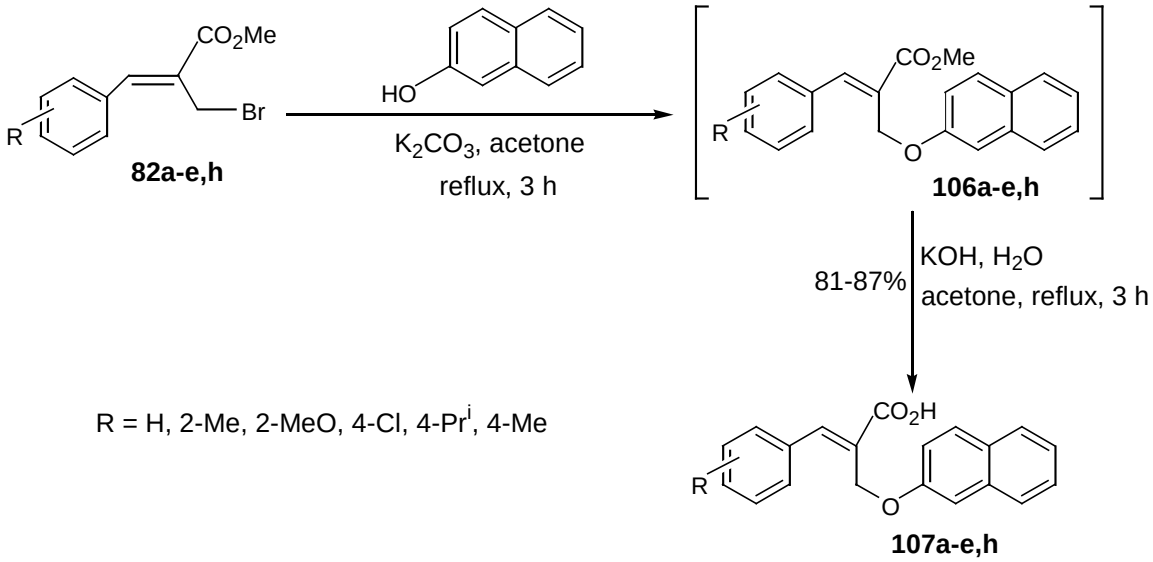
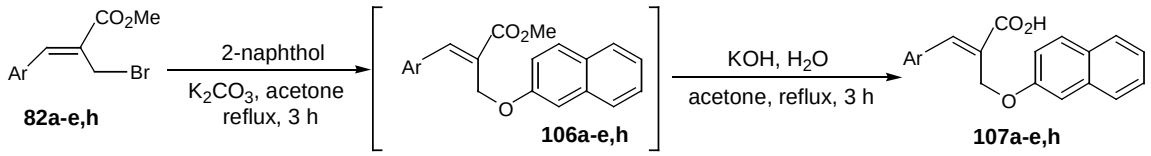


Table 11: Crystal data and structure refinement for 108c

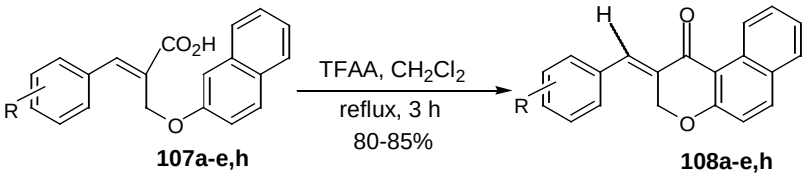
Identification code	: **108c**
Empirical formula	: $C_{21}H_{16}O_3$
Formula Weight	: 316.34
Temperature	: 293(2)K
Wavelength	: 0.71073 A^0
Crstal system, space group	: Monoclinic, P2 (1) / c
Unit cell dimensions	: a = 7.397 (2); α = 90 deg.
	: b = 11.371 (4); β = 97.131 (5) deg.
	: c = 18.895 (6); γ = 90 deg.
Volume	: 1576.9 (9) $A^{0\,3}$
Z, Calculated density	: 4, 1.332 g/cm^3
Absorption coefficient	: 0.082 mm^{-1}
F(000)	: 664
Crystal size	: 0.40 x 0.26 x 0.24 mm
Theta range for data collection	: 2.09 to 25.03 deg.
Limiting indices	: -8 < = h < = 8, -13 < = k < = 13, -22 < = 1 < = 22
Reflections collected / unique	: 8992 / 2765 [R (int) = 0.048]
Completeness to theta = 25.03	99.2%
Absorption correction	: Empirical
Max. and min. transmission	: 0.9791 and 0.9655
Refinement method	: Full-matrix least-squares on F^2
Data / restrains / parameters	: 2765 / 0 / 281
Goodness-of-fit on F^2	: 0.944
Final R indices [I>2sigma(I)]	: R1 = 0.0379, wR = 0.0875
R indices (all data)	: R1 = 0.0590, wR2 = 0.0960
Largest diff. peak and hole	: 0.119 and -0.197 e. A^{-3}

Table 12: Synthesis of (2*E*)-2-(naphthoxymethyl)-3-arylprop-2-enoic acids[a,b]



(Z) **Allylbromide**	**Ar**	**E-Alkenoic acid**[b,c]	**Yield %**[d]
82a	C_6H_5	**107a**	87
82b	2-MeC_6H_4	**107b**	83
82c	2-MeOC_6H_4	**107c**	81
82d	4-ClC_6H_4	**107d**	82
82e	4-i-PrC_6H_4	**107e**	85
82h	4-MeC_6H_4	**107f**	84

a) All reactions were carried out in 2 mmol scale of allyl bromides with 2-naphthol (2.4 mmol) in the presence of K_2CO_3 (4 mmol) in acetone at reflux temperature for 3 hours followed by hydrolysis of the resulting ester using aq. KOH in acetone at reflux temperature for 3 hours without isolation of ester b) All the compounds were obtained as colorless solids and were characterized by IR, ^{1}H NMR and ^{13}C NMR spectral data. c) The (*E*)-stereochemistry for th compound **107** were assigned on the basis ^{1}H NMR spectral analysis. (See foot note '£' page no : 70) d) Isolated yields of pure acids after crystallization (10% EtOAc in hexanes).



107a-e,h **108a-e,h**

E:Z = 90-100:0-10

R = H, 2-Me, 2-MeO, 4-Cl, 4-Pr[i], 4-Me

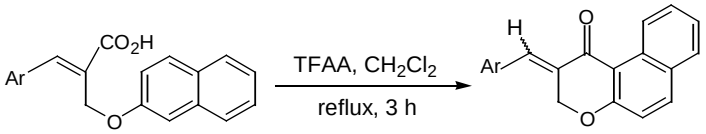
Eq. 31

The structure of these compounds were established by IR, ^{1}H NMR (spectrum # 19 and 21 for compounds **108c** and **108 e**), ^{13}C NMR (spectrum #20 and 22 for compounds **108c** and **108 e**), mass spectral data (LCMS), and elemental analysis.

[þ] For continuity and easy understanding the (*E*)-alkenoic esters, acids and bischromanones obtained from **82a-e,h** were numbered as **106a-e,h, 107a-e,h** and **108a-e,h** respectively.

[¢] The *E/Z* selectivity was determined by the integration ratio of isomeric *β*-vinylic proton signals in ^{1}H NMR spectra of the crude as well as crystallized products. It is well documented in the literature that in the ^{1}H NMR spectrum of 3-benzylidenechroman-4-ones the vinylic proton *cis* to the carbonyl group appears at ~ δ 7.7, while the corresponding *trans β*-proton appears at ~ δ 6.7.[109,110] . In the case of compound **108b-e,h,** the ^{1}H NMR spectra of the crude as well as crystallized products, the *β*-vinylic proton *cis* to carbonyl group (*E*-isomer) appeared at δ 7.81-8.05 with high intensity while the same proton *trans* to carbonyl group (*Z*-isomer) appeared at δ 6.83-7.18 with low intensity. The compounds 108 b-e,h were obtained as a mixturte of *(E)* and *(Z)* isomers (E/Z = 90-98: 2-10) In the case of compound **108a** 100% *(E)*-selectivity was determined by the absence of *(Z)*-olefinic proton signal in ^{1}H NMR spectrum of crude as well as pure product. [In the ^{1}H NMR of the crude as well as crystallized product, the *β*-vinylic proton signal appeared at δ 7.91 (i.e. *(E)*-olefinic proton) and there was no peak observed in the range δ 6.83-7.18 (i.e *(Z)*-olefinic proton)].

Table 13: Synthesis of 5:6-benzo[h]chroman-4-ones[a,b]



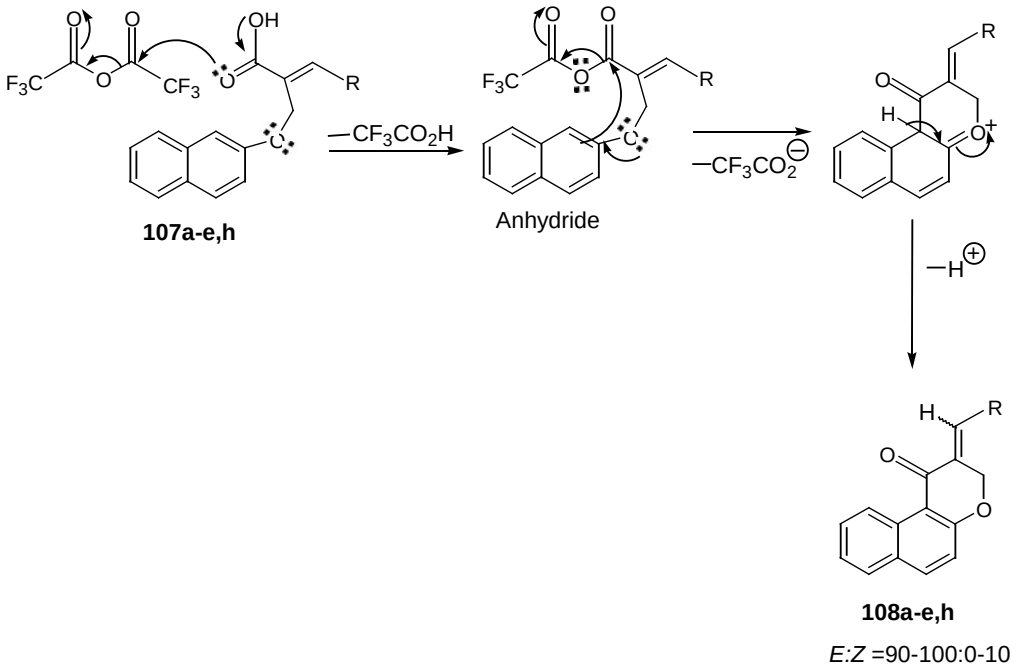
107a-e,h **108a-e,h**

***(E)*- Alkenoic acid**	**Ar**	**Benzochromanone[c]**	***E : Z*[d]**	**Yield %[e]**
107a	C_6H_5	**108a**	100 : 0	84
107b	2-MeC_6H_4	**108b**	90 : 10	81
107c	2-MeOC_6H_4	**108c**	96 : 4	80
107d	4-ClC_6H_4	**108d**	98 : 2	85
107e	4-i-PrC_6H_4	**108e**	98 : 2	83
107h	4-MeC_6H_4	**108h**	90 : 10	82

a) All the reactions were carried out on 1 mmol scale of the acid **(107a-e,h)** with TFAA (3 mmol) in CH_2Cl_2 at reflux temperature for 3 hours. b) All the products gave satisfactory IR, ^{1}H NMR, ^{13}C NMR, mass spectral data and elemental analysis. c) The products **108a-e,h** were obtained as pale yellow crystalline solids. d) ^{1}H NMR spectra of the crude products indicated the presence of 2-10% minor *(Z)*-isomer along with the major *(E)*-isomer. (See the foot note '¢' in page no : 74). e) Yields of the pure products obtained after crystallization from EtoAc-hexanes (2:1 ratio).

A possible mechanism for the intramolecular Friedel-Crafts reaction is presented in Scheme 56. Thus, we have developed a new protocol for the synthesis of 5:6-benzochroman-4-ones using the Baylis-Hillman adducts.

Scheme56



Conclusions:

All the objectives mentioned in the beginning of this chapter have been achieved with considerable success. We have successfully developed a facile synthesis of sterically hindered tetrahydrobenzodipyrandiones (**80a-g**) (angular products) starting from the Baylis-Hillman bromides (**82a-h**) and 1,4-dihydroxybenzene (**77**) as key synthons**,** in a three step process with exclusive (*E*)-stereochemistry. A plausible mechanism for the formation of sterically hindered angular products in preference to the less hindered linear products has been proposed. We have developed a simple synthesis of substituted 7:8-benzochroman-4-one (**99a-g**) frameworks using Baylis-Hillman bromides and 1-naphthol as the strating materials. We have also described a facile methodology for the synthesis of 5:6-benzochroman-4-one frameworks (**108a-e,h**) using Baylis-Hillman bromides and 2-naphthol as the starting materials. A plausible mechanistic pathways for the synthesis of 7:8-benzochroman-4-one (**99a-g**) and 5:6- benzochroman-4-one frameworks (**108a-e,h**) have also been presented. Our studies clearly demonstrate the applications of the Baylis-Hillman bromides as useful synthons in the synthesis of heterocyclic compounds containing oxygen in the ring.

EXPERIMENTAL

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

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

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

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

Nuclear Magnetic Resonance Spectra: Proton magnetic resonance spectra and carbon-13 magnetic resonance spectra were recorded on a BRUKER-AVANCE-200 and BRUKER-AVANCE-400 spectrometers. ^{1}H NMR (200 MHz/400 MHz) spectra for all the samples were measured in chloroform-d, unless otherwise mentioned, with TMS (δ = 0 ppm) as internal standard. ^{13}C NMR (50 MHz/100 MHz) spectra for all the samples were measured in chloroform-d, unless otherwise mentioned, with its middle peak of the triplet (δ = 77.10 ppm) as internal standard. Spectral assignments are as follows: (1) chemical shifts on the δ scale, (2) standard abbreviation for multiplicity, that is, s = singlet, d = doublet, t = triplet, q = quartet, sept = septet, m = multiplet, dd = doublet of doublet, td = triplet of doublet, dt = doublet of triplet, b = broad, d of ABq = doublet of

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

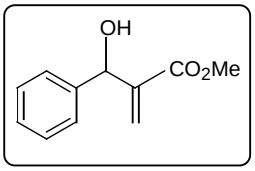
Mass Spectral Analysis: Mass spectra were recorded either on VG7070H mass spectrometer using EI technique or on Auto spec mass spectrometer using LSIMS technique (EI) or on shimadzu LCMS 2010A mass spectrometer.

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

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

Methyl 3-hydroxy-2-methylene-3-phenylpropanoate (81a):

A solution of benzaldehyde (200 mmol, 21.22 g), methyl acrylate (300 mmol, 25.82 g) and DABCO (15 mol%, 30 mmol, 3.36 g) was kept at room temperature for 8 days. To the reaction mixture ether (50 mL) was added and washed successively with 2N HCl, aqueous $NaHCO_3$ solution and water. Organic layer was dried over anhydrous Na_2SO_4. Solvent was removed under reduced pressure and the residue thus obtained was purified by column chromatography (silica gel, 10% EtOAc in hexanes) to provide **81a** in 77% (29.60 g) yield, as a colorless liquid.



IR (neat) : ν 3447, 1716, 1630 cm^{-1}

^1H NMR (400 MHz) : δ 3.03 (bs, 1H), 3.68 (s, 3H), 5.53 (s, 1H), 5.84 (s, 1H), 6.31 (s, 1H), 7.19-7.45 (m, 5H).

^{13}C NMR (50 MHz) : δ 51.75, 72.51, 125.46, 126.83, 127.70, 128.32, 141.65, 142.47, 166.68.

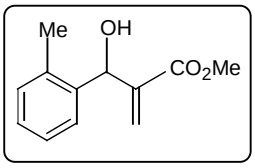
Methyl 3-(2-methylphenyl)-3-hydroxymethylenepropanoate (81b):

This molecule was obtained as a colourless viscous liquid *via* Baylis-Hillman reaction of 2-methylbenzaldehyde with methyl acrylate in the presence of catalytic amount of DABCO following a similar procedure described for the molecule **81a**.

Reaction time : 8 days

Yield : 74%

IR (neat) : ν 3449, 1722, 1630 cm^{-1}

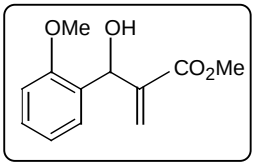


^{1}H NMR (400 MHz) : δ 2.34 (bs, 3H), 2.94 (bs, 1H), 3.77 (s, 3H), 5.63 (s, 1H), 5.82 (s, 1H), 6.34 (s, 1H), 7.14-7.32 (m, 3H), 7.39-7.46 (m, 1H).

^{13}C NMR (100 MHz) : δ 19.07, 51.99, 69.07, 126.08, 126.15, 126.34, 127.78, 130.43, 135.71, 138.92, 141.86, 167.09.

Methyl 3-(2-methoxyphenyl)-3-hydroxy-2-methylenepropanoate (81c):

This compound was obtained as a colorless viscous liquid *via* the treatment of 2-methoxybenzaldehyde with methyl acrylate in the presence of DABCO (cat.) following a similar procedure described for the molecule **81a.**



Reaction time : 10 days

Yield : 75%

IR (neat) : ν 3493, 1722, 1631 cm^{-1}

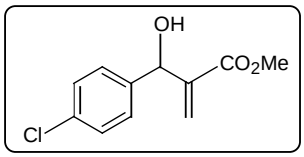
^{1}H NMR (400 MHz) : δ 3.54 (s, 3H), 3.63 (s, 3H), 3.64 (bs, 1H), 5.58 (s, 1H), 5.73 (s, 1H), 6.13(s, 1H), 6.70 (d, 1H, *J* = 8.0 Hz), 6.75-6.83 (m, 1H), 7.05-7.14 (m, 1H), 7.16-7.22 (m, 1H).

^{13}C NMR (50 MHz) : δ 51.67, 55.26, 67.85, 110.55, 120.56, 125.39, 127.50, 128.74, 129.30, 141.59, 156.56, 166.94.

Methyl 3-(4-chlorophenyl)-3-hydroxy-2-methylenepropanoate (81d):

This molecule was obtained as a colorless viscous liquid *via* the treatment of 4-chloro benzaldehyde with methyl acrylate in the presence of DABCO as a catalyst following a similar procedure described for the molecule **81a**.

Reaction time : 8 days



Yield : 76%

IR (neat) : ν 3481, 1718, 1630 cm^{-1}

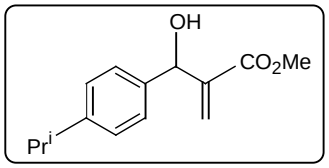
^{1}H NMR (400 MHz) : δ 3.23 (b, 1H), 3.71 (s, 3H), 5.51 (s, 1H), 5.83 (s, 1H), 6.33 (s, 1H), 7.30 (s, 4H).

^{13}C NMR (50 MHz) : δ 51.99, 72.44, 126.14, 128.04, 128.54, 133.54, 139.92, 141.79, 166.60.

Methyl 3-(4-isopropylphenyl)-3-hydroxy-2-methylenepropanoate (81e):

This compound was obtained as a colorless viscous liquid *via* the treatment of 4-isopropylbenzaldehyde with methyl acrylate in the presence of catalytic amount of DABCO following a similar procedure described for the molecule **81a.**

Reaction time : 8 days



Yield : 72%

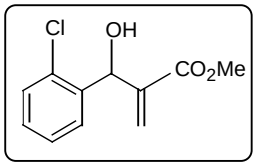
IR (neat) : ν 3429, 1716, 1633 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.22 (d, 6H, *J* = 6.8 Hz), 2.88 (s, 1H), 3.03 (bs, 1H), 3.68 (s, 3H), 5.51 (s, 1H), 5.85 (s, 1H), 6.30 (s, 1H), 7.18 (d, 2H, *J* = 8.2 Hz), 7.26 (d, 2H, *J* = 8.2 Hz).

^{13}C NMR (50 MHz) : δ 23.95, 33.80, 51.87, 72.92, 125.71, 126.48, 126.60, 138.76, 142.15, 148.44, 166.77.

Methyl 3-(2-chlorophenyl)-3-hydroxy-2-methylenepropanoate (81f):

Treatment of 2-chlorobenzaldehyde with methyl acrylate in the presence of DABCO as a catalyst following a similar procedure described for the molecule **81a** provided the title compound **81f** as a colorless liquid.



Reaction time : 8 days

Yield : 71%

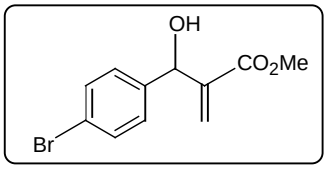
IR (neat) : ν 3437, 1724, 1631 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.50 (bs, 1H), 3.75 (s, 3H), 5.58 (s, 1H), 5.96 (s, 1H), 6.32 (s, 1H), 7.21-7.36 (m, 3H), 7.51-7.57 (m, 1H).

^{13}C NMR (100 MHz) : δ 52.11, 69.14, 126.95, 127.02, 128.15, 129.01, 129.45, 132.81, 138.37, 140.71, 166.98.

Methyl 3-(4-bromophenyl)-3-hydroxy-2-methylenepropanoate (81g):

The Baylis-Hillman coupling of 4-bromobenzaldehyde with methyl acrylate in the presence of DABCO (cat.) following a similar procedure described for the molecule **81a** provided the title compound as a colorless liquid.



Reaction time : 8 days

Yield : 75%

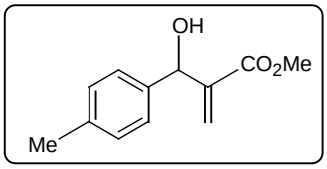
IR (neat) : ν 3435, 1714, 1631cm^{-1}

^{1}H NMR (400 MHz) : δ 3.10 (bs, 1H), 3.75 (s, 3H), 5.55 (s, 1H), 5.84 (s, 1H), 6.36 (s, 1H), 7.28 (d, 2H, *J* = 8.4 Hz), 7.49 (d, 2H, *J* = 8.4 Hz).

^{13}C NMR (100 MHz) : δ 52.06, 72.57, 121.73, 126.32, 128.37, 131.51, 140.39, 141.60, 166.60.

Methyl 3-hydroxy-2-methylene-3-(4-methylphenyl)propanoate (81h):

This molecule was obtained as a colorless solid *via* the reaction between 4-methyl benzaldehyde and methyl acrylate using DABCO as a catalyst following a similar procedure described for the molecule **81a**.



Reaction time : 8 days

Yield : 72%

IR (neat) : ν 3503, 1718, 1630 cm^{-1}

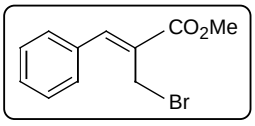
^{1}H NMR (400 MHz) : δ 2.31 (s, 3H), 3.60 (s, 3H), 3.88 (bs, 1H), 5.47 (s, 1H), 5.90 (s, 1H), 6.28 (s, 1H), 7.11 (d, 2H, *J* = 8.0 Hz), 7.22 (d, 2H, *J* = 8.0 Hz).

^{13}C NMR (50 MHz) : δ 20.70, 51.36, 72.00, 124.78, 126.48, 128.67, 136.91, 138.39, 142.23, 166.31.

Methyl (2*Z*)-2-(bromomethyl)-3-phenylprop-2-enoate (82a):

This compound was prepared according to the literature procedure.[103]

To a stirred mixture of methyl 3-hydroxy-2-methylene-3-phenylpropanoate (**81a**) (40 mmol, 7.6 g) in dichloromethane (60 mL) was added hydrobromic acid (48%; 100 mmol 8.09 g) followed by a drop wise addition of concentrated sulfuric acid (40 mmol 3.9 g) at $0^{0}C$. After stirring 12 hours at room temperature the reaction mixture was poured into ice cold water and then extracted with ether (3 x 15 mL). Combined organic layer was dried over anhydrous Na_2SO_4 and solvent was evaporated. The crude product thus obtained, was purified by column chromatography (silica gel, 2% EtoAc in hexanes) to provide **82a** in 89% (9.04 g) yield, as a colorless oil.



IR (neat) : ν 1718, 1626 cm^{-1}

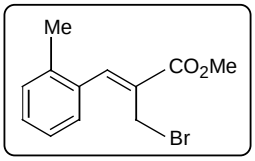
^{1}H NMR (400 MHz) : δ 3.91 (s, 3H), 4.42 (s, 2H), 7.45-7.75 (m, 5H), 7.85 (s, 1H).

^{13}C NMR (50 MHz) : δ 26.72, 52.39, 128.90, 129.63, 134.28, 142.88, 166.53.

Methyl (2*Z*)-2-(bromomethyl)-3-(2-methylphenyl)prop-2-enoate (82b):

This compound was prepared *via* the treatment of methyl 3-hydroxy-2-methylene-3-(2-methylphenyl)propanoate (**81b**) with 48% HBr in the presence of sulfuric acid following the similar procedure described for the molecule **82a,** as a colorless liquid.

Reaction time : 12h



Yield : 87%

IR (neat) : ν 1718, 1625 cm^{-1}

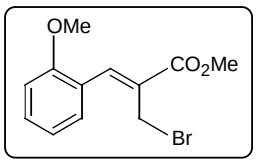
^{1}H NMR (400 MHz) : δ 2.30 (s, 3H), 3.89 (s, 3H), 4.28 (s, 2H), 7.19-7.35 (m, 3H), 7.52-7.62 (m, 1H), 7.91 (s, 1H).

^{13}C NMR (50 MHz) : δ 19.90, 26.62, 52.43, 126.09, 127.96, 129.37, 130.34, 133.54, 137.30, 142.13, 166.48.

Methyl (2*Z*)-2-(bromomethyl)-3-(2-methoxyphenyl)prop-2-enoate (82c):

The reaction of methyl 3-hydroxy-2-methylene-3-(2-methoxyphenyl)propanoate (**81c**) with 48% HBr in the presence of conc. H_2SO_4 following the similar procedure described for the molecule **82a**, provided the title compound as a colourless liquid.

Reaction time : 12h



Yield : 78%

IR (neat) : ν 1711, 1625 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.85 (s, 3H), 3.87 (s, 3H), 4.37 (s, 2H), 6.93 (d, 1H, *J* = 8.4 Hz), 7.01-7.12 (m, 1H), 7.34-7.47 (m, 1H), 7.64-7.75 (m, 1H), 8.03 (s, 1H).

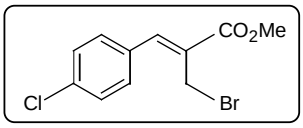
^{13}C NMR (50 MHz) : δ 27.37, 52.28, 55.55, 110.76, 120.69, 123.43, 128.45, 129.47, 131.24, 138.88, 158.02, 166.68.

Methyl (2*Z*)-2-(bromomethyl)-3-(4-chlorophenyl)prop-2-enoate (82d):

This was prepared *via* the treatment of methyl 3-hydroxy-2-methylene-3-(4-chlorophenyl)propanoate (**81d**) with 48% HBr and conc. H_2SO_4 following the similar procedure described for the molecule **82a** as a colorless liquid.

Reaction time : 12h

Yield : 79%



IR (neat) : ν 1716, 1626 cm^{-1}

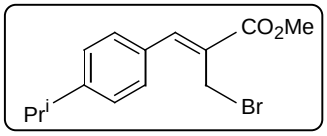
^{1}H NMR (400 MHz) : δ 3.88 (s, 3H), 4.34 (s, 2H), 7.43 (d, 2H, *J* = 8.8 Hz), 7.51 (d, 2H, *J* = 7.84 Hz), 7.76 (s, 1H).

^{13}C NMR (50 MHz) : δ 26.28, 52.55, 129.22, 130.95, 132.69, 135.80, 141.50, 166.36.

Methyl (2*Z*)-2-(bromomethyl)-3-(4-isopropylphenyl)prop-2-enoate (82e):

Treatment of methyl 3-hydroxy-2-methylene-3-(4-isopropylphenyl)propanoate (**81e**) with 48% HBr in the presence of concentrated sulfuric acid following the similar procedure described for the molecule **82a** provided the title compound **82e** as a colorless liquid.

Reaction time : 12h



Yield : 80%

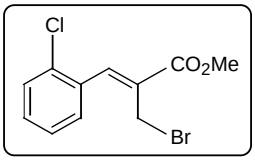
IR (neat) : ν 1716, 1624 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.14 (d, 6H, *J* = 7.2 Hz), 2.81 (sept, 1H, *J* = 7.2 Hz), 3.73 (s, 3H), 4.29 (s, 2H), 7.19 (d, 2H, *J* = 8.0 Hz), 7.39 (d, 2H, *J* = 8.0 Hz), 7.67 (s, 1H).

^{13}C NMR (50 MHz) : δ 23.70, 27.00, 34.06, 52.28, 127.04, 127.91, 130.02, 131.87, 143.05, 150.93, 166.75.

Methyl (2*Z*)-2-(bromomethyl)-3-(2-chlorophenyl)prop-2-enoate (82f):

This compound was obtained by the reaction of methyl 3-(2-chlorophenyl)-3-hydroxy-2-methylenepropanoate (**81f**) with 48% HBr in the presence of concentrated sulfuric acid following the similar procedure described for the molecule **82a**, as a colorless viscous liquid.



Reaction time : 12h

Yield : 82%

IR (neat) : ν 1716, 1633 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.85 (s, 3H), 4.22 (s, 2H), 7.10-7.48 (m, 3H), 7.60-7.73 (m, 1H), 7.87 (s, 1H).

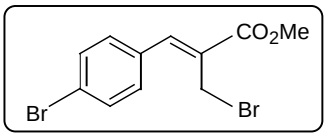
^{13}C NMR (100 MHz) : δ 26.26, 52.60, 127.05, 129.58, 129.86, 130.50, 130.63, 132.86, 134.51, 139.53, 166.07.

Methyl (2*Z*)-2-(bromomethyl)-3-(4-bromophenyl)prop-2-enoate (82g):

This was prepared *via* the treatment of methyl 3-hydroxy-2-methylene-3-(4-bromophenyl)propanoate (**81g**) with 48% HBr in the presence of concentrated sulfuric acid following the similar procedure described for the molecule **82a** as a colorless liquid.

Reaction time : 12h

Yield : 88%



IR (neat) : ν 1716, 1624 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.87 (s, 3H), 4.33 (s, 2H), 7.42 (d, 2H, *J* = 8.4 Hz), 7.58 (d, 2H, *J* = 8.4 Hz), 7.72 (s, 1H).

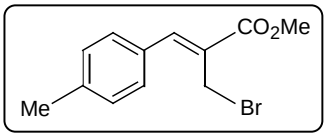
^{13}C NMR (50 MHz) : δ 26.40, 52.60, 124.13, 129.30, 131.16, 132.16, 133.06, 141.47, 166.24.

Methyl (2*Z*)-2-(bromomethyl)-3-(4-methylphenyl)prop-2-enoate (82h):

This compound was obtained by the reaction of methyl 3-(4-methylphenyl)-3-hydroxy-2-methylenepropanoate (**81h**) with 48% HBr in the presence of conc. sulfuric acid following the similar procedure described for the molecule **82a**, as a colorless oil.

Reaction time : 12h

Yield : 92%



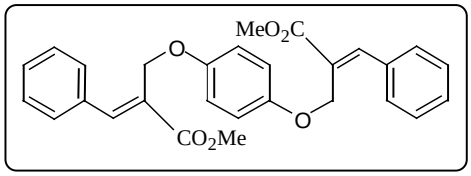
IR (neat) : ν 1720, 1626 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.26 (s, 3H), 3.74 (s, 3H), 4.28 (s, 2H), 7.13 (d, 2H, *J* = 8.0 Hz), 7.35 (d, 2H, *J* = 8.0 Hz), 7.66 (s, 1H).

^{13}C NMR (50 MHz) : δ 21.40, 26.96, 52.30, 127.91, 129.66, 129.85, 131.50, 140.07, 143.07, 166.75

1,4-Bis[(2*E*)-2-methoxycarbonyl-3-phenylprop-2-enyloxy]benzene (83a):

A mixture of methyl (2*Z*)-2-(bromomethyl)-3-phenylprop-2-enoate (**82a**) (5 mmol, 1.27 g), anhydrous K_2CO_3 (6 mmol, 0.82 g), 1,4-dihydroxybenzene (2 mmol, 0.22 g) in acetone (3 mL) was heated under reflux with stirring for 6 hours. The reaction was monitored by TLC. Then the reaction mixture was cooled to room temperature. Acetone was removed under reduced pressure. The residue was diluted with water (25 mL), and extracted with ethyl acetate (3 x 25 mL). The combined organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and crude product thus obtained was purified by crystallization [ethyl acetate/hexanes (1:2)] to provide the diester **83a** in 83% (0.76 g) yield, as a light brown solid.



Mp : 105-107^{0}C

IR (KBr) : ν 1714, 1631 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.88 (s, 6H), 4.82 (s, 4H), 6.95 (s, 4H), 7.37-7.45 (m, 6H), 7.50-7.56 (m, 4H), 8.07 (s, 2H).

^{13}C NMR (100 MHz) : δ 52.25, 63.43, 116.02, 127.38, 128.67, 129.58, 129.74, 134.40, 145.48, 153.00, 167.62.

1,4-Bis[(2*E*)-2-methoxycarbonyl-3-(2-methylphenyl)prop-2-enyloxy]benzene (83b):

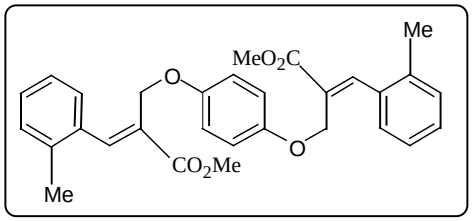
This compound obtained as a light brown solid *via* the reaction of methyl (2*Z*)-2-(bromo methyl)-3-(2-methylphenyl)prop-2-enoate (**82b**) with 1,4-dihydroxybenzene in the presence of K_2CO_3 following similar procedure described for the molecule **83a**.

Reaction time : 6h

Yield : 80%

Mp : 110-112^{0}C

IR (KBr) : ν 1716, 1637 cm^{-1}



^{1}H NMR (400 MHz) : δ 2.32 (s, 6H), 3.86 (s, 6H), 4.68 (s, 4H), 6.81 (s, 4H), 7.10-7.44 (m, 8H), 8.10 (s, 2H).

^{13}C NMR (100 MHz) : δ 20.01, 52.26, 63.86, 116.14, 126.08, 128.38, 129.19, 129.44, 130.18, 133.79, 137.25, 144.13, 153.12, 167.55.

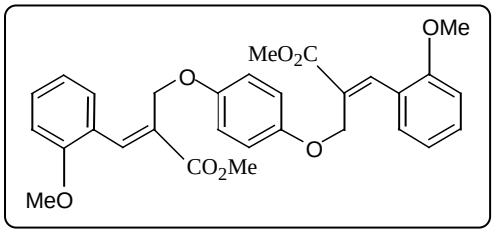
1,4-Bis[(2*E*)-2-methoxycarbonyl-3-(2-methoxyphenyl)prop-2-enyloxy]benzene (83c): Reaction of methyl (2*Z*)-2-(bromomethyl)-3-(2-methoxyphenyl)prop-2-enoate (**82c**) with 1,4-dihydroxybenzene in the presence of K_2CO_3 following similar procedure described for the molecule **83a,** provided the title compound as a light brown solid.

Reaction time : 6h

Yield : 84%

Mp : 138-140^{0}C

IR (KBr) : ν 1720, 1626 cm^{-1}

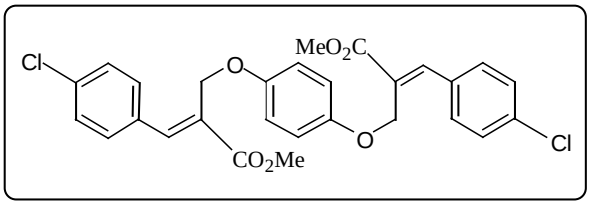


^{1}H NMR (400 MHz) : δ 3.84 (s, 6H), 3.86 (s, 6H), 4.74 (s, 4H), 6.80-6.98 (m, 8H), 7.30-7.40 (m, 2H), 7.44-7.52 (m, 2H), 8.22 (s, 2H).

^{13}C NMR (100 MHz) : δ 52.17, 55.52, 64.10, 110.45, 116.09, 120.67, 123.66, 127.27, 130.52, 131.18, 141.28, 153.13, 157.90, 167.75.

1,4-Bis[(2*E*)-2-methoxycarbonyl-3-(4-chlorophenyl)prop-2-enyloxy]benzene (83d):

Treatment of methyl (2*Z*)-2-(bromomethyl)-3-(4-chlorophenyl)prop-2-enoate (**82d**) with hydroquinone in the presence of K_2CO_3 following similar procedure described for the molecule **83a,** furnished the title compound as a light brown solid.



Reaction time : 6h

Yield : 80%

Mp : 120-122^{0}C

IR (KBr) : ν 1718, 1641 cm^{-1}

^{1}H NMR (200 MHz) : δ 3.86 (s, 6H), 4.76 (s, 4H), 6.92 (s, 4H), 7.36 (d, 4H, *J* = 8.8 Hz), 7.44 (d, 4H, *J* = 8.8 Hz), 7.98 (s, 2H).

^{13}C NMR (100 MHz) : δ 52.37, 63.43, 116.19, 128.03, 129.00, 131.11, 132.91, 135.82, 144.11, 153.04, 167.45 .

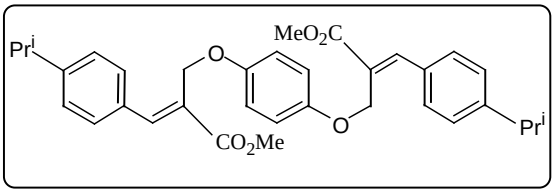
1,4-Bis[(2*E*)-2-methoxycarbonyl-3-(4-isopropylphenyl)prop-2- enyloxy]benzene (83e):

This was obtained as a light brown solid *via* the treatment of methyl (2*Z*)-2-(bromo methyl)-3-(4-isopropylphenyl)prop-2-enoate (**82e**) with 1,4-dihydroxybenzene in the presence of K_2CO_3 following similar procedure described for the molecule **83a**.

Reaction time : 6h

Yield : 83%

Mp : 120-122^{0}C



IR (KBr) : ν 1711, 1626 cm^{-1}

^{1}H NMR (400 MHz) : δ 1.27 (d, 12H, *J* = 7.2 Hz), 2.86-3.05 (m, 2H), 3.87 (s, 6H), 4.83 (s, 4H), 6.98 (s, 4H), 7.27 (d, 4H, *J* = 8.4 Hz), 7.47 (d, 4H, *J* = 8.4 Hz), 8.05 (s, 2H).

^{13}C NMR (100 MHz) : δ 23.75, 34.01, 52.22, 63.49, 116.01, 126.40, 126.86, 130.09, 132.00, 145.70, 150.85, 153.03, 167.86.

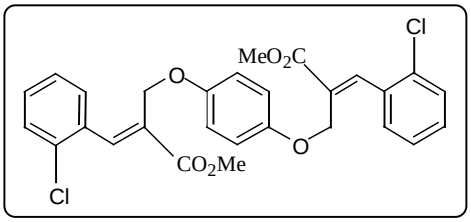
1,4 –Bis[(2*E*)-2-methoxycarbonyl-3-(2-chlorophenyl)prop-2-enyloxy]benzene (83f):

This was prepared by the reaction of methyl (2*Z*)-2-(bromomethyl)-3-(2-chlorophenyl) prop-2-enoate (**82f**) with hydroquinone in the presence of K_2CO_3 following similar procedure described for the molecule **83a,** as a light brown solid.

Reaction time : 6h

Yield : 81%

Mp : 118-120^{0}C



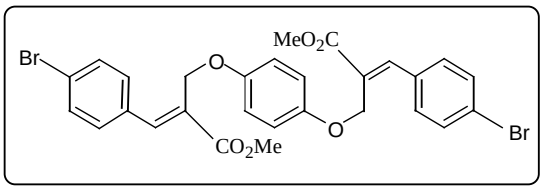
IR (KBr) : ν 1722, 1643 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.86 (s, 6H), 4.68 (s, 4H), 6.85 (s, 4H), 7.20-7.35 (m, 4H), 7.43 (d, 2H, *J* = 6.8 Hz), 7.53 (d, 2H, *J* = 8.0 Hz), 8.12 (s, 2H).

^{13}C NMR (100 MHz) : δ 52.34, 63.70, 116.01, 126.89, 129.28, 129.54, 130.56, 130.69, 133.00, 134.35, 141.82, 152.96, 167.03.

1,4-Bis[(2*E*)-2-methoxycarbonyl-3-(4-bromophenyl)prop-2-enyloxy]benzene (83g):

This was prepared by the reaction of methyl (2*Z*)-2-(bromomethyl)-3-(4-bromophenyl) prop-2-enoate (**82g**) with hydroquinone in the presence of K_2CO_3 following similar procedure described for the molecule **83a,** as a light brown solid.



Reaction time : 6h

Yield : 82%

Mp :160-162^{0}C

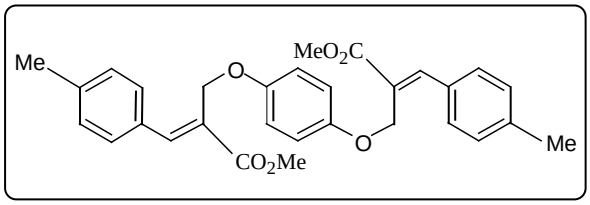
IR (KBr) : ν 1734, 1684 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.84 (s, 6H), 4.75 (s, 4H), 6.91 (s, 4H), 7.36 (d, 4H, *J* = 8.4 Hz), 7.50 (d, 4H, *J* = 8.4 Hz), 7.95 (s, 2H).

^{13}C NMR (100 MHz) : δ 52.44, 63.35, 116.13, 124.19, 128.03, 131.31, 132.20, 133.32, 144.26, 152.98, 167.42.

1,4-Bis[(2*E*)-2-methoxycarbonyl-3-(4-methylphenyl)prop-2-enyloxy]benzene (83h):

This was obtained as a light brown solid by the treatment of methyl (2*Z*)-2-(bromo methyl)-3-(4-methylphenyl)prop-2-enoate (**82h**) with hydroquinone in the presence of K_2CO_3 following similar procedure described for the molecule **83a.**



Reaction time : 6h

Yield : 81%

Mp : 108-110^{0}C

IR (KBr) : ν 1718, 1631 cm^{-1}

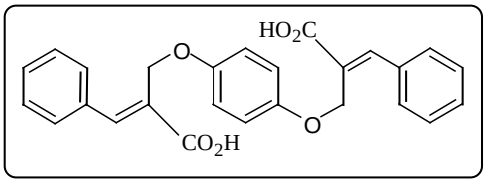
^{1}H NMR (400 MHz) : δ 2.36 (s, 6H), 3.84 (s, 6H), 4.79 (s, 4H), 6.93 (s, 4H), 7.19 (d, 4H

J = 8.0 Hz), 7.40 (d, 4H, *J* = 8.0 Hz), 8.02 (s, 2H).

^{13}C NMR (100 MHz) : δ 21.33, 52.18, 63.49, 116.00, 126.40, 129.42, 129.89, 131.59, 139.97, 145.64, 153.00, 167.77.

1,4-Bis[(2*E*)-2-carboxy-3-phenylprop-2-enyloxy]benzene (84a):

To a stirred solution of 1,4-bis[(2*E*)-2-methoxycarbonyl-3-phenylprop-2-enyloxy]-benzene (**83a**) (1 mmol, 0.49 g) in acetone (1 mL) was added aqueous KOH solution (0.3 g in 1mL water) at room temperature and the reaction was heated under reflux for 3 hours. Reaction mixture was cooled to room temperature and solvent was removed under pressure. The reaction mixture was diluted with cold conc. HCl (5 mL) and extracted with ethyl acetate (3 x 10 mL). Combined organic layer was dried over anhydrous Na_2SO_4. Solvent was evaporated and crude solid thus obtained was purified by crystallization [ethyl acetate/hexanes (1:2)] to afford **84a** in 81% (0.35g) yield, as a colorless crystalline solid.



Mp : 250-252^{0}C

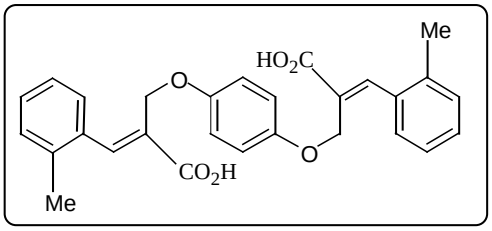
IR (KBr) : ν 3400-2500, 1674, 1620 cm^{-1}

^{1}H NMR (400 MHz) : δ 4.70 (s, 4H), 6.95 (s, 4H), 7.35-7.60 (m, 10H), 7.94 (s, 2H), 12.82 (bs, 2H).
(DMSO - d_6)

^{13}C NMR (50 MHz) : δ 63.40, 115.96, 128.35, 128.99, 129.82, 134.51, 144.09, 152.82, 168.31.
(DMSO – d_6)

1,4-Bis[(2*E*)-2-carboxy-3-(2-methylphenyl)prop-2-enyloxy]benzene (84b):

This compound was obtained as a white crystalline solid *via* the hydrolysis of 1,4-bis[(2*E*)-2-methoxycarbonyl-3-(2-methylphenyl)prop-2-enyloxy]benzene (**83b**) using KOH in water / acetone following the similar procedure described for the molecule **84a**



Reaction time : 3h

Yield : 78%

Mp : 234-236^{0}C

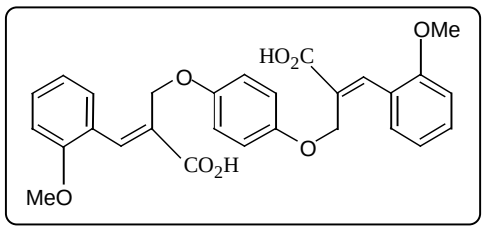
IR (KBr) : ν 3500-2500, 1685, 1626 cm^{-1}

^{1}H NMR(400 MHz) (DMSO – d_6) : δ 2.26 (s, 6H), 4.56 (s, 4H), 6.81 (s, 4H), 7.15-7.22 (m, 2H), 7.26-7.35 (m, 6H), 7.97 (s, 2H).

^{13}C NMR (50 MHz) (DMSO – d_6) : δ 19.69, 63.55, 115.80, 126.09, 128.77, 129.26, 129.44, 130.31, 133.84, 137.08, 142.66, 152.75, 168.09.

1,4-Bis[(2*E*)-2-carboxy-3-(2-methoxyphenyl)prop-2-enyloxy]benzene (84c):

Hydrolysis of 1,4-bis[(2*E*)-2-methoxycarbonyl-3-(2-methoxyphenyl)prop-2-enyloxy]-benzene (**83c**) using KOH in water / acetone following the similar procedure described for the molecule **84a** provided the title compound as a white crystalline solid.



Reaction time : 3h

Yield : 75%

Mp : 235-238^{0}C

IR (KBr) : ν 3500-2400, 1684, 1606 cm^{-1}

^{1}H NMR(400 MHz) : δ 3.85 (s, 6H), 4.67 (s, 4H), 6.87 (s, 4H), 6.88-6.95 (m, 4H),
($CDCl_3$ & DMSO-d_6 in 4:1 ratio)
6.98 (d, 2H, *J* = 8.8 Hz), 7.32-7.40 (m, 2H), 7.41-7.46 (m, 2H),
8.11 (s, 2H).

^{13}C NMR (100 MHz) : δ 53.94, 62.13, 109.25, 114.18, 118.88, 121.77, 126.16, 128.41,
($CDCl_3$ & DMSO-d_6 in 4:1 ratio)
129.67, 138.51, 151.24, 156.12, 166.87.

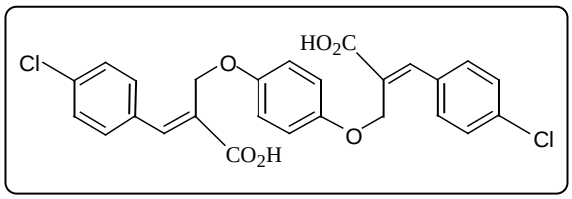
1,4-Bis[(2*E*)-2-carboxy-3-(4-chlorophenyl)prop-2-enyloxy]benzene (84d):

This compound was obtained by hydrolysis of 1,4-bis[(2*E*)-2-methoxycarbonyl-3-(4-chlorophenyl)prop-2-enyloxy]benzene (**83d**) using KOH in water / acetone following the similar procedure described for the molecule **84a** as a white crystalline solid.

Reaction time : 3h

Yield : 74%

Mp : 239-242^{0}C



IR (KBr) : ν 3500-2400, 1676, 1616 cm^{-1}

^{1}H NMR (400 MHz) : δ 4.69 (s, 4H), 6.94 (s, 4H), 7.50 (d, 4H, *J* = 8.8 Hz), 7.55 (d, 4H,
(DMSO – d_6)
J = 8.8 Hz), 7.91 (s, 2H).

^{13}C NMR (50 MHz) : δ 63.29, 116.04, 128.99, 131.51, 133.36, 134.63, 142.70, 152.82,
(DMSO – d_6)
168.14.

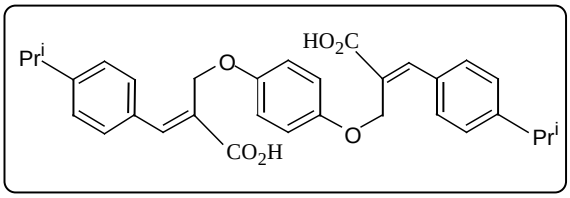
1,4-Bis[(2*E*)-2-carboxy-3-(4-isopropylphenyl)prop-2-enyloxy]benzene (84e):

Hydrolysis of 1,4-bis[(2*E*)-2-methoxycarbonyl-3-(4-isopropylphenyl)prop-2-enyloxy]-benzene (**83e**) using KOH in water / acetone following the similar procedure described for the molecule **84a** furnished the title compound **84e** as a white crystalline solid.

Reaction time : 3h

Yield : 76%

M.P : 240-242^{0}C



IR (KBr) : ν 3400-2400, 1682, 1606 cm^{-1}

^{1}H NMR (200 MHz) (DMSO – d_6) : δ 1.17 (d, 12H, *J* = 5.4 Hz), 2.81-3.08 (m, 2H), 4.71 (s, 4H), 6.97 (s, 4H), 7.30 (d, 4H, *J* = 6.8 Hz), 7.47 (d, 4H, *J* = 6.8 Hz), 7.92 (s, 2H), 12.75 (bs, 2H).

^{13}C NMR (50 MHz) (DMSO – d_6) : δ 23.67, 33.41, 63.29, 115.81, 126.87, 127.33, 129.98, 132.03, 145.21, 150.46, 152.77, 168.36.

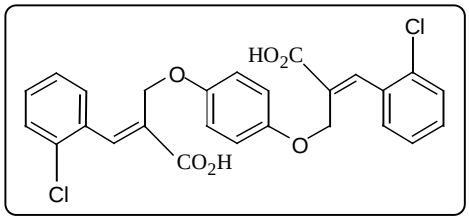
1,4-Bis[(2*E*)-2-carboxy-3-(2-chlorophenyl)prop-2-enyloxy]benzene (84f):

This molecule was obtained *via* the hydrolysis of 1,4-bis[(2*E*)-2-methoxycarbonyl-3-(2-chlorophenyl)prop-2-enyloxy]benzene (**83f**) using KOH in water / acetone following the similar procedure described for the molecule **84a** as a white crystalline solid.

Reaction time : 3h

Yield : 78%

Mp : 238-240^{0}C



IR (KBr) : ν 3500-2400 , 1689 , 1630 cm^{-1}

^{1}H NMR (400 MHz) (DMSO – d_6) : δ 4.60 (s, 4H), 6.85 (s, 4H), 7.35-7.41 (m, 2H), 7.41-7.48 (m, 2H), 7.50 (d, 2H, *J* = 7.2 Hz), 7.57 (d, 2H, *J* = 8.0 Hz), 7.95 (s, 2H), 13.05 (bs, 2H).

^{13}C NMR (50 MHz) (DMSO – d_6) : δ 63.44, 115.89, 127.57, 129.75, 130.66, 131.20, 132.84, 133.48, 140.00, 152.76, 167.71.

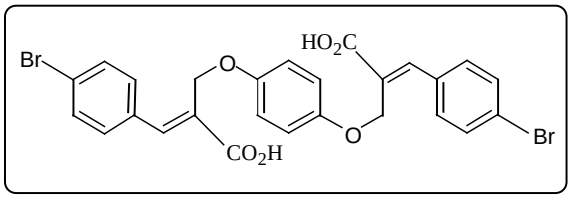
1,4-Bis[(2*E*)-2-carboxy-3-(4-bromophenyl)prop-2-enyloxy]benzene (84g):

Treatment of 1,4-bis[(2*E*)-2-methoxycarbonyl-3-(4-bromophenyl)prop-2-enyloxy]benzene (**83g**) using KOH in water / acetone following the similar procedure described for the molecule **84a** provided the title compound **84g** as a white crystalline solid.

Reaction time : 3h

Yield : 77%

Mp : 228-230^{0}C



IR (KBr) : ν 3500-2400 , 1680 , 1639 cm^{-1}

^{1}H NMR (400 MHz) (DMSO – d_6) : δ 4.69 (s, 4H), 6.94 (s, 4H), 7.48 (d, 4H, *J* = 8.0 Hz), 7.64 (d, 4H, *J* = 8.0 Hz), 7.89 (s, 2H), 12.99 (bs, 2H).

^{13}C NMR (100 MHz) (DMSO – d_6) : δ 63.19, 115.98, 123.38, 128.99, 131.72, 131.90, 133.66, 142.79, 152.73, 168.14.

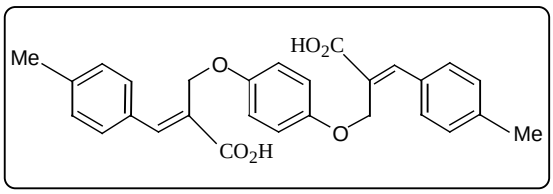
1,4-Bis[(2*E*)-2-carboxy-3-(4-methylphenyl)prop-2-enyloxy]benzene (84h):

This was obtained by hydrolysis of 1,4-bis[(2*E*)-2-methoxycarbonyl-3-(4-methylphenyl)-prop-2-enyloxy]benzene (**83h**) using KOH in water / acetone following the similar procedure described for the molecule **84a** as a white crystalline solid.

Reaction time : 3h

Yield : 79%

Mp : 248-250^{0}C



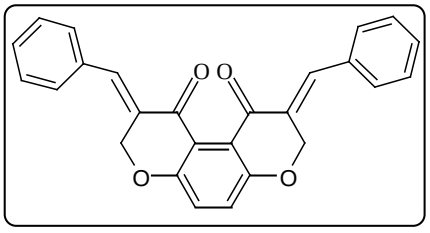
IR (KBr) : ν 3200-2500, 1676, 1606 cm^{-1}

^{1}H NMR (400 MHz) (DMSO–d_6) : δ 2.29 (s, 6H), 4.67 (s, 4H), 6.94 (s, 4H), 7.22 (d, 4H, *J* = 7.8 Hz), 7.41 (d, 4H, *J* = 7.8 Hz), 7.89 (s, 2H), 12.74 (bs, 2H).

^{13}C NMR (50 MHz) (DMSO – d_6) : δ 21.16, 63.38, 115.89, 127.35, 129.62, 129.93, 131.71, 139.81, 144.28, 152.82, 168.46.

7,12-Bisbenzylidene-5,14-dioxatricyclo[8.4.0.0^{4,9}]tetradeca-1,3,9-triene-8,11-dione (80a):

To a stirred solution of 1,4-bis[(2*E*)-2-carboxy-3-phenylprop-2-enyloxy]benzene (**84a**) (0.5 mmol, 0.215 g) in dichloromethane (2 mL) under nitrogen atmosphere, TFAA (1.38 mmol, 0.2 mL) was added and the reaction was heated under reflux for 5 hours. Then the reaction mixture was cooled to room temperature. The solvent was evaporated under reduced pressure and diluted with aq. K_2CO_3 solution (3 mL) and extracted with ethyl acetate (3 x 10 mL). Combined organic layer was dried over anhydrous Na_2SO_4. After evaporation of solvent, the compound was crystallized from ethyl acetate/hexanes (1:2) to provide product **80a** in 83% (0.164 g) yield, as a light yellow solid.



Mp : 225-228^{0}C

IR (KBr) : ν 1668, 1615 cm^{-1}

^{1}H NMR(400 MHz) : δ 5.19 (s, 4H), 6.95 (s, 2H), 7.05–7.40 (m, 10H), 7.78 (s, 2H).

^{13}C NMR(50 MHz) : δ 68.09, 122.23, 125.24, 128.75, 129.49, 129.94, 131.99, 134.48, 137.75, 158.43, 179.39.

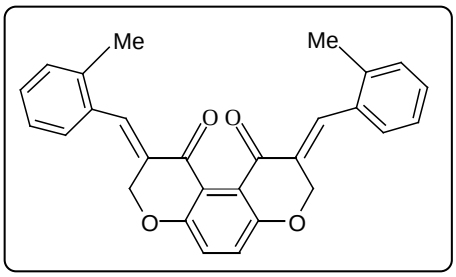
LCMS (m/z) : 395 $(M+H)^+$

Analysis calcd. for $C_{26}H_{18}O_4$: C, 79.18; H, 4.56

Found : C, 79.19; H, 4.57

7,12-Bis(2-methylbenzylidene)-5,14-dioxatricyclo[8.4.0.0^{4,9}]tetradeca-1,3,9-triene-8,11-dione (80b):

This was prepared *via* the treatment of 1,4-bis [(2*E*)-2-carboxy-3-(2-methylphenyl)prop-2-enyloxy]benzene (**84b**) with TFAA following similar procedure described for the molecule **80a** as a yellow crystalline solid.



Reaction time : 5h

Yield : 81%

Mp : 238-240^{0}C

IR (KBr) : ν 1685, 1614 cm^{-1}

^{1}H NMR (400 MHz) : δ 2.37 (s, 6H), 5.19 (s, 4H), 7.04 (d, 2H, *J* = 7.2 Hz), 7.08 (s, 2H), 7.21-7.36 (m, 6H), 8.05 (s, 2H).

^{13}C NMR (100 MHz) : δ 20.06, 68.22, 122.30, 125.48, 125.87, 128.78, 129.55, 130.62, 132.08, 133.58, 137.37, 138.35, 158.78, 179.51.

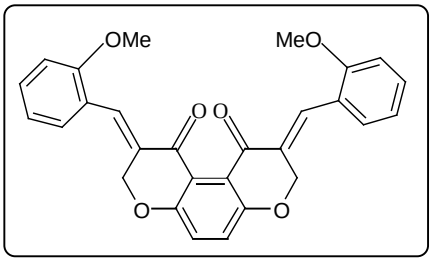
LCMS (m/z) : 423 $(M+H)^+$

Analysis calcd. for $C_{28}H_{22}O_4$: C, 79.62; H, 5.21

Found : C, 79.56; H, 5.26

7,12-Bis(2-methoxybenzylidene)-5,14-dioxatricyclo[8.4.0.0^{4,9}]tetradeca-1,3,9-triene-8,11-dione (80c):

Treatment of 1,4-bis [(2*E*)-2-carboxy-3-(2-methoxyphenyl)prop-2-enyloxy]benzene (**84c**) with TFAA following similar procedure described for the molecule **80a** provided the title compound as a white crystalline solid.



Reaction time : 5h

Yield : 84%

Mp : 231-234^{0}C

IR (KBr) : ν 1680 , 1615 cm^{-1}

^{1}H NMR (400 MHz) : δ 3.86 (s, 6H), 5.18 (s, 4H), 6.92-7.04 (m, 4H), 7.05 (s, 2H), 7.08-7.15 (m, 2H), 7.34-7.44 (m, 2H), 8.06 (s, 2H).

^{13}C NMR(50 MHz) : δ 55.53, 68.63, 111.08, 120.35, 122.46, 123.69, 125.05, 130.36, 131.12, 131.89, 134.20, 158.26, 158.57, 179.48.

LCMS (m/z) : 455 $(M+H)^+$

Analysis calcd. for $C_{28}H_{22}O_6$: C, 74.00 ; H, 4.84

Found : C, 75.04; H, 3.52

7,12-Bis(4-chlorobenzylidene)-5,14-dioxatricyclo[8.4.0.0^{4,9}]tetradeca-1,3,9-triene-8,11-dione (80d):

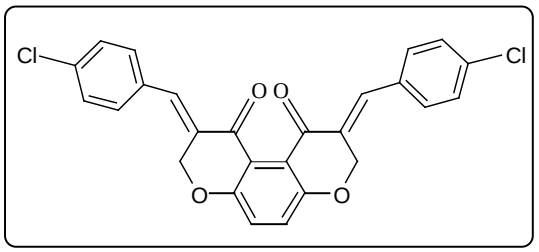
Treatment of 1,4-bis [(2*E*)-2-carboxy-3-(4-chlorophenyl)prop-2-enyloxy]benzene (**84d**) with TFAA following similar procedure described for the molecule **80a** furnished the title compound **80d** as a yellow crystalline solid in 77% yield.

Reaction time : 5h

Yield : 77%

Mp : 227-231^{0}C

IR (KBr) : ν 1689, 1615 cm^{-1}



^{1}H NMR(400 MHz) : δ 5.29 (s, 4H), 7.10 (s, 2H), 7.26 (d, 4H, *J* = 8.4 Hz), 7.43 (d, 4H, *J* = 8.4 Hz), 7.84 (s, 2H).

^{13}C NMR (50 MHz) : δ 68.00, 122.04, 125.56, 129.18, 131.24, 132.43, 132.91, 135.80, 136.55, 158.65, 179.31.

LCMS (m/z) : 463 $(M+H)^+$; 465 $(M+H+2)^+$

Analysis calcd. for $C_{26}H_{16}O_4Cl_2$: C, 67.53; H, 3.46

Found : C, 67.35 ; H, 3.47

7,12-Bis(4-isopropylbenzylidene)-5,14-dioxatricyclo[8.4.0.0^{4,9}]tetradeca-1,3,9-triene-8,11-dione (80e):

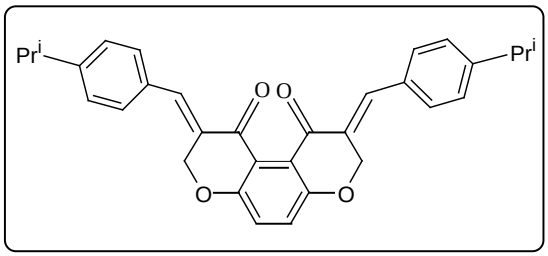
This was obtained as a yellow crystalline solid in 83% yield *via* the treatment of 1,4-bis [(2*E*)-2-carboxy-3-(4-isopropylphenyl)prop-2-enyloxy]benzene (**84e**) with TFAA following similar procedure described for the molecule **80a**.

Reaction time : 5h

Yield : 75%

Mp : 228-230^{0}C

IR (KBr) : ν 1682 , 1615 cm^{-1}



^{1}H NMR(400 MHz) : δ 1.28 (d, 12H, *J* = 6.8 Hz), 2.96 (sept, 2H, *J* = 6.8 Hz), 5.35 (s, 4H), 7.08 (s, 2H), 7.27 (d, 4H, *J* = 8.8 Hz), 7.31 (d, 4H, *J* = 8.8 Hz), 7.89 (s, 2H).

^{13}C NMR(50 MHz) : δ 23.83, 34.14, 68.22, 122.38, 125.15, 126.92, 130.29, 131.29, 132.09,137.88, 150.86, 158.36, 179.65.

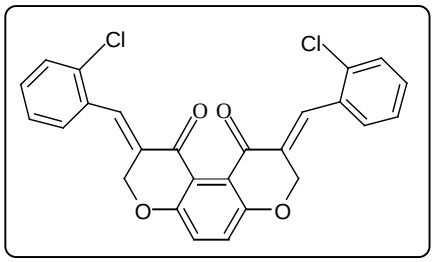
LCMS (m/z) : 479 $(M+H)^+$

Analysis calcd. for $C_{32}H_{30}O_4$: C, 80.33; H, 6.27

Found : C, 80.36; H, 6.23

7,12-Bis(2-chlorobenzylidene)-5,14-dioxatricyclo[8.4.0.0^{4,9}]tetradeca-1,3,9-triene-8,11-dione (80f):

This compound was prepared *via* the treatment of 1,4-bis[(2*E*)-2-carboxy-3-(2-chlorophenyl)prop-2-enyloxy]benzene (**84f**) with TFAA following similar procedure described for the molecule **80a** as a yellow crystalline solid.



Reaction time : 5h

Yield : 80%

Mp : 230-232^{0}C

IR (KBr) : ν 1680, 1618 cm^{-1}

^{1}H NMR(400 MHz) : δ 5.03 (s, 4H), 6.96 (s, 2H), 6.97-7.05 (m, 2H), 7.10-7.28 (m, 4H), 7.30-7.42 (m, 2H), 7.91 (s, 2H).

^{13}C NMR(50 MHz) : δ 68.03, 121.97, 125.56, 126.67, 130.11, 130.50, 132.99, 133.16, 135.01, 158.79, 178.78.

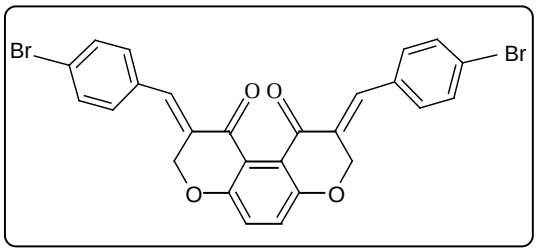
LCMS (m/z) : 463 $(M+H)^+$; 465 $(M+H+2)^+$

Analysis calcd. for $C_{26}H_{16}O_4Cl_2$: C, 67.53; H, 3.46

Found : C, 67.39; H, 3.46

7,12-Bis(4-bromobenzylidene)-5,14-dioxatricyclo[8.4.0.0^{4,9}]tetradeca-1,3,9-triene-8,11-dione (80g):

This was prepared *via* the treatment of 1,4-bis[(2*E*)-2-carboxy-3-(4-bromophenyl)prop-2-enyloxy]benzene (**84g**) with TFAA following similar procedure described for the molecule **80a** as a yellow crystalline solid in 82% yield.



Reaction time : 5h

Yield : 82%

Mp : 235-238^{0}C

IR (KBr) : ν 1682, 1608 cm^{-1}

^{1}H NMR(400 MHz) : δ 5.28 (s, 4H), 7.10 (s, 2H), 7.19 (d, 4H, *J* = 8.0 Hz), 7.59 (d, 4H, *J* = 8.0 Hz), 7.82 (s, 2H).

^{13}C NMR(50 MHz) : δ 67.99, 122.03, 124.08, 125.55, 131.42, 132.12, 132.46, 133.31, 136.56, 158.58, 179.23.

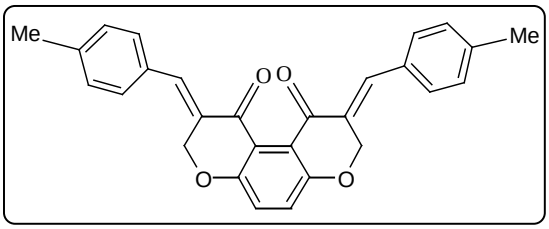
LCMS (m/z) : 553 $(M+H)^+$; 555 $(M+H+2)^+$

Analysis calcd. for $C_{26}H_{16}O_4Br_2$: C, 56.52; H, 2.89

Found : C, 56.94 ; H, 2.91

7,12-Bis(4-methylbenzylidene)-5,14-dioxatricyclo[8.4.0.0^{4,9}]-tetradeca-1,3,9-triene-8,11-dione (80h):

Reaction of of 1,4-bis [(2*E*)-2-carboxy-3-(4-methylphenyl)prop-2-enyloxy]benzene (**84h**) with TFAA following similar procedure described for the molecule **80a** gave the title compound **80h** as a yellow crystalline solid in 83% yield.



Reaction time : 5h

Yield : 83%

Mp : 230-232^{0}C

IR (KBr) : ν 1682, 1615 cm^{-1}

^{1}H NMR(400 MHz) : δ 2.41 (s, 6H), 5.34 (s, 4H), 7.08 (s, 2H), 7.16-7.48 (m, 8H), 7.88 (s, 2H).

^{13}C NMR(100 MHz) : δ 21.50, 68.19, 122.32, 125.12, 129.52, 130.13, 131.20, 131.66, 137.88, 140.00, 158.30, 179.61.

LCMS (m/z) : 423 $(M+H)^+$

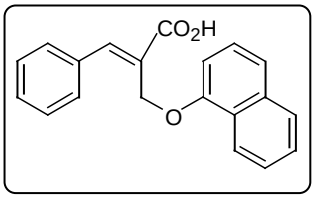
Analysis calcd. for $C_{28}H_{22}O_4$: C, 79.62; H, 5.21

Found : C, 79.50; H, 5.25

(2*E*)-2-(Naphthoxymethyl)-3-phenylprop-2-enoic acid (98a):

To a stirred mixture of methyl (2*Z*)-2-(bromomethyl)-3-phenylprop-2-enoate (**82a**) (2 mmol, 0.510 g) and anhydrous K_2CO_3 (4 mmol, 0.552 g) in acetone (3 mL), α-naphthol (2.4 mmol, 0.346 g) was added and the reaction mixture heated under reflux (the reaction was monitored by TLC). After 3 hours reaction mixture was cooled to room temperature. Then 50% aq KOH solution (1 mL) was added to the above reaction mixture and heated under reflux for three hours. Reaction mixture was cooled to room temperature and the solvent was removed under pressure. The reaction mixture was diluted with cold conc. HCl (5 mL) and extracted with ethyl acetate (3 x 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 [30% ethyl acetate in hexane] to provide the acid **98a** in 80% (0.49g) yield as a white crystalline solid.



M.P : 148-150^0 C

IR (KBr) : ν 3500-2500, 1676, 1626 cm^{-1}

^{1}H NMR(400 MHz) (DMSO – d_6) : δ 4.98 (s, 2H), 7.06 (d, 1H, *J* = 7.6 Hz), 7.32-7.62 (m, 9H), 7.89 (d, 1H, *J* = 7.8 Hz), 8.05 (s, 1H), 8.07 (d, 1H, *J* = 7.6 Hz), 12.87 (bs, 1H).

^{13}C NMR(50 MHz) (DMSO – d_6) : δ 63.29, 105.83, 120.53, 121.65, 125.26, 125.57, 126.38, 126.69, 127.66, 128.20, 128.93, 129.75, 134.30, 134.57, 144.52, 153.95, 168.38.

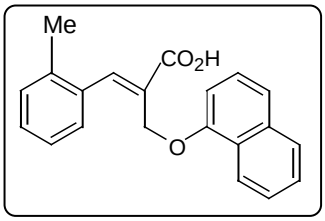
(2*E*)-2-(Naphthoxymethyl)-3-(2-methylphenyl)prop-2-enoic acid (98b):

This acid was prepared *via* the treatment of methyl (2*Z*)-2-(bromomethyl)-3-(2-methylphenyl)prop-2-enoate (**82b**) and α-naphthol in the presence of anhydrous K_2CO_3 in acetone and subsequent hydrolysis of the resulting ester using KOH following the similar procedure described for the molecule **98a** as a white crystalline solid.

Reaction time : (3 + 3) h

Yield : 82%

Mp : 120-122^{0}C



IR (KBr) : ν 3500-2500, 1685, 1628 cm^{-1}

^{1}H NMR(200 MHz) : δ 2.36 (s, 3H), 4.94 (s, 2H), 6.78 (d, 1H, *J* = 7.82 Hz), 7.00-7.60

(m, 8H), 7.71-7.93 (m, 1H), 8.29 (d, 1H, *J* = 8.8 Hz), 8.34 (s, 1H).

^{13}C NMR(50 MHz) : δ 20.02, 63.00, 105.43, 120.73, 122.33, 125.29, 125.85, 125.93, 126.24, 126.46, 127.43, 127.57, 129.18, 129.81, 130.29, 133.59, 134.63, 137.47, 146.71, 154.35, 172.84.

(2*E*)-2-(Naphthoxymethyl)-3-(2-methoxyphenyl)prop-2-enoic acid (98c):

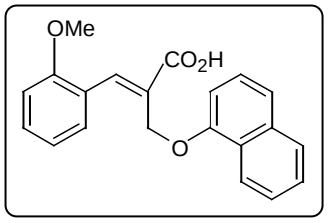
Treatment of methyl (2*Z*)-2-(bromomethyl)-3-(2-methoxyphenyl)prop-2-enoate (**82c**) with α-naphthol in the presence of anhydrous K_2CO_3 in acetone followed by the hydrolysis of the resulting ester following the similar procedure described for the molecule **98a** furnished the required acid as a white crystalline solid.

Reaction time : (3 + 3) h

Yield : 84%

Mp : 180-183^{0}C

IR (KBr) : ν 3500-2500, 1672, 1622 cm^{-1}

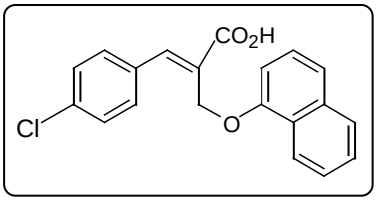


^{1}H NMR(400 MHz) : δ 3.81 (s, 3H), 4.95 (s, 2H), 6.72-6.89 (m, 3H), 7.24-7.36 (m, 2H)
($CDCl_3$ & DMSO – d_6 4:1 ratio) 7.37-7.52 (m, 4H), 7.76 (d, 1H, *J* = 8.0 Hz), 8.24 (d, 1H, *J* = 8.04 Hz), 8.30 (s, 1H).

^{13}C NMR(100 MHz) : δ 54.94, 63.03, 104.69, 110.05, 119.77, 119.99, 121.63, 123.18,
($CDCl_3$ & DMSO – d_6 4:1 ratio) 124.56, 125.16, 125.44, 125.82, 126.80, 127.04, 129.58, 130.57, 133.86, 140.55, 153.78, 157.28, 168.49.

(2*E*)-2-(Naphthoxymethyl)-3-(4-chlorophenyl)prop-2-enoic acid (98d):

This acid was obtained as a white crystalline solid *via* the treatment of methyl (2*Z*)-2-(bromomethyl)-3-(4-chlorophenyl)prop-2-enoate (**82d**) with α-naphthol in the presence of anhydrous K_2CO_3 in acetone followed by the hydrolysis with KOH following the similar procedure described for the molecule **98a.**



Reaction time : (3 + 3) h

Yield : 81%

Mp : 172-175^{0}C

IR (KBr) : ν 3500-2500, 1680, 1622cm^{-1}

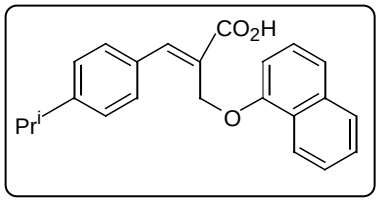
^{1}H NMR(400 MHz) ($CDCl_3$ & DMSO – d_6 4:1 ratio) : δ 4.95 (s, 2H), 7.03 (d, 1H, *J* = 7.6 Hz), 7.32-7.60 (m, 8H), 7.85 (d, 1H, *J* = 7.6 Hz), 8.00 (s, 1H), 8.02 (d, 1H, *J* = 8.8 Hz), 12.96 (bs, 1H).

^{13}C NMR (100 MHz) ($CDCl_3$ & DMSO–d_6 4:1 ratio) : δ 61.99, 104.45, 119.66, 120.98, 124.34, 124.60, 125.09, 125.55, 126.51, 127.64, 127.92, 130.09, 132.30, 133.45, 134.27, 142.70, 153.05, 167.65.

(2*E*)-2-(Naphthoxymethyl)-3-(4-isopropylphenyl)prop-2-enoic acid (98e):

Treatment of methyl (2*Z*)-2-(bromomethyl)-3-(4-isopropylphenyl)prop-2-enoate (**82e**) with α-naphthol in the presence of anhydrous K_2CO_3 in acetone and subsequent hydrolysis of the resulting cinnamic ester following the similar procedure described for the molecule **98a** provided the title compound **98e** as a white crystalline solid.

Reaction time : (3 + 3) h



Yield : 83%

Mp : 136-140^{0}C

IR (KBr) : ν 3500-2500, 1682, 1622 cm^{-1}

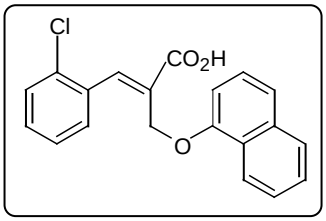
^{1}H NMR (400 MHz) (DMSO – d_6) : δ 1.08 (d, 6H, *J* = 6.8 Hz), 2.76 (sept, 1H, *J* = 6.8 Hz), 4.94 (s, 2H), 7.01 (d, 1H, *J* = 7.6 Hz), 7.15 (d, 2H, *J* = 8.4 Hz), 7.35-7.56 (m, 6H), 7.86 (d, 1H, *J* = 8.00 Hz), 8.04 (s, 1H), 8.09 (d, 1H, *J* = 8.4 Hz).

^{13}C NMR(100 MHz) (DMSO – d_6) : δ 23.44, 33.20, 62.98, 105.44, 120.25, 121.39, 124.95, 125.33, 126.18, 126.45, 126.71, 126.83, 127.44, 129.76, 131.86, 134.04, 144.45, 150.38, 153.65, 168.27.

(2*E*)-2-(Naphthoxymethyl)-3-(2-chlorophenyl)prop-2-enoic acid (98f):

This α,β- unsaturated acid was obtained as a white crystalline solid *via* the treatment of methyl (2*Z*)-2-(bromomethyl)-3-(2-chlorophenyl)prop-2-enoate (**82f**) with α-naphthol in the presence of anhydrous K_2CO_3 in acetone followed by the subsequent hydrolysis of the resulting cinnamic ester by following the similar procedure described for the molecule **98a.**

Reaction time : (3 + 3) h



Yield : 84%

Mp : 128-132 ^{0}C

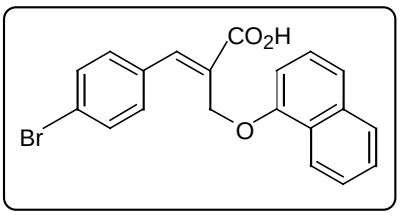
IR (KBr) : ν 3500-2500, 1691, 1630 cm^{-1}

^{1}H NMR (400 MHz) : δ 4.88 (s, 2H), 6.76 (d, 1H, *J* = 7.6 Hz), 7.05-7.12 (m, 1H), 7.17-7.27 (m, 1H), 7.28-7.35 (m, 1H), 7.36-7.48 (m, 4H), 7.56 (d, 1H, *J* = 7.2 Hz), 7.75-7.80 (m, 1H), 8.24 (d, 1H, *J* = 7.6 Hz), 8.36 (s, 1H), 11.58 (bs, 1H).

^{13}C NMR (50 MHz) : δ 62.88, 105.31, 120.88, 122.19, 125.37, 125.83, 126.51, 127.11, 127.48, 128.59, 129.73, 130.73, 130.95, 132.91, 134.58, 134.66, 144.48, 154.14, 172.47.

(2*E*)-2-(Naphthoxymethyl)-3-(4-bromophenyl)prop-2-enoic acid (98g):

Reaction between methyl (2*Z*)-2-(bromomethyl)-3-(4-bromophenyl)prop-2-enoate (**82g**) with α-naphthol in the presence of anhydrous K_2CO_3 in acetone and subsequent hydrolysis of the resulting cinnamic ester following the similar procedure described for the molecule **98a** provided the title compound as a white crystalline solid.



Reaction time : (3 + 3) h

Yield : 86%

Mp : 190-194^{0}C

IR(KBr) : ν 3500-2500, 1678, 1628 cm^{-1}

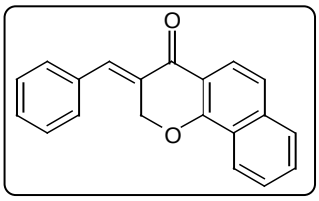
^{1}H NMR (400 MHz) ($CDCl_3$ & DMSO – d_6 4:1 ratio) : δ 4.25 (bs, 1H), 4.97 (s, 2H), 6.88 (d, 1H, *J* = 7.6 Hz), 7.33-7.52 (m, 8H), 7.79 (d, 1H, *J* = 8.0 Hz), 8.04 (s, 1H), 8.21 (d, 1H, *J* = 8.0 Hz).

^{13}C NMR(100 MHz) ($CDCl_3$ & DMSO – d_6 4:1 ratio) : δ 62.34, 104.76, 120.05, 121.47, 123.18, 124.67, 125.07, 125.39, 125.89, 126.86, 128.08, 130.65, 131.28, 133.12, 133.87, 143.24, 153.48, 168.12.

3-Benzylidene-7:8-tetrahydrobenzochroman-4-(4H)-one (99a):

To a stirred solution of (2*E*)-2-(naphthoxymethyl)-3-phenylprop-2-enoic acid (**98a**) (1 mmol, 0.304 g) in anhydrous CH_2Cl_2 (2 mL) under nitrogen atmosphere, TFAA (3 mmol, 0.41 mL) was added and the reaction was heated under reflux for 3 hours. Then the reaction mixture was cooled to room temperature and diluted with ethyl acetate (30 mL) and washed successfully with water and aq. K_2CO_3 solution. Organic layer was dried over anhydrous Na_2SO_4. After evaporation of solvent, the crude product was crystallized from ethyl acetate/hexane (1:2) to provide the pure product **99a** in 85% (0.243 g) yield as a light yellow crystalline solid.

E : Z : 90 : 10 [determined by the integration of isomeric olefinic proton singlets at δ 7.00 (*Z*-isomer) & 7.95 (*E*-isomer) in the ^{1}H NMR spectrum of the crude as well as crystallized sample. It was further confirmed by integration of isomeric CH_2 proton doublets at δ 5.24 (*Z*- isomer) & δ 5.60 (*E*-isomer)].



Mp : 115-120^{0}C

IR (KBr) : ν 1658, 1620 cm^{-1}

^{1}H NMR (400 MHz) (*Z* & *E* mixture) : δ <u>5.24</u> & 5.60 (2d, 2H, *J* = 2.0 Hz), <u>7.00</u> & 7.95 (2s, 1H)*, 7.32-7.69 (m, 8H), 7.79-7.85 (m, 1H), <u>7.99</u> & 8.02 (2d, 1H, *J* = 8.0 Hz), 8.27 & <u>8.32</u> (2d, 1H, *J* = 8.0 Hz).

**They are two unresolved triplets but look like singlets*

The underlined chemical shift values with low intensity arise due to the presence of minor (Z)-isomer

^{13}C NMR(50 MHz) (*Z* & *E* mixture) : δ 68.34, <u>75.79,</u> 116.39, <u>117.54</u>, <u>121.40</u>, 121.57, 122.59, 123.49,

123.55, 124.87, 126.27, 127.87, 127.93, 128.06, 128.77, 129.42, 129.64, 129.70, 130.00, 130.54, 134.37, 134.54, 137.03, 137.45, 139.81, 159.30, 181.84.

Major peak at δ 68.34 (allylic carbon) and minor peak at δ 75.79 (allylic carbon) are attributed to the major (E)- and minor (Z)-isomers respectively. Similarly, the underlined chemical shift values with low intensity arise due to the presence of minor (Z)-isomer.

LCMS (m/z) : 287 $(M+H)^+$

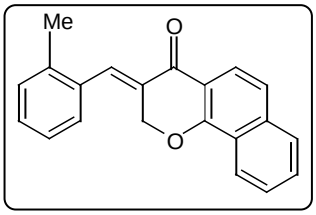
Analysis calcd. for $C_{20}H_{14}O_2$: C, 83.91; H, 4.89

Found : C, 83.96; H, 4.85

3-(2-Methylbenzylidene)-7:8-tetrahydrobenzochroman-4-(4H)-one (99b):

This was prepared *via* the treatment of (2*E*)-2-(naphthoxymethyl)-3-(2-methylphenyl)-prop-2-enoic acid (**98b**), TFAA and dry CH_2Cl_2 following the similar procedure described for the molecule **99a** as a light yellow crystalline solid.

E : Z : 90 : 10 [determined by the integration of isomeric methylene proton doublets at δ 5.29 (*Z*-isomer) & 5.46 (*E*-isomer) in the ^{1}H NMR spectrum of the crude as well as crystallized sample].



Reaction time : 3h

Yield : 80%

Mp : 150-152 ^{0}C

IR (KBr) : ν 1666, 1618 cm^{-1}

^{1}H NMR(400 MHz) (*Z* & *E* mixture) : δ 2.34 & 2.40 (2s, 3H), 5.29 & 5.46 (2d, 2H, 1.6 Hz), 7.08 (d, 1H, *J* = 7.2 Hz), 7.14 & 8.05 (2s, 1H)*, 7.20-8.10 (m, 8H), 8.27 & 8.34 (2d, 1H, *J* = 8.4 Hz).

**They are two unresolved triplets but look like singlets.*

The underlined chemical shift values with low intensity arise due to the presence of minor (Z)-isomer

^{13}C NMR (50 MHz) (*Z* & *E* mixture) : δ 19.99, 68.41, <u>74.67</u>, <u>108.63</u>, 116.51, 121.56, 122.58, 123.47, 124.93, 125.75, 126.22, 127.89, 128.93, 129.39, 129.66, 130.56, 130.90, 133.57, 136.31, 137.47, 138.08, 159.52, 182.08.

Major peak at δ 68.41 (allylic carbon) and minor peak at δ 74.67 (allylic carbon) are attributed to the major (E)- and minor (Z)-isomers respectively.

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

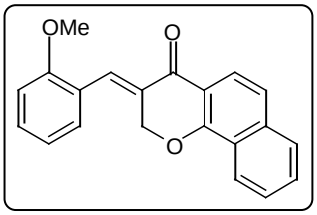
Analysis calcd. for $C_{21}H_{16}O_2$: C, 84.00 ; H, 5.33

Found : C, 84.08 ; H, 5.33

3-(2-Methoxybenzylidene)-7:8-tetrahydrobenzochroman-4-(4H)-one (99c):

Treatment of methyl (2*E*)-2-(naphthoxymethyl)-3-(2-methoxyphenyl)prop-2-enoic acid (**98c**), TFAA and dry CH_2Cl_2 following the similar procedure described for the molecule **99a** provided the title compound **99c** as a light yellow crystalline solid.

E : Z : 96 : 4 [determined by the integration of isomeric olefinic proton singlets at δ 7.12 (*Z*-isomer) & 7.95 (*E*-isomer) in the ^{1}H NMR spectrum of the crude as well as crystallized sample. It was further confirmed by integration of isomeric CH_2 proton doublets at δ 5.14 (*Z*-isomer) & δ 5.34 (*E*-isomer)



Reaction time : 3h

Yield : 81%

Mp : 102-104^{0}C

IR (KBr) : ν 1668, 1614 cm^{-1}

^{1}H NMR (400 MHz) (*Z* & *E* mixture) : δ <u>3.72</u> & 3.76 (2s, 3H), <u>5.14</u> & 5.34 (2d, 2H, *J* = 2.0 Hz), 6.72-7.60 (m, 7H), <u>7.12</u> & 7.95 (2s, 1H), 7.68 & <u>7.77</u> (2d, 1H, *J* = 8.4 Hz), <u>7.88</u> & 7.92 (2d, 1H, *J* = 8.4 Hz), 8.14 & <u>8.20</u> (2d, 1H, *J* =

8.4 Hz).

The underlined chemical shift values with low intensity arise due to the presence of minor (Z)-isomer.

^{13}C NMR (100 MHz) : δ 55.50, 68.80, 75.36, 110.18, 110.93, 116.53, 119.94, 120.27,
(*Z & E* mixture)
121.22, 121.37, 122.59, 122.64, 123.46, 123.61, 124.90, 126.13,
127.80, 127.86, 129.19, 129.49, 129.53, 130.46, 130.93, 131.08,
131.50, 133.40, 135.06, 137.35, 158.18, 159.38, 182.05.

Major peak at δ 68.80 (allylic carbon) and minor peak at δ 75.36 (allylic carbon) are attributed to the major (E)- and minor (Z)-isomers respectively. Similarly, the underlined chemical shift values with low intensity arise due to the presence of minor (Z)-isomer.

LCMS (m/z) : 317 $(M+H)^+$

Analysis calcd. for $C_{21}H_{16}O_3$: C, 79.74 ; H, 5.06

Found : C, 79.69 ; H, 5.06

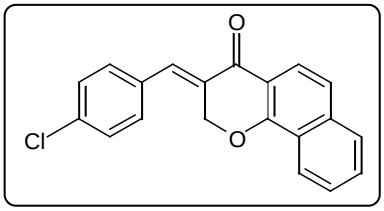
3-(4-Chlorobenzylidene)-7:8-tetrahydrobenzochroman-4-(4H)-one (99d):

Treatment of methyl (2*E*)-2-(naphthoxymethyl)-3-(4-chlorophenyl)prop-2-enoic acid (**98d**) , TFAA and dry CH_2Cl_2 following the similar procedure described for the molecule **99a** furnished the expected chromanone **99d** as a light yellow crystalline solid.

E : Z : 70 : 30 [determined by the integration of isomeric olefinic proton singlets at δ 6.94 (*Z*-isomer) & 7.87 (*E*-isomer) in the ^{1}H NMR spectrum of the crude as well as crystallized sample. It was further confirmed by integration of isomeric CH_2 proton doublets at δ 5.24 (*Z*-isomer) & δ 5.57 (*E*-isomer)

Reaction time : 3h

Yield : 84%



Mp : 172-174 ^{0}C

IR (KBr) : ν 1666, 1620 cm^{-1}

^{1}H NMR (400 MHz) (*Z* & *E* mixture) : δ 5.24 & 5.57 (s, 2H), 6.94 & 7.87 (2s, 1H)*, 7.20-7.85 (m, 8H), 7.97 & 8.01 (2d, 1H, *J* = 8.4 Hz), 8.28 & 8.32 (2d, 1H, *J* = 8.8 Hz).

**They are two unresolved triplets but look like singlets.*

The underlined chemical shift values with low intensity arise due to the presence of minor (Z)-isomer

^{13}C NMR(100 MHz) (*Z* & *E* mixture) : δ 68.22, 75.69, 116.36, 116.98, 121.57, 121.76, 122.51, 122.56, 123.52, 123.59, 124.87, 126.38, 127.94, 128.00, 128.32, 129.12, 129.80, 129.84, 129.99, 131.07, 131.24, 132.01, 132.81, 133.00, 135.55, 135.60, 137.47, 137.53, 138.37, 159.36, 181.59.

Major peak at δ 68.22 (allylic carbon) and minor peak at δ 75.69 (allylic carbon) are attributed to the major (E)- and minor (Z)-isomers respectively. Similarly, the underlined chemical shift values with low intensity arise due to the presence of minor (Z)-isomer.

LCMS (m/z) : 321 $(M+H)^{+}$; 323 $(M+H+2)^{+}$

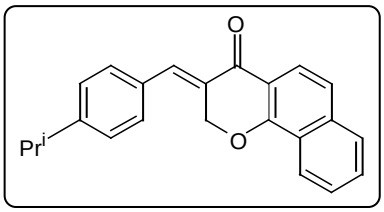
Analysis calcd. for $C_{20}H_{13}O_2Cl$: C, 75.00 ; H, 4.06

Found : C, 74.98 ; H, 4.05

3-(4-Isopropylbenzylidene)-7:8-tetrahydrobenzochroman-4-(4H)-one (99e):

This ketone was prepared as a light yellow crystalline solid *via* the treatment of (2*E*)-2-(naphthoxymethyl)-3-(4-isopropylphenyl)prop-2-enoic acid (**98e**), TFAA and dry CH_2Cl_2 following the similar procedure described for the molecule **99a**.

E : Z : 98 : 2 [determined by the integration of isomeric olefinic proton singlets at δ 6.94 (*Z*-isomer) & 7.90 (*E*-isomer) in the ^{1}H NMR spectrum of the crude as well as crystallized sample. It was further confirmed by integration of isomeric CH_2 proton doublets at δ 5.20 (Z-isomer) & δ 5.59 (E-isomer).



Reaction time : 3h

Yield : 82%

Mp : 135-140 ^{0}C

IR (KBr) : ν 1668, 1626 cm^{-1}

^{1}H NMR (400 MHz) (*Z* & *E* mixture) : δ <u>1.26</u> & 1.28 (d, 6H, *J* = 6.8Hz), 2.90-3.02 (m, 1H), <u>5.20</u> & 5.59 (2d, 2H, *J* = 2.0 Hz), <u>6.94</u> & 7.90 (two unresolved triplets, s, 1H), 7.20-7.30(m, 4H), 7.44 (d, 1H, *J* = 8.8 Hz), 7.45-7.53 (m, 1H), 7.55-7.63 (m, 1H), 7.78 (d, 1H, *J* = 8.4 Hz), 8.00 (d, 1H, *J* = 8.8 Hz), 8.24 (d, 1H, *J* = 8.32 Hz).

The underlined chemical shift values with low intensity arise due to the presence of minor (Z)-isomer.

^{13}C NMR (100 MHz) (*Z* & *E* mixture) : δ 23.87, 34.16, 68.49, <u>76.05</u>, 116.48, 121.52, 122.67, 123.51, 124.93, 126.24, 126.93, 127.95, 129.65, 129.80, 130.31, 132.16, 137.15, 137.45, 150.74, 159.26, 181.94.

Major peak at δ 68.49 (allylic carbon) and minor peak at δ 76.05 (allylic carbon) are attributed to the major (E)- and minor (Z)-isomers respectively. Similarly, the underlined chemical shift values with low intensity arise due to the presence of minor (Z)-isomer.

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

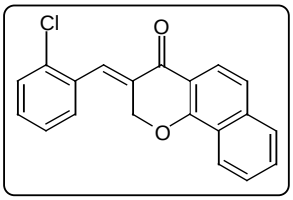
Analysis calcd. for $C_{23}H_{20}O_2$: C, 84.14 ; H, 6.09

Found : C, 84.13 ; H, 6.09

3-(2-Chlorobenzylidene)-7:8-tetrahydrobenzochroman-4-(4H)-one (99f):

This was obtained as a light yellow crystalline solid *via* the treatment of methyl (2*E*)-2-(naphthoxymethyl)-3-(2-chlorophenyl)prop-2-enoic acid (**98f**), TFAA and dry CH_2Cl_2 following the similar procedure described for the molecule **99a.**

E : Z : 90 : 10 [determined by the integration of isomeric olefinic proton singlets at δ 7.15 (*Z*-isomer) & 8.02 (*E*-isomer) in the ^{1}H NMR spectrum of the crude as well as crystallized sample. It was further confirmed by integration of isomeric CH_2 proton doublets at δ 5.29 (*Z*-isomer) & δ 5.42 (*E*-isomer)



Reaction time : 3h

Yield : 83%

Mp : 184-187^{0}C

IR (KBr) : ν 1668, 1616 cm^{-1}

^{1}H NMR (400 MHz) (*Z* & *E* mixture) : δ 5.29 & 5.42 (2s, 2H), 7.15 & 8.02 (2s, 1H), 7.19-8.10 (m, 9H), 8.25 & 8.33 (d, 1H, *J* = 8.4 Hz).

The underlined chemical shift values with low intensity arise due to the presence of minor (Z)-isomer.

^{13}C NMR (100 MHz) (*Z* & *E* mixture) : δ 68.27, 74.56, 116.42, 121.56, 121.71, 122.41, 122.52, 123.49, 123.61, 124.86, 126.11, 126.32, 126.68, 127.89, 127.95, 129.07, 129.78, 129.80, 130.11, 130.38, 130.48, 131.57, 132.14, 133.05, 134.06, 134.98, 135.65, 137.50, 159.55, 181.66.

Major peak at δ 68.27 (allylic carbon) and minor peak at δ 74.56 (allylic carbon) are attributed to the major (E)- and minor (Z)-isomers respectively. Similarly, the underlined chemical shift values with low intensity arise due to the presence of minor (Z)-isomer.

LCMS (m/z) : 321 $(M+H)^+$; 323 $(M+H+2)^+$

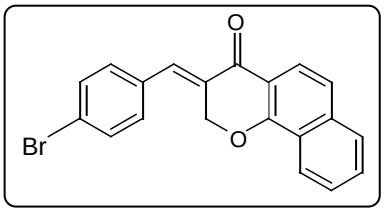
Analysis calcd. for $C_{20}H_{13}O_2Cl$: C, 75.00; H, 4.06

Found : C, 75.12 ; H, 4.01

3-(4-Bromobenzylidene)-7:8-tetrahydrobenzochroman-4-(4H)-one (99g):

This compound was obtained as a light yellow crystalline solid *via* the treatment of methyl (2*E*)-2-(naphthoxymethyl)-3-(4-bromophenyl)prop-2-enoic acid (**98g**), TFAA and dry CH_2Cl_2 following the similar procedure described for the molecule **99a.**

E : Z : 97 : 3 [determined by the integration of isomeric CH_2 proton doublets at δ 5.24 (*Z*-isomer) & 5.60 (*E*-isomer) in the ^{1}H NMR spectrum of the crude as well as crystallized sample].



Reaction time : 3h

Yield : 85 %

Mp : 215-218 ^{0}C

IR (KBr) : ν 1666, 1626 cm^{-1}

^{1}H NMR 400 MHz) (*Z & E* mixture) : δ <u>5.19</u> & 5.51 (d, 1H, *J* = 2.0 Hz), <u>6.88</u> & 7.81 (2s, 1H),7.19 (d, 2H, *J* = 8.4 Hz), 7.44 (d, 1H, *J* = 8.4 Hz), 7.51-7.65 (m, 4H), 7.78 (d, 1H, *J* = 8.4 Hz), 7.97 (d, 1H, *J* = 8.4 Hz), 8.24 (d, 1H, *J* = 8.4 Hz).

The underlined chemical shift values with low intensity arise due to the presence of minor (Z)-isomer.

^{1}H NMR spectrum shows a singlet at 6.88 with low intensity (<3%) indicating that its stereochemical purity is atleast 97%.

^{13}C NMR (100 MHz) (*Z & E* mixture) : δ 68.18, 116.30, 121.72, 122.51, 123.48, 123.81, 124.82, 126.35, 127.96, 129.81, 131.11, <u>131.25</u>, 131.41, 132.03, 133.39, 135.57, 137.48, 159.31, 181.49.

Major peak at δ 68.18 (allylic carbon) is attributed to the major (E)-isomer. Similarly, the underlined chemical shift values with low intensity arise due to the presence of minor (Z)-isomer.

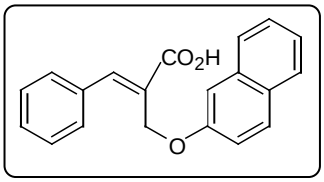
LCMS (m/z) : 365 $(M+H)^+$; 367 $(M+H+2)^+$

Analysis calcd. for $C_{20}H_{13}O_2Br$: C, 65.93 ; H, 3.71

Found : C, 65.78 ; H, 3.55

(2*E*)-2-(Naphthoxymethyl)-3-phenylprop-2-enoic acid (107a):

To a stirred mixture of methyl (2*Z*)-2-(bromomethyl)-3-phenylprop-2-enoate (**82a**) (2 mmol, 0.510 g) and anhydrous K_2CO_3 (4 mmol, 0.552 g) in acetone (3 mL), β-naphthol (2.4 mmol, 0.346 g) was added and the reaction mixture heated under reflux (the reaction was monitored by TLC). After 3 hours reaction mixture was cooled to room temperature. Then 50% aq KOH solution (1 mL) was added to the above reaction mixture and heated under reflux. After 3 hours, the reaction mixture was cooled to room temperature. The solvent was removed under pressure. The reaction mixture was diluted with cold conc. HCl (5 mL) and extracted with ethyl acetate (3 x 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 [30% ethyl acetate in hexane] to provide the acid **107a** in 87% (0.53 g) yield as a white crystalline solid.



Mp : 146-148^{0}C

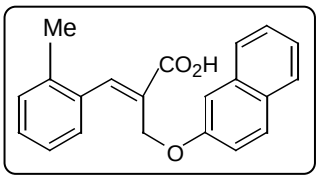
IR (KBr) : ν 3500-2500, 1682, 1626 cm^{-1}

^{1}H NMR (400 MHz) (DMSO – d_6) : δ 4.91 (s, 2H), 7.20-7.90 (m, 12H), 8.04 (s, 1H).

^{13}C NMR (50 MHz) (DMSO – d_6) : δ 63.01, 107.37, 118.92, 123.93, 126.63, 126.93, 127.72, 128.20, 128.96, 129.63, 129.78, 134.51, 144.39, 156.37, 168.35.

(2*E*)-2-(Naphthoxymethyl)-3-(2-methylphenyl)prop-2-enoic acid (107b):

This was prepared *via* the treatment of methyl (2*Z*)-2-(bromomethyl)-3-(2-methylphenyl)prop-2-enoate (**82b**) with anhydrous K_2CO_3 and β-naphthol in acetone and subsequent hydrolysis the resulting cinnamic ester with KOH following the similar procedure described for the molecule **107a** as a white crystalline solid.



Reaction time : (3 + 3) h

Yield : 83%

Mp : 114-116 ^{0}C

IR (KBr) : ν 3500-2500, 1693, 1630 cm^{-1}

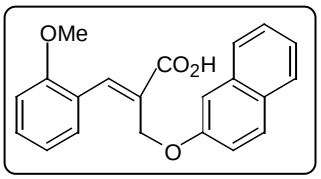
^{1}H NMR (400MHz) (DMSO – d_6) : δ 2.20 (s, 3H), 4.00 (bs, 1H), 4.71 (s, 2H), 6.90-7.38 (m, 7H), 7.55-7.73 (m, 4H), 8.00 (s, 1H).

^{13}C NMR (50 MHz) (DMSO – d_6) : δ 19.62, 63.16, 107.28, 118.86, 122.84, 123.87, 126.08, 126.29, 126.57, 126.78, 127.69, 128.75, 129.29, 129.45, 130.36, 133.90, 137.03, 142.94, 156.34, 168.11.

(2*E*)-2-(Naphthoxymethyl)-3-(2-methoxyphenyl)prop-2-enoic acid (107c):

This acid was prepared *via* the treatment of methyl (2*Z*)-2-(bromomethyl)-3-(2-methoxyphenyl)prop-2-enoate (**82c**) with anhydrous K_2CO_3 and β-naphthol in acetone and subsequent hydrolysis of the resulting cinnamic ester with KOH following the similar procedure described for the molecule **107a** as a white crystalline solid.

Reaction time : (3 + 3) h



Yield : 81%

Mp : 138-142^{0}C

IR (KBr) : ν 3500-2500, 1674, 1628 cm^{-1}

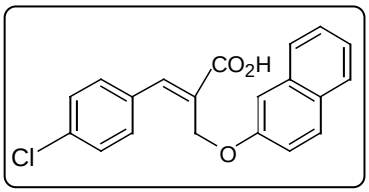
^{1}H NMR (400MHz) (DMSO – d_6) : δ 3.83 (s, 3H), 4.87 (s, 2H), 6.85-6.92 (m, 1H), 7.06 (d, 1H, *J* = 8.4 Hz), 7.22-7.26 (m, 1H), 7.30-7.49 (m, 5H), 7.75 (d, 1H, *J* = 8.0 Hz), 7.80-7.88 (m, 2H), 8.17 (s, 1H).

^{13}C NMR (50 MHz) (DMSO – d_6) : δ 55.77, 63.32, 107.22, 111.47, 118.96, 120.65, 123.20, 123.90, 126.63, 126.87, 127.72, 127.87, 128.84, 129.60, 129.90, 131.66, 134.48, 140.06, 156.40, 157.83, 168.35.

(2*E*)-2-(Naphthoxymethyl)-3-(4-chlorophenyl)prop-2-enoic acid (107d):

This acid was prepared *via* the treatment of methyl (2*Z*)-2-(bromomethyl)-3-(4-chlorophenyl)prop-2-enoate (**82d**) with anhydrous K_2CO_3 and β-naphthol in acetone and followed by the hydrolysis of the resulting cinnamic ester with KOH following the similar procedure described for the molecule **107a** as a white crystalline solid.

Reaction time : (3 + 3) h



Yield : 82%

Mp : 194-198^{0}C

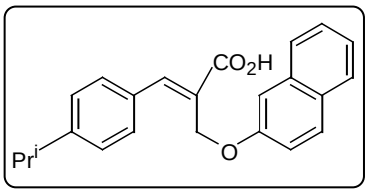
IR (KBr) : ν 3500-2500, 1684, 1628 cm^{-1}

^{1}H NMR (400MHz) (DMSO – d_6) : δ 4.94 (s, 2H), 7.17 (dd, 1H, *J* = 2.4 & 8.8 Hz), 7.30-7.46 (m, 7H), 7.68 (s, 1H), 7.77-7.84 (m, 3H).

^{13}C NMR (100 MHz) (DMSO – d_6) : δ 64.50, 107.22, 119.20, 123.59, 126.44, 126.90, 127.69, 128.57, 128.66, 129.32, 130.90, 132.54, 134.63, 135.97, 137.21, 156.86, 170.62.

(2*E*)-2-(Naphthoxymethyl)-3-(4-isopropylphenyl)prop-2-enoic acid (107e):

Treatment of methyl (2*Z*)-2-(bromomethyl)-3-(4-isopropylphenyl)prop3-phenylprop-2-enoate (**82e**) with β-naphthol in the presence of anhydrous K_2CO_3 in acetone and subsequent hydrolysis of the resulting ester with KOH following the similar procedure described for the molecule **107a** furnished the title compound as a white crystalline solid.



Reaction time : (3 + 3) h

Yield : 85%

Mp : 138-142 ^{0}C

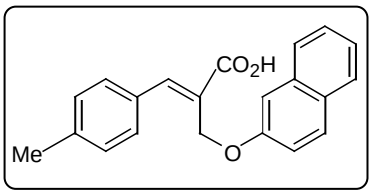
IR (KBr) : ν 3500-2500, 1682, 1626 cm^{-1}

^{1}H NMR(400 MHz) (CDCl$_3$ & DMSO- d_6 in 4:1 ratio) : δ 1.19 (d, 6H, *J* = 6.8 Hz), 2.72-2.95 (septet, 1H, *J* = 6.8 Hz), 4.94 (s, 2H), 7.17-7.50 (m, 8H), 7.70 (d, 1H, *J* = 8.0 Hz), 7.76 (d, 2H, *J* = 8.6 Hz), 8.02 (s, 1H).

^{13}C NMR (50 MHz) (CDCl$_3$ & DMSO – d_6 in 4:1 ratio) : δ 22.58, 32.64, 61.81, 106.11, 117.91, 122.58, 125.28, 125.67, 126.43, 127.85, 128.25, 128.79, 131.01, 133.34, 143.83, 149.44, 155.32, 167.66.

(2*E*)-2-(Naphthoxymethyl)-3-(4-methylphenyl)prop-2-enoic acid (107h):

This cinnamic acid was obtained as a white crystalline solid *via* the treatment of methyl (2*Z*)-2-(bromomethyl)-3-(4-methylphenyl)prop-2-enoate (**82h**) with anhydrous K_2CO_3 and β-naphthol in acetone followed by the hydrolysis of the resulting ester following the similar procedure described for the molecule **107a**.



Reaction time : (3 + 3) h

Yield : 84%

Mp : 150-155^{0}C

IR (KBr) : ν 3500-2500, 1682, 1628 cm^{-1}

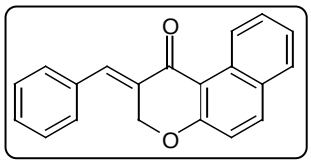
^{1}H NMR (400 MHz) (DMSO – d_6) : δ 2.28 (s, 3H), 4.88 (s, 2H), 7.17-7.50 (m, 8H), 7.78 (d, 1H, *J* = 8.0 Hz), 7.85 (d, 2H, *J* = 8.02 Hz), 7.97 (s, 1H).

^{13}C NMR (100 MHz) (DMSO – d_6) : δ 20.82, 62.79, 107.00, 118.70, 123.69, 126.42, 126.67, 126.87, 127.50, 128.60, 129.39, 129.63, 131.44, 134.22, 139.66, 144.37, 156.07, 168.21.

2-Benzylidene-5:6-tetrahydrobenzochroman-4-(4H)-one (108a):

To a stirred solution of (2*E*)-2-(naphthoxymethyl)-3-phenylprop-2-enoic acid (**107a**) (1 mmol, 0.304 g) in dry CH_2Cl_2 (2 mL) under nitrogen atmosphere, TFAA (3 mmol, 0.42 mL) was added and the reaction was heated under reflux for 3 hours.Then the reaction mixture was cooled to rt and diluted with ethyl acetate (30 mL) and washed successfully with water, aq. K_2CO_3. Organic layer was dried over anhydrous Na_2SO_4. After evaporation of solvent, the crude product was crystallized from ethyl acetate/hexane (1:2) to provide the pure product **108a** in 84% yield (0.24 g) as a light yellow crystalline solid.

Mp : 101-104 ^{0}C



IR (KBr) : ν 1655, 1616 cm^{-1}

E : *Z* : 100 : 0

^{1}H NMR (400 MHz) *(E-isomer)* : δ 5.33 (2d, 2H, *J* = 2.4 Hz), 7.04 (d, 1H, *J* = 8.8 Hz), 7.28 (d, 2H, *J* = 6.8 Hz), 7.35-7.43 (m, 4H), 7.60-7.68 (m, 1H), 7.72 (d, 1H, *J* = 8.4 Hz), 7.87 (d, 1H, *J* = 8.8 Hz), 7.91 (s, 1H), 9.44 (d, 1H, *J* = 8.0 Hz).

^{13}C NMR (50 MHz) (*E-isomer*) : δ 67.49, 114.33, 118.74, 125.03, 126.53, 128.50, 128.71, 129.25, 129.51, 129.66, 129.85, 131.99, 132.23, 134.75, 136.72, 137.40, 163.21, 182.49.

LCMS (m/z) : 287 $(M+H)^+$

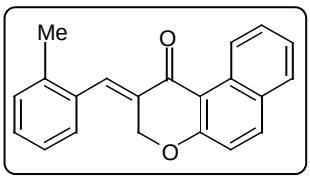
Analysis calcd. for $C_{20}H_{14}O_2$: C, 83.91 ; H, 4.89

Found : C, 83.79; H, 4.87

2-(2-Methylbenzylidene)-5:6-tetrahydrobenzochroman-4-(4H)-one (108b):

This was prepared as a light yellow crystalline solid *via* the treatment of (2*E*)-2-(naphthoxymethyl)-3-(2-methylphenyl)prop-2-enoic acid (**107b**) with TFAA following the similar procedure described for the molecule **108a.**

Reaction time : 3h



Yield : 81%

Mp : 133-138 ^{0}C

IR (KBr) : ν 1658, 1620 cm^{-1}

E : Z : 90 : 10 [determined by the integration of isomeric CH_2 doublets at δ 4.98 (*Z*- isomer) & δ 5.12 (*E*- isomer)]

^{1}H NMR (400 MHz) (*Z* & *E* mixture) : δ 2.18 & 2.25 (s, 3H), 4.98 & 5.12 (2d, 2H, *J* = 2.4 Hz), 6.85-7.95 (m, 10H), 9.34 & 9.37 (2d, 1H, *J* = 8.6 Hz).

The underlined chemical shift values with low intensity arise due to the presence of minor (Z)-isomer.

^{13}C NMR (50 MHz) (*Z* & *E* mixture) : δ 14.30, 19.92, 67.56, 74.00, 114.28, 118.74, 125.00, 125.73, 126.56, 128.47, 128.81, 129.22, 129.49, 129.66, 130.49, 132.11, 132.45, 133.83, 135.99, 137.37, 137.96, 163.45, 182.74.

The underlined chemical shift values are attributed to the minor (Z)-isomer.

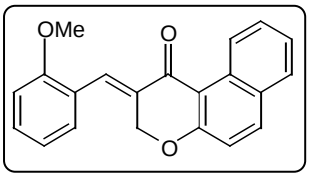
LCMS (m/z) : 301 $(M+H)^+$

Analysis calcd. for $C_{21}H_{16}O_2$: C, 84.00 ; H, 5.33

Found : C, 84.00 ; H, 5.35

2-(2-Methoxybenzylidene)-5:6-tetrahydrobenzochroman-4-(4H)-one (108c):

This was prepared as a light yellow crystalline solid *via* the treatment of (2*E*)-2-(naphthoxymethyl)-3-(2-methoxyphenyl)prop-2-enoic acid (**107c**) with TFAA following the similar procedure described for the molecule **108a.**



Reaction time : 3h

Yield : 80%

M.P : 104-107 ^{0}C

IR (KBr) : ν 1657, 1610 cm^{-1}

E : Z : 96 : 4 [determined by the integration of isomeric CH_2 doublets at δ 5.05

(*Z*- isomer) & δ 5.21 (*E*- isomer)]

^{1}H NMR (400 MHz) : δ <u>3.73</u> & 3.81 (2s, 3H), <u>5.05</u> & 5.21 (2d, 2H, *J* = 2.4 Hz), <u>7.18</u> & 8.05 (2s, 1H), <u>6.84</u> & 6.91 (2d, 1H, *J* = 8.4 Hz), 6.94-6.99 (m, 1H), 7.01-7.10 (m, 2H), 7.22-7.70 (m, 3H), 7.71 (d, 1H, *J* = 8.0 Hz), 7.85 (d, 1H, *J* = 9.0 Hz), 9.49 (d, 1H, *J* = 8.4 Hz).
(*Z* & *E* mixture)

The underlined chemical shift values with low intensity arise due to the presence of minor (Z)-isomer.

^{13}C NMR (50 MHz) : δ 55.53, 68.00, 110.96, 114.35, 118.79, 120.30, 123.89, 124.93, 126.58, 128.45, 129.42, 129.61, 130.36, 130.92, 132.11, 133.10, 137.20, 158.14, 163.35, 182.81.
(*E-isomer*)

Peak at δ 68.00 (allylic carbon) is attributed to the major (E)- isomer.

LCMS (m/z) : 317 $(M+H)^{+}$

Analysis calcd. for $C_{21}H_{16}O_3$: C, 79.74 ; H, 5.06

Found : C, 79.82; H, 4.95

2-(4-Chlorobenzylidene)-5:6-tetrahydrobenzochroman-4-(4H)-one (108d):

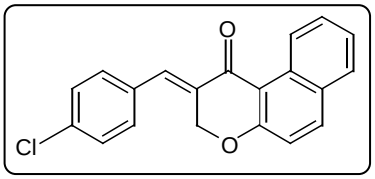
This was prepared as a light yellow crystalline solid *via* the treatment of (2*E*)-2-(naphthoxymethyl)-3-(4-chlorophenyl)prop-2-enoic acid (**107d**) with TFAA following the similar procedure described for the molecule **108a**.

Reaction time : 3h

Yield : 85%

Mp : 170-175 ^{0}C

IR (KBr) : ν 1664, 1610 cm^{-1}



E : *Z* : 98 : 2 [determined by the integration of isomeric olefinic proton singlets at δ 6.85 (*Z*-isomer) & 7.85 (*E*- isomer) in the ^{1}H NMR spectrum of the crude as well as crystallized sample. It was further confirmed by integration of isomeric CH_2 proton at δ 5.06 (*Z*-isomer) & δ 5.34 (*E*-isomer)

^{1}H NMR (400 MHz) (*Z* & *E* mixture) : δ 5.06 & 5.34 (2d, 2H, *J* = 2.4 Hz), 6.85 & 7.85 (s, 1H), 7.00-8.00 (m, 9H), 9.41 & 9.43 (d, 1H, *J* = 8.8 Hz).

The underlined chemical shift values with low intensity arise due to the presence of minor (Z)-isomer.

^{13}C NMR (100 MHz) (*Z* & *E* mixture) : δ 67.39, 74.55, 114.31, 118.74, 123.52, 125.20, 126.53, 128.35, 128.59, 129.08, 129.68, 131.12, 131.65, 131.99, 132.77, 133.23, 135.34, 137.25, 137.64, 163.31, 182.27.

Major peak at δ 67.39 (allylic carbon) and minor peak at δ 74.55 (allylic carbon) are attributed to the major (E)- and minor (Z)-isomers respectively. Similarly, the underlined chemical shift values with low intensity arise due to the presence of minor (Z)-isomer.

LCMS (m/z) : 321 $(M+H)^+$; 323 $(M+H+2)^+$

Analysis calcd. for $C_{20}H_{13}O_2Cl$: C, 75.00; H, 4.06

Found : C, 74.91 ; H, 4.02

2-(4-Isopropylbenzylidene)-5:6-tetrahydrobenzochroman-4-(4H)-one (108e):

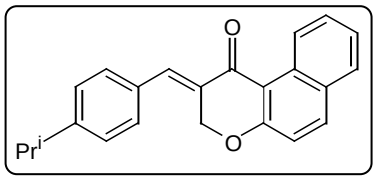
Treatment of (2*E*)-2-(naphthoxymethyl)-3-(4-isopropylphenyl)prop-2-enoic acid (**107d**) with TFAA following the similar procedure described for the molecule **108a** provided the title compound as a colorless solid.

Reaction time : 3h

Yield : 83%

Mp : 128-132 ^{0}C

IR (KBr) : ν 1684, 1630 cm^{-1}



E : Z : 98 : 2 [determined by the integration of isomeric CH_2 doublets at δ 5.07 (*Z*- isomer) & δ 5.26(*E*- isomer)]

^{1}H NMR (400 MHz) : δ 1.17 (d, 6H, *J* = 7.2 Hz), 2.83 (septet, 1H, *J* = 7.2 Hz), 5.07 & 5.26 (2d, 2H, *J* = 2.4 Hz), 6.94 (d, 1H, *J* = 8.8 Hz), 7.13 (d, 2H, *J* = 8.0 Hz), 7.18 (d, 2H, *J* = 8.0 Hz), 7.27-7.35 (m, 1H), 7.50-7.57 (m, 1H), 7.62 (d, 1H, *J* = 8.0 Hz), 7.75 (d, 1H, *J* = 8.8 Hz), 7.81 (s, 1H), 9.37 (d, 1H, *J* = 8.5 Hz).
(*Z* & *E* mixture)

The underlined chemical shift values with low intensity arise due to the presence of minor (Z)-isomer.

^{13}C NMR (100 MHz): δ 23.79, 34.03, 67.56, 114.34, 118.72, 124.93, 126.51, 126.80, 128.45, 129.40, 129.61, 130.11, 131.42, 131.96, 132.25, 136.71, 137.22, 150.44, 163.05, 182.49.
(E isomer)

Peak at δ 67.56 (allylic carbon) is attributed to the major (E)-isomer respectively.

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

Analysis calcd. for $C_{23}H_{20}O_2$: C, 84.14 ; H, 6.09

Found : C, 84.24; H, 6.09

2-(4-Methylbenzylidene)-5:6-tetrahydrobenzochroman-4-(4H)-one (108h):

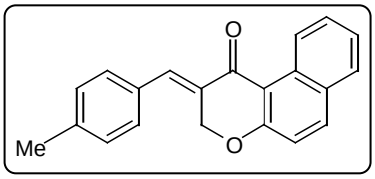
This was prepared as a light yellow crystalline solid *via* the treatment of (2*E*)-2-(naphthoxymethyl)-3-(4-methylphenyl)prop-2-enoic acid (**107h**) with TFAA following the similar procedure described for the molecule **108a**.

Reaction time : 3h

Yield : 82%

Mp : 142-146 ^{0}C

IR (KBr) : ν 1657, 1620 cm^{-1}



E : Z : 90 : 10 [determined by the integration of isomeric olefinic proton singlets at δ 6.84 (*Z*-isomer) & 7.90 (*E*- isomer) in the ^{1}H NMR spectrum of the crude as well as crystallized sample. It was further confirmed by integration of isomeric CH_2 proton doublets at δ 5.03 (Z- isomer) & δ 5.37 (*E*-isomer)]

^{1}H NMR (400 MHz) (*Z* & *E* mixture) : δ 2.34 & 2.39 (2s, 3H), 5.03 & 5.37 (2d, 2H, *J* = 2.4 Hz), 7.04-7.48 (m, 6H), 7.59-7.78 (m, 2H), 6.84 (s) & 7.85-7.92 (m) [2H], 9.43 & 9.55 (2d, 1H, *J* = 8.8 Hz).

The underlined chemical shift values with low intensity arise due to the presence of minor (Z)-isomer. Signal arising from (E)-olefinic proton merges with the multiplet at 7.85-7.92.

^{13}C NMR (50 MHz) (*Z* & *E* mixture) : δ 21.49, 67.62, 74.85, 114.40, 118.66, 118.77, 124.89, 125.01, 126.37, 126.54, 128.51, 128.84, 129.49, 129.67, 130.03, 130.38 131.44, 131.92, 132.00, 136.88, 137.33, 138.92, 139.68, 163.13, 182.63.

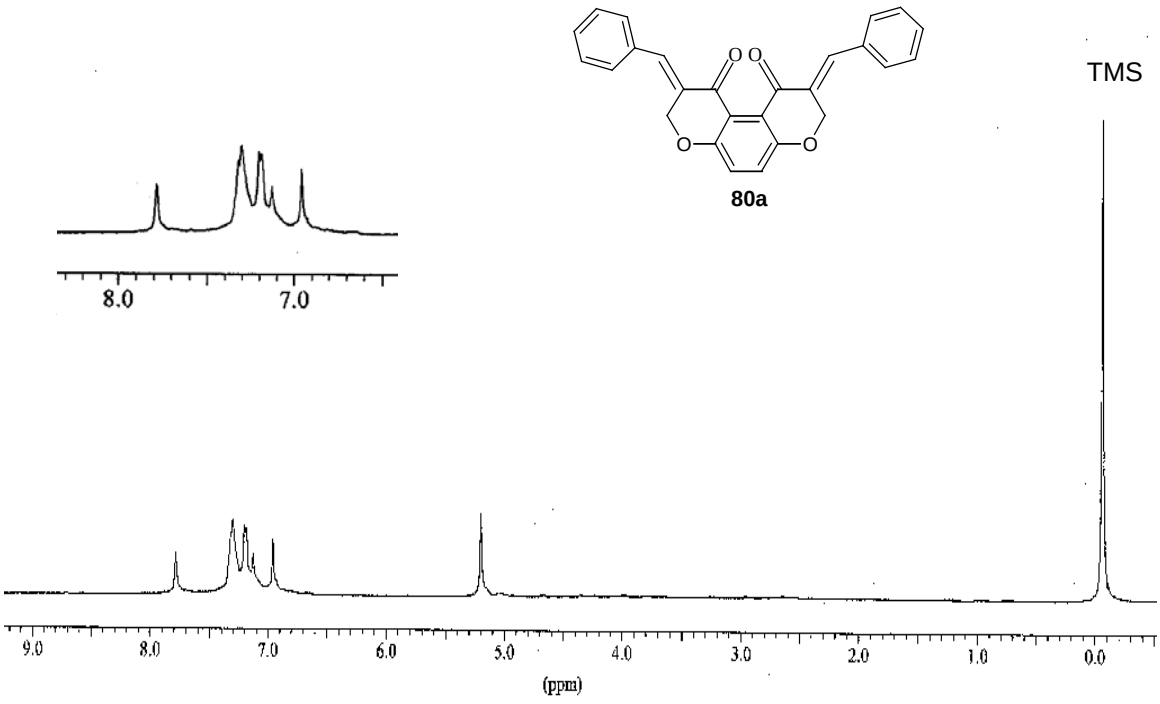
Major peak at δ 67.62 (allylic carbon) and minor peak at δ 74.85 (allylic carbon) are attributed to the major (E)- and minor (Z)-isomers respectively. Similarly, the underlined chemical shift values with low intensity arise due to the presence of minor (Z)-isomer

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

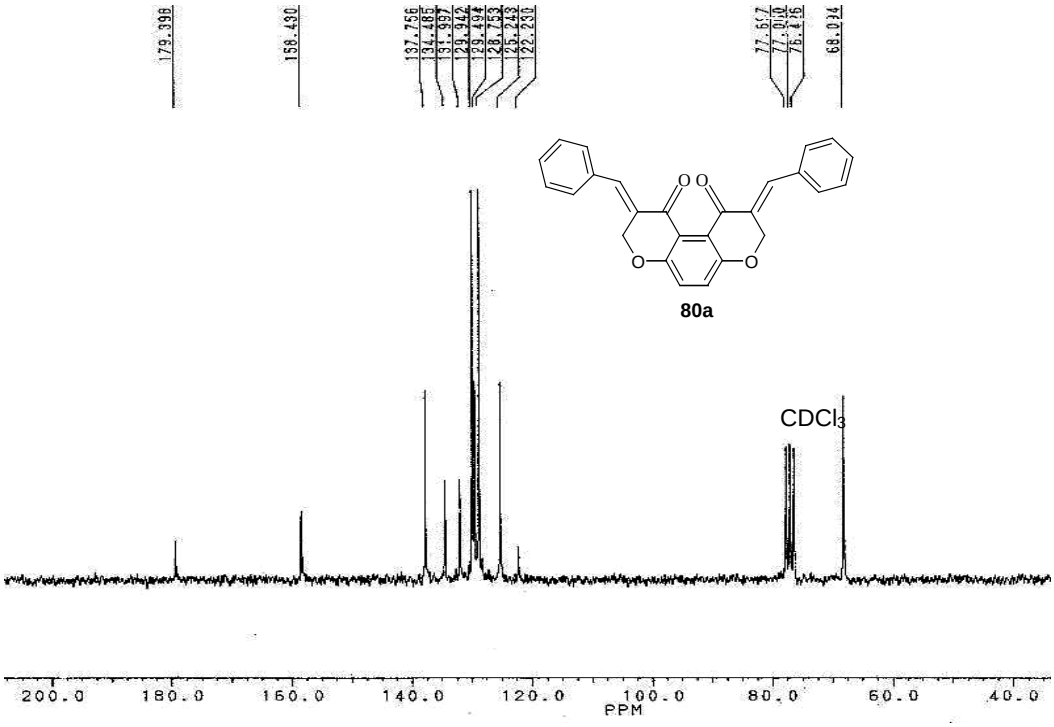
Analysis calcd. for $C_{21}H_{16}O_2$: C, 84.00 ; H, 5.33

Found : C, 84.10 ; H, 5.31

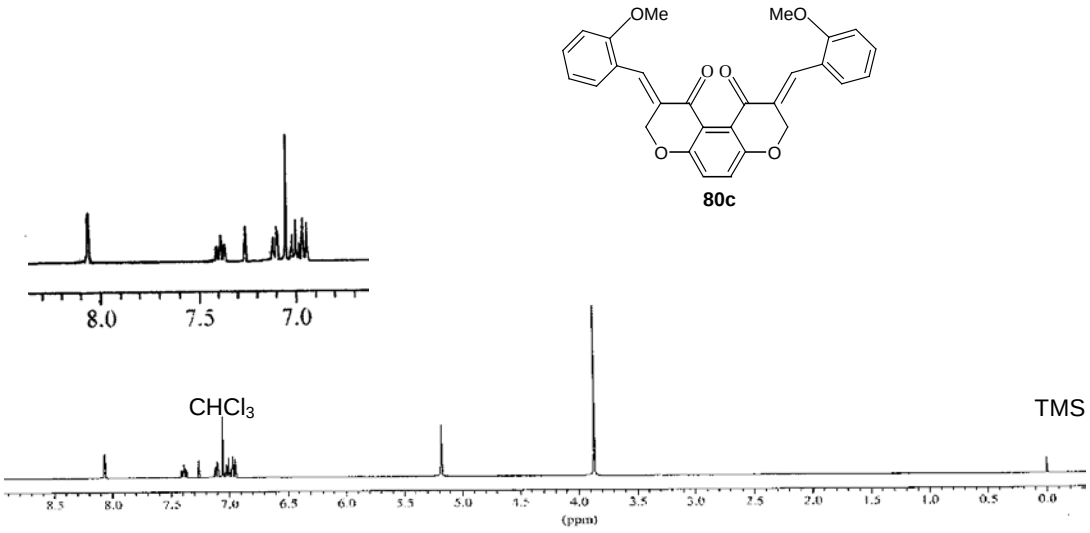
Spectrum 1: ^{1}H NMR of **80a**



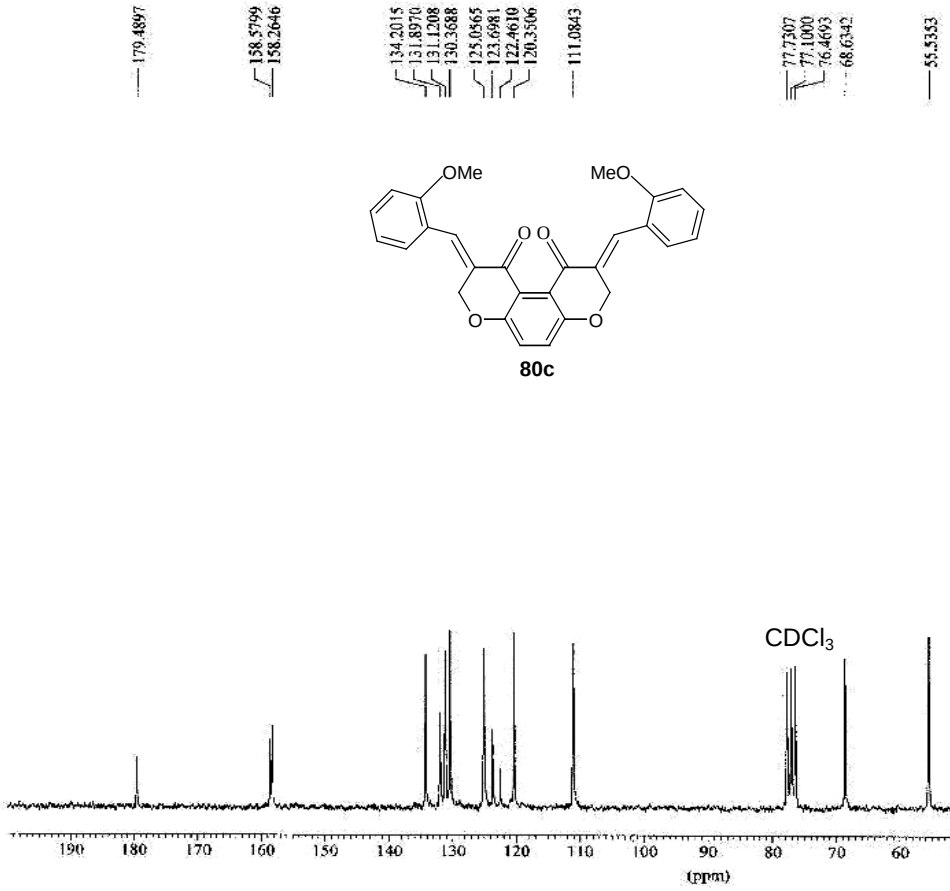
Spectrum 2: ^{13}C NMR of **80a**



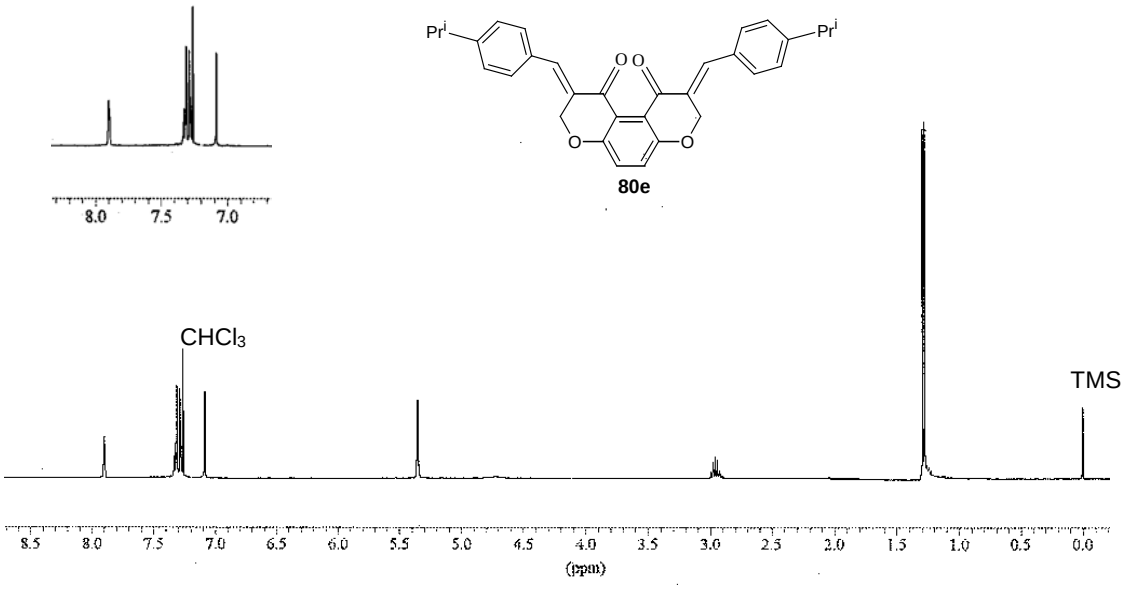
Spectrum 3: ^{1}H NMR of **80c**



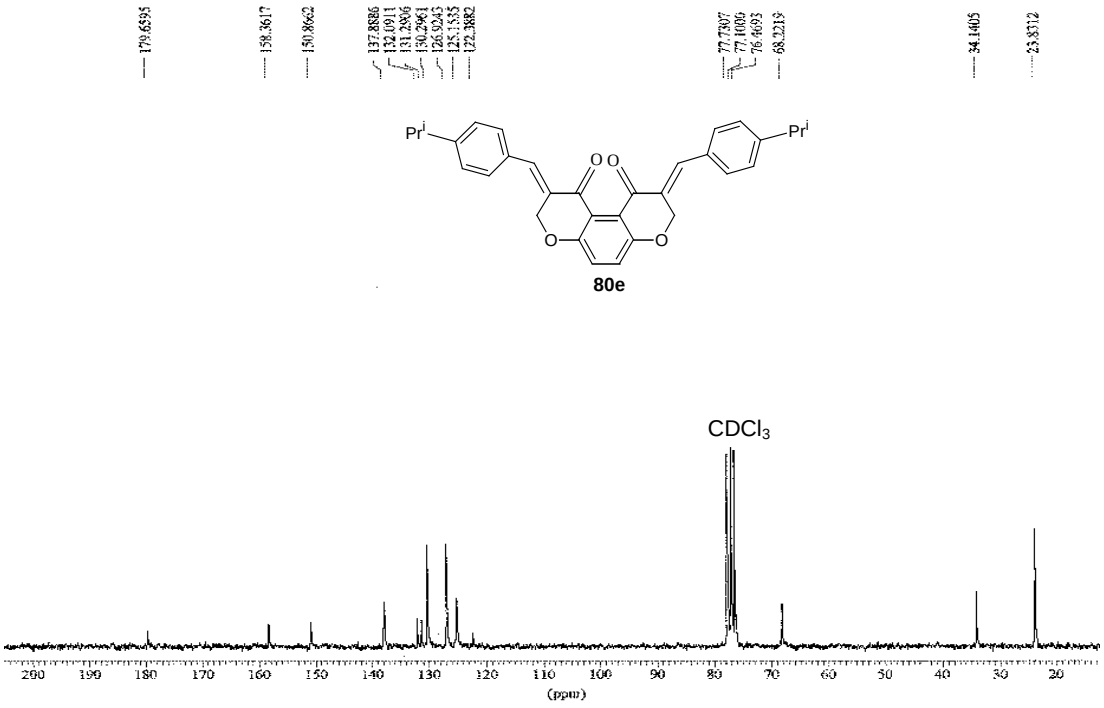
Spectrum 4: ^{13}C NMR of **80c**



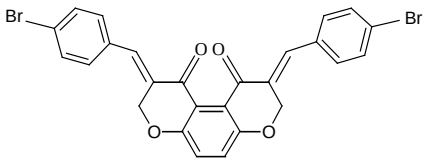
Spectrum 5: ^{1}H NMR of **80e**



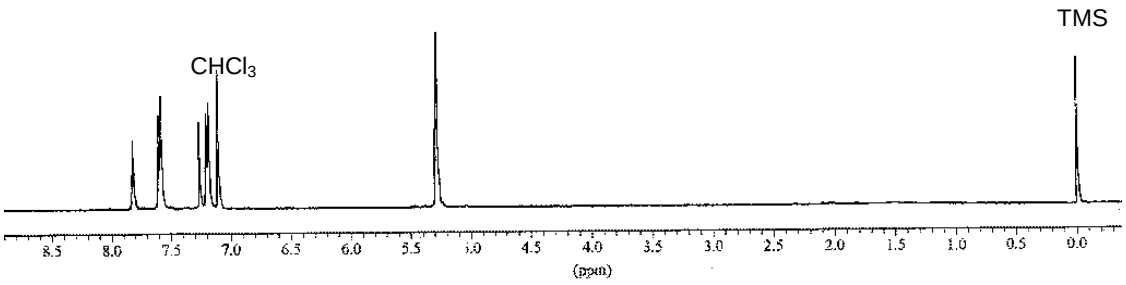
Spectrum 6: ^{13}C NMR of **80e**



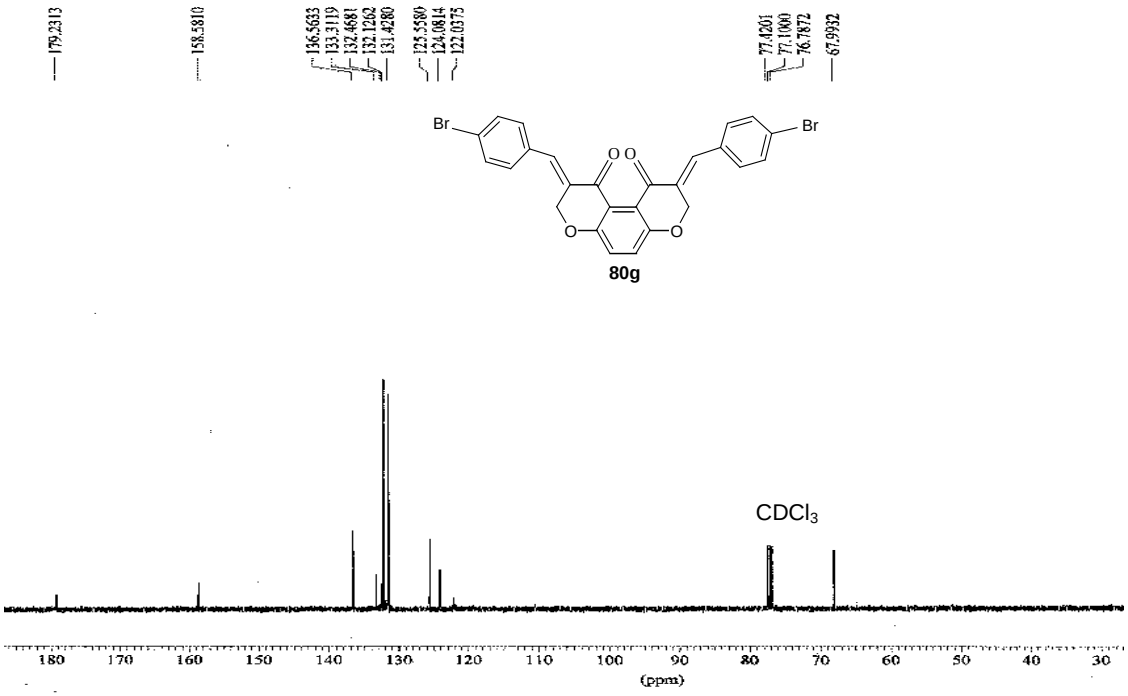
Spectrum 7: ^{1}H NMR of **80g**



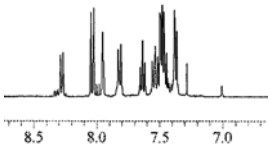
80g

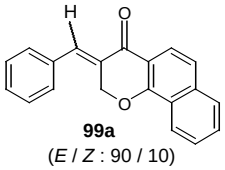


Spectrum 8: ^{13}C NMR of **80g**

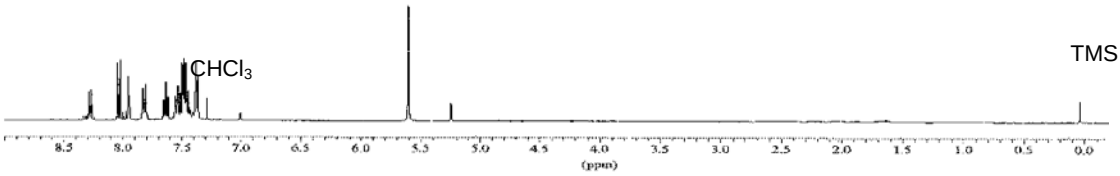


Spectrum 9: ^{1}H NMR of **99a**

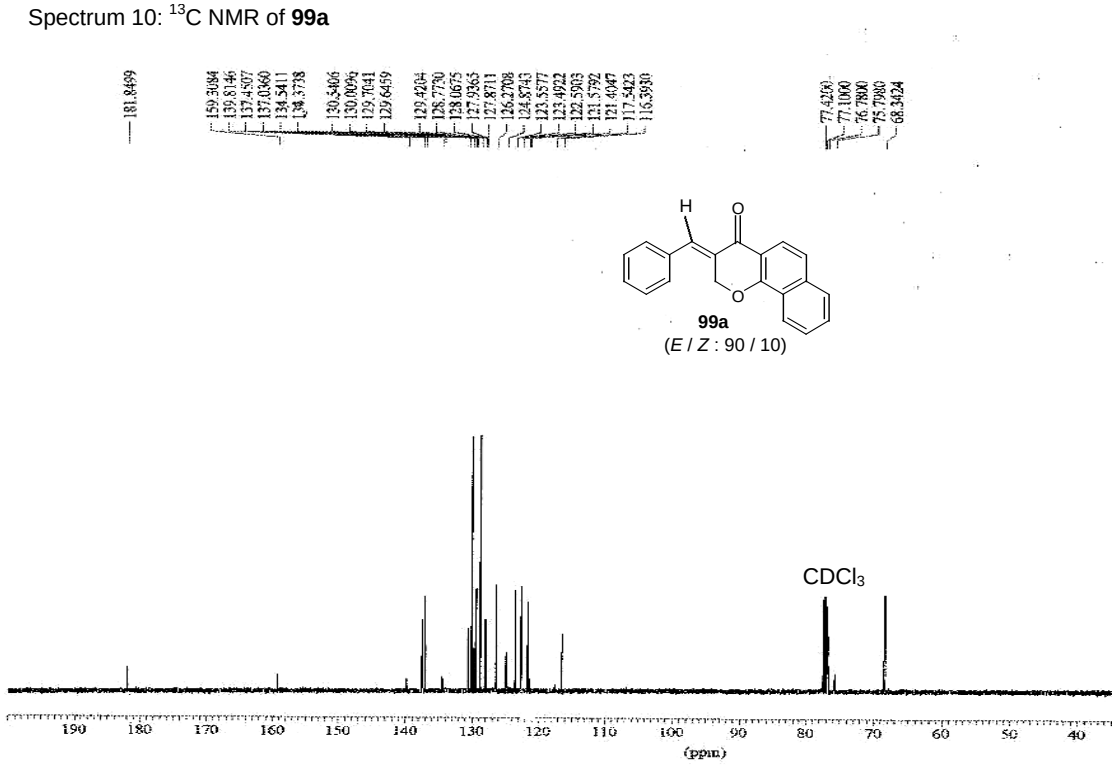




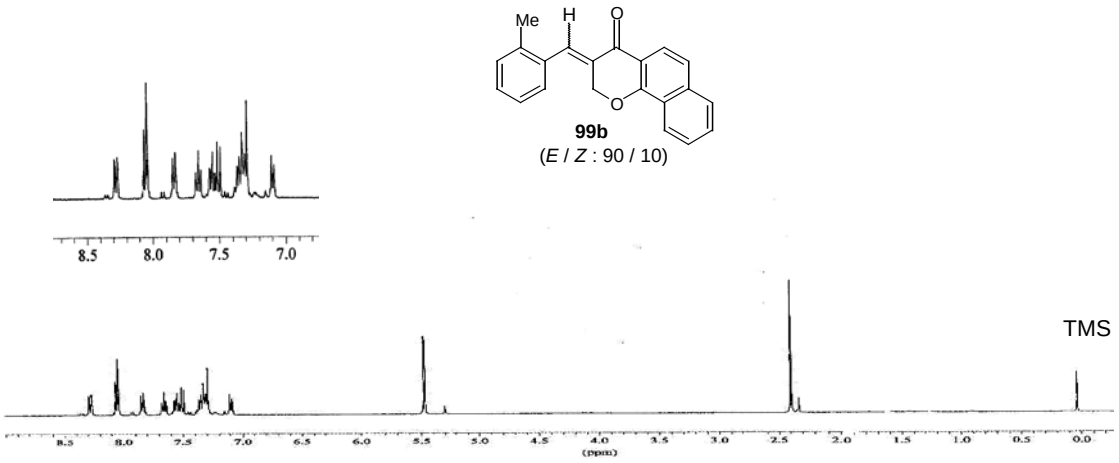
99a
(*E* / *Z* : 90 / 10)



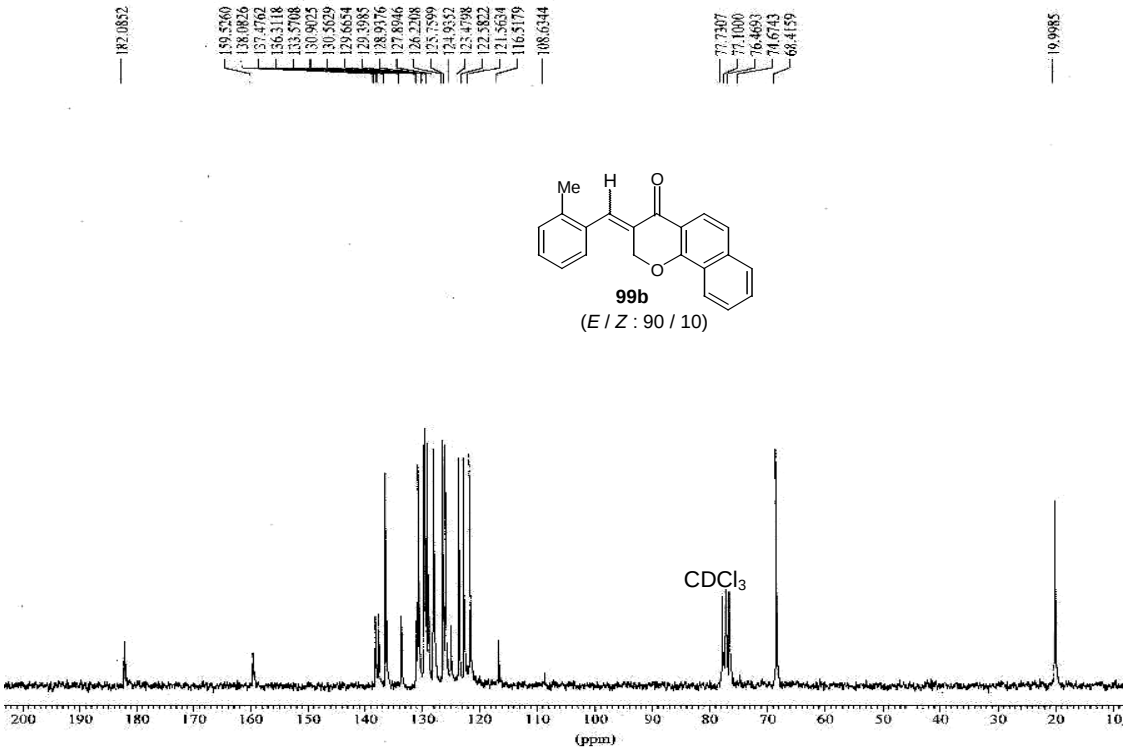
Spectrum 10: ^{13}C NMR of **99a**



Spectrum 11: ^{1}H NMR of **99b**

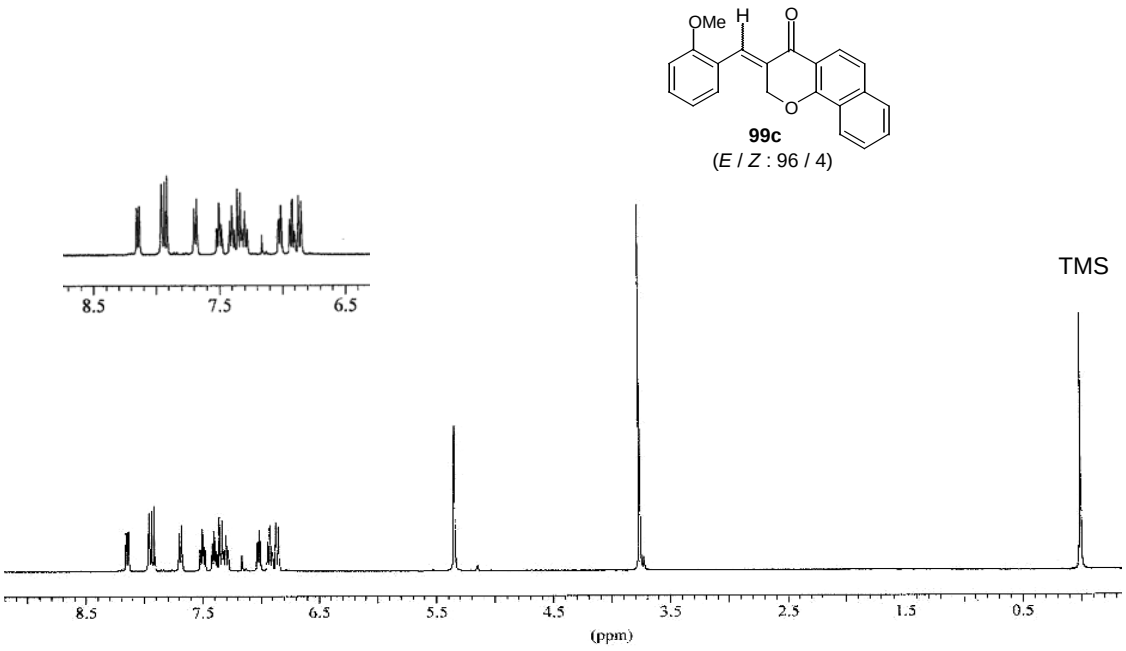


Spectrum 12: ^{13}C NMR of **99b**

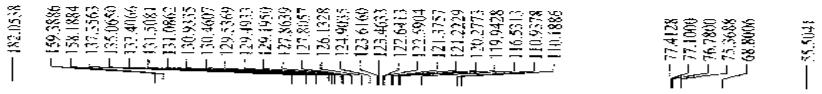


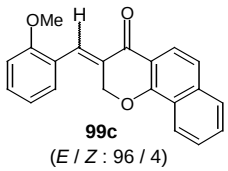
99b
(*E* / *Z* : 90 / 10)

Spectrum 13: ^{1}H NMR of **99c**

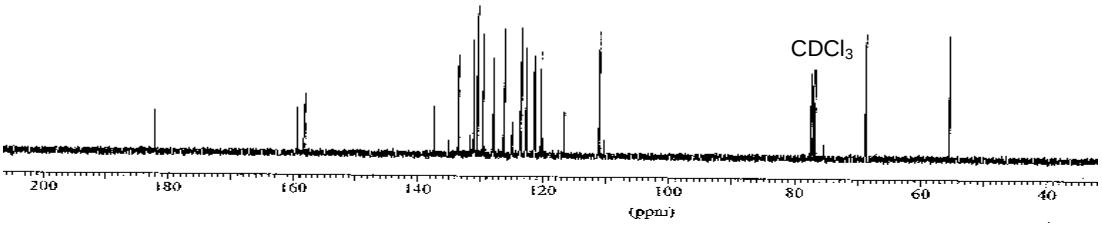


Spectrum 14: ^{13}C NMR of **99c**

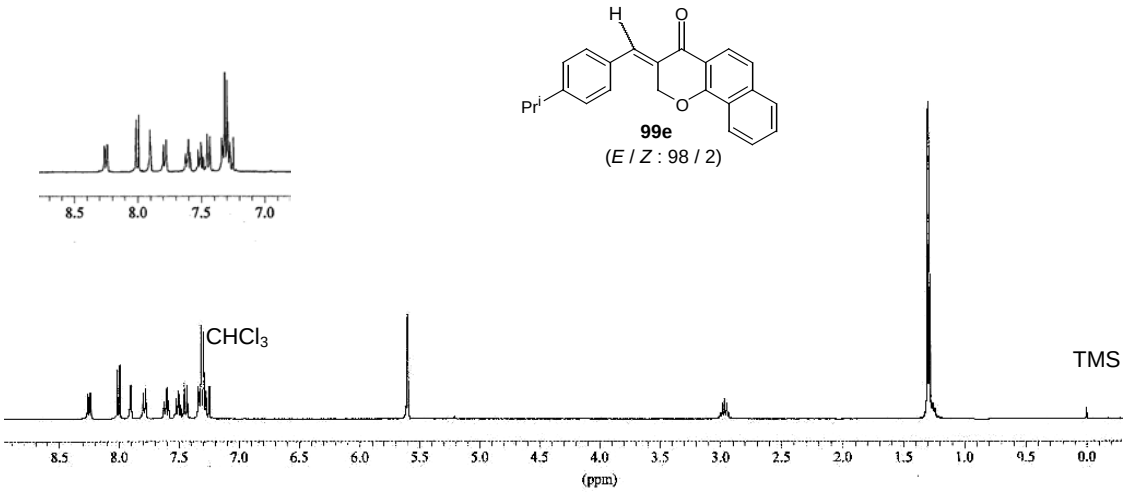




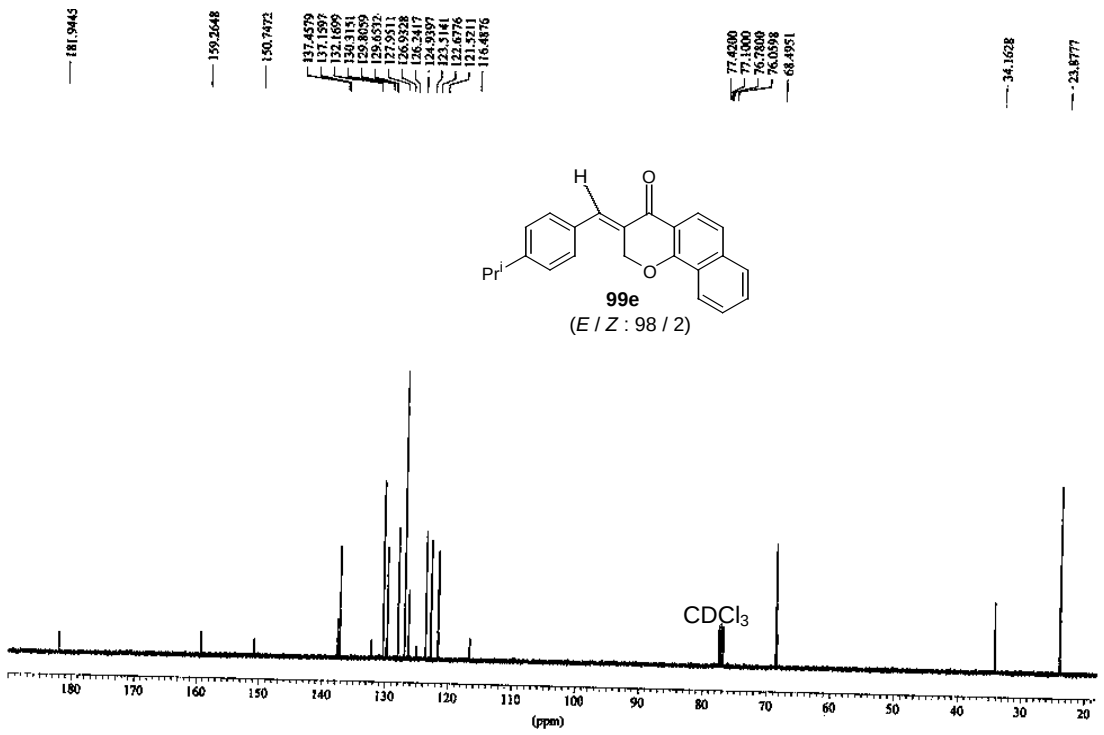
99c
(*E* / *Z* : 96 / 4)



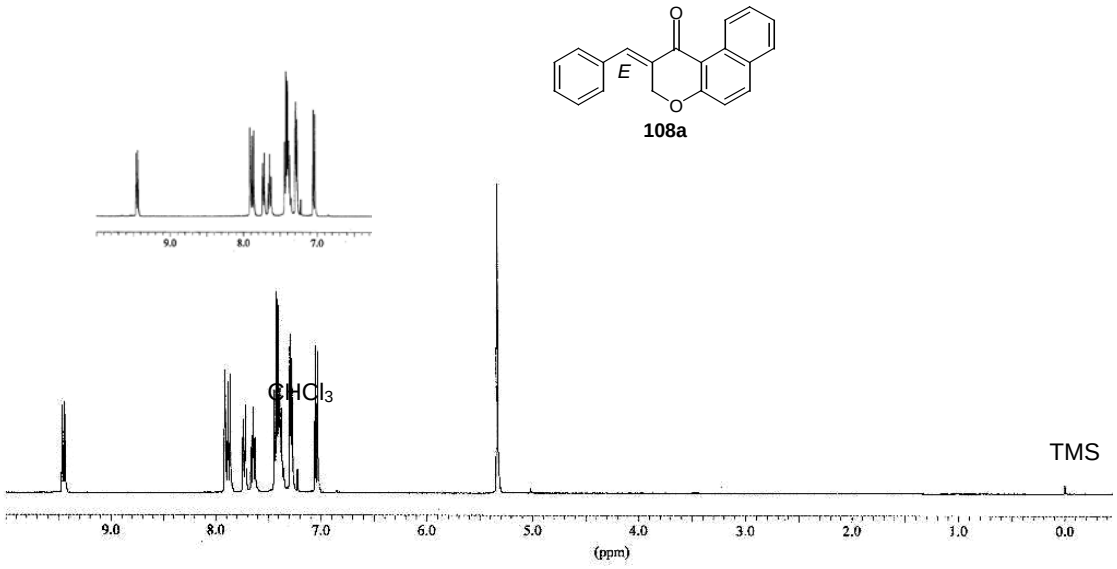
Spectrum 15: ^{1}H NMR of **99e**



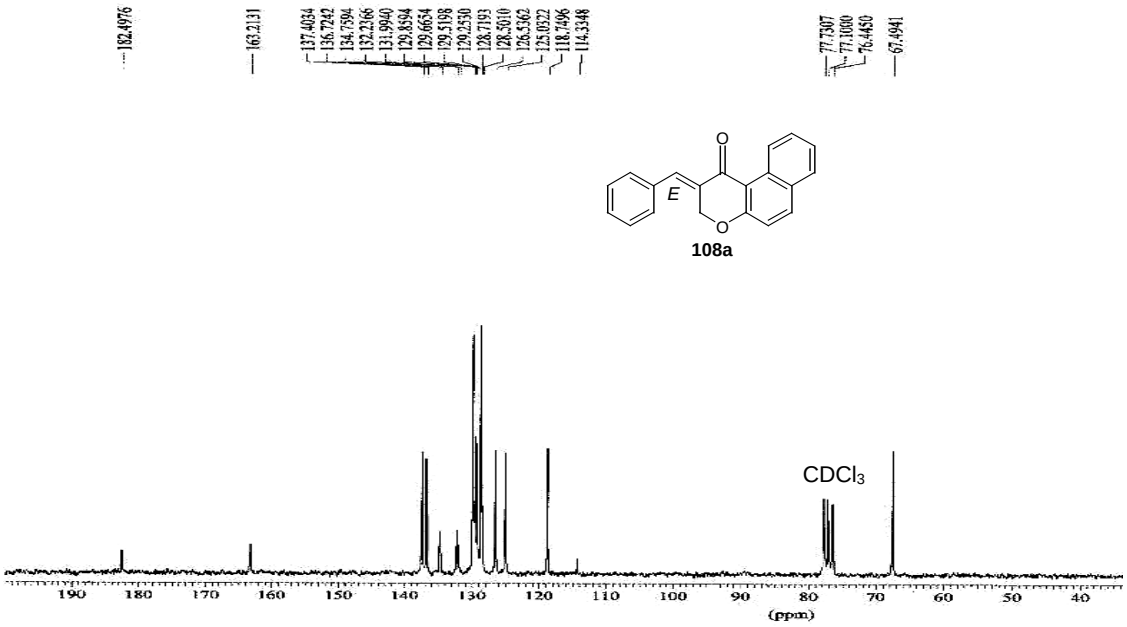
Spectrum 16: ^{13}C NMR of **99e**



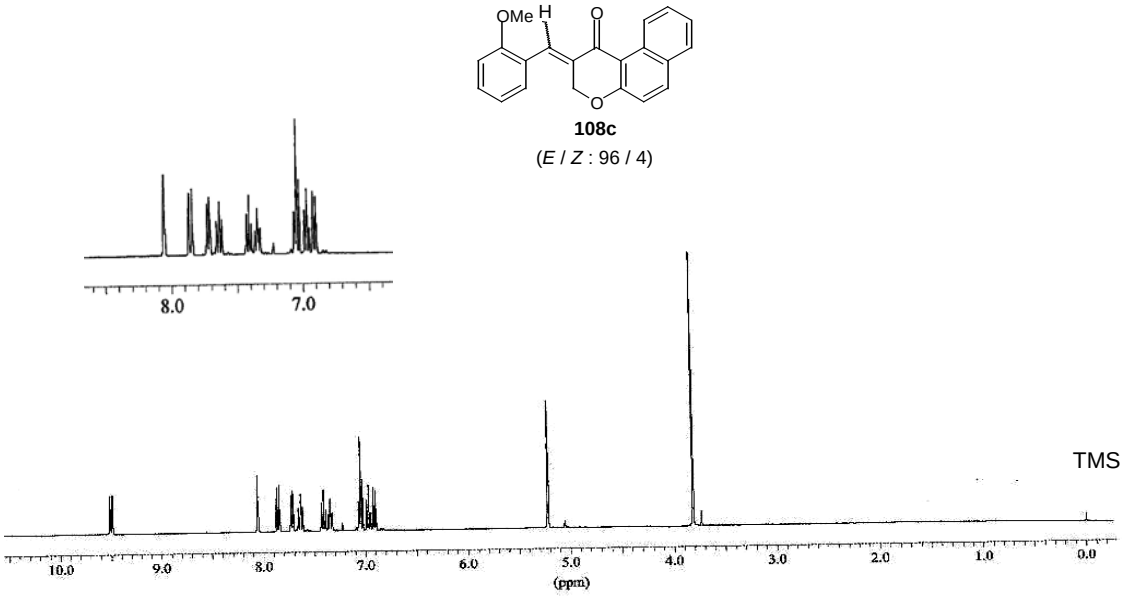
Spectrum 17: ^{1}H NMR of **108a**



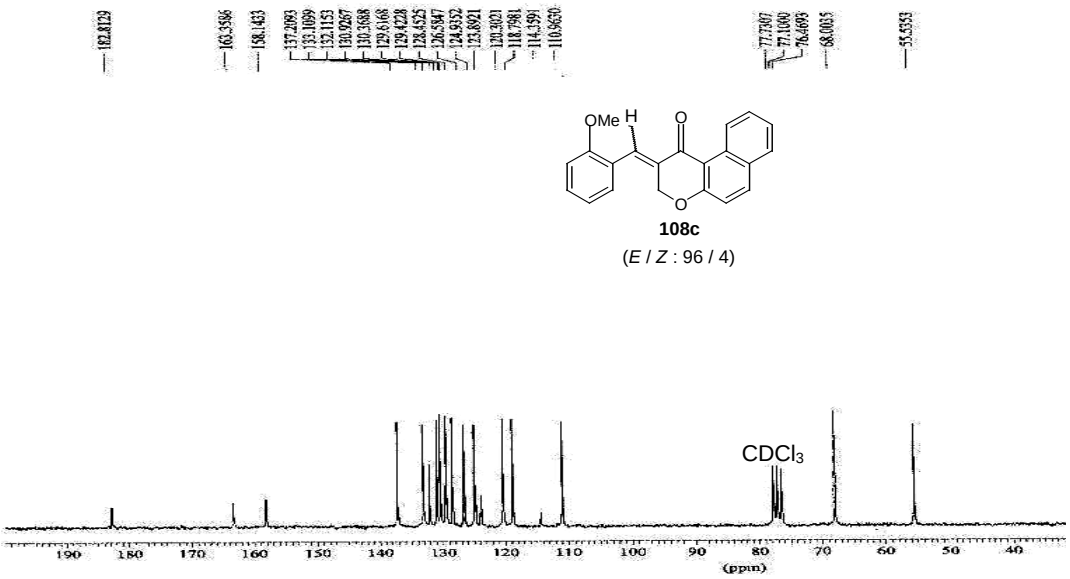
Spectrum 18: ^{13}C NMR of **108a**



Spectrum 19: ^{1}H NMR of **108c**



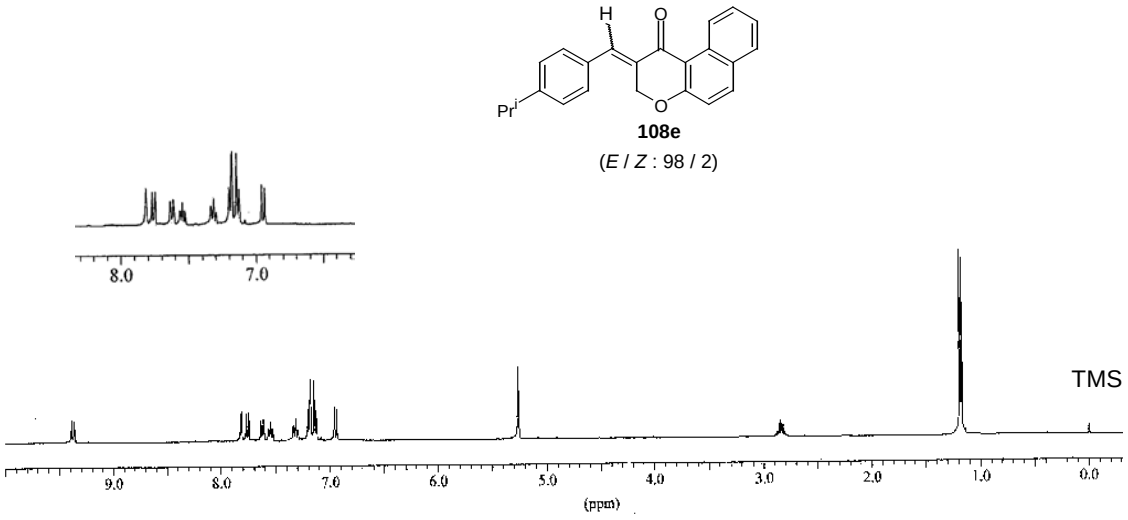
Spectrum 20: ^{13}C NMR of **108c**



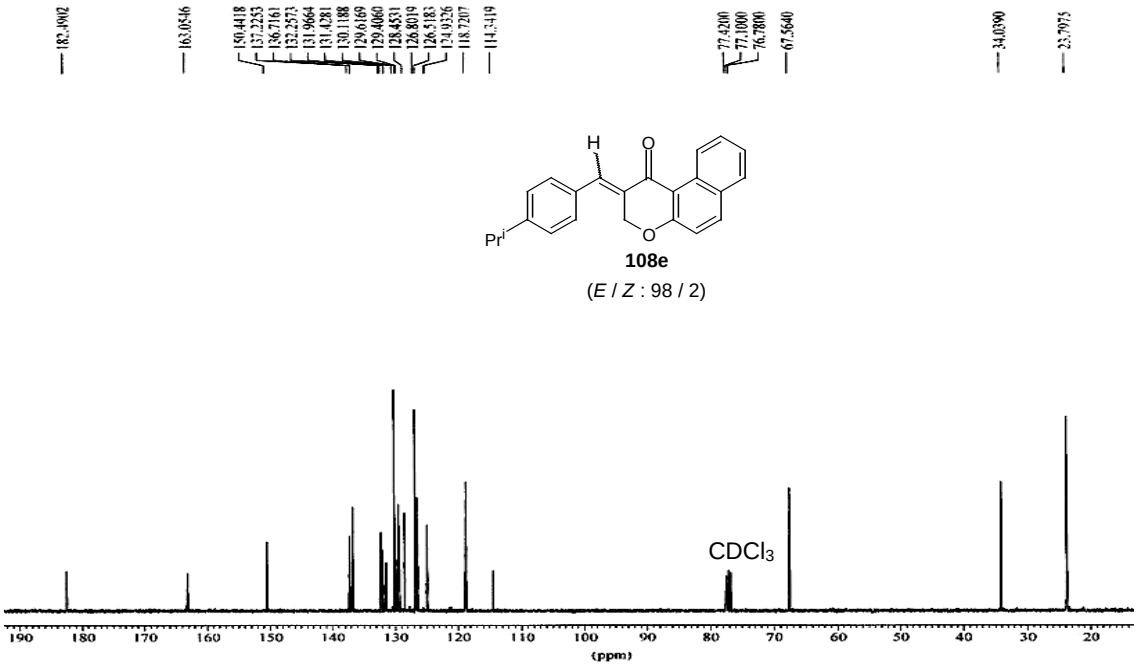
108c

(*E* / *Z* : 96 / 4)

Spectrum 21: ^{1}H NMR of **108e**



Spectrum 22: ^{13}C NMR of **108e**



108e

(*E* / *Z* : 98 / 2)

APPENDIX

(X-RAY CRSTALLOGRAPHIC DATA)

Table 1: Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for molecule **80a**. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

atom	X	Y	Z	U(eq)
O(1)	6852(2)	10589(2)	1745(1)	67(1)
O(2)	6380(2)	9031(2)	3180(1)	66(1)
O(3)	2688(2)	10978(2)	4027(1)	61(1)
O(4)	1413(2)	8223(3)	734(1)	70(1)
C(1)	2467(3)	10297(3)	3208(2)	51(1)
C(2)	3641(3)	9371(3)	1973(1)	48(1)
C(3)	7702(3)	11637(3)	4617(1)	49(1)
C(4)	3924(3)	10001(3)	2831(1)	46(1)
C(5)	5551(3)	10035(3)	3376(1)	49(1)
C(6)	6019(3)	11272(3)	4185(1)	47(1)
C(7)	5230(3)	9543(3)	1486(1)	51(1)
C(8)	665(3)	9807(4)	2769(2)	62(1)

C(9)	6126(3)	8270(3)	248(1)	56(1)
C(10)	4700(3)	8395(3)	657(1)	55(1)
C(11)	352(3)	9067(4)	1962(2)	65(1)
C(12)	1827(3)	8850(3)	1553(2)	54(1)
C(13)	8748(3)	12916(3)	5366(1)	51(1)
C(14)	2608(3)	7389(4)	370(2)	60(1)
C(15)	6139(3)	7181(3)	-532(1)	53(1)
C(16)	7882(4)	7532(3)	-818(1)	58(1)
C(17)	10427(4)	12808(3)	5689(2)	61(1)
C(18)	4604(3)	12113(3)	4386(2)	58(1)
C(19)	4572(4)	5731(4)	-989(2)	68(1)
C(20)	4767(4)	4738(4)	-1698(2)	69(1)
C(21)	8267(4)	14304(3)	5756(2)	64(1)
C(22)	11551(4)	13994(4)	6377(2)	74(1)
C(23)	11047(5)	15347(4)	6760(2)	80(1)
C(24)	6495(5)	5124(4)	-1968(2)	75(1)
C(25)	9410(5)	15497(4)	6443(2)	76(1)
C(26)	8068(4)	6530(4)	-1526(2)	74(1)

Table II: Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for molecule **80b**. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

atom	X	Y	Z	U(eq)
O(1)	8536(4)	-466(2)	2272(1)	48(1)
O(2)	7934(4)	2812(2)	2535(1)	57(1)
O(3)	2788(4)	830(2)	3589(1)	57(1)
O(4)	7332(4)	2765(3)	3630(1)	66(1)
C(1)	10253(6)	148(3)	2280(2)	47(1)
C(2)	9917(5)	1381(3)	2215(2)	38(1)
C(3)	8355(6)	1835(3)	2541(2)	41(1)
C(4)	7164(5)	993(3)	2817(2)	37(1)
C(5)	5746(6)	1305(3)	3181(2)	40(1)
C(6)	5854(6)	2323(4)	3526(2)	45(1)
C(7)	4047(6)	2651(4)	3777(2)	45(1)
C(8)	2386(6)	2018(4)	3583(2)	52(1)
C(9)	4325(6)	559(4)	3292(2)	44(1)

C(10)	4400(7)	-548(4)	3094(2)	51(1)
C(11)	5832(6)	-863(3)	2770(2)	49(1)
C(12)	7227(6)	-101(3)	2628(2)	40(1)
C(13)	10794(6)	2079(3)	1890(2)	42(1)
C(14)	12400(6)	1887(3)	1532(2)	44(1)
C(15)	12466(7)	2424(4)	1037(2)	55(1)
C(16)	13995(8)	2256(5)	714(2)	70(2)
C(17)	15447(8)	1578(5)	869(2)	72(2)
C(18)	15414(7)	1059(4)	1360(2)	60(1)
C(19)	13886(6)	1215(4)	1683(2)	49(1)
C(20)	10879(9)	3157(5)	856(2)	89(2)
C(21)	4051(6)	3424(4)	4162(2)	46(1)
C(22)	2435(6)	3905(3)	4449(2)	41(1)
C(23)	2551(6)	4092(3)	4996(2)	48(1)
C(24)	1047(7)	4592(4)	5249(2)	59(1)
C(25)	-528(7)	4894(4)	4970(2)	64(1)
C(26)	-645(7)	4710(4)	4435(2)	59(1)
C(27)	828(6)	4206(4)	4175(2)	51(1)
C(28)	4253(8)	3761(5)	5312(2)	75(2)

Table III: Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for molecule **80f**. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

atom	X	Y	Z	U(eq)
Cl(1)	4755(2)	4076(1)	10292(1)	98(1)
Cl(2)	10760(2)	3019(1)	5801(1)	124(1)
O(1)	8537(4)	-700(2)	7295(1)	66(1)
O(2)	7890(4)	2569(2)	7504(1)	75(1)
O(3)	2828(4)	644(2)	8608(1)	69(1)
O(4)	7232(4)	2617(3)	8620(1)	86(1)
C(1)	10226(6)	-84(3)	7303(2)	62(1)
C(2)	9882(5)	1130(3)	7216(2)	49(1)
C(3)	8306(5)	1591(3)	7530(2)	51(1)
C(4)	7166(5)	787(3)	7826(2)	49(1)
C(5)	5716(5)	1114(3)	8191(2)	50(1)
C(6)	5791(6)	2154(4)	8525(2)	58(1)
C(7)	4010(6)	2487(4)	8770(2)	58(1)
C(8)	2382(6)	1818(4)	8593(2)	66(1)
C(9)	4327(6)	372(4)	8305(2)	55(1)

C(10)	4416(7)	-734(4)	8121(2)	63(1)
C(11)	5847(6)	-1062(3)	7803(2)	63(1)
C(12)	7220(6)	-314(3)	7649(2)	55(1)
C(13)	10783(6)	1819(3)	6873(2)	58(1)
C(14)	12370(7)	1636(3)	6527(2)	58(1)
C(15)	12553(7)	2184(4)	6035(2)	69(1)
C(16)	14078(9)	2078(5)	5714(2)	92(2)
C(17)	15501(8)	1418(4)	5887(2)	90(2)
C(18)	15359(7)	871(4)	6376(2)	71(1)
C(19)	13861(6)	975(4)	6685(2)	61(1)
C(20)	3998(6)	3297(3)	9144(2)	59(1)
C(21)	2436(6)	3793(3)	9434(2)	54(1)
C(22)	2649(6)	4187(4)	9963(2)	60(1)
C(23)	1227(8)	4691(4)	10250(2)	80(2)
C(24)	-460(7)	4833(4)	9994(2)	83(2)
C(25)	-704(7)	4467(4)	9459(2)	76(1)
C(26)	714(6)	3961(4)	9191(2)	65(1)

Table IV: Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for molecule **99b**. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

atom	X	Y	Z	U(eq)
O(1)	8562(1)	2295(2)	6599(1)	54(1)
O(2)	9152(1)	7212(2)	5350(1)	61(1)
C(1)	8881(2)	2130(3)	5782(2)	51(1)
C(2)	8675(2)	3917(3)	5294(2)	43(1)
C(3)	9004(2)	5717(3)	5717(2)	45(1)
C(4)	9080(2)	5599(3)	6614(2)	44(1)
C(5)	9317(2)	7248(4)	7106(2)	58(1)
C(6)	9260(2)	7215(4)	7924(2)	63(1)
C(7)	8952(2)	5540(4)	8328(2)	54(1)
C(8)	8878(2)	5462(5)	9185(2)	72(1)
C(9)	8583(2)	3834(5)	9549(2)	79(1)
C(10)	8348(2)	2201(5)	9088(2)	69(1)
C(11)	8399(2)	2218(4)	8258(2)	55(1)
C(12)	8706(2)	3879(3)	7862(2)	45(1)
C(13)	8795(2)	3952(3)	6999(1)	42(1)

C(14)	8201(2)	3980(3)	4553(2)	46(1)
C(15)	7831(2)	2354(3)	4053(1)	45(1)
C(16)	6870(2)	2362(4)	3674(2)	50(1)
C(17)	6567(2)	789(4)	3200(2)	59(1)
C(18)	7179(2)	-756(4)	3090(2)	62(1)
C(19)	8118(2)	-755(4)	3462(2)	61(1)
C(20)	8438(2)	784(4)	3940(2)	53(1)
C(21)	6174(2)	4022(4)	3765(2)	72(1)

Table V: Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for molecule **108c**. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

atom	x	y	z	U(eq)
O(1)	3252(2)	-527(1)	273(1)	70(1)
O(2)	-683(1)	327(1)	1499(1)	70(1)
O(3)	1725(1)	4077(1)	1708(1)	62(1)
C(1)	595(2)	-15(1)	1196(1)	51(1)
C(2)	541(2)	-1115(1)	781(1)	49(1)
C(3)	-906(2)	-1973(1)	771(1)	50(1)

C(4)	-2264(2)	-1946(2)	1237(1)	63(1)
C(5)	-3633(3)	-2765(2)	1186(1)	78(1)
C(6)	-3743(3)	-3653(2)	673(1)	81(1)
C(7)	-2435(3)	-3729(2)	228(1)	71(1)
C(8)	-986(2)	-2911(1)	268(1)	55(1)
C(9)	406(3)	-3013(2)	-183(1)	64(1)
C(10)	1795(2)	-2239(2)	-154(1)	63(1)
C(11)	1854(2)	-1282(1)	326(1)	54(1)
C(12)	3846(2)	174(2)	891(1)	65(1)
C(13)	2300(2)	699(1)	1222(1)	50(1)
C(14)	2363(2)	1738(1)	1563(1)	51(1)
C(15)	3891(2)	2555(1)	1728(1)	49(1)
C(16)	3520(2)	3756(1)	1836(1)	50(1)
C(17)	4922(2)	4533(2)	2050(1)	60(1)
C(18)	6708(2)	4141(2)	2150(1)	67(1)
C(19)	7108(2)	2985(2)	2039(1)	66(1)
C(20)	5709(2)	2205(2)	1831(1)	58(1)
C(21)	1285(3)	5301(2)	1738(1)	67(1)

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Synopsis

Organic chemistry, particularly synthetic organic chemistry, has become one of the most powerful and important branches of science. Construction of carbon-carbon bond indeed occupies the most important place in organic chemistry due to its fundamental role in building and assembling various structural carbon frameworks to provide all kinds of natural and unnatural molecules including the most complex molecules. The evolving trends in organic chemistry particularly in synthetic organic chemistry clearly emphasize the need for discovering novel and efficient carbon-carbon bond forming reactions involving the concepts of selectivity, that is, constructing a carbon-carbon bond at the required place in a substrate which has more than one competing sites for the formation of carbon-carbon bonds. For easy understanding let us consider methyl vinyl ketone (MVK) as a substrate for constructing carbon-carbon bonds. There are five sites where one can construct carbon-carbon bonds and there are methods available in the literature for the construction of C-C bonds at the required places.

Another important requirement in the present day context of organic chemistry is the concept of atom-economy. This concept has gained unique importance and in fact, has become one of the essential requirements for development of any novel C-C bond forming reactions. The Baylis Hillman reaction is one such carbon-carbon bond forming reaction developed in recent years well equipped with the concept of selectivity and atom-economy. Thus this reaction provides the procedure to construct carbon-carbon bonds at α-position of activated alkenes (like methyl vinyl ketone) in atom-economical

fashion and indeed this reaction has become one of the most powerful synthetic tools for construction of carbon-carbon bonds. This thesis deals with the studies towards development of novel methodologies for synthesis of oxygen heterocycles using the Baylis-Hillman adducts and consists of three chapters, that is, 1. Introduction 2. Objectives, Results and Discussion 3. Experimental.

In the first chapter, a brief literature survey on the developments and recent applications of the Baylis-Hillman reaction is described.

The second chapter deals with objectives, results and discussions and describes our studies towards the application of the Baylis-Hillman bromides in synthesis of heterocyclic compounds containing oxygen in the ring with the following main objectives.

Objectives:

1) To develop a novel and facile methodology for the synthesis of tetrahydrodipyrandione derivatives [7,12-bisarylidene-5,14-dioxatricyclo[8.4.0.$0^{4,9}$]tetradeca-1,3,9-triene-8,11-dione] using the Baylis-Hillman bromides as starting materials.

2) To develop a simple methodology for the synthesis of 7:8-benzochroman-4-one frameworks using the Baylis-Hillman bromides as synthons.

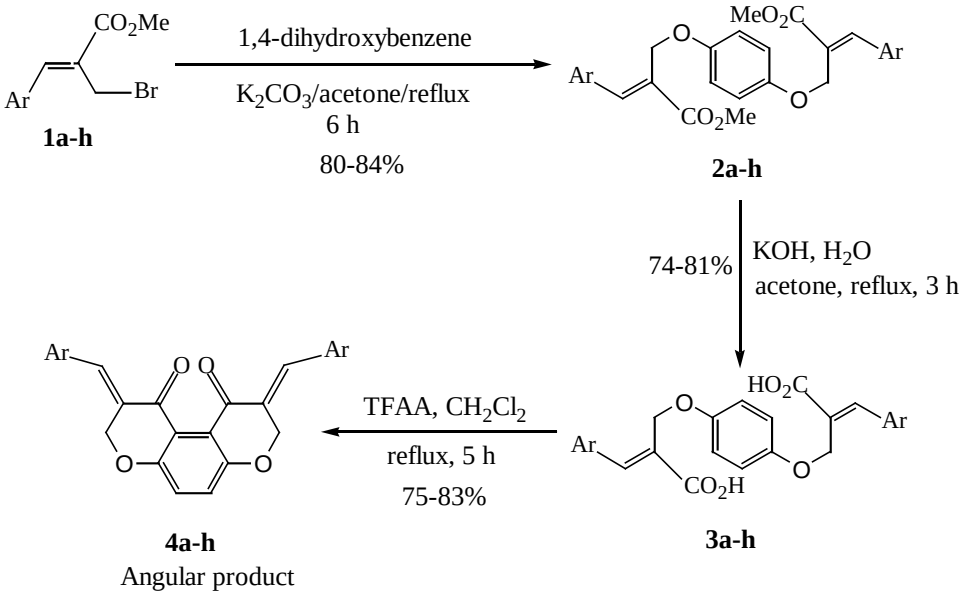
3) To develop facile methodology for the synthesis of 5:6-benzochroman-4-one derivatives using the Baylis-Hillman bromides as starting materials.

A facile synthesis of tetrahydrobenzodipyrandiones from the Baylis-Hillman bromides:

Tetrahydrobenzodipyrandione framework has attracted the attention of organic chemists because some of these compounds possess interesting psychotropic, antithrombic and

antihistaminic properties. The medicinal importance of these compounds containing tetrahydrobenzodipyrandione framework has attracted our attention and we have therefore developed a simple methodology for synthesis of these frameworks starting from the Baylis-Hillman bromides following the reaction sequence as shown in Scheme 1.

Scheme 1



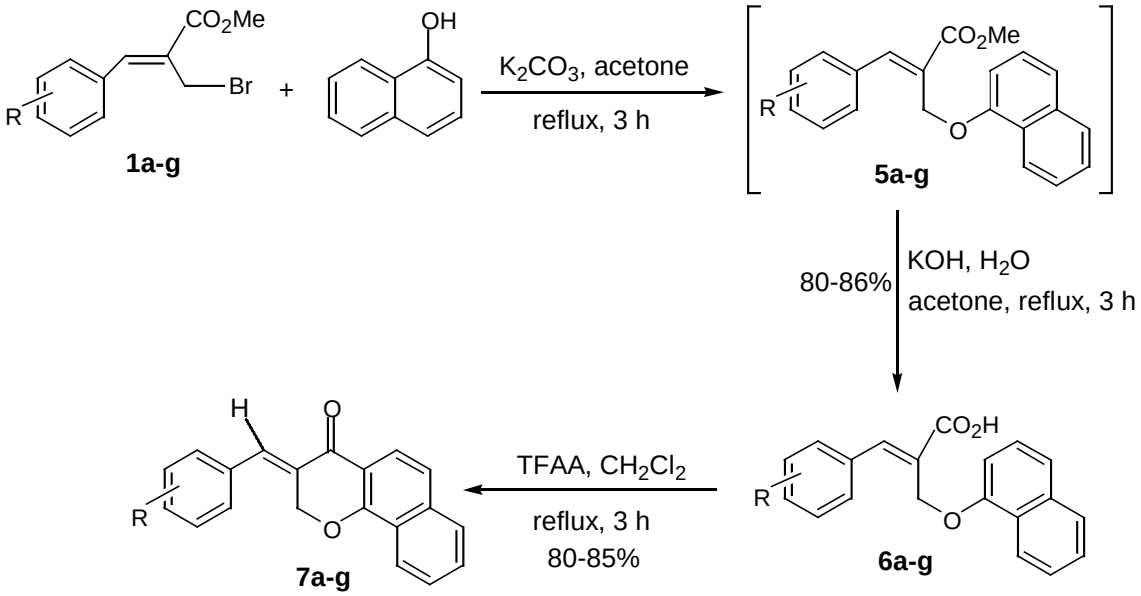
Ar = Ph, 2-MeC_6H_4, 2-$OMeC_6H_4$, 4-ClC_6H_4, 4-i-PrC_6H_4, 2-ClC_6H_4, 4-BrC_6H_4, 4-MeC_6H_4

Development of facile synthesis of 7:8-benzochroman-4-one frameworks from Baylis-Hillman bromides:

The 7:8- benzochroman-4-one derivatives occupy an interesting place in oxygen heterocyclic chemistry because of presence of this framework in a number of biologically active natural products. Fascinated by the medicinal importance of these derivatives, we have developed simple methodologies for obtaining 7:8-benzochroman-4-one derivatives

using Baylis-Hillman bromides and 1-naphthol as versatile starting materials following the reaction sequence as described in Schemer 2.

Scheme 2



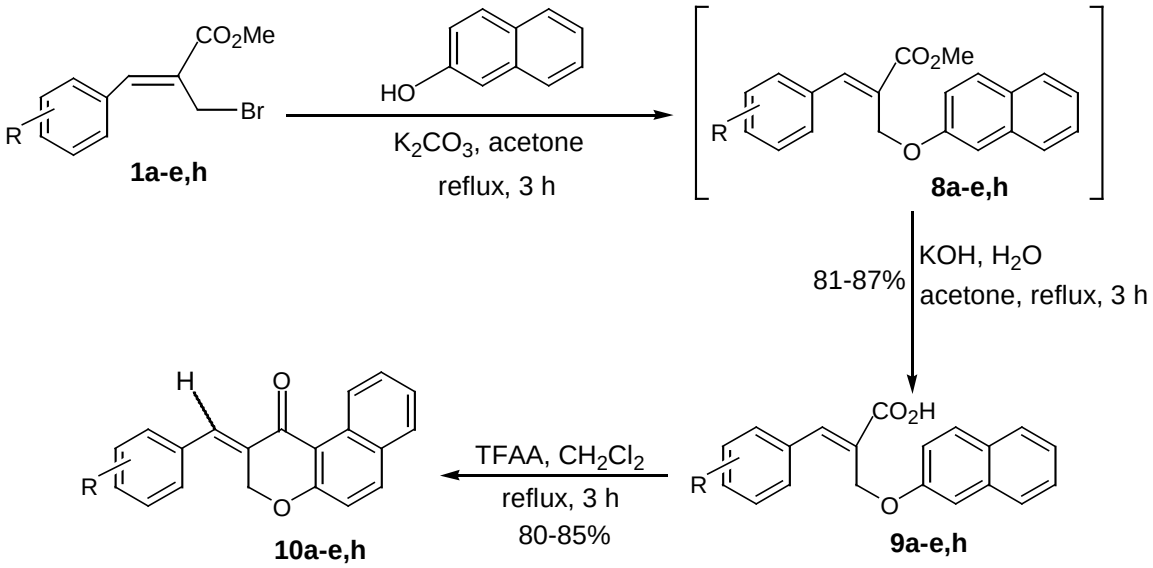
R = H, 2-Me, 2-OMe, 4-Cl, 4-Pr^{i}, 2-Cl, 4-Br

E:Z = 70-98:2-30

Novel and facile synthesis of 5:6-benzochroman-4-one frameworks using Baylis-Hillman bromides:

The 5:6-benzochroman-4-one framework is another important skeleton has attracted the attention of organic and medicinal chemists owing to the antimicrobial activity against trichomonads, gram-positive and gram-negative bacteria and fungi. We have therefore developed a facile methodology for obtaining 5:6-benzochroman-4-one frameworks using the Baylis-Hillman bromides and 2-naphthol as the key synthons.

Scheme 3



R = H, 2-Me, 2-MeO, 4-Cl, 4-Pr^{i}, 4-Me

E:Z = 90-100:0-10

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