Review Article in Organic Chemistry

Recent Advances in Reformatsky Reaction and Grignard Reaction on Coumarins and other Uncommon Electrophilic Centre.

L.N. Dutta**, N.C. Sinha#, Mrs. M. Bhattacharyya, P.K. De, R. K. Shit*

Abstract:

The ever increasing large scale isolation of naturally occurring coumarin having diversified skeleton pattern with manifold biological and industrial application throws a challenge for their synthesis. Recent advancement for the synthesis of various derivatives of coumarin through the application of organozinc and organomagnesium reagents well reputed for their high stereo and chemoselectivity are presented in this review.

Keywords: biological, coumarin, diversified, naturally, stereo selectivity.

L.N. Dutta**, Retired Professor, J.U to whom the review article is dedicated,

N.C. Sinha#, Retired Associate Professor, Department of Chemistry, S.C College, B.U and Guest Lecturer, J.U to whom all correspondence to be made

Email: sinhanitai1234@gmail.com

R. K. Shit*, Associate Professor, Department of Chemistry, Vidyasagar College

Email: rshit123@gmail.com

Introduction:

Coumarins a well defined naturally occurring compounds [1,2] widely distributed in plant families and incorporates an α, ß unsaturated lactone moiety fused with an aromatic nucleus. The studies on Coumarins have received a tremendous impetus due to its manifold biological as well as pharmacological properties such as anticoagulant [3], antibacterial [4,5] anti hypertension [6,7] hypolepidemic [8], and allied activities [9,10,11] and also wide industrial applications as brightsner [12] luminescence properties [13] photochemical activities [14,15].

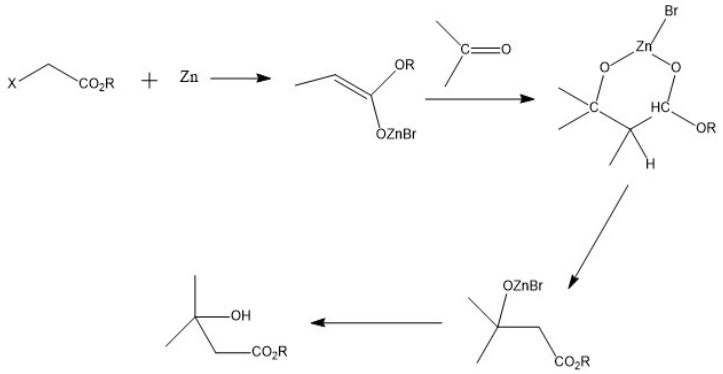
The coumarins with substitution in lactone moiety at position 3 and 4 exhibit antimalerial activities. Various 2,2 disubstituted chromen derivatives and dihydro coumarin derivatives also have interesting biological as well as pharmacological activities [9,10] (compounds 1-15 in table 1) [16-25] The coumarins with prenyl and isoprenyl five carbon chain substituted at aromatic nucleus constitute a well defined family having vast members of photochemicals and enlisted with other diversified natural products [26-30] e.g. alkaloids & terpenoids.

A large varieties of naturally occurring coumarins having furan ring fused with the aromatic nucleus such as Psoralen [31], Holofordin [31], Isohalofordin [32] Sesibericine Toddaculin [34], Pennarin [34], Neushoutol [35] have been encountered in nature. Recently various allyl, prenyl type of side chain attached to the basic Coumarins moiety have been successfully isolated in nature [36] e.g. Osthenal, Murrayon & Aurepetol.

Thus the ever increasing isolation of coumarins having diversified skeleton pattern with various biological properties throws a challenge for this synthesis. This prompted us to carry systematic literature survey by exploiting well known reactivity of suitable anionic reagent [37] towards the electrophilic centre of coumarins. It is well known that various organozinc and organomagnesium reagents [38,39] find almost routine use due to their high degree of chemoselectivity [40, 41] in attacking various types of carbonyl system. It is logical that the reaction coumarin bearing carbonyl functionality with various organozinc and organomagnesium reagents should result in the formation of some new coumarins. Thus this will not only develop an effective and new synthetic methodology in elaborating side chain in coumarin but also corroborate high degree of chemoselectivity of these reagents and rated high for day to day use in synthetic organic chemistry and medicinal chemistry. The present article deals with the systematic and up to date literature survey of Grignard and Reformatsky reaction on coumarin derivatives and other uncommon electrophilic centre have been judiciously documented in the Review article in two parts.

Reformatsky reaction of coumarins and other uncommon electrophilic centre

Reformatsky reaction [42, 43] may be described as a reaction of carbonyl compounds with bromozine enolate reagent afforded a β– hydroxyester.



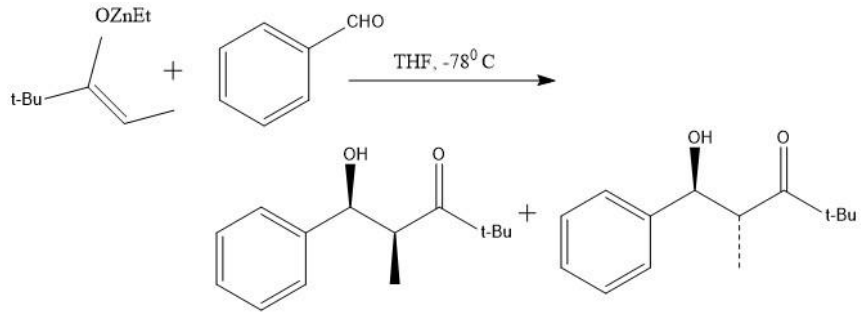
Scheme – 1

Reformatsky reaction is generally carried out in aprotic [43,44, 45] solvent such as aromatic hydrocarbon, ether, tetrahydrofuran, 1, 4 dioxan, DMSO, HMPT etc.

Since the Reformatsky reaction has been successfully investigated by many workers [46, 47] a wealth of knowledge can be found regarding the structure and reactivity of the bromozinc enolate used nature of different aprotic solvent [48] employed and types of Zn metal added in some excellent monograph & review articles [43, 46, 49].

Stereochemistry in Reformatsky Reaction

The stereochemical implication of Reformatsky reactions comprehensively reviewed. The effect of reaction conditions on the ratio erythreo and threo of β – hydroxyesters has been studied by large number of workers [50 - 57] and most of the results can be rationalized by metal-chelate structure incorporating minimum possible interaction of the groups.

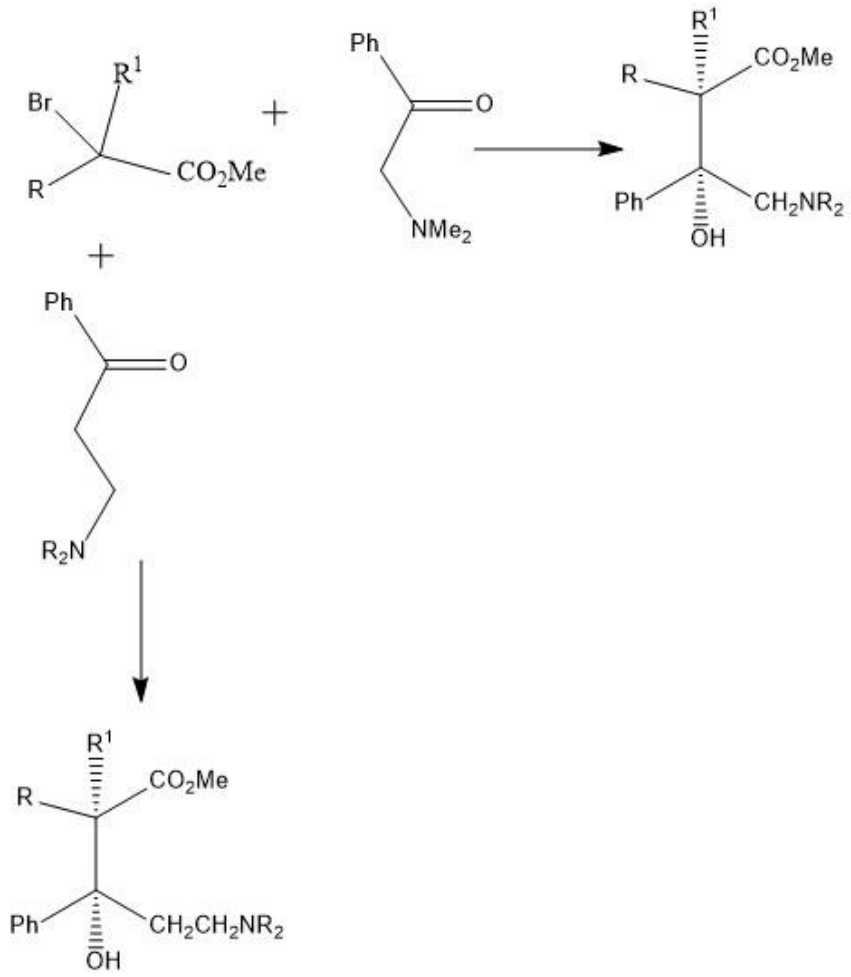


Scheme-2

Considering the mechanistic picture of the reaction it is difficult to predict whether the reaction is kinetically controlled or thermodynamically controlled. A large number of workers reported that a direct evidence for an initial kinetic controll and slower equilibration of threo and erythreo is being observed and they reported erythreo happens to be the predominant products [50 - 60] The stereoelectronic factors in Reformatsky reacttion have been observed. Aromatic α or β – aminoketones having prochiral carbonyl centre reacts with various bromozinc enolates and the products isolated on α – aminoketone is similar to β – aminoketone and the products characterized in which the erythreo is the predominant products [61,62] .The stereoselectivity observed with α – aminoketons is inferior to that of β –aminoketone and the stereoselectivity is maximum when the reacting α – haloester is derived from isovalerate under kinetically controlled condition [61 , 62]. The formation of products can be explained via bicyclic transition state.

Scheme-3

The asymmetric synthesis has also been achieved in Reformatsky reaction when a prochiral carbonyl compounds is treated with Retormatsky reagent in presence chiral electron donar (+) spertine)



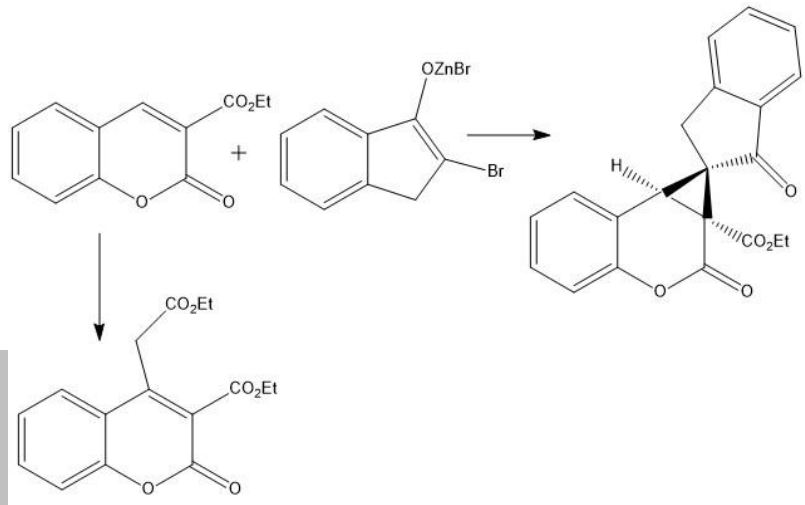
Scheme-3

Reformatsky Reaction on coumarin system and other electrophilic centre

The Reformatsky reaction on carbonyl or nitrile function has been widely studied and need no comments. Reformatsky reaction on coumarin with additional carbonyl functionality capable of participating in consecutive reactions are going interest due the high degree of chemoselectivity as well as regioselectivity. The major extension of Reformatsky reaction has been achieved by the use of electrophile other than aldehyde and ketone such as coumarin system, amino ketone, amide, lactones, nitrones, azirins, thiophenes, etc.

The Reformatsky reaction is of enormous research interest though it has been found limiid applicalions in coumarin system. A few reports of Reformatsky

reaction of Coumarin-3-carboxylate [63, 64] by and large lead to 3,4 addition products in Michael fashion without touching lactone moiety afforded dihydrocoumarin derivative. Very recently [65] zinc enolate obtained from 2,2 dibromo-1- indanone reacted with coumarin-3- carboxylate also lead to3,4 addition products afforded Spiro counpound in the form of single geometrical isomer.



Scheme-4

Recently a new general approach [64, 67] has been introduced for introducing side chain in coumarins utilizing various bromozinc enolates as chemo, regio & stereoselective reagent. Coumarins, bearing alkyl, aryl or formyl group on reaction with bromozinc enolates of α – bromoacetate, propionate, butyrate afforded to the corresponding diastereoisomeric alcohol and or the olefinic products in high degree of chemoselectivity.

The β – hydroxyester bearing-tertiary hydroxy group are liable to form product mixture on dehydration and the regioselectivity is distinctly in favour of β , γ unsaturated ester in case of α bromoacetate involving Petersion olefination [68]. Some interesting results and unusual chemoselectivity has been observed during Reformatsky reaction on acylcoumarins using bulkier bromozinc enolates.

The extension of the Reformatsky reaction has been achieved by the use of uncommon electrophiles using indole [71], amide[71], lactone[72] , [73], azirin [69 , 70] nitrones [75], alkyne & thiophen[75]. Despite the complication and complexities of such electrophile the addition of Reformatsky reaction of azirin and indoles are

very [69 , 70 , 71] interesting and a number of products from azirin such as aziridin, azitidone and diazipenone have been isolated using α – bromoacetate, (Table-3).

Various functionally substituted allyl propagryl and alkyl pyranols and furanols were prepared from pyrones and a furanone [72 ,73]utilizing bromozinc enolates (Table - 3). Nitrile containing additional electrophilic site such as halogen and ester group reacts with bromozinc enolates afforded lactam[74]. Despite the complexities of nitrones as electrophilic centre various is oxazolididone[75], are successfully prepared by using Reformatsky reagents. Thus nitrones RCH = N (O)R^1 [R = Me, R^1 = p-$C1C_6H_4$,p=$OMeC_6H_4$, or R=Me,Et,Me_2CH, $PhCH_2$,R^1 = Ph] underwent Reformatsky reaction with $R^2CR^3BrCO_2R^4$ [R^2=R^3=H, R^4=Et, CMe_2 : R^2=R^3=Me, R^4=Et] leading to isoxazolidinone (Table – 3).

An interesting singmatropic shift occurred during the addition of $RR^1CBrCO_2CHR^2CH=CHR^3$ ([76, 77]) [R=R^1=H, Me; R^2R^3=H, R=R^2=Me; R^1=R^3=H] to a suspenson zinc in refluxing beenzene afforded unsaturated carboxylate $R^2CH=CHR^3CRR^1$ CO_2ZnBr via 3,3 sigmatropic shift[76]

Recently varities of amides are a found to react with the bromozinc enolates. Reformatsky reaction with various bromozinc enolate with phthalimide has been studeed using different solvent[79].

An exhaustive literature survey reveals that a few number of research publications on this rection of Reformatsky reagents with various coumarin derivatives and other uncommon electrophilie centre have been reported.

Thus the review article include the nature of the products formed & their stereochemistry, nature of the substrate has been compiled all these data in a Tabular form. (Table 2&3)

Grignard Reaction on Coumarin system

The action of Grignard reagents on coumarins was extensively studied by Houben[78] and Shriner[79] and the research work published on coumarins has been represented in the excellent book of Kharash and Reinmuth[80]. Since these publications no extensive review has appeared on the reaction of organomagnesium reagent on coumarin. Hence it is worthwhile to take up thorough literature survey in order to gain insight on the up to date knowledge in this highly interesting field.

Before going into the proper subject let us have a look at structure[81 , 82] and mode of formation of the reagent and the solvent used [83,84]. The organomagnesium reagents are prepared by the oxidative addition of organic

halides to pure magnesium metal in polar dry solvent. In the reaction zerovalent Mg is oxidised to divalent state.

$Mg^{o} + RX \rightarrow RMg^{+2}\text{-}X$

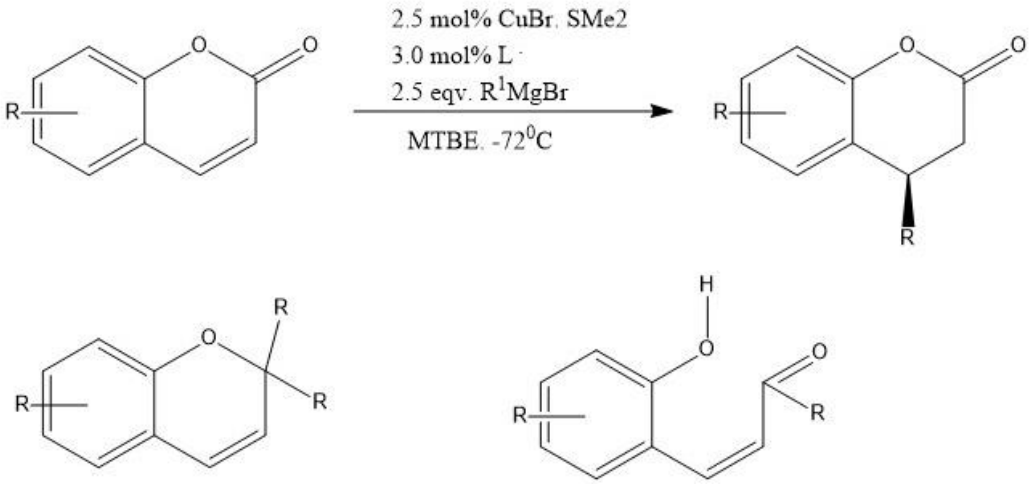
The Grignard reagent thus obtained is a source of carbanion and hence it reacts successfully with various electrophilic centre, generally offered by carbonyl or nitrile functionalities. This step can be formally understood as an insertion reaction involving unsaturated bond of carbonyl or nitrile into the Carbon-Magnesium bond of Grignard reagent.

The mechanism of reaction between organomagnesium reagent and carbonyl function has been reported in the literature [89 , 90]. There is a considerable evidences that Grignard reagent adds to carbonyl compounds via polar mechanism and there are many evidences that branched Grignard reagents react via SET mechanism [90 , 91].

Despite these complication and complexities the reaction of organo magnesium comounds with various substrates are well established [92]. The scope of addition of organomagnesium compounds to various aldehydes and ketones are well documented [93, 94] and the stereochemistry of addition is determined by steric approach control [95] while the applicability of product development control in this fields has been recorded with reservation [96], the assymetric synthesis have been achieved in this reaction on achiral or prochiral ketones in the presence of chiral electron donor [96].

Organomagnesium compounds show a greater tendency than organolithium compounds towards 1, 4 addition to α ,β unsaturated carbonyl compounds and α ,β – unsaturated δ lactones. A few reports of 1, 2 addition have been reported. It has been found [97] that the addition of Grignard reagent to α , β – unsaturated carbonyl compound gave 1, 2 addition product along with the tautomeric 1,4 adduct.

Thus the Grignard reagent behaves as a softer base than alkyllithium as the former attacks more preferentially the softer acid [98 , 99] centre i.e. β carbon of α , β unsaturated coumarin which has typical member having lactone-moiety, on reaction with Grignard reagent mainly leads to benzopyran derivatives via 1,2 addition together with some ketophenol via 1,4 addition[100].



Scheme – 5

The reaction of Grignard reagents with coumarin has drawn wide attention. This is virtually very few reports on reaction of coumarin bearing another functionality. The high nucleophilic character and low chemoselective nature of Grignard reagent than organozinc reagent, The Grignard reaction of coumarin having one electron deficient keto or aldehyde functionality was studied. The hot carbanion of Grignard reagent failed to divulge any degree of chemoseleclivity as the reagent attack both lactone & carbonyl group. But it is pleasant surprise that Grignard reaction using alkylmagnesium halide on 7-methoxy-8-acetylcoumarin furnishes-z-cinnamate ester as highly unusual products with unexpected chemoselectivity. Hence it has been considered worthwhile to compile all these data available from literature on this subject in tabular form[101 - 127] (Table-5).

The short and comprehensive review intends to demonstrate the various applicability and great varsitility of organozinc and organomagnesium reagents. Among these two reagents organozinc reagents show better chemoselective reagent than organomagnesium reagent on coumarin derivative. Hence it is logical that the reaction of coumarin and other uncommon electrophilic centre such as indole, amides azirines, nitrones, lactones, alkynes & thiophenes, etc with various organozic and organomagneisum reagents under ambident condition results in the formation of new compounds and unusual, and unexpected fundings have been recorded [66 , 67, 101,102,103-105] This review also give some information in the progress of diastereo as well as enantioselective

synthesis of acyclic and other system and also further corroborate the high degree of chemoselectivities of these reagents.

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Table – 1 Some selected compounds of Coumarin with Pharmacological and Industrial properties

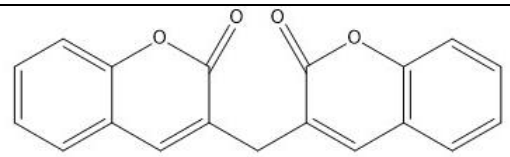
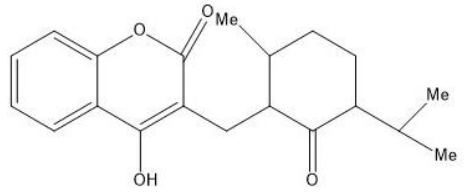
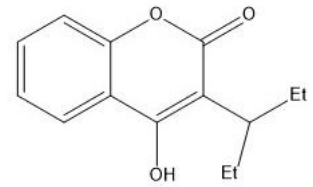
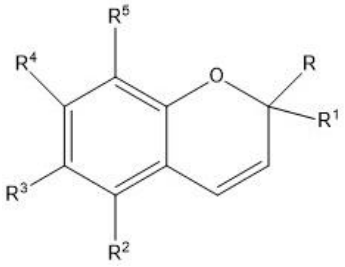
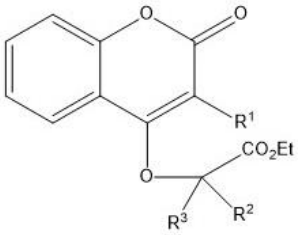
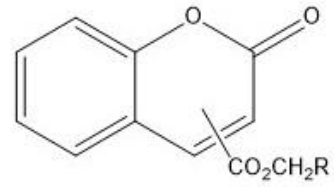
Substrates	Properties	Ref
	Anticoagulant	16,17
	Anticoagulant	16,17
	Hypo epidemic1	17
	Anti allergic	17a
	Anti inflammatory	18
	Anti hypertension	19

Table – 1 Some selected compounds of Coumarin with Pharmacological and Industrial properties

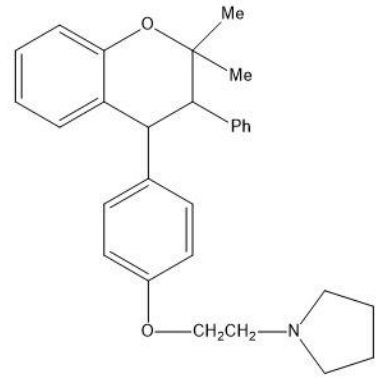
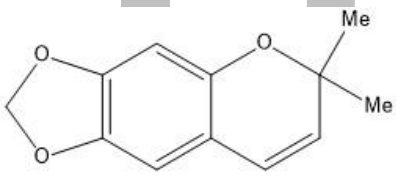
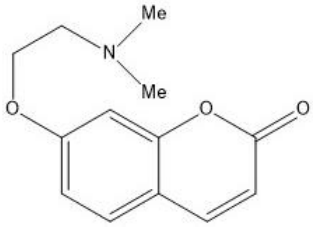
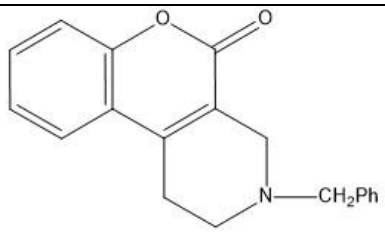
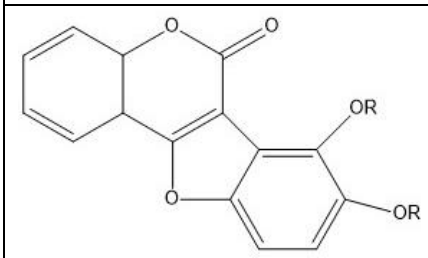
Substrates	Properties	Ref
	Anti inflammatory Schistomiacide	20 20
	Metamorphosis activity of insect	21
	Hypertensive	22
	Hypertensive	22
	Hypertensive	22

Table – 1 Some selected compounds of Coumarin with Pharmacological and Industrial properties

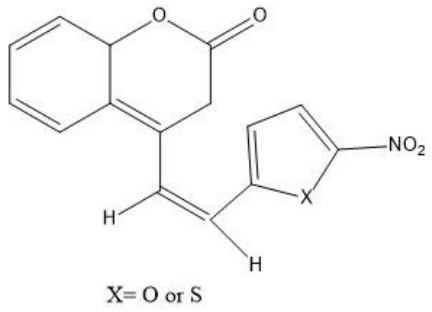
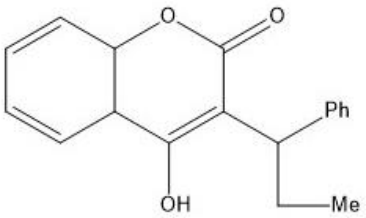
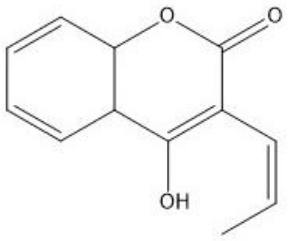
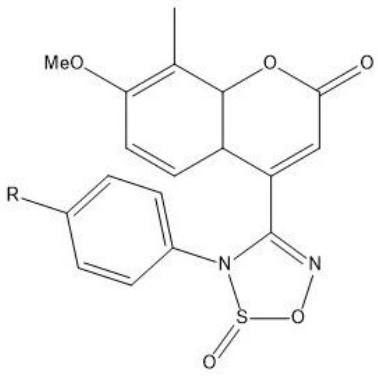
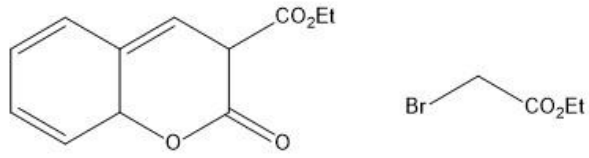
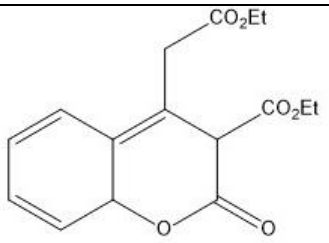
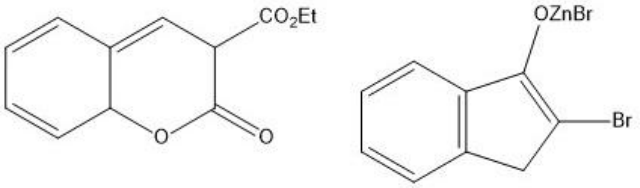
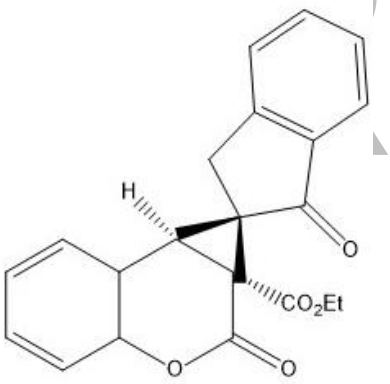
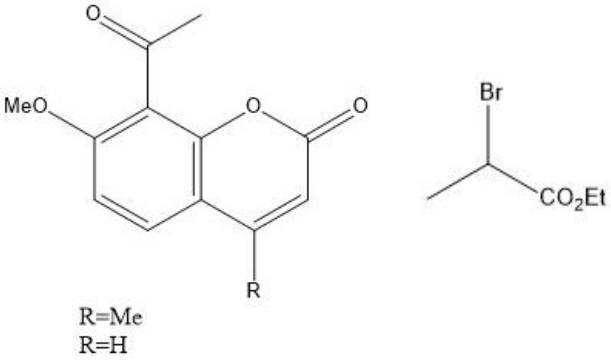
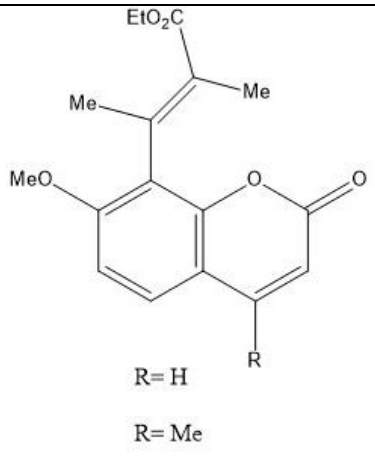
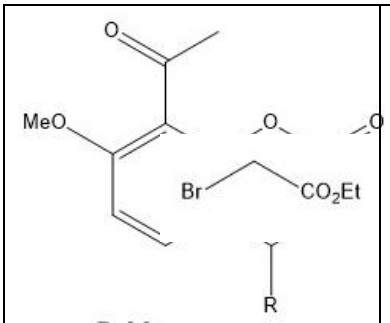
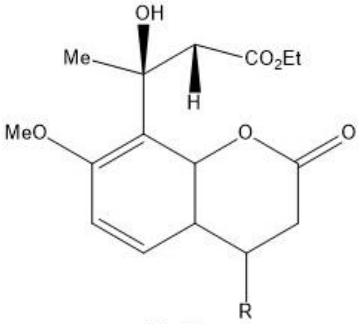
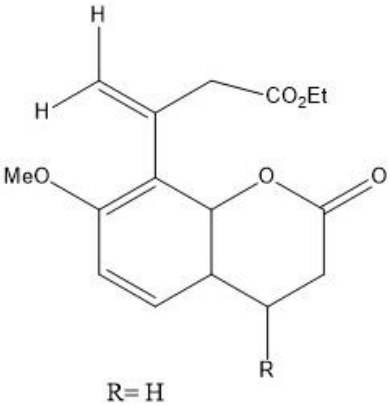
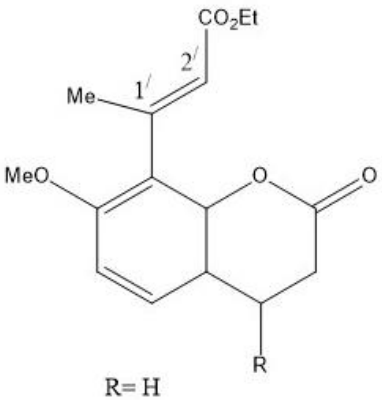
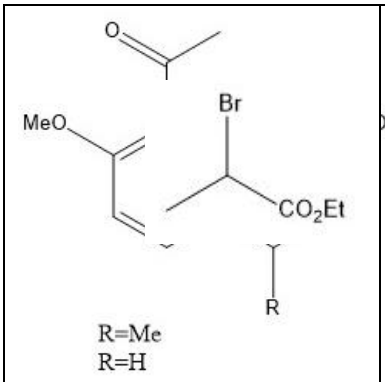
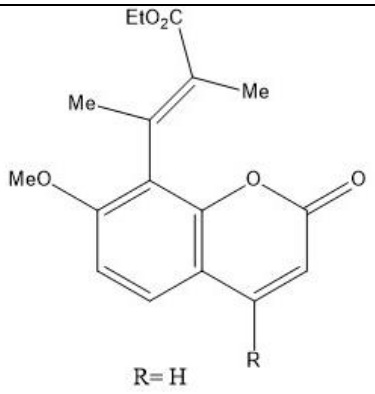
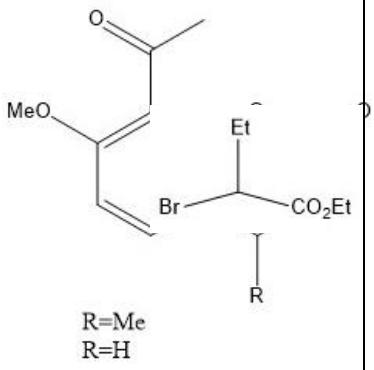
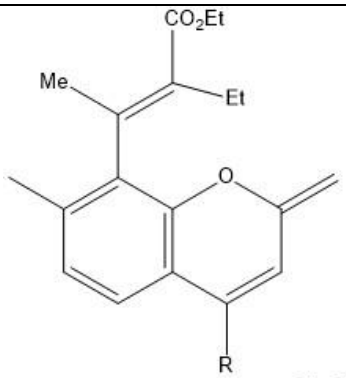
Substrates	Properties	Ref
	Anti tubercular	23
	Anti coagulant	23a
 	Anti inflammatory & Anti microbial	24,25

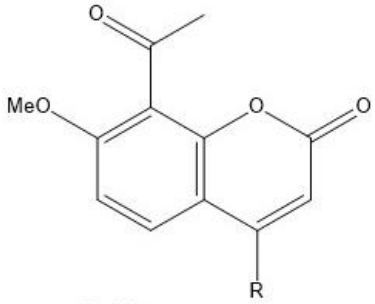
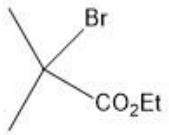
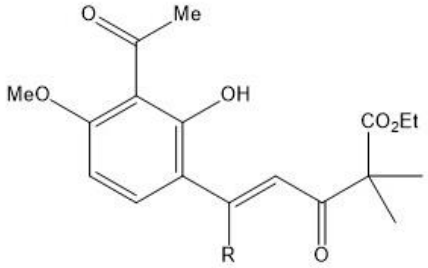
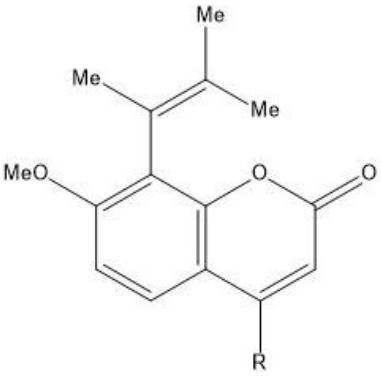
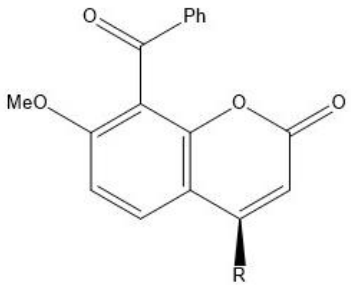
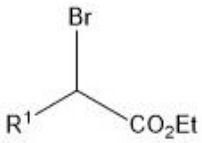
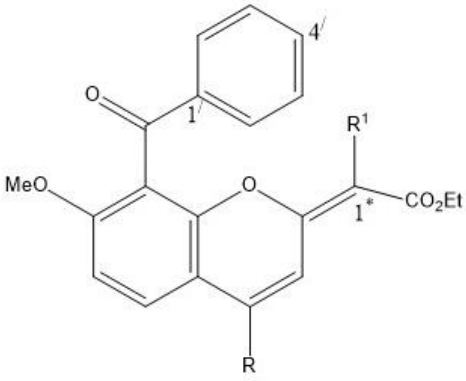
Table - 2 Selected Examples of Reformatsky Reaction with Coumarins/uncommon electrophiles

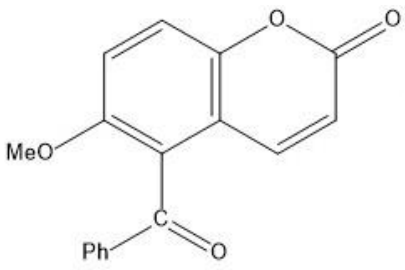
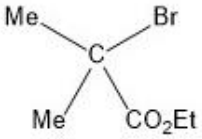
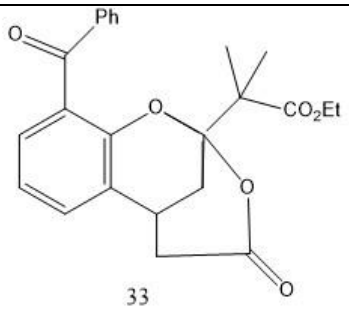
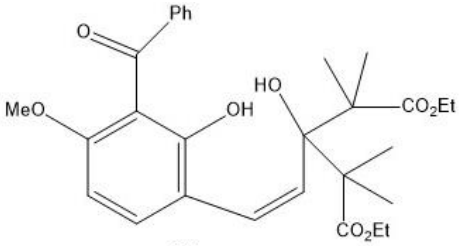
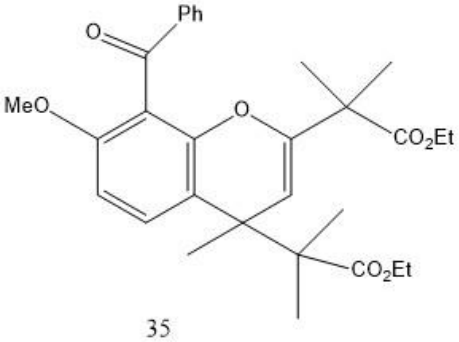
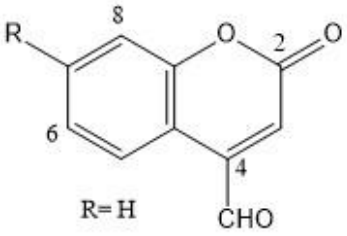
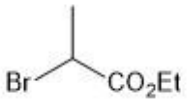
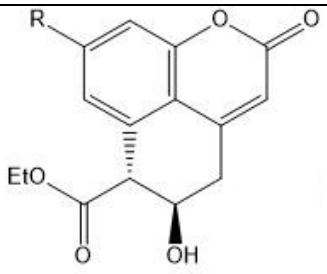
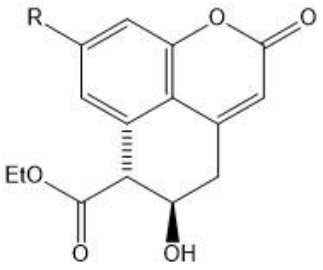
Substrates	Products	Ref
		63
		65
		66

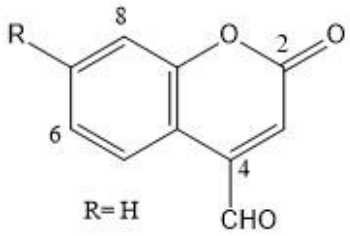
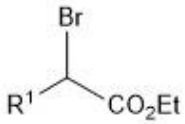
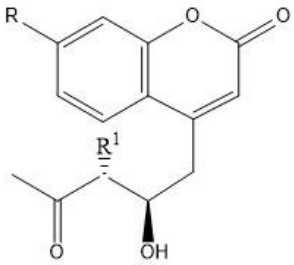
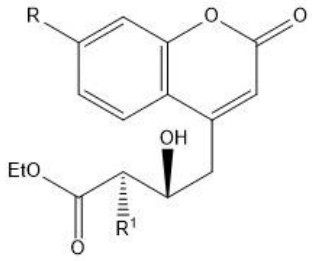
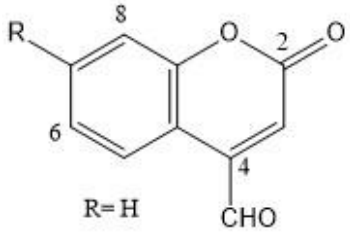
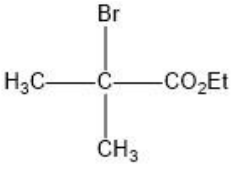
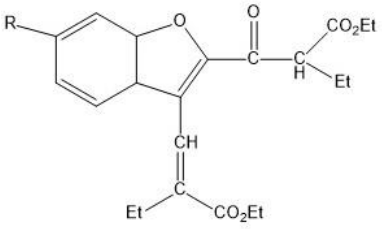
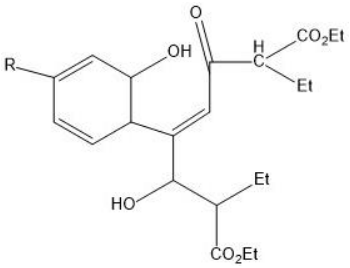
Table

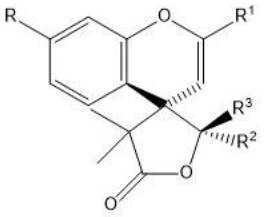
 R=Me R=H	 R= H R= Me  R= H R= Me  R= H R= Me	66

 R=Me R=H	 R= H R= Me	6 6
 R=Me R=H	 R= H R=Me	6 6

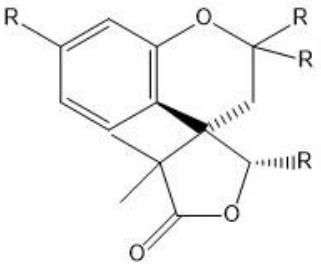
  R=Me R=H	 R=H  R=H R= Me	66
  R= H, Me	 R= H R^1= H R= Me R^1=H R=H R^1= Me R=Me R^1=Me R=H R^1= Et R= Me R^1= Et	66a

 	 33  34  35	66a
 R= H R= OMe 	 	67

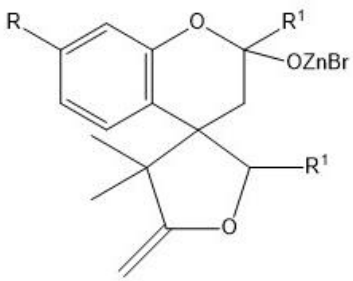
Substrates	Products	Ref
  R= H R= OMe	  R^1 = Me, Et, $CHMe_2CH$ R= H, Me	67
  R= H R= OMe	 	67



R=R^2=H, R^3=CMe$_2$CO$_2$Et
R=R^3=H, R^2=CMe$_2$CO$_2$Et
R=OMe, R^1=R^3=CMe$_2$CO$_2$Et, R$_2$=H

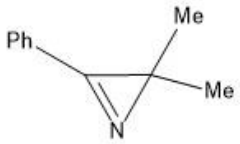
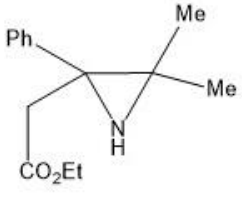
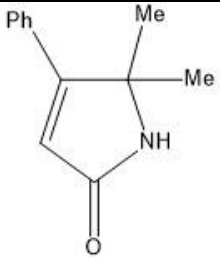
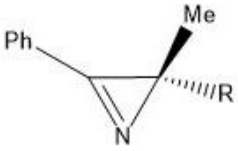
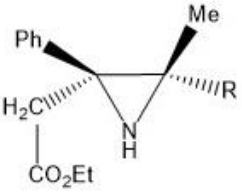
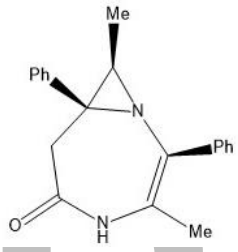
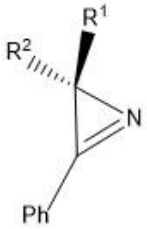
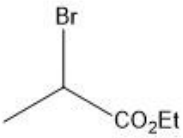
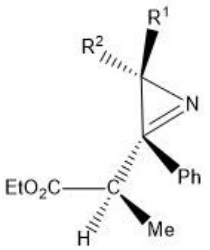
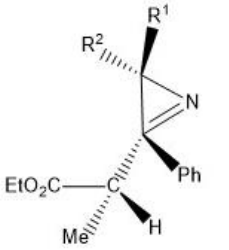
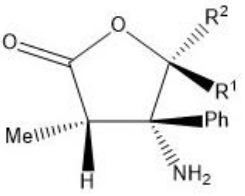
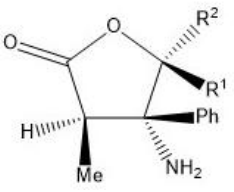


R=CMe$_2$CO$_2$Et



R=H, OMe, R^1=CMe$_2$CO$_2$Et

Table -3 Selected Examples of Reformatsky Reaction with Coumarins/uncommon electrophiles

Substrates	Products	Ref
 	 	69
 	 	69
 	   	70

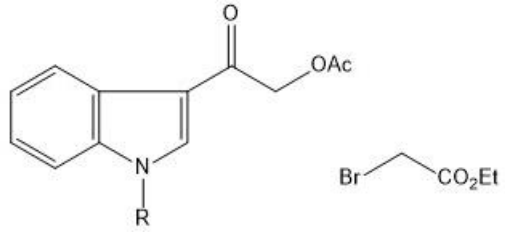
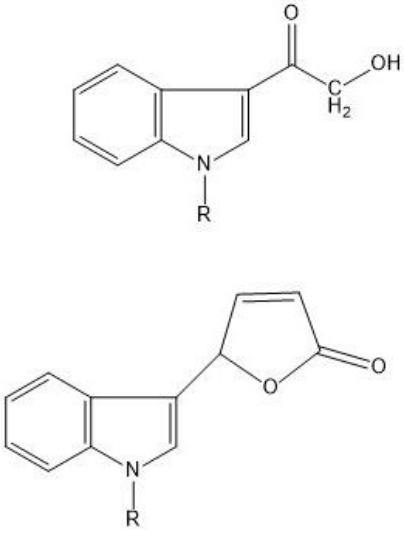
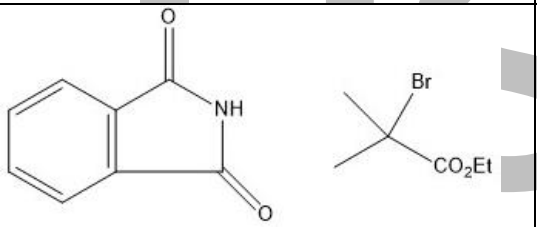
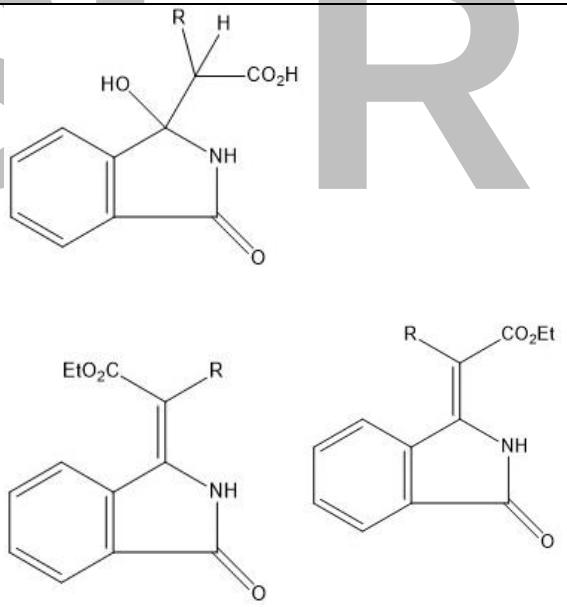
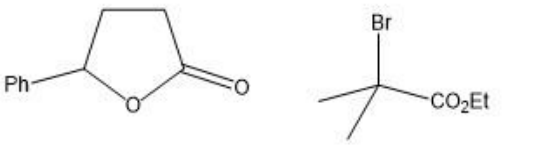
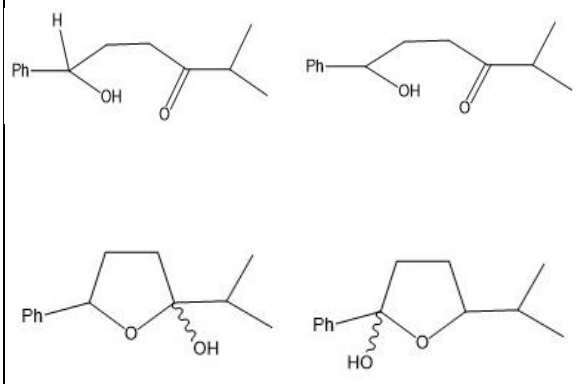
		71

Table -3 Selected Examples of Reformatsky Reaction with Coumarins/uncommon electrophiles

Substrates	Products	Ref
		77
		72

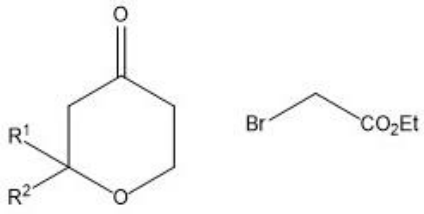
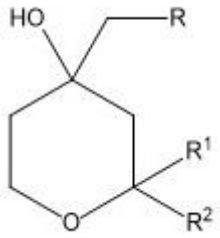
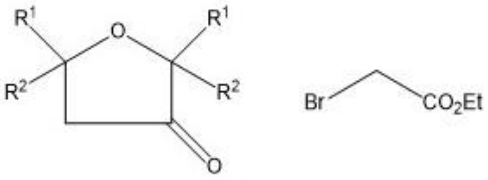
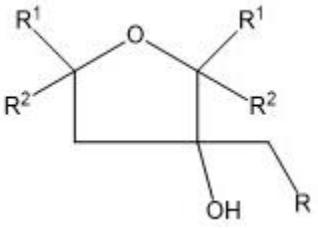
		73
		73

Table -3 Selected Examples of Reformatsky Reaction with Coumarins/uncommon electrophiles

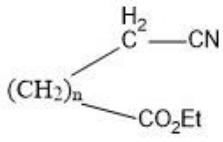
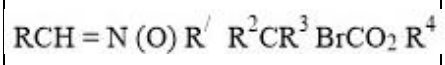
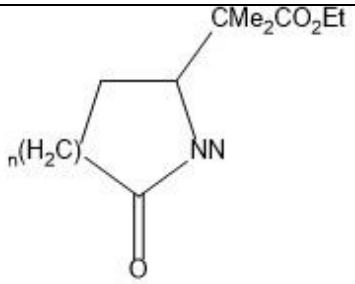
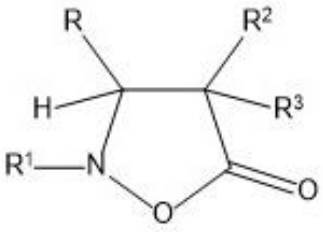
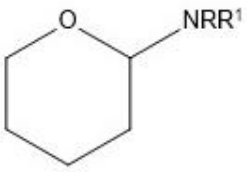
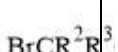
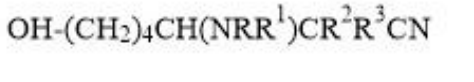
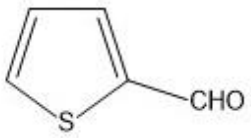
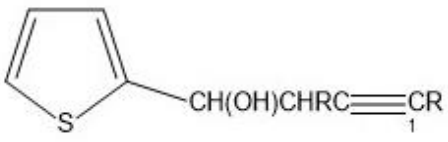
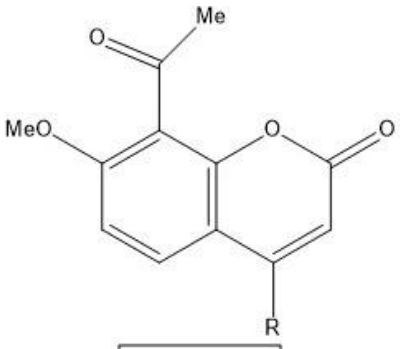
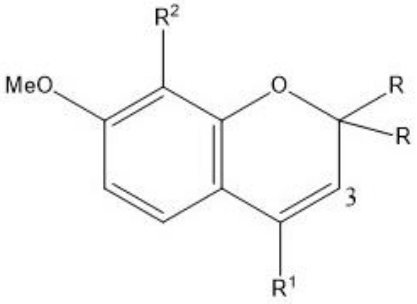
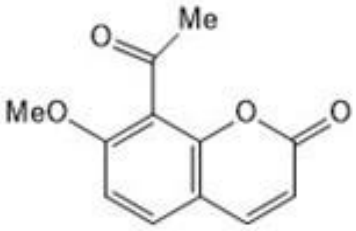
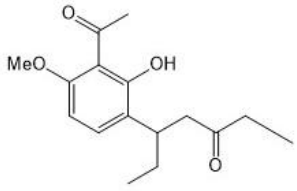
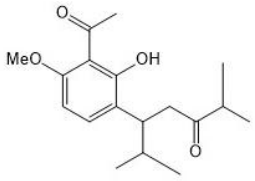
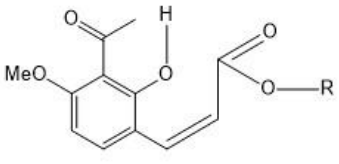
Substrates	Products	Ref
 		74
	 R= Me. R′ = p-OMe-C_6H_4 or, R= Me, Et, $CHMe_2$, $CHPh_2$, R′= Ph R^2= R^3= H, R^4=Et/, CMe ; R^2=R^3= Me, R^4=Et	75
 	 R= Me. R′ = p-OMe-C_6H_4 or, R= Me, Et, $CHMe_2$, $CHPh_2$, R′= Ph R^2= R^3= H, R^4=Et/, CMe ; R^2=R^3= Me, R^4=Et	75
 	 R= Me. R′ = p-OMe-C_6H_4 or, R= Me, Et, $CHMe_2$, $CHPh_2$, R′= Ph	75

Table -4 Selected Examples of Grignard Reaction with Coumarins

Substrates	Products	Ref
 RMgX R= Me, Et, Me_2CH_2, Ph, P-anisyl	 R= Ph, R^1= H_1 R2= $MeC^{1/}(OH)Ph$ R= P-Anisyl, R^1 H R2=MeC(OH)Anisyl-P R,R_1= Me, R_2=$MeC^{1/}$=$C^{2/}(H_2)$ R=Et, R^1=Me, R^2=$MeC^{1/}(OH)Et$ R=Pr^i, R^1= Me, R^2=$MeC^{1/}$, $C^{2/}Me_2$ R=$(CH_2)_2Ph$, R^1= Me R^2= $MeC^{1/}(OH)(CH_2)_2Ph$ R= Ph, R^1= Me, R^2= MeC(OH)Ph R=P-Anisyl, R^1= Me R2=P-Anisyl$C^{1/}$=$C^{2/}H_2$	101, 102
	  	101

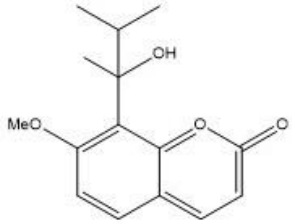
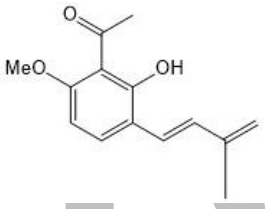
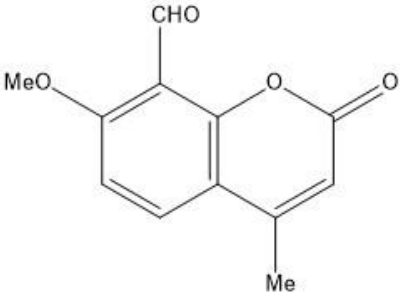
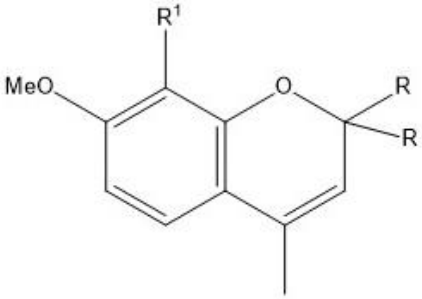
	 	

Table -4 Selected Examples of Grignard Reaction with Coumarins

Substrates	Products	Ref
 RMgX R= Me, Et,i-Pr,Ph, p-Anisyl	 R= Me, R^1=Me=CH_2 R=Et, R^1=MeC(OH)Et R= $CHMe_2$, R_1=Me=$C(Me)_2$ R=Ph, R_1=MeC(OH)Ph R=p-Anisyl, R^1= p-Anisyl C=CH_3 R=Me, R^1=CH(OH)Me R=Et, R^1=CH(OH)Et R=$CHMe_2$, R^1= CH(OH)CMe_2 R=Ph, R^1=CH(OH)CPh_2 R=p-Anisyl, R_1=CH(OH)C p-Anisyl	102

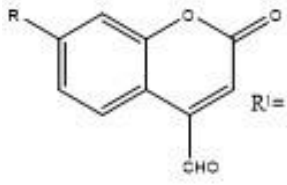
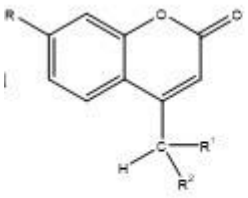
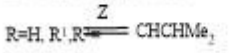
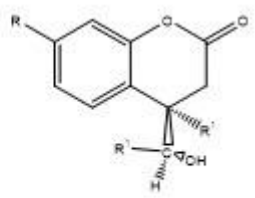
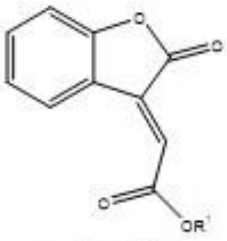
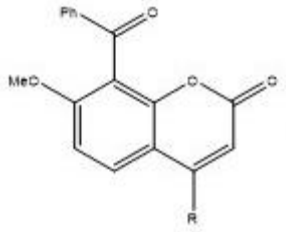
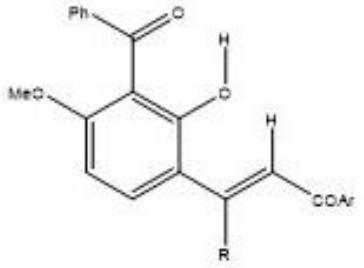
 R^1-MgX R^1= Ph, Et,Pr^i, Bu^i, p-Anisyl R=H R=OMe	 R,R^1=H, R^2=OH R=OMe, R^1=H, R^2=OH R=H, R^1=Ph, R^2=OAc R=OMe, R^1=Ph, R^2=OH R=H, R^1=p-Anisyl, R^2=OAc R=OMe, R^1=p-Anisyl, R^2=OH R=H, R^1=Et, R^2=OH R=OMe, R^1=Et, R^2=OH R=OMe, R^1=Pr^i, R^2= OH R=OMe, R^1=Pr^i, R^2=OAc  R=H, R^1,R= CHCHMe$_2$ R= OMe, R^1=Bu^i, R^2=OH  R=H, R^1=Me R=OMe, R^1=Mr R=OMe, R^1=Et  R=H, R^1=Pr^i R=OMe, R^1=Pr^i	126

Table -4 Selected Examples of Grignard Reaction with Coumarins

Substrates	Products	Ref
 ArMgBr R=H R=Me	 Ar=Ph, R=H Ar= p-OMeC_6H_4, R=H	126

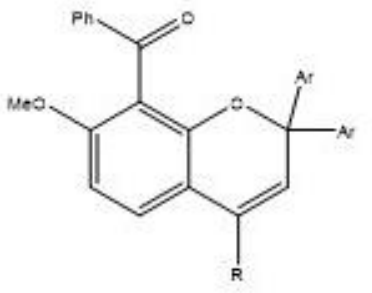
	 R=H, Ar= Ph R=Me, Ar=Ph R=Me, Ar= p-OMeC$_6$H$_4$	

Table -4 Selected Examples of Grignard Reaction with Coumarins

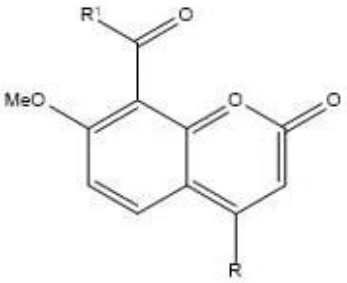
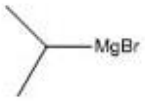
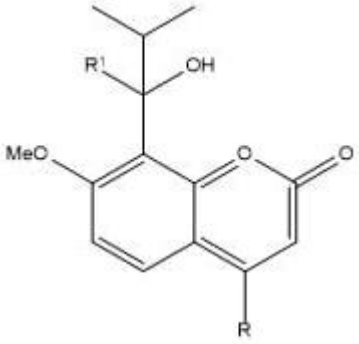
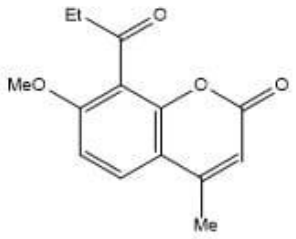
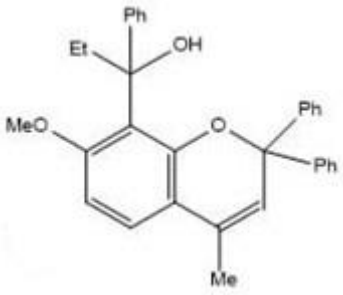
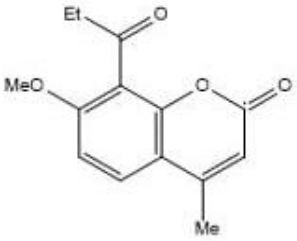
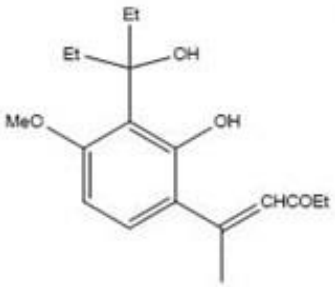
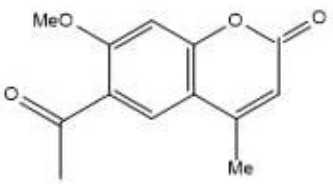
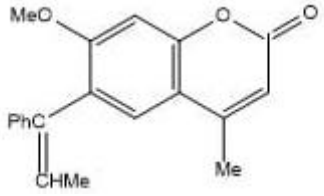
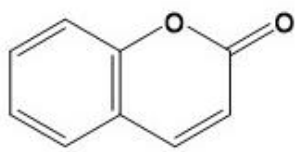
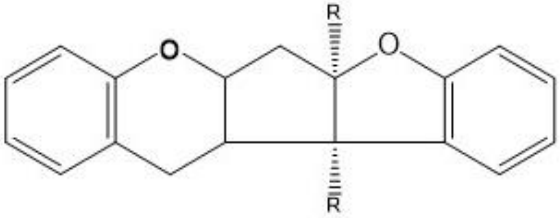
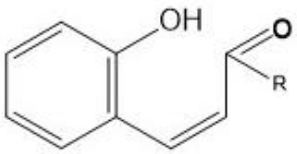
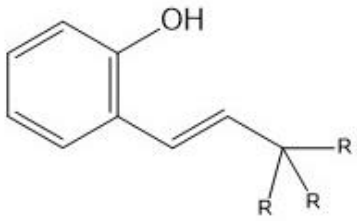
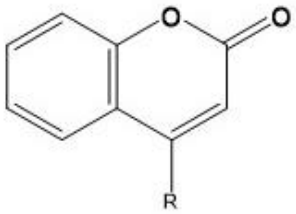
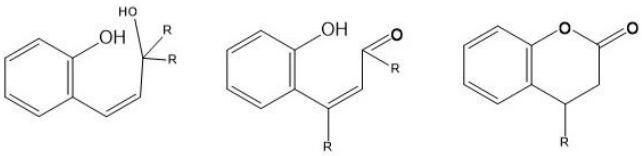
Substrates	Products	Ref
  R= H, R^1=Me R=Me, R^1=Me R=H, R^1= Ph R=Me, R^1=Ph	 R= H, R^1=Me R=Me, R^1=Me R=H, R^1= Ph R=Me, R^1=Ph	127
 PhMgBr		127
 EtMgBr		127
 PhMgBr		127

Table-5 Selected Examples of Grignard Reaction with Coumarins

Substrates	Products	Ref
 RMgX (R=Me, Ph)		103, 104
RMgX (R=Ph, $CHMe_2$)		105
RMgX (R=Me,Pr, Ph, allyl)		
RMgX (R=$PhCl_2CH_2$, i-Pr)		105
RMgX		105

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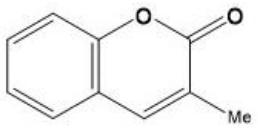
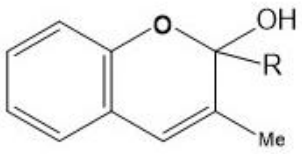
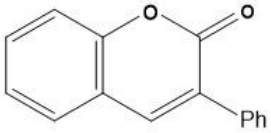
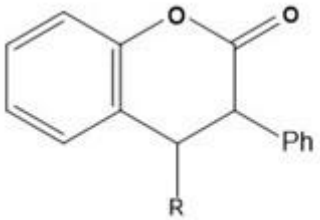
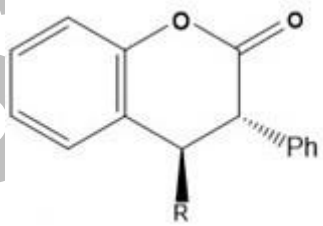
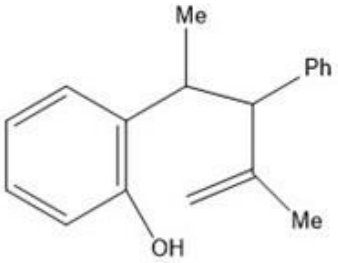
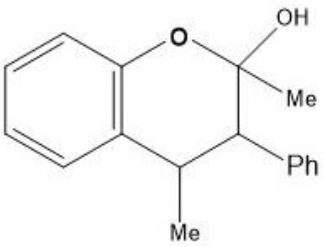
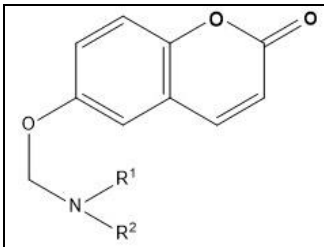
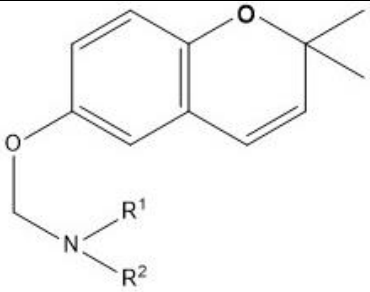
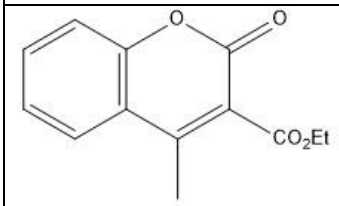
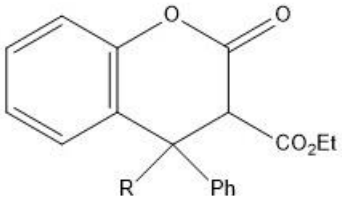
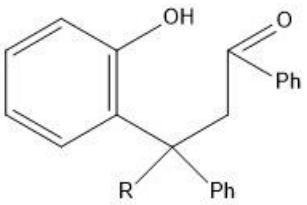
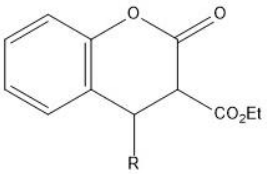
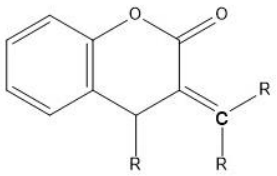
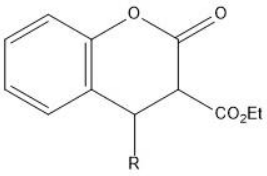
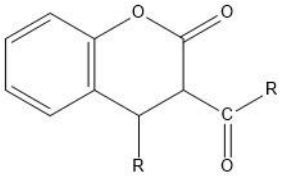
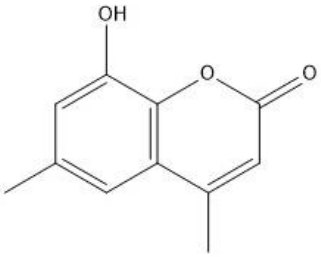
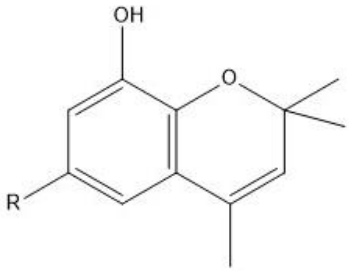
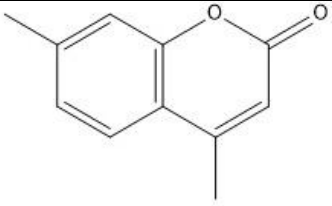
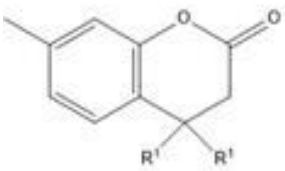
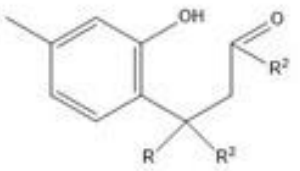
 RMgX (R=Ph, p-Anisyl, napthyl)		108, 109
 RMgX R=Et, Me_2CH, Me_3C	 	109
RMgX R=Me	 	110

 RMgX R=1-bromo napthalene		111
 PhMgX	 	112
RMgX R=p-anisyl	 	113
RMgX (R=Me_3C)	 	114
 RMgX R=Me		115
	 	115

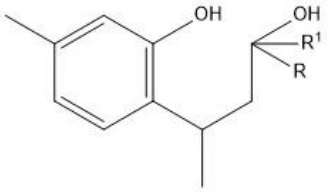
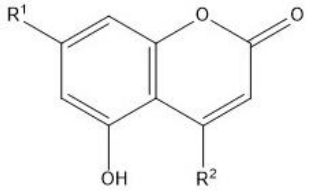
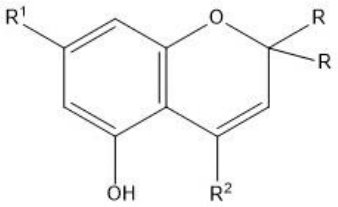
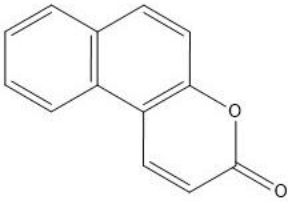
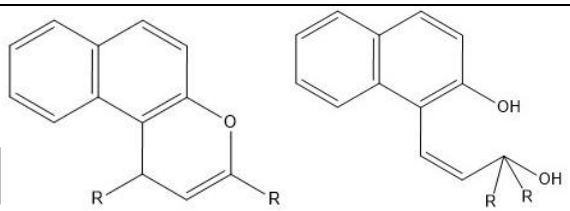
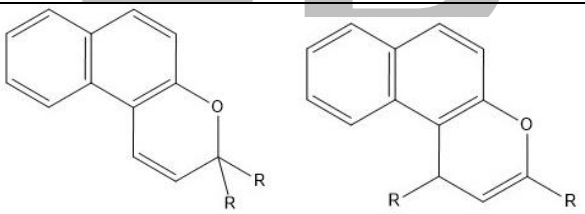
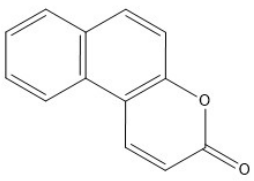
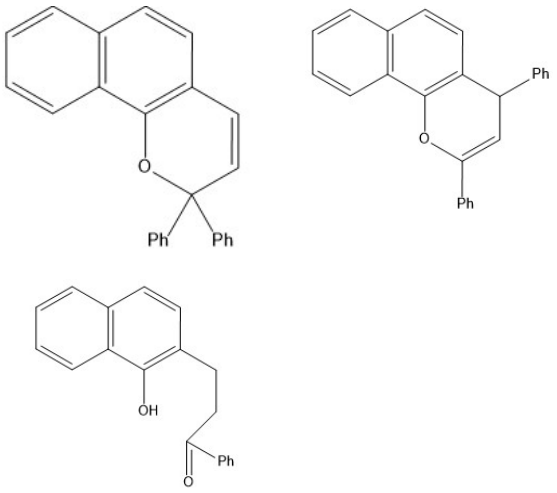
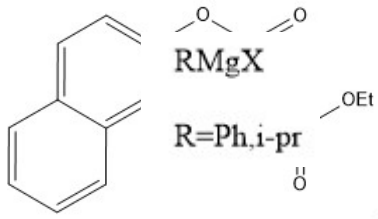
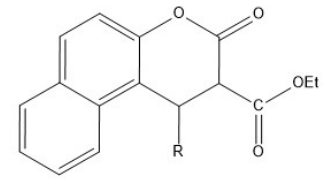
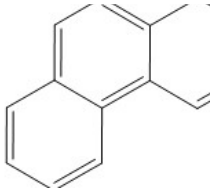
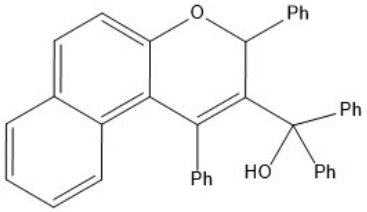
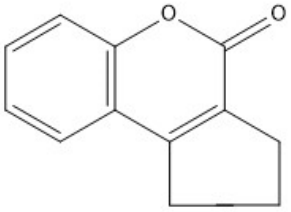
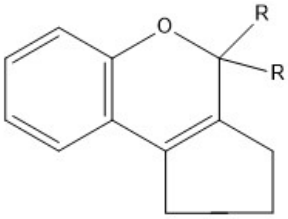
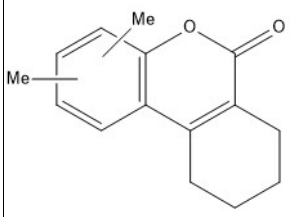
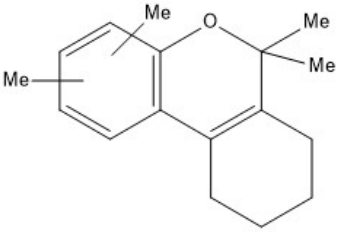
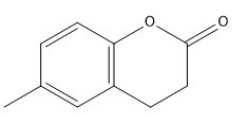
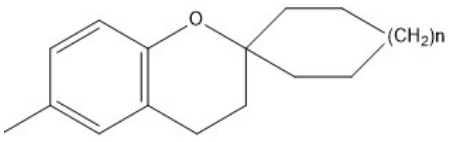
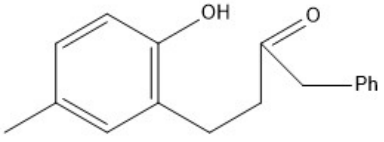
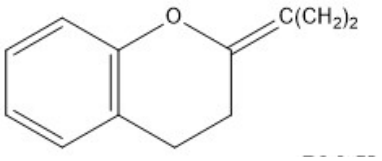
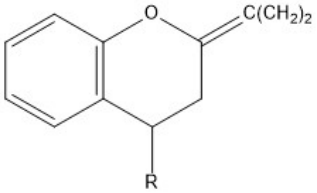
R^1MgX R^1= Et, Me2CH, Cyclohexyl		
 RMgX R= Me,Ph		115
 RMgX R=o,m-anisyl		116
RMgX R=p-anisyl		117

Table-5 Selected Examples of Grignard Reaction with Coumarins

Substrates	Products	Ref
 PhMgX X=Br		118, 119

 RMgX R=Ph,i-pr RMgX R=Ph	  	120
  RMgX R=Me		121
 RMgX R=Me		122
 $BrCH_2(CH_2)nCH_2CH_2MgBr$ $PhCH_2MgBr$ n=1,2	 	123 124

 RMgX R=Me,Et,Ph,Me2CH		125