Chapter –3

Synthesis of novel Azetidinone derivatives from Coumarin moiety.
β-Lactam (2-Azetidinones) antibiotic research was opened when Scottish scientist Sir Alexander Fleming observed that *Pencillium notatum* produces an inhibitory growing effect and partial lysis on *Staphylococci colonies*.¹ Thus, 2-Azetidinones are four-membered cyclic amides derived from 3-amino-propanoic acids. The first member of this class of compounds was synthesized ² by Staudinger in 1907. However, until the discovery of penicillin by Fleming in 1929, the importance of β-lactams as antibiotics was not recognized.¹

Therefore, the following demonstration of the chemotherapeutic properties of penicillin (1), a search for an antibiotic producing organism was made by Professor Brotzu³ in Sardinia. He examined the microbial flora of the sea water near a sewage outlet, supposing that the process of self-purification of water might be due to bacterial antagonism. He reported the discovery of cephalosporin (2) which produced anti-bacterial material that has activity against certain Gram-positive as well as Gram-negative organisms. Brotzu³ believed that his results offered hopeful prospects. The experiments with the Sardinian’s cephalosporins were carried out at Oxford University laboratories and proved to contain an acidic antibiotic which was readily extractable in organic solvents.⁴

---

Resistance to penicillin and cephalosporin\textsuperscript{5-7} and the possibility that antibiotics might occur in nature, prompted scientists to start screening microorganisms for new compounds. This resulted in the detection and isolation of clavulanic acid\textsuperscript{8} (3), thienamycin\textsuperscript{9} (4) and olivanic acid\textsuperscript{10} (5) from the genus \textit{Streptomyces}.

Molecular geometry and dimensions of 2-Azetidinone

On the basis of X-ray diffraction analysis, 2-azetidinone ring has a planar structure.\textsuperscript{11} Thus, the confirmation from similar studies proves the molecular dimensions as shown below-
With the introduction of a carbonyl function, substitution in the 4-membered ring as in 2-azetidinone, the π-bonding molecular orbital of the >C=O bond overlaps with p-orbital of the N-atom, creating a Csp²-N bond to permit the correct geometry for overlapping, thus leading to a planar structure. The dipole moment of 2-azetidinone is 4.152.
Molecular Spectra

_Ultraviolet (UV)_

The UV spectrum of 2-azetidinone with N-phenyl substitution exhibited a strong absorption maxima near 250 nm, which undergoes a bathochromic shift if substituents like halogen and methoxy group are presenting the _p_-position of the phenyl ring. The chromophore for the absorption must be aryl-N-CO group, in which the possibilities of overlap of the orbitals are aromatic system, the _p_-orbital on the _sp^2_ nitrogen and _π_-orbitals of the carbonyl group.\(^{12}\)

_Infrared (IR)_

The IR spectra of 2-azetidinone(s) exhibits a very strong band in the region 1760-1723 cm\(^{-1}\), characteristic for >C=O group. The other bands at 2986 and 3002 cm\(^{-1}\) are attributed to C-H group and those at 1182 cm\(^{-1}\) to C-N- group.\(^{11}\)

_Nuclear Magnetic Resonance (_H NMR)_

The influence of the stereochemistry on β-lactams was obtained from a study of the NMR spectrum of 1-\(p\)-bromo phenyl-3,3-dimethyl-2-azetidinone, which display a singlet for two methyl groups at δ 1.38 ppm and another singlet for two methylene protons at δ 3.35 ppm. The equivalence of the methyl substituents at C\(_3\) and also of the two protons at C\(_4\) is consistent with the planarity of the β-lactam ring and the planarity of the 3 valencies of N atom.
The NMR spectra of o-bromo phenyl-2-azetidinone also displays a singlet at δ 3.82 ppm for methylene group. This again reveals the planarity of the β-lactam ring. The methylene protons will be equivalent to each other if (a) the (o-bromo) phenyl ring lies substantially in the plane of the β-lactam ring or (b) the phenyl ring rotates around its axis fast enough to provide a sharp peak as the time averaged signal for the methylene protons.

Thus, the lowering of the temperature to -34 °C failed to resolve this methylene signal or even to broaden it. In the NMR spectrum of p-bromophenyl-2-azetidinone, the C₃ and C₂ protons occur as two triplets centered at δ 3.06 ppm and δ 3.52 ppm respectively, again revealing the symmetry of the ring system.¹²

Natural β-Lactams

Discovery of penicillin (1) was followed by the isolation of cephalosporin C¹³ (2a), which resembles the former in its stereospecific bicyclic disposition of the molecule. Recently, deacetoxy cephalosporin C (2b)¹⁴,¹⁵ 3-alkylthiomethyl cephalosporins¹⁶,¹⁷ (2c) and (2d) and cephamyrtins¹⁸-²² (6) have been added to the list. Another fused bicyclic β-lactam system with an oxazolidine ring, namely clavulanic acid²³ (7a) and its isomer isoclavulanic acid²⁴ (7b) was reported. Monocyclic β-lactams, such as steroidal alkaloids pachystermin A²⁵ (8a) and pachystermin B²⁵ (8b) wild-fire toxin²⁶ (9), nocardicins²⁷ (10) and bleomycins²⁸-³⁰ (11) were discovered. Thus, the occurrence of β-lactams in nature seems to be not unusual and it is likely that many more naturally occurring β-lactams will be isolated in future.
Acetidinone Derivatives
The recent and the advanced increase in both the spectrum of β-lactam antibiotics and the number of the known producing organisms are due to the development of new and more sensitive screening techniques. Further progress had been added by continuous synthetic derivatization to monocyclic β-lactam compounds. Many methods had been reported in the literature. Some of these methods will be listed in this study.

**Ketene-imine cycloaddition**

The ketene-imine cycloaddition was reported by Staudinger\textsuperscript{31} to be a smooth well-documented route to the synthesis of substituted β-lactam derivatives. In an effort to investigate a suitably substituted monocyclic β-lactam as a minimum requirement for biological activity, many scientists\textsuperscript{32-35} reported the trans stereoselective synthesis of butadienyl azetidinones (12) and their Diels-Alder cycloaddition. This included the preparation of a series of Schiff's bases and their reaction with dienylketene to produce a trans azetidinone (12). This involved the in situ formation of the ketene and its subsequent addition to the imine.

\[ R' \]
Wasserman cyclization

Joyeau et al., studied the stability of 2-azetidinones to enzymatic ring opening by β-lactamases. They suggested that a halogen α to the carbonyl would increase the IR absorption of the C=O, one of the criteria for the reactivity of the β-lactam in this aspect. Fluorine substitution, which will not introduce a large steric hindrance, is particularly interesting for a possible biological effect and possible stability towards β-lactamase. β-Bromopropionamide derivative (13) was prepared, which can be cyclized by Wasserman procedure using sodium hydride to give the N-(3-carboxy-6-methylphenyl) 3-difluoro-2-azetidinone (14).36

\[
\begin{align*}
\text{BrCH}_2\text{COCOOEt} & \overset{\text{SF}_4}{\longrightarrow} \text{BrCH}_2\text{CF}_2\text{COOEt} \\
\text{N} & \overset{\text{ClSO}_2\text{H}}{\longrightarrow} \text{H}_2\text{NAr} \\
\end{align*}
\]

Synthesis of oxamazine β-lactams

The ω-substituted derivatives at the nitrogen are usually more susceptible to nucleophilic attack at the β-lactam carbonyl than the N-alkyl derivatives. The first indication that a heteroatom on the nitrogen could include chemical activation and provides biological activity, was obtained by the significant activity of monobactams. Subsequently, Woulfe and Miller37 described the synthesis of the oxamazines (15a) and (15b), a totally synthetic class of heteroatom activated β-lactam antibiotics.
Modification of Staudinger ketene-imine cyclization

Yoshioka et al., described the facile synthesis of 4-fluoromethyl-1-sulfo-2-azetidinones, starting with the commercially available fluoro ethanol (16).\(^ {38}\) Swern oxidation of (16) with oxalyl chloride and DMSO followed by treatment with dimethoxy benzylamine gave an imine (17) which was cyclized with phthalimido acetyl chloride to give the \(\beta\)-lactam (18).\(^ {39}\) This was followed by oxidative cleavage and sulfonation to give the desired sulfo derivative (19).\(^ {40}\)
Synthesis of β-lactams from imidates

Cardellini and his group reported the synthesis of alkoxy β-lactams via acid chloride imine route. Imidates (20) such as substituted N-phenyl formimidate, were reacted with acid chlorides to produce β-lactam (21). The major feature of this synthesis is its high stereoselectivity, only trans 4-alkoxy-β-lactams were formed.41

\[
RO—\text{CH}═N—C₆H₅ + X—C₂H₅—Cl \xrightarrow{\text{Et₃N/CH₂Cl₂}} X—\text{CH}═N—C₆H₅
\]

(20)

Acid chloride addition reaction

Bose et al., has applied a method to prepare β-lactams which involved the reaction between benzylideneaniline and few selected acid to produce (22) and (23).42

\[
\text{CH}_2X + \text{CHR} + \text{Et}_3\text{N} \xrightarrow{\text{COC}} X—\text{CH}═N—\text{Ar}
\]

(22)

\[
\text{HC}═\text{CHR} + \text{Et}_3\text{N} \xrightarrow{\text{COC}} X—\text{CH}═N—\text{Ar}
\]

(23)
Synthesis of azido $\beta$-lactams

This involves the annelation of imino compounds with azido acetyl chloride to afford (24).

\[
\begin{align*}
N_3\text{CH}_2\text{COOEt} + \text{H}_2\text{CS} & \xrightarrow{\text{Et}_3\text{N}} \text{Saccharyl chloride} \\
\text{H}_2\text{C} & \xrightarrow{\text{N}} \text{O} \\
\text{Et} & \xrightarrow{\text{N}} \text{C}_6\text{H}_5 \\
(24)
\end{align*}
\]

Since azido acetyl chloride is prone to explosive decomposition, especially during purification by distillation under reduced pressure, saccharyl chloride can be successfully employed for the preparation of 3-azido-2-azetidinones (25) from imines and azido acetic acid as reported by Manhas et al.\textsuperscript{43}

\[
\begin{align*}
N_3\text{CH}_2\text{COOEt} + \text{C}_6\text{H}_5\text{SO}_{\text{Cl}} & \xrightarrow{\text{Et}_3\text{N}} \\
\text{R} & \text{H} \xrightarrow{\text{R}} \text{N} \xrightarrow{\text{R}} \text{R} \\
(25)
\end{align*}
\]

Free radical cyclization

Recently, ring closure reactions leading to 4-membered rings, have been considerably studied. Annibale and his group\textsuperscript{44} investigated the intramolecular addition of free radicals to double bonds to give the $\beta$-lactam. They generated radicals (26) from enamides by treatment with Mn(OAc)\textsubscript{3}.2H\textsubscript{2}O. The key step in this reaction is the cyclization of (26) to (27). The final product (28) showed trans stereochemical relationship to substituents at C\textsubscript{3} and C\textsubscript{4} as demonstrated by $^1$H NMR coupling constants.
β-Lactam formation using microwave irradiation

The formation of 2-azetidinones by the reaction of an acid chloride, Schiff's base and a triethylamine seems to involve multiple pathways, some of which are very fast at higher temperatures. When it is conducted in domestic microwave ovens, high level irradiation leads to preferential formation of trans β-lactams (29) in several cases when the Schiff's base is derived from an aryl aldehyde rather than glyceraldehydes acetonide.45

\[
\text{Ph–CH₂–O–CH₂–C–Cl + Ph–CH=–N–CH₂–Ph} \xrightarrow{\text{Microwave irradiation}} \text{Ph–CH₂–O} \quad \text{Ph–CH₂–O} \\
(29)
\]

Synthesis of β-lactams from Passerini reaction

The reaction of carbonyl compounds with 3-aminopropanoic acids, followed by treatment with a suitable isocyanide afforded β-lactam derivatives. This reaction is called Passerini reaction and it was useful for the preparation of monocyclic and bicyclic β-lactams (31) and (33) respectively. The reaction envisages formation of a cyclic compound (30),
which on trans annular acyl migration gave β-lactam (31). It is noteworthy that the configuration of the newly formed asymmetric center in the penicillin analogue (33) is predetermined by the steric disposition of the reacting molecule.46

Conversion of ring compounds into β-lactams

I. Ring expansion of 3-membered rings.

The aziridine (34) in the presence of thionylchloride or oxalylicloride rearranges to β-lactam (35) in benzene, possibly via a mixed anhydride which undergoes ring expansion. The conversion is stereospecific and yields are good.47
The reaction of azirine and carbene was used in the synthesis of β-lactam. Thus, addition of trichloromethide ions to several azirines, followed by base catalyzed ring closure of the intermediate gave azetines which were converted into the corresponding β-lactam (36). The nature of substituents in the azirine ring influences the course of reaction.

\[ \text{R}_1\text{N} = \text{Ph; R}_2 = \text{Me; R}_3 = \text{H} \]
\[ \text{b, R}_1 = \text{Ph; R}_2 = \text{H; R}_3 = \text{H} \]
\[ \text{c, R}_1 = \text{Ph; R}_2 = \text{Ph; R}_3 = \text{H} \]

Diaziridines (37) reacted with ketenes to give β-lactam (38) and the reaction follows ketene-imine type interaction.

\[ \text{R}_1\text{R}_2\text{N} = 2\text{C} = \text{O} \]
\[ \text{R}_1 = \text{R}_2 = \text{Et; R}_3 = \text{Ph} \]

A new expansion of an α-lactam to a β-lactam system was reported. Thus, thermal fragmentation of (39) produced isocyanide (42), besides other products, which on cycloaddition to either (40) or its rearranged product (41) gave the corresponding β-lactam (43) which was characterized by degradation and alternative synthesis.
Cycloalkanones (44) are known to undergo ring expansion to lactams by Schmidt reaction or Beckmann rearrangement. It was found that cyclopropanone hemiacetal with sodium azide in acetone at pH 5.5 (KH$_2$PO$_4$/NaOH buffer) gave azetidin-2-one (45) in 21% yield.$^{51}$

\[
\text{Cycloalkanone} + \text{EtOH} \xrightarrow{\text{NaN$_3$/H}} \text{H$_2$O} \xrightarrow{\text{NaN$_3$/H}} \text{H$_2$N$_2$} \xrightarrow{\text{NaN$_3$/H}} \text{RCHO} + \text{R-N=CH}_2
\]

Similarly, the compound (46) on treatment with hydroxylamine, followed by subsequent tosylation afforded $\beta$-lactams (47).$^{52}$

Cyclopropanone with aminoacid esters was converted into $\beta$-lactams by similar ring expansion.$^{53}$ It is noteworthy that diphenylcyclopropenone (48) with ammonia or methylamine at room temperature gave azetidin-2-ones (49).$^{54}$
Wolf rearrangement\textsuperscript{55,56} of 3-diazopyrrolidine-2,4-diones (50) in the presence of tert-butylcarbazate, afforded $\beta$-lactams (51).

Reagent induced ring contraction has been reported recently. For example, the compound (52) was converted into (53) by oxidation with periodate and this reaction has been extended to several mono and bicyclic $\beta$-lactams.\textsuperscript{57}

Photolytic ring contraction of pyrazolidin-3-one systems was reported recently.\textsuperscript{58} This method has been extended to the synthesis of a novel system (55), from the compound (54) and other bicyclic and spiro cyclic $\beta$-lactams.\textsuperscript{59} Treatment of pyrazolidinones (56) successively with base and glyme, Mercury (II) oxide and 2,4,6-trimethylbenzenesulphonylhydroxyl amine gave $\beta$-lactams (57).\textsuperscript{60}
Conversion of azetidine derivatives into azetidin-2-ones.

Perfluoroisobutene with benzylidene aniline under drastic conditions gave the azetidine (58) which on hydrolysis afforded the corresponding β-lactam (59).

In another method, the compound (60) was treated with imines and the resulting azetidinylidene ammonium salt afforded β-lactams (64), on hydrolysis.
Recently, oxygenation of azetidine dianions (66) afforded β-lactams (69).63

![Chemical structure](image)

R = t-Bu, n-C₅H₁₁, PhCH₂CH₂, C₆H₁₁, C₈H₁₅

The reaction of chlorosulfonyl isocyanate (CSI) with alkenes provides β-lactams (70) in quantity, and the products have frequently been used for ring-opening polymerization to generate nylon-3 materials. Prior uses of this approach have focused almost entirely on β-lactams with purely hydrocarbon substituents.64

![Chemical structure](image)

Application of Staudinger ketene-imine cycloaddition reaction to bis-o-allyloxyarylideneamines afforded the corresponding bisallyloxyazetidinones as the cis-cis diastereomers (71), exclusively obtained as a mixture of cis-syn-cis and cis-anti-cis. RCM of the latter using Grubbs’ catalysts afforded the corresponding macrocyclic bisazetidinones in good yields.65
New oxidative dearomatization procedures leading to spiro β-lactams (72) and oxindoles were developed. By a variation of the oxidative reaction conditions, the usefulness of phenolic amides derived from 4-aminophenol in the synthesis of structurally different types of molecules was demonstrated.66
A brief review of the literature available on the chemical structure and the biological activity of 2-azetidinone and their derivatives are presented below.

Singh _et al._, have synthesized some new 1,3,3-trisubstituted 4-(2'-hydroxyphenyl)-2-azetidinones (73) and screened for anti-bacterial and anti-fungal activities against the different strains. Some the azetidinone derivatives have shown good anti-microbial activities against the panel of microorganisms. They also synthesized of new 1-alkyl/cyclohexyl-3,3-diaryl-10-methylspiro[azetidine-2,3'-indoline]-2',4-diones from the reactions of 2-diazo-1,2-diarylethanones with 1-methyl-3-(alkyl/cyclohexylimino)indolin-2-ones under thermal conditions. All the synthesized compounds were screened for their anti-bacterial and anti-fungal activities against bacterial strains _Bacillus subtilis, Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa_ and fungal strains _Candida albicans, Saccharomyces cerevisiae_. The compound (74) with two 4-methylphenyl groups and an isopropyl group on 2-azetidinone ring carbon and nitrogen, respectively showed activity against three organisms.

\[ \text{Ar} = \text{4-MeC}_{6}H_{4}, R = \text{CHMe}_{2} \]

(74)
Broccolo, *et al.*, have synthesized a series of 4-Alkyliden-azetidin-2-ones from 4-acetoxy-azetidinones and diazoesters. The *in vitro* anti-bacterial activity of the new agents was evaluated against 43 recent clinical isolates of antibiotic susceptible and resistant Gram-positive and Gram-negative pathogens by determining their minimum inhibitory concentrations (MICs). The most active compound showed MIC values ranging from 0.25 to 32 mg/L against some of the bacterial species tested. Interestingly, some compounds demonstrated similar activity against methicillin susceptible and resistant strains of *Staphylococcus aureus* suggesting possible alternative mechanisms of action of these agents, supported by cytotoxicity and preliminary scanning electron microscopy studies.69

Ashok Kumar *et al.*, have synthesized a series of azetidinone derivatives from the Quinazolinone nucleus. All the compounds have been screened for their anti-inflammatory and analgesic activities at the dose of 50 mg/kg po. These compounds have shown better anti-inflammatory (28.55-34.21%) and analgesic (27.35-34.11%) activities. Out of these nine compounds, compound (76) has shown 34.21% anti-inflammatory activity and is associated with almost the same degree of analgesic (34.11%) activity.70
Desai et al., have synthesized efficient and rapid synthesis of novel azetidin-2-ones under microwave as well as conventional methods from 2-{(1H-benzimidazol)-yl-thio}-N'-2-(substituted phenyl) hydrazide with chloroacetylchloride were carried out in DMF-benzene solvent in the presence of Et$_3$N catalyst. The synthesized compounds were tested for their \textit{in vitro} anti-bacterial activity against three strains of bacteria (gram + ve, gram -ve) and anti-fungal activities against three strains of human pathogenic fungi. Five compounds of the obtained series showed high \textit{in vitro} anti-microbial activity.\textsuperscript{71}

Indrani Banik, et al., have stereoselectively synthesized novel β-lactams using polyaromatic imines following the Staudinger reaction. As a measure of cytotoxicity, some of these compounds have been assayed against nine human cancer cell lines. Structure activity study has revealed that 1-N-chryselyn and 1-N-phenanthrenyl 3-acetoxy-4-aryl-2-azetidinones have potent anti-cancer activity. The presence of the acetoxy group at C$_3$ of the β-lactams has proven to be obligatory for their anti-cancer activity.\textsuperscript{72}
Indrani Banik et al., have synthesized a series 3-chloro-4-aryl-1-{5-[[1,3,4]thiadiazino[6,5-b]indol-3-ylamino]methyl}-1,3,4-thiadiazol-2-yl}azetidin-2-one from indole-2,3-dione with thiosemicarbazide. These compounds were evaluated for their anti-inflammatory, ulcerogenic and analgesic activities. Compound (79) has showed most active anti-inflammatory and analgesic activities with better ulcerogenic activity than phenylbutazone, while this compound was found to be associated with lesser degree of anti-inflammatory and analgesic activities as compared to indomethacin.\(^{73}\)

A series of 3-chloro-4-(3-methoxy-4-acetyloxyphenyl)-1-[3-oxo-3-(phenylamino)propanamido] azetidin-2-ones (80) and 3-chloro-4-[2-hydroxy-5-(nitro substituted phenylazo)phenyl]-1-phenylazetidin-2-ones (81) were synthesized using appropriate synthetic route. The anti-microbial activity of the synthesized compounds was screened against several microbes. Several of these molecules showed potent anti-microbial activity.
against *Bacillus anthracis*, *Staphylococcus aureus* and *Candida albicans* and significant structure activity relationship (SAR) trends. The chloro moiety of compound improved their antimicrobial activity significantly.\(^7\)

\[
R^1 = \text{-H, 2-Cl, 3-Cl, 4-Cl, 2-NO}_2, \text{3-NO}_2, \text{4-NO}_2
\]

\[
R^2 = \text{-H, 4-Cl, 4-Br, 4-F}
\]

Wang *et al.*, have synthesized fourteen new 2-azetidinone derivatives (82) and their cholesterol absorption inhibition activities were evaluated. Most of them showed comparable effects in lowering the levels of total cholesterol in the serum.\(^5\)

\[
R_1 = \text{-OMe, -H, -Cl, -4-Cl, -6Me, -4F, -6Br}
\]

\[
R_2 = \text{-Me, Cl, H, -F}
\]

Dong Xiao *et al.*, have synthesized a series of spiro piperidine azetidinone derivatives (83) and evaluated as potential TRPV1 antagonists. An important issue of plasma stability was investigated and resolved. Further focused SAR study lead to the discovery of a potent antagonist with good oral pharmacokinetic profile in rat.\(^6\)
Allan Urbach et al. have synthesized a series of novel 2-azetidinones (β-lactams) bearing short alkenyl chains at C₃ and N₁ and evaluated in vitro as inhibitors of human FAAH. Compound (84) (1-(4'-pentenoyl-3-(4'-pentenyl)-2-azetidinone)) featured an IC₅₀ value of 4.5 μM and a good selectivity for FAAH (fatty acid amide hydrolase) versus MGL (monoacylglycerol lipase).

The research work carried out during the present investigation has been described in Scheme-1.

The required 4-bromomethylcoumarins (1a-e) were prepared by Pechmann cyclisation of phenol and 4-bromoethylacetoacetate at 0-5 °C. The 4-bromoethylacetoacetate in turn was obtained by the bromination of ethylacetoacetate in dry ether at 0-5 °C.

4-bromomethylcoumarins (1a-e) were reacted with equimolar quantity of p-hydroxy benzaldehyde in presence of dry acetone and anhydrous K₂CO₃ to obtain 4-(2-oxo-2H-chromen-4-ylmethoxy)-benzaldehydes (2a-e). Compounds (2a-e) on treatment with anilines in presence of a drop of glacial acetic acid did not yield 4-(4-phenyliminomethyl-phenoxymethyl)-chromen-2-ones (4a-y).
But compounds (4a-y) were prepared by reacting (1a-e) 4-phenyliminomethyl-phenols (5a-e) in presence of dry acetone and anhydrous K₂CO₃ in good yield. Compounds (4a-y) when refluxed with a cold solution of chloro acetyl chloride in presence of catalytic quantity of triethyl amine in dioxane gave 3-Chloro-4-[4-(2-oxo-2H-chromen-4-yl-methoxy)-phenyl]-1-phenyl-azetidin-2-ones (5a-y) (Scheme-1).

SCHEME-1

Where R = 6-CH₃, 7-CH₃, 6-Cl, 5,6-Benz, 7,8-Benz
R' = -H, -CH₃, -OCH₃, -Cl, -Br
Melting points of all the synthesized compounds were determined in open capillaries and are uncorrected. Infrared spectra were recorded using KBr pellets on *Nicolet 5700 FT-IR* instrument. The $^1$H NMR and $^{13}$C NMR spectra were recorded on *Brucker Avance-300 (300 MHz)* model spectrophotometer in CDCl$_3$ and DMSO as solvent and TMSi as internal standard with $^1$H resonant frequency of 300 MHz and $^{13}$C resonant frequency of 75MHz. The chemical shifts were measured in $\delta$ ppm downfield from internal standard TMSi at $\delta=0$. The TLC was performed on neutral alumina silica gel 60 $F_{254}$ (Merck). The mobile phase was ethyl acetate and n-hexane (1:1) and detection was made using UV light and iodine vapours. The resulting compounds were purified by column chromatography. For column chromatography Merck silica gel (0.040-0.063mm) was used. All the compounds gave C, H and N analysis within ±0.4% of the theoretical values.

This part deals with preparation of following compounds.

(a) 4-Bromoethylacetoacetate
(b) 4-Bromoethylcoumarins. (General method)
(c) (2-Oxo-2H-chromen-ylmethoxy)-benzaldehydes. (General method)
(d) Preparation of 4-(4-Phenyliminomethyl-phenoxy methyl)-chromen-2-ones. (General method)
(e) Preparation of 3-Chloro-4-[4-(2-oxo-2H-chromen-4-ylmethoxy)-phenyl]-1- phenyl- azetidin-2-ones. (General method)
(a) **Preparation of 4-Bromoethylacetoacetate**

Liquid bromine (20.5 ml, 0.38 mol) was added with stirring during the course of one hour to an ice cold solution of ethylacetoacetate (50 ml, 0.38 mol) in 60 ml of dry ether. Reaction mixture was allowed to stand at room temperature for about 24 hours. It was decomposed with crushed ice; Separated ether layer was washed with water and dried over anhydrous calcium chloride. Solvent was removed under reduced pressure and pale yellow coloured 4-bromoethylacetoacetate which was lachrymatory in nature was stored in dark coloured bottle.

(b) **Preparation of 4-Bromoethylcoumarins (1a-e)**

To a mixture of equimolar quantity of substituted phenols (0.1 mol) and 4-bromoethylacetoacetate (20.8 ml, 0.1 mol) was added drop wise sulphuric acid (30 ml) with stirring and maintaining the temperature between 0-5 °C. The reaction mixture was allowed to stand in ice chest overnight and deep red coloured solution was poured into the stream of crushed ice. Solid separated was filtered and washed with water and then with cold ethanol so as to get a colourless compound. All the substituted 4-bromomethylcoumarins (1a-e) were recrystallized from acetic acid.

(c) **Preparation of (2-Oxo-2H-chromen-ylmethoxy)-benzaldehydes (2a-e)**

p-Hydroxy benzaldehyde (1.22g, 0.01 mol) and anhydrous K$_2$CO$_3$ (1.38 g, 0.01 mol) were stirred in dry acetone 25 ml for 30 minutes. 4-Bromomethyl coumarins (2a-e) (0.01mol) were added and stirring was continued for 24 hours. The reaction mixture was concentrated to one fourth of the original volume and poured into ice water. The solid separated was filtered and washed with 50% HCl to neutralize excess of potassium.
carbonate. Then, it was washed with 100 ml of cold water and dilute ethanol. The crude product was dried and recrystallized from DMF.

(d) Preparation of 4-(4-Phenyliminomethyl-phenoxymethyl)-chromen-2-ones (4a-y)

4-Phenyliminomethyl phenols (3a-e) (10 mmol) and anhydrous K$_2$CO$_3$ (1.38g, 10 mmol) were stirred in dry acetone (25 ml) for 30 min. 4-Bromomethylcoumarins (1a-e) (2.52g, 10 mmol) was added and stirring was continued for 24h. The reaction mixture was concentrated and poured onto crushed ice (100g). The solid separated was filtered and washed with 5% HCl (10 ml) to neutralize excess of potassium carbonate, then washed with 100 mL of cold water and with dilute ethanol. The crude product was dried and recrystallized from DMF.

(e) Preparation of 3-Chloro-4-[4-(2-oxo-2H-chromen-4-ylmethoxy)-phenyl]-1-phenyl-azetidin-2-ones (5a-y)

The mixture of 4-(4-Phenyliminomethyl-phenoxymethyl)-chromen-2-ones (0.01 mol) and triethylamine (0.01 mol) was dissolved in dioxane (50 ml), cooled and stirred. To this well-stirred cold solution of chloroacetyl chloride (0.01 mmol) was added drop wise within a period of 20 min. The reaction mixture was then stirred for an additional 3 hrs and left at room temperature for 48 hrs. The resultant mixture was concentrated, cooled, poured into ice cold water, filtered and then dried. The product thus obtained was purified by column chromatography over silica gel using 30% ethyl acetate: 70% benzene as an eluent. Recrystallization was done from suitable solvent which gave 2-azetidinones (5a-y).

The physical constants and analytical data of synthesized compounds (5a-y) have been given in Table-1.
**Table-1 Physical and Analytical Data of 2-azetidinone derivatives**

<table>
<thead>
<tr>
<th>Entry</th>
<th><strong>Product</strong></th>
<th>R</th>
<th>Ar</th>
<th>Yield (%)</th>
<th>m. p (°C)</th>
<th>Mol. Formula/ Mol. Wt</th>
<th>Elem. Analysis (Cal./Found)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5a</td>
<td>6-CH_{3}</td>
<td>Ph</td>
<td>88.00</td>
<td>138-140</td>
<td>C_{29}H_{20}ClNO_{4}</td>
<td>70.09 4.49 3.14</td>
</tr>
<tr>
<td>2</td>
<td>5b</td>
<td>7-CH_{3}</td>
<td>Ph</td>
<td>71.00</td>
<td>114-116</td>
<td>C_{29}H_{20}ClNO_{4}</td>
<td>70.08 4.52 3.17</td>
</tr>
<tr>
<td>3</td>
<td>5c</td>
<td>6-Cl</td>
<td>Ph</td>
<td>62.80</td>
<td>118-120</td>
<td>C_{29}H_{17}Cl_{2}NO_{4}</td>
<td>64.39 3.67 3.00</td>
</tr>
<tr>
<td>4</td>
<td>5d</td>
<td>5,6-Benzo</td>
<td>Ph</td>
<td>74.10</td>
<td>198-200</td>
<td>C_{29}H_{20}ClNO_{4}</td>
<td>72.27 4.18 2.92</td>
</tr>
<tr>
<td>5</td>
<td>5e</td>
<td>7,8-Benzo</td>
<td>Ph</td>
<td>65.12</td>
<td>232-234</td>
<td>C_{29}H_{20}ClNO_{4}</td>
<td>72.26 4.20 2.90</td>
</tr>
<tr>
<td>6</td>
<td>5f</td>
<td>6-CH_{3}</td>
<td>4-MeC_{6}H_{4}</td>
<td>64.20</td>
<td>132-134</td>
<td>C_{29}H_{22}ClNO_{4}</td>
<td>70.51 4.82 3.05</td>
</tr>
<tr>
<td>7</td>
<td>5g</td>
<td>7-CH_{3}</td>
<td>4-MeC_{6}H_{4}</td>
<td>71.80</td>
<td>208-210</td>
<td>C_{29}H_{22}ClNO_{4}</td>
<td>70.50 4.84 3.04</td>
</tr>
<tr>
<td>8</td>
<td>5h</td>
<td>6-Cl</td>
<td>4-MeC_{6}H_{4}</td>
<td>82.4</td>
<td>183-185</td>
<td>C_{29}H_{19}Cl_{2}NO_{4}</td>
<td>65.01 3.99 2.92</td>
</tr>
<tr>
<td>9</td>
<td>5i</td>
<td>5,6-Benzo</td>
<td>4-MeC_{6}H_{4}</td>
<td>71.12</td>
<td>220-222</td>
<td>C_{30}H_{22}ClNO_{4}</td>
<td>72.65 4.47 2.82</td>
</tr>
<tr>
<td>10</td>
<td>5j</td>
<td>7,8-Benzo</td>
<td>4-MeC_{6}H_{4}</td>
<td>65.20</td>
<td>110-112</td>
<td>C_{30}H_{22}ClNO_{4}</td>
<td>72.65 4.47 2.82</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>5k</td>
<td>6-CH₃</td>
<td>4-MeOC₆H₄</td>
<td>63.8</td>
<td>170-172</td>
<td>C₂₇H₂₂ClNO₅ 477</td>
<td>68.14</td>
</tr>
<tr>
<td>12</td>
<td>5l</td>
<td>7-CH₃</td>
<td>4-MeOC₆H₄</td>
<td>70.8</td>
<td>98-100</td>
<td>C₂₇H₂₂ClNO₅ 477</td>
<td>68.14</td>
</tr>
<tr>
<td>13</td>
<td>5m</td>
<td>6-Cl</td>
<td>4-MeOC₆H₄</td>
<td>63.4</td>
<td>130-132</td>
<td>C₂₈H₁₉Cl₂NO₅ 497</td>
<td>62.92</td>
</tr>
<tr>
<td>14</td>
<td>5n</td>
<td>5,6-Benzoyl</td>
<td>4-MeOC₆H₄</td>
<td>61.02</td>
<td>282-284</td>
<td>C₂₉H₂₂ClNO₅ 512</td>
<td>70.38</td>
</tr>
<tr>
<td>15</td>
<td>5o</td>
<td>7,8-Benzoyl</td>
<td>4-MeOC₆H₄</td>
<td>70.13</td>
<td>195-197</td>
<td>C₂₉H₂₂ClNO₅ 512</td>
<td>70.38</td>
</tr>
<tr>
<td>16</td>
<td>5p</td>
<td>6-CH₃</td>
<td>4-ClC₆H₄</td>
<td>73.35</td>
<td>174-176</td>
<td>C₂₆H₁₉Cl₂NO₄ 480</td>
<td>65.01</td>
</tr>
<tr>
<td>17</td>
<td>5q</td>
<td>7-CH₃</td>
<td>4-ClC₆H₄</td>
<td>69.93</td>
<td>132-133</td>
<td>C₂₆H₁₉Cl₂NO₄ 480</td>
<td>65.01</td>
</tr>
<tr>
<td>18</td>
<td>5r</td>
<td>6-Cl</td>
<td>4-ClC₆H₄</td>
<td>88.12</td>
<td>175-177</td>
<td>C₂₅H₁₆Cl₃NO₄ 500</td>
<td>59.96</td>
</tr>
<tr>
<td>19</td>
<td>5s</td>
<td>5,6-Benzoyl</td>
<td>4-ClC₆H₄</td>
<td>67.56</td>
<td>122-124</td>
<td>C₂₉H₂₂Cl₂NO₄ 516</td>
<td>67.45</td>
</tr>
<tr>
<td>20</td>
<td>5t</td>
<td>7,8-Benzoyl</td>
<td>4-ClC₆H₄</td>
<td>71.46</td>
<td>180-182</td>
<td>C₂₉H₂₂Cl₂NO₄ 516</td>
<td>67.45</td>
</tr>
<tr>
<td>21</td>
<td>5u</td>
<td>6-CH₃</td>
<td>4-BrC₆H₄</td>
<td>77.16</td>
<td>167-168</td>
<td>C₂₆H₁₉BrClNO₄ 524</td>
<td>59.51</td>
</tr>
<tr>
<td>22</td>
<td>5v</td>
<td>7-CH₃</td>
<td>4-BrC₆H₄</td>
<td>69.78</td>
<td>237-238</td>
<td>C₂₆H₁₉BrClNO₄ 524</td>
<td>59.51</td>
</tr>
<tr>
<td>23</td>
<td>5w</td>
<td>6-Cl</td>
<td>4-BrC₆H₄</td>
<td>64.68</td>
<td>159-160</td>
<td>C₂₆H₁₉BrCl₂NO₄ 545</td>
<td>55.07</td>
</tr>
<tr>
<td>24</td>
<td>5x</td>
<td>5,6-Benzoyl</td>
<td>4-BrC₆H₄</td>
<td>80.34</td>
<td>192-193</td>
<td>C₂₉H₁₉BrClNO₄ 560</td>
<td>62.11</td>
</tr>
<tr>
<td>25</td>
<td>5y</td>
<td>7,8-Benzoyl</td>
<td>4-BrC₆H₄</td>
<td>70.23</td>
<td>230-231</td>
<td>C₂₉H₁₉BrClNO₄ 560</td>
<td>62.11</td>
</tr>
</tbody>
</table>
The present synthetic strategy begins with the generation of required 4-bromomethylcoumarins (1a-e) by Pechmann cyclization of phenols with 4-bromoacetoacetate. Condensation of (1a) with 4-hydroxy benzaldehyde in presence of anhydrous K$_2$CO$_3$ yielded (2-oxo-2H-chromen-4-ylmethoxy) benzaldehydes (2a-e). In the IR Spectrum of 4-(2-oxo-2H-chromen-4-ylmethoxy)-benzaldehyde (2a), the lactone carbonyl stretching frequency was observed at 1718 cm$^{-1}$, whereas the aldehydic carbonyl stretching appeared at 1690 cm$^{-1}$. In the $^1$H NMR spectrum of compound (2a), a singlet was observed at $\delta$ 2.38 ppm due to C$_6$-CH$_3$ protons. The C$_4$-CH$_2$ protons were observed downfield as a singlet at $\delta$ 5.31 ppm. The C$_3$-H of coumarin appeared at $\delta$ 6.64 ppm. The aldehydic proton appeared as a singlet at $\delta$ 9.95 ppm. The $^{13}$C NMR spectral data of compound (2a) is given in the experimental section. In view of the poor reactivity of the p-carbonyl group observed in 4-aryloxymethyl coumarins, pre-functionalized phenols (3a-e) (obtained by the reaction of p-formyl phenol and aromatic amines) were used for room temperature allylic S$_N$ reaction under standard acetone, K$_2$CO$_3$ conditions generating the required precursors (4a-y) in high yields. The IR spectrum of 6-Methyl-4-(4-phenyliminomethyl-phenoxymethyl)-chromen-2-one (4a) (R = 6-CH$_3$, R$_1$ = H) showed lactone carbonyl stretching frequency at 1709 cm$^{-1}$ and stretching frequency for C=N group at 1615 cm$^{-1}$. The PMR spectrum of (4a) exhibited a singlet due to -CH$_3$
protons at $\delta$ 2.24 ppm, C$_4$-CH$_2$ at $\delta$ 5.16 ppm and C$_3$-H at $\delta$ 6.33 ppm. The aromatic protons resonated in the range of $\delta$ 7.04-8.32 ppm. The azomethine proton appeared downfield as a singlet at $\delta$ 9.85 ppm. The azomethine group in (4a-y) underwent cycloaddition with chloroacetylchloride in presence of triethylamine (Et$_3$N) as a catalyst in dioxane afforded 3-Chloro-4-[4-(2-oxo-2H-chromen-4-ylmethoxy)-phenyl]-1-phenyl-azetidin-2-ones (5a-y) (Scheme-1). The IR spectrum of 3-Chloro-4-[4-(6-methyl-2-oxo-2H-chromen-4-ylmethoxy)-phenyl]-1-phenyl-azetidin-2-one (5a), the bands at 1768 cm$^{-1}$ (C=O of $\beta$-lactum) and coumarin carbonyl stretching at 1722 cm$^{-1}$. In the PMR spectra of compound (5a), the doublet peak was observed at $\delta$ 5.34 ppm due to the >CH-Cl in the $\beta$-lactam ring; in $^{13}$C NMR spectra of compound (5a), peaks at $\delta$ 53.3 ppm was observed due to >CH-Cl, 184.4 ppm (cyclic, >C=O) and 162.1 ppm (heteroaromatics) in the $\beta$-lactam moiety. The mass spectra of compound (5a) showed the molecular ion peak at 445[M]$^+$. The various new compounds synthesized during the present investigation are listed in Table-1.

**4-(6-Methyl-2-oxo-2H-chromen-4-ylmethoxy)-benzaldehyde (2a)**

![Structure of 4-(6-Methyl-2-oxo-2H-chromen-4-ylmethoxy)-benzaldehyde](image)

Colourless solid, m.p.218-219 °C, IR (KBr, $v$ cm$^{-1}$): 3046 (=$CH-$), 2778 (CH of CHO) 1718 (C=O of coumarin), 1690 (C=O of aldehyde), 1534 (C=C) cm$^{-1}$, 1022 (C-O-C); $^1$H NMR (300MHz, CDCl$_3$, $\delta$ ppm): 2.38 (s, 3H, CH$_3$), 5.31 (s, 2H, CH$_2$O), 6.64 (s, 1H, C$_3$H), 7.12-7.97 (m, 7H, Ar-H), 9.95 (s,1H, CHO); $^{13}$C NMR (75 MHz, CDCl$_3$, 118
4-(7-Methyl-2-oxo-2H-chromen-4-ylmethoxy)-benzaldehyde (2b)

Colourless solid, m.p. 223-225°C, IR (KBr, ν cm⁻¹): 2922 (=CH-), 2858 (CH of -CHO), 1722 (C=O of coumarin), 1685 (C=O of aldehyde), 1606 (C=C), 1022 (C-O-C) cm⁻¹; ¹H NMR (300MHz, CDCl₃, δ ppm): 1.73 (s, 3H, CH₃), 5.31 (s, 2H, CH₂O), 6.60 (s, 1H,C₃H), 7.11-7.91 (m, 7H, Ar-H), 9.93 (s, 1H, CHO); ¹³C NMR (75 MHz, δ ppm, CDCl₃): 18.6, 71.6, 110.4, 113.80, 119.3, 128.1, 129.0, 129.9, 131.5, 148.2, 155.4, 159.6, 166.3, 172.0; ESI-MS: 294 (M⁺); Anal. Calcd for C₁₈H₁₄O₄: C, 73.45; H, 4.76; Found C, 73.46; H, 4.80 %.

4-(6-chloro-2-oxo-2H-chromen-4-ylmethoxy)-benzaldehyde (2c)

Colourless solid, m.p. 220-222°C, IR (KBr, ν cm⁻¹): 3062 (=CH-), 2808 (CH of CHO), 1722 (C=O of coumarin), 1698 (C=O of aldehyde), 1571 (C=C), 1021 (C-O-C) cm⁻¹; ¹H NMR (300MHz, CDCl₃, δ ppm): 5.25 (s, 2H, CH₂O), 6.73 (s, 1H,C₃H), 7.21-7.91 (m, 7H, Ar-H), 9.90 (s, 1H, CHO); ¹³C NMR (75 MHz, CDCl₃, δ ppm): 83.4, 110.0, 116.0, 126.0, 135.1, 138.3, 148.2, 158.4, 161.0, 167.7, 192.0; ESI-MS: 315 [M+1]⁺; Anal. Calcd for C₁₇H₁₁ClO₄: C, 64.87; H, 3.57, Cl, 11.28; Found C, 64.91; H, 3.62, Cl, 11.32 %.
4-(3-Oxo-3H-benzo[f]chromen-1-ylmethoxy)-benzaldehyde (2d)

Light yellow solid, m.p.222-224°C, IR (KBr, \( \nu \) cm\(^{-1} \)): 3080 (=CH-), 2836 (CH of -CHO), 1712 (C=O of coumarin), 1695(C=O of aldehyde), 1562 (C=C), 1031 (C-O-C) cm\(^{-1} \); \(^1\)H NMR (300MHz, CDCl\(_3\), \( \delta \) ppm): 5.75 (s, 2H, CH\(_2\)), 6.94 (s, 1H, C\(_3\)-H), 7.13-8.15 (m, 10H, Ar-H), 8.96 (s, 1H, -CHO); \(^13\)C NMR (75 MHz, CDCl\(_3\), \( \delta \) ppm): 73.4, 101.2, 111.3, 115.0, 116.4, 120.8, 122.1, 125.3, 127.6, 128.9, 129.7, 130.6, 135.5, 145.7, 157.5, 166.3, 178.2; ESI-MS: 330 (M\(^+\)); Anal. Calcd for C\(_{21}\)H\(_{14}\)O\(_4\): C, 76.34; H, 4.24; Found C, 76.37; H, 4.21%.

4-(2-Oxo-2H-benzochromen-4-ylmethoxy)-benzaldehyde (2e)

Light reddish crystals, m.p.248-249°C, Yield 77%; IR (KBr, \( \nu \) cm\(^{-1} \)): 3052 (=CH-), 1718 (C=O of coumarin), 1707 (C=O of aldehyde), 1569 (C=C), 1028 (C-O-C) cm\(^{-1} \); \(^1\)H NMR (300MHz, CDCl\(_3\), \( \delta \) ppm): 5.48 (s, 2H, CH\(_2\)), 6.80 (s, 1H,C\(_3\)-H), 7.08-8.89 (m, 10H, Ar-H), 9.92 (s,1H, CHO); \(^13\)C NMR (75 MHz, CDCl\(_3\), \( \delta \) ppm): 76.7, 103.5, 111.1, 114.7, 115.0, 119.5, 121.4, 122.9, 126.8, 127.5, 128.1, 129.0, 129.4, 130.3, 135.6, 146.5, 156.7, 159.7, 173.5; ESI-MS: 330 (M\(^+\)); Anal. Calcd for C\(_{21}\)H\(_{14}\)O\(_4\): C, 76.34; H, 4.24; Found C, 76.34; H, 4.25%.
6-Methyl-4-(4-phenyliminomethyl-phenoxymethyl)-chromen-2-one (4a)

Colorless crystals from DMF;
Yield 81%; m.p. 215–217 °C;
IR (KBr, \( \nu \text{ cm}^{-1} \)):
- 3087 (=CH),
- 1718 (C=O of coumarin),
- 1605 (C=C),
- 1123 (C-O-C) cm\(^{-1}\);
\(^1\)H NMR (300MHz, DMSO-d\(_6\), \( \delta \) ppm):
- 2.32 (s, 3H, C\(_6\)-CH\(_3\)),
- 5.31 (s, 2H, CH\(_2\)-O),
- 6.43 (s, 1H, C\(_3\)-H),
- 7.10-8.32 (m, 12H, Ar-H),
- 9.83 (s, 1H, -CH=N);
\(^{13}\)C NMR (75 MHz, DMSO-d\(_6\), \( \delta \) ppm):
- 18.8,
- 77.03,
- 103.06,
- 112.20,
- 118.12,
- 121.20,
- 122.6,
- 125.56,
- 126.30,
- 127.2,
- 128.5,
- 130.31,
- 132.10,
- 145.12,
- 153.0,
- 157.21,
- 160.02,
- 161.12,
- 163.42;
ESI-MS: 370 [M+1]\(^+\); Anal.
Calcd for C\(_{24}\)H\(_{19}\)N\(_3\)O\(_3\): C, 78.01; H, 5.14, N, 3.79; Found C, 78.04; H, 5.17, N, 3.81%.

6-Chloro-4-(4-phenyliminomethyl-phenoxymethyl)-chromen-2-one (4c)

Colorless crystals from DMF;
Yield 77%; m.p. 233–234 °C;
IR (KBr, \( \nu \text{ cm}^{-1} \)):
- 2922 (=CH),
- 1721 (C=O of coumarin),
- 1608 (C=N),
- 1513 (C=C),
- 1154 (C-O-C);
\(^1\)H NMR (300MHz, DMSO-d\(_6\), \( \delta \) ppm):
- 5.16 (s, 2H, CH\(_2\)-O),
- 6.26 (s, 1H, C\(_3\)-H),
- 6.85-8.05 (m, 12H, Ar-H),
- 9.13 (s, 1H, -CH=N) ppm;
\(^{13}\)C NMR (75 MHz, DMSO-d\(_6\), \( \delta \) ppm):
- 80.12,
- 105.23,
- 113.16,
- 120.03,
- 121.36,
- 122.0,
- 124.13,
- 125.32,
- 126.2,
- 127.4,
- 129.23,
- 134.10,
- 146.23,
- 151.45,
- 155.32,
- 159.32,
- 160.87,
- 166.32;
ESI-MS: 390 [M+1]\(^+\); Anal.
Calcd for C\(_{23}\)H\(_{16}\)N\(_3\)O\(_3\): C, 70.93; H, 4.11, N, 3.59; Found C, 70.96; H, 4.09, N, 3.62%.
Azetidinone Derivatives

4-(4-phenyliminomethyl-phenoxymethyl)-benzo[h] chromen-2-one (4e)

Reddish colour crystals from DMF; Yield 83%; m.p. 203-204 °C; IR (KBr, ν cm⁻¹): 3034(=CH) 1719 (C=O of coumarin), 1622 (C=N), 1519 (C=C), 1122 (C-O-C); ¹H NMR (300MHz, DMSO-d₆, δ ppm): 4.94 (s, 2H, CH₂-O), 6.19 (s, 1H, C₃-H), 6.88-8.23 (m, 15H, Ar-H), 8.76 (s, 1H, -CH=N) ppm; ¹³C NMR (75 MHz, DMSO-d₆, δ ppm) 70.21, 100.95, 110.20, 116.07, 119.67, 121.05, 121.37, 122.18, 123.32, 124.00, 125.65, 126.54, 128.54, 131.45, 133.65, 144.45, 152.31, 157.43, 160.06, 163.23, 167.18; ESI-MS: 406 [M+1]⁺; Anal. Calcd for C₂₇H₁₉NO₃: C, 79.97; H, 4.68, N, 3.45; Found C, 79.99; H, 4.71, N, 3.47%.

7-Methyl-4-(4-(p-tolylimino-methyl)-phenoxymethyl)-chromen-2-one (4g)

Colourless crystals from DMF; 3067 (=CH), 1709 (C=O coumarin), 1611 (C=N), 1507 (C=C), 1109 (C-O-C) cm⁻¹; ¹H NMR (300MHz, DMSO-d₆, δ ppm): 1.87 (s, 3H, C₇-CH₃), 2.34 (s, 3H, CH₃), 5.07 (s, 2H, CH₂-O), 6.23 (s, 1H, C₃-H), 6.89-7.66 (m, 11H, Ar-H), 9.03 (s, 1H, -CH=N) ppm; ¹³C NMR (75 MHz, DMSO-d₆, δ ppm) 15.9, 22.5, 78.12, 104.65, 113.45, 119.65, 121.45, 122.32, 124.56, 125.32, 126.54, 129.32, 130.5, 136.65, 137.54, 149.32, 150.12, 156.45, 159.65, 162.32, 165.43; ESI-MS: 384 [M+1]⁺; Anal. Calcd for C₂₅H₂₁NO₃: C, 78.29; H, 5.48, N, 3.65; Found C, 78.32; H, 5.50, N, 3.67%.
**1-(4-p-Tolylimino-methyl)-phenoxymethyl]-benzo [f] chromen-3-one (4i)**

Yellow colour crystals from DMF; Yield 83%; m.p. 224-225 °C; IR (KBr, v cm⁻¹): 3067 (=CH), 1722 (C=O coumarin), 1614 (C=N), 1523 (C=C), 1116 (C-O-C); ¹H NMR (300MHz, DMSO-d₆, δ ppm): 4.57 (s, 2H, CH₂-0), 6.33 (s, 1H, C₃-H), 7.05-8.34 (m, 14H, Ar-H), 9.04 (s, 1H, -CH=N); ¹³C NMR (75 MHz, DMSO-d₆, δ, ppm): 16.9, 77.43, 103.43, 112.30, 115.15, 116.43, 119.32, 120.06, 121.34, 122.54, 124.00, 124.96, 127.23, 128.36, 129.83, 130.23, 132.54, 147.23, 149.33, 155.32, 159.06, 160.25, 162.32; ESI-MS: 420 [M+1]⁺; Anal. Calcd for C₂₈H₂₁N₀₃: C, 80.16; H, 5.01, N, 3.34; Found C, 80.18; H, 5.03, N, 3.32 %.

**4-{4-[4-Methoxy-phenylimino)-methyl]-phenoxymethyl]-6-methylchromen-2-one (4k)**

Yield 69%; m.p. 205-206 °C; IR (KBr, v cm⁻¹): 3024 (=CH), 1712 (C=O coumarin), 1613 (C=N), 1512 (C=C), 1114 (C-O-C); ¹H NMR (300MHz, DMSO-d₆, δ ppm): 2.32 (s, 3H, C₆-CH₃), 3.13 (s, 3H, OCH₃), 4.87 (s, 2H, CH₂-0), 6.23 (s, 1H, C₃-H), 6.83-7.65 (m, 11H, Ar-H), 8.65 (s, 1H, -CH=N); ¹³C NMR (75 MHz, DMSO-d₆, δ, ppm): 19.14, 51.23, 79.34, 101.32, 111.43, 115.55, 119.23, 121.32, 123.13, 125.78, 126.84, 128.76, 130.32, 133.13, 143.23, 146.67, 156.32, 159.54, 161.23, 165.31, 166.43; ESI-MS: 400 [M+1]⁺; Anal. Calcd for C₂₅H₂₁NO₄: C, 75.15; H, 5.26, N, 3.50; Found C, 75.18; H, 5.29, N, 3.53%.
4-{4-[(4-Methoxy-phenylimino)-methyl]-phenoxymethyl}-benzo[h] chromen-2-one (4o)

Reddish crystals from DMF; Yield 65%; m.p. 203-204 °C; IR (KBr, v cm⁻¹): 1728 (C=O coumarin), 1603 (C=N), 1515 (C=C), 1132 (C-O-C); ¹H NMR (300MHz, DMSO-d₆, δ ppm): 3.59 (s, 3H, OCH₃), 4.81 (s, 2H, CH₂-O), 6.51 (s, 1H, C₃-H), 6.72-7.83 (m, 14H, Ar-H), 8.97 (s, 1H, -CH-N); ¹³C NMR (75 MHz, DMSO-d₆, δ ppm) 54.04, 77.19, 104.55, 114.24, 115.54, 117.88, 120.45, 121.46, 122.92, 124.58, 127.43, 130.05, 134.65, 145.65, 150.54, 157.33, 159.63, 160.04, 163.45, 164.23; ESI-MS: 436 [M+1⁺]; Anal. Calcd for C₂₈H₂₁NO₄: C, 77.23; H, 4.86, N, 3.21; Found C, 77.26; H, 4.88, N, 3.24 %.

4-{4-[(4-Chloro-phenylimino)-methyl]-phenoxymethyl}-6-methyl-chromen-2-one (4p)

Colorless crystals from DMF; Yield 69%; m.p. 244-245 °C; IR (KBr, v cm⁻¹): 1709 (C=O coumarin), 1615 (C=N), 1502 (C=C), 1109 (C-O-C) cm⁻¹; ¹H NMR (300MHz, DMSO-d₆, δ ppm): 2.24 (s, 3H, C₆-CH₃), 5.16 (s, 2H, CH₂-O), 6.33 (s, 1H, C₃-H), 7.04-8.32 (m, 11H, Ar-H), 9.85 (s, 1H, -CH=N) ppm; ¹³C NMR (75 MHz, DMSO-d₆, δ ppm): 18.8, 81.4, 106.0, 113.6, 119.4, 122.8, 126.9, 128.9, 130.9, 134.6, 135.8, 146.8, 150.7, 156.6, 160.1, 162.3, 164.1; ESI-MS: 404 [M+1⁺]; Anal. Calcd for C₂₉H₂₁O₃Cl: C, 71.38; H, 4.49, N, 3.47; Found C, 71.40; H, 4.51, N, 3.50 %.
6-Chloro-4-{4-[4-Chloro-phenylimino]-methyl-phenoxymethyl}-
chromen-2-one (4r)

Colourless crystals from DMF; Yield 72 %; m. p. 214-216 °C; IR (KBr, ν cm⁻¹)
: 1721 (C=O of coumarin), 1612 (C=N); ¹H NMR (300MHz, DMSO-d₆, δ ppm): 4.59 (s, 2H, CH₂-O), 6.38 (s, 1H, C₃-H), 6.94-7.92 (m, 11H, Ar-H), 9.95 (s, 1H, -CH=N) ppm; ¹³C NMR (75 MHz, δ ppm, DMSO-d₆): 75.5, 109.1, 111.3, 116.9, 120.3, 124.7, 126.2, 129.3, 134.7, 136.3, 146.5, 147.5, 154.1, 157.4, 160.0, 162.3; ESI-MS: 425 [M+1]⁺; Anal. Calcd for C₂₃H₁₅O₃Cl₂N: C, 65.11; H, 3.57; N, 3.30; Found C, 65.13; H, 3.55, N, 3.33 %.

4-{4-[4-Bromo-phenylimino]-methyl-phenoxymethyl}-7-methyl-
chromen-2-one (4v)

Colourless crystals from DMF; Yield 65%; m. p. 245-247 °C; IR (KBr, ν cm⁻¹) : 1724 (C=O of coumarin), 1616 (C=N); ¹H NMR (300MHz, DMSO-d₆, δ ppm): 2.21 (s, 3H, C₇-CH₃), 5.18 (s, 2H, CH₂-O), 6.42 (s, 1H, C₃-H), 7.00-8.25 (m, 11H, Ar-H), 9.17 (s, 1H, -CH=N); ¹³C NMR (75 MHz, δ ppm, DMSO-d₆): 19.7, 80.5, 106.5, 113.8, 117.6, 122.7, 126.7, 128.3, 130.7, 135.8, 138.9, 148.9, 153.2, 156.2, 158.8, 159.2, 161.4; ESI-MS: 449 [M+1]⁺; Anal. Calcd for C₂₄H₁₈O₃Br: C, 64.30, H, 4.05, N, 3.11; Found C, 64.29, H, 4.09, N, 3.11 %.
Azetidinone Derivatives

4-{4-[(4-Bromo-phenylimino)-methyl]-phenoxy-methyl}-benzo[h]chromen-2-one (4y)

Reddish crystals from DMF; Yield 72%; m. p. 237-238 °C;
IR (KBr, v cm⁻¹) : 1731 (C=O of coumarin), 1601 (C=N); ¹H NMR (300MHz, DMSO-d₆, δ ppm): 4.61 (s, 2H, CH₂-O), 6.32 (s, 1H, C₃-H), 6.94-7.92 (m, 14H, Ar-H), 9.64 (s, 1H, -CH=N); ¹³C NMR (75 MHz, δ ppm, DMSO-d₆): 80.3, 107.7, 110.1, 113.3, 116.0, 119.3, 123.3, 125.4, 126.8, 129.2, 131.9, 138.2, 145.3, 151.3, 153.4, 154.7, 157.7, 162.5; ESI-MS: 485 [M+H]+; Anal. Calcd for C₂₇H₁₈O₃BrN: C, 66.95; H, 3.75; N, 2.89; Found C, 66.93; H, 3.77; N, 2.93 %.

3-Chloro-4-{4-(6-methyl-2-oxo-2H-chromen-4-ylmethoxy)-phenyl}-1-phenyl-azetidin-2-one (5a)

Colorless shiny crystals from DMF; IR (KBr, v cm⁻¹): 3089 (=CH-), 1768 (>C=O of β-lactam), 1722 (>C=O of coumarin), 1520 (C=C), 782 (-C-Cl); ¹H NMR (300MHz, CDCl₃, δ ppm): 2.38 (s, 3H, C₆-CH₃), 4.98 (s, 2H, CH₂-O), 5.05 (d, 1H, -N-CH), 5.34 (d, 1H, -CH-Cl), 6.65 (s, 1H,C₃-H), 6.88-7.96 (m, 12H, Ar-H); ¹³C NMR (75 MHz, CDCl₃) δ ppm) : 21.0, 53.3, 62.0, 79.8, 108.4, 115.2, 119.21, 121.2, 125.2, 126.65, 127.21, 128.1, 128.90, 134.0, 135.21, 140.2, 148.4, 158.2, 162.1, 184.4; ESI-MS: 446 [M+H]+.
3-Chloro-4-[4-(7-methyl-2-oxo-2H-chromen-4-ylmethoxy)-phenyl]-1-phenyl-azetidin-2-one (5b)

Colourless crystals from DMF;
IR (KBr, $\nu$ cm$^{-1}$): 3099 (=CH-), 1752 (>C=O of $\beta$-lactam), 1724 (>C=O of coumarin), 1498 (C=C), 752 (-C-Cl) cm$^{-1}$; $^1$H NMR (300MHz, CDCl$_3$, $\delta$ ppm): 2.19 (s, 3H, C$_7$-CH$_3$), 4.21 (s, 2H, CH$_2$-O), 4.55 (d, 1H, -NCH), 5.48 (d, 1H, -CH-C1), 6.56 (s, 1H,C$_3$-H), 7.19-7.55 (m, 12H, Ar-H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ ppm: 23.4, 56.7, 60.4, 82.0, 106.7, 114.0, 119.43, 122.0, 123.32, 125.12, 126.8, 127.23, 128.8, 132.8, 136.12, 142.0, 149.0, 157.7, 160.6, 173.7; ESI-MS: 446 [M+1]$^+$.

3-Chloro-4-[4-(6-chloro-2-oxo-2H-chromen-4-ylmethoxy)-phenyl]-1-phenyl-azetidin-2-one (5c)

Colourless crystals from DMF;
IR (KBr, $\nu$ cm$^{-1}$): 3088 (=CH-), 1765 (>C=O of $\beta$-lactam), 1722 (>C=O of coumarin), 1500 (C=C), 782 (-C-Cl) cm$^{-1}$; $^1$H NMR (300MHz, CDCl$_3$, $\delta$ ppm): 4.79 (s, 2H, CH$_2$-O), 5.20 (d, 1H, -NCH), 5.47 (d, 1H, -CH-C1), 6.40 (s, 1H,C$_3$-H), 7.12- 7.92 (m, 12H, Ar-H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ ppm: 60.2, 63.6, 79.6, 108.3, 113.2, 121.1, 123.6, 126.4, 127.21, 128.02, 128.93, 134.56, 138.62, 145.83, 150.3, 155.9,161.12, 164.4, 178.9; ESI-MS: 466 [M+1]$^+$. 

127
**Azetidinone Derivatives**

3-Chloro-4-[4-(3-oxo-3H-benzo[f]chromen-1-ylmethoxy)-phenyl]-1-phenyl-azetidin-2-one (5d)

- Light yellow crystals from DMF;
- IR (KBr, $\nu$ cm$^{-1}$): 3122 (=CH-), 1762 (>C=O of β-lactam), 1730 (>C=O of coumarin), 1521 (C=C), 792 (-C-Cl) cm$^{-1}$;
- $^1$H NMR (300MHz, CDCl$_3$, $\delta$ ppm): 4.57 (s, 2H, CH$_2$-O), 5.08 (d, 1H, -N-CH), 5.40 (d, 1H, -CH-Cl), 6.36 (s, 1H,C$_3$-H), 6.86- 8.35 (m, 15H, Ar-H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ ppm: 56.75, 64.92, 79.11, 106.63, 110.81, 116.71, 117.23, 120.03, 122.6, 123.34, 124.45, 126.02, 128.23, 128.54, 129.32, 131.23, 133.45, 140.2, 149.62, 151.23, 157.3, 160.1, 161.12, 170.2; ESI-MS: 482 [M+1]$^+$. 

3-Chloro-4-[4-(3-oxo-2H-benzo[h]chromen-4-ylmethoxy)-phenyl]-1-phenyl-azetidin-2-one (5e)

- Reddish crystals from DMF; IR (KBr, $\nu$ cm$^{-1}$): 3122 (=CH-), 1747 (>C=O of β-lactam), 1726 (>C=O of coumarin), 1507 (C=C), 781 (-C-Cl); $^1$H NMR (300MHz, CDCl$_3$, $\delta$ ppm): 4.62 (s, 2H, CH$_2$-O), 5.32 (d, 1H, -N-CH), 5.44 (d, 1H, -CH-Cl), 6.20 (s, 1H, C$_3$-H), 6.70- 7.97 (m, 15H, Ar-H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ ppm: 60.0, 63.5, 80.0, 99.8, 107.2, 113.1, 116.23, 119.23, 120.45, 121.34, 122.04, 125.02, 126.21, 127.12, 128.23, 128.90, 130.3, 134.12, 135.31, 142.03, 148.54, 150.8, 158.7, 160.21, 163.2, 172.0; ESI-MS: 482 [M+1]$^+$. 

128
3-Chloro-4-[4-(6-methyl-2-oxo-2H-chromen-4-ylmethoxy)-phenyl]-1-p-tolyl-azetidin-2-one (5f)

Colourless shiny crystals from DMF; IR (KBr, $\nu$ cm$^{-1}$): 3089 (=CH-), 1749 (>C=O of \(\beta\)-lactam), 1722 (>C=O of coumarin), 1520 (C=C), 782 (-C-C1) cm$^{-1}$; $^{1}$H NMR (300MHz, CDCl$ _3$, $\delta$ ppm): 2.17 (s, 3H, C$_6$-CH$_3$), 2.38 (s, 3H, CH$_3$), 4.57 (s, 2H, CH$_2$-O), 5.12(d, 1H, -N-CH), 5.49 (d, 1H, -CH-C1), 6.55 (s, 1H,C$_3$-H), 6.78-7.75 (m, 11H, Ar-H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ ppm: 19.2, 23.2, 59.1, 63.6, 82.5, 103.6, 110.0, 111.93, 121.2, 125.2, 126.43, 127.1, 128.32, 129.32, 131.28, 134.4, 135.34, 138.23, 140.21, 148.42, 158.26, 160.21, 162.13, 184.44; ESI-MS: 460 [M+1]$^+$. 

3-Chloro-4-[4-(7-methyl-2-oxo-2H-chromen-4-ylmethoxy)-phenyl]-1-p-tolyl-azetidin-2-one (5g)

Colourless shiny crystals from DMF; IR (KBr, $\nu$ cm$^{-1}$): 3102 (=CH-), 1764 (>C=O of \(\beta\)-lactam), 1717 (>C=O of coumarin), 1501 (C=C), 766 (-C-Cl) cm$^{-1}$; $^{1}$H NMR (300MHz, CDCl$_3$, $\delta$ ppm): 2.26 (s, 3H, C$_7$-CH$_3$), 2.41 (s, 3H, CH$_3$), 4.62 (s, 2H, CH$_2$-O), 5.06 (d, 1H, -N-CH), 5.51 (d, 1H, -CH-Cl), 6.40 (s, 1H,C$_3$-H), 6.68- 7.56 (m, 11H, Ar-H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ ppm: 20.0 22.7, 60.3, 63.9, 80.8, 106.0, 109.12, 112.32, 119.01, 122.27, 124.53, 125.50, 126.52, 131.04, 133.03, 136.53, 138.34, 142.23, 150.3, 154.5, 157.7, 160.0, 162.12, 171.3; ESI-MS: 460 [M+1]$^+$. 

129
Azetidinone Derivatives

3-Chloro-4-[4-(6-chloro-2-oxo-2H-chromen-4-ylmethoxy)-phenyl]-1-p-tolyl-azetidin-2-one (5h)

Colourless shiny crystals from DMF; IR (KBr, \( \nu \) cm\(^{-1} \)): 2993 (=CH-), 1759 (>C=O of \( \beta \)-lactam), 1709 (>C=O of coumarin), 1487 (C=C), 804 (-C-Cl) cm\(^{-1} \); \(^1\)H NMR (300MHz, CDCl\(_3\), \( \delta \) ppm): 2.20 (s, 3H, CH\(_3\)), 4.32 (s, 2H, CH\(_2\)-O), 4.78 (d, 1H, -N-CH), 5.37 (d, 1H, -CH-Cl), 6.26 (s, 1H,C\(_3\)-H), 6.82-7.68 (m, 11H, Ar-H); \(^13\)C NMR (75 MHz, CDCl\(_3\)) \( \delta \) ppm: 17.91, 56.04, 61.62, 77.94, 109.10, 112.70, 120.24, 126.02, 127.34, 128.52, 130.04, 134.62, 138.03, 146.03, 158.81, 159.32, 163.3, 169.7; ESI-MS: 481 [M+1]+.

3-Chloro-4-[4-(3-oxo-3H-benzo[f]chromen-1-ylmethoxy)-phenyl]-1-p-tolyl-azetidin-2-one (5i)

Yellow crystals from DMF; IR (KBr, \( \nu \) cm\(^{-1} \)): 3102 (=CH-), 1764 (>C=O of \( \beta \)-lactam), 1726 (>C=O of coumarin), 1507 (C=C), 779 (-C-Cl) cm\(^{-1} \); \(^1\)H NMR (300MHz, CDCl\(_3\), \( \delta \) ppm): 2.17 (s, 3H, CH\(_3\)), 4.47 (s, 2H, CH\(_2\)-O), 5.07 (d, 1H, -N-CH), 5.45 (d, 1H, -CH-Cl), 6.42 (s, 1H,C\(_3\)-H), 6.65-8.06 (m, 14H, Ar-H); \(^13\)C NMR (75 MHz, CDCl\(_3\)) \( \delta \) ppm: 19.4, 52.3, 59.2, 78.6, 106.9, 114.2, 117.4, 120.0, 123.3, 127.0, 129.9, 136.2, 143.4, 148.2, 153.1, 158.7, 160.5, 165.3, 173.0; ESI-MS: 496 [M+1]+.
3-Chloro-4-[4-(2-oxo-2H-benzo[h]chromen-4-ylmethoxy)-phenyl]-1-p-tolyl-azetidin-2-one (5j)

Reddish crystals from DMF; IR (KBr): ν 3115 (=CH-), 1759 (>C=O of β-lactam), 1722 (>C=O of coumarin), 1495 (C=C), 787 (-C-Cl) cm⁻¹; ¹H NMR (300MHz, CDCl₃, δ ppm): 2.25 (s, 3H, CH₃), 4.55 (s, 2H, CH₂-O), 5.12 (d, 1H, -N-CH), 5.52 (d, 1H, -CH-Cl), 6.30 (s, 1H,C₃-H), 6.70-7.91 (m, 14H, Ar-H); ¹³C NMR (75 MHz, CDCl₃) δ ppm: 21.0, 60.1, 64.1, 80.2, 107.0, 112.9, 115.64, 116.34, 120.1, 121.4, 122.8, 124.5, 127.7, 130.2, 133.2, 135.0, 138.6, 150.2, 155.3, 159.1, 160.7, 163.8, 169.6; ESI-MS: 496 [M+H]⁺.

3-Chloro-1-[4-methoxy-phenyl]-4-[4-(6-methyl-2-oxo-2H-chromen-4-ylmethoxy)-phenyl]-azetidin-2-one (5k)

Colourless shiny crystals from DMF; IR (KBr): ν 3089 (=CH-), 1753 (>C=O of β-lactam), 1716 (>C=O of coumarin), 1479 (C=C), 779(-C-Cl) cm⁻¹; ¹H NMR (300MHz, CDCl₃, δ ppm): 2.09 (s, 3H, C₆-CH₃), 3.56 (s, 3H, OCH₃), 4.74 (s, 2H, CH₂-O), 5.05 (d, 1H, -N-CH), 5.51 (d, 1H, -CH-Cl), 6.37 (s, 1H,C₃-H), 6.70-7.88 (m, 11H, Ar-H); ¹³C NMR (75 MHz, CDCl₃) δ ppm: 20.3, 51.9, 60.2, 63.7, 80.8, 107.0, 111.3, 113.8, 120.7, 127.0, 128.6, 140.4, 146.9, 155.3, 158.1, 160.5, 163.0, 171.0; ESI-MS: 477 [M+1]⁺.
Azetidinone Derivatives

3-Chloro-1-[4-methoxy-phenyl]-4-[4-(7-methyl-2-oxo-2H-chromen-4-ylmethoxy)-phenyl]-azetidin-2-one (5I)

Colourless shiny crystals from DMF; IR (KBr, ν cm⁻¹): 3105 (=CH-), 1746 (>C=O of β-lactam), 1710 (>C=O of coumarin), 1501 (C=C), 782 (-C-Cl) cm⁻¹; ¹H NMR (300MHz, CDCl₃, δ ppm): 2.21 (s, 3H, C₇-CH₃), 3.71 (s, 3H, OCH₃), 4.53 (s, 2H, CH₂-O), 4.93 (d, 1H, -N-CH), 5.33 (d, 1H, -CH-C₁), 6.30 (s, 1H, C₃-H), 6.66-7.70 (m, 11H, Ar-H); ¹³C NMR (75 MHz, CDCl₃) δ ppm: 21.0, 47.7, 59.1, 62.0, 83.1, 105.9, 112.1, 115.2, 121.1, 122.5, 124.2, 126.3, 127.2, 128.8, 132.1, 134.7, 138.3, 150.1, 156.0, 159.0, 160.7, 162.3, 169.3; ESI-MS: 477 [M+H]+.

3-Chloro-4-[4-(6-chloro-2-oxo-2H-chromen-4-ylmethoxy)-phenyl]-1-(4-methoxy-phenyl)-azetidin-2-one (5m)

Colourless shiny crystals from DMF; IR (KBr, ν cm⁻¹): 3091 (=CH-), 1747 (>C=O of β-lactam), 1716 (>C=O of coumarin), 1487 (C=C), 779 (-C-Cl) cm⁻¹; ¹H NMR (300MHz, CDCl₃, δ ppm): 3.50 (s, 3H, OCH₃), 4.61 (s, 2H, CH₂-O), 5.04 (d, 1H, -N-CH), 5.41 (d, 1H, -CH-C₁), 6.51 (s, 1H, C₃-H), 6.76-7.88 (m, 11H, Ar-H); ¹³C NMR (75 MHz, CDCl₃) δ ppm: 50.3, 60.2, 63.6, 80.6, 105.9, 113.5, 116.2, 120.4, 121.9, 127.1, 128.5, 130.1, 133.0, 135.1, 145.7, 155.3, 159.2, 160.0, 163.1, 170.7; ESI-MS: 497 [M+H]+.
3-Chloro-1-(4-methoxy-phenyl)-4-[4-(3-oxo-3H-benzo[f]chromen-1-ylmethoxy)-phenyl]-1-p-tolyl-azetidin-2-one (5n)

Yellow crystals from DMF; IR (KBr, v cm\(^{-1}\)): 3118 (=CH-), 1750 (>C=0 of β-lactam), 1731 (>C=O of coumarin), 1515 (C=C), 792 (-C-C\(_1\)) cm\(^{-1}\); \(^1\)H NMR (300MHz, CDCl\(_3\), δ ppm): 3.41 (s, 3H, OCH\(_3\)), 4.53 (s, 2H, CH\(_2\)-O), 5.16(d, 1H, -N-CH), 5.51 (d, 1H, -CH-C\(_1\)), 6.30 (s, 1H,C\(_3\)-H), 6.85-7.91 (m, 14H, Ar-H); \(^13\)C NMR (75 MHz, CDCl\(_3\) δ ppm: 53.1, 60.0, 63.3, 80.4, 108.0, 112.7, 114.7, 121.2, 123.0,126.6, 127.3, 128.9, 133.4, 137.0, 145.3, 150.2, 157.1, 159.7, 163.7, 168.2; ESI-MS: 512 [M+1]\(^+\).

3-Chloro-1-(4-methoxy-phenyl)-4-[4-(2-oxo-2H-benzo[h]chromen-4-ylmethoxy)-phenyl]-azetidin-2-one (5o)

Pale red crystals from DMF; IR (KBr, v cm\(^{-1}\)): 3104 (=CH-), 1763 (>C=O of β-lactam), 1722 (>C=O of coumarin), 1506 (C=C), 786 (-C-Cl) cm\(^{-1}\); \(^1\)H NMR (300MHz, CDCl\(_3\), δ ppm): 3.63 (s, 3H, OCH\(_3\)), 4.67 (s, 2H, CH\(_2\)-O), 4.78 (s, 1H, -N-CH), 5.23 (d, 1H, -CH-C\(_1\)), 6.23 (d, 1H,C\(_3\)-H), 6.76-7.83 (m, 14H, Ar-H); \(^13\)C NMR (75 MHz, CDCl\(_3\) δ ppm: 47.7, 56.3, 61.2, 82.1, 107.3, 113.0, 115.8, 118.2, 121.6, 123.4,126.3, 127.7, 129.2, 133.7, 135.3, 148.3, 156.0, 159.1, 162.3, 170.3; ESI-MS: 512 [M+1]\(^+\).
3-Chloro-1-[4-chloro-phenyl]-4-[4-(6-methyl-2-oxo-2H--chromen-4-ylmethoxy)- phenyl] - azetidin-2-one (5p)

Colourless shiny crystals from DMF, IR (KBr, \( \nu \) cm\(^{-1} \)): 3107 (=CH\(-\)), 1764(>C=O of \( \beta \)-lactam), 1723 (>C=O of coumarin), 1503 (C=C), 782 (-C-Cl) cm\(^{-1} \);

\( ^1 \text{H} \) NMR (300MHz, CDCl\(_3\), \( \delta \) ppm): 2.22 (s, 3H, C\( _6 \)-CH\( _3 \)), 4.63 (s, 2H, CH\(_2\)-O), 4.95 (d, 1H, -N-CH), 5.29 (d, 1H, -CH-C1), 6.21 (s, 1H,C\(_3\)-H), 6.67-7.92 (m, 11H, Ar-H); \( ^{13} \text{C} \) NMR (75 MHz, \( \delta \) ppm, CDCl\(_3\)): 17.9, 57.3, 61.0, 63.7, 80.2, 104.2, 111.2, 119.3, 120.4, 126.3, 129.3, 130.5, 140.4, 147.1, 157.0, 158.7, 162.1, 173.2; ESI-MS: 481 [M+1]+.

3-Chloro-1-[4-chloro-phenyl]-4-[4-(7-methyl-2-oxo-2H--chromen-4-ylmethoxy)- phenyl] - azetidin-2-one (5q)

Colourless shiny crystals from DMF, IR (KBr, \( \nu \) cm\(^{-1} \)): 3089 (=CH\(-\)), 1758 (>C=O of \( \beta \)-lactam), 1703 (>C=O of coumarin), 1489 (C=C), 780 (-C-Cl) cm\(^{-1} \);

\( ^1 \text{H} \) NMR (300MHz, CDCl\(_3\), \( \delta \) ppm): 2.03 (s, 3H, C\( _7 \)-CH\( _3 \)), 4.44 (s, 2H, CH\(_2\)-O), 5.12 (d, 1H, -N-CH), 5.42 (d, 1H, -CH-C1), 5.89 (s, 1H,C\(_3\)-H), 6.76- 7.79 (m, 11H, Ar-H); \( ^{13} \text{C} \) NMR (75 MHz, \( \delta \) ppm, CDCl\(_3\)): 21.0, 57.3, 63.7, 81.2, 102.3, 113.0, 116.8, 121.0, 125.7, 127.8, 132.6, 139.3, 145.9, 156.2, 157.5, 160.4, 167.5; ESI-MS: 481[M+1]+.
3-Chloro-4-[4-(6-chloro-2-oxo-2H-chromen-4-ylmethoxy)-phenyl]-1-(4-chloro-phenyl)-azetidin-2-one (5r)

Colourless shiny crystals from DMF, IR (KBr, v cm\(^{-1}\)): 3089 (=CH\(-\)), 1751 (>C=O of \(\beta\)-lactam), 1718 (>C=O of coumarin), 1497 (C=C), 791 (-C-Cl) cm\(^{-1}\);

\(^1\)H NMR (300MHz, CDCl\(_3\), \(\delta\) ppm): 4.12 (s, 2H, CH\(_2\)-O), 4.79 (d, 1H, -N-CH), 5.19 (d, 1H, -CH-Cl), 6.09 (s, 1H,C\(_3\)-H), 6.59-7.76 (m, 11H, Ar-H);

\(^13\)C NMR (75 MHz, \(\delta\) ppm, CDCl\(_3\)): 53.8, 61.2, 79.3, 107.3, 112.0, 120.3, 122.6, 125.7, 127.2, 129.9, 133.3, 137.3, 146.8, 155.7, 159.8, 163.6, 179.6; ESI-MS: 502 [M+2]\(^+\).

3-Chloro-1-(4-chloro-phenyl)-4-[4-(3-oxo-3H-benzo[f]chromen-1-ylmethoxy)-phenyl]-azetidin-2-one (5s)

Light brown crystals from DMF, IR (KBr, v cm\(^{-1}\)): v 3133 (=CH\(-\)), 1753 (>C=O of \(\beta\)-lactam), 1725 (>C=O of coumarin), 1506 (C=C), 785 (-C-Cl) cm\(^{-1}\);

\(^1\)H NMR (300MHz, CDCl\(_3\), \(\delta\) ppm): 4.34 (s, 2H, CH\(_2\)-O), 4.78 (d, 1H, -N-CH), 5.30 (d, 1H, -CH-Cl), 6.19 (s, 1H,C\(_3\)-H), 6.64-7.83 (m, 14H, Ar-H);

\(^13\)C NMR (75 MHz, \(\delta\) ppm, CDCl\(_3\)): 57.6, 64.1, 80.4, 104.2, 111.8, 115.2, 116.4, 120.1, 124.3, 126.4, 127.7, 130.5, 133.4, 134.6, 139.4, 150.9 156.7, 160.1, 165.7, 171.0; ESI-MS: 518 [M+2]\(^+\).
**3-Chloro-1-(4-chloro-phenyl)-4-[4-(2-oxo-2H-benzo[h]chromen-4-ylmethoxy)-phenyl]-azetidin-2-one (5t)**

Light reddish crystals from DMF, IR (KBr, \(\nu\) cm\(^{-1}\)): 3088 (=\(\text{CH-}\)), 1747 (>\(\text{C=O}\) of \(\beta\)-lactam), 1718 (>\(\text{C=O}\) of coumarin), 1478 (C=C), 779 (-C-Cl) cm\(^{-1}\);

\(^1\)H NMR (300MHz, CDCl\(_3\), \(\delta\) ppm): 4.56 (s, 2H, CH\(_2\)-O), 4.91 (d, 1H, -N-CH), 5.41 (d, 1H, -CH-C1), 6.37 (s, 1H, C3-H), 6.71-7.92 (m, 14H, Ar-H);

\(^{13}\)C NMR (75 MHz, \(\delta\) ppm, CDCl\(_3\)): 53.9, 62.6, 78.3, 102.4, 110.1, 113.9, 115.3, 119.7, 123.5, 125.0, 127.0, 130.8, 132.7, 135.7, 140.7, 147.7, 154.5, 157.7, 160.1, 168.3; ESI-MS: 518 [M+2]\(^+\).

**1-(4-Bromo-phenyl)-3-Chloro-4-[4-(6-methyl-2-oxo-2H-chromen-4-ylmethoxy)-phenyl]-azetidin-2-one (5u)**

Colourless shiny crystals from DMF, IR (KBr, \(\nu\) cm\(^{-1}\)): 3089 (=\(\text{CH-}\)), 1756 (>\(\text{C=O}\) of \(\beta\)-lactam) 1713 (>\(\text{C=O}\) of coumarin), 1457 (C=C), 775 (-C-Cl) cm\(^{-1}\);

\(^1\)H NMR (300MHz, CDCl\(_3\), \(\delta\) ppm): 1.78 (s, 3H, C\(_6\)-CH\(_3\)), 4.57 (s, 2H, CH\(_2\)-O), 4.88 (d, 1H, -N-CH), 5.38 (d, 1H, -CH-C1), 6.09 (s, 1H, C\(_3\)-H), 6.85-7.68 (m, 11H, Ar-H);

\(^{13}\)C NMR (75 MHz, \(\delta\) ppm, CDCl\(_3\)): 20.4, 60.2, 64.6, 77.5, 106.7, 113.9, 116.7, 123.7, 127.7, 129.9, 133.6, 138.9, 147.7, 158.4, 160.1, 161.7, 167.6; ESI-MS: 525 [M+1]\(^+\).
Azetidinone Derivatives

1-(4-Bromo-phenyl)-3-Chloro-4-[4-(7-methyl-2-oxo-2H—chromen-4-ylmethoxy)-phenyl] - azetidin-2-one (5v)

Colourless shiny crystals from DMF, IR (KBr, \( \nu \text{ cm}^{-1} \)): 3105 (\( =\text{CH} - \)), 1747 (>C=O of \( \beta \)-lactam), 1722 (>C=O of coumarin), 1418 (C=C), 779 (-C-Cl) cm\(^{-1}\); \( ^1 \text{H NMR} \) (300MHz, CDCl\(_3\), \( \delta \text{ ppm} \)): 1.92 (s, 3H, \( C_7-\text{CH}_3 \)), 4.39 (s, 2H, \( \text{CH}_2-\text{O} \)), 5.06 (d, 1H, -N-CH), 5.27 (d, 1H, -CH-Cl), 6.22 (s, 1H, C\(_3\)-H), 6.76-7.79 (m, 11H, Ar-H); \( ^{13} \text{C NMR} \) (75 MHz, \( \delta \text{ ppm, CDCl}_3 \)): 21.5, 59.7, 63.3, 82.0, 106.7, 110.7, 117.8, 121.6, 126.7, 128.8, 131.7, 141.6, 146.8, 155.8, 159.1, 160.0, 164.5; ESI-MS: 525 [M+1]^+.

1-(4-Bromo-phenyl)-3-Chloro-4-[4-(6-chloro-2-oxo-2H—chromen-4-ylmethoxy)-phenyl] - azetidin-2-one (5w)

Colourless shiny crystals from DMF, IR (KBr, \( \nu \text{ cm}^{-1} \)): 3078 (\( =\text{CH} - \)), 1749 (>C=O of \( \beta \)-lactam), 1712 (>C=O of coumarin), 1444 (C=C), 789 (-C-Cl) cm\(^{-1}\); \( ^1 \text{H NMR} \) (300MHz, CDCl\(_3\), \( \delta \text{ ppm} \)): 4.34 (s, 2H, \( \text{CH}_2-\text{O} \)), 4.93 (d, 1H, -N-CH), 5.32 (d, 1H, -CH- Cl), 6.26 (s, 1H,C\(_3\)-H), 6.76-7.78 (m, 11H, Ar-H); \( ^{13} \text{C NMR} \) (75 MHz, \( \delta \text{ ppm, CDCl}_3 \)): 57.9, 60.9, 83.1, 106.8, 114.6, 119.6, 121.7, 124.6, 126.9, 130.5, 132.6, 138.2, 143.7, 153.9, 158.1, 160.4, 164.9; ESI-MS: 547 [M+2]^+.
Metidinone (Derivatives)

1-(4-Bromo-phenyl)-3-chloro--4-[4-(3-oxo-3H-benzo[f]chromen-1-ylmethoxy)-phenyl]- azetidin-2-one (5x)

Light yellow crystals from DMF, IR (KBr, $\nu$ cm$^{-1}$): 3110 (=CH-), 1766 (>C=0 of \(\beta\)-lactam), 1720 (>C=O of coumarin), 1454 (C=C), 779 (-C-Cl) cm$^{-1}$; 

$^1$H NMR (300MHz, CDCl$_3$, $\delta$ ppm): 4.60 (s, 2H, CH$_2$-O), 5.13 (d, 1H, -N-CH), 5.37 (d, 1H, -CH-Cl), 6.35 (s, 1H,C$_3$-H), 6.61-7.76 (m, 14H, Ar-H); 

$^{13}$C NMR (75 MHz, $\delta$ ppm, CDCl$_3$): 58.5, 61.9, 78.9, 106.5, 113.9, 114.6, 115.9, 119.6, 124.2,125.9, 127.9, 131.6, 133.0, 134.9, 140.8, 150.3 155.2, 159.5, 160.5, 164.3; ESI-MS: 562 [M+2]$^+$. 

Light brown crystals from DMF, IR (KBr, $\nu$ cm$^{-1}$): 3093 (=CH-), 1757 (>C=O of \(\beta\)-lactum), 1722 (>C=O of coumarin), 1467 (C=C), 787 (-C-Cl) cm$^{-1}$; $^1$H NMR (300MHz, CDCl$_3$, $\delta$ ppm): 4.25 (s, 2H, CH$_2$-O), 5.14 (d, 1H, -N-CH), 5.31 (d, 1H, -CH-Cl), 6.32 (s, 1H,C$_3$-H), 6.73-7.88 (m, 14H, Ar-H); $^{13}$C NMR (75 MHz, $\delta$ ppm, CDCl$_3$): 55.9, 60.7, 79.9, 103.9, 112.0, 113.6, 115.8, 118.9, 122.1,125.7, 126.9, 129.7, 132.5, 135.6, 138.6, 146.7 155.9, 159.6, 160.4, 163.2; ESI-MS: 562 [M+2]$^+$. 

138
Spectrum 1: IR Spectrum of compound (3a).

Spectrum 2: IR Spectrum of compound (2b).
Spectrum 3: $^1$H NMR (300MHz) Spectrum of compound (2b) in CDCl$_3$.

Spectrum 4: IR Spectrum of compound (4b).
Spectrum 5: $^1$H NMR (300MHz) Spectrum of compound (4b) in CDCl$_3$.

Spectrum 6: IR Spectrum of compound (5b).
Spectrum 7: $^1$H NMR (300MHz) Spectrum of compound (5b) in CDCl$_3$.

Spectrum 8: $^{13}$C NMR (75MHz) Spectrum of compound (5b) in CDCl$_3$. 
Spectrum 9: MS Spectrum of compound (5b).
1. H.T. Clarke, J.R. Johnson and R. Robinson, 

2. H. Staudinger, 

3. G. Brotzu, 

4. E.P. Abraham and G.G.F. Newton, 

5. P.H. Lambert and F.W. O'Grady, 

6. A.S. Ghosh, A.K. Kar and M. Kundu, 

7. K. Marumo, A. Tekeda, Y. Nakamura and K. Nakaya, 

8. T.T. Hawarth, A.G. Brown and T.J. King, 


10. A.G. Brown, D.F. Corbett, J. Eglington and T.T. Haworth, 

11. M. Acloea Palafox, J.L. Nunez and M. Gil, 

12. M.S. Manhas, S. Jeng and A.K. Bose, 

13. E.P. Abraham, 
14. R. Nagarajan, L.D. Boeck, R.L. Hamill, C.E. Higgens and K.S. Yang, 
*J. C. S. Chem. Commun.*, 1974, 321

15. C.E. Higgens, R.L. Hamill, T.H. Sands, M.M. Hoehn, N.E. Devis, 
R. Nagarajan and L.D. Boeck, 

16. T. Kanzaki, T. Fukita, H. Shirafuji, Y. Fujisawa and K. Kitano, 

17. T. Kanzaki, T. Fukita, K. Kitano, K. Katamoto, K. Nara and Y. Nakao, 

18. R. Nagarajan, L.D. Boeck, M. Gorman, R.L. Hamill, C.E. Higgens, 
M.M. Hoehn, W.M. Stark and J.J. Whitney, 

19. G. Alhers-Schoenberg, B.H. Arisen and J.L. Smith, 

20. T. W. Miller, R. T. Goegelman, R. G. Weston, I. Putter and F. J. Wolf, 

and G.A. Koppel, 

22. H. Fukase and H. Iwasaki, 

23. T.T. Howarth. A.G. Brown and T.J. King, 
*J. C. S. Chem. Commun.*, 1976, 266.

24. A.G. Brown. T.T. Howarth, I. Stirling and T.J. King, 

25. T. Kikuchi and S. Uyeo, 

26. W.W. Stewart, 

27. M. Hashimoto, T. Komori and I. Kamiya, 
28. T. Takita, Y. Muraoka, T. Yoshioka, A. Fujii, K. Maeda and H. Umezawa,  

29. M.L. Coetzee, G.P. Sartiano, K. Klein and P. Ove,  

30. Y. Muraoka, A. Fujii, T. Yoshioka, T. Takita and H. Umezawa,  

31. H. Staudinger and F. Enke,  
*Die Ketene, Stuttgart*, Germany, 1912.

32. A.K. Sharma and S.N. Mazumdar,  

33. A. Arrieta, F.P. Cassio and B. Lecea,  
*J. Org. Chem.*, 1999, **64** (6), 1831.

34. R. Singh and J.M. Nuss,  

35. J. Anaya, S.D. Gero, M. Grande, J.M. Hernando and N.M. Laso,  

36. R. Joyeau, H. Molines R. Labia and M. Wakselman,  

37. S.R. Woulfe and M.J. Miller,  

38. K. Yoshioka, T. Miyawaki, S. Kishimoto, T. Matsuo and M. Ochiai,  
*J. Org. Chem.*, 1984, **49**(8), 1427.

39. A.J. Mancuso, S.L. Huang and D. Swern,  

40. A.S. Gajare, S.B. Bhawsar, D.B. Shinde and M.S. Shingare,  

41. M. Cardellini, F. Claudi and F.M. Moracci,  
*Synthesis*, 1984, 1070.

42. A.K. Bose, Y.H. Chiang and M.S. Manhas,  


57. D.R. Bender, L.F. Bjeldanes, D.R. Knapp and H. Rapoport, 


59. C.E. Hatch and P.Y. Johnson, 

60. P.Y. Johnson, N.R. Schmuff and C.E. Hatch, 

61. A.K. Mukerjee and R.C. Srivastava, 

62. M. Depoortere, J. Marchandbrynaert and L. Ghosez, 

63. H.H. Wasserman and B.H. Lipshutz, 

64. Myung-ryul Lee, S.S. Stahl and S.H. Gellman, 

   and Elizabeth John, 

66. J. Liang, J.Chen, F. Du, X. Zeng, L. Li, and H. Zhang, 
   *Organic Lett.*, 10.1021/ol901005x (Article in press)

67. G.S. Singh and T. Pheko, 
   *Indian Journal of Chemistry, Section B*, 2008, **47**(1), 159.

68. Girija S. Singh and Patrick Luntha, 

69. F. Broccolo, G. Cainelli, G. Caltabiano, C.E.A. Cocuzzo, 
   and A. Quintavalla, 

70. Ashok Kumar, C.S. Rajput and S.K. Bhati, 
71. K.G. Desai and K.R. Desai, 

72. I. Banik, F.F. Becker and B.K. Banik, 

73. S.K. Bhati1 and Ashok Kumar, 

74. A.K. Halve, D. Bhadauria and R. Dubey, 

75. Y.Wang, H. Zhang, W. Huang, J. Kong, J. Zhou and B. Zhang, 

76. D. Xiao, A. Palani, R. Aslanian, B.A. McKittrick, A.T. McPhail, 
C.C. Correll, P.T. Phelps, J.C. Anthes and D. Rindgen, 

77. A. Urbach, G.G. Muccioli, E. Stern, D.M. Lambert and J.M. Brynaert, 