# SUMMERY

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## Chapter-1 General Introduction

### Coumarin

Chroman or 'Coumarin' is an aromatic heterocyclic organic compound. It is a bicyclic structure, consisting of benzene ring fused to a six member oxygen heteroatom. The benzopyrones can be subdivided into the benzo-α-pyrones to which the coumarin belongs and the benzo-γ-pyrones of which the flavonoids are principal members. Coumarin is generally known as Benzo-2-pyrone or Chromen-2-one. Coumarin comprises a very large class of compounds found throughout the plant kingdom. Coumarin and the benzopyrone is representative of very diverse and potentially useful groups of drugs. These molecules generally have a broad range of technological and biological activities which includes antimicrobial, antifungal, anticancer, anticoagulant and cardiovascular, anti inflammatory, anti viral, antioxidant activities.

The study of coumarin, its various derivatives and other nitrogen containing heterocycles is of great interest for synthesis, antimicrobial, antifungal and anticancer activity.

### Pyridine

Pyridine is a basic heterocyclic organic compound with the chemical formula $C_5H_5N$. It is structurally related to benzene, with one group (=CH-) replaced by a nitrogen atom. Pyridine is a prototypical electron-poor six member ring heterocycle. The pyridine ring occurs in many important compounds including azines and vitamins niacin and pyidoxal.Pyridine is widely used as a precursor to agrochemicals and pharmaceuticals and is also important solvent and reagent. Pyridine is added in ethanol to make it unsuitable for drinking purpose. It is also used in *In Vitro* synthesis of DNA.

**Benzothiazol**

Benzothiazol is among the usually occurring heterocyclic nuclei in many marine and natural plant products. It's a weak base heterocyclic compound. It consist of a 5-member 1, 3 thiadiazole ring fused with a benzene ring and is an aromatic compound with the formula $C_7H_5NS$. Benzothiazol is a privileged bicycliclic ring system with multiple applications. The benzothiazol ring is potential component in nonlinear optics.2-amino benzothiazol scaffold is one of privileged structure in medicinal chemistry.

**Objectives of the Work:**

- Synthesis of coumarin and Naphthopyrone derivatives.
- Synthesis of various amide derivatives from 3-amino methyl pyridine and 3-amino methyl pyridine clubbed with 2-amino benzothiazole moiety.
- Antibacterial and anticancer evaluation of various synthesized compounds.
- The structures of all the synthesized compounds have been established using various analytical methods like IR, $^{1}$H NMR, $^{13}$C NMR, Mass, Elemental analyses and Single Crystal X-Ray Diffraction.

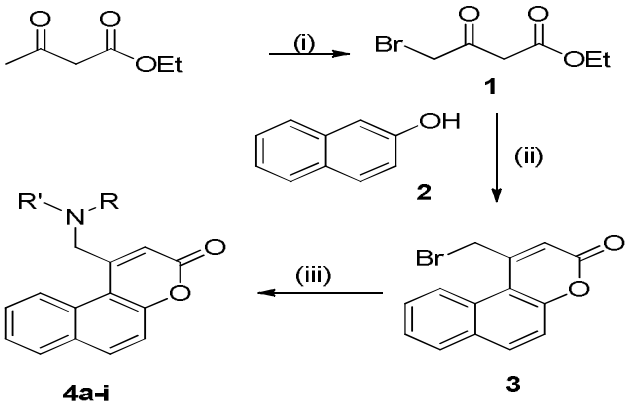
**CHAPTER-2 : Synthesis of some new 4-aminomethy-3[H]-benzo(f)-chromen-3-one derivatives and their antibacterial and anticancer evaluation.**

Naphthopyrone showed various biological activities like non steroidal human progesterone receptor agonists and antihypertensive activity.

**Synthesis of 1-(bromomethyl)-3H-benzo[f]chromen-3-one :**

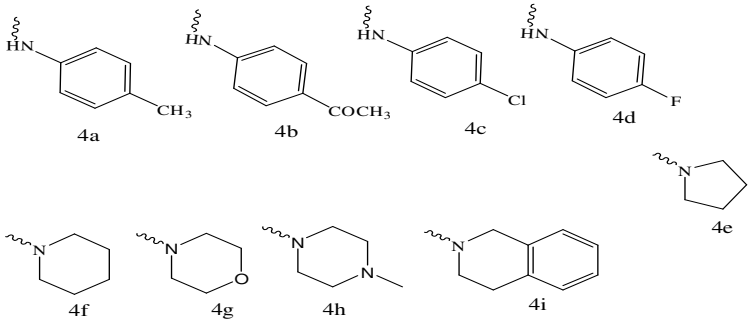
Ethyl 4-bromo-3-oxobutanoate**1** was obtained as red oil by bromination of ethyl acetoacetate using $Br_2$.Thus, obtained compound **1** was used as such for Pechmann reaction with β-naphtho **2** in conc. $H_2SO_4$ to obtain 1-(bromomethyl)-3H-benzo[f]chromen-3-one **3** .The desire compounds were synthesized by substitution reaction of 1-(bromomethyl)-3H-benzo[f]chromen-3-one **3**with different amines.

**Scheme-1**




Reagents & Conditions: (i) $Br_2$, 0 °C to r.t. 18 h; (ii) 2, Conc. $H_2SO_4$, 0 °C to r.t. 48 h; (iii) primary or secondary amine, TEA, DMF, r.t. 16 h.

Where R=




**Confirmation of 4-amino methyl benzocoumarin compound**

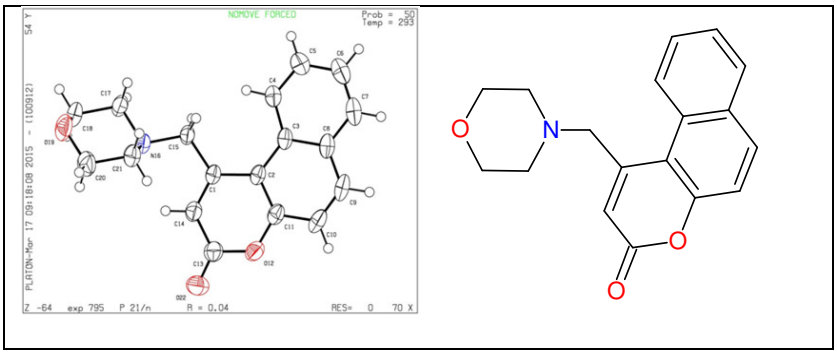



**Figure-1:** Single crystal XRD structure of 1-(morpholin-4-ylmethyl)-3*H*-benzo[*f*]chromen-3-one.

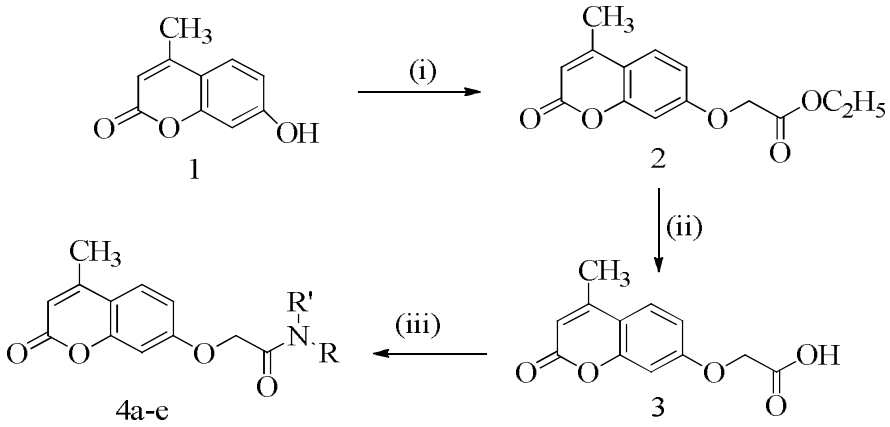
**Antibacterial and anticancer evaluation**: All Synthesized compounds were screened against 2 Gm +ve bacteria, 2 Gm –ve bacteria and one fungus at Micro Care Lab, Surat and also screened for anticancer activity against Brest cancer cell line MCF-75, lung

cancer cell line A549 and melanoma cell line A375 using MTT assay method at Department of Zoology, Faculty of Science, The M. S. University of Baroda.

**CHAPTER-3: Synthesis of some new derivatives of Coumarinyloxy acetamide and their antimicrobial & anticancer evaluation.**

The compounds of this chapter were synthesized by condensing the various substituted aromatic and aliphatic amines with [(4-methyl-2-oxo-2*H*-chromen-7-yl) oxy] acetyl chloride at room temperature.

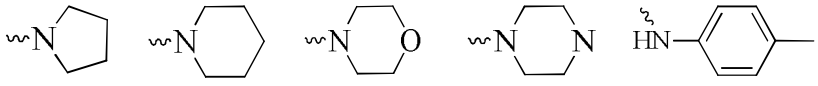
**Scheme-2**




**Scheme-2** Synthesis of carboxy acetamide derivatives of 4-methyl-7-hydroxy coumarin compounds.

**Reagents & Conditions**: (i) $ClCH_2COOC_2H_5$, $K_2CO_3$, DMF reflux; (ii) Ethanolic KOH (15 %), reflux; (iii) (1) ClCOCOCl, DMC at 0-5°C, 30 min, RT,4 h; (2) RR'NH, TEA, DCM.

Where in R, R'=




4a 4b 4c 4d 4e

**Confirmation of 2-(4-methyl-2-oxo-2H-chromen-7-yloxy) acetate intermediate**

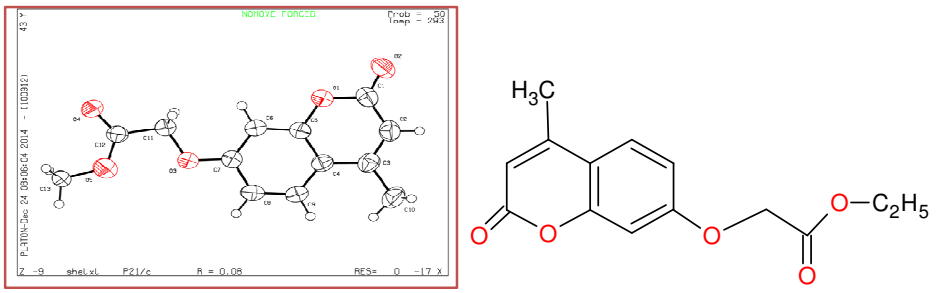
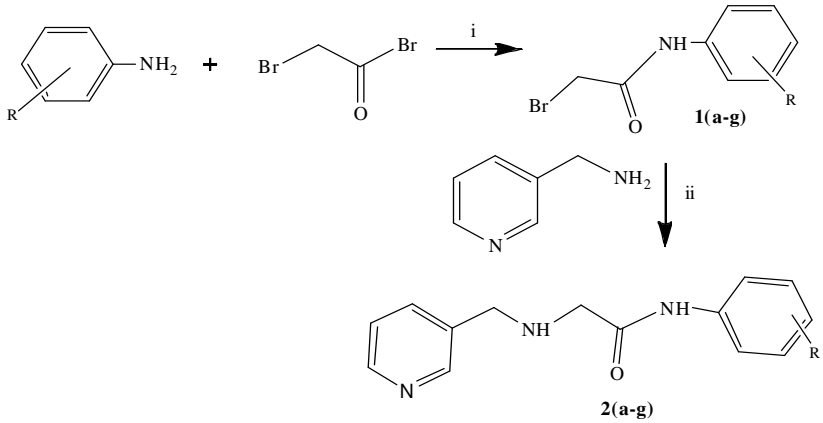


**Figure-2:** Single crystal XRD structure of 2-(4-methyl-2-oxo-2H-chromen-7-yloxy) acetate

**CHAPTER- 4: Synthesis of some new amide derivatives of 3-amino methyl pyridine and their antimicrobial & anticancer evaluation.**

**Scheme-3**



**Scheme-3:** Synthesis of *N*-substituted phenyl-2-[(pyridin-3-ylmethyl) amino] acetamide

**Reagents & conditions:** (i)TEA, Stirring at 0- 5 °C 30 min, RT, 2 h ,DCM ,(ii)TEA, RT Stirring 8h, DMF. Where in R=

| Compound | -R | Compound | -R |
|---|---|---|---|
| **2a** | 4-Cl | **2d** | 4-$CH_3$ |
| **2b** | 4-F | **2e** | 3-F |
| **2c** | 3-Cl | **2f** | 3-$NO_2$ |
| | | **2g** | 4-$COCH_3$ |

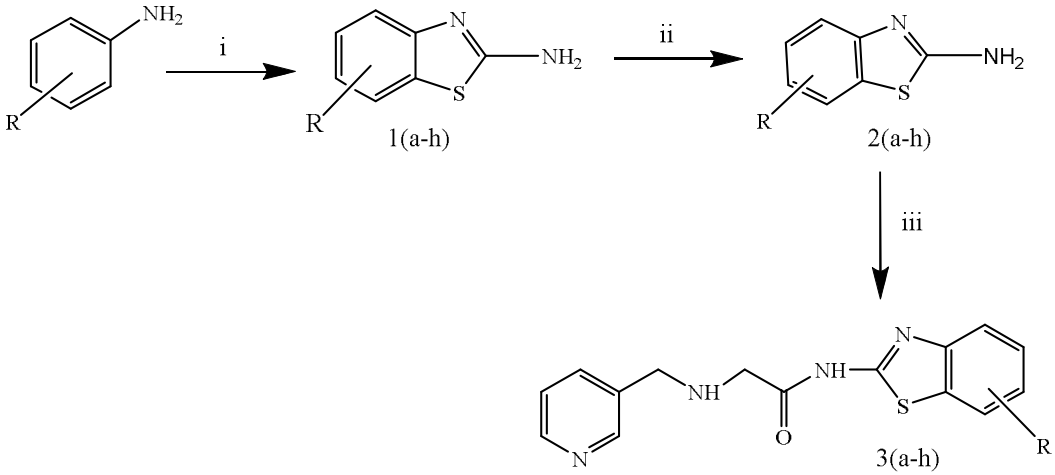
**Antimicrobial and anticancer Evaluation:** All Synthesized compounds were screened against 2 Gm +ve bacteria, 2 Gm –ve bacteria and one fungus at Micro Care Lab, Surat and also screened for anticancer activity against cancer cell lines using MTT assay.

**CHAPTER-5: Synthesis and antimicrobial & anticancer evaluation of some new N-(benzo[d]thiazol-2-yl)-2-{(pyridine-3-yl methyl) amino} acetamide**

Pyridine nucleus has been extensively explored for their applications in the field of Medicine, agriculture and industrial chemistry. Pyridine derivatives are useful as multi drug resistance (MDR) reversal in tumour cell in cancer therapy. A number of important pharmaceuticals also contain the fused rings of pyridine from the basis of some important alkaloids. e.g. quinine and morphine.

Benzothiazole is among the usually occurring heterocyclic nuclei in many marine and natural plant products. It's a weak base heterocyclic compound. It consist of a 5-member 1, 3 thiadiazole ring fused with a benzene ring and is an aromatic compound with the formula $C_7H_5NS$. Benzothiazole is a privileged bicyclic ring system with multiple applications.2-amino benzothiazole scaffolds is one of privileged structure in medicinal chemistry.

**Scheme-4**




**Scheme-4:** Synthesis of various N-(benzo[d] thiazol-2-yl) -2 -{(pyridine-3-ylmethyl) amino} acetamide derivatives.

Where in, R=

| **Compound** | **-R** |
|---|---|
| **3a** | H |
| **3b** | 4-$CH_3$ |
| **3c** | 6-Cl |
| **3d** | 4-Cl |
| **3e** | 6-F |
| **3f** | 6-$OC_2H_5$ |
| **3g** | 6-Br |
| **3h** | 4-$CH_3$-6- $NO_2$ |

**Reagents and Conditions:** (i) KSCN, $Br_2$ in Acetic acid, 0-5°C, RT string, RT 8-10 hrs. Liq. $NH_3$ (25%). (ii) $BrCOCH_2Br$, TEA, DCM, string at 0-5°C; 30min, RT string 10 hrs.(iii) TEA, DMF, 3-amino methyl pyridine, R.T. String 12 hrs.

**Antimicrobial and anticancer Evaluation:**

All the Synthesized compounds were screened against two Gram-Positive bacteria, two Gram- Negative bacteria and one fungus *(C. albicans)* at Micro Care Lab (Advanced Diagnostics), Surat. The anticancer activity of compounds was carried out against one lung cancer cell line A549 and three different leukemic cancer cell lines namely KG1, K562 and MOLT-3 at Department of Bioscience. *Veer Narmad South Gujarat University (*VNSGU).Surat,Gujarat.