Online : ISSN 2349-669X
Print : ISSN 0973-9874

J.Pharm.Chem

CODEN: JPCOCM

# Journal of Pharmacy and Chemistry

(An International Research Journal of Pharmaceutical and Chemical Sciences)
Indexed in Chemical Abstract and Index Copernicus (IC Value 5.28)
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# Journal of Pharmacy and Chemistry

(An International Research Journal of Pharmaceutical and Chemical Sciences)

Volume 15 • Issue 2 April – June 2021

## CONTENTS

# BIOLOGICAL EFFECTS OF VARIOUS HETEROCYCLIC COMPOUNDS

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## ABSTRACT

Heterocyclic compounds are the most numerous and diverse group of organic compounds in the field of organic chemistry. Till date, several heterocyclic compounds are recognized, and the number is exponentially growing due to extensive synthetic research and their synthetic usefulness. These compounds play a vital part in a variety of areas. Mainly in medicinal chemistry and biochemistry. The present review focuses on the synthesis, biological consequences and unexplored enormous biological activities of different heterocyclic compounds.

***Keywords:*** Benzoate, Benzopyrimidine, β-Enaminones, Coumarins, Heterocyclic compounds, Pyrimidinone, Pyrazoles,Quinolones.

## INTRODUCTION

Heterocyclic compounds are cyclic organic compounds that include minimum one heteroatom. The most popular heteroatoms are oxygen, Sulphur and nitrogen, although heterocyclic rings of other heteroatoms are often well-recognized. Due to their activity in a number of diseases, heterocyclic compounds are considered one of the most significant groups of organic compounds that are used in a variety of biological fields. The heterocyclic ring is present in the main skeleton of biological molecules like DNA & RNA, chlorophyll, hemoglobin, vitamins, and many others. Numerous heterocyclic compounds, such as triazine derivatives, being used as anti-microbial herbicides, urinary antiseptics, and anti-inflammatory agents in the treatment of a range of illnesses. Benzimidazole derivatives have been documented to have several biological activities, including antiviral, antifungal, antibacterial and anthelmintic properties [1].

Medical chemistry is a growing field in chemistry as a consequence of the convergence of chemistry with medical problems in an effort to explain modern diseases and how to cure them. Isolating and purifying active materials from plant and animal tissues, as well as microorganisms and their fermentation products, became the object of interest of researchers all over the world when this division of modern chemistry started. Medical chemistry is focused on conventional branches of chemistry, particularly organic chemistry, biology, and even some physics [2]. Heterocyclic compounds play an important function in medicinal chemistry.

Heterocycles have been identified as a crucial structural factor in medicinal chemistry, as well as in biomolecules such as natural products, vitamins, enzymes, and biologically active compounds with antiallergic, antifungal, anti-inflammatory, antioxidant, antidiabetic, antibacterial, anticonvulsant, enzyme inhibitors, herbicidal function, anti-HIV, anticancer properties, and insecticidal agents.

## 1. Coumarins and its derivatives

Coumarins (Fig.1) & its derivatives are a fascinating heterocyclic compoundtype. These compounds are the type of lactone that have a benzenering fused to a pyrone-ring and basically possess a conjugated system througha number of electrons and strong charge-transport property [3]. The coumarin scaffold's flexibility and versatility allow it enticing beginning line fora number offunctions [4]. Coumarins are used forcosmetics, fragrances, and industrial chemicals. Many of their compounds are used for fragrance in tobacco also for alcohols [5]. However, natural goods, organic chemistry, and medical chemistry [6] define their most significant function. Coumarin extraction, synthesis, and assessment has become a very fascinating and increasingly evolving field [7].

Furthermore, several coumarins and its derivatives are being extensively investigated as therapeutic candidates for medications with good pharmaceutical efficiency, low drug toleranceand side effects,broad range, less toxicity, stronger curative effects, high bio-availability and so on, for managing a range of diseases [8]. Numerous attempts have been performed to produce coumarin-based anticoagulants, anti-neurodegenerative, antioxidants [9], antimicrobial (antiviral, antiparasitic and antifungal) [10], analgesic, antidiabetic, and anti-inflammatory agents [11] and anticancer [12].

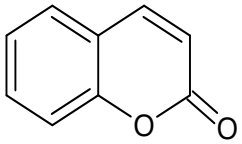


*Fig.1: Structure of 2H-1-benzopyran-2-one*

**a. (6-Fluoro-2-oxo-2H-chromen-4-yl) methyl diethylcarbamodithioate: (Fig. 2)**

The chemical formula of this compound is$C_{15}H_{16}FNO_2S_2$. In the asymmetric unit, this compound crystallized with two separate molecules. The ethyl groups are oriented slightly in both of them. The chromene rings are planar including the highest variance from the ring planes for atoms C9A & C9B, respectively, being 0.014 (2) and 0.018 (2). The carbamodithioate-moiety [(N–C(S)–S] of molecules A or B forms dihedral angles of 80.01 (7) & 76.97 (8) with the mean plane of the chromene ring, respectively. The two molecules are connected in the crystal by C–HS hydrogen bond, creating a ladder structure that propagates along the a-axis. Inside the ladder, there are offset interactions including the B molecules coumarin rings [intercentroid distances range around 3.705 (2) – 3.860 (1) A] [13].

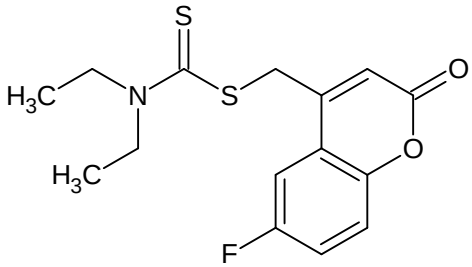


*Fig.2: Structure of (6-fluoro-2-oxo-2H-chromen-4-yl) methyl diethylcarbamodithioate*

**b. (7, 8-Dimethyl-2-oxo-2H-chromen-4-yl) methyl morpholine-4-carbodithioate: (Fig. 3)**

The chromene unit in the title compound, $C_{17}H_{19}NO_3S_2$, forms an 88.48 (5) dihedral angle with the better plane with the morpholine-ring. As shown by the S–C–N–C torsion angle of 171.64(8), the carbodithioate group adopts an antiperiplanar conformationin accordance with the morpholine ring. The chair conformation is adopted by the morpholine moiety. C–HO & C–HS hydrogen bonds, as well as C–H interaction, are found in the crystalline structure [14].

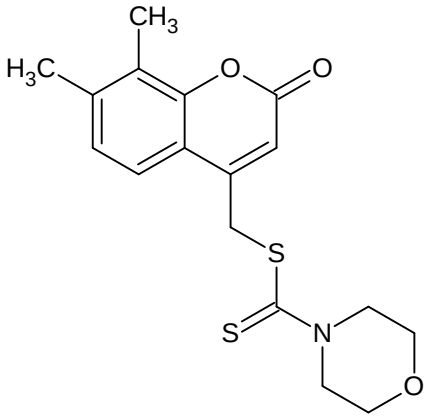


*Fig. 3: Structure of (7,8-dimethyl-2-oxo-2H-chromen-4-yl) methyl morpholine-4-carbodithioate*

## 2. β–Enaminones

β–Enaminones (vinylogous amides) are flexible substances that are utilized for their therapeutic activities as well as building blocks in the syntheses of heterocyclic and natural ingredients [15-19]. Stereoselective syntheses of β–enaminones are highly attractive since their chemical and biological qualities are based on alkene stereochemistry. A propargylic hydroxyl amine (Ar=p-tol, R=n-Bu) could reconfigure within basic requirements to offer the Cbz safe enaminone as a single (Z) diastereomer through initial experiments focused on developing an affected access to trisubstituted isoxazoles [20].

In organic synthesis, β-enaminones have been commonly used as primary intermediates. They have been used as synthons for a broad spectrum of heterocycles [16] and medicinal substances with anti-epileptic[18], molluscicidal, and larvicidal activities [19], as well as intermediates in the synthesis of naturally produced alkaloids. Their significance as useful bioactive compounds, β-enaminone synthesis has gained significant attention. Direct-condensation of b-dicarbonyl compound with amines in refluxing aromatic hydrocarbons with azeotropic elimination of water is the most well-known and commonly utilized path to β-enaminones [20]. Recently, a systematic analysis of all methods for synthesizing the title compounds were released [21]. Evidently, all these methods have significant or minor disadvantages, such as harsh reaction conditions, poor yields, time-consuming work-up techniques, low selectivity, the frequency of several side reactions, and the need for chromatography for adduct purification. Furthermore, since certain Lewis acid catalyzed reactions do not recycle the catalyst, these methods are environmentally unsound, particularly for large-scale reaction [22]. Despite the fact that various methods for synthesizing β-enaminones are usable, the production of another quick, high-yielding, nonpolluting preparation remains crucial.

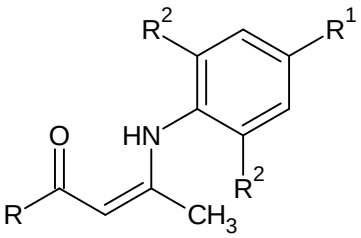


*Fig.4: General structure of β-Enaminones*

**a. (2E)-3-Anilino-1-(2-chlorophenyl)-3-(methylsulfanyl) prop-2-en-1-one. (Fig. 5)**

The dihedral angle between the aromatic rings in the title compound, $C_{16}H_{14}ClNOS$, is 86.34(9) and an intra molecular N–HO hydrogen bond seals a S(6) ring. The Cl atom and the methyl sulfanyl group are on the same side of the molecule. C–HO hydrogen bonds bind the molecules in the crystal, creating (010) double sheets [23].

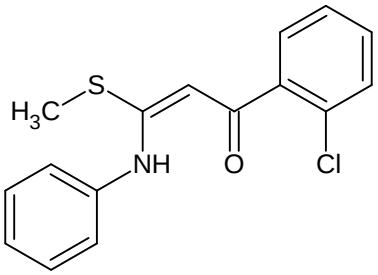


*Fig.5: Structure of (2E)-3-anilino-1-(2-chlorophenyl)-3-(methylsulfanyl) prop-2-en-1-one*

### 3. Benzoate derivatives

Benzoate is the simplest representative of a group of benzoates that comprises a fundamental benzoic acid center that is lacking a proton to yield a -1 charge. It is the benzoic acid's conjugate base. It is a xenobiotic metabolite in humans and a plant metabolite in plants.

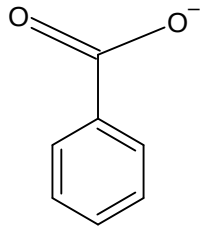


*Fig.6: Structure of Benzoate*

**a. 2-(4-Methylphenyl)-2-oxoethyl 3,4-dimethoxybenzoate. (Fig.7)**

The dihedral angle between the mean planes of the two aromatic rings in the title compound, $C_{18}H_{18}O_5$, is 66.55. Intermolecular C–HO interactions describe the crystal packaging. For the synthesis of this compound, Potassium carbonate was introduced to the 3,4-dimethoxybenzoic acid in water solution and the mixture was mixed for half an hour. Thereafter, the mixture was further heated under reflux for 6 hours with a solution of 2-bromo-1-(p-tolyl) ethanone in ethanol. Ethanol was extracted under decreased pressure after the synthesis was finished. Filtration was used to extract the crystals, and ethanol was used to recrystallize them [24].

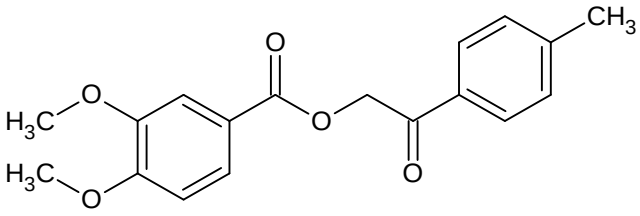


*Fig.7: Structure of 2-(4-methylphenyl)-2-oxoethyl 3,4-dimethoxybenzoate*

**b. Methyl 2-(benzoyloxy)benzoate. (Fig.8)**

The dihedral angle between the two aryl rings in the title compound, $C_{15}H_{12}O_4$, is 68.19 degrees (9). C–H interactions connect molecules in the crystal, creating chains along the b-axis path. The chains are bound by offset π–π interactions [25].

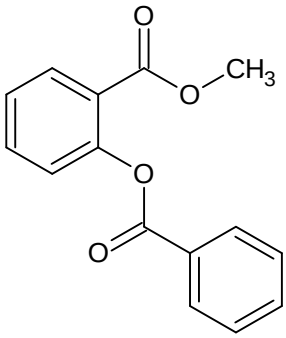


*Fig.8: Structure of methyl 2-(benzoyloxy) benzoate*

### 4. Quinolone derivatives

Quinolones (Fig.9) are a relatively broad, rapidly expanding, and fascinating class of anti-bacterial drugs that have a significant effect on anti-microbial chemotherapy in recent years [26-28]. This is just so they can have all the characteristics of an ideal antibiotic, such as high efficacy, a wide range of action, better bioavailability, oral and intravenous formulations, high serum amounts, a large amount of circulation indicating tissue concentration, and a low risk of side effects.

More studies have been conducted in order to render these possible characteristics a reality.

The first representative of the quinolones, nalidixic acid [29], was discovered as a by-product of antimalarial study in 1962, and it was considered successful against certain Gram-negative micro-organisms and possess pharmaco-kinetic properties for controlling urinary tract infections (UTIs).

Quinolones were a discarded group of anti-microbials, until the development of fluoroquinolones in the 1970-1980. When opposed to previous drugs, fluoroquinolones have a wider range of action and better pharmacokinetics. Quinolones have evolved from a limited and undesirable group of medicines used mostly to treat urinary tract infections (UTIs) to molecules of wide antibacterial action [30].

The number of agents in production has risen dramatically in recent years, with more than 10,000 molecules patented to date. Thousands of molecules have been identified during the next four decades and are now referred to as "quinolones," notwithstanding the fact that they are purely derivatives of any of the 4-quinolone or 1, 8-napthyridine ring structures. As a result, quinolones reflect the new age of antibiotic drug growth. These have undoubtedly contributed on our understanding of anti-microbial science than any other type of antibiotics & anti-microbial chemotherapeutic agents since they have been commonly applied as well as extensively researched.

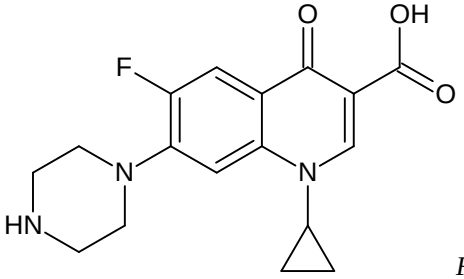


*Fig.9: Structure of 1-cyclopropyl-6-fluoro-4-oxo-7-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid*

**a. 2-(2-Chlorobenzoyl)-1-(3,4-dimethoxyphenyl)-3iodoquinolin-4(1H)-one. (Fig.10)**

The iodoquinolinyl moiety forms dihedral angles of 87.44 (10) and 88.64 (10) degrees with the chloro- and methoxy-substituted benzene rings, respectively, in the title compound $C_{24}H_{17}ClINO_4$. As shown by the C–C–O–C torsion angle values of -16.2 and 177.6°, the methoxy groups are found in synperiplanar& antiperiplanar conformations according to the benzene ring they are attached. The methoxybenzene C–H···O (quinolinyl) hydrogen bonds in the crystal structure are fairly strong, resulting in helical supramolecular chains along the a-axis path. The 3D molecular packing is strengthened by additional C–H···O interactions and stacking [31].

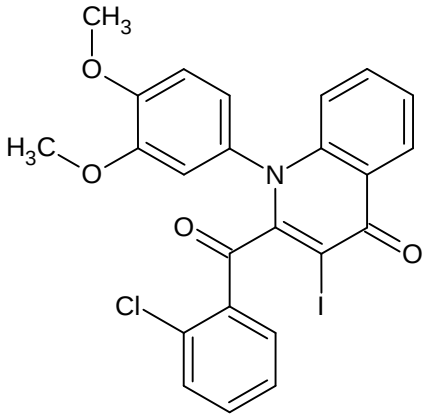


*Fig.10: Structure of 2-(2-chlorobenzoyl)-1-(3,4-dimethoxyphenyl)-3-iodoquinolin-4(1H)-one*

## 5. Acrylonitrile derivatives

Acrylonitrile (Fig.11) is a popular bulk chemical that is used to make a variety of chemicals and polymers. Global annual demand is about 6 million tons, with a current price of about €1900 /ton. Its key industrial development (SOHIO process) is focused on the high temperature (400–500°C) conversion of propene and ammonia in the presence of metal oxide catalysts. Using microwave irradiation, the first example of acrylonitrile synthesis from a non-fossil source (glycerol) was recently published (47 percent conversion, 80 percent selectivity).However, to add the nitrogen functionality, hydrogen peroxide and ammonia were needed.

It is also used in the production of carbon fibers. By using the SOHIO technique, almost all ACN is now made using propylene [32]. However, natural fuels are used to make propylene, which results in CO2 emissions that causes global warming. Finding a viable replacement for limited fossil resources is a major potential obstacle. While biomass is a sustainable resource, there are currently only a few process choices for the development of ACN. [33]

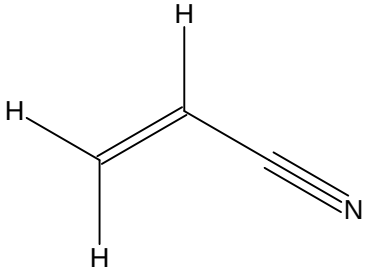


*Fig.11: Structure of prop-2-enenitrile*

**a. 2-(4-chlorophenyl)- 3-(4-methoxyphenyl)-3-(methylsulfanyl)-acrylonitrile. (Fig.12)**

The aromatic rings in the compound, $C_{17}H_{14}ClNOS$, are oriented to one another by 64.22 degrees. The ACN group (C=C–C≡N) is planar within about 0.003Å, with the S and methyl C atoms being displaced 0.2317 and 0.637 Å, respectively, from this plane. Inversion dimers are formed in the crystal as molecules are joined by pairs of C–H···π interactions. There is no other intermolecular interaction that are important [34].

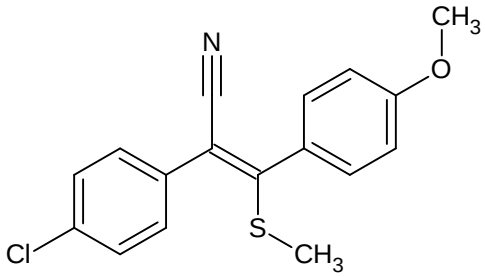


*Fig.12: Structure of 2-(4-chlorophenyl)-3-(4-methoxyphenyl)-3-(methylsulfanyl)-acrylonitrile*

## 6. Pyrazoles

Pyrazoles are 5-membered diazoles aromatic compounds with a wide range of biochemical properties, as well as a long and fascinating background. Indeed, phenazone 1 (Scheme 1), the first pyrazole found, was commercially successful as a pharmaceutical usage. In 1884, the substance was discovered to have antipyretic effects, and the patent rights were sold to Farbwerke. However, it was only recently known as a pyrazole after it hit the market. As Knorr tried to make a tetrahydroquinoline by reacting phenyl hydrazine with acetoacetic ester, he accidentally prepared phenazone.

This heterocyclic motif's popularity has undoubtedly grown as a result of its positive and intriguing start. The synthesis of 1,3-dicarbonyl compounds were quickly discovered to be relevant to production of variousheterocyclic compounds and used in the synthesis of numerous compounds having wide range of applications. The regulation of regiochemistry of N-substituted pyrazoles is a specific drawback of this approach in terms of pyrazole production.

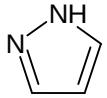


*Fig.13: Structure of 1H-pyrazole*

**a. N'-Benzoyl-5-methyl-1,3-diphenyl-1Hpyrazole-4-carbohydrazide. (Fig.14)**

The pyrazole ring in the compound ($C_{24}H_{20}N_4O_2$) forms dihedral angles of 47.57° & 30.56°, respectivelywith its N-bound and C-bound phenyl groups. The

C–N–N–C group that connects the two carbonyl has an 81.5° torsion angle. The carbonyl groups and their adjacent pyrazole & phenyl rings have torsion angles of 125.89° and 164.22°, respectively. Pairs of molecules are joined in the crystal by N–H···O hydrogen bonds to form $R^2_2(10)$ ring motifs, which then bind to form chains that spread parallel to the c-axis [35].

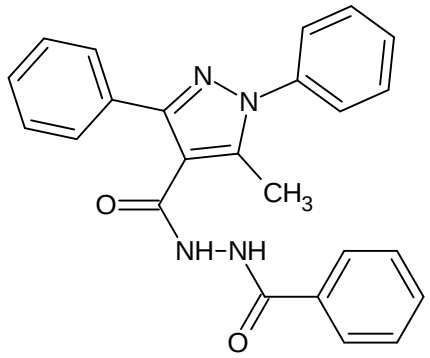


*Fig.14: Structure of N'-benzoyl-5-methyl-1,3-diphenyl-1H-pyrazole-4-carbohydrazide*

CONCLUSION

Heterocyclic compounds have a wide range of application in medicinal chemistry. Its unexplored array of benefits needs to be discovered and put into implication. The present review is an attempt to compile such various compounds and its derivatives. Theseheterocyclic derivatives are believed to have potential actionsagainst fungal and bacterial infection, inflammatory and allergy conditions, cancer, and others. However, the information about these derivatives and its applications are sparsely available in literature widening the scope for future research.

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