

ISSN:2320-3714 Volume:3 Issue:1 July 2022 Impact Factor:5.7 Subject:Science

A Critical analysis on Synthesis of Some New Heterocyclic Compounds

Rahul Sharma Research Scholar

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Abstract

The synthesis of a few brand-new heterocyclic compounds is described in the current paper. Two categories of heterocyclic compounds are the main topics of this paper. Most heterocyclic compounds are known to be either drugs or co-drugs. The two types of heterocyclic compounds are aliphatic and aromatic. A carbocyclic compound is a natural cyclic compound that has carbon particles organized in rings. The cyclic analogs of amines, ethers, thio ethers, amides, and so on are the aliphatic heterocyclics. Heterocyclic substances can be employed as diuretics, anthelmintics, antimalarials, and many other things.

Among the important natural and synthesised chemicals for medicinal use, heterocyclic compounds have a unique niche. For more than a century, the goal of study has been the synthesis of diverse heterocycles. The foundation of medical, chemical, and pharmaceutical research is the chemistry of heterocyclic molecules and the methods used to make them. Heterocyclic nuclei have a remarkable capacity to behave as reactive pharmacophores as well as biomimetic pharmacophores, which has made them essential components of many medications.

Keywords: Heterocyclic compounds, Synthesis, Biological activities, Antibacterial study.



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1. Introduction

In our daily lives, heterocyclic compounds receive a great deal of attention. One or more hetero atoms can be found in the structure of heterocyclic substances. They could have cyclic or non-cyclic characteristics. Applications for heterocyclic compounds are very diverse. They are mostly used as veterinary goods, agrochemicals, and medications. They also explore uses for the materials as co-polymers, dyes, antioxidants, designers, and sanitizers. They serve as the means by which other organic molecules are synthesised. Some natural products, including alkaloids like vinblastine, morphine, and reserpine as well as antibiotics like penicillin and cephalosporin, have a heterocyclic moiety.

Heterocyclic substances are abundant in nature, essential to life, and they play a dynamic part in every living cell's metabolism. Pyrimidines and purines, which are heterocyclic bases, are also found in DNA, the genetic material. Various heterocyclic compounds, both counterfeit and regular, have pharmacological action and are utilized in medication.

Heterocyclic compounds are widely employed in a variety of industries, including those of medicines, agrochemicals, and veterinary products. They are used as sanitizers, designers, antioxidants, corrosion inhibitors, copolymers, and dyestuffs, among other things. They serve as the means by which other organic molecules are synthesised.

With the greater part of all realized synthetic compounds being heterocycles, this gathering of substances is critical. Heterocycles are available in many meds, most of nutrients, various regular items, biomolecules, and biologically dynamic substances, for example, antitumor, antiinfection, calming, stimulant, antimalarial, hostile to HIV, antimicrobial, antibacterial, antifungal, antiviral, antidiabetic, herbicidal, fungicidal, and insecticidal specialists. Moreover, they are commonly found as an essential underlying part in engineered drugs and agrochemicals.

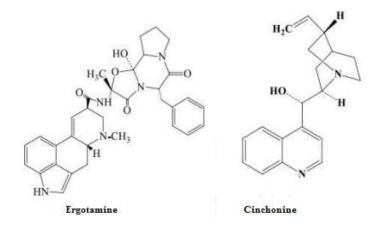
Most of heterocycles have critical purposes in materials science, like colors, fluorescence sensors, brighteners, data capacity specialists, polymers, and logical reagents. They additionally



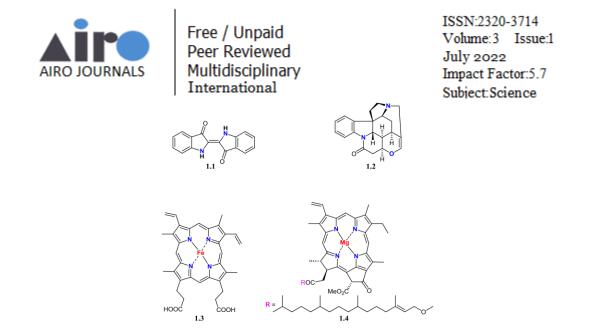
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have utilizes in supramolecular science and polymer science, especially in formed polymers. They additionally capability as natural transmitters, semiconductors, atomic wires, photovoltaic cells, natural light-emanating diodes (OLEDs), light-gathering frameworks, optical information transporters, synthetically programmable switches, and fluid translucent substances.

Due to their synthetic value as organ catalysts, metal ligands, protecting groups, chiral auxiliaries, synthetic intermediates, and synthetic intermediates, heterocycles are also of major importance. Therefore, there has been a lot of focus on creating new, effective processes for making heterocycles. The majority of naturally occurring heterocyclic compounds with diverse biological activities are alkaloids.



Organic synthesis relies heavily on heterocyclic substances. Nearly 50% of all chemical molecules that are now understood have at least one heterocyclic ring. Numerous heterocyclic substances are found in nature and play an important role in biological processes, such as the replication mechanism of nucleic acid bases, which are derived from the pyrimidine and purine ring systems. Numerous dyes and pigments contain a heterocyclic moiety, including indigo (1.1), strychnine (1.2), haemoglobin (1.3), and chlorophyll (1.4). 1 Heterocyclic compounds are also present in certain vitamins, penicillin, and several amino acids like histidine, tryptophan, and proline.



Researchers place great emphasis on the oxygen, nitrogen, and sulfur-bearing heterocycles among the various heterocycles because they include highly stable aromatic compounds with a variety of biological uses, including medicines, agricultural products, veterinary products, as well as sensitizers, developers, antioxidants, and copolymers, among others. Due to their chemotherapeutic potential in the creation of novel antimicrobials, compounds with heterocyclic nuclei have drawn a lot of research in recent years. 4-5 The majority of the heterocyclic compounds from the classes benzimidazole, benzothiazole, benzoxazole, and quinoline that have oxygen, nitrogen, and sulphur as heteroatoms have exhibited a wide range of bioactivities. Due to their easy accessibility, varied chemical reactivity, and wide spectrum of biological functions, these heterocycles have received substantial study.

2. Recent Synthetic Protocols

An incredibly diverse range of scientific fields are impacted by the dynamic and expanding field of organic chemistry. It began as the chemistry of life, which was believed to be distinct from laboratory chemistry. Organic chemistry can be defined as the study of the relationship between a carbon compound's structure and characteristics. Accordingly, "Synthesis is the core of Chemistry." The purpose of organic synthesis is to give this study access to these molecules in a pure form, either by extraction from natural resources or via synthesis.



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One of the pillars of the natural sciences is organic synthesis. Novel approaches and effective pathways for molecule synthesis are provided by synthetic organic chemistry. New organic compounds are produced as a result of excellent synthetic reactions, frequently opening up entirely new chemistries. In the form of pharmaceuticals, food items, cosmetics, dyes, paints, agrochemicals, biomolecules, and high-tech materials like polymers, organic synthesis has produced useful things. With their knowledge and expertise, chemists have created a wide range of new materials that are significantly superior to and more beneficial than natural items, including high-tech polymers, designer pharmaceuticals, genetic materials, and alternative energy sources.

Last but not least, organic synthesis aims to create the most cost-effective path for the industrial synthesis of a good for which there is a clear need. To individuals who perform chemistry in industry, education, and research today, the green chemistry revolution is posing a huge number of obstacles. However, there are just as many possibilities to learn and use new chemistry as there are problems, helping to restore chemistry's badly damaged reputation. In this perspective, I'd like to offer a new concept in chemistry: the task facing modern organic chemists is not just the synthesis of organic compounds, but also the creation of novel, eco-friendly processes.

Green science, otherwise called feasible science, is a way to deal with synthetic designing and exploration that advances the improvement of merchandise and systems that diminish the utilization and creation of perilous compounds. Green science plans to decrease and stay away from contamination at its source, rather than ecological science, which concentrates on the science of the common habitat and of dirtying compounds in nature. Any synthetic decision ought to be made with an eye toward limiting gamble and expanding adequacy. Natural science, which centers around synthetic peculiarities in the climate, is unique in relation to this. Supercritical water oxidation, on-water reactions, and dissolvable free reactions are several events of applied green science. The use of supercritical carbon dioxide as a green dissolvable, liquid hydrogen peroxide for clean oxidations, and the use of hydrogen in upside down combination were the three critical movements in green science noted by Ryoji Noyori in 2005.



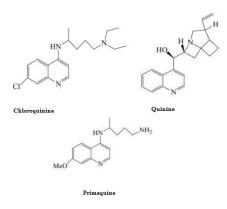
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To obtain the environmental benefits that are now necessary in terms of safe chemistry, chemists and others must devise new methods. This requires a clever methodology that means to build the utilization of inexhaustible assets, broaden item solidness and recyclability, limit or dispense with the arrival of unsafe synthetic compounds into the climate, and lessen the material and energy power of substance cycles and items. The disclosure and advancement of new manufactured pathways utilizing elective feed stocks or more particular science, the distinguishing proof of elective response conditions and the conservation of assets, the evasion of harmful reagents as well as poisonous solvents26 for further developed selectivity and energy minimization, and the plan of less harmful and intrinsically more secure synthetic compounds are a portion of the difficulties looked by scientists.

3. Heterocyclic Compounds' Applications For Biological Activity

3.1. Heterocyclic compounds as antimalarial

One of the most severe, difficult-to-treat diseases that humanity is now dealing with is malaria. The disease affects between 300 million and 500 million people worldwide and results in 120 million clinical cases each year. Without exaggeration, it can be said that the drug quinine has relieved more human suffering than any other inhibitor. One of the most effective antimalarial medications ever created is chloroquinine, a main medication in the 4-aminoquinoline class. The medication of the 8-aminoquinoline class known as primaquinine forms a peptide bond with the amino group in order to bind to amino acids. It is notable that these amino corrosive subsidiaries have higher movement and less poisonousness.





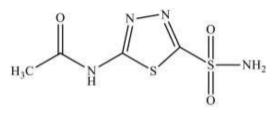
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3.2. Heterocyclic compounds as Diuretic agents

The drugs known as diuretics aid in lowering the body's water content. A strong carbonic anhydrase inhibitor, acetazolamide controls liquid emission in the treatment of a few convulsive problems and advances diuresis when there is strange liquid maintenance. Acetazolamide is a nonbacteriostatic sulfonamide, and that implies that it has a substance structure and pharmacological movement that are totally different from those of bacteriostatic sulfonamides. It is not a mercurial diuretic drug. The carbonic anhydrase enzyme in the central nervous system (CNS) may be directly inhibited by acetazolamide, which would increase arterial oxygen tension via reducing carbon dioxide tension in the pulmonary alveoli. The reduction in hydrogen ions available for active transport in the renal tubule lumen, which results from the inhibition of carbonic anhydrase, is what causes the diuretic action. As a result, the urine becomes more alkaline and the outflow of bicarbonate, salt, potassium, and water increases.

3.3. Heterocyclic compounds as anthelmintic

The parasitic worms known as helminthes are remembered to contaminate two billion individuals universally, only in immature tropical or semitropical countries. Ailing health, iron deficiency, hindered development, mental hindrance, and expanded helplessness to different sicknesses are completely brought about by helminthic diseases.



Acetazolamide

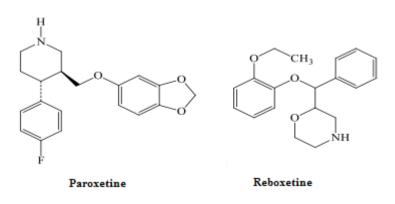
The different sorts of heterocyclics utilized as anthelmintics incorporate benzimidazole, pyrazine, isoquinoline, tetrahydropyramidine, tetrahydroquinolone, piperidine, piperazine, triazoles, and indoleisoxazole subordinates. The benzamidazole anthelminitic drug with the most elevated action is albendazole.



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3.4. Heterocyclic compounds as antidepressants

A mental medication called an energizer is utilized to treat temperament problems such critical wretchedness and dysthymia. They are most often associated with drugs like monoamine oxidase inhibitors (MAOI), tricyclic antidepressants (TCAs), particular serotonin reuptake inhibitors (SSRIs), tetracyclic antidepressants (TeCAs), and serotonin norepinephrine reuptake inhibitors (SNRIs). Probably the best antidepressants with heterocyclic moiety in their designs incorporate paroxetine and reboxetine. A few compounds of piperidine and pyrimidine likewise have energizer properties. Various little atom nano-peptide adversary heterocyclics have been found and creature conduct testing have exhibited their energizer adequacy.



4. Experimental

- Synthesis of compounds [1]: 2-phenyl-4H-benzo[d][1,3]oxazin4-one arrangement [1].
 This substance was made utilizing a strategy depicted in the writing.
- Synthesis of compounds [2] and [3]: phthalic anhydride or 2-phenyl-4Hbenzo[d][1,3]oxazin-4-one mixed in equimolar proportions (5 mmol) with glycine in glacial acetic acid (30 mL). Refluxing the mixture took (4-5) hours. The reaction mixture was then mixed with 30 ml of ice-cold distilled water before the compounds were dried, filtered, and crystallized again from 100% ethanol.
- Synthesis of compounds (4) and (5): In the presence of dry benzene (10 mL), a mixture of compounds (2) or (3) (20 mmol) was taken with (5 ml) of thionyl chloride and



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refluxed for four hours. After cooling, the excess benzene and thionyl chloride were extracted under vacuum. The goods were gathered as crystals.

- Synthesis of compounds [6] and [7]: Refluxing was done for six hours with a stirring mixture of compound [4] or [5] (30 mmol) and 80% hydrazine hydrate (150 mmol) in dry benzene (30 mL). The surplus hydrazine hydrate and solvent were removed under reduced pressure after cooling, the residue washed with ether, and the resulting chemicals were then recrystallized from ethanol to produce solid products.
- Synthesis of 5-(2,2-dimethyl-1,3-dioxolan-4- yl)-3,4-di-hydroxyfuran-2(5H)-one[8]: Dry (HCl) swiftly bubbled while moving for 20 minutes in a 250 ml flask that also contained 100 ml of dry acetone and 10 g of L-ascorbic acid. The supernatant was decanted after being added (80ml of n-hexane), moved, and refrigerated in a (snow aqueous). The sediment has been washed four times with 154 mL of a 7:4 v/v hexaneacetone mixture before being refrigerated in an aqueous snow bath and having the excess liquid removed after each addition. The final sediment has been dehydrated under low pressure to produce (8) (78%) as a white solid with a melting point between 210 and 212 °C. Rf (0.68) (benzene: methanol, 1:1 v/v).
- Synthesisof2-(2,2-dimethyl-1,3-dioxolan-4-yl)- 5-oxo-2,5-ihydrofuran-3,4-diyl bis(4-nitrobenzoat) [9]: This compound was made in accordance with the available literature (35). After compound (8) (10g, 46mmol) in dry pyridine (50mL) had cooled, moving (24g, 129mmol) of (p-nitrobenzoyl chloride was added. The next mixture was agitated for two hours, then kept at room temperature in a dark place (22 hrs). The mixture was added to ice water and stirred for 20 minutes before the oil layer was extracted using chloroform (2150 mL) and washed with water, HCl (5%) (2100 mL), saturated watery NaHCO3 (100 m), and water. Over anhydrous MgSO4, dehydrate. Chloroform has been evaporated. Reconstituted from 100% ethanol, the residue yielded (9) (44%) as a dark solid with a melting point of (102-104 °C). Rf (0.76; v/v, 1:1 methanol: benzene).
- Synthesis of 2-(1,2dihydroxyethyl)-5-oxo-2,5- dihydro-furan-3,4-diyl bis(4nitrobenzoate) [10]: A mixture of (65%) acetic acid (30mL) and 100% ethanol (10mL) was used to dissolve compound [9] (10g, 19.45mmol), and the mixture was agitated for



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(48) hours at room temperature. The TLC demonstrated that the intraction (benzene: methanol, 3:2) was successful. Filter the mixture, add 40 mL of benzene to the resultant solution, and allow it to volatilize four more times. Re-crystallizing the residue from 100% ethanol produced [10] (67%) as a dark brown solid with a m.p. (122-124 °C) Rf (0.46) (3:2 benzene: methanol).

- Synthesis of 2-formyl-5-oxo-2,5-dihydrofuran3,4-diylbis (4-nitrobenz-oate)[11]: Dropwise, at 0 degrees Celsius, and while stirring, a solution of compound (10) (10g, 21mmol) in (abs. ethanol) (60mL) was added to the solution of (NaIO4) (5.6g, 26mmol) in distilled water (60mL). After stirring for one minute, 0.5 mL of ethylene glycol has been added dropwise (15 min). Stirring continued for a while at room temperature (1 h). A (40mL) of distilled water was added to the mixture, which was then filtered, the yield was removed using (ethyl acetate, 3–50mL), the extracts were then dehydrated using (anhydrous MgSO4), the solvent was then removed, and the residue was recrystallized using absolute ethanol to yield the compound (11) (54%) as a yellow solid with a melting point of (194–196 °C). Rf (0.73) (benzene: methanol, v/v, 1.55).
- Synthesis of Schiff bases (12-17): To create the Schiff bases compounds, a combination of the compounds (6) and (7) (0.001mol) with different aldehydes (0.001mol) was broken up in (30mL) outright ethanol and (3) drops of chilly acidic corrosive was refluxed for (48) hours. The dissolvable was then volatilized, and the leftover material was then recrystallized from outright ethanol. Table lists the nomenclature and physical characteristics of synthesised Schiff bases (1).
- Synthesis of 1,3-oxazepine compounds [12Ox17Ox]: Equimolar groupings of Schiff bases (12-17) and phthalic anhydride (0.2 mmol each) were joined with 15 mL of 1,4-dioxane and refluxed for 24 hours. To make 1,3-oxazepine compounds, the brilliant strong that came about subsequent to eliminating the dissolvable was recrystallized from 100 percent ethanol. Table lists the 1,3-oxazepine compounds' names and physical characteristics (1).
- Synthesis of 1H-tetrazol compounds [12T,15T,17T]: Schiff bases [12–17] (0.5 mmol) dissolved in sodium azide (0.5 mmol) in 30 mL of THF (NaN3). For 6 to 8 hours, the

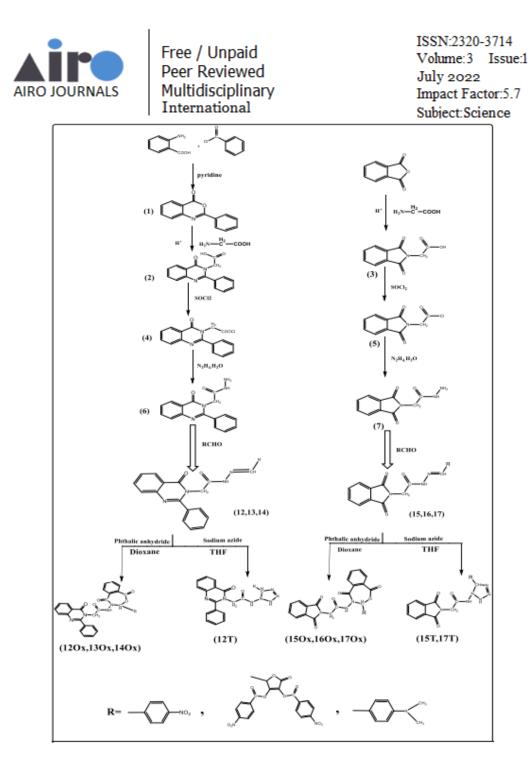


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mixture was refluxed at (55 to 65 0C). The mix was cooled to room temperature, the leftover dissolvable was dissipated, followed by a water wash, filtration, and recrystallization of the filtrate from pure ethanol. The nomenclature and physical characteristics of compounds [12T,15T,17T] are provided in Table (1).

5. Result and Discussion

The synthesis of different quinoline subordinates is displayed in Scheme (1). As per distributed research, 2-phenyl-4Hbenzo[d][1,3]oxazin-4-one [1] was created (30). M.P. also, FT-IR both recognized the compound, which is reliable with the writing. The arrangement of compounds [2] and [3] involved the response of glycine and quinazoline with phthalic anhydride in chilly acidic corrosive. The liquefying temperatures and FT-IR spectroscopy of compounds [2] and [3] are utilized to portray their designs. The FT-IR range of [2] and [3] uncovered groups of retention at (3200-2400 cm-1, (3300-2400 cm-1), and appearance at (1685, 1654) cm-1 for carbonyl gatherings, separately, because of OH carboxyl gatherings. The compounds [4] and [5] were created from [2] and [3] using benzene as the solvent and thionyl chloride as the catalyst. By using FT-IR, these compounds 'structures were verified. By treating compounds [4] and [5] with hydrazine hydrate, compounds [6] and [7] were created.



[SCHEME 1]

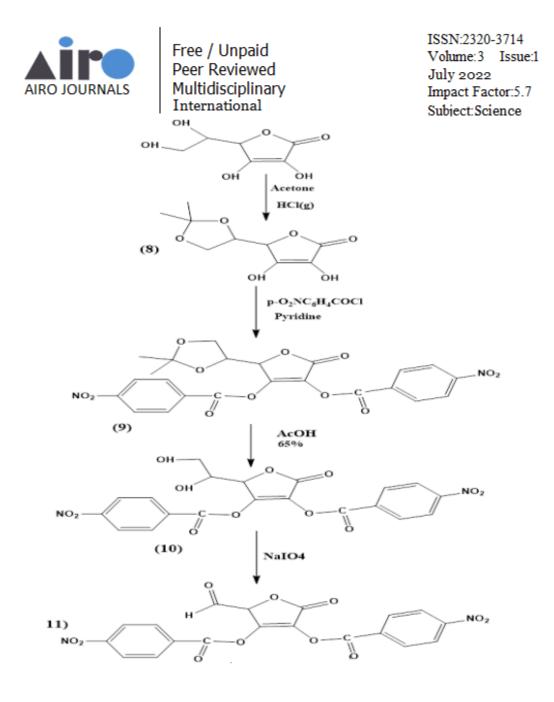




Table: 1. Nomenclature, m.ps, molecular weight, color of some of prepared compounds Y



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Comp.	Chemical name	Molecular weight g/mol C	m.p(⁰ C)	Color	Yield (%)
1	2-phenyl-4H-benzo[d][1,3]oxazin-4-one	223	118- 120	Bright Yellow	72%
2	2-(4-oxo-2-phenylquinazolin-3(4H)-yl)acetic acid	280	167-169	White	95%
3	2-(1,3-dioxoisoindolin-2-yl)acetic acid	205	192-194	White	96%
4	2-(4-oxo-2-phenylquinazolin-3(4H)-yl)acetyl chloride	298.5	115-117	Dark brown	83%
5	2-(1,3-dioxoisoindolin-2-yl)acetyl chloride	223.5	80-82	Dark brown	92%
6	2-(4-oxo-2-phenylquinazolin-3(4H)- yl)acetohydrazide	294	177-180	Pale Brown	78%
7	2-(1,3-dioxoisoindolin-2-yl)acetohydrazide	219	267- 270	Pale Brown	82%
8	5-(2,2-dimethyl-1,3-dioxolan-4-yl)-3,4- dihydroxyfuran-2(5H)-one	216	208-210	White	90%
9	-2-(2,2-dimethyl-1,3-dioxolan-4-yl)-5-oxo2,5- dihydrofuran-3,4-diyl bis(4-nitrobenzoat)	514	120- 125	Brown	75%
10	2-(1,2dihydroxyethyl)-5-oxo-2,5- dihydrofuran-3,4- diyl bis(4-nitrobenzoate)	474	142- 145	Deep Brown	67%
14 Ox	N-(3-(4-(dimethylamino)phenyl)-1,5-dioxo1,5- dihydrobenzo[e][1,3]oxazepin-4(3H)-yl)- 2-(4-oxo- 2-phenylquinazolin-3(4H)- yl)acetamide	560	134- 137	Orange	84%
15 Ox	2-(1,3-dioxoisoindolin-2-yl)-N-(3-(4- nitrophenyl)- 1,5-dioxo-1,5- dihydrobenzo[e][1,3]oxazepin-4(3H)- yl)acetamide	487	280- 283	Yellow	72%
16 Ox	2-(4-(2-(1,3-dioxoisoindolin-2-yl)acetamido)- dioxo-1,3,4,5- yl)-5-oxo2,5-dihydrofuran-3,4-diyl nitrobenzoate) 1,5- dioxo-1,3,4,5- bis(4-	791	170-173	Deep Brown	69%
17 Ox	N-(3-(4-(dimethylamino)phenyl)-1,5-dioxo1,5- dihydrobenzo[e][1,3]oxazepin-4(3H)-yl)- 2-(1,3- dioxoisoindolin-2-yl)acetamide	485	182- 185	Orange	81%



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6. Conclusion

Polymers, adhesives, molecular engineering, medicinal chemistry, dyestuff, and photographic sciences are just a few of the fields where heterocyclic compounds play a significant role. Quinoxalines, Oxoindolines, Triazoles, and Isooxazoles are among the heterocyclic compounds that are significant chemotherapeutic agents and have a wide range of clinical applications including antimicrobial, anticancer, antiviral, and anti-AIDS, antitubercular, sedative/hypnotic/antiepileptic, cardiac, as well as analgesics, diuretics, antibiotics, metabolic electrolytes, etc.

In this work, various novel heterocyclic compounds including subsidiaries of tetrazole and oxazepin were made. FTIR and 1HNMR ghastly examinations were utilized to recognize the presence of practical gatherings. These synthetic compounds' dissolving focuses have been recognized and revealed. The engineered synthetic substances' antibacterial properties had been researched.

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