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المجلة العراقية لبحوث السوق وحماية المستهلك

SYNTHESIS AND CHARACTERIZATION OF NEW HETEROCYCLIC DERIVATIVES FROM 7- HYDROXY -4- METHYL COUMARIN AND STUDY ANTIOXIDANT ACTIVITY FOR SOME SYNTHETIC COMPOUNDS

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ABSTRACT

7-Hydroxy-4-methyl coumarin(H_1) compound have been synthesized by resorcinol and ethyl acetoacetate reaction. 4-methyl-2-oxo-2H-chromen-7-yl 2-chloroacetate(H_2) is highly reactive compounds. It has been used as intermediate in some reactions. It has been synthesized and reacted with hydrazine hydrate to produce4-methyl-2-oxo-2H-chromen-7-yl 2-hydrazinylacetate (H_3).Schiff Bases Compound (H_4) is synthesized by reacting the compound (H_3) with P-hydroxy benzaldehyde, then reacted(H_4) with sodium azide, mercaptoacetic acid, chloroacetyl chloride and anhydrides such as (3- nitro phathalic anhydride, maleic anhydride, succinic anhydride) which produced tetrazole(H_5), thiazolidinone (H_6), β–Lactam (H_7), and Oxazepine Compounds(H_8-H_{10}) respectively. The prepared derivatives have been identified by FT-IR, ^{1}HNMR. Some of these compounds have bene screened for their antioxidant activity.

Keywords*:* Coumarin, Sschiff bases, tetrazole, Thiazolidinone, β–Lactam,Oxazepine.

تحضير وتشخيص مشتقات حلقية غير متجانسة جديدة من 7 – هيدروكسي – 4- مثيل كومارين ودراسة نشاط مضادات الاكسدة لبعض منها

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الخلاصة:

في هذا العمل تم تحضير 7- هيدروكسي4- مثيل كومارين من الريسورسينول المتفاعل مع الاثيل اسيتو اسيتيت ثم مفاعلته مع الكلورو اسيتل كلورايد وتكوين مركب وسطي يعتبر من المركبات شديده التفاعل. يتم تفاعل المركب الناتج مع هيدرات الهيدرازين لتكوين مشتق الهيدرازين، بعد ذلك يتم تخلق قواعد شيف من خلال تفاعل بارا هيدروكسي بنزلديهايد مع مشتق الهيدرازين. يتم ادخال قواعد شيف في سلسله من التفاعلات مع (الصوديوم ازيد ،مركبتو اسيتك اسد، كلورو اسيتل كلورايد اضافه الى بعض الانهدريدات المختلفه مثل 3- نايترو فثالك انهدريد،المالك انهدريد،السكسنك انهدريد) ليعطي مشتقات حلقيه جديده مختلفه والتي تضمنت(التترازول، الثايازوليدين، البيتا لاكتام، الاوكسازبينات).تم تشخيص هذه المركبات في طيف الرنين النووي المغناطيسي وطيف الاشعه تحت الحمراء وفحص بعض المركبات لمعرفه نشاطها المضاد للاكسده.

الكلمات المفتاحية: الكومارين، قواعد شيف، التترازول، الثايازولدين، البيتا لاكتام، الاوكسازبينات..

INTRODUCTION

Cyclic organic molecules with heteroatoms are known as heterocyclic compounds, these compounds have been some elements such as carbon, nitrogen, oxygen and sulfur. Pharmacological characteristics of the heterocyclic compounds are diverse and they are utilized to treat a variety of illnesses. The heterocyclic ring is a crucial structural element of the vast

* البحث مستل من رسالة ماجستير للباحث الاول.

majority of pharmaceuticals which used in modern medicine. Nitrogen-containing heterocyclic rings stand out among these molecules despite their ease of synthesis due to their broad dispersion and biological characteristics. For example, of these are "Schiff bases" which have "azomethine," as a function of group nitrogen connected to an alkyl or aryl group but not to hydrogen and contains a carbon-nitrogen double bond (>C=N-). German chemist Hugo Schiff first described these chemicals in 1864, hence his name was used to refer to them **(Muzammil &Trivedi, 2015).** The general formula R1R2C=NR3 **(Kolapwar, 2017)** describes the bulk of Schiff bases, while the general formula R1CH=NR2 describes some of them, in which the carbon atom is connected with a hydrogen atom rather than an alkyl or aryl group **(Hameed *et al*., 2017)** .These are the byproducts of primary amines condensation with ketones or aldehydes **(Dalia *et al*., 2018).** Schiff bases that are stable in nature are often those that result from the condensation of aromatic amines and aromatic aldehydes **(Kakanejadifard *et al*., 2018).** A multitude of biological properties, such as antifungal, analgesic, and anti-inflammatory, have been attributed to Schiff bases **(Malik *et al*., 2018).** The simplest structure of tetrazolates, with the formula CH_2N_4, is a five-ring heterogeneous molecule that contains four nitrogen atoms, one carbon atom, and hydrogen atoms **(Shah &modi, 2021).** Tetrazoles have both acceptor and electrical donor properties which characterized by the nitrogen-rich conjugated system**.** Due to their widespread application in a variety of industries which including pharmacology, medicine, photography, and prospective use as components of explosives and rocket propellants due to their high energy characteristics, tetrazole derivatives have attracted significant attention as prime heterocycles **(Dippold *et al*., 2016).** A five-membered ring called thiazolidinone, having a pentagonal ring with multiple heteroatoms, such as a sulfur atom at position 1, a nitrogen atom at position 3, and carbonyl groups at positions 2, 4, or 5. **(Rawnaq *et al*., 2022).** The thiazolidinedione nucleus is extensively implicated in biologically active substances that have anti-tumor, analgesic, antibacterial, anti-HIV, anti-fungal, and anti-inflammatory properties **(Rawnaq *et al*., 2022)**. One of the most often prescribed medication classes, beta-lactam antibiotics which have a wide range of clinical uses. The fight against bacterial infectious diseases was fundamentally altered by their introduction beginning in the 1930s of the twentieth century. These days, the cost of these antibiotics has been estimated annually which comes about chillon USD which is 65% of the antibiotics market. **(Thakuria & lahon, 2022).** However, the usage of these products conflicts with the alarming antibiotic resistance phenomena, a problem for world health.this sentens oxyazepine compound is aseven – membered ring that contains five carbon atoms,oxygen and nitrogen in the first and third position**.**. Oxazepine's synthesis has been studied and reported over time. It is created by the reaction between Schiff base or hydrazone and various anhydrides **(Nagham, 2013).** The biological activities of oxyazepine derivatives, such as those of antifungal, hypnotic muscle relaxants, inflammatory, and antibacterial agents, were shown to change dramatically**.**

MATERIALS AND METHODS

A wide range of firms, including Thomas Baker, Merck, BDH, GCC, and Scharlau, contributed the chemicals that were used in the study. further purification is not required Uncorrected electrothermal melting point equipment was used to get the melting point values (Stuart Germany). TLC plates 60 F245 (E. Merck) were coated with aluminum and iodine vapor was used as a mobile phase. The FTIR Shimadzu was used to acquire infrared spectra on a KBrb disk in the 400-4000 cm-1 band (Japan). A Bruker DMX-500 spectrophotometer was used to investigate the HNMR spectra of the chemicals produced (500 bMHZ, solvent DMSO-d6).

Synthesis of 7-Hydroxy-4-methyl coumarin(H_1)

Resorcinol (3g, 0.1 mole) and concentrated H_2SO_4 (15mL) were cooled to about 5 °C, ethyl acetoacetate (4,8 mL) was added dropwise over the course of 30 min, the reaction mixture was stirred for 4 hours, then poured into ice/cold water where the solid product was separated, filtered out, and dried **(Kidwai *et al.*, 2000).** The crude product is then re-crystallized using a 1:1 ethanol/water ratio**.**The physical propertiesof compound (H_1) are listed in (Table1).

FT-IR (KBr)/cm^{-1})(H_1): 3128 (OH.phenol), 3029 (C-H aromatic), 2918, 2808 (C-H aliphatic), 1797(C=O lactone), 1597 (C=C aromatic).

Synthesis of 4-methyl-2-oxo-2H-chromen-7-yl 2-chloroacetate(H2)

Chloroacetyl chloride (0.008 mol, 2.25mL) was gradually added to a combination of (0.004 mol, 5 g) from compound (H_1) in (25mL) dry pyridine, then cooling in ice bath at (0-5) °C and stirring for 4 h **(Mohammed & Zmam, 2012)**. The mixture was placed into ice water, then the solid was filtered out,dried, and purified from the ethanol and water (1:1). The physical properties of compound [H_2] are listed in (Table1).

FT-IR (KBr)/cm^{-1})(H_2): 3030 (C-H aromatic), 2925, 2845 (C-H aliphatic), 1700 (C=O lactone), 1797 (C=O ester), 1589 (C=C aromatic), 1234 (C-O), 840 (C-Cl).

Synthesis of 4-methyl-2-oxo-2H-chromen-7-yl 2-hydrazinylacetate(H_3)

The compound (H_2) (3 g, 0.01 mole) was dissolved in absolute ethanol (24.5 mL) and stirred for 10 minutes at 25°C. Next, about (0.02 mole, 0.36 mL) of hydrazine hydrate ($N_2H_4.H_2O$) (80%) was added . The reaction mixture was refluxed for 6 hours, tested on lead paper, cooled to room temperature, filtered, and recrystallized from absolute ethanol **(Ahmed, 2015).** The physical properties of compound [H_3] are listed in (Table1).

FT-IR (KBr)/cm^{-1})(H_3):3479,3433 (NH_2),3199 (NH), 3066 (C-H aromatic), 2970, 2833 (C-H aliphatic), 1735 (C=O ester), 1700 (C=O lactone), 1597 (C=C aromatic), 1273 (C-O).

Synthesis of Schiff Bases Compound (H_4)

A mixture of compound (H_3) (3.4 g., 0.01mole) and P-hydroxybenzaldehyde (2.1 g., 0.01mole) in absolute ethanol (10mL) is refluxed for 8 hrs. In the presence of few drops of glacial acetic acid, the progress of the reaction was monitored by TLC **(Al-Azzawi &Raheem, 2017)**. After cooling the product, was filtered off, dried and purified by recrystallization from absolute ethanol**.** The physical properties of compound (H_4) are listed in (Table1).

FT-IR (KBr)/cm^{-1})[H_4]:3450 (OH phenol),3124 (NH), 3074 (C-H aromatic), 2927, 2804 (C-H aliphatic), 1678 (C=N), 1597 (C=C aromatic), 1234 (C-O).

Synthesis of Tetrazole Compound (H5)

Ten milliliters oftetrahydrofuran (THF) were used to dissolve the Schiff base (H_4) (0.00149mol, 0.8g), and sodium azide (0.1g) was then added. The mixture was stirred for 9 to 10 hours at 60 to 70 degrees Celsius in a water bath.T.L.C. tested the reaction once it had finished. The mixture was filtered, dried, and the resulting products were purified with ethanol **(Ibtisam & Iman, 2016).** The physical properties of compound [H_5] are listed in (Table1).

FT-IR (KBr)/cm^{-1})(H_5):3387 (OH phenol),3146 (NH), 3050 (C-H aromatic), 2933, 2845 (C-H aliphatic), 2357,2318 (N=N-N), 1705 (C=O ester), 1700 (C=O lactone), 1589 (C=C aromatic1597 (C=C aromatic), 1234 (C-O).compound Characterization was donevia1H-NMR spectra which gave [H_5] δ (6.70-7.70) ppm due to (m, 7H,Ar-H), δ(6.58) ppm as (s,1 H, Hcoumarine), δ(6.07) ppm as (s,1H,CHmethine), δ(4.92)ppm due to (s,1H,OHphenol),

δ(3.55)ppm due to(s,2H,CHmethylene), δ(2.51) ppm due to(s,1H,NHtetrazol ring), δ(2.40) ppm due to(s,1H,NHamine), δ(2.34)ppm (DMSO), δ(1.75)ppm due to(s,3H,CHmethyl).

Synthesis of Thiazolidinone Compound (H_6)

The Schiff bases (H_4) (0.00187mol, 1g) were dissolved in 10 mL dry benzene, and 0.26 mL of mercaptoacetic acid was added after that. The mixture was refluxed for (12–14) h. As soon as the reaction was complete, T.L.C. testing was done. The reaction mixture was filtered, and the solid that resulted was recrystallized and then derided **(Saleh *et al*., 2020).** The physical properties of compound [H_5] are listed in (Table1).

FT-IR (KBr)/cm^{-1})(H_6):3575 (OH phenol), 3155 (NH), 3012 (C-H aromatic), 2911, 2804 (C-H aliphatic), 1797 (C=O ester), 1700 (C=O lactone), 1597 (C=C aromatic).

Synthesis of β–Lactam Compound(H_7)

Schiff bases (H_4) (0.00149mol, 0.8g) and triethylamine (0.5 mL) were dissolved in dimethyl formamide (10 mL), After adding dropwise amounts of chloroacetyl chloride and stirring the reaction mixture for 6-7 h, it was allowed to cool for 48 h before being poured into water with crushed ice. Following that, the solid precipitate was filtered, washedwith water, and then was cleaned with ethanol and water (1:1) **(Mohammed & Zmam, 2012)**. The physical properties of compound (H_5) are listed in (Table1). FT-IR (KBr)/cm^{-1})(H_7): 3603 (OH phenol), 3100 (NH), 3032 (C-H aromatic), 2935, 2825 (C-H aliphatic), 1693 (C=O ester), 1666 (C=O lactone), 1604 (C=O amid), 1593 (C=C aromatic), 1261 (C-O), 856 (C-Cl).

Synthesis of Oxaze pine Compounds (H_8-H_{10}).

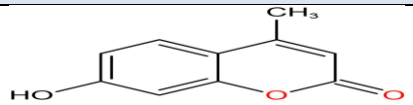
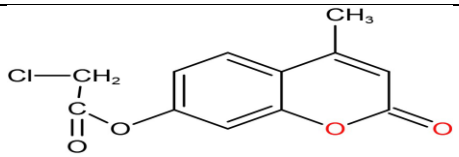
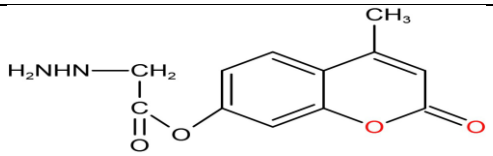
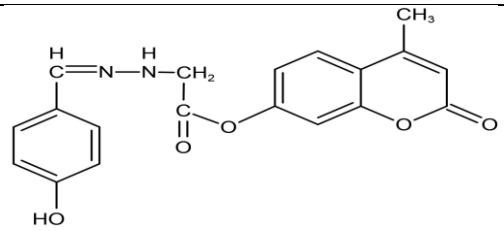
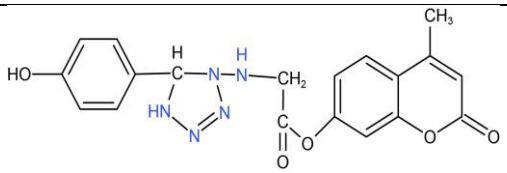
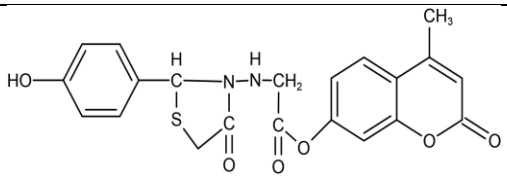
In (10mL) of dry benzene, a combination of Schiff bases (H_4) (0.00187mol, 0.8g) and different anhydrides (3- nitro phthalic anhydride (0.4g), maleic anhydride (0.25g), succinic anhydride (0.26g) were dissolved. The mixture was refluxed for 5–6 hours. When the reaction was finished, T.L.C. checked it. Take a ride after the reaction, the mixture was filtered, and the solid that was produced was recrystallization **(ABBAS & JBER, 2020).** The physical properties of compound (H_5) are listed in (Table1).

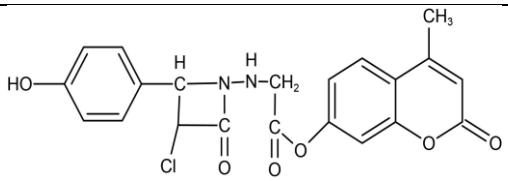
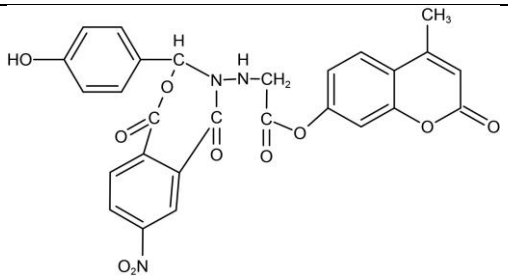
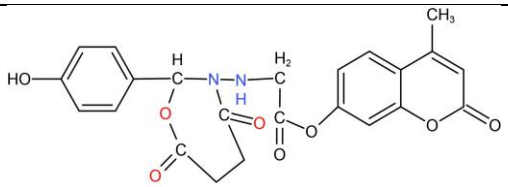
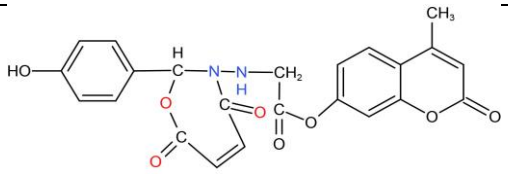
FT-IR (KBr)/cm^{-1})(H_8):3336 (OH phenol), 3155 (NH), 3078 (C-H aromatic), 2900, 2889 (C-H aliphatic), 1748 (C=O ester), 1700 (C=O lactone),1678 (C=O lactam),1512 (C=C aromatic), 1288 (C-O),1535,1388 (C-NO_2). Compound Characterization (H8) was donevia1H-NMR spectra which gave [H_8] δ (7.58-8.60) ppm due to (m, 9H,Ar-H), δ(6.15) ppm as (s,1 H, Hcoumarine), δ(6.96) ppm as (s,1H,CHmethine), δ(5.70)ppm due to (s,1H,OHphenol), δ(3.51)ppm due to(s,2H,CHmethylene), δ(2.56)ppm due to(s,3H,CHmethyl), δ(2.39)ppm (DMSO), and δ(2.20) ppm due to(s,1H,NHamine).

FT-IR (KBr)/cm^{-1})(H_9):3489 (OH phenol), 3100 (NH), 3029 (C-H aromatic), 2922, 2870 (C-H aliphatic), 1797 (C=O ester), 1700 (C=O lactone),1600 (C=O lactam),1512 (C=C aromatic), 1566(C=C aliphatic), 1238 (C-O). Compound Characterization (H_9) was donevia1H-NMR spectra which gave [H_9] δ (7.35-8.50) ppm due to (m, 7H,Ar-H), δ(6.80)ppm due to(d,2H,CHoxazepine ring), δ(6.15) ppm as (s,1 H, Hcoumarine), δ(6.72) ppm as (s,1H,CHmethine), δ(5.55)ppm due to (s,1H,OHphenol), δ(3.50)ppm due to(s,2H,CHmethylene), δ(2.52)ppm due to(s,3H,CHmethyl), δ(2.33)ppm (DMSO), and δ(2.30) ppm due to(s,1H,NHamine).

FT-IR (KBr)/cm^{-1})(H_{10}):3336 (OH phenol),3128 (NH), 3032 (C-H aromatic), 2935, 2808 (C-H aliphatic), 1780 (C=O ester), 1732 (C=O lactone),1693 (C=O lactam),1593(C=C aromatic), 1211 (C-O) (Table, 1).

Table (1): The Physical properties of compounds.

Comp No.	Nomenclature & Formula for Structure	Yield (%)	Color	Melting point
H_1	 7-hydroxy-4-methyl-2H-chromen-2-one	63	Light yellow	182-184
H_2	 4-methyl-2-oxo-2H-chromen -7-yl 2-chloroacetate	56	Brown	161-163
H_3	 4-methyl-2-oxo-2H- chromen-7-yl 2-hydrazinylacetate	68	Dark yellow	215-217
H_4	 4-methyl-2-oxo-2H-chromen-7-yl 2-{2-[(4-hydroxyphenyl) methylidene]hydrazin-1-yl}acetate	73	Brown	167-169
H_5	 4-methyl-2-oxo-2H-chromen-7-yl 2-{[5-(4-hydroxyphenyl)-4,5-dihydro-1H-1,2,3,4-tetrazol-1-yl]amino}acetate	56	Dark brown	157-159
H_6	 4-methyl-2-oxo-2H-chromen-7-yl 2-{[2-(4-hydroxyphenyl)-4-oxo-1,3- thiazolidin-3-yl]amino}acetate	58	Brown	Oily

H_7	 4-methyl-2-oxo-2H-chromen-7-yl 2-{[3-chloro-2-(4-hydroxyphenyl) -4-oxoazetidin-1-yl]amino}acetate	62	Dark yellow	148-150
H_8	 4-methyl-2-oxo-2H-chromen-7-yl 2-{[3-(4-hydroxyphenyl)-7-nitro -1,5-dioxo-1,3,4,5-tetrahydro-2,4-benzoxazepin-4-yl]amino}acetate	81	Yellow	135-137
H_9	 4-methyl-2-oxo-2H-chromen-7-yl 2-{[2-(4-hydroxyphenyl)- 4,7-dioxo-1,3-oxazepan-3-yl] amino} acetate	69	Brown	135-137
H_{10}	 4-methyl-2-oxo-2H-chromen-7-yl 2-{[2-(4-hydroxyphenyl)- 4,7-dioxo-2,3,4,7-tetrahydro-1,3-oxazepin-3-yl]amino}acetate	78	Yellow	168-170

RESULTS AND DISCUSSION

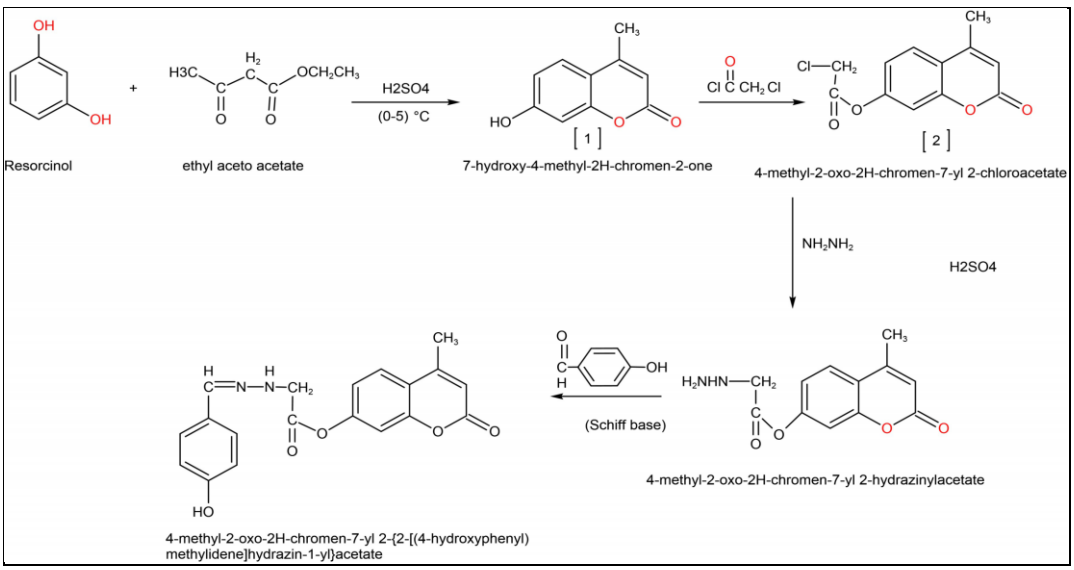
The vehicles were diagnosed by FTIR and HNMR, and the results appeared in the following picture: FT-IR (KBr)/cm^{-1}): 3128 (OH phenol), 3029 (C-H aromatic), 2918, 2808 (C-H aliphatic), 1797(C=O lactone), 1597 (C=C) aromatic for the compound [H_1].compound[H_2] which gave 3030 (C-H aromatic), 2925, 2845 (C-H aliphatic), 1797 (C=O lactone), 1700 (C=O ester), 1589 (C=C aromatic), 1234 (C-O), 840 (C-Cl) [H_2]. Compound[H_3] which gave 3479,3433 (NH_2),3199 (NH), 3066 (C-H aromatic), 2970, 2833 (C-H aliphatic), 1735 (C=O ester), 1700 (C=O lactone), 1597 (C=C aromatic), 1273 (C-O) .Compound[H_4] which gave 3450 (OH phenol),3124 (NH), 3074 (C-H aromatic), 2927, 2804

(C-H aliphatic), 1678 (C=N), 1597 (C=C aromatic), 1234 (C-O). compound[H_5] which gave 3387 (OH phenol),3146 (NH), 3050 (C-H aromatic), 2933, 2845 (C-H aliphatic), 2357,2318 (N=N-N), 1705 (C=O ester), 1700 (C=O lactone), (C=C aromatic1597, 1234 (C-O) (scheme, 1).Compound Characterization [H_5] was donevia1H-NMR spectra which gave [H_5] δ (6.70-7.70) ppm due to (m, 7H,Ar-H), δ(6.58) ppm as (s,1 H, Hcoumarine), δ(6.07) ppm as (s,1H,CHmethine), δ(4.92)ppm due to (s,1H,OHphenol), δ(3.55)ppm due to(s,2H,CHmethylene), δ(2.51) ppm due to(s,1H,NHtetrazol ring), δ(2.40) ppm due to(s,1H,NHamine), δ(2.34)ppm (scheme, 2). Compound [H_6] which gave 3575 (OH phenol), 3155 (NH), 3012 (C-H aromatic), 2911, 2804 (C-H aliphatic), 1797 (C=O ester), 1700 (C=O lactone), 1597 (C=C aromatic), 1273 (C-O),1064 (C-S) (scheme, 2). Compound [H_7] which gave 3603 (OH phenol), 3100 (NH), 3032 (C-H aromatic), 2935, 2825 (C-H aliphatic), 1693 (C=O ester), 1666 (C=O lactone), 1604 (C=O amid), 1593 (C=C aromatic), 1261 (C-O), 856 (C-Cl).Compound [H_8] FT-IR (KBr)/cm^{-1}):3336 (OH phenol), 3155 (NH), 3078 (C-H aromatic), 2900, 2889 (C-H aliphatic), 1748 (C=O ester), 1700 (C=O lactone),1678 (C=O amid),1512 (C=C aromatic), 1288 (C-O),1535,1388 (C-NO_2). Compound Characterization [H_8] was donevia1H-NMR spectra which gave [H_8] δ (7.58-8.60) ppm due to (m, 9H,Ar-H), δ(6.15) ppm as (s,1 H, Hcoumarine), δ(6.96) ppm as (s,1H,CHmethine), δ(5.70)ppm due to (s,1H,OHphenol), δ(3.51)ppm due to(s,2H,CHmethylene), δ(2.56)ppm due to (s,3H,CHmethyl), δ(2.39)ppm (DMSO), and δ(2.20) ppm due to(s,1H,NHamine) (scheme, 3). Compound [H_9] which gave 3489 (OH phenol), 3100 (NH), 3029 (C-H aromatic), 2922, 2870 (C-H aliphatic), 1797 (C=O ester), 1700 (C=O amide),1600 (C=O lactam),1512 (C=C aromatic), 1566(C=C aliphatic), 1238 (C-O). Compound Characterization [H_9] was donevia1H-NMR spectra which gave [H9] δ (7.35-8.50) ppm due to (m, 7H,Ar-H), δ(6.80)ppm due to(d,2H,CHoxazepine ring), δ(6.15) ppm as (s,1 H, Hcoumarine), δ(6.72) ppm as (s,1H,CHmethine), δ(5.55)ppm due to (s,1H,OHphenol), δ(3.50)ppm due to(s,2H,CHmethylene), δ(2.52)ppm due to(s,3H,CHmethyl), δ(2.33)ppm (DMSO), and δ(2.30) ppm due to(s,1H,NHamine).Compound [H10] FT-IR (KBr)/cm^{-1}):3336 (OH phenol),3128 (NH), 3032 (C-H aromatic), 2935, 2808 (C-H aliphatic), 1780 (C=O ester), 1732 (C=O lactone),1693 (C=O lactam),1593(C=C aromatic), 1211 (C-O) for the compound[H_{10}] (table, 2).

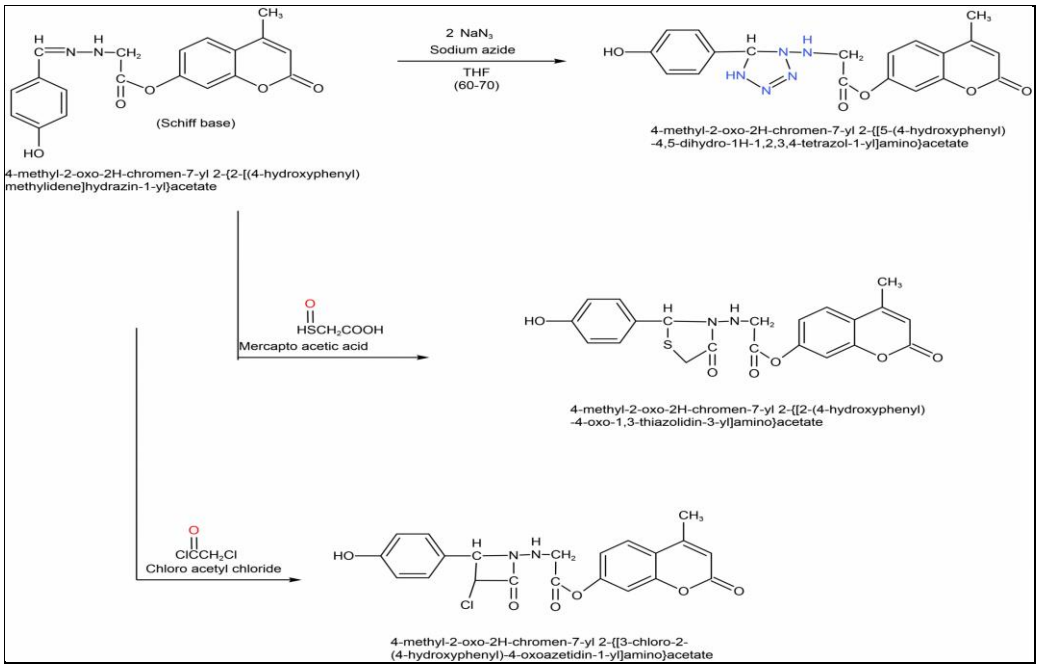
Table (2): FT-IR spectra for compounds(H_1-H_{10})

Comp NO.	FT-IR Spectrum Data, cm-1						
	v(NH)	v(C-H) Arom.	v(C-H) Aliph.	V(OH) phenol	v(C=O)	v(C=N)	v(C=C)
H1	-	3029	2918-2808	3128	1797 lactone	-	1597
H2	-	3030	2925-2845	-	1700 ester	-	1589
H3	3479-3433	3066	2970-2833	-	1735 ester	-	1597
H4	3124	3074	2927-2804	3450	1732 ester	1678	1597
H5	3146	3050	2933-2845	3387	1705 ester	-	1597

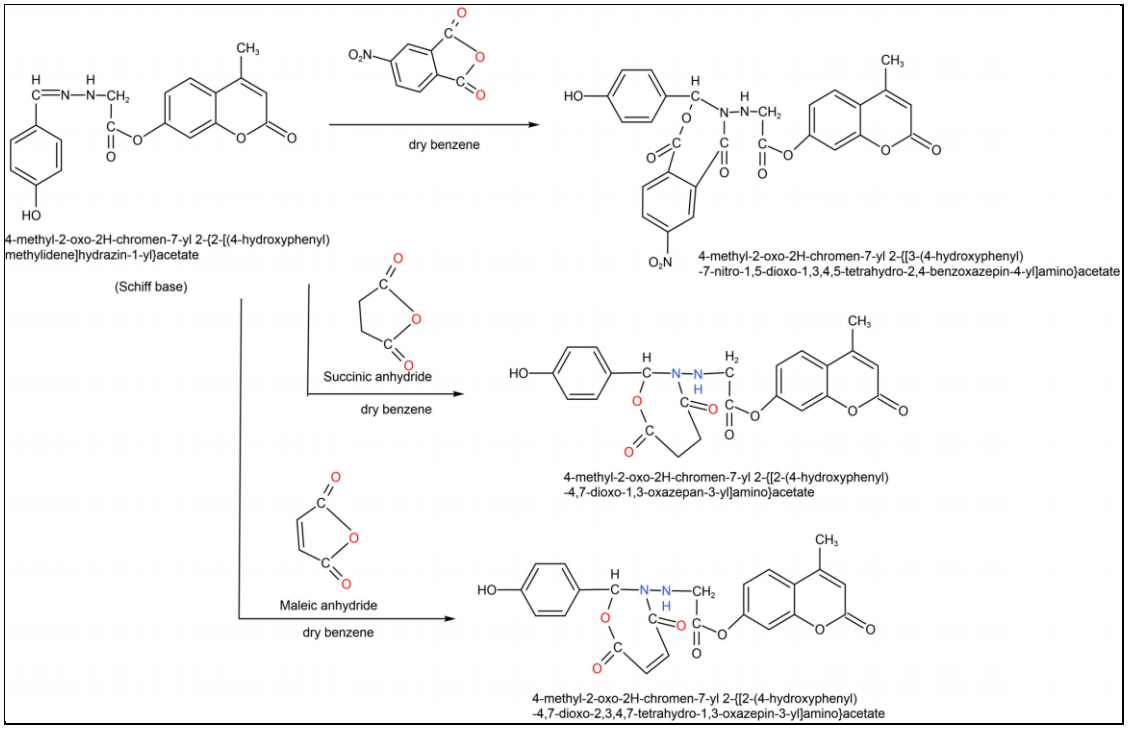
H6	3155	3012	2911-2804	3575	1797	-	1597
H7	3100	3032	2935-2825	3603	1693 ester 1604 amid	-	1593
H8	3155	3078	2900-2889	3336	1748 Ester 1678 amid	-	1512
H9	3100	3029	2922-2870	3489	1797 Ester 1700 amide	-	1512
H10	3128	3032	2935-2808	3336	1780 Ester 1693 amid	-	1593



Scheme (1): Path way for Synthesis Schiff Bases Compound (H_4).



Scheme (2): Path way for Synthesis tetrazole, Beta-lactam, andThiazolidin Compounds.



Scheme (3) Path way for Synthesis Oxazepine Compounds.

Antioxidant activity

The Blois method was modified to carry out the experiment. Free Radical Scavenging Activity in the DPPH (1958). 2mL of the aqueous extracts at varied concentrations (50-100 g/mL) had been combined with 1 mL of 0.1 mM solution of DPPH (Alfa Aesar, Japan) in MeOH. The mixture had spent 30 minutes growing in the dark environment. To create the blank, distilled water was combined with 1 mL of DPPH solution **(Hani *et al*, 2018).** The absorbance at 517 nm was calculated using a UV spectroscopy in comparison to a blank. A decreased absorbance of the reaction mixture indicates 1% inhibition of the free radical of DPPH. India-based Merck's VitaminC was utilized as the reference; triplicate samples were created and measured. The following equation was used to compute the percentage of scavenging activity of each extract on the DPPH radical as%inhibition of DPPH 1%.

$$\textbf{Inhibition } (\%) = \frac{\mathbb{A}\mathbb{o}-\mathbb{A}\mathbb{S}}{\mathbb{A}\mathbb{o}} \times 100$$

Ao: is the absorption of control
As: is the absorption of the tested extract solution.

Some of the produced compounds had their antioxidant properties investigated, and the results were displayed in the following (Table3).

Table (3): DPPH radical scavenging assay of compounds **(H_5, H_8, H_9).**

No.com	50 (µg/mL)	100 (µg/mL)	150 (µg/mL)
H_5	0.182	0.264	0.347
H_8	0.102	0.13	0.282
H_9	0.14	0.2	0.277
Ascorbic acid	**0.24**	**0.45**	**0.8**

CONCLUSION

Novel heterocyclic compounds have been created successfully with rings of 5, 6, and 7 to manufacture Schiff bases (tetrazole, thiazolidinone, -Lactam, and oxyzepine). Spectral data are used to supplement characterization (FT-IR, ^{1}HNMR). For their antioxidant properties, some of these compounds have been tested.

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