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Synthesis and Characterization of New Spiroheterocyclic from Isatin and Evaluation of its Antifungal and Antibacterial Activity

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ABSTRACT

This investigation introduced six chalcones, characterized by substituted acetophenone and substituted benzaldehyde. These chalcones were utilized to prepare six spiroheterocyclic compounds. Thin-layer chromatography was utilized to monitor the reactions, and mass spectroscopy analysis techniques, carbon nuclear magnetic resonance, proton nuclear magnetic resonance, and Fourier-transform infrared spectroscopy were used to characterize the structures. Additionally, the biological efficacy of spiroheterocyclic compounds prepared against bacteria and fungi was studied.

1-Introduction

The term "spiro" refers to polycyclic compounds where two dissimilar rings share a common carbon atom [1], and the planes of the two rings are forced, by the spiro atom, to almost face each other. Spiro compounds are a desirable subclass of heterocyclic scaffolds. In particular, spiropyrrolidine analogs are present in many naturally occurring products and synthetic compounds that are important for biological processes, and they have a variety of biological and pharmacological effects [2]. Spiroheterocyclic compounds are prevalent in many natural products [3], including hormones, vitamins, and alkaloids [4]. They exhibit unique characteristics that are crucial to various fields, such as biology, where they can inhibit acetylcholinesterase and demonstrate anticancer, anti-mycobacterial, and antibacterial properties, and materials research [5], where they exhibit anticoagulant and spasmolytic activities [6]. Heterocyclic chemistry is one of the most complex subfields of chemistry, and heterocyclic compounds represent the broadest and most diverse family of chemical substances.

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The robust characteristics of heterocyclic compounds inhibit their facile polymerization or hydrolysis. Heterocyclic compounds constitute a large class of cyclic compounds containing one or more non-carbon atoms, including nitrogen, oxygen, sulfur, or phosphorus [7]. The stability of synthesized heterocyclic compounds must be verified, as they must be stable inside the intricate physiological system of the body. The stability of the compounds was assessed by analyzing their UV-visible spectra. The relationship between absorbance and wavelength, as well as between percent concentration and duration (in hours), was determined [8]. In such a complicated situation, isatins may represent the only class of heterocyclic compounds that has been extensively used in the design and synthesis of various spirocyclic frameworks [9]. The term "chalcone" refers to a group of ketones (flavonoids) characterized by two aromatic rings, namely, A and B, and a three-carbon, unsaturated carbonyl group. Chalcone is also known as benzyl acetophenone and benzylideneacetophenone [10]. A unique unsaturated carbonyl known as chalcone is a precursor to numerous heterocyclic compounds and has physiologically active or beneficial qualities. Chalcones' medicinal qualities and simple preparation have drawn special attention from researchers for many years. The most popular and commonly used method to create

chalcone is Claisen–Schmidt condensation, which involves the condensation of ketone and aldehydes, resulting in minimal work-up and few byproducts [11]. The synthesis of a chalcone derivative with a heterocyclic scaffold is the focus of numerous scholars. Several studies have reported the biological and pharmacological activities of chalcones containing heterocyclic scaffolds, including antibacterial, antioxidant, and antifungal activities [12]. The synthesis, characterization, and computational research of chalcones and heterocyclic compounds are fascinating. Extensive research has been conducted on theoretical and experimental grounds on computational studies in elucidating the reactivity of heterocycles, mechanisms, and analysis of biological activities [13].

2- EXPERIMENTAL SECTION: MATERIALS

All chemicals utilized in this study were of analytical grade. They included isatin,4-nitrobenzaldehyde,4-aminoacetophenon,4-chlorobenzaldehyde,3-aminoacetophenon,2,4-dichlorobenzaldehyde,4-bromoacetophenone,4-chlorobenzaldehyde,diethylamine,formaldehyde, glycine, sodium hydroxide, methanol, and ethanol.

Instrumentation

1- Melting point measurements: Melting points were determined using an open capillary tube and are uncorrected. Stuart SMP11-SMP30,Sabart, UK/Anbar University, College of Science, Department of Chemistry.

2- Infrared spectrophotometer (FT-IR): Measurements were conducted at the Department of Chemistry at Al-Anbar University using the FT Spectrophotometer. The model was placed directly on the lens of the Shimadzu IR-8400s Fourier instrument.

3- Proton nuclear magnetic resonance spectrometry (^{1}H NMR): The 1HNMR spectra were recorded by using a 400 MHz NMR spectrometer from Brucker Biospin GmbH (USA), with DMSO (Iran) as the solvent.

4- Carbon 13 nuclear magnetic resonance spectrometer (13CNMR): The13CNMR spectra were recorded by using a 400 MHz NMR spectrometer from Brucker Biospin GmbH (Germany), with DMSO (Iran) as the solvent.

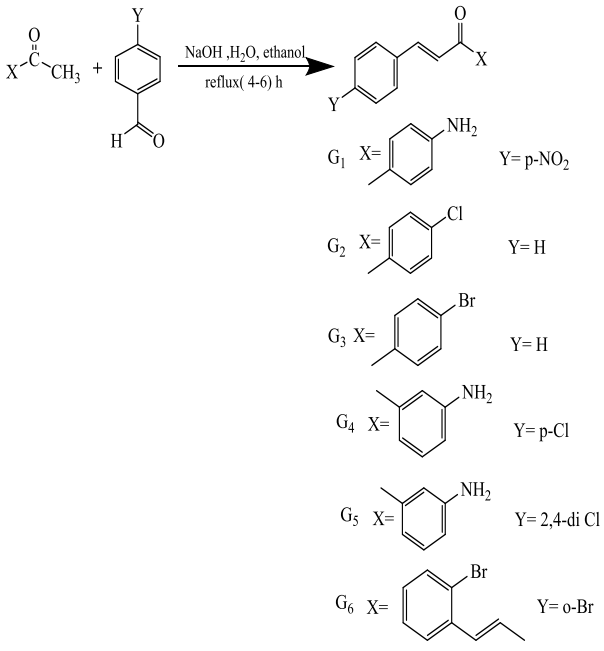
5- Mass spectroscopy: Mass spectra 5973 Network Mass Selective Detector, Center for Microanalysis in Iran (USA).

6-Thin-layer chromatography (TLC): The purity of the synthesized compounds was confirmed by TLC on Echo silica gel F254 plates, with spot development using iodine vapor in various solvents.

Synthesis Procedures:

Preparing Chalcon (G_1 -G_6)

In general, 40% sodium hydroxide solution in water and rectified spirit are added to a flask equipped with a mechanical stirrer. Crushed ice was used to form a bath around the flask. With steady stirring, substituted acetophenones (0.01 M) were poured into the solution and added with substituted benzaldehydes (0.01 M). The mixture was vigorously agitated while being held at 25 °C for 4–6 h, or until the slurry was thick enough to stop stirring. The stirrer was removed, and the mixture of the reaction was maintained at 8 °C overnight. The products (G1–G6) were filtered via a Buchner funnel using suction, followed by a wash in ice-cold ethanol that is neutral to litmus and a rinse in cold water. The process of reforming the raw material from ethanol [14] is shown by the following scheme (1).



Scheme 1: Synthesis of chalcone (G_1–G_6)

(E)-1-(4-aminophenyl)-3-(4-nitrophenyl)prop-2-en-1-one (G_1)

Orange color, mp 147 °C–150 °C, FT-IR spectrum of compound shows the following bands:

stretched vibration band of NH at 3386.72–3485.19 cm^{-1}, stretched vibration band of C-H art at 3012.86–3045.61 cm^{-1}, stretched vibration band of C-H ale at 2932.85–2982.85 cm^{-1}, stretched vibration band of C=O at 1635.50 cm^{-1}, stretched vibration band of C=N at 1315.80–1340.29 cm^{-1}, and stretched vibration band of o.o.p at 824.18–853.26 cm^{-1}.

(E)-1-(4-chlorophenyl)-3-phenylprop-2-en-1-one (G_2)

White color, mp 58 °C–60 °C, FT-IR spectrum of compound shows the following bands: stretched vibration band of C-H art at 3062.23–3094.53 cm^{-1}, stretched vibration band of C-H ale at 2360.68–2419.13 cm^{-1}, stretched vibration band of C=O at 1646.69 cm^{-1}, stretched vibration band of C=C at 1578.77 cm^{-1}, stretched vibration group of C-C at 1277.58–1300.84 cm^{-1}, stretched vibration band of C-Cl at 726.30 cm^{-1}, and stretched vibration band of o.o.p at 691 cm^{-1}.

(E)-1-(4-bromophenyl)-3-phenylprop-2-en-1-one (G_3)

White color, mp 69 °C–72 °C, FT-IR spectrum of compound shows the following bands: stretched vibration band of C-H art at 3028.82–3058.31 cm^{-1}, stretched vibration band of C-H ale at 2950.84 cm^{-1}, stretched vibration band of C=O at 1654.26 cm^{-1}, stretched vibration band of C=C at 1581.59 cm^{-1}, stretched vibration band of C-Br at 757.97 cm^{-1}, and stretched vibration band of o.o.p at 664.02 cm^{-1}.

(E)-1-(3-aminophenyl)-3-(4-chlorophenyl)prop-2-en-1-one (G_4)

Yellowish white color, mp 138 °C–140 °C, FT-IR spectrum of compound shows the following bands: stretched vibration band of N-H at 3615.95 cm^{-1}, stretched vibration band of C-H art at 3086.60–3127.60 cm^{-1}, stretched vibration band of C-H ale at 2919.98 cm^{-1}, stretched vibration band of C=O at 1667.77 cm^{-1}, stretched vibration band of C=C at 1577.15 cm^{-1}, stretched vibration band of C-Cl at 728.38 cm^{-1}, and stretched vibration band of o.o.p at 682.72 cm^{-1}.

(E)-1-(3-aminophenyl)-3-(2,4-dichlorophenyl)prop-2-en-1-one (G_5)

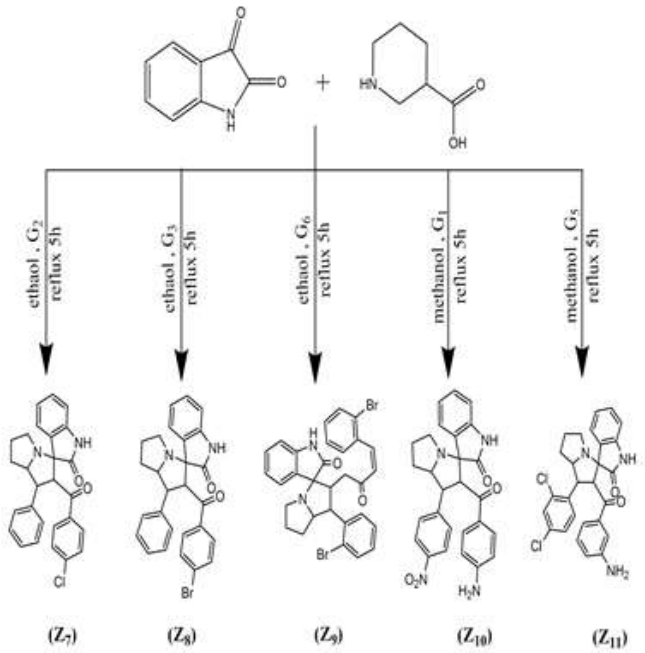
Light yellow color, mp 133 °C–135 °C, FT-IR spectrum of compound shows the following bands: stretched vibration band of N-H at 3289.77–3368.71 cm^{-1},stretched vibration band of C-H art at 3025.57–3065.66 cm^{-1}, stretched vibration band of C-H ale at 2863.16 cm^{-1}, stretched vibration band of C=O at 1655.29 cm^{-1}, stretched vibration band of C-Cl at 781.37 cm^{-1}, and stretched vibration band of o.o.p at 821.38 cm^{-1}

(1E,4E)-1,5-bis(2-bromophenyl)penta-1,4-dien-3-one (G_6)

Yellow color, mp 62 °C–65 °C, FT-IR spectrum of compound shows the following bands: stretched vibration band of C-H art at 3025.90–3058.78 cm^{-1}, stretched vibration band of C-H ale at 2919.03 cm^{-1}, stretched vibration band of C=O at 1669.20 cm^{-1}, stretched vibration band of C=C at 1558.06–1587.49 cm^{-1}, stretched vibration band of C-Brl at 753.08 cm^{-1}, and stretched vibration band of o.o.p at 974.85 cm^{-1}.

General Procedure for the synthesis of compounds (Z_7 - Z_{11})

Formation of nitrogen-containing heterocycles via intermolecular 1,3-dipolar cycloaddition processes. Here, isatin and L-proline were combined with chalcones, which were produced by the reaction of substituted benzaldehydes with acetophenones [15], as shown by the following scheme (2).



Scheme (2): Synthesis of spiroheterocyclic from isatin **2'-(4-chlorobenzoyl)-1'-phenyl-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (Z_7)**

Off white color, FT-IR spectrum displays the following bands: stretched vibration band of N-H at 3155.16–3184.20 cm^{-1}, stretched vibration band of C-H ar at 3080.26 cm^{-1}, stretched vibration band of C-H al at 2911.96–2958.14 cm^{-1}, stretched vibration band of C=O keton at 1710.40 cm^{-1}, stretched vibration band of C=O amid at 1649.80 cm^{-1}, stretched vibration band of C=C at 1403.73–1465.16 cm^{-1}, stretched vibration band of C-N at 1251.23 cm^{-1}, and stretched vibration band of C-Cl at 743.33 cm^{-1}. 1H NMR (400 MHz, DMSO-d6) δ 10.3 (s, 1H,NH), 8.2 (d, 2H,), 7.5 (d, 2H,), 6.9-7.2 (m, 9H, aromatic), 4.4 (d, 1H), 4.1 (m, 1H), 4 (t, 1H), 3 (t, 2H), 1.7 (m, 2H), 1.8 (m, 2H). 13C NMR (100 MHz, DMSO-d6) δ 197.8, 175.4, 139.4, 139.0, 138.3, 135.3, 129.5, 129.0, 128.8, 127.4, 126.9, 124.7, 124.4, 123.3, 111.6, 78.7, 70.2, 66.7, 51.2, 50.5, 28.8, 24.7.

2'-(4-bromobenzoyl)-1'-phenyl-1',2',5',6',7',7a'hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (Z_8)

Light yellow color, mp 178 °C–180 °C, FT-IR spectrum shows the following bands: stretched vibration band of N-H at 3227.60–3226.82 cm^{-1}, stretched vibration band of C-H ar at 3029.23–3066.79 cm^{-1}, stretched vibration band of C-H ale at 2963.68 cm^{-1}, stretched vibration band of C=O keton at 1712.03 cm^{-1}, stretched vibration band of C=O amid at 1618.12 cm^{-1}, stretched vibration band of C=C at 1448.46–1462.30 cm^{-1}, stretched vibration band of C-N at 1256.86 cm^{-1}, and stretched vibration band of C-Br at 790.77 cm^{-1}. 1H NMR (400 MHz, DMSO-d6) δ 10.25 (s, 1H,NH), 6.42–7.87 (m, 13H, aromatic,), 1.07–4.84 (m, 9H,). 13C NMR (100 MHz, DMSO-d6) δ 197.9, 175.4, 140.0, 138.3, 135.7, 131.8, 129.5, 128.8, 127.4, 126.9, 126.7, 124.6, 124.4, 123.3, 110.9, 78.7, 70.2, 66.7, 51.2, 50.7, 29.2, 24.8.

(1'R,2'R,3R,7a'R)-1'-(2-bromophenyl)-2'-((Z)-3-(2bromophenyl)acryloyl)-1',2',5',6',7',7a'-exahydrospiro[indoline-3,3'-pyrrolizin]-2-one (Z_9)

White color, mp 177 °C–180 °C, FT-IR spectrum displays the following bands: stretched vibration band of N-H at 3195.02 cm^{-1}, stretched vibration band of C-H ar at 3029.06–3089.49 cm^{-1}, stretched vibration band of C-H al at 2867.01–2963.83 cm^{-1}, stretched vibration band of C=O keton at 1709.11 cm^{-1}, stretched vibration band of C=O amid at 1617.78 cm^{-1}, stretched vibration band of C=C at 1440.66–1470.34 cm^{-1}, stretched vibration band of C-N at 1253.46 cm^{-1}, and stretched vibration band of C-Br at 749.20 cm^{-1}. 1H NMR (400 MHz, DMSO-d6) δ 10.5 (s, 1H,NH), 6.55–7.30 (m, 12H, aromatic,), 1.03–3.84 (m, 9H,).13C NMR (100 MHz, DMSO-d6) δ 140.0, 137.0, 133.6, 132.5, 131.7, 129.6, 129.4, 128.7, 128.4, 127.9, 127.3, 124.7, 124.6, 124.2, 123.4, 111.03, 78.17, 67.52, 64.87, 50.76, 48.86, 29.52, 25.01.

2'-(4-aminobenzoyl)-1'-(4-nitrophenyl)-1',2',5',6',7',7a' hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (Z_{10})

Dark brown, mp 280 °C–284 °C, FT-IR spectrum shows the following bands: stretched vibration band of N-H at 3346.27–3474.12 cm^{-1}, stretched vibration band of C-H ar at 3046.16 cm^{-1}, stretched vibration band of C-H al at 2880.06 cm^{-1}, stretched vibration band of C=O keton at 1711.59 cm^{-1}, stretched vibration band of C=O amid at 1609.36 cm^{-1}, stretched vibration band of C=C at 1414.24–1451.40 cm^{-1}, stretched vibration band of $-NO_2$ at 1325.73 cm^{-1}, stretched vibration band of C-N) at 1230.30 cm^{-1}, and stretched vibration band of C-Br at 739.82 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.2-6.7 (d, 2H,), 6.9–7.2 (m, 4H, aromatic), 5.2 (s, 2H, NH_2), 4.4 (d, 1H), 4–4.1 (m, 2H), 3 (m, 4H), 1.8 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 198.3, 175.3, 152.2 ,146.7, 142.7, 140.0 ,130.0, 128.8, 127.7, 124.6, 124.4, 124.1, 123.2, 114.1, 111.6.

2'-(3-aminobenzoyl)-1'-(2,4-dichlorophenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (Z_{11})

Dark purple color, FT-IR spectrum of compound shows the following bands: stretched vibration band of N-H at 3191.31 cm^{-1}, stretched vibration band of C-H ar at 3062.33 cm^{-1}, stretched vibration band of C-H al at 2967.04 cm^{-1}, stretched vibration band of C=O keton at 1711.89 cm^{-1}, stretched vibration band of C=O amid at 1614.63 cm^{-1}, stretched vibration band of C=C at 1466.00 cm^{-1}, stretched vibration band of C-N at 1258.81 cm^{-1}, and stretched vibration band of C-Cl at 748.95 cm^{-1}

3- RESULTS AND DISCUSSION

A small library of six chalcones (G_1–G_6) was prepared using substituted acetophenones and substituted benzaldehydes in 40% sodium hydroxide solution in water, and rectified spirit was added at 25 °C for 4–6 h. Six final compounds (Z_7–Z_{11}) were prepared through the formation of nitrogen-containing heterocycles via intermolecular 1,3-dipolar

cycloaddition processes. Here, isatin and L-proline were combined with chalcones. The reflux of the reaction components in ethanol for 1–6 h yielded modest to good yields of G_1–G_6 and Z_7–Z_{11}, all of which could be isolated by simple filtration of the directly precipitated products. The purity of these compounds were 90%–98% based on the FTIR spectrum, and these compounds were recrystallized to provide well-formed needles ranging from white to brown. Substituted spiroheterocyclics were synthesized by intermolecular 1,3-dipolar cycloaddition processes. Isatin and L-proline were coupled with chalcones, which were produced by the reaction of substituted benzaldehydes with acetophenones. In brief, 1 mmol prepared chalcones was reacted with 1 mmol isatin and 1 mmol L-proline in refluxing ethanol to provide the desired compounds. TLC was used to monitor the completion of the reaction. The reaction mixture was cooled. The condensate was filtered and purified by recrystallization from ethanol. FTIR and NMR experiments were conducted to achieve the structural determination and signal assignments of the final products (Z_7–Z_{11}). The physical characteristics of some of the synthesized derivatives are presented. The structure of the synthesized systems was determined by melting points and spectroscopic data from 'H NMR, FT-IR, mass spectrometry, ^{13}C NMR techniques, and antibacterial and antifungal activity tests.

Test for antibacterial activity:

Commercially available nutrient agar (Acumedia/LAB) was produced in accordance with conventional protocols to create nutrient agar plates. To prepare nutrient agar, 28 g was added to 1L of distilled water in a conical flask and heated until it fully dissolved. Cotton was used to seal the flask, and the medium was autoclaved for 20 min at 121°C and 15 bound/inch of pressure to sanitize it. The medium was then chilled to between 45 °C and 55 °C, placed into a Petri dish (approximately 15–20 mL), and allowed to cool and solidify. The medium was prepared for the development of bacteria.

In this study, four different types of bacteria were used to investigate the effect of bacterial growth inhibition (*Pseudomonas aeruginosa* and *Staphylococcus aureus* [Gram-positive], *Escherichia coli* [Gram-negative], and *Streptococcus* spp. [Gram-positive]) following the strategy of Kirby–Bauer [16]. In the sensitivity test, four colonies of the aforementioned bacterial species were moved to the nutritional medium (nutritional agar). Thereafter, the medium was incubated for 15–16 h at 37 °C. Subsequently, normal saline solution was diluted. Lastly, 0.1 mL of the bacterial suspension was evenly dispersed across the surface of the nutrient agar plate. The dishes were left to stand for around 30 min [17].

After being removed from the filter flask, the tablets were immersed in solutions with different amounts of the chemical components. The antibacterial activity of theses chemical compounds will be investigated to quantify their inhibitory effects. The chemical compounds under study were initially dissolved in a solvent (N,N-dimethyl formamide [DMF]). The tablets saturated with the solutions were then placed on the agar surface with appropriate spacing and incubated for 20–24 h. The four prior species were inhibited using the antibiotics (gentamycin and tetracycline), which are approved by WHO tests and utilized in public health laboratories. After measuring the inhibition zone and carrying out the experiment three times, the measurement rate was established. Table 1 lists the results of the preliminary screening tests and examines the inhibition zones induced by the different substances.

Table (1): Antibacterial activity data of the same prepared spiro compounds

	Gram negative									
	Escherichia coli					*Pseudomonas aeruginosa*				
	Concentration (mg/mL)					Concentration (mg/mL)				
compound	1.25	2.5	5	12.5	25	1.25	2.5	5	12.5	25
Z_8	*	*	10	16	21	*	*	9	14	20
Z_{10}	*	*	13	15	21	*	*	*	13	18
Gentamycin	7	12	20	27	31	12	14	20	28	30
Tetracycline	5	9	17	23	27	7	11	13	15	24
DMF	*	*	*	*	*	*	*	*	*	*

* No bacterial growth was observed.

	Gram positive									
	Staphylococcus aureus					*Streptococcus spp.*				
	Concentration (mg/mL)					Concentration (mg/mL)				
compound	1.25	2.5	5	12.5	25	1.25	2.5	5	12.5	25
Z_8	8	13	16	22	27	*	8	14	18	25
Z_{10}	*	10	14	21	25	8	17	23	28	31
Gentamycin	10	15	27	36	39	13	14	29	31	34
Tetracycline	11	17	29	34	36	10	12	26	30	35
DMF	*	*	*	*	*	*	*	*	*	*

* No bacterial growth was observed

Test for antifungal activity:

The agar dilution method, as reported in the literature [18], was utilized to evaluate antifungal activity with minor modifications. This process was used to determine whether the chemicals generated adversely affect the radial growth of the mycelium in the test organisms. Both cultivars were cultivated on potato dextrose agar (PDA), and they were used for fungal pathogenicity tests. According to the manufacturer's instructions, 39 g of PDA was dissolved in 1 L of distilled water, autoclaved at 121 °C for 20 min, pressed with 15 pounds, and cooled to 45 °C in a water bath. After the flask cooled, 42 mg/L ampicillin was added to stop bacterial growth [19].

The synthesized compounds were dissolved in DMF, and sterile filter sheets were saturated with these different concentrated solutions. The medium was used in a laminar flow cabinet and placed into a 90 mm sterile plastic Petri dish. It was then left to set at a temperature between 40 °C and 45 °C. A 6 mm plug of 5-day-old cultures was then added to the center of each test plate, with one plug for each pathogen. The control consisted of a plate containing a 6 mm plug of fungus in the basal medium [20].

In a growth cabinet, plates were incubated at 25 °C±2 °C for 5 (*Aspergillus niger*) and 7 days (*Candida albicans*). The screening process was conducted twice, and each assay was performed in duplicate. Radial mycelial growth was calculated daily for 5 (*A. niger*) and 7 days (*C. albicans*) by adding the two perpendicular colony diameters for each replicate. The values, which are presented in millimeter diameters each day, were used to calculate the percentage of mycelial growth inhibition using the formula below:

$$\% \text{ mycelial growth inhibition} = \frac{G_{Control} - G_{Test}}{G_{Control}} * 100$$

Where: $G_{Control}$ = Average diameter of the fungal colony of the control. G_{Test} = Average diameter of the fungal colony treated with the prepared compounds.

The preliminary screening tests results are shown in Table (2), which also shows the inhibition zones generated by the various substances. The data from two screening trials were combined and averaged.

Table (2): Percentage mycelial growth inhibition data of the prepared spiro compounds

	Candida albicans					*Aspergillus niger*				
	Concentration (mg/mL)					Concentration (mg/mL)				
compound	1.25	2.5	5	12.5	25	1.25	2.5	5	12.5	25
Z_8	11	19	41	52	67	*	13	29	40	51
Z_{10}	24	35	45	54	62	27	45	61	55	51
Fluconazole	14	20	47	64	76	13	22	43	65	72
DMF	*	*	*	*	*	*	*	*	*	*

4-Conclusions

1. Chalcones are utilized as starting materials for the synthesis of all heterocyclic compounds. They are produced by reacting substituted benzaldehyde with substituted acetophenone in good yields with NaOH.

2. The six rings are created by reacting a large number of chemicals with the initially prepared chalcone compounds.
3. The data from mass spectroscopy, FT-IR, 13C-NMR, and ^{1}H-NMR provide strong support for the synthesis of the synthesized compounds.
4. Tests for antibacterial and antifungal activity yielded good results.

5-Reference

[1] M. A. Borad, M. N. Bhoi, N. P. Prajapati, and H. D. Patel, "Review of synthesis of spiro heterocyclic compounds from isatin," *Synth. Commun.*, vol. 44, no. 7, pp. 897–922, 2014, doi: 10.1080/00397911.2013.843196.

[2] R. Raju, R. Raghunathan, N. Arumugam, A. I. Almansour, and R. S. Kumar, "Regio-and stereoselective synthesis of novel β-lactam engrafted spiroheterocyclic hybrids via one-pot three component cycloaddition strategy," *Tetrahedron Lett.*, vol. 61, no. 52, p. 152661, 2020.

[3] T. Kumar, N. Satam, and I. N. N. Namboothiri, "Hauser–Kraus Annulation of Phthalides with Nitroalkenes for the Synthesis of Fused and Spiro Heterocycles," *European J. Org. Chem.*, vol. 2016, no. 20, pp. 3316–3321, 2016.

[4] A. M. Abdella, A. M. Abdelmoniem, I. A. Abdelhamid, and A. H. M. Elwahy, "Synthesis of heterocyclic compounds via Michael and Hantzsch reactions," *Journal of Heterocyclic Chemistry*, vol. 57, no. 4. pp. 1476–1523, 2020. doi: 10.1002/jhet.3883.

[5] Y. Villarreal, B. Insuasty, R. Abonia, A. Ortiz, P. Romo, and J. Quiroga, "Three-component one-pot synthesis of new spiro[indoline-pyrrolidine] derivatives mediated by 1,3-dipolar reaction and DFT analysis," *Monatshefte fur Chemie*, vol. 152, no. 5, pp. 497–506, 2021, doi: 10.1007/s00706-021-02765-z.

[6] B. S. Bashar *et al.*, "Application of novel Fe3O4/Zn-metal organic framework magnetic nanostructures as an antimicrobial agent and magnetic nanocatalyst in the synthesis of heterocyclic compounds," *Front. Chem.*, vol. 10, no. October, pp. 1–17, 2022, doi: 10.3389/fchem.2022.1014731.

[7] M. Adlu and I. Yavari, "One-pot, mild and efficient multicomponent synthesis of novel various spiro-nitrogen heterocycle compounds," *Bull. Chem. Soc. Ethiop.*, vol. 37, no. 1, pp. 115–122, 2023.

[8] R. A. Dabhi, M. P. Dhaduk, V. D. Bhatt, and B. S. Bhatt, "Synthetic approach toward spiro quinoxaline-β-lactam based heterocyclic compounds: Spectral characterization, SAR, pharmacokinetic and biomolecular interaction studies," *Journal of Biomolecular Structure and Dynamics*. 2022. doi: 10.1080/07391102.2022.2086176.

[9] G. S. Singh and Z. Y. Desta, "Isatins as privileged molecules in design and synthesis of spiro-fused cyclic frameworks," *Chem. Rev.*, vol. 112, no. 11, pp. 6104–6155, 2012, doi: 10.1021/cr300135y.

[10] R. Pereira, A. M. S. Silva, D. Ribeiro, V. L. M. Silva, and E. Fernandes, "Bis-chalcones: A review of synthetic methodologies and anti-inflammatory effects," *Eur. J. Med. Chem.*, vol. 252, p. 115280, 2023.

[11] S. Farooq and Z. Ngaini, "Recent synthetic methodologies for chalcone synthesis (2013-2018)," *Curr. Organocatalysis*, vol. 6, no. 3, pp. 184–192, 2019.

[12] K. Mezgebe, Y. Melaku, and E. Mulugeta, "Synthesis and Pharmacological Activities of Chalcone and Its Derivatives Bearing N-Heterocyclic Scaffolds: A Review," *ACS omega*, 2023.

[13] S. M. Reddy, "Elucidating reaction mechanism of some Oxa Thia Aza Heterocycles and Chalcone derivatives through Computational Techniques," 2023.

[14] A. K. A. Al-naseeri, "Synthesis and Characterization of Some New Pyrazoline and Isoxazoline Derivatives as Antibacterial Agents Abstract : Introduction : Materials and Methods : Biological Evaluation :," vol. 13, no. 3. 2016.

[15] A. Alizadeh, A. Roosta, and M. Halvagar, "Four-Component Regio- and Diastereoselective Synthesis of Pyrrolizidines Incorporating Spiro-Oxindole/Indanedione via 1,3-Dipolar Cycloaddition Reaction of Azomethine Ylides," *ChemistrySelect*, vol. 4, no. 1. pp. 71–74, 2019. doi: 10.1002/slct.201803418.

[16] M. T. Brandl, "Fitness of human enteric pathogens on plants and implications for food safety," *Annu. Rev. Phytopathol.*, vol. 44, pp. 367–392, 2006, doi: 10.1146/annurev.phyto.44.070505.143359.

[17] M. T. Brandl, "Fitness of human enteric pathogens on plants and implications for food safety," *Annu. Rev. Phytopathol.*, vol. 44, pp. 367–392, 2006.

[18] L. Yang, Y. Liu, C. Sternberg, and S. Molin, "Evaluation of enoyl-acyl carrier protein reductase inhibitors as Pseudomonas aeruginosa quorum-quenching reagents," *Molecules*, vol. 15, no. 2, pp. 780–792, 2010, doi: 10.3390/molecules15020780.

[19] R. J. Lamont, G. N. Hajishengallis, and H. F. Jenkinson, *Oral microbiology and immunology.*, no. Ed. 2. ASM press, 2014.

[20] P. D. Marsh, M. A. O. Lewis, D. W. Williams, and M. V Martin, *Oral microbiology E-book*. Elsevier health sciences, 2009.

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تحضير وتوصيف مركبات حلقية حلقية غير متجانسة جديدة من الايزاتين وتقييم فعاليتها المضادة للفطريات والبكتيريا

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الخلاصة:

البحث الحالي قدم ستة جالكونات، محضرة من الأسيتوفينون المستبدل والبنزالدهيد المستبدل، تم استخدام هذه الجالكونات لتحضير ستة مركبات حلقية غير متجانسة، تم استخدام كروماتوغرافيا الطبقة الرقيقة لمراقبة التفاعلات، وتم استخدام تقنيات التحليل الطيفي الكتلي، والرنين المغناطيسي النووي الكربوني ، والرنين المغناطيسي النووي البروتوني ، والتحليل الطيفي للأشعة تحت الحمرا لتوصيف جميع الهياكل. بالإضافة إلى ذلك، تمت دراسة الفعالية البيولوجية للمركبات الحلقية غير المتجانسة المحضرة ضد البكتيريا والفطريات.

الكلمات المفتاحية : الإيساتين، الجالكونات، المركبات الحلقية الغير متجانسة.