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Antioxidant and Antimicrobial Activities of New Ethers, 1,3-Diazetidene-4-One and Thiazolidine-4-one Derivatives Containing Imidazobenzothiazole.

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Abstract

The synthesis of novel thiazolidinones **6-8A**, diazetidenes **9-11A**, and ethers **13-18A** was described using 2-aminobenzathiazole and 4-bromophenacyl bromide as starting materials. The reaction of 2-aminobenzathiazole with 4-bromophenacyl bromide afforded the product **A1** in 80% yield. Position 5 at the product **A1** 5-(4-bromophenyl)imidazo(2,1-b)benzothiazole used to form carbaldehyede group **A2** under Vilsmeier-Huck conditions. Schiff bases **3-5A** were then produced via condensation of **A1** various aromatic amines. The products **3-5A** were reacted with naphthyl isocyanate and thioacetic acid to give the compounds **6-8A** (77-90% yields) and **9-11A** (92-97% yields), respectively. The product **2A** was reduced with $NaBH_4$ to provide the corresponding alcohol **12A** in an excellent yield (97%). This was followed by the reaction with aryl halides *via* the Williamson reaction to afford the desired ethers **13-18A** in yields ranging from 50 to 96%. All of the prepared compounds were characterized by FT-IR spectroscopy, and some of them were characterized by ^{1}H NMR and ^{13}C NMR spectroscopy. A few products were evaluated for their antifungal, antibacterial, and antioxidant activities.

Keywords: Antioxidant, Biological activity, Diazetidene, Ethers, Thiazolidinone.

الفعاليات المضادة للأكسدة و المضادة للميكروبات لمشتقات جديدة من الايثرات، و مشتقات 1,3-دايازيتيدين و ثيازوليدين-4-اون التي تحتوي على ايميدازو بنزو ثايازول

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الخلاصة

تم وصف تحضير مشتقات جديدة من ثايازوليدين **6-8A**، دايازيتيدين **9-11A** و الايثرات **13-18A** بأستخدام 2-امينو بنزوثايازول و 4-بروموفيناسيل برومايد كمواد اولية. اعطى تفاعل 2-امينو بنزوثايازول مع 4-بروموفيناسيل برومايد المركب **A1** بمنتوج (80%). استخدم الموقع 5 في المركب **A1** 5-(4-بروموفينيل)ايميدازو(2,1-b)بنزوثايازول لتحضير مجموعة الكارب الديهايد **A2** تحت ظروف هاك-فلس ماير. تم بعد ذلك تحضير قواعد شف **3-5A** عبر تكثيف المركب **A1** لمختلف الامينات الاروماتية. تم تفاعل المركبات **3-5A** مع نفثيل ايزوسيانات وحمض الثايو اسيتيك لاعطاء المركبات **6-8A** بنسبة (77-90%) والمركبات **9-11A** بنسبة (92-97%)، على التوالي. تم اختزال المركب **A2** بأستخدام بورهيدريد الصوديوم لتحضير الكحول **A12** بمنتوج ممتاز (97%). بأتباع ذلك التفاعل مع هاليدات الاريل عبر تفاعل ويليامسون لتحضير الايثرات المرغوبة **13-18A** في نسب تتراوح من 50 الى 96%. تم تمييز و تشخيص

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جميع المركبات المحضرة باستخدام التحليل الطيفي FT–IR ، وتم تشخيص البعض بأستخدام التحليل الطيفي ^{1}H NMR و ^{13}C NMR . كما تم اختبار و تقييم عدد من المركبات لمعرفة الفعالية المضادة للفطريات و البكتيريا و مضادات الأكسدة.

1. Introduction

Heterocyclic compounds represent a major family of organic compounds with significant and well-known biological activity and a wide spectrum of synthetic, pharmacological, and industrial applications. The biological actions of the benzothiazole moiety, which is a versatile moiety, include antibacterial [1], antifungal [2], and antiviral [3] activities. Benzothiazole modifications have produced several compounds with a variety of biological activities [4]. Imidazo[2,1-b]benzothiazole derivatives are repeatedly encountered as bioactive molecules because such derivatives indicate a noticeable role in medicinal and organic chemistry, as they manifest in logically chosen pharmaceutical mediators [5] and naturally occurring substances. In addition, the experimental observations on the biological activity of imidazo[2,1-b]benzo[d]thiazole derivatives also showed their probable role as particular kinase inhibitors [6-18]. Also, some of these compounds were reported as antiviral and immune-supportive agents, such as frentizole [19]. The Vilsmeier-Haack (V-H) reagent is used for chlorination, as well as various condensations, cyclizations, and rearrangements [20-24]. It is a useful technique for adding the formyl group to compounds that are activated aromatic or heteroaromatic. In this study, the formyl group was added to position 5 of the parent chemical to produce 6-(4-bromophenyl)imidazo[2,1-b]benzothiazole-5-carbaldehyde. This 5-carbaldehyde then interacted with various amines to generate Schiff bases as intermediary molecules in the presence of a few drops of glacial acetic acid. Thiazolidinones, which are derived from thiazoles, are among the most actively researched groups of five-membered heterocyclic compounds that contain a carbonyl group, a nitrogen atom, and a sulfur atom [25]. A study of the literature found that thiazolidine derivatives are significant heterocyclic compounds with a lengthy history in medicinal chemistry. Thiazolidine-4-ones, in particular, are a class of heterocyclic compounds that have a wide range of pharmacological activities [26]. Furthermore, a wide range of biological activities are exhibited by molecules with thiazolidine nuclei, including anti-tumor [27], anti-HIV [28], antibacterial [29], antimicrobial [30], anti-convulsant [31], antioxidant [32,33], anti-inflammatory [34], and analgesic [35] properties. β-lactams are four-membered cyclic structures of heterocycles containing nitrogen atoms and a carbonyl group called azetidine-2-one that hold great promise in medicinal chemistry due to their desirable pharmacokinetic effects [36]. Diazetine molecules have been used. Since 1940, the most often recommended medications for the treatment of bacterial infections have been β-Lactam antibiotics, β-Lactam are life-saving drugs that have been widely used to treat [37]. Heterocyclic compounds that contain the imidazo moiety and their fused derivatives constitute the main class of organic compounds with their medical and biological properties; therefore, the development of some novel fused heterocycles is the main goal of the present work.

2. Experimental

2.1. Instruments and chemicals

All the chemicals utilized were purchased from CDH, Sigma Aldrich, BDH, Fluka, and Merck companies. TLC was performed on Merck silica gel 60 F_{254} and visualized by iodine vapors. Melting points are uncorrected and were recorded in open capillary tubes using Gallenkamp melting point equipment. The FT-IR spectral data were recorded using a Shimadzu FT-IR-8400 at the College of Science, University of Baghdad. The ^{1}H NMR and ^{13}C NMR spectral data were recorded on a Varian ultra-shield (400 and 500 MHz spectrometer) at the University of Basrah in Iraq. Chemical shifts are expressed in ppm

downfield from tetramethylsilane (TMS) as an internal standard or deuterated DMSO as a reference. Melting points are uncorrected and were recorded in open capillary tubes using Gallenkamp melting point equipment.

2.2. Chemistry

*2.2.1. Synthesis 6-(4-bromophenyl) imidazo[2,1-b]benzathiazole (**1A**) [38]*

In a round bottomed flask, 2-aminobenzathiazole (3.0 mmol) and 4-bromophenacyl bromide (3.0 mmol) were combined and mixed in absolute EtOH (80-100 mL) before being heated at reflux for 13-15 hours. The reaction was monitored by TLC (ethyl acetate: petroleum ether, 2:1). The reaction mixture was then basified with NaOH (5%) till the pH reached 10-11. The solid crude material was filtered, washed with hot distilled water, dried, and recrystallized from ethanol into the desired product **1A**. Table 1 displays the physical characteristics of product **1A**.

*2.2.2. Synthesis of imidazo[2,1-b]benzthiazole-5-carbaldehyde (**2A**)*

In a round bottomed flask, a solution of phosphorus oxychloride (0.012 mol) in DMF (7 mL) at a temperature of 0 to 5 °C. A solution of compound **1A** (0.012 mol) in DMF (7 mL) was then slowly added with stirring. The reaction mixture was heated at 45-50 °C for 2 hours. The completion of the reaction was determined by TLC (eluent with petroleum ether/ethyl acetate, 2:1). The reaction mixture was subsequently cooled and added to crush ice. The solid crude material was filtered, washed with water, and recrystallized from ethanol to give the title product **2A**. Table 1 lists the physical properties of product **2A**.

*2.2.3. Synthesis of Schiff base derivatives **3-5A*** [39]

In a round-bottomed flask, a solution of compound **2A** (0.001 mol) in EtOH (25 mL) with a few drops of glacial acetic acid was heated for 10 minutes. Different primary amines (0.001 mol) were added to the solution before refluxing for 10-30 hours. The reaction mixture was poured onto crushed ice before filtration of the solid crude material. Table 1 shows the physical properties of products **3-5A**.

*2.2.4. Synthesis of 4-thiazolidinone derivatives **6-8A***

To a mixture of Schiff bases **3-5A** (0.0002 mol) and 2-mercaptoacetic acid (0.0002 mol) in EtOH (10 mL), $ZnCl_2$ (0.0002 mol) was gradually added. The reaction mixture was then heated to reflux for 17-25 hours. The solid crude material was then filtered, washed with water, and recrystallized from EtOH. Table 1 shows the physical properties of products **6-8A**.

*2.2.5. Synthesis of β-azalactam derivatives **9-11A***

In a round-bottomed flask, a mixture of Schiff bases **3-5A** (0.0016 mol) and 1-naphthyl isocyanate (0.0016 mol) in THF (10 mL) was refluxed for 10-22 hours. The solvent was then evaporated, filtered, and dried to afford the derivatives ***9-11A***. The physical properties of these products (***9-11A***) are listed in Table 5.

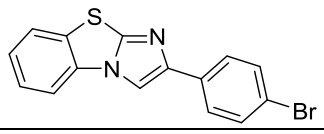
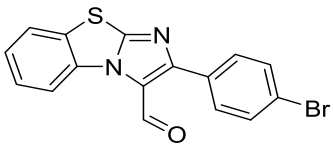
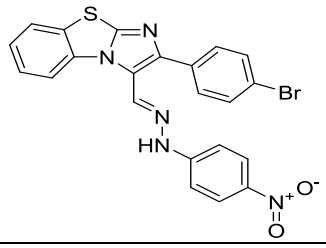
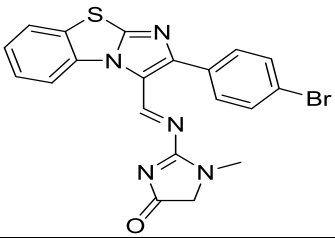
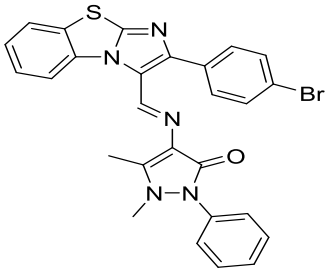
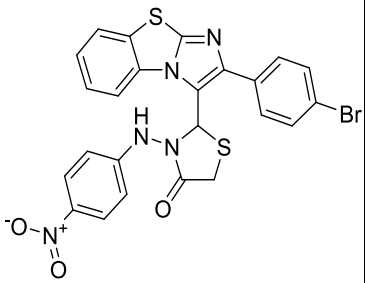
*2.2.6. Synthesis of (2-(4-bromophenyl)benzo[d]imidazo[2,1-b]thiazol-3-yl)methanol (**12A**)* [41]

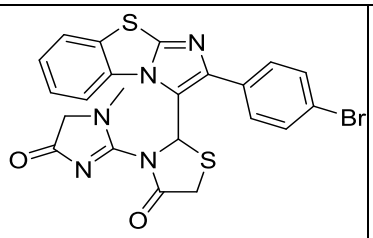
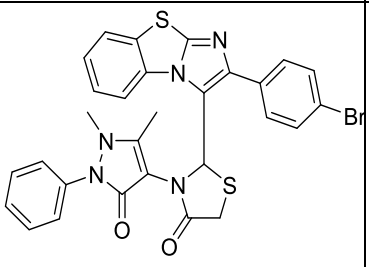
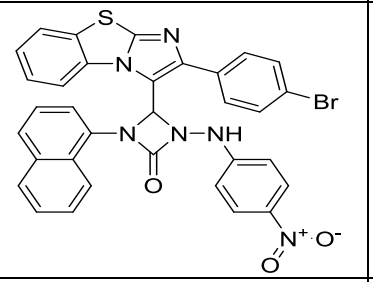
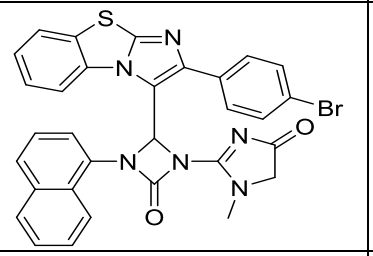
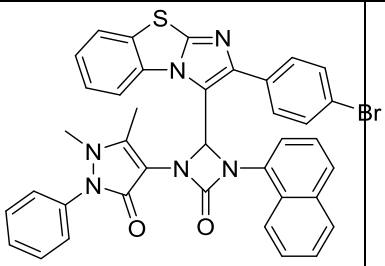
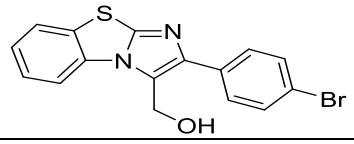
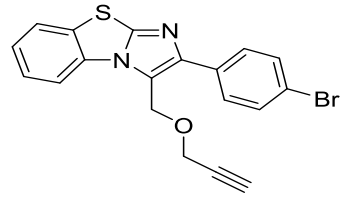
To a solution of aldehyde **2A** (0.001 mol) in MeOH (10 mL) at 5 °C, $NaBH_4$ (0.001 mol) was slowly added. The reaction mixture was then heated to reflux for 5 hours. The solution was acidified using HCl to pH = 1, then basified with ammonia. The solvent was concentrated *in vacuo* and the organic layer was extracted with dichloromethane before evaporation to obtain the sold derivatives. The physical properties of product **12A** are displayed in Table 5.

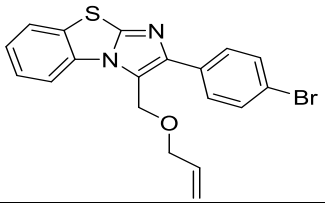
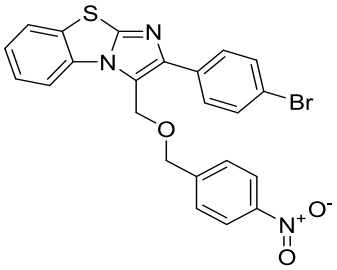
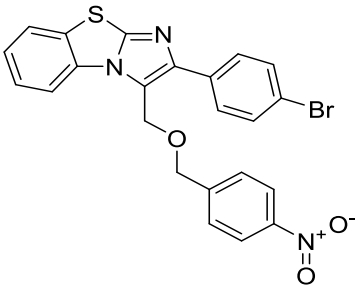
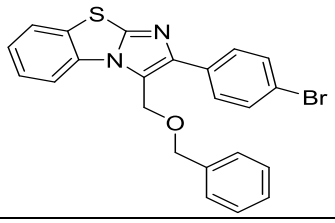
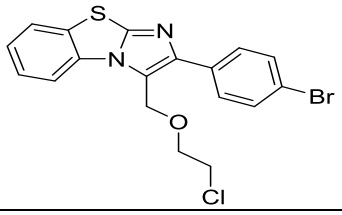
*2.2.7. Synthesis of ether derivatives (**13-18A**)*

A mixture of compound **12A** (0.009 mol), appropriate alkyl halide (0.002 mol), and sodium carbonate (0.003 mol) in EtOH (10 mL) was refluxed for 25 hours. The reaction mixture was then cooled before evaporating the solvent to form the desired compounds **13-18A**. Table 1 shows the physical properties of products **13-18A**.

Table 1: compounds' physical qualities (1-18A)

No.	Structure	Molecular formula	Molecular weight (g/mole)	Color	m.p. (℃)	Time (h)	Yield (%)
1A		$C_{15}H_9BrN_2S$	329.22	Orange	125	13-15	80
2A		$C_{16}H_9BrN_2OS$	357.23	Light yellow	150	1-2	85
3A		$C_{22}H_{14}BrN_5O_2S$	492.35	Orange	130	10	62
4A		$C_{20}H_{14}BrN_5OS$	452.33	Pale yellow	104	32	69
5A		$C_{27}H_{20}BrN_5OS$	542.46	Pale Orange	127	22	56
6A		$C_{24}H_{16}BrN_5O_3S_2$	566.45	Light Brown	138	17	90

7A		$C_{22}H_{16}BrN_5O_2S_2$	526.43	Light Orange	123	22	86
8A		$C_{29}H_{22}BrN_5O_2S_2$	616.55	Brown	160	25	77
9A		$C_{33}H_{21}BrN_6O_3S$	661.53	Light Orange	160	10	95
10A		$C_{31}H_{21}BrN_6O_2S$	621.51	Pale Yellow	273	22	92
11A		$C_{38}H_{27}BrN_6O_2S$	711.64	Pale Yellow	248	10	97
12A		$C_{16}H_{11}BrN_2OS$	359.24	Yellowish-orange	172	5	97
13A		$C_{19}H_{13}BrN_2OS$	397.29	Off white	205	25	75

14A		$C_{19}H_{15}BrN_2OS$	399.31	Pale Yellow	318	25	50
15A		$C_{23}H_{16}BrN_3O_3S$	494.36	Orange	185	25	53
16A		$C_{23}H_{16}BrN_3O_3S$	494.36	Off white	350	25	95
17A		$C_{23}H_{17}BrN_2OS$	449.37	Pale Yellow	360	25	96
18A		$C_{18}H_{14}BrClN_2OS$	421.74	Off white	165	25	50

2.3. Antifungal and antibacterial activities [40]

Some synthetic substances underwent antimicrobial susceptibility testing using the "good diffusion strategy". Two different bacterial strains, *staphylococcus aureus* as a gram-positive and *klebsiella pneumonia* as a gram-negative, were utilized as test organisms for the compounds. Specimens were grown for 24 hours at a temperature of 37 °C on Muller-Hinton agar medium. The samples were planted on PDA medium for 3-5 days at a temperature of 28 °C in order to test for a pathogenic fungal strain known as *Candida*. Agar plates were surface inoculated uniformly with 100 µL frome both culture of tested microorganism [41]. Some of the outcomes were favorable, as indicated in Table 4.

2.4. Antioxidant activity

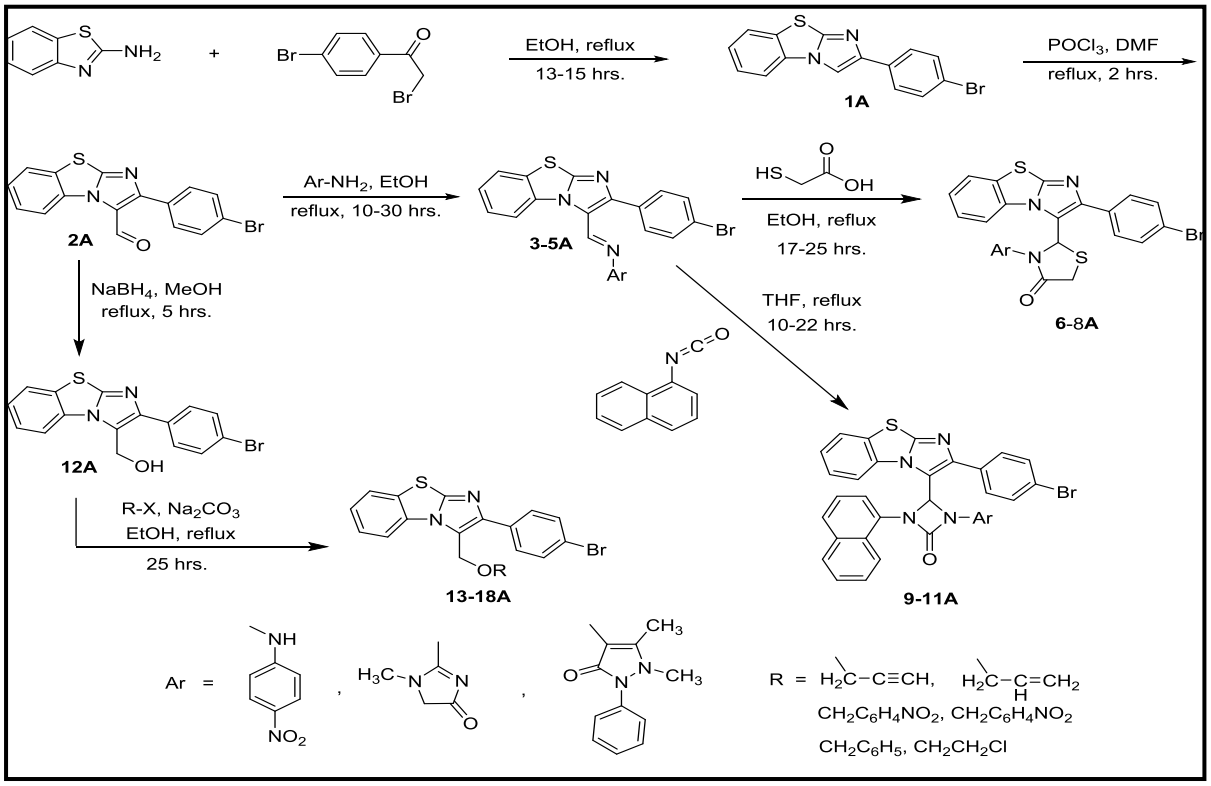
Antioxidant activity and a significant scavenging percentage against the DPPH free radical were found in some of the newly synthesized compounds [42]. DPPH (1,1-Diphenyl-2-picryl-hydrazyl): DPPH (4 mg) was dissolved in 100 mL of methanol, and by shielding the aluminum foil test tubes, the solution was kept shielded away from light. Various concentrations (100, 50, 25, 12.5, and 6.25 ppm) were prepared from 1 to 8 by dissolving 1

mg of the compound and then dissolving it with 10 mL of methanol to prepare 100 ppm. This concentration was then diluted to prepare the above-mentioned concentrations. Ascorbic acid (vitamin C): Similar concentrations of the prepared compounds were prepared.

3. Results and discussion

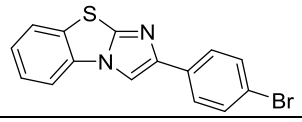
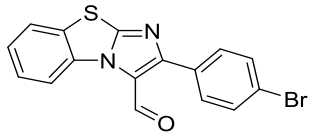
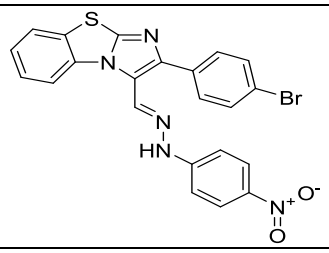
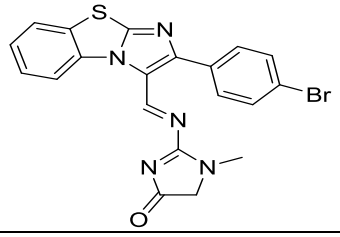
3.1. Chemistry

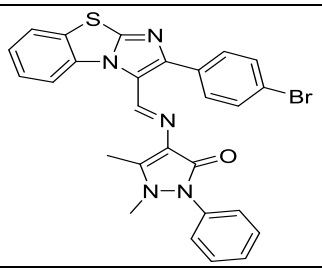
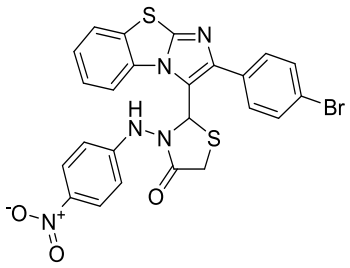
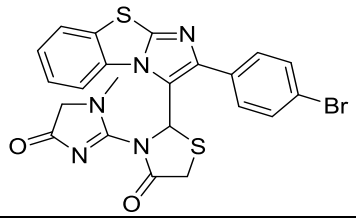
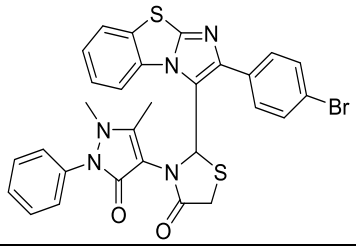
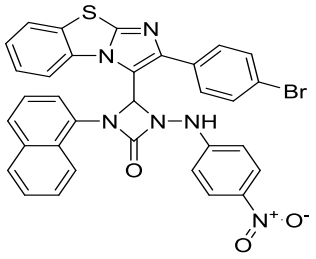
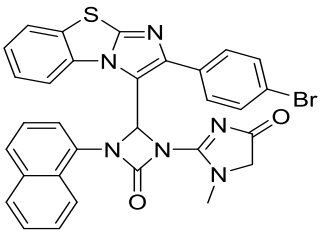
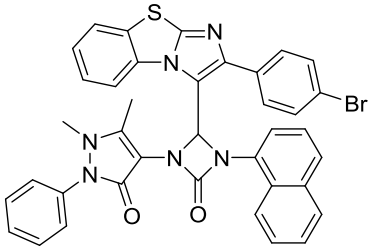
The preparation of new thiazolidinones **6-8A**, β-lactams **9-11A**, and ethers **13-18A** derived from imidazobenzothiazole was successfully achieved using 2-aminobenzothiaozle as a starting material (Scheme 1). To access these derivatives, compound **1A** was synthesized in 80% yields using a well-established method by the reaction of 2-aminobenzothiaozle with *p*-bromophenacyl bromide. The FT-IR spectral data of compound **1A** shows that the stretching absorptions of the NH_2 group at 3400 cm^{-1} for 2-aminobenzothiaozle and the C=O group at 1700 cm^{-1} for *p*-bromophenacyl bromide vanished, respectively; new stretching absorptions are found at 1679 to 1662 cm^{-1} due to the C=N of the imidazo moiety. Table 2 lists all the details of the FT-IR spectral data. Vilsmeier-Huck conditions were then employed on compound **1A** to afford the desired product **2A** in 85% yield. The FT-IR spectral data of compound **2A** showed stretching vibrations at 1697 cm^{-1} and 2885 cm^{-1} for the C=O and C-H of the aldehyde group, respectively. The ^{1}H NMR spectral data of compound **2A** showed a singlet signal at 10 ppm for the C-H aldehyde proton, and the ^{13}C NMR spectral data showed a signal at 183.87 ppm for the C-H aldehyde carbon. The Schiff base derivatives **3-5A** were obtained in the third step by the condensation of compound **2A** with different aromatic aldehydes. The FT-IR spectral data of compounds **3-5A** showed the disappearance of the absorption bands of the C=O aldehyde group at **2A,** and the appearance of new absorption bands at 2980-2834 cm^{-1} and 1610-1668 cm^{-1} belong to the stretching absorptions of the C=N and C-H imine groups. The ^{1}H NMR and ^{13}C NMR spectral data of compound **3A** revealed a signal at 8.3 ppm and a signal at 133.6 ppm, respectively, attributed to the imine group. The fourth step involved the ring closure of Schiff bases **3-5A** with thioglycolic acid and naphthyl isocyanate to provide the desired thiazolidinones **6-8A** (77-90% yields) and β-lactams **9-11A** (92-97% yields), respectively. The FT-IR spectral data of thiazolidinones **6-8A** showed the appearance of new absorption bands at 1722-1735 cm^{-1} that correspond to the carbonyl group and the disappearance of the imine absorption bands of reactants. The ^{1}H NMR spectrum of compound **6A** shows a signal at 5.9 that belongs to the C-H proton of the thiazolidinone ring. The ^{13}C NMR spectrum of compound **6A** revealed new signals at 57.5 and 168.8 ppm attributed to the C-H and C=O of the thiazolidinone ring. The FT-IR spectral data of β-lactams **9-11A** showed the appearance of new absorption bands at 1687-1703 cm^{-1} belonging to the C=O group. The ^{1}H NMR spectral data of compound **9A** showed a signal at 6.98 for the C-H proton of the four-membered ring, while the ^{13}C NMR spectral data of compound **9A** revealed signals at 156.3 and 79.7 ppm for the C=O and C-H of the four-membered ring, respectively. The ether derivatives **13-18A** were accessed by a two-step reaction using compound **2A**. The first step included a reduction of compound **2A** with $NaBH_4$ to afford the corresponding alcohol derivative **12A** in 97% yield. The ^{1}H NMR spectral data of compound **12A** showed that the aldehyde absorption band at 1697 cm^{-1} of the C=O group had disappeared, and a new band at 3471-3429 cm^{-1} belonging to the O-H group appeared. The second step for accessing the ether derivatives included the S_N^2 reaction (known as the Williamson reaction) between compound **12A** and alkyl and aryl halides, resulting in the title derivatives **13-18A**. These compounds (**13-18A**) were characterized by FT-IR spectroscopy, which showed that the absorption band of O-H disappeared and new absorption bands for the C-O-C group appeared at 1010-1151 cm^{-1}. All the details of the FT-IR spectral data are shown in Table 2.



Scheme 1 : Synthesis of compounds **1-18A**

Table 2: FT-IR spectral data (υ, cm^{-1}) of compounds **1-18A**

No.	Structure	C-H Aromatic	C-H Aliphatic	C=C Aromatic	C=N Imine	Other bands
1A		3055	-	1596 1492	1639	1147 (C-N) 746 (C-S-C) 642 (C-Br)
2A		3040	-	1556 1483	1647	1697 (C=O) 2889 (C-H) aldehyde 646 (C-Br) 746 (C-S-C)
3A		3047	2979 2833	1575 1492	1610 1635	1537 (NO_2 asym.) 1325 (NO_2 sym.) 3479 (N-H) 642 (C-Br) 746 (C-S-C)
4A		3070	2989 2858	1575 1492	1668 1639	1695 (C=O) 649 (C-Br) 748 (C-S-C)

5A		3070	2983 2850	1595 1492	1643 1639	1560 (C=C) olefin 1662 (C=O) 648 (C-Br) 748 (C-S-C)
6A		3070	2966 2895	1595 1492	1637	1537 (NO_2 asym.) 1325 (NO_2 sym.) 1724 (C=O) 3467 (N-H) 642 (C-Br) 746 (C-S-C) 829 (C-S-N)
7A		3070	2933 2783	1595 1487	1665	1706 (C=O) amide 1722 (C=O) ketone 648 (C-Br) 752 (C-S-C) 829 (C-S-N)
8A		3074	2974 2885	1590 1494	1637	1568 (C=C) olefin 1735 (C=O) amide 642 (C-Br) 746 (C-S-C) 829 (C-S-N)
9A		3051	2981 2856	1595 1496	1631	1537 (NO_2 asym.) 1325 (NO_2 sym.) 3433 (N-H) 1552 (C=C) olefin 1687 (C=O) 648 (C-Br) 748 (C-S-C)
10A		3053	2989 2890	1571 1496	1623	1560 (C=C) olefin 1631 (C=O) amide 1701 (C=O) amide 649 (C-Br) 744 (C-S-C)
11A		3053	2981 2877	1595 1498	1625	1554 (C=C) olefin 1673 (C=O) amide 1703 (C=O) amide 646 (C-Br)

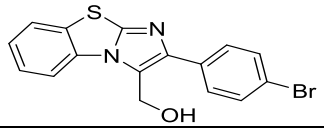
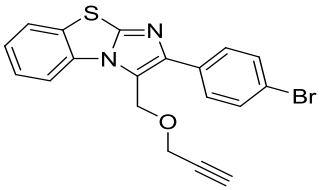
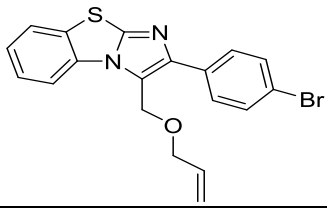
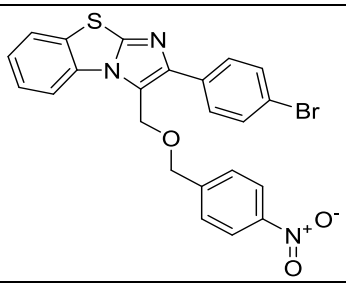
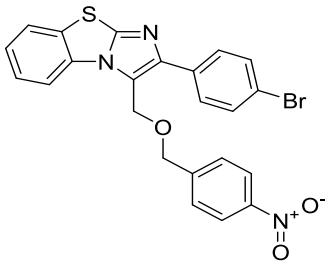
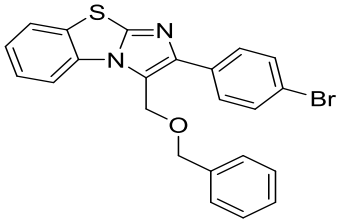
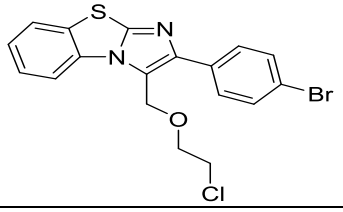
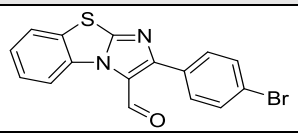
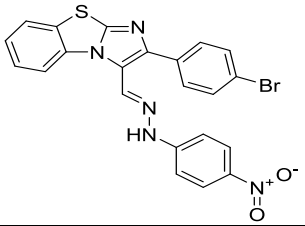
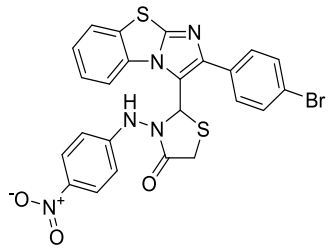
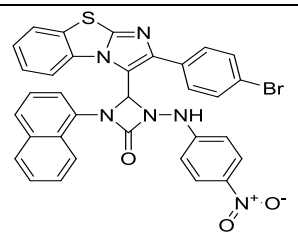
						744 (C-S-C)
12A		3047	2940 2864	1562 1483	1539	3429 (OH broad) 644 (C-Br) 748 (C-S-C)
13A		3053	2970 2865	1577 1492	1627	3288 (H-C≡C) 2279 (C≡C) 1010-1033 (C-O) 648 (C-Br) 746 (C-S-C)
14A		3055	2979 2860	1579 1492	1652	1579 (C=C) 1070-1147 (C-O) 642 (C-Br) 746 (C-S-C)
15A		3053	2979 2891	1595 1492	1645	1535 (NO_2 asym.) 1340 (NO_2 sym.) 1070-1147 (C-O) 642 (C-Br) 746 (C-S-C)
16A		3064	2975 2890	1575 1444	1639	1525 (NO_2 asym.) 1348 (NO_2 sym.) 1072-1145 (C-O) 649 (C-Br) 746 (C-S-C)
17A		3060	2987 2891	1595 1427	1629	1068-1151 (C-O) 636 (C-Br) 748 (C-S-C)
18A		3072	2983 2890	1568 1492	1645	1070-1147 (C-O) 829 (C-Cl) 646 (C-Br) 746 (C-S-C)

Table 3: ^{1}H NMR and ^{13}C NMR spectral data (δ, ppm) of compounds **2A**, **3A**, **6A**, **9A**, and **13A**

No.	Structure	^{1}H NMR	^{13}C NMR
2A		9.75 (s, 1H, CHO), 8.0-7.43 (m, 8H, Ar-H)	188.9 (C=O), 155.5 (C=N), 133.6-121.8 (Ar-C)
3A		8.1 (s, 1H, HC=N), 8.8 (s, N-H), 7.3-8 (m, 12H, Ar-H)	147.6 (C=N imidazo ring), 110-145.5 (Ar-C), 133.6 (C=N imine)
6A		10.1 (s, N-H), 8.0-7.1 (m, 12H, Ar-H), 5.9 (s, 1H, HC-N, HC-S), 4.39 (s, 2H, CH_2)	168.8 (C=O) amide, 155.5 (C=N), 111.4-138,3 (Ar-C), 57.5 (C-N, C-S), 39.33 (CH_2)
9A		10.1 (s, N-H), 7.1-8 (m, 19H, Ar-H), 6.98 (s, 1H, β-lactam ring)	156.3 (C=O amide), 155.5 (C=N), 111.4-142.7 (Ar-C), 79.7 (CH, β-lactam ring)

3.2. Antifungal and antibacterial activities

According to the findings, the majority of the compounds analyzed have strong antifungal and antibacterial activities. These fungi and bacteria were selected because they have tremendous therapeutic value for a wide range of ailments and are resistant to many different antibiotics and chemical treatments. Because the generated chemicals can suppress the bacteria and fungi by altering their concentrations, they have biological activity against the chosen bacteria and fungi, as demonstrated in Table 4.

Table 4: Antifungal and antibacterial activities of some of the tested prepared compounds (**4A**, **5A**, **7A**, **8A**, **10A**, **11A**, **12A**, and **14A**)

No.	Antibacterial activity test		Antifungal activity test
	Staphylococcus aureus **(Gram-positive bacteria)**	***Klebsiella pneumonia*** **(Gram-negative bacteria)**	***Candida albicans***
4A	9	10	10
5A	15	10	11
7A	14	11	11
8A	19	13	12
10A	15	10	15
11A	15	10	15
12A	12	9	10
14A	13	9	10
DMSO	-ve	-ve	-ve
Amoxicillin	9	9	10

3.3. Antioxidant activity

In order to perform the antioxidant activity for some of the prepared compounds, the DPPH technique was employed, and ascorbic acid was used as the positive standard. Free radical scavenging activity was specified according to the literature [16] with a little modification. A compound extract (0.5 mL) was added to a DPPH solution in ethanol that contained 1 mL and 2 mL of 0.013 g/L DPPH. At 30 minutes, the decrease in DPPH was detected at 517 nm in comparison to a blank experiment. The absorbance of the sample divided by that of the DPPH control at the same time and multiplied by 100 is used to compute the percentage of residual radical in the medium. The results of antioxidant activity showed significant scavengers of free radicals. The relationship between the *in vitro* percentage inhibition and the concentration of the potent hits (25, 50, and 100 µg/mL) is summarized in Table 10.

Table 5: Antioxidant activity for some of the synthesized compounds **3A**, **6A**, **9A**, **12A**, and **13A**

No.	Concentration (mg/mL)		
	25 (mg/mL)	**50 (mg/mL)**	**100 (mg/mL)**
3A	36	50	85
6A	20	15	18
9A	10	18	10
12A	20	15	10
13A	65	20	60
Ascorbic acid	80.95	89.25	93.54

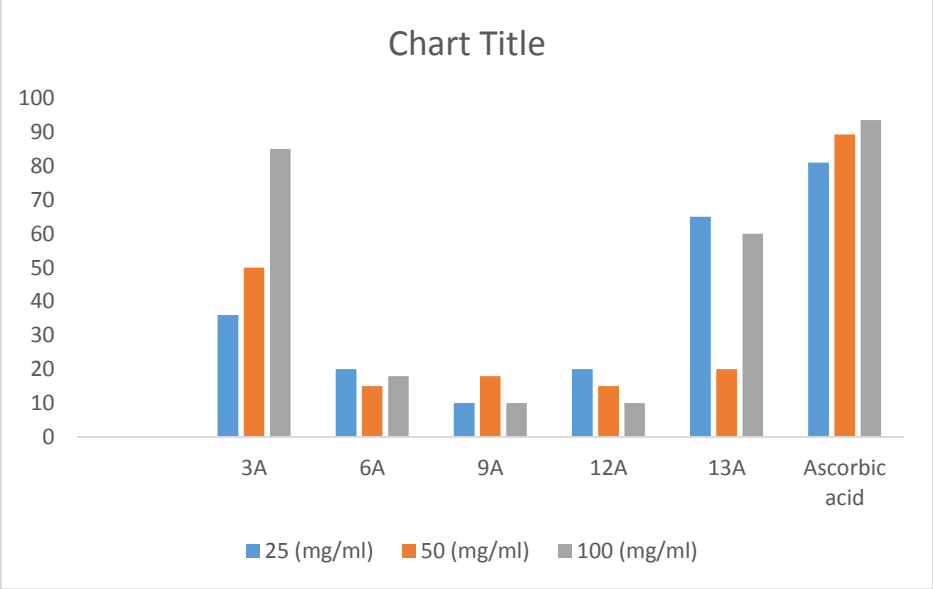


Figure 1: Antioxidant of compounds **3A, 6A, 9A, 12A,** and **13A**

4. Conclusion

A series of different products were synthesized, including thiazolidinones **6-8A**, β-lactams **9-11A**, and ethers **13-18A**, on an imidazobenzothiazole fused system over four steps starting from 2-aminobenzothiaozle. Some of the prepared compounds displayed good antifungal, antibacterial, and antioxidant properties. For example, compounds show that they have biological activity against the chosen fungus and bacteria. The effectiveness of these compounds was compared with that of an antibiotic for bacteria and fungi, amoxicillin, to

determine the pharmacological effectiveness of these compounds. The results of antioxidant activity showed significant scavengers of free radicals. These imidazo benzothiazole compounds therefore showed moderate anti-oxidant and good antibacterial agent agreement with the medication metronidazole (amoxicillin).

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