Synthesis and Studies of Some Newly Heterocyclic Compounds and their Biologically Activity

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Abstract

A series of isolated/fused heterocyclic compounds have been prepared such as new pyrazole, isoxazole, pyrimidine, via the cycloaddition reaction of α, β-unsaturated ketone derivatives. However, it contains also the preparing of new thiazolidine and β-lactam derivatives via the cycloaddition reaction of nitroso derivatives.These derivatives have been based on 2- aminobenzimidazole. The structure assignments of these compounds based on chemical and spectroscopic evidence. The detailed synthesis and spectroscopic data were reported.

Keywords: Pyrazole, Isoxazolo, Pyrimidine, Pyrimidine thione, Spiro thiazolodine, Spiro β-lactam

Introduction

The importance of heterocyclic compounds in various aspects is beyond estimation and there is always continuous need for the discovery of new heterocyclic compounds to satisfy the requirement of intensive development in industry and various biological aspects. In the recent years, many biologically active exhibiting interesting medicinal properties for benzimidazoles. The potential treatments of human diseases have been disclosed. For example pyrrolobenzimidazoles[1-5], thiazolobenzimidazoles[6], pyrimidobenzimidazoles[7], and pyridobenzimidazoles were reported as potent antitumor agents[8]. Furthermore, pyrrolobenzimidazoles[9], pyridobenz-imidazoles[10], were found to be useful in treating central nervous system disorders. Pyridobenzimidazoles have alsoanxiolytic activity in human[11-13], and pyrimidobenzimidazoles were anti-rheumatic agents[14]. Also,1,2,4-triazinobenzimidazoles was found to bereductase ados inhibitors[15] and to possess antimicrobial activity[16].

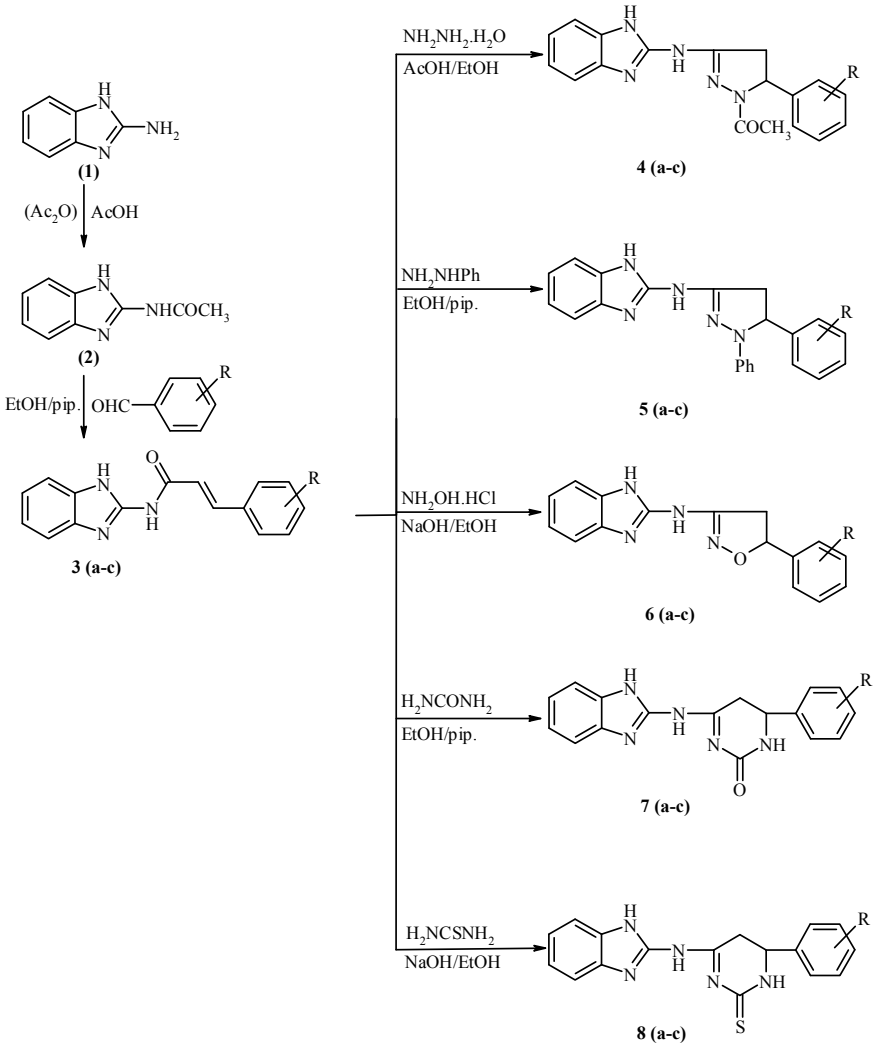
Biological activity

Biological screening of some selected synthesis compounds and structure-activity relationship studies: Sample of selected compounds (5c, 6c, 7c, 10b, 10c, 11b, 11c) was chosen to study the biological activities and the relation between the chemical structures of these tested compounds as bactericides and fungicides. These compounds were dissolved in DMSO (10 mg/10 ml). Then transferred to filter paper disc. The antibacterial activity was determined against Bacillus cereus, Staphylococcus aureus, Micrococcus luteus, Pseudomonas aeruginosa, Escherichia coli and Serratia marcescens, while the antifungi activity was determined against Candide albicans, Geotrichum candidum, Trichophyton rubrum, Fusarium oxysporum, Scopulariopsis brevicaulis and Aspergillus flavus.

The results are listed in **Tables** (6 and 7). It is obvious, that all selected compounds are biologically active against bacteria expecting those of 7c, 10c, 11b, and 11c.

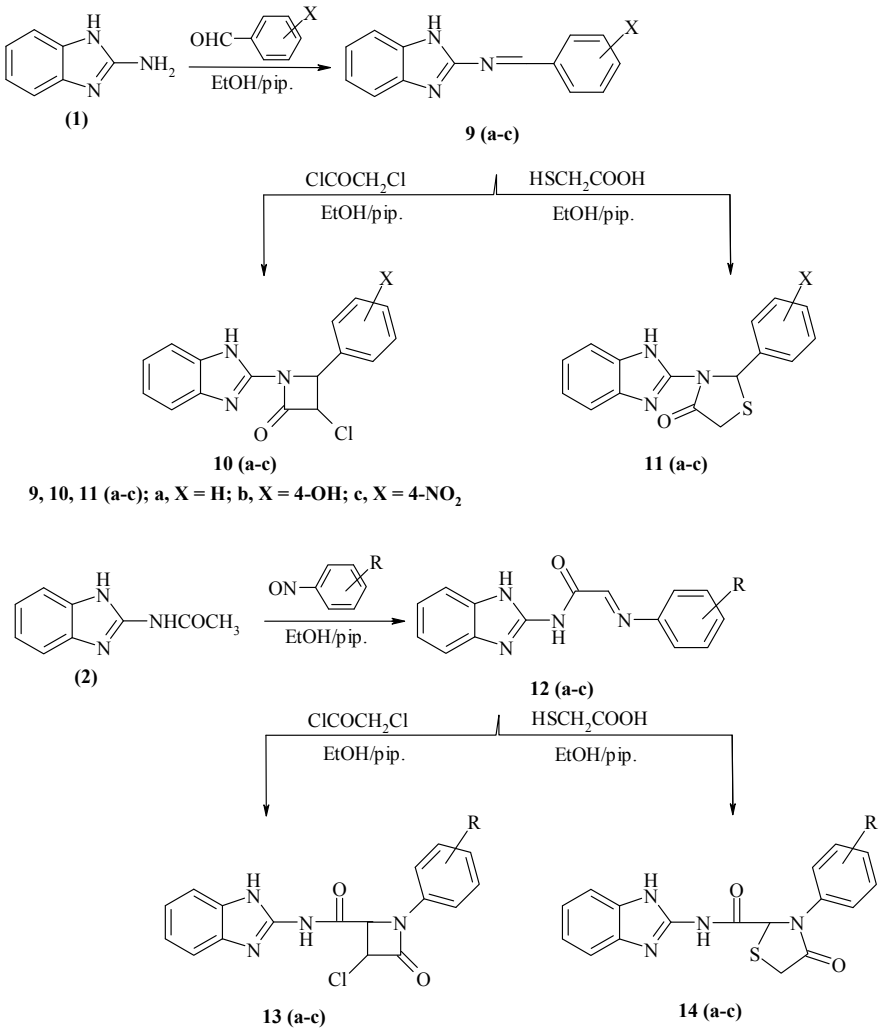
Experimental

All melting points for the synthesized compounds are (uncorrected) measured on a Gallen-Kamp melting point apparatus with a digital thermometer type MFB-595-010M. The elemental analysis was done on a Perken-Elmer 240ºC elemental analyzer system Gmbh VAR IDEL $V_{2.3}$ 2007 CHNS mode. (CairoUniversity). IR spectra were measured as KBr discs on a Pye Unicam Sp 1100 infrared spectrophotometer Shimadzu (υ. Cm^{-1}). ^{1}H-NMR spectra were recorded for $CDCl_3$ and DMSO solution on a varian T-60 NMR spectrometer using TMS as an internal reference (chemical shifts in δ ppm) at 450 MHz (CairoUniversity). Mass spectra were recorded on an Hp.Ms 5988 spectrometer. Elemental analysis was carried out at the microanalytical of CairoUniversity.



where 3, 4, 5, 6, 7, 8 (a-c):
a, R = H; b, R = OCH_3; c, R = 4-NO_2

Scheme 1



Scheme (2)

Synthesis of 2- aminobenzimidazole:

2-aminobenzimidazole was first obtained by pierron by the action of cyanogens bromide on o-phenylenediamine but did not attract the attention of researchers for a long time. Research on the chemistry of 2-aminobenzimidazoles has become more intense in recent years, when the high biological activity of some representative of this series was established[18].

Synthesis of *N1*-(1*H*-benzo(*d*)imidazole-2-yl)acetamide:

This compound was prepared in accordance with the methodology described in respective[19].

Synthesis of α,β-unsaturated ketone derivatives 3 (a-c):

N_1-(1*H*-benzo[*d*]imidazol-2-yl)-(*E*)-3-phenyl-2- propenamide. (3a)

N_1-(1*H*-benzo[d]imidazol-2-yl)-(*E*)-3-(4-methoxyphenyl)-2-propenamide. (3b)

N_1-(1*H*-benzo[*d*]imidazol-2-yl)-(*E*)-3-(4-nitrophenyl)-2- propenamide. (3c)

Equimolar amounts of compound (2) (0.01 mol) and aromatic aldehydes (benzaldehyde, 4-methoxybenzaldehyde and/or 4-nitrobenzaldehyde, 0.01 mol) were dissolved in ethanol (30 ml) and then piperidine (1 ml) was added. The reaction mixture was refluxed for 8-10 hrs, allowed to cool at room temperature, filtered, the ppt. washed several times with water, dried, collected and recrystallized to give **3 (a-c)**, **Tables (1-5)**.

Synthesis of N-acetylpyrazolino derivatives 4 (a-c):

1-[3-(1*H*-benzo[*d*]imidazol-2-ylamino)-5-phenyl-4,5-dihydro-1*H*-1-pyrazolyl]-1-ethanone. (4a)

1-[3-(1*H*-benzo[*d*]imidazol-2-ylamine)-5-(4-methoxy-phenyl)-4,5-dihydro-1*H*-1-pyrazolyl]-1-ethanone. (4b)

1-[3-(1*H*-benzo[*d*]imidazol-2-ylamino)-5-(4-nitro-phenyl)-4,5-dihydro-1*H*-1-pyrazolyl]-1-ethanone. (4c)

Equimolar amounts of **3 (a-c)** (0.01 mol) and hydrazine hydrate (0.01 mol) were dissolved in absolute ethanol (30 ml) and then glacial acetic acid (1 ml) was added, reflux the solution for 12-13hrs, the solution cooled and diluted with water. The precipitated products were collected and crystallized from proper solvent to give **4 (a-c)**, **Tables (1-5)**.

Synthesis of N-phenylpyrazolino derivatives 5 (a-c):

*N*2-(1,5-diphenyl-4,5-dihydro-1*H*-3-pyrazolyl)-1*H*-benzo[*d*]imidazol-2-amine (5a)

*N*2-[5-(4-methoxyphenyl)-1-phenyl-4,5-dihydro-1*H*-3-pyrazolyl]-1*H*-benzo[*d*]imidazol-2-amine (5b)

*N*2-[5-(4-nitrophenyl)-1-phenyl-4,5-dihydro-1*H*-3-pyrazolyl]-1*H*-benzo[*d*]imidazol-2-amine (5c)

Equimolar amount of appropriate **3(a-c)** (0.01 mol) and phenylhydrazine (0.01 mol) were dissolved in absolute ethanol (20 ml), then piperidine (0.5 ml) was added. The reaction mixture was refluxed for 10-12 hrs., Filtered hot, concentrated, cooled and acidified with acetic acid. The precipitated products were collected after dilution with water and crystallized from proper solvent to give **5 (a-c)**, **Tables (1-5)**.

Synthesis of ISO-oxazolo derivatives 6 (a-c):

*N*3-(1*H*-benzo[*d*]imidazol-2-yl)-5-phenyl-4,5-dihydro-3-isoxazolamine (6a).

*N*3-(1*H*-benzo[*d*]imidazol-2-yl)-5-(4-methoxyphenyl)-4,5-dihydro-3-isoxazolamine (6b).

*N*3-(1*H*-benzo[*d*]imidazol-2-yl)-5-(4-nitrophenyl)-4,5-dihydro-3-isoxazolamine (6c).

Equimolar amounts of appropriate **3(a-c)**, (0.01 mol) and hydroxylamine hydrochloride (0.01 mol) were dissolved in absolute ethanol (20 ml) using 1 gm of NaOH as catalysis, then reflux the solution for 10-12 hrs, filtered on hot, concentrated, and diluted with ice. The precipitated products were collected and crystallized from proper solvent to give **6 (a-c) Tables (1-5).**

Synthesis of pyrimidino derivatives 7 (a-c):

4-(1*H*-benzo[*d*]imidazol-2-ylamino)-6-phenyl-1,2,5,6-tetrahydro-2-pyrimidinone (7a)

4-(1*H*-benzo[*d*]imidazol-2-ylamino)-6-(4-methoxy-phenyl)-1,2,5,6-tetrahydro-2-pyrimidinone (7b).

4-(1*H*-benzo[*d*]imidazol-2-ylamino)-6-(4-nitrophenyl)-1,2,5,6-tetrahydro-2-pyrimidinone (7c).

Equimolar amounts of **3(a-c)** (0.01 mol) and urea (0.01 mol) were dissolved in absolute ethanol (20 ml), then pipredine (0.5 ml) was added, then refluxed the solution for 8-10 hrs., The precipitated products were filtered hot, concentrated, collected and crystallized from proper solvent to give **7 (a-c) Tables (1-5)**.

Synthesis of thiopyrimidino derivatives 8 (a-c):

4-(1*H*-benzo[*d*]imidazol-2-ylamino)-6-phenyl-1,2,5,6-tetrahydro-2-pyrimidinethione (8a)

4-(1*H*-benzo[*d*]imidazol-2-ylamino)-6-(4-methoxy-phenyl)-1,2,5,6-tetrahydro-2-pyrimidinethione (8b)

4-(1*H*-benzo[*d*]imidazol-2-ylamino)-6-(4-nitrophenyl)-1,2,5,6-tetrahydro-2-pyrimidinethione (8c)

Equimolar amounts of **3(a-c)** (0.01 mol) and thiourea (0.01 mol) were dissolved in absolute ethanol (20 ml), then pipredine(0.5 ml) was added, then refluxed the solution for 8-10 hrs., The precipitated products were filtered hot, concentrated, collected and crystallized from proper solvent to give **8 (a-c), Tables (1-5)**.

Synthesis of new Schiff Base derivatives 9 (a-c):

N-(1*H*-benzo[*d*]imidazol-2-yl)phenylmethanimine (9a).

4-(1*H*-benzo[*d*]imidazol-2-yliminomethyl)phenol (9b)

N-(1*H*-benzo[*d*]imidazol-2-yl)-4-nitrophenylmethanimine (9c)

An equimolar ratio of compound **(1)** (0.01 mol) and aromatic aldehydes (benzaldehyde, 4-hydroxybenzaldehyde, and 4-nitrobenzaldehyde) (0.01 mol) were dissolved in ethanol (30 ml), then piperidine (3-5 drops) was added. The reaction mixture was allowed to reflux for about 8-10 hrs., then, the solvent was evaporated under reduced pressure, The products were separated, collected and crystallized from ethanol to give **9 (a-c), Tables (1-5)**.

Synthesis of New Isolate β-Lactam derivatives 10 (a-c):

1-(1*H*-benzo[*d*]imidazol-2-yl)-3-chloro-4-phenyl-2-azetanone (10a).

1-(1*H*-benzo[*d*]imidazol-2-yl)-3-chloro-4-(4-hydroxy-phenyl)-2-azetanone (10b).

1-(1*H*-benzo[*d*]imidazol-2-yl)-3-chloro-4-(4-nitro-phenyl)-2-azetanone (10c)

Ethanolic solution **9 (a-c)** (0.01 mol) and chloroacetyl chloride (0.01 mol) which added drop by drop and stirred for 1h. In the presence of (0.5 ml) piperidine as a catalyst, was refluxed for 11-13 hrs, filtered hot, concentrated,and diluted with ice, filtered off and crystallized from the proper solvent to give **10 (a-c), Tables (1-5)**.

Synthesis of new Isolated Thiazolidinone derivatives 11 (a-c):

3-(1*H*-benzo[*d*]imidazol-2-yl)-2-phenyl-1,3-thiazolan-4-one (11a)

3-(1*H*-benzo[*d*]imidazol-2-yl)-2-(4-hydroxyphenyl)-1,3-thiazolan-4-one (11b)

3-(1*H*-benzo[*d*]imidazol-2-yl)-2-(4-nitrophenyl)-1,3-thiazolan-4-one (11c)

Equimolar amounts of **9(a-c)** (0.01 mol) and thioglycolic acid (0.01 mol), which added drop by drop with stirring, were dissolved in ethanol (30 ml), then piperidine (3-5 drops) were added, reflux the solution for 10-12 hrs. Cooled, diluted with water, filtered off, and crystallized from the proper solvent to give **11 (a-c), Tables (1-5)**.

Synthesis of new Schiff base 12 (a-c):

*N*1-(1*H*-benzo[*d*]imidazol-2-yl)-2-(1-hydroxy-2-naphthylimino)acetamide (12a).

*N*1-(1*H*-benzo[*d*]imidazol-2-yl)-2-(2-hydroxy-1-naphthylimino)acetamide (12b).

*N*1-(1*H*-benzo[*d*]imidazol-2-yl)-2-(4-hydroxyphenyl-imino)acetamide (12c).

Equimolar amounts of compound **2** (0.01 mol) and aromatic nitroso derivatives (4-nitrophenol, 2-nitroso-α-naphthol and/or 1-nitroso-β-naphthol, 0.01 mol) were dissolved in ethanol (30 ml), then piperidine (3-5 drops) were added. The reaction mixture was refluxed for 9-11 hrs, then, filtered on hot, concentrated and diluted with ice water. The precipitated products were collected and crystallized from the proper solvent to give **12 (a-c), Tables (1-5)**.

Synthesis of New Isolated β-Lactam derivatives 13 (a-c):

2-[3-chloro-1-(1-hydroxy-2-naphthyl)-4-Oxo-2-azetanyl-carboxamido]-1*H*-benzo[*d*]imidazole (13a).
2-[3-chloro-1-(2-hydroxy-1-naphthyl)-4-oxo-2-azetanyl-carboxamido]-1*H*-benzo[*d*]imidazole (13b).
2-[3-chloro-1-(4-hydroxyphenyl)-4-oxo-2-azetanyl-carboxamido]-1*H*-benzo[*d*]imidazole (13c).

Equimolar amount of compound **12 (a-c)** (0.01 mol) and chloroacetyl chloride (0.01 mol) was dissolved in ethanol (20 ml), then piperidine (3-5 drops) was added. The reaction mixture refluxed for 11-13 hrs, filtered hot, concentrated, and diluted with water. The precipitated products were collected and crystallized from the proper solvent to give **13 (a-c), Tables (1-5).**

Table (1): Physical and analytical data for the synthesized compounds (3_{a-c} , 4_{a-c} , 5_{a-c}).

Comp. NO.	Yield %	M.P (ºC)	Mol. Form. (Mol. Wt)	Elemental analysis [Calc. / Found (%)]			MS (M^+)
				C	H	N	
3a	51	280	$C_{16}H_{13}N_3O$ (263.290)	72.99 72.97	4.98 4.96	15.96 15.94	265
3b	63	148	$C_{17}H_{15}N_3O_2$ (293.320)	69.61 69.59	5.15 5.13	14.33 14.31	295
3c	53	188	$C_{16}H_{12}N_4O_3$ (308.290)	62.34 62.32	3.92 3.90	18.17 18.15	310
4a	48	154	$C_{18}H_{17}N_5O$ (319.360)	67.70 67.68	5.37 5.35	21.93 21.91	319
4b	58	292	$C_{19}H_{19}N_5O_2$ (349.39)	65.32 65.31	5.48 5.46	20.04 20.02	347
4c	45	280	$C_{18}H_{16}N_6O_3$ (364.36)	59.34 59.32	4.43 4.41	23.07 23.05	364
5a	58	>300	$C_{22}H_{19}N_5$ (353.42)	74.77 74.75	5.42 5.40	19.82 19.80	353
5b	65	210	$C_{23}H_{21}N_5O$ (383.45)	72.04 72.02	5.52 5.50	18.26 18.24	383
5c	52	102	$C_{22}H_{18}N_6O_2$ (398.42)	66.30 66.28	4.53 4.51	21.07 21.05	398

Synthesis of new Isolated Thiazolidinone derivatives 14 (a-c):

*N*2-(1*H*-benzo[*d*]imidazol-2-yl)-3-(1-hydroxy-2-naphthyl)-4-Oxo-1,3-thiazolane-2-carboxamide (14a)
*N*2-(1*H*-benzo[*d*]imidazol-2-yl)-3-(2-hydroxy-1-naphthyl)-4-oxo-1,3-thiazolane-2-carboxamide (14b)
*N*2-(1*H*-benzo[*d*]imidazol-2-yl)-3-(4-hydroxyphenyl)-4-oxo-1,3-thiazolane-2-carboxamide (14C)

Equimolar amount of compound **12 (a-c)** (0.01 mol) and mercaptoacetic acid (0.01mol) was dissolved in ethanol (20 ml), then piperidine (3-5 drops) was added, then reflux the solution for 9-11hrs,

filtered hot, concentrated, acidified and diluted with water. The precipitated prouducts were collected and crystallized from the proper solvent to give **14 (a-c), Tables (1-5).**

Biological Screening

The screened compounds were dissolved in DMSO to get a solution of 5% concentration. Filter paper disc (Waltman NO. 3 and 5 mm diameter) were saturated with this solution. The discs were placed on the surface of solidified Nutrient agar dishes seeded by the tested bacteria or Czapeks Dox agar dishes seeded by the tested fungi. The diameter of inhibition zones (mm) was measured at the end of the incubation period (24h- 48h) at 37ºC for bactria and for 4-7 days at 28ºC for fungi). Dishes saturated with DMSO were used as control. Chloramphenicol and Clotrimazole were used as reference substances. The biologically active compounds were diluted with DMSO to prepare a series of concentrations in order to determine the minimum inhibitory concentration (MTC) compound. MTCs were calculated[20] as mg/ml.

Table 2: Physical and analytical data for the synthesized compounds (6_{a-c} , 7_{a-c}, 8_{a-c}).

Comp. NO.	Yield %	M.P (ºC)	Mol. Form. (Mol. Wt)	Elemental analysis [Calc. / Found (%)]			MS (M^+)
				C	H	N	
6a	48	292	$C_{16}H_{14}N_4O$ (278.31)	69.05 69.03	5.07 5.05	20.13 20.11	278
6b	45	288	$C_{17}H_{16}N_4O_2$ (308.33)	66.20 66.18	5.21 5.19	18.15 18.13	326
6c	52	>300	$C_{16}H_{13}N_5O_3$ (323.30)	59.44 59.42	4.05 4.03	21.66 21.64	323
7a	46	212	$C_{17}H_{15}N_5O$ (305.33)	66.87 66.85	4.95 4.93	22.94 22.92	305
7b	62	209	$C_{18}H_{17}N_5O_2$ (335.36)	64.45 64.43	5.90 5.88	20.86 20.84	335
7c	56	160	$C_{17}H_{14}N_6O_3$ (350.33)	58.28 58.26	4.03 4.01	23.99 23.97	350
8a	48	180	$C_{17}H_{15}N_5S$ (321.39)	63.53 63.51	4.70 4.68	21.79 21.77	321
8b	65	>300	$C_{18}H_{17}N_5OS$ (351.42)	61.52 61.50	4.88 4.86	19.93 19.91	351
8c	43	178	$C_{17}H_{14}N_6O_2S$ (366.39)	55.73 55.71	3.85 3.83	22.94 22.92	366

Table 3: Physical and analytical data for the synthesized compounds (9_{a-c} , 10_{a-c} , 11_{a-c}).

Comp. NO.	Yield %	M.P (ºC)	Mol. Form. (Mol. Wt)	Elemental analysis [Calc. / Found (%)]			MS (M^+)
				C	H	N	
9a	52	>300	$C_{14}H_{11}N_3$ (221.26)	75.98 75.96	4.99 4.97	18.97 18.95	221
9b	60	290	$C_{14}H_{11}N_3O$ (237.26)	70.87 70.85	4.67 4.65	17.71 17.69	237
9c	56	268	$C_{14}H_{10}N_4O_2$ (266.25)	63.15 63.13	3.79 3.77	21.04 21.02	266
10a	62	210	$C_{16}H_{12}N_3OCl$ (297.74)	64.52 64.50	4.04 4.02	14.09 14.07	295
10b	46	>300	$C_{16}H_{12}N_3O_2Cl$ (313.74)	61.25 61.23	3.86 3.84	11.30 11.28	313
10c	53	>300	$C_{16}H_{11}N_4O_3Cl$ (342.74)	56.07 56.05	3.23 3.21	16.35 16.33	342
11a	44	292	$C_{16}H_{13}N_3OS$ (295.35)	65.05 65.03	4.42 4.40	14.21 14.19	294
11b	52	278	$C_{16}H_{13}N_3O_2S$ (311.35)	61.72 61.70	4.21 4.19	13.50 13.48	311
11c	63	162	$C_{16}H_{12}N_4O_3S$ (340.35)	56.46 56.44	3.55 3.53	16.46 16.44	340

Table 4: Physical and analytical data for the synthesized compounds (12_{a-c} , 13_{a-c} , 14_{a-c}).

Comp. NO.	Yield %	M.P (ºC)	Mol. Form. (Mol. Wt)	Elemental analysis [Calc. / Found (%)]			MS (M^+)
				C	H	N	
12a	53	148	$C_{19}H_{14}N_4O_2$ (330.34)	69.08 69.06	4.25 4.23	16.94 16.92	329
12b	64	124	$C_{19}H_{14}N_4O_2$ (330.34)	69.08 69.06	4.25 4.23	16.94 16.92	330
12c	68	188	$C_{15}H_{12}N_4O_2$ (280.28)	64.26 64.24	4.30 4.28	19.97 19.95	280
13a	46	292	$C_{21}H_{15}N_4O_3Cl$ (406.82)	62.00 61.58	3.72 3.70	8.71 8.69	406
13b	53	282	$C_{21}H_{15}N_4O_3Cl$ (406.82)	62.00 61.58	3.72 3.70	8.71 8.69	406
13c	61	278	$C_{17}H_{13}N_4O_3Cl$ (356.76)	57.23 57.21	3.67 3.65	15.70 15.68	356
14a	42	218	$C_{21}H_{16}N_4O_3S$ (404.44)	62.35 62.32	3.97 3.95	13.83 13.81	402

14b	48	230	$C_{21}H_{16}N_4O_3S$ (404.44)	62.35 62.32	3.97 3.95	13.83 13.81	402
14c	54	262	$C_{17}H_{14}N_4O_3S$ (354.38)	57.62 57.60	3.98 3.96	15.81 15.79	354

Table 5: IR (υmax/cm-1) and 1H-NMR data of synthesized compounds

Comp. No.	IR (υ_{max}/cm^{-1})	^{1}H-NMR (DMSO-d_6)
3b	3100-3500 cm^{-1} (NH, OH), 3018.6 cm^{-1} (CH aromatic), 2939.9 cm^{-1} (CH aliphatic), 1690.4 cm^{-1} (ketonic CO)	δ 8.27-7.30 (m, 8H, aromatic proton), δ 6-5.8(d, 2H, CH oleofinic proton), δ 5.60-5.40 (br, 1H, NH hetero nuclei proton), δ 4.2-4.00(br, 1H, NH), 3.354 (m, 3H, OCH_3).
3c	3412.5 cm^{-1} (OH), 3250.2 cm^{-1} (NH), 3069.2 cm^{-1} (CH aromatic), 2937 cm^{-1} (CH aliphatic), 1700.1 cm^{-1} (ketonic CO).	δ 8.27-7.30 (m, 8H, aromatic proton), δ 6-5.8(d, 2H, CH oleofinic proton), δ 5.60-5.40 (br, 1H, NH hetero nuclei proton), δ 4.2-4.00(br, 1H, NH) .
4b	3125.1 cm^{-1} (NH), 3021.9 cm^{-1} (CH aromatic), 2907.1 cm^{-1} (CH aliphatic), 1695.2 cm^{-1} (CO).	δ 8.27-7.30 (m, 8H, aromatic hydrogen), δ 5.8-6 (br, 1H, NH hetero nuclei proton), δ 4.2-4.00(br, 1H, NH), 3.354 (m, 6H, $2OCH_3$), δ 2.40-2.38 (br, 3H, CH_2 + CH).
5c	3124-3200 cm^{-1} (NH), 3021.9 cm^{-1} (CH aromatic), 2909 cm^{-1} (CH aliphatic).	δ 8.27-7.30 (m, 13H, aromatic proton), δ 5.8-6 (br, 1H, NH hetero nuclei proton), δ 4.2-4.00(br, 1H, NH), 3.354 (m, 3H, OCH_3), δ 2.40-2.38 (br, 3H, CH_2 + CH).
6b	3124-3200 cm^{-1} (NH), 3021.9 cm^{-1} (CH aromatic), 2909 cm^{-1} (CH aliphatic).	δ 8.27-7.30 (m, 8H, aromatic proton), δ 5.8-6 (br, 1H, NH hetero nuclei proton), δ 4.2-4.00(br, 1H, NH), 3.354 (m, 3H, OCH_3), δ 2.40-2.38 (br, 3H, CH_2 + CH).
7b	3441.4 cm^{-1} (OH), 3200 cm^{-1} (NH), 3099 cm^{-1} (CH aromatic), 1700.3 cm^{-1} (CO).	δ 11.38 (s, 2H, 2NH), δ 6.9-8.13 (m, 8H, aromatic proton), δ 5.41 (s, H, NH), δ 3.7-3.4 (m, 4H, CH + OCH_3), δ 2.8-2.7 (d, 2H, CH_2).
9a	3100-3500 cm^{-1} (NH), 3018.6 cm^{-1} (CH aromatic).	δ 10.9 (s, 1H, NH), δ 6.9-7.3 (m, 10H, aromatic proton + N=CH).
11a	3123-3200 cm^{-1} (NH), 3021.9 cm^{-1} (CH aromatic), 2907.1 cm^{-1} (CH aliphatic), 1734.2 cm^{-1} (C═O)	δ 10.9 (s, 1H, NH), δ 6.9-7.9 (m, 9H, aromatic proton), δ 4.0-4.2 (br, 3H, CH_2 + CH) .
12a	3424.1 cm^{-1} (OH), 3220 cm^{-1} (NH), 3020.9 cm^{-1} (CH aromatic), 1700.2 cm^{-1} (CO).	δ 10.9 (s, 1H, NH), δ 8.4 (m, 9H aromatic proton) δ 3.5 (br, H, NH).
14a	3438.5 cm^{-1} (OH), 3135.7 cm^{-1} (NH), 3031.5 cm^{-1} (CH aromatic), 2910.9 cm^{-1} (CH aliphatic), 1696.6 cm^{-1} (CO).	δ 10.9 (s, 1H, NH), δ 6.9-7.9 (m, 9H, aromatic proton), δ 4.0-4.2 (br, 3H, CH_2 + CH), δ 3.5 (br, H, NH).

Table 6: Antimicrobial activity (inhibition zone in mm)

Sample No. / organisms	5c	6c	7c	10c	11b	11c	10b	Cont.
Bacillus ceureus (+ve) AUMC No. B-52	0	10	0	0	0	0	8	30
Staphylococcus aureus (+ve) AUMC No. B-54	13	8	0	0	0	0	12	24
Micrococcus luteus (+ve) AUMC No. B-112	13	0	0	0	0	0	10	23
Pseudomonas aeruginosa (-ve) AUMC No. B-73	0	0	0	0	0	0	0	15
Escherichia coli (-ve) AUMC No. B-53	0	0	0	0	0	0	12	25
Serratia marcescens (-ve) AUMC No. B-55	0	0	0	0	0	0	0	34

Cont.* = chloramphenicol as antibacterial standard

Table 7: Antifungal activity (inhibition zone in mm)

Sample No. / organisms	5c	6c	7c	10c	11b	11c	10b	Cont.
Candida albicans AUMC No. 1299	28	10	12	12	10	0	10	24
Geotrichum candidum AUMC No. 226	27	0	0	12 p.i	0	0	8	24
Trichophyton rubrum AUMC No. 1804	45	0	0	14	0	18 p.i	10	36
Scopulariopsis brevicaulis AUMC No. 361	28	0	0	14	0	0	0	28
Fusarium oxysporum AUMC No. 5119	14	0	0	0	0	0	0	25
Aspergillus flavus AUMC No. 1276	16 p.i	0	0	12 p.i	0	0	0	26

p.i. = Partial Inhibition

Cont.* = Clotrimazole as antifungal standard

Results and Discussion

Our interest in preparing of the newly classes of β-lactams derivatives and thiazolidinone derivatives comes as a result of their importance as it was mentioned before. These compounds were prepared through the cycloaddition reaction of prepared Schiff bases with chloroacetyl chloride and/or thioglycolic acid respectively. 2-aminobenzimidazole was prepared by fusion of *o*-phenylene-diamine with urea. The reaction of 2- aminobenzimidazole with acetic anhydride and acetic acid afforded the corresponding compound *N*1-(1*H*-benzo (*d*) imidazole-2-yl) acetamide **(2)**[17]**.** The reaction of *N*1-(1*H*-

benzo (*d*) imidazole-2-yl) acetamide with a different aromatic aldehyde (benzaldehyde, anisaldehyde and/or 4-Nitro-benzaldehyde) under thermal piperidine catalysis and ethanol achieved the corresponding compound **3 (a-c)[Scheme 1]**. The structure of compound (3b) was confirmed by elemental analysis, IR, ^{1}H-NMR, and Mass spectra. The presence of active methelene group adjacent to a carbonyl group in compound **3 (a-c)** lead to the formation of new heterocyclic derivatives. This can be achieved by cycloaddition between equimolar ratios of compound **3 (a-c)** with hydrazine hydrate in the presence of a few drops of glacial acetic acid in ethanol achieved the corresponding compound **4 (a-c)[Scheme 1]**.The structures of these compounds (3a-c, 4a-c) were confirmed by elemental analysis, IR, ^{1}H-NMR and Mass spectra **Tables (1-5)**. The Cyclocondensation reaction of compounds **3 (a-c)** with phenylhydrazine using piperidine catalysis achieved the corresponding compounds **5 (a-c)[Scheme 1]**.The structures of these compounds were confirmed by elemental analysis, IR, ^{1}H-NMR and Mass spectra **Tables (1-5)**. Cyclocondensation reaction of **3 (a-c)** with hydroxylamine using EtOH as solvent and NaOH as a basic catalyst gave aryl-isoxazolo heterocyclic derivatives **6 (a-c)[Scheme 1]**.The structure of compound **6 (a-c)** was confirmed by elemental analysis; ^{1}H-NMR and Mass spectra **Tables (1-5)**. The Cyclocondensation reaction of an ethanolic solution of **(3a-c)** and urea in the presence of piperidine as a basic catalyst afforded arylpyrimidino derivatives **7 (a-c) Scheme (1)**.The structures of these compounds were confirmed by elemental analysis, IR, ^{1}H-NMR and Mass spectra **Tables (1-5)**. Cyclocondensation reaction of **3(a-c)** with thiourea using EtOH as solvent and NaOH (2-3 drops) as basic catalyst afforded thiopyrimidino derivatives **8(a-c)Scheme (1)**.The new Schiff bases were prepared by the reaction of *N*1-(1*H*-benzo (*d*) imidazole-2-yl) acetamide with an equimolar ratio of aromatic nitroso compound derivatives (2-nitroso-α-naphthol, 1-nitroso-*β*-naphthol, and 4-nitrosophenol) in ethanol and piperidine as a catalystafforded **9 (a-c)** and **12 (a-c)** derivatives. An ethanolic solution of 2- aminobenzimidazole reacts with an equimolar ratio of aromatic aldehyde such as (benzaldehyde, 4-hydroxybenzaldehyde and/or 4-Nitro-benzaldehyde) using piperidine as a catalyst to give Schiff bases **9 (a-c) [Scheme (2)]**. The structures of these compounds were confirmed by elemental analysis, ^{1}H-NMR and Mass spectra **Tables (1-5)**.The interaction of Schiff bases **9 (a-c)** and **12 (a-c)** with chloroacetyl chloride in the presence of piperidine as basic catalyst and ethanol as solvent afforded β-lactams derivatives of **10 (a-c)** and **13 (a-c)[Scheme 2]**. The structures of **10 (a-c)** and **13 (a-c)** were confirmed by their elemental analysis and Mass spectra, **Tables (1-5)**.The new isolated thiazolidinone derivatives**11(a-c)** and **14 (a-c)** were prepared through the cycloaddition of thioglycolic acid to previously prepared Schiff bases **9(a-c)** and **12(a-c)** respectively, in ethanol containing drops of piperidine as basic catalysis, **[scheme 2]**.The structures of **11 (a-c)** and **14 (a-c)** were confirmed by the elemental analysis, IR, Mass spectra and ^{1}H-NMR, **Tables (1-5)**.

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