Synthesis, Characterization and Evaluation of Antimicrobial Activity of Several New N-Substituted Carbazole

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Abstract

In this research, a series of some new compounds different heterocyclic new rings, sulfur, oxygen and nitrogen containing in structures, substituted-N-carbazole, through the prepared α-chloro-N-carbazolacetaimde (1) which was prepared by two methods. The first method by treated carbazole compound with sodium hydrite in DMF at 0°C to give a suspension of the sodium salt of carbazole and subsequent reaction with chloroacetyl chloride. The second method reaction carbazole compound with chloroacetyl chloride and potassium hydroxide by fusion. Then reaction compound (1) by two different ways. The first way involved direct reaction with substituted-2-aminobenzothiazole under certain conditions to give new compounds (2-8) and reaction of 5-substituted-2-amino-1,3,4-oxadiazole in the presence of potassium carbonate anhydrous to give new compounds (14-18) respectively. While the second way involved condensation compound (1) with hydrazine hydrate give the corresponding hydrazine derivative (19) which the conversion new Schiff base (20-23) were prepared through the reaction of hydrazine derivative (19) with aromatic aldehyde. Followed the cyclization of compounds (20-23) by used sodium azide in dry THF to give substituted tetrazoles (24-27) respectively. The prepared compounds identified by spectral methods [FTIR, ^{1}H-NMR, ^{13}C-NMR] and measurement some of its physical properties and some specific reaction, furthermore we were studied the effects of the preparing compounds on some strains of three types of bacteria and one yeast.

Keywords: carbazole, 2-aminobenzothiazole, 1,3,4-oxadiazole, Schiff base, tetrazole, antimicrobial.

Introduction

Carbazole and numerous derivatives are one of the most important fundamental structures in the field of organic physical properties and favorable conductive behavior such that numerous potential application [1], such as high density optical data storage, photonic application (photoconductivity, electroluminescence, and photorefraction) [2-4], transporting properties and their charge transfer (CT) complexes [5], and for their light-emitting properties [6]. Also carbazoles are a large and interesting group of organic compounds active among which one can find dyes stuffs [7], and plastics [8].

Several alkaloids based on a carbazole structure are know to possess interesting biological activities. Antitumor [9], abtibacterial [10], anti-inflammatory [11], anti-HIV activity [12] and cytotoxic activities [13] properties have been attributed to many of such compounds. On the hand 2-aminobenzothiazole substituted, 1,3,4-oxadiazoles, and tetrazole constitute a potential class of compounds which possess abroad field of biological interaction [14-16]. Many of them exhibit antibacterial, anticonvulsant, anticancer activities and are used to fight infections involving (AIDS) [17]. They are also applied in agriculture as herbicides, fungicides or insecticides [18]. Keeping these above facts in view it was through worth while to synthesize new compounds by incorporating carbazole and 2-aminobenzothiazoles derivatives or 1,3,4-oxadiazole or tetrazole ring in a single molecular framework. The resulted new molecules were expected to possess biological activity since they were built from two biological active compounds.

Experimental

Instruments

Melting points were determined Gallenkamp melting point apparatus and uncorrected. FTIR spectra were recorded on Shimadza FTIR 8400 Fourier infrared spectrophotometer as KBr disc. The ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a make Bruker model ultrashield 300 MHz,

using DMSO-d^6 as solvent and TMS as internal reference.

Chemical

Starting chemical compounds were obtained from Fluka or Aldrich.

Preparation of α-chloro-N-carbazoleacetamide (1)

This compound (1) was prepared by two ways:

Method (I) [19]

A solution of carbazole compound (2.7 gm., 0.016 mol.) in DMF (10 ml.) was cold to 0°C, and sodium hydride (0.38 g., 0.016 mol. 60% in mineral oil) was periodically added to the solution in small portions. Chloroacetylchloride (1.27 ml., 0.016 mol., 80% in toluene) was added to the slurry via syringe, and the reaction mixture was slowly warmed to room temperature. The reaction was quenched with water after 14 hrs., and the resulting solid was removed via filtration. And recrystallization from ethanol solvent. Physical properties are listed in Tables (1).

Method (II) [20]

A mixture of carbazole compound (2.7 gm., 0.016 mol.), anhydrous potassium hydroxide (1.73 gm., 0.016 mol.) and chloroacetyl chloride (1.27 ml., 0.016 mol.) in special Pyrex glass ampule. The ampoule is heated at (250-270)°C in oil bath for 5hrs., then the reaction mixture was poured into ice water, the separated precipitate was filtered and recrystalized from ethanol to give a dusty crystals. Physical properties are listed in Table (1).

Preparation of N-(2-aminoacetyl substituted benzothiazole-2-yl)carbazole (2-8)

A mixture of compound (1) (2 gm., 0.008 mol.) in absolute ethanol (25 ml.) and potassium carbonate anhydrous (1.02 gm., 0.008 mol.) was refluxed and added dropwise to a solution of (0.008 mol.) of substituted-2-aminobenzothiazole dissolved in (30 ml.) of absolute ethanol, the reaction mixture was refluxed for (8-10) hrs. after cooling the separated precipitate was filtered and recrystalized from a suitable solvent. Physical properties are listed in Tables (1, 7 and 8).

Preparation of 2-amino-5-substituted-1,3,4-oxadiazoles (9-13)

The titled compounds were prepared according to literature procedures [21] with minor modifications. An equimolar of semicarbazide hydrochloride and different aromatic aldehyde were dissolved in the mixture were refluxed for (1 hr.), then cooled and precipitated by water, filtered to obtain semicarbazone.

Semicarbazone (0.01 mol.) and sodium acetate (1.4 gm., 0.01 mol.) were dissolved (40-50) ml. of glacial acetic acid in a suitable round bottomed flask equipped with a dropping funnel for the addition of bromine, bromine (0.6 ml in 5 ml glacial acetic acid) was added dropwise with stirring and cooling. Stirring was continued for 1 hr. then the resulted solution was poured on ice water with vigorous stirring. The resulting solid was filtered, washed then dried and recrystallized from ethanol/water. Physical properties and FTIR spectral data of compound (9-13) are listed in Table (2).

Preparation of N-(2-aminoacetyl-5-substituted-1,3,4-oxadiazoles-2-yl)carbazole (14-18)

General

A mixture of compound (1) (1 gm., 0.004 mol.) in absolute ethanol (10 ml.) and potassium carbonate anhydrous (0.56 gm., 0.004 mol.) was refluxed and added dropwise to a solution of (0.004 mol.) of 2-amino -5-substituted-1,3,4-oxadiazole dissolved in (10 ml.) abs. ethanol, the mixture was refluxed for (6-8) hrs. The resulted mixture was cooled to room temperature before pouring into crushed ice. The obtained precipitate was filtered, washed thorough by with water and dried then was purified by recrystallization from a suitable solvent. Physical properties and FTIR spectral data are listed in Tables (3, 6 and 7).

Preparation of α-hydrazino-N-carbazoleacetamide (19)

To a solution of compound (1) (3 gm., 0.012 mol.) in absolute ethanol (25 ml.) hydrazine hydrate (1.5 ml., 0.024 ml.) was added with continuous stirring and the resulting mixture was refluxed on water bath for (4 hrs.) after cooling the mixture, white

precipitate was formed. The precipitate was filtered. Physical properties of the product is listed in Tables (4, 6 and 7).

Preparation of Schiff Base Derivatives of α-hydrazino-N-carbazoleacetamide (20-23)

To a hot stirred solution of the hydrazide (19) (1 gm., 0.004 mol.) in ethanol (10 ml.) appropriate aromatic aldehyde (0.004 mol.) was added with 3-4 drops of glacial acetic acid. The reaction mixture was heated to (70-80)°C for (4-6) hrs. The separated solid was filtered. Physical properties of the products are listed in Table (4).

Preparation of N-(2-aminoacetyl-5-substituted-1,2,3,4-tetrazole-1-yl)carbazole (24-27)

A mixture of (0.003 mol.) of appropriate Schiff base (20-23), dry THF (15 ml.) and sodium azide (0.2 gm., 0.003 mol.) was heated on water bath, the temperature of the water bath was controlled between (60-65)°C. The end of the reaction was checked by TLC. Physical properties of the products are listed in Tables (5, 6 and 7).

Antimicrobial Activity Test

The test was performed according to the disk diffusion method [22]. The some of the prepared compounds were tested against two strain of Gram +ve (*Staphyloccus aureus*, *Staphyloccus epiderunidis*) and one strain of Gram -ve bacteria (*Escherichia coli*) also tested against one strain of yeast (*Candidau*). Whatman No.1 filter paper disk of 5mm diameter were sterilized by autoclaving for 15 min. at 121°C. The sterile disk were impregnated with different compounds (800 µg/disk). Agar plats were surface inoculated uniformly with 100 µL from broth culture of the tested microorganism. The impregnated disk were placed on the medium suitably spaced a part and the plates incubated at 5°C for 1hr. to permit good diffution and then transferred to an incubator at 37°C for 24 hrs. The inhibition zones caused by the various compounds on the microorganisms were examined. The results are listed in Table (8).

Table (1)
Physical properties and FTIR spectral data of N-(2-aminoacetyl substituted benzothiazole-2-yl) carbazole (2-8).

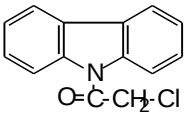
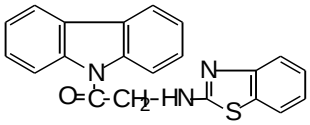
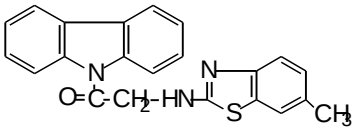
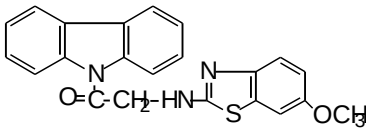
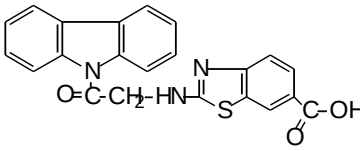
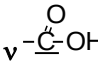
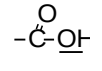
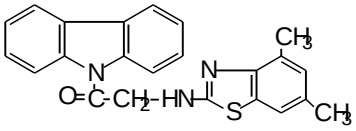
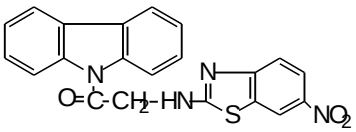
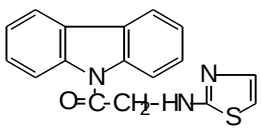
Comp. No.	*Comp. structure*	*Melting point*	*Color*	*Yield %*	*Major FTIR Absorptions cm^{-1}*				
					νN-H	*νC-H arom.*	*νC=O*	*νC=N*	*Other bands*
1		138-140	Yellow	80		3045	1695		**νC-H alph.** 2985 **νC-Cl** 656
2		176-177	Pale brown	88	3384	3051	1645	1527	**δN-H** 1602
3		156-157	Pale brown	90	3278	3051	1655	1537	**νC-H alph.** 2921 2854
4		179-180	Deep yellow	66	3419	3055	1660	1550	**νC-O-C** 1203
5		236-237	Pale brown	77	3377	3062	1670	1602	**ν**  1720  3294
6		93-94	Brown	60	3419	3049	1685	1625	**νC-H alph.** 2920 2850
7		170-171	Deep yellow	58	3336	3049	1700	1625	**νNO_2** asym. 1525 sym. 1330
8		222-223	Yellow	75	3338	3051	1701	1625	**νC-S 617**

Table (2)

Physical properties and FTIR spectral data of (2-amino-5-substituted-1,3,4-oxadiaole) (9-13).

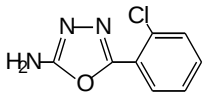
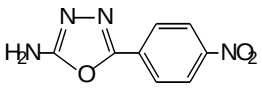
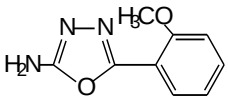
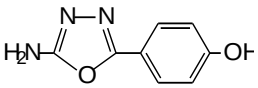
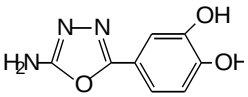
Comp. No.	Comp. structure	Melting point	Color	Yield %	Major FTIR Absorptions cm^{-1}			
					νN-H amine	νC=N	νC-O-C νC=N	Other bands
9		82-83	Green	53	3415 asym. 3390 sym.	1652	1223	**νC-Cl =1042** *o*-position = 721
10		82-73	Pale yellow	55	3423 asym. 3384 sym.	1652	1224	**νNO_2** asym. 1521 sym. 1348
11		112-113	Pale brown	92	3413 3355	1618	182 1269	
12		113-114	Light orange	95	3390 3340	1652	1305 1242	**νO-H phenolic 3472**
13		108-109	Pale pink	92	3390 3372	1639	1286	**νO-H phenolic 3472**

Table (3)

Physical properties and FTIR spectral data of N-(2-aminoacetyl-5-substituted-1,3,4-oxadiazoles-2-yl) carbazole (14-18).

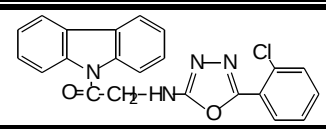
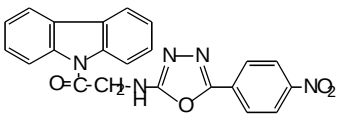
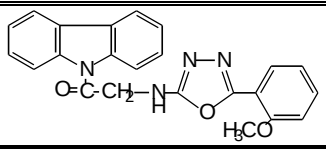
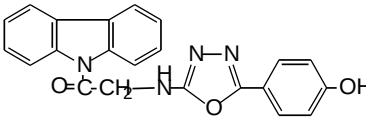
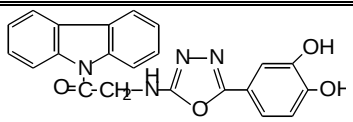
Comp. No.	Comp. structure	Melting point	Color	Yield %	Major FTIR Absorptions cm^{-1}				
					νN-H	νC=O	νC=N	νC-O-C	Other bands
14		203-204	Pale brown	90	3385	1685	1654	1164	**νC-Cl** 1042 *o*-position 722
15		197-198	Light yellow	95	3320	1674	1602	1162	**νNO_2** asym. 1520 sym. 1326 *p*-position 620
16		193-194	Pale brown	76	3315	1682	1662	1168	*o*-position 725
17		216-217	Pale brown	78	3318	1682	1602	1139	**νO-H 3419** *p*-position 842
18		223-225	Deep yellow	95	3372	1662	1603	1139	**νO-H** 3429

Table (4)

Physical properties and FTIR spectral data of Schiff base derivatives of α-hydrazino-N-carbazole acetamide (20-23).

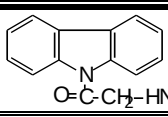
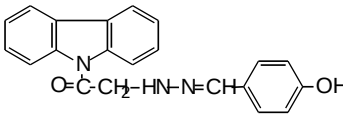
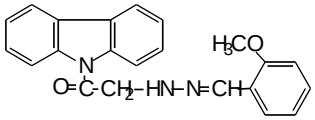
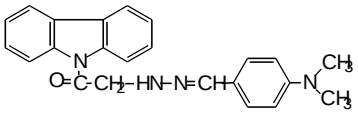
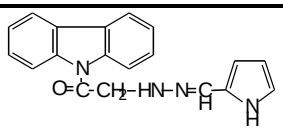
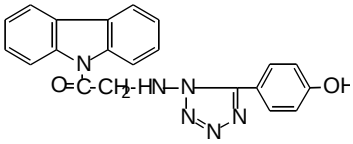
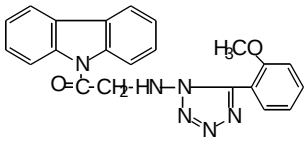
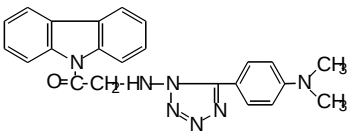
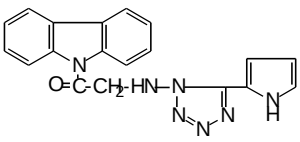
Comp. No.	Comp. structure	Melting point	Color	Yield %	Major FTIR Absorptions cm^{-1}				
					νN-H	νC-H arom.	νC=O	νC=N	Other bands
19		231-232	White	85	3192	3050	1692		**ν-NH_2** asym. 3407 Sym. 3235
20		174-175	Brown	95	3290	3070	1686	1602	**νO-H** 3419 *p*-position 815
21		180-181	Deep brown	90	3302	3055	1670	1600	**νC-O-C** 1157 *o*-position 743
22		70-72	Deep brown	95	3346	3053	1668	1600	**νC-N** 1373 *p*-position 813
23		160-161	Deep green	95	3321	3051	1672	1612	**νN-H pyrol** 3419

Table (5)

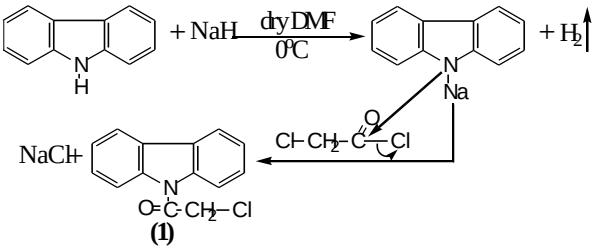
Physical properties and FTIR spectral data of N(2-aminoacetyl-5-substituted-1,2,3,4-tetrazole-1-yl) carbazole (24-27).

Comp. No.	Comp. structure	Melting point	Color	Yield %	Major FTIR Absorptions cm^{-1}				
					νN-H	νC=O	νC=N	ν tetrazol	Other bands
24		212-213	Brown	78	3419	1698	1602	1139	**νO-H** Overlap with **νN-H** *p*-position OH=814
25		200-201	Deep yellow	75	3421	1692	1602	1122	**νC-O-C** 1145
26		129-130	Deep brown	95	3415	1685	1662	1168	*p*-position 816
27		210-211	Black	95	3419	1679	1625	1126	**νN-H pyrole overlap with νN-H**

Results and Discussion

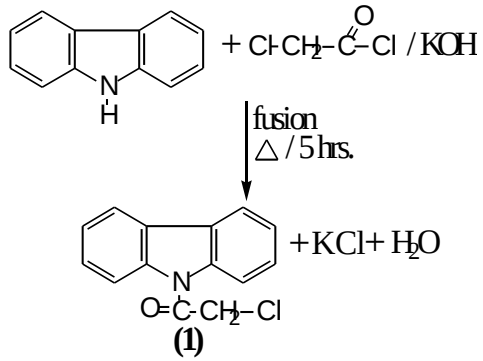
Carbazole and its derivatives are an important type nitrogen containing aromatic heterocyclic compounds which have attracted considerable attention on medicinal chemists due to their antimicrobial. For this purpose, new carbazole derivatives were synthesized and evaluated for antimicrobial activity.

As starting material α-chloro-N-carbazole (1) was prepared by two methods, in the first method reaction carbazole compound with sodium hydrite in dimethylformamad at 0°C to have sodium salt of carbazole and subsequent reaction addition of the chloroacetyl chloride according to the following equation [19]:



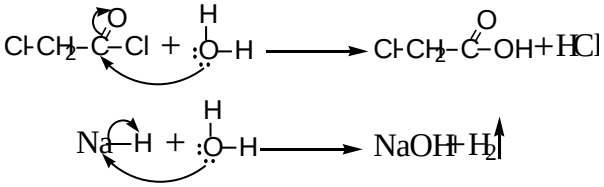
(1)

The second method by fusion carbazole compound with chloroacetyl chloride and potassium hydroxide according to the following equation:



(1)

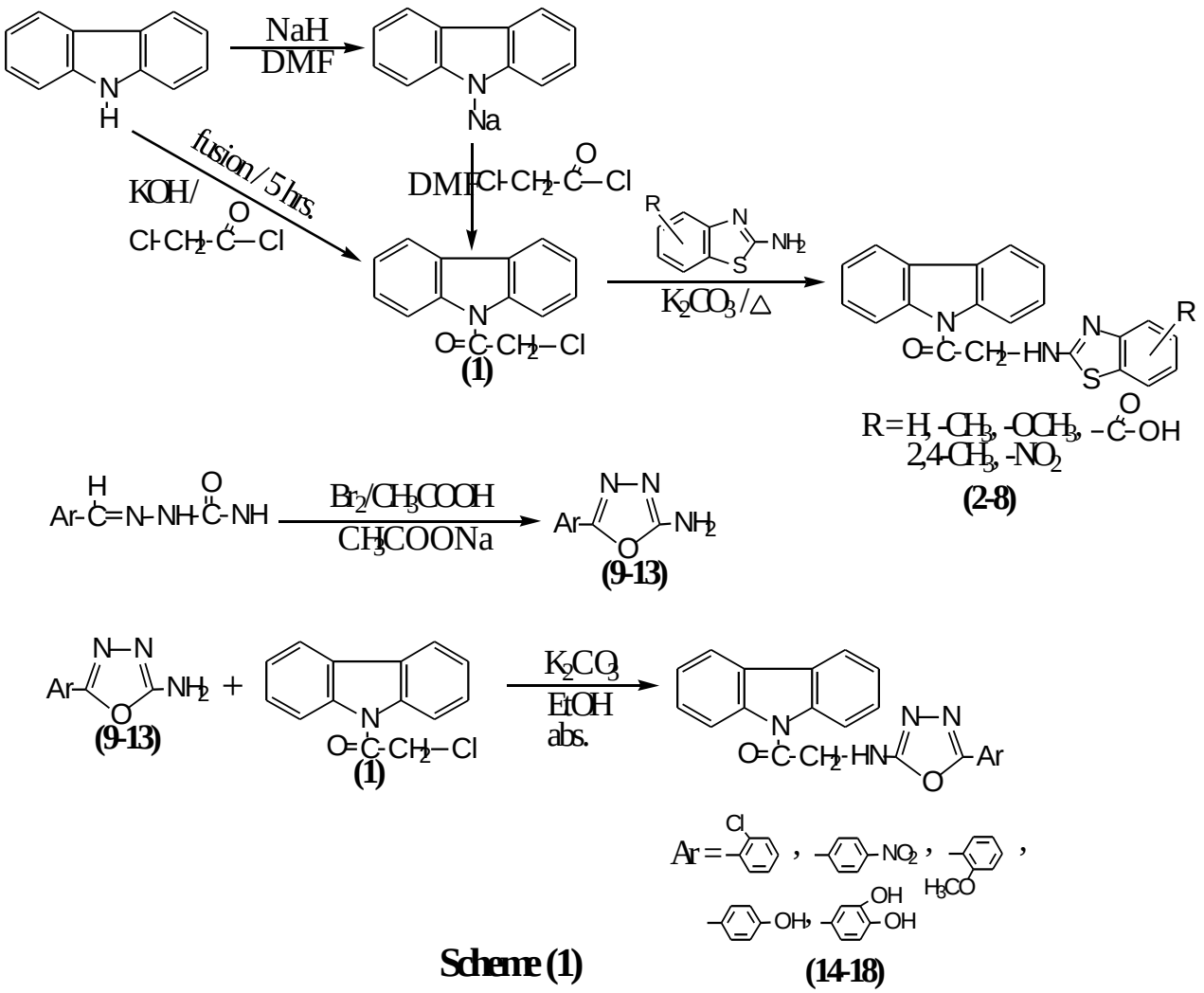
The first method better yield and purity than second method. The reaction should be carried in dry condition due to that the existence of water caused to water to react with all $Cl\text{-}CH_2\text{-}\overset{O}{\overset{\|}{C}}\text{-}Cl$ and NaH according to the following equation respectively.



The structure of compound (1) was confirmed by physical properties which are listed in Table (1). FTIR spectra showing the absorption at ν cm^{-1} (3045 for C-H aromatic; 2985 for C-H alph.; 1695 for C=O amides; 656 for C-Cl) and disappearance the absorption of $(>N\text{-}H)$ group other chemical test was carried out to characterize the prepared compound (1) such as sliver nitrate alcoholic test confirmed the presence of chloren group [23].

The prepared compounds (2-18) were colored solids with sharp melting points and afforded in good yields. Structures of the prepared compounds (2-8) were confirmed by FTIR, ^{1}H-NMR and ^{13}C-NMR spectroscopy [24]. FTIR spectra of compounds (2-8) showed clear absorption band at (3278-3419) cm^{-1}, (3049-3055) cm^{-1}, (1645-1701) cm^{-1}, and (1527-1625) cm^{-1} due to νNH, νC-H arom., νC=O and C=N respectively. And disappearance the absorption of νC-Cl group. While FTIR spectra of compound (14-18) show results listed in Table (3). ν cm^{-1} (3315-3385) for (N-H), (1602-1685) cm^{-1} for (C=O), (1602-1654) for C=N and (1139-1168) for (C-O-C) ether group in addition 1520 asym. for NO_2 group for compound (15); 3419 and 3429 for O-H group for compounds (17) and (18) respectively. In the other hand ^{1}H-NMR spectra data of compound (4) δ ppm in DMSO-d_6 solvent 3.30(s, 2H, $-\overset{O}{\overset{\|}{C}}\text{-}CH_2\text{-}$); 3.37 (s, 3H, -$OCH_3$); 7.12-7.49(m, 11H, Ar-H); 8.11(t, 1H, -NH-). Then reaction compound (1) by two different ways. The first way involved direct reaction with substituted-2-aminobenzothiazol under certain conditions to give new compounds (2-8) and reaction of 5-substituted-2-amino-1,3,4-oxadiazole in the presence of potassium carbonate anhydrous to

give new compounds (14-18). These reactions are summarized in Scheme (1).

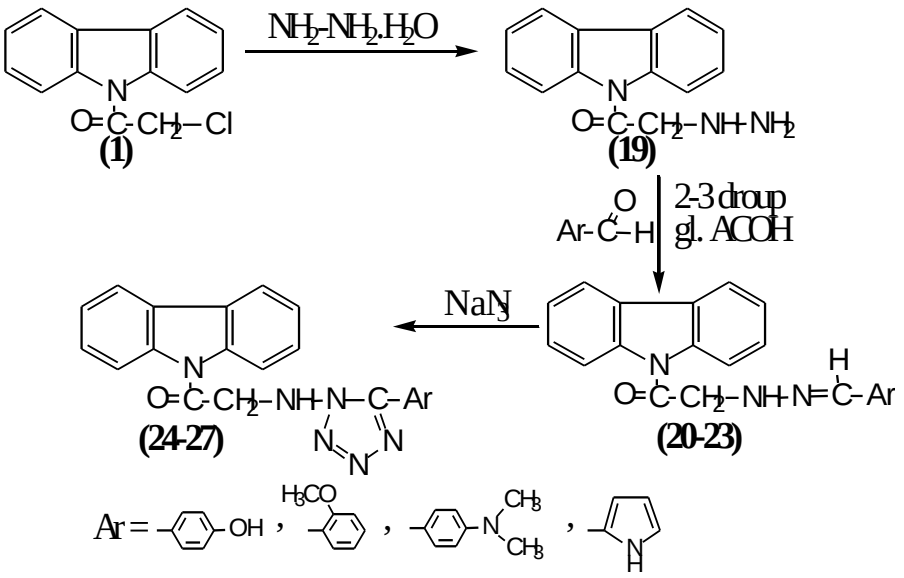


Scheme (1)

Also the compounds (5) δ ppm DMSO-d_6 solvent 3.33(s, 2H, $-\overset{O}{\overset{\|}{C}}-CH_2-$); 7.15-7.48(m, 11H, Ar-H); 8.30(s, 1H, -NH-); 11.27(s, 1H, $-\overset{O}{\overset{\|}{C}}-OH$). ^{13}C-NMR spectra of compounds (4) and (5) showed results were listed in Table (7).

^{1}H-NMR spectrum data of compound (15) δ ppm in DMSO-d_6 solvent 3.32(s, 2H, $-\overset{O}{\overset{\|}{C}}-CH_2-$); 7.15-7.5(m, 12H, Ar-H); 8.3-10 (s, 1H, -NH-). ^{13}C-NMR spectra results were listed in Table (7).

The second way condensation compound (1) with hydrazine hydrate give the corresponding hydrazine derivative (19) which the conversion new Schiff base (20-23) were prepared through the reaction of hydrazine derivative (19) with different aromatic aldehyde. Followed the cyclization of compounds (20-23) by used sodium azide in dry THF to give substituted tetrazole (24-27) respectively. Synthesis of these compound (19-27) can be summarized in Scheme (2).



Scheme (2)

The structure of compound (19) was confirmed by physical properties which are listed in Table (4). FTIR spectra showing the absorption at ν cm^{-1} (3467 asym. for $–NH_2$; 3192 for NH; 3050 C-H arom.; 1692 for C=O and disappearance the absorption of (C-Cl) group. While the ^{1}H-NMR spectra [15] of compound (19) δ ppm in DMSO-d_6 solvent: 3.25(s, 2H, $-\overset{O}{\overset{\|}{C}}-CH_2-$); 4.25(s, 2H, $-NH_2$); 7.1-7.5(m, 8H, Ar-H); 8.13(s, 1H, -NH-). ^{13}C-NMR spectra show results were listed in Table (7).

The Schiff base (20-23) were obtained good yield through the reaction of hydrazine (19) with different aromatic aldehyde Scheme (2). The FTIR spectrum of compounds (20-23) are listed in Table (4). All the spectrum data show disappearance the absorption of νNH_2 and appearance the absorption ν cm^{-1} (1600-1612) for C=N group. The Schiff base (20-23) were concerted to tetrazoles (24-27) derivative by the reaction with sodium azide in dry acetone afford intramolecular cyclization to give N-(2-aminoacetyl-5-substituted-1,2,3,4-tetrazole-1-yl) carbazole (24-27) were identified from FTIR spectra shows results listed in Table (5) ν cm^{-1} (3415-3421) for –NH-, (1679-1698) for C=O, (1602-1662) for C=N, (1122-1168) for tetrazole group for compounds (24-27), in addition νO-H and νN-H overlap with νN-H for compound (24) and (27) respectively. Also 1145 for νC-O-C group for compound (25). While the H-NMR spectra data of compound (24) δ ppm in DMSo-d_6 solvent: 3.11(d, 2H, $-\overset{O}{\overset{\|}{C}}-CH_2-$); 6.6-7.4(m, 12H, Ar-H); 7.92(s, 1H, -NH-); 9.48(s, 1H, -OH). Also H-NMR of compound (27) δ ppm in DMSO-d_6 solvent: 1.4(s, 6H, $-N\begin{matrix}CH_3\\CH_3\end{matrix}$); 3.30(s, 2H, $-\overset{O}{\overset{\|}{C}}-CH_2-$); 7.1-7.5(m, 12H, Ar-H); 8.31(s, 1H, -NH-). ^{13}C-NMR spectra for compounds (24) and (27) shows were listed in Table (7).

Antimicrobial Activity

The results of antimicrobial studies are show in Table (8). From the data it are clear that all compounds possess between height to moderate activity against of yeast (*Candidau*), while compounds (25) and (27) possess very high activity against one type of bacteria and compounds (2, 14, 16, 19 and 27) possess moderate activity two types of bacteria. As far as compounds (3, 7, 17 and 27) possess high activity against one types of bacteria while compounds (7, 14, 16, 17, 19 and 24) show inactive against one type of bacteria (*E. coli*).

Table (6)

^{1}H-NMR spectra data for some of the prepared compounds.

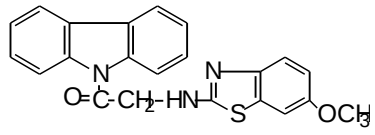
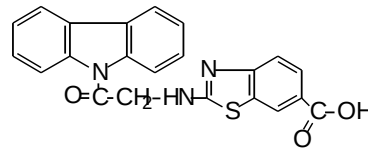
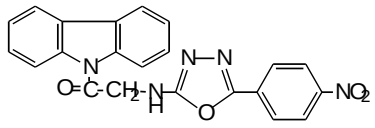
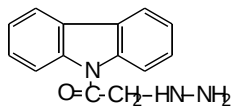
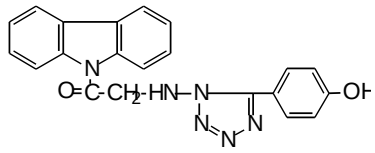
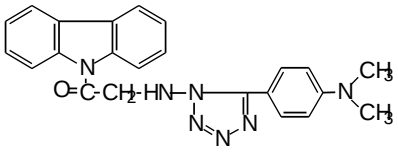
Comp. No.	*Compound structure*	*^{1}H-NMR (δ ppm) in DMSO-d_6 solvent*
4		3.30(s, 2H, -C(=O)-CH$_2$-); 3.73(s, 3H, -OCH$_3$); 7.12-7.49(m, 11H, Ar-H); 8.11(t, 1H, -NH-)
5		3.33(s, 2H, -C(=O)-CH$_2$-); 7.15-7.48(m, 11H, Ar-H); 8.3(s, 1H, -NH-); 11.27(s, 1H, -C(=O)-OH)
15		3.32(s, 2H, -C(=O)-CH$_2$-); 7.15-7.5(m, 12H, Ar-H); 8.3(s, 1H, -NH-)
19		3.25(s, 2H, -C(=O)-CH$_2$-); 4.25(s, 2H, -NH$_2$); 7.1-7.5(m, 8H, Ar-H); 8.13(s, 1H, -NH-)
24		3.11(s, 2H, -C(=O)-CH$_2$-); 6.6-7.4(m, 12H, Ar-H); 7.92(s, 1H, -NH-); 9.48(s, 1H, -OH)
26		1.4(s, 6H, -N(CH$_3$)CH$_3$); 3.3(s, 2H, -C(=O)-CH$_2$-); 7.1-7.5(m, 12H, Ar-H); 8.312(s, 1H, -NH-)

Table (7)

^{13}C-NMR spectra data for some of the prepared compounds.

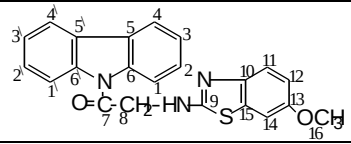
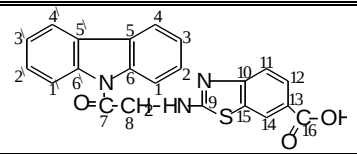
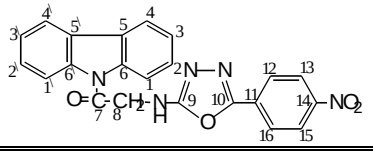
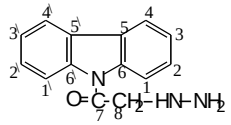
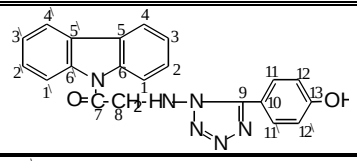
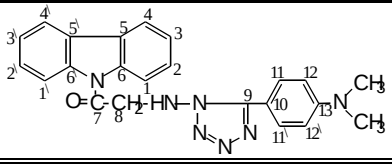
Comp. No.	*Compound structure*	*^{13}C-NMR (δ ppm) in DMSO-d_6 solvent*
4		55, 53 (C^{16}); 79.6(C^{8}); 110.86-120.06(C^{2}, C^{2}, $C^{2'}$, C^{3}, $C^{3'}$, C^{4} and $C^{4'}$); 125.36-139.68(C^{1}, $C^{1'}$, C^{5}, $C^{5'}$, C^{6}, $C^{6'}$, C^{10}, C^{11}, C^{12}, C^{14} and C^{15}); 158(C^{9}); 172.62(C^{7})
5		79.56(C^{8}); 107.88-120.05(C^{2}, $C^{2'}$, C^{3}, $C^{3'}$, C^{4} and $C^{4'}$); 122.36-139.71(C^{1}, $C^{1'}$, C^{5}, $C^{5'}$, C^{6}, $C^{6'}$, C^{10}, C^{11}, C^{12}, C^{13}, C^{14} and C^{15}); 158.64(C^{9}); 172.93(C^{7}); 180.76(C^{16})
15		79.82(C^{8}); 110.02-122.36(C^{2}, $C^{2'}$, C^{3}, $C^{3'}$, C^{4} and $C^{4'}$); 125.02-139.68(C^{1}, $C^{1'}$, C^{5}, $C^{5'}$, C^{6}, $C^{6'}$, C^{11}, C^{12}, $C^{12'}$, C^{13}, $C^{13'}$, C^{14}); 157.23(C^{9}); 158.03(C^{10}); 172.60(C^{7})
19		79.56(C^{8}); 109.71-122.87(C^{2}, $C^{2'}$, C^{3}, $C^{3'}$, C^{4} and $C^{4'}$); 125.92-129.35(C^{1}, $C^{1'}$, C^{5} and $C^{5'}$); 140.20(C^{6} and $C^{6'}$); 170.16(C^{7})
24		79.56(C^{8}); 110.86-120.6(C^{2}, $C^{2'}$, C^{3}, $C^{3'}$, C^{4} ,$C^{4'}$, C^{11} and $C^{11'}$); 125.42-131.48(C^{1}, $C^{1'}$, C^{5} ,$C^{5'}$, C^{10}, C^{12} and $C^{12'}$); 139.68(C^{6}, $C^{6'}$, C^{9} and $C^{9'}$); 172.93(C^{7})
26		38.71(C^{14} and $C^{14'}$); 79.55(C^{8}); 110.86-120.06(C^{2}, $C^{2'}$, C^{3}, $C^{3'}$, C^{4} ,$C^{4'}$, C^{11} and $C^{11'}$); 122.35-125.42(C^{1}, $C^{1'}$, C^{5} ,$C^{5'}$, C^{10}, C^{12} and $C^{12'}$); 139.68(C^{6}, $C^{6'}$, C^{9} and C^{13}); 172.82(C^{7}).

Table (8)

Results of antimicrobial activity of the tested prepared compounds.

Comp. No.	*Staph. aure*	*Staph. Epide*	*E. coli*	*Candidau*
2	++	-	++	+++
3	+++	++	+	++
7	+++	++++	-	++
14	++	++	-	++
16	++	++	-	++
17	+++	++	-	++
19	++	++	-	++
24	++	+	-	+++
25	++++	++	+	+++
27	+++	++	++	+++

Solvent: DMSO, [C]: 800 µg/ml.

Key to symbols: Very active = ++++ (inhibition zone 21-30 mm).

Highly active = +++ (inhibition zone 15-20 mm). Moderately active = ++ (inhibition zone 10-14 mm).

Slightly active = + (inhibition zone 6-9 mm). Inactive = - (inhibition zone <6 mm).

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الخلاصة

تضمن البحث سلسلة من بعض المركبات الحلقية غير المتجانسة جديدة حاوية على الكبريت، الاوكسجين والنتروجين في تركيبها معوضة بذرة نتروجين الكاربزول، وذلك من خلال تحضير الفا-كلورو-N-كاربزول است امايد (1) الذي حصلنا عليه بطريقتين، الطريقة الاولى بمعاملة مركب الكاربزول مع الصوديوم هيدريد في داي مثيل فورمامايد في درجة (صفر م°) ليعطي ملح الصوديوم للكاربزول العالق وتواصل التفاعل مع الكلورواسيتايل كلوريد وتم الحصول على المركب الرئيسي. اما الطريقة الثانية تفاعل مركب الكاربزول مع الكلورواسيتايل كلوريد وهيدروكسيد البوتاسيوم بطريقة الصهر. بعدها تفاعل المركب (1) بطريقتين، تضمنت الطريقة الاولى بالتفاعل المباشر مع معوضات-2-امينوبنزوثايزول تحت ظروف معينة حصلنا على المركبات (2-8)، وتفاعل 5-معوض-2-امينو-1و2و3-اوكساديايزول بوجود كاربونات البوتاسيوم اللامائية حصلنا على المركبات الجديدة (14-18) على التوالي. بينما تضمنت الطريقة الثانية تكاثف المركب (1) مع الهايدرازين المائي ليعطي مشتق الهايدرازين (19) الذي تم تحويله الى قواعد شف الجديدة (20-23) وذلك من خلال تفاعل مشتق الهايدرازين (19) مع الالديهايدات الاروماتية. الغلق الحلقي للمركبات (20-23) باستخدام ازايد الصوديوم في تتراهيدروفيوران الجاف نتجت معوضات التترازول (24-27). شخصت المركبات المحضرة بالطرق الطيفية [FTIR، ^{1}H-NMR، ^{13}C-NMR] وتعين بعض خواصها الفيزياوية واجراء بعض الكشوفات النوعية. كما تم دراسة تاثير هذه المركبات على ثلاثة انواع من البكتريا وواحدة من الخمائر.

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