Research Paper Chemistry

Antimicrobial Evaluation of some Prepared Fused Quinazolinone Derivatives

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ABSTRACT

Treatment of Anthranilic acid with chloroacetylchloride in presence of sodium acetate gave 2-(chloromethyl)-4H-benzo[d][1,3]oxazin-4-one [1], that fused with ammonium acetate to give 2-(aminomethyl)quinazolin-4(3H)-one [2]. The compound 2,3-dihydro-1H-pyrazino[2,1-b]quinazoline-4,6-dione [3] was prepared from cyclization of [2] with ethyl chloroacetate in presence of fused sodium acetate . Treatment of [3] with 1 mol and/or 2 mol of aromatic aldehydes in presence of pepridine yielded the corresponding 3-(arylidene)-2,3-dihydro-1H-pyrazino[2,1-b]quinazoline-4,6-dione [4] and 1,3-diarylidene-2,3-dihydro-1H-pyrazino[2,1-b]quinazoline-4,6-dione [5], respectively. Acetylation of [4] and [5] by the reaction with acetic anhydride gave the corresponding 2-acetyl-3-(arylidene)-2,3-dihydro-1H-pyrazino[2,1-b]quinazoline-4,6-dione [6] and 2-acetyl-1,3-diarylidene-2,3-dihydro-1H-pyrazino[2,1-b]quinazoline-4,6-dione [7] respectively. The electron impact mass spectra of the above series of compounds have also been recorded and their fragmentation pattern is discussed. The prepared compounds also exhibited antimicrobial activity.

Keywords : pyrazine, quinazolinone, mass spectra, Antimicrobial activity.

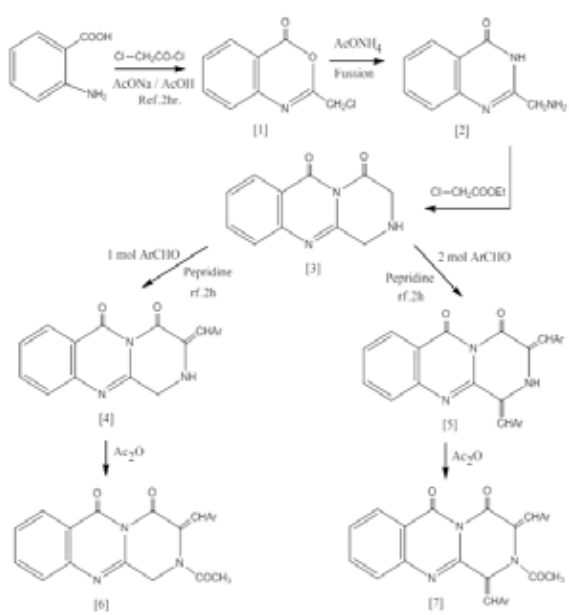
1- Introduction

Quinazolin-4(3H)-one and its derivatives are a class of heteroaromatic compounds that have drawn much attention due to their biological and pharmaceutical activities[1-11]. A brief survey on the biological activities of quinazolin-4(3H)-one derivatives showed anti-inflammatory[12-14], Antitumor[15-18], anti HIV[19], antibacterial[20-22], as well as CNS depressant and anticonvulsant activities[23, 24]. 4-Substituted quinazolines were also studied as anticancer agents for their strong ability to inhibit several receptor tyrosine kinases[25]. Derivatives of quinazolin-4-one are potential drugs which can possess hypnotic[26], analgesic[27], anthelmintic[28], neuroleptic[29], antiallergic, antimalarial and other effects[30, 31]. On the other hand, it was found that not only quinazoline derivatives showed chemotherapeutic activity, but also pyrazine[32] and pyrazolone[33] moieties possess this activity. Moreover, the increasing biological importance of quinazolinone derivatives particularly in chemotherapy, promoted us to develop and synthesize the new pyrazino[2,1-b] quinazoline-4,6-dione derivatives, with the aim of obtaining some novel heterocyclic systems with potentially enhanced biological properties. The electron impact (EI) ionization mass spectral fragmentations of some synthesized compounds were described.

2- Result and Discussion

2.1 Chemistry

The reaction of Anthranilic acid with chloroacetylchloride in presence of sodium acetate under reflux gave the corresponding 2-(chloromethyl)-4H-benzo[d][1,3]oxazin-4-one [1]. A monolysis of 2-chloromethyl-4-oxo-3,1-benzoxazinone (**1**) with ammonia from ammonium acetate and/or formamide under fusion led to the formation of 2-aminomethyl-4-oxo-quinozolinone(**2**). Cyclization of **2** with ethyl chloroacetate in presence of fused sodium acetate gave 2,3-dihydro-1H-pyrazino[2,1-b]quinazoline-4,6-dione [3] . Treatment of **3** with 1 mol and/or 2 mol of aromatic aldehydes in presence of pepridine yielded the corresponding 3-(arylidene)-2,3-dihydro-1H-pyrazino[2,1-b]quinazoline-4,6-dione [4] and 1,3-diarylidene-2,3-dihydro-1H-pyrazino[2,1-b]quinazoline-4,6-dione [5], respectively. Acetylation of **4** and **5** by the reaction with acetic anhydride gave the corresponding 2-acetyl-3-(arylidene)-2,3-dihydro-1H-pyrazino[2,1-b]quinazoline-4,6-dione [6] and 2-acetyl-1,3-diarylidene-2,3-dihydro-1H-pyrazino[2,1-b]quinazoline-4,6-dione [7] respectively. (Scheme I)



	a	b	c
Ar	C_6H_5	C_6H_4-CH_3-p	C_6H_4-OCH_3-p

Scheme I

2.2 Mass spectrometry:

All the spectra of synthesized compounds show relatively small molecular ions and peaks typical of a cleavage and rearrangement process type fragmentation[34-36]. The molecular

ions of [1]; (Fig.1), [2]; (fig.2), [3]; (Fig.3), [4a]; (fig.4) and [6a]; (Fig.5) fragmented further and involved pathway as illustrated in Scheme II, Where the molecular ion of 6] at m/z 345 fragmented to give the molecular ion of [4a] at m/z 303 by losing CH_2CO that broken and lose C_7H_4 to give the molecular ion of [3] at m/z 215 which fragmented to give the molecular ion of [2] at m/z 175. The later molecular ion broken to give the fragment of m/z 159 by losing NH_2. The fragment of m/z 159, which broken to give the fragment of m/z 145 (the base peak) by losing CH=NH. The fragment of m/z 145 was broken to give an ion of m/z 105 which further broke to give an ion at m/z 77. The later loss CH_2=CH to form the fragment of m/z 50.

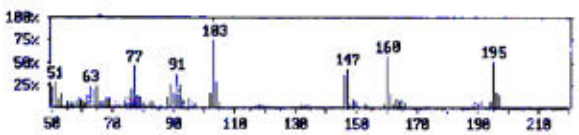


Fig.1 70 eV mass spectrum of compound [1]

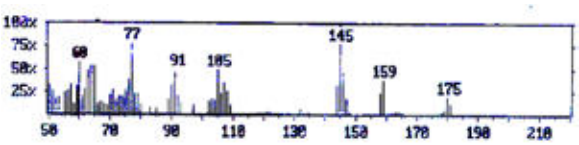


Fig.2 70 eV mass spectrum of compound [2]

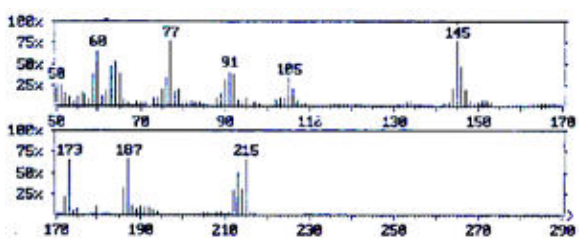


Fig.3 70 eV mass spectrum of compound [3]

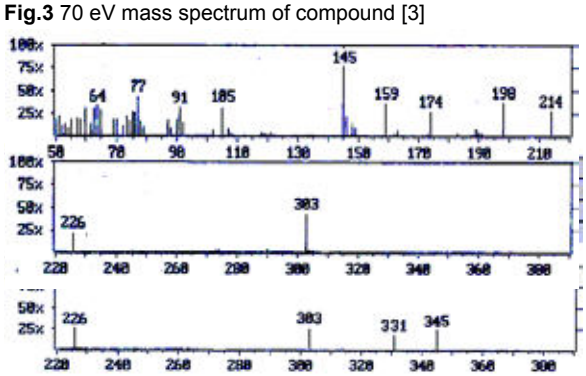
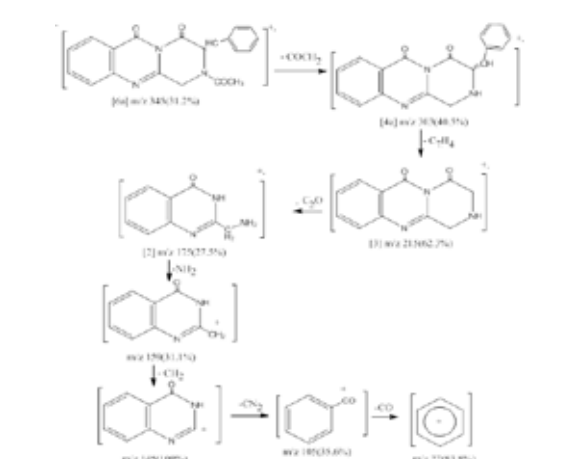


Fig.5 70 eV mass spectrum of compound [6a]



Scheme II. Main fragmentation pathway of compounds [2], [3], [4a] and [6a].

The molecular ions of [3]; (Fig.3), [5a]; (fig.6) and [7a]; (fig.7) fragmented further and involved pathway as illustrated in Scheme III, Where the molecular ion of [7a] at m/z 433 fragmented to give the molecular ion of [5a] at m/z 391 by losing $COCH_2$ that broken and lose 2 C7H4 to give the molecular ion of [3] at m/z 215. The later fragmented to give the fragment of m/z 187 by losing CO. The fragment of m/z 187, which broken to give the fragment of m/z 145 (the base peak) by losing CH=NH. The fragment of m/z 145 was broken to give an ion of m/z 105 which further broke to give an ion at m/z 77. The later loss CH_2=CH to form the fragment of m/z 50.

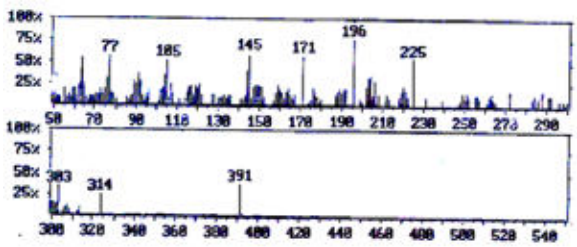


Fig.5 70 eV mass spectrum of compound [5a]

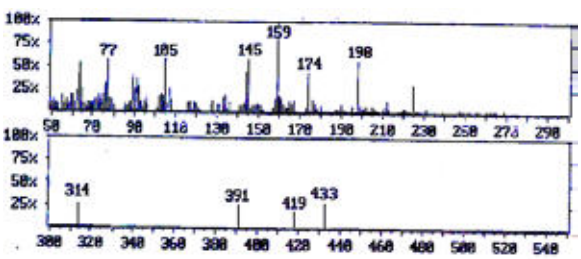
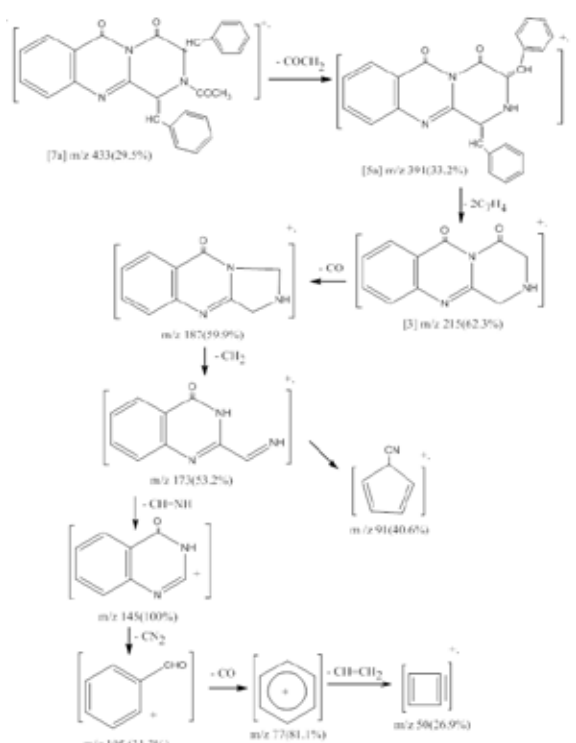


Fig.5 70 eV mass spectrum of compound [7a]



Scheme III. Main fragmentation pathway of compounds [3], [5a] and [7a].

3- Experimental section:

Melting points were determined in Capillaries with a Thomas Uni-melt apparatus uncorrected. NMR spectra were recorded on a general electric QE300 instrument and chemical shifts are given with respect to TMS. IR spectra were recorded on a Perkin-Elmer 1420 spectrometer and a Biorad FTS7 (KBr). Mass spectra were obtained on a Jeol JMSD-300 spectrometer operating at 70 eV. Microanalyses were conducted using an elemental analyzer 1106.

2-(chloromethyl)-4H-benzo[d][1,3]oxazin-4-one [1]

A mixture of Anthranilic acid (0.01 mol), chloroacetylchloride (0.01 mol) in presence of sodium acetate (0.02mol) was heated under reflux for 2 hr, and then cooled. The solid formed was filtered off, dried and purified by recrystallization with ethanol to give [1] as colorless crystals, yield 87%, m.p: 165°C; **IR** (KBR): 1722(C=O), 1630(C=N), 1605, 1592(C=C), 1120, 1075(C-O) cm^{-1}. **^{1}H-NMR** (DMSO-d6): δ2.91(s, 2H, CH_2), 7.25-7.33(d, 1H, Ar-H), 7.46-7.55(t, 1H, Ar-H), 7.72-7.83(t, 1H, Ar-H), 7.91-8.10(d, 2H, Ar-H) ppm. **MS** (m/z, %): 197(M^+2, 6.1), 196(M^+1,14.2), 195(M^+, 51.3), 191(17.4), 160(48.7), 147(25.8), 146(17.0), 103(100), 92(25.2), 91(37.4), 90(14.8), 77(45.2), 63(22.6), 51(27.8). Anal. Calcd. For $C_9H_6ClNO_2$: C, 55.26; H, 3.09; Cl, 18.13; N, 7.16 Found: C, 55.11; H, 2.89; Cl, 17.93; N, 7.12

2-(aminomethyl)quinazolin-4(3H)-one [2]

A mixture of [1] (0.01 mol) and ammonium acetate (0.02) was heated until fusion. The crude product was cooled, washed with water, filtered off and purified by ethanol to give [2] as white crystals, yield 75%, m.p: 245°C; **IR** (KBR): 3320-3300(NH_2), 3296(NH), 1722(C=O), 1630(C=N), 1605, 1592(C=C) cm^{-1}. **^{1}H-NMR** (DMSO-d6): δ2.75(s, 2H, CH_2), 7.45-7.72(m, 4H,Ar-H), 8.2(s, 2H, NH_2), 8.9(s, 1H, NH) ppm. **MS** (m/z,%): 176(M^+1,15.9), 175(M^+, 27.5), 159(31.1), 145(100), 105(35.6), 91(45.9), 77(83.8), 50(32.4). Anal. Calcd. For $C_9H_6N_3O$: C, 61.70; H, 5.18; N, 23.99 Found: C, 61.48; H, 4.98; N, 23.68

2,3-dihydro-1H-pyrazino[2,1-b]quinazoline-4,6-dione [3]

The reaction of [2] (0.01 mol) and ethylchloroacetate under reflux in presence of sodium acetate gave [3], pale yellow crystals yield 68%, m.p: 261°C; **IR** (KBr): 3229(NH), 1685-1710(C=O), 1630(C=N), 1585(C=C) cm^{-1}. **^{1}H-NMR** (DMSO-d6): δ2.46(s, 2H, CH_2C=N), δ3.31(s, 2H, CH_2C=O), 7.71-7.83(m, 4H,Ar-H), 8.4(s, 1H, NH) ppm. **MS** (m/z,%): 215(M^+, 62.3), 187(59.9), 173(53.2), 145(100), 105(31.3), 91(40.6), 77(81.1), 50(26.9). Anal.Calcd. for $C_{11}H_9N_3O_2$: C, 61.39; H, 4.22; N, 19.53 Found: C, 61.12; H, 4.08; N, 19.22

3-(arylidene)-2,3-dihydro-1H-pyrazino[2,1-b]quinazoline-4,6-dione [4]

A mixture of [3], (0.01 mole), aromatic aldehydes (such as benzaldehyde, anisaldehyde or 4-methoxybenzaldehyde) (0.01 mole) and piperdine (1 ml) was fused on a hot plate at 120-130 °C for 2hr. the reaction mixture was cooled and acidified with dilute hydrochloric acid (2N). The crude product was filtered off, washed with water, dried and purified by recrystallization with ethanol to give [4a-c].

Compound 4a as white crystals yield 75 %, m.p: 195 °C; IR (KBr): 3288(NH), 1712-1685(C=O), 1628(C=N), 1612, 1587(C=C) cm^{-1}. ^{1}H-NMR (DMSO-d6): δ2.2(s, 2H, CH_2C=N), 5.5(s, 1H, =CH), 7.2-7.87(m, 9H, Ar-H), 8.5(s, 1H, NH) ppm. MS (m/z, %): 303(M^+,49.5),226(23.7),214(25.1),198(38.5),174(32.7),159(42.5),145(100),105(35.4),91(32.5),77(47.3),64(42.5),50(22.5). Anal.Calcd. for $C_{18}H_{13}N_3O_2$: C, 71.28; H, 4.32; N, 13.85 Found: C, 71.10; H, 4.25; N, 13.67

Compound 4b as white crystals yield 83 %, m.p: 225 °C; IR (KBr): 3320(NH), 1720-1695(C=O), 1630(C=N), 1618, 1590(C=C) cm^{-1}. ^{1}H-NMR (DMSO-d6): δ1.8(s, 3H, CH_3), δ 2.34(s, 2H, CH_2C=N), 6.2(s, 1H, =CH), 7.17-7.68(m, 8H, Ar-H), 9.1(s, 1H, NH) ppm. MS (m/z, %): 317(M^+,31.5), 302(35.8), 225(51.5), 213(47.5), 197(100), 174(65.2), 159(54.6), 144(45.2), 105(74.5), 90(33.8), 77(54.2), 62(44.5), 50(41.2). Anal.Calcd. for $C_{19}H_{15}N_3O_2$: C, 71.91; H, 4.76; N, 13.24 Found: C, 71.68; H, 4.55; N, 13.14

Compound 4c as pale yellow crystals yield 63 %, m.p: 246 oC; IR (KBr): 3330(NH), 1705-1681(C=O), 1622(C=N), 1633, 1585(C=C), 1203, 1124(C-O) cm-1. 1H-NMR (DMSO-d6): δ 2.61(s, 2H, CH2C=N), δ3.5(s, 3H, CH3), 6.5(s, 1H, =CH), 7.1-7.79(m, 8H, Ar-H), 9.5(s, 1H, NH) ppm. MS (m/z, %): 333(M+,32.5), 319(51.5), 302(45.8), 225(53.5), 213(37.5), 197(60.5), 174(55.2), 159(44.6), 144(100), 105(73.5), 90(43.8), 77(50.2), 62(50.5), 50(47.2). Anal.Calcd. for C19H15N3O4: C, 68.46; H, 4.54; N, 12.61 Found: C, 68.23; H, 4.28; N, 12.54

1,3-diarylidene-2,3-dihydro-1H-pyrazino[2,1-b]quinazoline-4,6-dione [5]

A mixture of [3] (0.01 mole), aromatic aldehydes (such as benzaldehyde, anisaldehyde or 4-methoxybenzaldehyde) (0.02 mole) and piperdine (2 ml) was fused on a hot plate at 120-130 °C for 2hr. the reaction mixture was cooled and acidified with dilute hydrochloric acid (2N). The crude product was filtered off, washed with water, dried and purified by recrystallization with ethanol to give [5a-c].

Compound 5a as white crystals yield 82 %, m.p: 218 oC; IR (KBr): 3276(NH), 1710-1693(C=O), 1642(C=N), 1615, 1574(C=C) cm-1. 1H-NMR (DMSO-d6): δ5.7(s, 2H, =CH), 7.1-8.12(m, 14H, Ar-H), 12.5(s, 1H, NH) ppm. MS (m/z, %): 391(M+,50.1), 314(25.5), 303(27.7), 225(68.5), 196(100), 171(70.2), 145(65.5), 105(50.3), 77(60.3), 63(51.5), 50(22.5). Anal.Calcd. for C25H17N3O2: C, 76.71; H, 4.38; N, 10.74 Found: C, 76.58; H, 4.25; N, 10.64

Compound 5b as pale yellow crystals yield 58 %, m.p: 235 oC; IR (KBr): 3315(NH), 1700-1680(C=O), 1615(C=N), 1601, 1568(C=C) cm-1. 1H-NMR (DMSO-d6): δ2.2(s, 6H, CH3), δ 6.5(s, 2H, =CH), 7.1-7.95(m, 12H, Ar-H), 11.5(s, 1H, NH) ppm. MS (m/z, %): 419(M+,35.5), 404(25.9), 328(45.5), 316(42.6), 301(44.2), 225(34.5), 213(57.5), 196(56.2), 171(60.2), 145(100), 105(55.3), 77(45.3), 63(54.5), 50(21.5). Anal.Calcd. for C27H21N3O2: C, 77.31; H, 5.05; N, 10.02 Found: C, 77.12; H, 4.87; N, 9.89

Compound 5c as yellow crystals yield 61 %, m.p: 252 oC; IR (KBr): 3300(NH), 1712-1690(C=O), 1615(C=N), 1628, 1595(C=C), 1224, 1150(C-O) cm-1. 1H-NMR (DMSO-d6): δ3.21 (s, 6H, CH3), 6.2(s, 2H, =CH), 7.1-7.85(m, 12H, Ar-H), 13.1(s, 1H, NH) ppm. MS (m/z, %): 451(M+,33.5), 436(44.5), 420(55.2), 344(56.2), 332(64.5), 317(31.4), 302(29.8), 225(45.6), 214(32.7), 196(52.2), 171(65.2), 145(100), 105(51.3), 77(40.3), 63(50.5), 50(28.5). Anal.Calcd. for C27H21N3O4: C, 71.83; H, 4.69; N, 9.31 Found: C, 71.66; H, 4.52; N, 9.25

2-acetyl-3-(arylidene)-2,3-dihydro-1H-pyrazino[2,1-b]quinazoline-4,6-dione [6] and

2-acetyl-1,3-diarylidene-2,3-dihydro-1H-pyrazino[2,1-b] quinazoline-4,6-dione [7]

A mixture of [4a-c] and/or [5a-c] (0.01 mol) and acetic anhydride (0.01mol) was heated until fusion. The crude product was cooled, washed with water, filtered off and purified by ethanol to give [6a-c] and/or [7a-c], respectively.

Compound 6a as white crystals yield 70 %, m.p: 120 oC; IR (KBr): 1728-1664(C=O), 1630(C=N), 1618, 1557(C=C) cm-1. 1H-NMR (DMSO-d6): δ1.85(s, 3H, CH3), 2.5(s, 2H, CH2C=N), 6.3(s, 1H, =CH), 7.1-7.77(m, 9H, Ar-H) ppm. MS (m/z, %): 345(M+, 25.5), 331(22.5), 303(24.1), 226(25.2), 214(26.2), 196(47.3), 171(100), 145(48.3), 105(45.3),

77(49.5), 64(44.6), 50(23.5). Anal.Calcd. for C20H15N3O3: C, 69.56; H, 4.38; N, 12.17 Found: C, 69.41; H, 4.15; N, 12.10

Compound 6b as white crystals yield 65 %, m.p: 233 oC; IR (KBr): 1700-1686(C=O), 1611(C=N), 1601, 1584(C=C) cm-1. 1H-NMR (DMSO-d6): δ1.8(s, 3H, COCH3), δ2.2(s, 3H, CH3), δ 2.68(s, 2H, CH2C=N), 5.64(s, 1H, =CH), 7.1-7.84(m, 8H, Ar-H) ppm. MS (m/z, %): 359(M+, 31.5), 345(44.2), 317(35.5), 302(30.8), 225(41.5), 213(37.5), 197(46.8), 174(45.2), 159(100), 144(35.2), 105(64.5), 90(23.8), 77(58.2), 62(44.5), 50(41.2). Anal.Calcd. for C21H17N3O3: C, 70.18; H, 4.77; N, 11.69 Found: C, 70.05; H, 4.61; N, 11.52

Compound 6c as yellow crystals yield 60 %, m.p: 256 oC; IR (KBr): 1720-1685(C=O), 1610(C=N), 1641, 1573(C=C), 1220, 1154(C-O) cm-1. 1H-NMR (DMSO-d6): δ1.8(s, 3H, COCH3), 2.54(s, 2H, CH2C=N), δ4.2(s, 3H, OCH3), 6.4(s, 1H, =CH), 7.2-7.89(m, 8H, Ar-H)ppm. MS (m/z, %): 375(M+,30.5), 361(44.8), 333(48.5), 319(41.5), 302(45.8), 225(63.5), 213(29.5), 197(50.5), 174(45.2), 159(44.6), 144(100), 105(63.5), 90(63.8), 77(60.2), 62(53.5), 50(37.2). Anal.Calcd. for C21H17N3O4: C, 67.19; H, 4.56; N, 11.19 Found: C, 67.11; H, 4.29; N, 11.11

Compound 7a as white crystals yield 70 %, m.p: 173 oC; IR (KBr): 1719-1678(C=O), 1645(C=N), 1622, 1592(C=C) cm-1. 1H-NMR (DMSO-d6): δ1.9(s, 3H, CH3), 5.5(s, 2H, =CH), 7.1-7.73(m, 14H, Ar-H) ppm. MS (m/z, %): 433(M+,26.5), 419(23.5), 391(25.8), 314(25.5), 225(24.3), 198(62.5), 174(50.1), 159(100), 145(65.5), 105(63.5), 77(65.3), 65(64.6), 50(18.3). Anal.Calcd. for C27H19N3O3: C, 74.81; H, 4.42; N, 9.69 Found: C, 74.59; H, 4.28; N, 9.38

Compound 7b as yellow crystals yield 65 %, m.p: 254 oC; IR (KBr): 1710-1676(C=O), 1628(C=N), 1631, 1598(C=C) cm-1. 1H-NMR (DMSO-d6): δ1.7(s, 3H,CH3), 2.41(s, 6H, CH3), δ 6.3(s, 2H, =CH), 7.1-7.87(m, 12H, Ar-H) ppm. MS (m/z, %): 461(M+,28.5), 447(38.9), 419(35.5), 404(45.9), 328(55.5), 316(60.6), 301(54.2), 225(58.5), 213(57.5), 196(46.2), 171(58.2), 145(100), 105(55.3), 77(43.3), 63(44.5), 50(22.5). Anal.Calcd. for C29H23N3O3: C, 75.47; H, 5.02; N, 9.10 Found: C, 75.34; H, 4.87; N, 9.07

Compound 7c as yellow crystals yield 55 %, m.p: 293 oC; IR (KBr): 1716-1693(C=O), 1634(C=N), 1655, 1572(C=C), 1228, 1123(C-O) cm-1. 1H-NMR (DMSO-d6): δ1.9(s, 3H, COCH3), 4.13 (s, 6H, OCH3), 6.1(s, 2H, =CH), 7.1-7.88(m, 12H, Ar-H) ppm. MS (m/z, %): 493(M+,30.2), 479(50.8), 451(30.5), 436(41.5), 420(51.2), 344(36.2), 332(44.5), 317(51.4), 302(59.8), 225(65.6), 214(52.7), 196(72.2), 171(55.2), 145(100), 105(41.3), 77(45.3), 63(53.5), 50(25.5). Anal.Calcd. for C29H23N3O5: C, 70.58; H, 4.70; N, 8.51 Found: C, 70.37; H, 4.55; N, 8.42

4- Antimicrobial activity

In vitro antibacterial screening

Applying the agar plate diffusion technique[37,38] all of the compounds were screened in Vitro for antibacterial activity against Bacillus subtilis, Streptococcus Penumonia, Staphylococcus Aureas, E.Coli and Pseudomonas Solanarium. The compounds were tested at (10mg, 50mg and 100mg) concentrations and the activity was determined by measuring the zone of inhibition. The screening results given in table (1) where, the activities of compounds were compared with Streptomycin as antibacterial standard. The compound (7c) showed maximum antibacterial potency. Compounds 4b, 4c, 5b, 5c, 6b, 6c, 7b and 7c have more activity, Compounds 4a, 5a, 6a and 7a, have nearly activity and compounds 1, 2 and 3 have less activity compared with Streptomycin against all bacterial organisms.

In vitro antifungal screening

The compounds were evaluated for their in vitro antifungal activity against Aspergillus Nigaer, Candia albicans, and Penicillium Sp. using an agar dilution method[39]. The screening results given in table (2) where, the activities of compounds were compared with Ketoconazole as antifungal standard. The compound (7c) showed maximum antifungal potency. Compounds 4b, 4c, 5b, 5c, 6b, 6c, 7b and 7c have more activity, Compounds 4a, 5a, 6a and 7a, have nearly activity and compounds 1, 2 and 3 have less activity compared with Ketoconazole against all Fungal organisms.

Table(1) Antibacterial Activity

Comp.	Gram Positive Bacteria									Gram Negative Bacteria					
	Bacillus Subtilis			Streptococcus Penumonia			Staphylococcus Aureas			E.Coli			Pseudomonas Sp.		
	10mg	50mg	100mg	10mg	50mg	100mg	10mg	50mg	100mg	10mg	50mg	100mg	10mg	50mg	100mg
1		1	5		3	6			5			3			1
2		6	9		5	10			9		1	8		1	8
3	1	7	11	1	7	12	2	6	13	1	5	10	3	8	11
4a	4	8	17	3	10	15	5	15	19	7	15	21	7	13	26
4b	9	16	28	6	23	28	9	26	29	15	22	29	12	22	32
4c	15	21	34	11	26	31	14	29	35	14	25	32	15	21	35
5a	5	8	19	4	12	19	5	18	21	9	18	22	7	12	27
5b	10	19	26	10	24	28	12	29	33	15	26	30	11	28	38
5c	12	13	30	12	29	29	17	32	38	16	29	33	13	25	41
6a	4	7	18	3	11	18	4	15	18	7	17	21	6	11	26
6b	11	15	25	14	28	31	16	29	35	15	28	32	12	25	42
6c	12	20	36	15	24	33	11	33	37	19	25	33	15	28	35
7a	3	8	19	2	12	18	6	18	22	8	18	20	8	11	26
7b	12	14	28	7	26	20	15	28	38	17	23	31	11	26	39
7c	20	29	41	19	28	38	17	35	42	19	25	37	16	30	45
Streptomycin	3	7	18	2	11	17	4	16	20	8	17	22	6	12	27

Table (2) Antifungal Activity

Comp.									
	Aspergillus Nigaer			Penicillium Sp.			Candia albicans		
	10mg	50mg	100mg	10mg	50mg	100mg	10mg	50mg	100mg
1					1	3			3
2		1	5		7	9		1	9
3	1	7	11	1	12	15	2	9	11

4a	5	12	17	5	11	19	5	14	20
4b	12	19	25	14	25	28	15	28	34
4c	13	20	33	12	28	30	18	32	36
5a	6	13	21	8	13	21	5	16	22
5b	16	20	28	11	24	28	15	28	30
5c	18	22	30	13	30	32	19	30	41
6a	6	14	20	6	11	19	5	14	20
6b	11	19	28	20	28	28	20	25	37
6c	17	23	30	15	29	37	19	28	43
7a	6	14	21	8	13	22	7	16	22
7b	15	23	30	12	27	33	13	28	38
7c	18	29	37	15	31	41	22	35	45
Ketoconazole	8	13	18	7	17	21	6	17	21

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