Synthesis and antibacterial activity of novel quinoxalinone derivatives

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The reaction of 3-hydrazinocarbonylmethylquinoxalin-2(1H)-one with phthalic anhydride, certain aromatic aldehydes, isocyanates and phenyl isothiocyanate furnished corresponding imide, Schiff's, semi- and thiosemicabazide derivatives. Treatment of 3-[2-(phenylcarbamoyl)hydrazinocarbonylmethyl]quinoxalin-2(1H)-one with chloroacetic acid, sulfuric acid and sodium hydroxide yielded cyclised derivatives. Moreover, 3-[2-bromobenzylidenehydrazinocarbonyl-methyl]quinoxalin-2(1H)-one was cyclised to oxadiazolinyl derivative using acetic anhydride. Furthermore, 3-[5-sulfanylidene-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl]quinoxalin-2(1H)-one was employed as a precursor in the synthesis of some novel 2(1H)-quinoxalinones. Some of the newly prepared compounds were evaluated for *in vitro* antibacterial activity using ofloxacin as the reference standard.

Keywords: quinoxalinones, synthesis, antibacterial activity

Among the various classes of nitrogen containing heterocyclic compounds, quinoxaline derivatives have been shown to display a diverse array of pharmacological activities, among which are antibacterial,[1] antiviral,[2] antifungal,[3] antiprotozoal,[4] and anti-inflammatory activities.[5]

Moreover, five-membered heterocyclic compounds[6-9] act as highly functionalised scaffolds and are known pharmacophores of a number of biologically active and medicinally useful molecules.

Meanwhile, resistance to antimicrobial agents is now recognised as a major global public health problem. With the emergence of new bacterial strains to many currently available treatments, there is increasing interest in the discovery of novel antibacterial agents.[10]

Hence, it was considered worthwhile to prepare molecules having quinoxaline and oxadiazole/thiadiazole/triazole/thiazolidinone rings in an attempt to find an effective antibacterial agent.

The starting material, 3-hydrazinocarbonylmethyl-quinoxalin-2(1H)-one (**1**), was prepared via hydrazinolysis of 3-ethoxycarbonylmethylquinoxalin-2(1H)-one adopting a reported procedure.[11] Treatment of **1** with certain aromatic aldehydes gave 3-[3-arylidenehydrazinocarbonylmethyl] quinoxalin-2(1H)-ones **2a,b**. Cyclisation of compound **2a** with acetic anhydride yielded the corresponding 3-[(4-acetyl-5-(2-bromophenyl)-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl] quinoxalin-2(1H)-one (**3**) and was substantiated by spectral evidence. Thus, the ^{1}H NMR spectra revealed the absence of the two signals corresponding to azomethine (CH=N) and (CO–NH) protons of its precursors. Moreover, the appearance of a signal at δ 2.35 ppm corresponding to an acetyl group, in addition to a singlet signal at δ 7.20 ppm corresponding to the proton at position 2- of the oxadiazoline ring, were indicative of successful formation of the title compound **3**.

In addition, compound **1** was allowed to react with phthalic anhydride to afford 3-(N-imidocarbamoylmethyl)quinoxalin-2(1H)-one **4**.

Conversely, heating the acid hydrazide **1** with carbon disulfide in alcoholic potassium hydroxide gave 3-[5-sulfanylidene-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl]quinoxalin-2(1H)-one (**5**) as reported.[12] Attempted alkylation of **5** with benzyl chloride furnished 3-[(5-benzylsulfanyl-1,3,4-oxadiazol-2-yl)methyl]quinoxalin-2(1H)-one (**6**). Its ^{1}H NMR spectra showed the appearance of a singlet at δ 4.53 ppm integrating for two protons of SCH_2. Also, its mass spectrum showed a molecular ion peak at *m/z* 350. Meanwhile, alkylation of **5** with chloroacetic acid yielded 3-[(5-carboxymethylsulfanyl-1,3,4-oxadiazol-2-yl)methyl]quinoxalin-2(1H)-one (**7**). Oxidation of compound **7** with hydrogen peroxide in acetic acid afforded 3-[(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl]quinoxalin-2(1H)-one (**8**). Furthermore, compounds **9a,b** were prepared by the reaction of **5**[12] with formaldehyde and diethylamine or morpholine under Mannich conditions (Scheme 1).

When the acid hydrazide **1** was refluxed with phenylisocyanate in absolute ethanol for 6 hours 3-[2-(phenylcarbamoyl)hydrazinecarbonylmethyl]quinoxalin-2(1H)-one (**10**) was obtained. On the other hand, refluxing compound **1** with certain isocyanates for 24 hours yielded triazole derivatives **11a,b**. Cyclisation of the thiosemicarbazide derivative **12**[13] was achieved by the action of chloroacetic acid and sulfuric acid to yield 1,3-thiazolidin-4-one **13**, and 1,3,4-thiadiazole **14** derivatives respectively. Finally, the reaction of the reported cyclised compound **15**[13] with certain alkyl halides afforded the desired thioethers **16a,b** (Scheme 2).

Experimental

Melting points were obtained on a Griffin apparatus and are uncorrected. Microanalyses for C,H and N were carried out at the Microanalytical Centre, Cairo University. IR spectra were recorded on a Shimadzu 435 spectrometer, using KBr discs. ^{1}H NMR spectra were performed on a Joel NMR FXQ-200 MHz spectrometer, using TMS as the internal standard.

Mass spectra were recorded on a GCMP-QP1000 EX Mass spectrometer. Progress of the reactions were monitored by TLC using precoated aluminium sheet silica gel MERCK 60F 254 and was visualised by UV lamp.

General procedure for the synthesis of compounds **2a,b**

To a solution of compound **1** (2.18 g, 0.01 mol) in hot ethanol (20 mL), the appropriate aromatic aldehyde (0.01 mol) was added. The mixture was heated under reflux for 3 h, then allowed to cool to room temperature. The solid obtained was filtered, washed with ethanol and crystallised from dimethylformamide.

3-[2-Bromobenzylidenehydrazinocarbonylmethyl]quinoxalin-2(1H)-one (**2a**): Yield: 98%; m.p. 295–297 °C; IR: 3447–3196 (NH), 1678, 1630 (2C=O), 1603 (C=N); ^{1}H NMR (DMSO-d_6): 4.12 (s, 2H, CH_2), 5.73 (s, 1H, vinylic =CH), 6.50–7.31 (m, 8H, 8 ArH), 7.95, 8.04 (2 s, 1H, syn, anti isomers of azomethine N=CH), 9.57, 9.64 (2 s, 1H, CONH, D_2O exchangeable), 11.10 (s, 1H, N4H, D_2O exchangeable), 11.66, 12.06 (2 s, 1H, N_1H, OH, tautomers of quinoxaline, D_2O exchangeable), MS: *m/z* 386 (M + 2, 4.95%), 384 (M+, 4.97%). Anal. Calcd for $C_{17}H_{13}BrN_4O_2$: C, 53.00; H, 3.40; N, 14.54. Found: C, 53.00; H, 3.20; N, 14.50%.

3-[4-Hydroxybenzylidenehydrazinocarbonylmethyl]quinoxalin-2(1H)-one (**2b**): Yield: 69%; m.p. 279–281 °C; IR: 3447–3200 (NH), 1678, 1640 (2C=O), 1610 (C=N); ^{1}H NMR (DMSO-d_6): 4.11 (s, 2H, CH_2), 5.78 (s, 1H, vinylic =CH), 6.50–7.53 (m, 8H, 8ArH), 7.87, 7.96 (2 s, 1H, syn, anti isomers of azomethine N=CH), 9.88 (s, 1H, CONH, D_2O exchangeable), 11.02 (s, 1H, OH, D_2O exchangeable), 11.28 (s, 1H, N_4H, D_2O exchangeable), 11.67, 12.07 (2 s, 1H, N1H, OH, tautomers of quinoxaline, D_2O exchangeable). Anal. Calcd for

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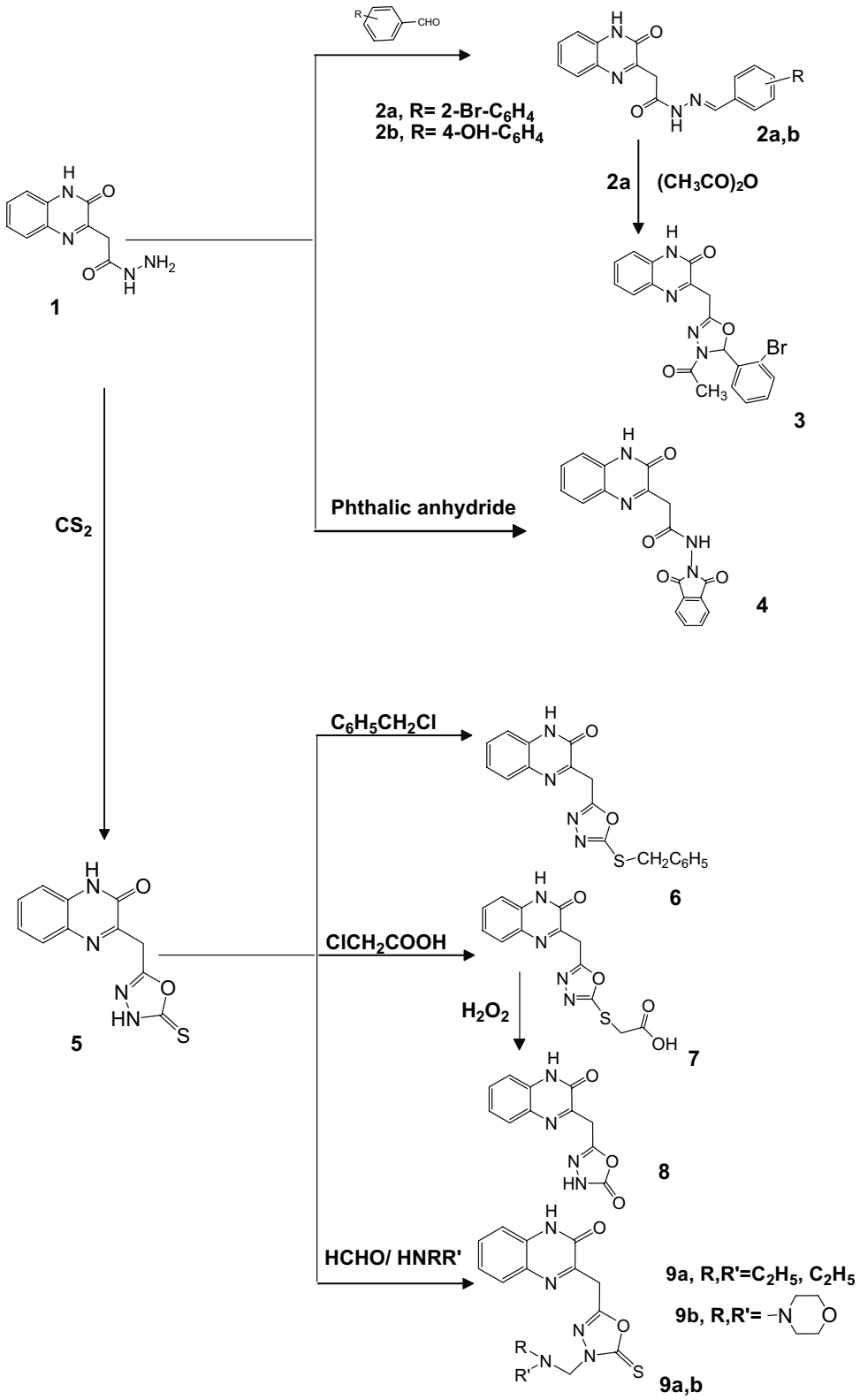


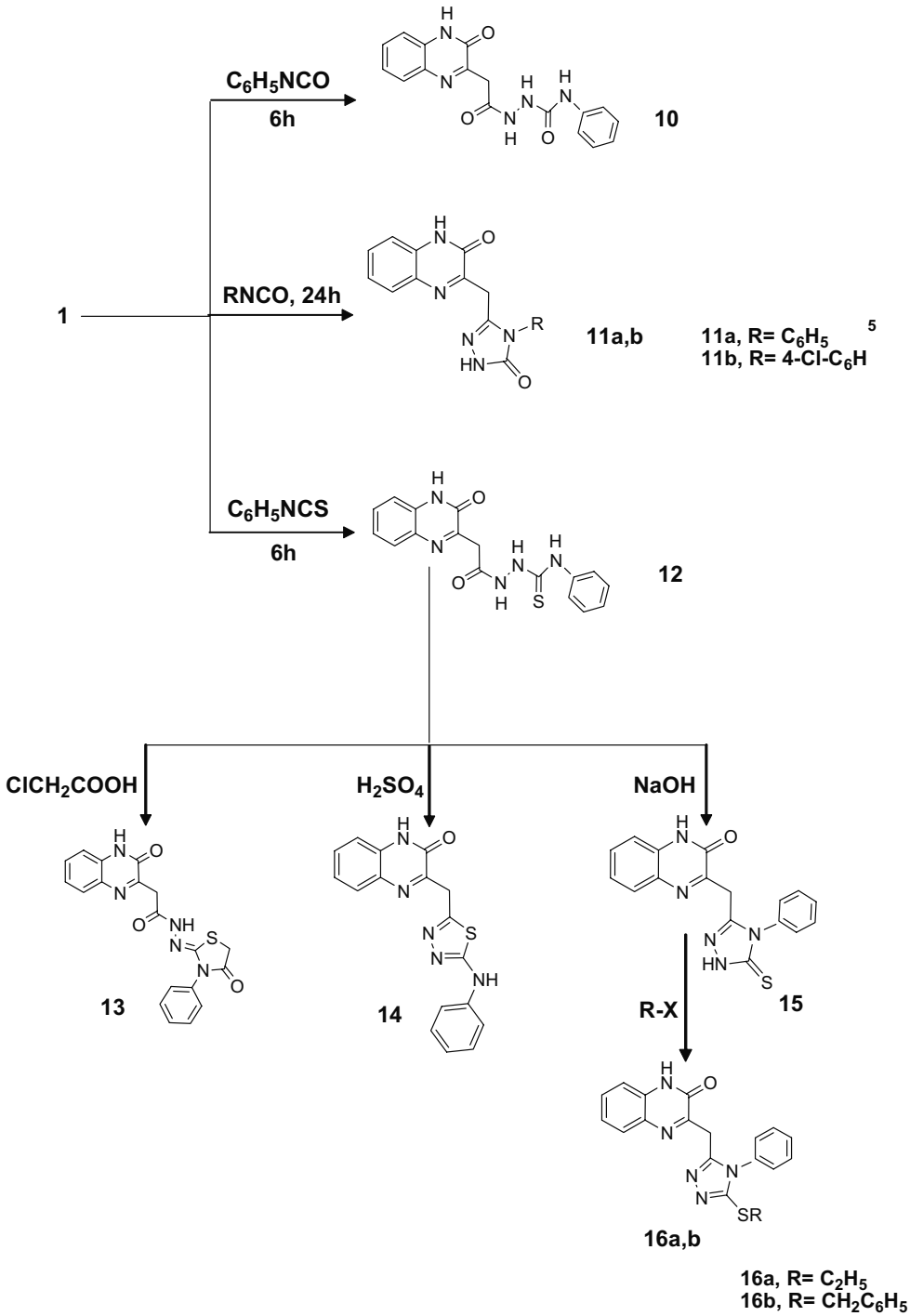
Scheme 1

$C_{17}H_{14}N_4O_3$: C, 63.35; H, 4.37; N, 17.38. Found: C, 63.55; H, 4.31; N, 17.35%.

3-[(4-Acetyl-5-(2-bromophenyl)-4,5-dihydro-1,3,4-oxadiazol-2-yl) methyl] quinoxalin-2(1H)-one (**3**): A mixture of compound **2a** (3.84 g, 0.01 mole) and acetic anhydride (6 mL) was heated under reflux for 2 h. The excess acetic anhydride was distilled off under reduced pressure, the obtained residue was triturated with petroleum ether (25 mL). The separated solid was filtered and crystallised from benzene/petroleum ether (40–60°).

Yield: 72%; m.p. 223–225 °C; IR: 3463 (NH), 1733, 1669 (2C=O), 1625 (C=N); ^{1}H NMR (DMSO-d_6): 2.35 (s, 3H, $COCH_3$), 3.77 (s, 2H, CH_2), 5.73 (s, 1H, vinylic =CH), 6.94–7.72 (m, 9H, 8ArH and one oxadiazoline H); 10.42 (s,1H, N_4H, D_2O exchangeable) and 11.56, 12.31 (2 s, 1H, N_1H, OH, tautomers of quinoxaline, D_2O exchangeable); MS: *m/z* 428 (M + 2, 2.15%), 427 (M + 1, 0.59%), 426 (M+, 2.18%). Anal. Calcd for $C_{19}H_{15}BrN_4O_3$: C, 53.41; H, 3.53; N, 13.11. Found: C, 53.64; H, 3.62; N, 13.14%.

3-[(1,3-Dioxo-2,3-dihydro-1H-isoindo-2-yl)aminocarbonyl-methyl] quinoxalin-2(1H)-one (**4**): To a solution of acid hydrazide **1** (1.09 g, 0.005 mol) in glacial acetic acid (10 mL), the appropriate



Scheme 2

acid anhydride (0.005 mol) was added and the mixture was heated under reflux for 4 h. After cooling, the reaction mixture was poured onto crushed ice (30 g). The solid separated was filtered, washed with water and crystallised from glacial acetic acid. Yield: 35%; m.p. 311–313 °C; IR: 3445–3130 (NH), 1720, 1680, 1640 (3C=O), 1601 (C=N); ^{1}H NMR (DMSO-d_6): 3.93 (s, 2H, CH_2); 5.83 (s, 1H, vinylic =CH); 6.96–7.96 (m, 8H, ArH); 10.62, 10.91 (2 s, 1H, NH, OH tautomers of –CONH, D_2O exchangeable); 11.41 (s, 1H, N_4H, D_2O exchangeable) and 11.69, 12.46 (2 s, 1H, N_1H, OH, tautomers of quinoxaline, D_2O exchangeable). Anal. Calcd for $C_{18}H_{12}N_4O_4$: C, 62.06; H, 3.47; N, 16.08. Found: C, 61.89; H, 3.37; N, 15.94%.

3-[(5-Benzylsulfanyl-1,3,4-oxadiazol-2-yl)methyl]quinoxalin-2(1H)-one (**6**): An equimolar amount of **5** (2.60 g, 0.01 mol) and benzyl chloride (1.26 g, 0.01 mol) in ethanolic potassium hydroxide (0.08 g KOH in 20 mL ethanol) was heated under reflux for 3 h. On cooling, the reaction mixture was poured onto crushed ice; the solid separated was filtered and crystallised from dioxane. Yield: 67%; m.p. 277–279 °C; IR: 3423 (NH), 1682 (C=O), 1637 (C=N); ^{1}H NMR (DMSO-d_6): 3.57 (s, 2H, CH_2), 4.53 (s, 2H, SCH_2), 6.05 (s, 1H, vinylic =CH), 7.04–7.49 (m, 9H, ArH), 10.38 (s, 1H, N_4H, D_2O exchangeable), 11.72 (s, 1H, N_1H, D_2O exchangeable); MS: *m/z* 351 (M + 1, 12.30%), 350 (M+, 26.10%). Anal. Calcd for $C_{18}H_{14}N_4O_2S$: C, 61.70; H, 4.02; N, 15.98. Found: C, 61.83; H, 4.14; N, 16.01%.

3-[(5-Carboxymethylsulfanyl-1,3,4-oxadiazol-2-yl)methyl] quinoxalin-2(1H)-one (**7**): To a solution of **5** (2.60 g, 0.01 mole) in ethanolic sodium hydroxide (0.4 g NaOH, 80 mL ethanol), monochloroacetic acid (0.94 g, 0.01 mole) was added. The reaction mixture was heated under reflux for 2 h, and diluted with water, then acidified with acetic acid and crystallised from dioxane. Yield: 66%; m.p. 242–244 °C; IR: 3420–2714 (OH, NH), 1753, 1665 (2C=O), 1611 (C=N); ^{1}H NMR (DMSO-d_6): 4.13 (s, 2H, CH_2), 4.31 (s, 2H, SCH_2), 5.88 (s, 1H, vinylic =CH), 7.00–7.79 (m, 4H, ArH), 11.65 (s, 1H, N_4H, D_2O exchangeable), 12.23, 12.57 (2 s, 1H, N1H, OH, tautomers of quinoxaline, D_2O exchangeable), 13.09 (s, 1H, COOH,

D_2O exchangeable); MS: *m/z* 320 (M + 2, 7.04%), 319 (M + 1, 10.23%), 318 (M+, 69.69%). Anal. Calcd for $C_{13}H_{10}N_4O_4S$: C, 49.05; H, 3.16; N, 17.60. Found: C, 48.91; H, 3.27; N, 17.64%.

3-[(5-Oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl]quinoxalin-2(1H)-one (**8**): To a solution of **7** (3.18 g, 0.01 mol) in glacial acetic acid (10 mL), H2O2 (5 mL) was added. The solution was left overnight with stirring, the solvent was removed under vacuum and the solid was crystallised from chloroform. Yield: 52%; m.p. 237–239 °C; IR: 3397–3107 (NH); 1709, 1677 (2C=O), 1604 (C=N); ^{1}H NMR (DMSO-d_6): 4.17 (s, 2H, CH_2), 6.02 (s, 1H, vinylic =CH), 6.96–7.72 (m, 4H, ArH), 10.36 (s, 1H, NH, D_2O exchangeable), 11.70 (s, 1H, N_4H, D_2O exchangeable), 12.56 (s, 1H, N_1H, D_2O exchangeable); MS: *m/z* 245 (M + 1, 3.87%), 244 (M+, 14.78%). Anal. Calcd for $C_{11}H_8N_4O_3$: C, 54.10; H, 3.30; N, 22.94. Found: C, 54.07; H, 3.36; N, 23.11%.

General procedure for the synthesis of compounds **9a,b**

To a solution of 5 (2.60 g, 0.01 mol) in absolute ethanol (200 mL), formaldehyde (10 mL, 40%) was added. The mixture was heated to give a clear solution, then the corresponding secondary amine (0.01 mol) was added and the reaction mixture was stirred at room temperature. The solid separated was filtered and crystallised from chloroform.

3-[(4-(Diethylamino)methyl)-5-sulfanylidene-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl]quinoxalin-2(1H)-one (**9a**): Yield: 53%; m.p. 288–290 °C; IR: 3449 (NH), 1671(C=O), 1611(C=N), 1224 (C=S); ^{1}H NMR (DMSO-d_6): 1.07–1.12 (t, 6H, *J* = 7.2 Hz, $N(CH_2CH_3)_2$); 3.89–3.91 (q, 4H, *J* = 7.2 Hz, $N(CH_2CH_3)_2$); 4.30 (s, 2H, CH_2); 4.41 (s, 2H, NCH_2N); 6.01 (s, 1H, vinylic =CH), 7.02–7.33 (m, 4H, ArH); 11.21 (s, 1H, N_4H, D2O exchangeable), 11.47 (s, 1H, N_1H, D_2O exchangeable); MS: *m/z* 347 (M + 2, 12.03%), 346 (M + 1, 30.96%), 345 (M+, 9.64%). Anal. Calcd for $C_{16}H_{19}N_5O_2S$: C, 55.63; H, 5.54; N, 20.27. Found: C, 55.49; H, 5.30; N, 20.51%.

3-[(4-(Morpholin-4-yl)methyl)-5-sulfanylidene-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl]quinoxalin-2(1H)-one (**9b**): Yield: 37%; m.p. 249–251 °C; IR: 3446 (NH), 1669 (C=O), 1611 (C=N), 1225 (C=S); ^{1}H NMR (DMSO-d_6): 3.08–3.11 (m, 4H, CH_2OCH_2), 3.54–3.77 (m, 4H, CH_2NCH_2), 4.32 (s, 2H, CH_2), 4.96 (s, 2H, NCH_2N), 5.83 (s, 1H, vinylic =CH), 7.01–7.77 (m, 4H, ArH), 10.25 (s, 1H, N_4H, D_2O exchangeable),11.41 (s, 1H, N_1H, D_2O exchangeable). Anal. Calcd for $C_{16}H_{17}N_5O_3S$: C, 53.47; H, 4.76; N, 19.48. Found: C, 53.56; H, 4.73; N, 19.45%.

3-[2-(Phenylcarbamoyl)hydrazinecarbonylmethyl]quinoxalin-2(1H)-one (**10**): Compound **1** (6.54 g, 0.03 mol) was heated under reflux with phenyl isocyanate (0.03 mol) in absolute ethanol (60 mL) for 6 h. On cooling, the solid separated was filtered and crystallised from acetic acid/water. Yield: 90%; m.p. 260–262 °C; IR: 3425–3270 (NH), 1681, 1637 (2C=O), 1613 (C=N); ^{1}H NMR (DMSO-d_6): 3.77 (s, 2H, CH_2), 5.72 (s, 1H, vinylic =CH), 6.97–7.72 (m, 9H, ArH), 9.40, 9.84, 10.45(3 s, 3H, 3NH, D_2O exchangeable), 11.56 (s, 1H, N_4H, D_2O exchangeable),12.63 (s, 1H, N1H, D_2O exchangeable); MS: *m/z* 337 (M+, 1.63%). Anal. Calcd for $C_{17}H_{15}N_5O_3$: C, 60.52; H, 4.48; N, 20.76. Found: C, 60.52; H, 4.29; N, 20.55%.

General procedure for the synthesis of compounds **11a,b**

A mixture of compound **1** (2.18 g, 0.01 mol) and the appropriate isocyanate derivative (0.012 mol) was heated under reflux in absolute ethanol (50 mL) for 24 h. The formed precipitate was filtered and crystallised from ethanol.

3-[(4-Phenyl-5-oxo-1,5-dihydro-1,2,4-triazol-3-yl)methyl]quinoxalin-2(1H)-one (**11a**): Yield: 95%; m.p. 261–263 °C; IR: 3448 (NH), 1772, 1684 (2C=O), 1609 (C=N); ^{1}H NMR (DMSO-d_6): 3.80 (s, 2H, CH2), 5.74 (s, 1H, vinylic =CH), 7.00–7.75 (m, 9H, ArH), 9.43, 9.60 (2 s, 1H, NH, OH, D_2O exchangeable), 10.48 (s, 1H, N_4H, D_2O exchangeable), 11.59, 12.66 (2 s, 1H, N_1H, OH, tautomers of quinoxaline, D_2O exchangeable). Anal. Calcd for $C_{17}H_{13}N_5O_2$: C, 63.94; H, 4.10; N, 21.93. Found: C, 63.75; H, 4.24; N, 21.74%.

3-[(4-(4-Chlorophenyl)-5-oxo-1,5-dihydro-1,2,4-triazol-3-yl)methyl]quinoxalin-2(1H)-one (**11b**): Yield: 97%; m.p. 233–235 °C; IR: 3425 (NH), 1773, 1683 (2C=O), 1613 (C=N); ^{1}H NMR (DMSO-d_6): 3.71 (s, 2H, CH_2), 5.64 (s, 1H, vinylic =CH); 6.98–7.81(m, 8H, ArH), 9.19 (s, 1H, NH, D_2O exchangeable); 11.46 (s, 1H, N_4H, D_2O exchangeable),11.68, 12.16(s, brs, 1H, N_1H, OH, tautomers of quinoxaline, D_2O exchangeable); MS: *m/z* 353 (M+, 0.51%). Anal. Calcd for $C_{17}H_{12}ClN_5O_2$: C, 57.71; H, 3.41; N, 19.79. Found: C, 57.59; H, 3.60; N, 19.90%.

3-[2-(4-Oxo-3-phenyl-1,3-thiazolidin-2-ylidene)hydrazinecarbonylmethyl]quinoxalin-2(1H)-one (**13**): A mixture of phenylthiosemicarbazide **12** (3.53 g, 0.01 mol) and monochloroacetic acid (0.94 g, 0.01 mol), in absolute ethanol (30 mL) was stirred at room temperature for 1 h., anhydrous sodium acetate (0.82 g, 0.01 mol) was then added and the reaction mixture was heated under reflux for 10 h. The solid separated was filtered and crystallised from ethanol. Yield: 63%; m.p. 230–232 °C; IR: 3448–3141 (NH), 1713, 1624 (2C=O), 1603 (C=N); ^{1}H NMR (DMSO-d_6): 4.16 (s, 2H, CH_2), 4.42 (s, 2H, SCH_2), 6.03 (s, 1H, vinylic =CH), 7.06–7.71 (m, 9H, ArH), 10.37 (s, 1H, CONH, D_2O exchangeable), 11.70 (s, 1H, N_4H, D_2O exchangeable), 11.90, 12.55 (2 s, 1H, N_1H, OH, tautomers of quinoxaline, D_2O exchangeable), MS: *m/z* 395 (M + 2, 3.56%), 393 (M+, 3.56%). Anal. Calcd for $C_{19}H_{15}N_5O_3S$: C, 58.00; H, 3.84; N, 17.80. Found: C, 58.02; H, 4.01; N, 18.01%.

3-[(5-Phenylamino-1,3,4-thiadiazol-2-yl)methyl]quinoxalin-2-(1H)-one (**14**): A solution of phenylthiosemicarbazide 12 (3.53 g, 0.01 mol) in conc. sulfuric acid (10 mL) was kept at room temperature for 4 h, while stirring at intervals. Thereafter, it was poured onto crushed ice, and neutralised with 10% NaOH. The separated solid was filtered and crystallised from ethanol. Yield: 70%; m.p. 282–284 °C; IR: 3447–3283 (NH), 1675 (C=O), 1624 (C=N); ^{1}H NMR (DMSO-d_6): 3.82 (s, 2H, CH_2), 5.77 (s, 1H, vinylic =CH), 7.01–7.76 (m, 9H, ArH), 10.48 (s, 1H, NH, D_2O exchangeable), 11.59 (s, 1H, N_4H, D_2O exchangeable),12.66 (s, 1H, N_1H, D_2O exchangeable); MS: *m/z* 337(M + 2, 3.85%), 336(M + 1, 5.84%), 335(M+, 24.19%). Anal. Calcd for $C_{17}H_{13}N_5OS$: C, 60.88; H, 3.90; N, 20.88. Found: C, 61.01; H, 4.00; N, 20.69%.

General procedure for the synthesis of compounds **16a,b**

A mixture of equimolar amount of compound **15** (1.675 g, 0.005 mol) and the appropriate alkyl or aryl halide (0.005 mol) in alcoholic potassium hydroxide (0.28 g KOH in 20 mL ethanol) was heated under reflux for 3 h. The reaction mixture was cooled, poured onto crushed ice, the solid separated was filtered and crystallised from acetone.

3-[(5-Ethylsulfanyl-4-phenyl-1,5-dihydro-1,2,4-triazol-3-yl)-methyl]-quinoxalin-2(1H)-one (**16a**)

Yield: 60%; m.p. 266–268 °C; IR: 3173 (NH), 1677(C=O), 1635 (C=N); ^{1}H NMR (DMSO-d6): 1.29–1.36 (t, 3H, *J* = 7.2 Hz, CH_2CH_3), 3.09–3.16 (q, 2H, *J* = 7.2 Hz, CH_2CH_3), 3.57 (s, 2H, CH_2), 5.57 (s, 1H, vinyl =CH), 6.94–7.66 (m, 9H, ArH), 11.12 (s, 1H, N_4H, D_2O exchangeable), 11.49 (s, 1H, N_1H, D_2O exchangeable). Anal. Calcd for $C_{19}H_{17}N_5OS$: C, 62.79; H, 4.71; N, 19.26. Found: C, 62.61; H, 4.68; N, 19.18%.

3-[5-(Benzylsulfanyl-4-phenyl-1,5-dihydro-1,2,4-triazol-3-yl)methyl]-quinoxalin-2(1H)-one (**16b**): Yield: 49%; m.p. 247–249 °C; IR: 3168 (NH), 1678 (C=O), 1631 (C=N); ^{1}H NMR (DMSO-d_6): 3.56 (s, 2H, SCH_2), 5.55 (s, 1H, vinylic =CH), 6.92–7.63 (m, 14H, ArH), 11.07 (s, 1H, N_4H, D_2O exchangeable), 11.45 (s, 1H, N_1H, D_2O exchangeable); MS: *m/z* 427 (M + 2, 1.20%), 426 (M + 1, 4.92%), 425 (M+, 15.20%). Anal. Calcd for $C_{24}H_{19}N_5OS$: C, 67.74; H, 4.50; N, 16.45. Found: C, 67.69; H, 4.50; N, 16.61%.

Evaluation of anti-inflammatory activity

The minimal inhibitory concentrations (MIC) of 12 compounds against different bacterial isolates(*Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Bacillus subtilis*) were determined by the agar-dilution method according to the National Committee for Clinical Laboratory Standards.[14]

Minimal inhibitory concentration (MIC) measurement

Mueller Hinton agar plates containing two- fold serial dilution of the respective compounds were surface inoculated with about 10^4 CFU of the test organism per spot and incubated at 37 °C for 18 hours. The plates were then observed for the presence or absence of microbial growth. The lowest concentration showing no growth was taken as the minimal inhibitory concentration (MIC).

Results of antimicrobial activity

The results of antimicrobial testing revealed that all compounds showed weak antibacterial activity. On the other hand, compounds **14** and **16b** were the most active against *Pseudomonas aeruginosa*.

The authors thank Dr Amal E. Saafan, Department of Microbiology and Immunology, Faculty of Pharmacy, Beni-Swief University for help in performing the anti-microbial testing.

Received 29 June 2009; accepted 17 August 2009
Paper 09/0659 doi: 10.3184/030823409X12510409044803
Published online: 8 September 2009

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