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RESEARCH ARTICLE

Synthesis and antimicrobial studies of *s*-triazine based heterocycles

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Abstract

In an effort to discover new candidates with improved antimicrobial activities we report here the synthesis and *in vitro* biological evalution of various series of 2-(*N*-methylamino)-4-(*N*,*N*-dimethylamino)-6-(arylthioureido)-*s*-triazine **(5a–j)** and (*N*-methylamino)-4-(*N*,*N*-dimethylamino)-6-(arylureido)-*s*-triazine **(6a–j)**. All the synthesized compounds were screened *in vitro* for their antibacterial activity against two different gram-positive bacteria (*S. aureus*, *B. subtilis*) and two different gram-negative bacteria (*P. aeruginosa*, *E. coli*) using the broth dilution method.

Keywords: *s-triazine; thiourea; urea; antimicrobial activity*

Introduction

Research on new substances possessing antibacterial activity has attracted considerable attention owing to the continuing increase in bacterial resistance. Further, infection caused by various microorganisms poses a serious challenge to the medical community, and the need for an effective therapy has led to the search for novel antimicrobial agents.

In this work, we report the synthesis and biological activity of substituted *s*-triazine derivatives. Substituted *s*-triazine constitutes an important class of compounds having anticancer[1], antitumor[2], antimicrobial[3], antibacterial[4], antimalarial[5], and herbicidal activities[6]. They are also used for the treatment of human immunodeficiency virus (HIV) infection[7]. Thiourea derivatives also exhibit anti-HIV[8], antiviral[9], antibacterial[10], and antifungal[11] activities.

In the design of new compounds, the development of hybrid molecules through the combination of different pharmacophores in one structure may lead to compounds with increased antimicrobial activity. The synthesized compounds were tested against two gram-positive bacteria (*Staphylococcus aureus*, *Bacillus subtilis*) and two gram-negative bacteria (*Pseudomonas aeruginosa*, *Escherichia coli*) using the broth dilution method.

Materials and methods

All chemicals were of analytical grade and used directly. All the reported melting points were taken in open capillaries and were uncorrected. The completion of reaction was checked by thin layer chromatography (TLC) using silica gel-G coated Al-plates (0.5 mm thickness; Merck) and spots were visualized under ultraviolet (UV) radiation. Infrared (IR) spectra were recorded on a Bruker Tensor series Fourier transform (FT-IR) spectrometer using KBr pellets. 1H nuclear magnetic resonance (NMR) spectra were recorded on a 300 MHz Bruker Ultrashield spectrometer using tetramethylsilane (TMS) as internal standard (chemical shift in δ, ppm). C, H, N elemental analysis was carried out on a PerkinElmer 2400.

Chemistry

The triazines described were synthesized starting from cyanuric chloride (2,4,6-trichloro-1,3,5-triazine) (**1**) and different nucleophiles (Scheme 1). The chlorine atoms of cyanuric chloride can be replaced successively by substituted or nonsubstituted amino groups. The nucleophiles can selectively displace the different chlorines by control of the reaction temperature[12]. In general, the first chlorine can

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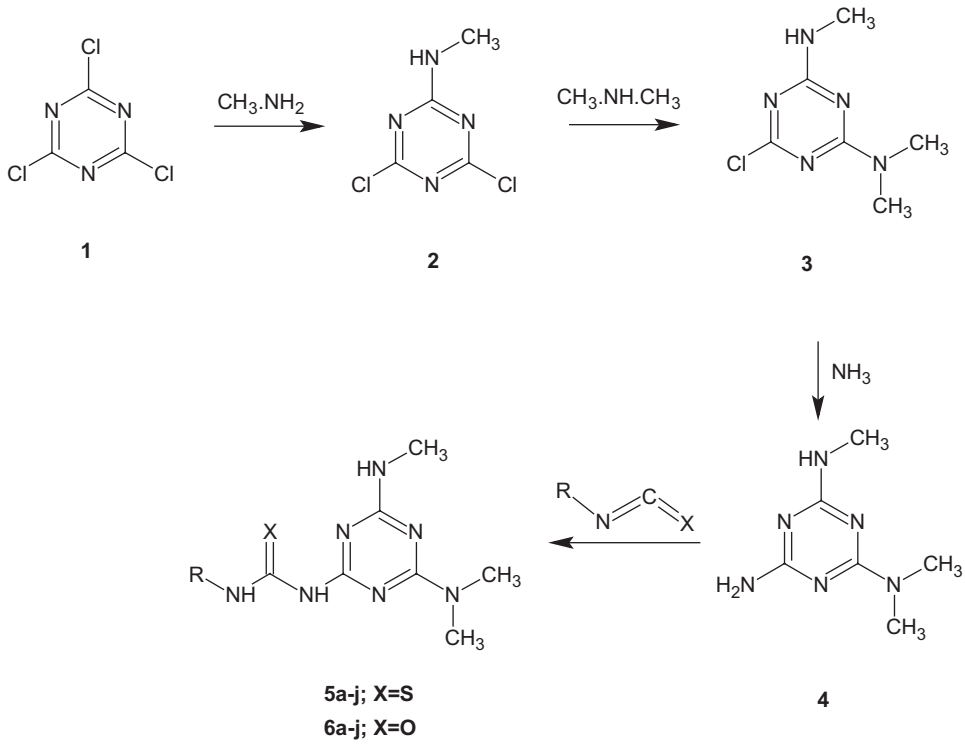

Scheme 1. Synthesis of compounds **5** and **6**.

be displaced when the temperature is maintained at 0°C, the second between 25 and 50°C, and the third substitution at 65–67°C[13]; due to reactivity the temperature can exceed 80°C. Another important factor that has to be considered for the preparation of the different derivatives is the nature of the reactive group and the order of entry of the group. Next, different amino groups were introduced. A less reactive amino was introduced before a more reactive one[14]; hence, in these reactions the least reactive was introduced first, i.e. methylamine, dimethylamine, followed by ammonia.

2-(N-methylamino)-4,6-dichloro-*s*-triazine (2)
To a solution of cyanuric chloride **(1)** (0.05 mol, 9.2 g), in acetone (50 mL) at 0–5°C, a solution of methylamine (0.05 mol, 1.55 g) in acetone was added and the pH was maintained neutral by the addition of 10% $NaHCO_3$. The reaction mixture was stirred for 4 h at 0–5°C. The progress of the reaction was monitored by TLC using acetone/toluene (9:1) as eluent. After completion of the reaction the resultant mixture was poured on crushed ice. The product was filtered, washed with water, and crystallized from ethanol to give **(2)**: M.P. 160°C, yield 85% (found: N, 31.21%, $C_4H_4N_4Cl_2$, required N, 31.30%).

2-(N-methylamino)-4-(N,N-dimethylamino)-6-chloro-*s*-triazine (3)
To a solution of **(2)** (0.05 mol, 9.0 g) in acetone (50 mL), a solution of dimethylamine (0.05 mol, 2.3 g) in acetone was added and stirred at 40–45°C. The pH was maintained neutral by the addition of 10% $NaHCO_3$. The reaction mixture was stirred for 6 h at 25–35°C. The progress of the reaction was monitored by TLC using acetone/toluene (9:1) as eluent. After completion of the reaction, the resultant mixture was poured on crushed ice. The product was filtered, washed with water, and crystallized from ethanol to give solid needles **(3)**: M.P. 202°C, yield 80% (found: N, 37.28%, $C_6H_{10}N_5Cl$, required N, 37.33%).

2-(N-methylamino)-4-(N,N-dimethylamino)-6-(amino)-*s*-triazine (4)
A mixture of **(3)** (0.005 mol) and ammonia (0.005 mol) in dioxane (50 mL) was refluxed in a water bath at 80–90°C for 6 h. The progress of the reaction was monitored by TLC using acetone/toluene (9:1) as eluent. After completion of the reaction, the resultant mixture was poured on crushed ice. The product was filtered, washed with water, and crystallized from ethanol to give solid needles **(4)**: M.P. 225°C, yield 70% (found: N, 49.87%, $C_6H_{10}N_5Cl$, required N, 49.96%).

General procedure for 2-(N-methylamino)-4-(N,N-dimethylamino)-6-(arylthioureido)-*s*-triazine (5a–j)
A mixture of **(4)** (0.005 mol) and aryl isothiocynate (0.005 mol) in tetrahydrofuran (THF; 30 mL) was refluxed for 8 h. The progress of the reaction was monitored by TLC using acetone/toluene (9:1) as eluent. After completion of the reaction, the solvent was evaporated by distillation and the resultant solid was crystallized from ethanol.

5a M.P. 180°C, yield 72% (found: C 51.40, H 5.63, N 32.40, $C_{13}H_{17}N_7S$, calc: C 51.47, H 5.65, N 32.32%). IR (KBr) cm^1, 1540 (C=S), 1562 (C=N), 3300 (NH), 1330 (N-CH_3), 2890

(C-H), 3045 (C-H-Ar); ^{1}H NMR (DMSO-d_6, δ) ppm, 2.80 (s, 6H, N-$(CH_3)_2$), 2.50 (s, 3H, N-CH_3), 6.95 (d, 2H, Ar-H), 7.28 (d, 2H, Ar-H), 7.80 (s, 1H, Ar-NH), 9.02 (s, 1H, Ar-NH-CS), 9.20 (s, 1H, -CSNH-).

5b M.P. 182°C, yield 72% (found: C 46.15, H 4.78, N 29.15, $C_{13}H_{17}N_7SCl$, calc: C 46.22, H 4.77, N 29.02%). IR (KBr) cm^1, 1545 (C=S), 1560 (C=N), 3300 (NH), 1325 (N-CH_3), 2885 (C-H), 3055 (C-H-Ar), 798 (C-Cl); ^{1}H NMR (DMSO-d_6, δ) ppm, 2.79 (s, 6H, N-$(CH_3)_2$), 2.56 (s, 3H, N-CH_3), 6.84 (d, 2H, Ar-H), 7.28 (d, 2H, Ar-H), 7.82 (s, 1H, Ar-NH), 9.03 (s, 1H, Ar-NH-CS), 9.17 (s, 1H, -CSNH-).

5c M.P. 176°C, yield 67% (found: C 46.20, H 4.75, N 29.10, $C_{13}H_{17}N_7SCl$, calc: C 46.22, H 4.77, N 29.02%). IR (KBr) cm^1, 1550 (C=S), 1562 (C=N), 3334 (NH), 1328 (N-CH_3), 2884 (C-H), 3058 (C-H-Ar), 790 (C-Cl); ^{1}H NMR (DMSO-d_6, δ) ppm, 2.77 (s, 6H, N-$(CH_3)_2$), 2.50 (s, 3H, N-CH_3), 6.83 (d, 2H, Ar-H), 7.24 (d, 2H, Ar-H), 7.81 (s, 1H, Ar-NH), 9.03 (s, 1H, Ar-NH-CS), 9.14 (s, 1H, -CSNH-).

5d M.P. 184°C, yield 70% (found: C 46.30, H 4.76, N 29.05, $C_{13}H_{17}N_7SCl$, calc: C 46.22, H 4.77, N 29.02%). IR (KBr) cm^1, 1540 (C=S), 1563 (C=N), 3300 (NH), 1330 (N-CH_3), 2883 (C-H), 3056 (C-H-Ar), 800 (C-Cl); ^{1}H NMR (DMSO-d_6, δ) ppm, 2.78 (s, 6H, N-$(CH_3)_2$), 2.48 (s, 3H, N-CH_3), 6.82 (d, 2H, Ar-H), 7.25 (d, 2H, Ar-H), 7.82 (s, 1H, Ar-NH), 9.01 (s, 1H, Ar-NH-CS), 9.15 (s, 1H, -CSNH-).

5e M.P. 175°C, yield 70% (found: C 52.85, H, 6.01, N, 30.95, $C_{14}H_{20}N_7S$, calc: C 52.98, H 6.03, N 30.89%). IR (KBr) cm^1, 1542 (C=S), 1562 (C=N), 3310 (NH), 1332 (N-CH_3), 2880 (C-H), 3054 (C-H-Ar), 1382 (C-CH_3). ^{1}H NMR (DMSO-d_6, δ) ppm, 2.78 (s, 6H, N-$(CH_3)_2$), 2.48 (s, 3H, N-CH_3), 6.82 (d, 2H, Ar-H), 7.25 (d, H, Ar-H), 7.82 (s, 1H, Ar-NH), 9.01 (s, 1H, Ar-NH-CS), 9.15 (s, 1H, -CSNH-).

5f M.P. 172°C, yield 70% (found: C 52.91, H 6.02, N 30.78, $C_{14}H_{20}N_7S$, calc: C 52.98, H 6.03, N 30.89%). IR (KBr) cm^1, 1543 (C=S), 1560 (C=N), 3315 (NH), 1330 (N-CH_3), 2883 (C-H), 3055 (C-H-Ar), 1380 (C-CH_3). ^{1}H NMR (DMSO-d_6, δ) ppm, 2.75 (s, 6H, N-$(CH_3)_2$), 2.44 (s, 3H, N-CH_3), 6.82 (d, 2H, Ar-H), 7.30 (d, 2H, Ar-H), 7.82 (s, 1H, Ar-NH), 2.37 (s, 3H, Ar-CH_3), 9.09 (s, 1H, Ar-NH-CS), 9.24 (s, 1H, -CSNH-).

5g M.P. 189°C, yield 70% (found: C 52.89, H 6.04, N 30.92, $C_{14}H_{20}N_7S$, calc: C 52.98, H 6.03, N, 30.89%). IR (KBr) cm^1, 1545 (C=S), 1562 (C=N), 3330 (NH), 1332 (N-CH_3), 2880 (C-H), 3058 (C-H-Ar), 1382 (C-CH_3). ^{1}H NMR (DMSO-d_6, δ) ppm, 2.76 (s, 6H, N-$(CH_3)_2$), 2.46 (s, 3H, N-CH_3), 6.80 (d, 2H, Ar-H), 7.35 (d, 2H, Ar-H), 7.80 (s, 1H, Ar-NH), 2.38 (s, 3H, Ar-CH_3), 9.07 (s, 1H, Ar-NH-CS), 9.20 (s, 1H -CSNH-).

5h M.P. 185°C, yield 65% (found: C 50.52, H 5.73, N 29.52, $C_{14}H_{20}N_7OS$, calc: C 50.43, H 5.74, N 29.41%). IR (KBr) cm^1, 1540 (C=S), 1565 (C=N), 3335 (NH), 1330 (N-CH_3), 2885 (C-H), 3050 (C-H-Ar), 1380 (C-CH_3), 1225 (C-O-C). ^{1}H NMR (DMSO-d_6, δ) ppm, 2.78 (s, 6H, N-$(CH_3)_2$), 2.48 (s, 3H, N-CH_3), 6.85 (d, 2H, Ar-H), 7.45 (d, 2H, Ar-H), 7.85 (s, 1H, Ar-NH), 3.34 (s, 3H, Ar-OCH_3), 9.08 (s, 1H, Ar-NH-CS), 9.24 (s, 1H, -CSNH-).

5i M.P. 179°C, yield 65% (found: C 50.35, H 5.75, N 29.35, $C_{14}H_{20}N_7OS$, calc: C 50.43, H 5.74, N 29.41%). IR (KBr) cm^1, 1545 (C=S), 1560 (C=N), 3332 (NH), 1334 (N-CH_3), 2880 (C-H), 3052 (C-H-Ar), 1382 (C-CH_3), 1220 (C-O-C). ^{1}H NMR (DMSO-d_6, δ) ppm, 2.74 (s, 6H, N-$(CH_3)_2$), 2.44 (s, 3H, N-CH_3), 6.86 (d, 2H, Ar-H), 7.39 (d, 2H, Ar-H), 7.85 (s,1, Ar-NH), 3.44 (s, 3H, Ar-OCH_3), 9.08 (s, 1H, Ar-NH-CS), 9.28 (s, 1H, -CSNH-).

5j M.P. 190°C, yield 65% (found: C 44.95, H 4.64, N 32.22, $C_{13}H_{17}N_8O_2S$, calc: C 44.82, H 4.63, N 32.16%). IR (KBr) cm^1, 1540 (C=S), 1565 (C=N), 1540 (C-N0$_2$) 3300 (NH), 1330 (N-CH_3), 1142 (C-C), 2882 (C-H), 3050 (C-H-Ar), 1380 (C-CH_3), 1225 (C-O-C). ^{1}H NMR (DMSO-d_6, δ) ppm, 2.85 (s, 6H, N-$(CH_3)_2$), 2.54 (s, 3H, N-CH_3), 6.94 (d, 2H, Ar-H),7.42 (d, 2H, Ar-H), 8.12 (s, 1H, Ar-NH), 9.09 (s, 1H, Ar-NH-CS), 9.24 (s, 1H, -CSNH-).

General procedure for 2-(N-methylamino)-4-(N, N-dimethylamino)-6-(arylthioureido)-*s*-triazine (6a–j)

A mixture of **(4)** (0.005 mol) and aryl isocynate (0.005 mol) in THF (30 mL) was refluxed for 8 h. The progress of the reaction was monitored by TLC using acetone/toluene (9:1) as eluent. After completion of the reaction, the solvent was evaporated by distillation and the resultant solid was crystallized from ethanol.

6a M.P. 178°C, yield 72% (found: C 51.23, H 5.98, N 34.22, $C_{13}H_{17}N_7O$, calc: C 51.34, H 5.96, N 34.12%). IR (KBr) cm^1, 1558 (C=O), 1560 (C=N), 3300 (NH), 1332 (N-CH_3), 2895 (C-H), 3040 (C-H-Ar); ^{1}H NMR (DMSO-d_6, δ) ppm, 2.82 (s, 6H, N-$(CH_3)_2$), 2.53 (s, 3H, N-CH_3), 6.98 (d, 2H, Ar-H), 7.29 (d, 2H, Ar-H), 7.85 (s, 1H, Ar-NH), 9.08 (s, 1H, Ar-NH-CO), 8.14 (s, 1H, -CONH-).

6b M.P. 183°C, yield 65% (found: C 48.65, H 5.02, N 30.52, $C_{13}H_{17}N_7OCl$, calc: C 48.53, H 5.01, N 30.47%). IR (KBr) cm^1, 1560 (C=O), 1559 (C=N), 3332 (NH), 1330 (N-CH_3), 2890 (C-H) 790 (C-Cl), 3045 (C-H-Ar); ^{1}H NMR (DMSO-d_6, δ) ppm, 2.80 (s, 6H, N-$(CH_3)_2$), 2.58 (s, 3H, N-CH_3), 6.8 3(d, 2H, Ar-H), 7.28 (d, 2H, Ar-H), 7.82 (s, 1H, Ar-NH), 9.06 (s, 1H, Ar-NH-CO), 8.16 (s, 1H, -CONH-).

6c M.P. 175°C, yield 60% (found: C 48.42, H 5.03, N 30.40, $C_{13}H_{17}N_7OCl$, calc: C 48.53, H 5.01, N 30.47%). IR (KBr) cm^1, 1562 (C=O), 1560 (C=N), 3330 (NH), 1332 (N-CH_3), 2890 (C-H), 795 (C-Cl), 3042 (C-H-Ar); ^{1}H NMR (DMSO-d_6, δ) ppm, 2.82 (s, 6H, N-$(CH_3)_2$), 2.56 (s, 3H, N-CH_3), 6.82 (d, 2H, Ar-H), 7.26 (d, 2H, Ar-H), 7.80 (s, 1H, Ar-NH), 9.09 (s, 1H, Ar-NH-CO), 8.12 (s, 1H, -CONH-).

6d M.P. 180°C, yield 60% (found: C 48.68, H 5.02, N 30.58, $C_{13}H_{17}N_7OCl$, calc: C 48.53, H 5.01, N 30.47%). IR (KBr) cm^1, 1565 (C=O), 1563 (C=N), 3335 (NH), 1335 (N-CH_3), 2895 (C-H), 790 (C-Cl), 3045 (C-H-Ar); ^{1}H NMR (DMSO-d_6, δ) ppm, 2.85 (s, 6H, N-$(CH_3)_2$), 2.52 (s, 3H, N-CH_3), 6.97 (d, 2H, Ar-H), 7.26 (d, 2H, Ar-H), 7.83 (s, 1H, Ar-NH), 9.08 (s, 1H, Ar-NH-CO), 8.12 (s, 1H, -CONH-).

6e M.P. 185°C, yield 63% (found: C 56.98, H 6.34, N 32.64, $C_{14}H_{20}N_7O$, calc: C 55.80, H 6.36, N 32.54%). IR (KBr) cm^1, 1562 (C=O), 1563 (C=N), 3330 (NH), 1332 (N-CH_3), 2892 (C-H), 1380 (C-CH_3), 3045 (C-H-Ar); ^{1}H-NMR (DMSO-d_6, δ) ppm, 2.82 (s, 6H, N-$(CH_3)_2$), 2.54 (s, 3H, N-CH_3), 6.96 (d, 2H, Ar-H), 7.30 (d, 2H, Ar-H), 7.80 (s, 1H, Ar-NH), 2.38 (s, 3H, Ar-CH_3), 9.05 (s, 1H, Ar-NH-CO), 8.13 (s, 1H, -CONH-).

6f M.P. 190°C, yield 54% (found: C 55.78, H 6.38, N 32.42, $C_{14}H_{20}N_7O$, calc: C, 55.80, H 6.36, N 32.54%). IR (KBr) cm^1, 1564 (C=O), 1568 (C=N), 3338 (NH), 1336 (N-CH_3), 2890 (C-H), 1382 (C-CH_3), 3052 (C-H-Ar); ^{1}H NMR (DMSO-d_6, δ) ppm, 2.84 (s, 6H, N-$(CH_3)_2$), 2.52 (s, 3H, N-CH_3), 6.94 (d, 2H, Ar-H), 7.32 (d, 2H, Ar-H), 7.82 (s, 1H, Ar-NH), 2.34 (s, 3H, Ar-CH_3), 9.04 (s, 1H, Ar-NH-CO), 8.12 (s, 1H, -CONH-).

6g M.P. 185°C, yield 58% (found: C 55.89, H 6.37, N 32.47, $C_{14}H_{20}N_7O$, calc: C 55.80, H 6.36, N 32.54%). IR (KBr) cm^1, 1560 (C=O), 1564 (C=N), 3332 (NH), 1334 (N-CH_3), 2894 (C-H), 1380 (C-CH_3), 3052 (C-H-Ar); ^{1}H NMR (DMSO-d_6, δ) ppm, 2.82 (s, 6H, N-$(CH_3)_2$), 2.54 (s, 3H, N-CH_3), 6.92 (d, 2H, Ar-H), 7.30 (d, 2H, Ar-H), 7.84 (s, 1H, Ar-NH), 2.32 (s, 3H, Ar-CH_3), 9.06 (s, 1H, Ar-NH-CO), 8.14 (s,1H, -CONH-).

6h M.P. 174°C, yield 50% (found: C 53.15, H 6.04, N 30.98, $C_{14}H_{20}N_7O_2$, calc: C 52.99, H 6.03, N 30.90%). IR (KBr) cm^1, 1568 (C=O), 1567 (C=N), 3330 (NH), 1338 (N-CH_3), 2898 (C-H), 1388 (C-CH_3), 3058 (C-H-Ar); ^{1}H NMR (DMSO-d_6, δ) ppm, 2.72 (s, 6H, N-$(CH_3)_2$), 2.44 (s, 3H, N-CH_3), 6.82 (d, 2H, Ar-H), 7.42 (d, 2H, Ar-H), 7.82 (s,1H, Ar-NH), 3.46 (s, 3H, Ar-OCH_3), 9.02 (s, 1H, Ar-NH-CO), 8.12 (s,1H,-CONH-).

6i M.P. 178°C, yield 52% (found: C 52.90, H 6.02; N 30.85, $C_{14}H_{20}N_7O_2$, calc: C 52.99, H 6.03, N 30.90%). IR (KBr) cm^1, 1564 (C=O), 1565 (C=N), 3332 (NH), 1334 (N-CH_3), 2894 (C-H), 1388 (C-CH_3), 3052 (C-H-Ar); ^{1}H NMR (DMSO-d_6, δ) ppm, 2.74 (s, 6H, N-$(CH_3)_2$), 2.42 (s, 3H, N-CH_3), 6.80 (d, 2H, Ar-H), 7.44 (d, 2H, Ar-H), 7.84 (s, 1H, Ar-NH), 3.52 (s, 3H, Ar-OCH_3), 9.06 (s, 1H, Ar-NH-CO), 8.14 (s, 1H,-CONH-).

6j M.P. 189°C, yield 67% (found: C 46.88, H 4.84, N 33.83, $C_{14}H_{20}N_8O_3$, calc: C 48.98, H 4.85, N 33.72%). IR (KBr) cm^1, 1560 (C=O), 1566 (C=N), 1542 (C-NO_2), 3300 (NH), 1330 (N-CH_3), 2880 (C-H), 3052 (C-H-Ar); ^{1}H NMR (DMSO-d_6, δ) ppm, 2.74 (s, 6H, N-$(CH_3)_2$), 2.42 (s, 3H, N-CH_3), 6.80 (d, 2H, Ar-H), 7.44 (d, 2H, Ar-H), 8.12 (s, 1H, Ar-NH), 9.09 (s, 1H, Ar-NH-CO), 8.16 (s, 1H, -CONH-).

Antibacterial activity

All the synthesized compounds were screened for their minimum inhibitory concentration (MIC, μg/mL) against two gram-positive (*Staphylococcus aureus* ATCC 25923 and *Bacillus subtilis* ATCC 6633) and two gram-negative (*Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853) bacteria by the broth dilution method as recommended by the National Committee for Clinical Laboratory Standards (NCCLS)[15]. Penicillin and streptomycin were used as standard antibacterial agents. Solutions of the tested compounds and reference drugs were dissolved in dimethylsulfoxide (DMSO) at prepared concentrations of 100, 50, 25, 12.5, and 6.25 μg/mL. The chemical compound–broth medium in serial test tube dilution inoculated with each bacterium was incubated on a rotary shaker at 37°C for 24 h at 150 rpm. The incubation chamber was kept humid. At the end of the incubation period, MIC values were recorded as the lowest concentration of the substance that gave no visible turbidity, i.e. no growth of inoculated bacteria.

Results and discussion

The MIC values of tested compounds against certain bacteria are shown in Table 1. A series of novel compounds **5a–j** and

Table 1. *In vitro* antimicrobial activity of newly synthesized compounds.

			MIC (μg/mL)			
			Gram-positive bacteria		Gram-negative bacteria	
Compound	R	X	*S. aureus* ATCC 25923	*B. subtilis* ATCC 6633	*P. aeruginosa* ATCC 27853	*E. coli* ATCC 25922
5a	C_6H_5	*S*	25	50	50	50
5b	2-Cl.C_6H_5	*S*	12.5	25	—	25
5c	3-Cl.C_6H_5	*S*	50	25	—	25
5d	4-Cl.C_6H_5	*S*	6.25	6.25	—	50
5e	2-$CH_3C_6H_5$	*S*	50	25	—	25
5f	3-$CH_3C_6H_5$	*S*	25	50	—	
5g	4-$CH_3C_6H_5$	*S*	12.5	25	—	25
5h	2-$OCH_3C_6H_5$	*S*	25	50	—	50
5i	4-$OCH_3C_6H_5$	*S*	6.25	12.5	—	50
5j	4-$NO_2C_6H_5$	*S*	25	6.25	—	25
6a	C_6H_5	*O*	12.5	25	25	25
6b	2-Cl.C_6H_5	*O*	6.25	6.25	—	50
6c	3-Cl.C_6H_5	*O*	25	12.5	—	50
6d	4-Cl.C_6H_5	*O*	12.5	25	—	50
6e	2-$CH_3C_6H_5$	*O*	12.5	6.25	—	50
6f	3-$CH_3C_6H_5$	*O*	25	12.5	—	25
6g	4-$CH_3C_6H_5$	*O*	6.25	50	25	50
6h	2-$OCH_3C_6H_5$	*O*	12.5	25	—	50
6i	4-$OCH_3C_6H_5$	*O*	12.5	50	—	50
6j	4-$NO_2C_6H_5$	*O*	6.25	6.25	—	25
Penicillin			1.562	1.562	6.25	12.5
Streptomycin			6.25	6.25	3.125	3.125

6a–j were prepared and tested for their *in vitro* antibacterial activity against four strains of bacteria (gram +ve, gram –ve). Among the synthesized compounds, **5d**, **6b**, and **6j** were very active against gram-positive bacteria. Compounds **5i** and **6e** also showed a good deal of activity against gram-positive bacteria, while only three compounds (**5a**, **6a**, and **6g**) showed activity against *P. aeruginosa*. The results as reported in Table 1 conclude that the tested compounds showed good activivity against gram-positive bacteria, while they were moderately active against *E. coli* and much less active against *P. aeruginosa* of gram-negative bacterial strain.

In conclusion, it has been shown that the potency and selectivity of these compounds make them valid leads for synthesizing new compounds that possess better activity. Further structure–activity and mechanistic studies should prove fruitful.

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