Synthesis and antimicrobial activity of new substituted 1,3,5-triazine derivatives

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Abstract: A series of di- and tri-substituted 1,3,5-triazine derivatives has been synthesized from the reaction of 2,4-dichloro-6-(trityloxy)-1,3,5-triazine with some cyclic secondary amines as morpholine, piperidine and piperazine in the presence of anhydrous potassium carbonate by nucleophilic substitution reaction. The reaction of 2,4-dichloro-6-(trityloxy)-1,3,5-triazine with 2-aminothiazole, 2-aminobenzothiazole, hydrazine hydrate, were also studied. The structures of the new products were characterized by common analytical and spectroscopic methods. The antimicrobial activity of prepared compounds against gram positive bacteria Staphylococcus aureus and Candida albicans were investigated.

Keywords: Synthesis, Triazine derivatives, 2-Aminothiazole, 2-Aminobenzothiazole, Secondary amines, Hydrazine hydrate, Antimicrobial activities.

Introduction

Triazinyl derivatives are very common compounds which are known long time ago, the innovation in the area of preparing functionalized 1,3,5-Triazine derivatives for special kind of application became an interesting target. They are covering a wide area of applications as pharmaceutical, textile, plastic, and rubber industries, and are used as pesticides, dyestuffs, optical bleaches, opto-electronic, explosives, and surface active agents.¹⁻⁷ The morpholine and piperidine skeleton containing species important in the synthesis of organic compounds,⁸⁻¹⁰ including pharmaceuticals,¹¹⁻¹⁸ have selective enzyme inhibition, antimicrobial and antifungal activities.¹⁹⁻二十五 Numerous papers have shown that the benzothiazole nucleus possesses a potent anticancer activity against human cancer.²⁶⁻⁻³²

Cyanuric chloride (1, 3, 5-Triazine) is an inexpensive, commercially available reagent used for the preparation of variety of x-triazine derivatives. The ease of displacement of chlorine atoms in cyanuric chloride by various nucleophiles enhances the utility of this reagent for the preparation of mono-, di- and tri-substituted 1,3,5-triazine derivatives under controlled temperature conditions.³³,³⁴ In this work we are presenting the synthesis of new asymmetrical triazinyl compounds based on triphenylmethanol which combine with different heterocyclic amine by nucleophilic substitution reaction. All prepared compounds were characterized by all spectroscopy tools and the antimicrobial activity of prepared compounds against gram positive bacteria Staphylococcus aureus and Candida albicans were investigated.
Materials

The reagent grade chemicals were obtained from commercial sources and purified by either distillation or recrystallization before use. Purity of synthesized compounds has been checked by thin layer chromatography. Melting points were determined on an electrical digital- melting point apparatus (Stuart/melting point SMP 30) and uncorrected. 1H NMR spectra are recorded in CDCl3 or DMSO-d6 on a Varian MERCURY 300 spectrometer using TMS as internal standard. The chemical shifts are reported as parts per million (ppm) and mass spectra were determined on a Finnigan MAT SSQ 7000 (EI 70 eV) spectrometer.

Experimental

2,4-Dichloro-6-(trityloxy)-1,3,5-triazine (3)

s-triazine (1) (0.05 mol), Na2CO3 (0.1 mol) and 100 ml anhydrous THF were fed into a 500 ml glass flask equipped with a separating funnel. Triphenylmethanol (2) (0.05 mol) dissolved in 50 ml THF, and the obtained solution was added drop wise into the flask. The reaction temperature was kept at 0-5°C, and the mixture was stirred for about 5 h until the start material disappear examined by TLC. The inorganic material was filtered off and the filtrate triturated with water to give 3 (yield: 70.2%), mp 296-298 °C. Anal. Calcd for C26H25ClN2O: C, 68.04; H, 5.05; Cl, 12.69; N, 12.31. Found: C, 68.18; H, 5.11; Cl, 12.79; N, 12.34. IR cm-1: 3022 (CH, aromatic), 1609 (C=N), 1292 (C-O, stretching). 13C NMR (DMSO): δ 7.15 – 7.29 (m, 15ArH). 1H NMR (300 MHz, DMSO): δ 7.15 – 7.29 (m, 15ArH).

General procedures for the preparation of compounds 5a-c

4-(4-chloro-6-(trityloxy)-1,3,5-triazin-2-yl)morpholine (5a)

In three nicked 100 ml round flask a solution of compound 3 (0.02 mol) in dry acetone (20 ml) and anhydrous potassium carbonate (2 g) were added, a solution of the morpholine (4a) (0.02 mol) in 10 ml acetone was added dropwise to the mixture. The reaction mixture was stirred at room temperature for about 3 h. The inorganic material filtered off and the solvent was evaporated under reduced pressure, then the ice water (10 ml) was added to the semi dry precipitate. The solid was collected by vacuum filtration, washed with water, dried and recrystallized from chloroform/n-hexane to give a colorless crystalline product of 5a (yield: 70%), mp 161-163°C. Anal. Calcd for C26H25ClN2O: C, 68.04; H, 5.05; Cl, 12.69; N, 12.31. Found: C, 68.18; H, 5.11; Cl, 12.79; N, 12.34. IR cm-1: 3022 (CH, aromatic), 1610 (C=N), 1292 (C-O, stretching). 1H NMR (300 MHz, DMSO): δ 7.15 – 7.29 (m, 15ArH), 3.43 (t, JH-H = 6.8 Hz, 4 H, -CH2-N-CH2-), 7.19 – 7.30 (m, 15 CH ArH). MS: m/z (relative intensity) 371 (M1+, 27%), 243 (75, OCPH3), 228 (10), 204 (27), 178 (15), 165 (100), 152 (8), 115 (8), 105 (17), 87 (27), 70 (19).

2-chloro-4-((piperidin-1-yl)-6-(trityloxy)-1,3,5-triazine (5b)

Compound 5b was prepared from reaction of 3 and piperidine (4b) using the same procedure as described for the preparation of 5a. A white solid was separated. Yield: 73%; mp 172-174°C. Anal. Calcd for C26H25ClN3: C, 70.97; H, 5.51; Cl, 7.76; N, 12.26. Found: C, 71.07; H, 5.62; Cl, 7.81; N, 12.31. IR cm-1: 3025 (CH, aromatic), 1605 (C=N), 1299 (C-O, stretching). 1H NMR (DMSO): δ 1.43 (m, 6H, CH2 at position 3,4 and 5- of piperidine ring), 3.69 (m, 4H, -CH2-N-CH2-), 7.12 – 7.38 (m, 15 CH ArH). 13C NMR: 23.81, 24.67, 45.24, 48.40, 55.59, 126.21, 127.93, 129.95, 148.50, 173.66. MS: m/z (relative intensity) 454 (M1+, 5%), 369 (5), 302 (10), 243 (100, OCPH3), 228 (10), 202 (5), 178 (12), 165 (77), 152 (10), 115 (10), 85 (20), 77 (25).

2-chloro-4-((piperazin-1-yl)-6-(trityloxy)-1,3,5-triazine (5c)

Compound 5c was formed from reaction of 3 and piperazine (4c) using the same procedure as described for the preparation of compound 5a. A white solid crystal was separated. Yield: 75%; mp 161-163°C. Anal. Calcd for C26H25ClN4: C, 68.19; H, 5.28; Cl, 7.74; N, 15.29. Found: C, 68.27; H, 5.38; Cl, 7.79; N, 15.33. IR cm-1: 3055, 3025 (CH, aromatic), 1612 (C-N), 1596 (C=C), 1238 (C-O, stretching). 1H NMR (300 MHz, CDCl3): 2.72 (t, JH-H = 6.6 Hz, 4 H, -CH2-N-CH2-), 2.96 (t, JH-H = 6.6 Hz, 4 H, -CH2-N-CH2-), 3.55 (s, 1H, NH), 3.69 (m, 4H, -CH2-N-CH2-), 7.12 – 7.38 (m, 15 CH ArH). 13C NMR: 23.81, 24.67, 45.24, 48.40, 55.59, 126.21, 127.93, 129.95, 148.50, 173.66. MS: m/z (relative intensity) 454 (M1+, 5%), 369 (5), 302 (10), 243 (100, OCPH3), 228 (10), 202 (5), 178 (12), 165 (77), 152 (10), 115 (10), 85 (20), 77 (25).
General procedures for the preparation of compounds 6a-c.

4,4’-(6-(trityloxy)-1,3,5-triazine-2,4-diyl)dimorpholine (6a)

In three nicked flsk 100 ml a solution of compound 3 (0.02 mol) in dry toluene (20 ml) and potassium carbonate anhydrous (2 g) were added, the morpholine (4a) (0.04 mol) in 10 ml toluene was added dropwise to the mixture at room temperature. The reaction temperature was gradually raised to boiling point until the complete disappearance of 3. After 10 h the inorganic solids was filtered off and the solvent was evaporated under reduced pressure, then the mixture was poured to 30 ml of ice water. The solid was collected by vacuum filtration, washed with water, dried and recrystallized from acetone/n-hexane to give a colorless crystalline product of N-(4-chloro-6-(trityloxy)-1,3,5-triazin-2-yl)thiazol-2-amine (6a) (yield: 65%), mp 154-156°C. Anal. Calcd for C_{12}H_{13}N_{3}O: C, 76.01; H, 6.98; N, 13.85. Found: C, 76.12; H, 7.09; N, 13.92. IR cm\(^{-1}\): 3025 (CH, aromatic), 1609 (C=N), 1567 (C=C), 1298 (C-O, stretching).\(^1\)\(^\text{H}\)NMR (300 MHz, DMSO): \(\delta\) 1.4 (m, 12 H, 6 CH\(_2\)), 2.50 (m, 8 H, 2 -CH\(_2\)N-CH\(_2\)), 7.12–7.38 (m, 15 CH ArH). MS: \(m/z\) (relative intensity) 506 (M\(^+\), 83%), 463 (25), 243 (100%, OCPh\(_3\)), 178 (25), 165 (25), 154 (35), 90 (21), 77 (19).

2,4-di(piperazin-1-yl)-6-(trityloxy)-1,3,5-triazine (6b)

Compound 6b was yielded from reaction of 3 and piperazine (4b) by the same procedure as described for the preparation of compound 6a as a white solid. Yield: 67%; mp 154-156°C. Anal. Calcd for C\(_{12}\)H\(_{15}\)N\(_3\)O: C, 76.01; H, 6.98; N, 13.85. Found: C, 76.12; H, 7.09; N, 13.92. IR cm\(^{-1}\): 3025 (CH, aromatic), 1609 (C=N), 1567 (C=C), 1298 (C-O, stretching).\(^1\)\(^\text{H}\)NMR (300 MHz, DMSO): \(\delta\) 1.4 (m, 12 H, 6 CH\(_2\)), 2.50 (m, 8 H, 2 -CH\(_2\)N-CH\(_2\)), 7.12–7.38 (m, 15 CH ArH). MS: \(m/z\) (relative intensity) 506 (M\(^+\), 83%), 463 (25), 243 (100%, OCPh\(_3\)), 178 (25), 165 (25), 154 (35), 90 (11), 77 (19).

2,4-di(piperdin-1-yl)-6-(trityloxy)-1,3,5-triazine (6c)

Compound 6c was prepared from the reaction of 3 and piperidine (4b) by the same procedure similar to the procedure described for compound 6a. A white solid of 6c was separated. Yield: 70%; mp 148-150°C. Anal. Calcd for C\(_{12}\)H\(_{15}\)N\(_3\)O: C, 76.98; H, 6.55; N, 19.3. Found: C, 76.11; H, 6.61; N, 19.38. IR cm\(^{-1}\): 3156 (NH), 3028 (CH, aromatic), 1608 (C=N), 1596 (C=C), 1348 (C-O, stretching).\(^1\)\(^\text{H}\)NMR (300 MHz, CDCl\(_3\)): \(\delta\) 2.82 (t, J\(_{HH}\) = 6.4 Hz, 8 H, 2 -CH\(_2\)N-CH\(_2\)), 3.36 (t, J\(_{HH}\) = 6.4 Hz, 8 H, 2 -CH\(_2\)O-CH\(_2\)), 7.11 – 7.24 (m, 15 CH ArH). MS: \(m/z\) (relative intensity) 509 (M\(^+\), 40%), 463 (29), 441 (23), 178 (59), 165 (25), 154 (5), 90 (11), 77 (19).

General procedures for the preparation of compounds 9 and 10

The mixture of compound 3 (0.02 mol) and 2-aminobenzothiazole (7) (0.02 mol) in dry acetone (20 ml) in the presence of anhydrous potassium carbonate (2 g) was stirred at room temperature for about 5 h. The inorganic solids was filtered off and the solvent was evaporated under reduced pressure, then the solid was collected by vacuum filtration, dried and recrystallized from chloroform/petroleum ether 40-60°C to give a colorless crystalline product of N-(4-chloro-6-(trityloxy)-1,3,5-triazin-2-yl)benzo[d]thiazol-2-amine (9) (yield: 72%), mp 246-248°C. Anal. Calcd for C\(_{20}\)H\(_{15}\)ClN\(_3\)O: C, 63.62; H, 3.84; Cl, 7.51; N, 14.84; S, 6.79. Found: C, 63.75; H, 3.89; Cl, 7.55; N, 14.88; S, 6.81%. IR cm\(^{-1}\): 3166 (NH), 3024 (CH, aromatic), 1606 (C=N), 1323 (C-O, stretching).\(^1\)\(^\text{H}\)NMR (300 MHz, CDCl\(_3\)): \(\delta\) 6.81, 7.10 (2s, 2 CH, thiazole ring), 7.21 – 7.27 (m, 15 ArH), 10.28 (s, 1H, NH). MS: \(m/z\) (relative intensity) 471 (M\(^+\) 27%), 302 (5), 243 (27, OCPh\(_3\)), 228 (7), 178 (18), 165 (85), 152 (15), 115 (17), 103 (27), 98 (33), 77 (100).

N-(4-chloro-6-(trityloxy)-1,3,5-triazin-2-yl)benzo[d]thiazol-2-amine (10)

Compound 10 was prepared from the reaction of 3 with 2-aminobenzothiazole (8) using the same procedure as described for the preparation of 9. A white solid of compound 10 was separated. Yield: 67%; mp 182-184°C. Anal. Calcd for C\(_{20}\)H\(_{15}\)ClN\(_3\)O: C, 66.72; H, 3.86; Cl, 6.79; N, 13.42; S, 6.14. Found: C, 66.75; H, 3.91; Cl, 6.82; N, 13.45; S, 6.19. IR cm\(^{-1}\): 3176 (NH), 3055 (CH, aromatic), 1614 (C=N), 1548 (C=C), 1355 (C-
O, stretching). 1H NMR (300 MHz, DMSO): δ 7.18 – 7.35 (m, 16 CH ArH), 7.44 (t, J = 7.4 Hz, 1H, ArH of benzothiazole ring), 7.70, 7.90 (2d, J = 7.2 Hz, 2H, ArH of benzothiazole ring), 12.06 (s, 1H, NH). MS: m/z (relative intensity) 522 (M+ 69%), 318 (5), 277 (100), 243 (15, OCPPh3), 199 (31), 183 (23), 152 (25), 107 (10), 77 (75).

2-chloro-4-hydrazinyl-6-(trityloxy)-1,3,5-triazine (11)

To a stirred solution of compound 3 (0.04 mol) in absolute ethanol (30 ml), the hydrazine hydrate (0.04 mol) in 10 ml absolute ethanol was added dropwise during 15 min. The reaction mixture was stirred at room temperature for about 2 h. The solvent was evaporated under reduced pressure, and then the ice water (10 ml) was added. The solid was collected by vacuum filtration, washed with water, dried and crystallized from chloroform to give a colorless crystalline product of 11 (yield: 80%), mp 219-221°C. Anal. Calcd for C22H18ClN5O: C, 65.43; H, 4.49; Cl, 8.78; N, 17.34. Found: C, 65.55; H, 4.53; Cl, 8.80; N, 17.38. IR cm⁻¹: 3328 (NH2), 3175 (NH), 3060 (CH, aromatic), 1610 (C=N). 1H NMR (300 MHz, DMSO): δ 3.83 (s, 2H, NH2), 7.14 – 7.27 (m, 15 ArH), 8.68 (s, 1H, NH). MS: m/z (relative intensity) 405 (M+ 90%), 358 (10), 343 (5), 258 (5), 245 (95, OCPPh3), 230 (10), 204 (5), 180 (22), 167 (100), 154 (8), 117 (8), 92 (10), 79 (12), 72(19). The same product obtained when the reaction takes place without solvent at room temperature.

2,4-dihydrazinyl-6-(trityloxy)-1,3,5-triazine (12)

To a stirred solution of 3 (0.05 mol) in dry toluene (30 ml) and anhydrous sodium carbonate (2 g), a solution of (0.1 mol) of hydrazine monohydrate in dry toluene (10 ml) was added dropwise. The resulting mixture was heated under reflux for about 5 h. The solid was collected and dried to give 12 (77% yield), recrystallized from acetone and n-hexane, mp 189-190°C. Anal. Calcd for C22H21N7O: C, 66.15; H, 5.30; N, 24.55. Found: C, 66.19; H, 5.34; N, 24.59. IR cm⁻¹: 3246 (NH, NH2), 3054 (=CH), 1618 (C=C). 1H NMR (300 MHz, CDCl3): δ 2.52 (s, 4H, 2 NH2), 6.01 (s, 2H, 2 NH), 7.11–7.28 (m, 15 ArH), MS: m/z (relative intensity) 400 (M+ 65%), 372 (M+ - N2, 15%), 244 (30), 205 (18), 166 (100), 116 (15), 106 (22), 88 (32), 78 (29).

2.3 Microorganisms and growth conditions

One Gram- positive bacteria, Staphylococcus aureus ATCC 6538 and one yeast, Candida albicans EMCC105 were used to check the antimicrobial potential of the samples. Bacterial strain was cultured overnight at 37°C in Nutrient broth medium (5 g peptone, 3 g meat extract and 1000 ml distilled water) while yeast strain was cultured overnight at 28°C using Sabouraud’s dextrose medium (5 g peptone, 20 g dextrose and 1000 ml distilled water). For antimicrobial test 15 gram of agar was added to above media to prepare Nutrient agar and Sabouraud’s dextrose agar plates.

Antimicrobial Assay

The antimicrobial activity was determined by disc diffusion method. Briefly, 100 il of suspension of the tested microorganisms, containing 10⁶ colony-forming units (CFU)/ml of bacteria and 10⁵ CFU/ml of yeast were spread on nutrient agar and sabouraud’s dextrose agar plates, respectively. The samples were suspended in (DMF). The discs (6 mm in diameter) was individually impregnated with diluted samples and leave them to evaporate the solvent then, placed them on the agar plates which had previously been inoculated with the tested microorganisms. The disc with only solvent was used as a negative control. Plates were incubated at 37°C for bacteria and at 28°C for yeast for 24h. Antimicrobial activity was evaluated by measuring the diameter of the growth inhibition zones and comparing to the control. The obtained results are compared with the reference antibiotics, cephradine.

Results and discussions

2,4-Dichloro-6-(trityloxy)-1,3,5-triazine (3) was synthesized by interaction a molar ratio of cyanuric chloride 1 and triphenylmethanol 2 in dry tetrahydrofuran in the presence of sodium carbonate anhydrous at 0-5°C for 5 h (Scheme 1). The structure of 3 was elucidated by elemental analyses and different spectroscopic tools (IR, NMR and MS). Correct elementary analysis and molecular weight determination for 3 corresponded to C22H15Cl2N3O; MS: m/z 408, M+. Its IR spectrum (KBr, cm⁻¹) revealed the presence of strong absorption
bands at 3053, 3029 (CH, aromatic), 1596 (C=C), 1286 (C-O, stretching) and at 756 (Cl-C). The $^1$H NMR spectrum of 3 (DMSO, $\delta$ ppm) showed a multiplet at $\delta$ 7.15–7.29 attributed to 15 aromatic protons.

Scheme 1

The reaction of 2,4-dichloro-6-(trityloxy)-1,3,5-triazine (3) with molar ratio of cyclic secondary amines (4) in dry acetone in the presence of potassium carbonate as a base at room temperature led to the formation of compound (5) (Scheme 2). The structure of compound 5 was proved by elemental analyses and different spectroscopic methods. Correct elementary analysis and molecular weight determination for 5a as an example corresponded to C$_{26}$H$_{23}$ClN$_4$O$_2$; MS: m/z 371, M$^+$ - morpholine). Its IR spectrum (KBr, cm$^{-1}$) revealed the presence of strong absorption bands at 3022 (CH, aromatic), 1609 (C=N). The $^1$H NMR spectrum of 5a (CDCl$_3$, $\delta$ ppm) showed the two triplets at $\delta$ 2.93 (t, $J_{HH}$ = 6.8 Hz, 4 H, -CH$_2$-N-CH$_2$-) and 3.43 (t, $J_{HH}$ = 6.8 Hz, 4 H, -CH$_2$-O-CH$_2$-) ppm. Additionally, the signal formed by protons of the CH group of aromatic rings was observed as multiplets at $\delta$ 7.11-7.24 ppm due to the high overlap of aromatic protons.

Scheme 2

Treatment of 3 with 2-aminothiazole (7) in dry acetone in the presence of anhydrous potassium carbonate at room temperature for about 5 h. produced the compound 9 in a good yields. Compound 9 shows characteristic absorption bands in the infrared spectra at 3166 cm$^{-1}$ for the NH group. In the $^1$H NMR spectra of compound 9, the two protons of the thiazole ring were appeared as two singlets at chemical shift 6.81 and 7.10 ppm. Additionally, it was observed in a downfield chemical shift ($\delta$ 10.28 ppm) the signal produced by protons of the NH group of this compound. By the same manner, the reaction of compound 3 with 2-
aminobenzothiazole (8) led to the formation of a white solid of N-(4-chloro-6-(trityloxy)-1,3,5-triazin-2-yl)benzo[d]thiazol-2-amine (10). The structure of compound 10 was established from IR, MS and $^1$HNMR spectroscopic data. The infrared spectra show a characteristic absorption bands at 3176 cm$^{-1}$ for the N-H group. The $^1$H NMR spectrum shows the multiplets at $\delta$ 7.18–7.35 ppm attributed to 16 phenyl protons, the benzothiazole protons appeared as a triplet at $\delta$ 7.44 ppm with coupling constant 7.4 Hz and two doublets at $\delta$ 7.70, 7.90 ppm with coupling constant 7.4 Hz. The NH proton was appeared as a singlet at $\delta$ 12.06 ppm.

Scheme 3

Upon treatment of compound 3 with a different molar ratio of hydrazine hydrate in ethanol absolute at room temperature (1:1 molar ratio) a colorless crystals was afforded of 2-chloro-4-hydrazinyl-6-(trityloxy)-1,3,5-triazine (11) in a good yield while (1:2 molar ratio) of compound 3 in dry toluene compound 2,4-dihydrazinyl-6-(trityloxy)-1,3,5-triazine (12) was separated as shown in (Scheme 4). The structural of compound 11 was confirmed according to the results obtained from mass, $^1$HNMR and IR spectra as well as elemental analysis. The gross formula C$_{22}$H$_{18}$ClN$_5$O is confirmed by its mass spectrum (M$^+$ at m/z 405 (M$^+$ 90%), the IR spectrum of 11 revealed two absorption bands at $\nu$ = 3328 (NH$_2$), 3175 (NH) cm$^{-1}$. The $^1$H NMR spectrum is in accordance with the suggested structure which is showed two singlets at $\delta$ 3.83 and 8.68 ppm for NH$_2$ and NH protons respectively, while the phenyl protons appeared as multiplets at $\delta$ 7.14–7.27 ppm. When the same reaction was carried out using excess of hydrazine monohydrate in boiling dry toluene and anhydrous sodium carbonate gave 2,4-dihydrazinyl-6-(trityloxy)-1,3,5-triazine (12) (Scheme 4). The structure of the newly synthesized dihydrazinyl 12 was elucidated using all the analytical and spectral data, which were showed that the synthesized compound was in full agreement with the proposed structure. The $^1$H NMR spectrum of 12 showed two singlets at $\delta$ 2.52 and 6.01 ppm corresponding to 2 NH$_2$ and 2 NH groups, respectively while the aromatic protons appear as a multiplet at $\delta$ 7.11–7.28 ppm.
The antibacterial activity

The antibacterial activity data of s-triazine derivatives (Table 1) against tested organisms displayed significant activity with a wide degree of variation. It is found that compounds 5a and 6c displayed substantial activity against gram positive bacteria Staphylococcus aureus and Candida albicans, while the s-triazine derivatives 10, 11 and 12 are inactive towards both tested organism. Against Candida albicans compounds 3, 5b and 9 has been found to possess significant activity; comparatively no activity has been reported against gram positive bacteria Staphylococcus aureus. Remaining s-triazine derivatives in this series, compounds 6a and 6b displayed least activity against all the tested organisms. Thus, it is obvious from the structure-activity profile of substituted s-triazines; a small structural variation may induce an effect on antimicrobial activity.

Table 1: Antimicrobial activity of the chemical samples at 250 µg/disc.

<table>
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<th>Chemical samples</th>
<th>Tested organisms</th>
<th>Zone of inhibition (mm)</th>
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<td>Staphylococcus aureus</td>
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<td>Candida albicans</td>
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<td>3</td>
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<td>5a</td>
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<td>6a</td>
<td>12</td>
<td>12</td>
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<td>5b</td>
<td>-</td>
<td>8</td>
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<td>6b</td>
<td>10</td>
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<td>5c</td>
<td>-</td>
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<td>6c</td>
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<td>9</td>
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<td>11</td>
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<td>12</td>
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Table 2: Antimicrobial activity of the most active chemical samples at different concentrations

<table>
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<th>Samples</th>
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<th>Candida albicans</th>
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<td>Zones of inhibition (mm) at different concentration (µg/disc)</td>
<td>Zones of inhibition (mm) for different concentration (µg/disc)</td>
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<tr>
<td>5a</td>
<td>250 125 60 30 15</td>
<td>250 125 60 30 15</td>
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<tr>
<td></td>
<td>30 25 22 18 15</td>
<td>20 18 16 13 10</td>
</tr>
<tr>
<td>6c</td>
<td>26 23 20 13 10</td>
<td>20 19 14 12 10</td>
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<tr>
<td>Reference (cephradine)</td>
<td>_ 50 45 43 38</td>
<td>_ 45 40 33 30</td>
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Conclusion

The sequential replacement of three chlorine atoms on cyanuric chloride with different nucleophiles provides the synthesis of a variety of substituted s-triazine molecules. In light of its operational simplicity and efficiency, this reliable method is expected to have a broad utility due to the scope of applications of the s-triazines. Antimicrobial activity of the newly compounds were investigated.

Acknowledgments

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