Synthesis and antimicrobial activities of pyrido[2,3-\textit{d}]pyrimidine, pyridotriazolopyrimidine, triazolopyrimidine, and pyrido[2,3-\textit{d}:6,5\textit{d}']dipirimidine derivatives

Anhar Abdel-Azim \textsuperscript{a}, Marwa Sayed El-Gendy \textsuperscript{a} and Abdou Osman Abdelhamid \textsuperscript{b,*}

\textsuperscript{a} Department of Chemistry, Faculty of Science (Girls), Ahar University, Nasr City, Cairo, 11754, Egypt
\textsuperscript{b} Department of Chemistry, Faculty of Science, Cairo University, Giza, 12613, Egypt

*Corresponding author at: Department of Chemistry, Faculty of Science, Cairo University, Giza, 12613, Egypt. Tel.: +20.2.1095209750; Fax: +202.35676573. E-mail address: abdelhamid45@gmail.com (A.O. Abdelhamid).

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ABSTRACT
A new series of pyridotriazolopyrimidines were synthesized via reaction of hydrazonoyl halides with pyrido[2,3-\textit{d}]-dipirimidine. The structures of the newly synthesized compounds were established by elemental analysis, spectral data and alternative synthetic routes whenever possible. Some of synthesized compounds were also screened in vitro for their antimicrobial activity against a variety of bacterial and fungal samples.

KEYWORDS
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1. Introduction
Previously, it was reported that pyrido[2,3-\textit{d}]pyrimidines possess a broad spectrum of biological activity. They are used as antiallergic [1], antiasmatic agents [2], antihypertensive [3], anti-inflammatory [4], anticancer and antiviral [5-8], diuretic [9] and anticoagulant agents [10,11]. Other than their biological importance, they are valuable for synthesis of polyfunctional heterocyclic compounds. As an extension of our study [12-18] and our program aiming at the synthesis of different heterocyclic derivatives, we report herein the convenient synthesis of some new triazolo[4,3-\textit{a}]pyrimidin-5(\textit{f})-one, pyrido[2,3-\textit{d}]:[1,2,4]triazolo[4,3-\textit{a}]pyrimidin-5-one and 1,2,4-triazolino[4,5-\textit{a}]-1,2,4-triazolino[4,5-\textit{a}]-1,2,4-triazolino[5',5'-1,2']pyrimidino[5',4',5-\textit{f}][pyridino[2,3-\textit{d}]pyrimidin-4-\textit{d}]-dipirimidine derivatives.

2. Experimental
2.1. Instrumentation
All melting points were determined on an electrothermal apparatus and are uncorrected. IR spectra were recorded (KBr discs) on a Shimadzu FT-IR 8201 PC spectrophotometer. \textit{H} and \textit{C} NMR spectra were recorded in CDCl\textsubscript{3} and (CD\textsubscript{3})\textsubscript{SO} solutions on a Varian Gemini 300 MHz and JNM-LA 400 FT-NMR system spectrometer and chemical shifts are expressed in ppm units using TMS as an internal reference. Mass spectra were recorded on a GC-MS QP1000 EX Shimadzu. Elemental analyses were carried out at the Micro analytical Center of Cairo University. Hydrazonoyl halides 5a-e [19-23] were prepared as previously reported.

2.2. Synthesis
2.2.1. Synthesis of pyrido[2,3-\textit{d}] pyrimidines (4a-c)
A mixture of equimolecular amounts of 6-amino-2-thioxo-2,3-dihydro-1H-pyrimidin-4-one [24] (1) (5 mmol) and the appropriate of 2-benzylidenemalononitrile (2a), 2-(benz[d]thiazol-2-yl)3-phenylacrylonitrile (2b) and 3-phenyl-2-(4-thiazolyl)3-phenylacrylonitrile (2c) (5 mmol) in absolute ethanol (10 mL) containing triethylamine (3 drops) was heated under reflux for 3 h. The reaction mixture was concentrated and cooled. The solid obtained was filtered off, washed with ethanol and recrystallized from N,N-dimethylformamide to give 4a-c, respectively (Scheme 1).
8-Amino-3-benzoyl-7-cyano-5-oxo-1,6-diphenyl-1,5-dihydropyrido[2,3-d][1,2]triazolo[4,3-alpyrimidine (10e): Color: Red (from ethanol). Yield: 83%. M.p.: 180-181 °C. FT-IR (KBr, v cm⁻¹): 3300, 3222 (NH), 3038 (CH, aromatic). 1H NMR (300 MHz, DMSO-δ, δ ppm): 1.30 (t, 3H, J = 7.5 Hz, CH₃), 2.00 (q, 2H, J = 7.5 Hz, CH₂), 6.76 (br, 2H, NH), 7.02-8.2 (m, 19H, ArH's). Anal. calcd. for C₂₈H₂₀N₇O₂: C, 69.6; H, 3.54; S, 5.08. Found: C, 69.3; H, 3.46; S, 4.99%.

8-Amino-7-(benzothiazol-2-yl)-5-oxo-1,6-diphenylpyridopyrido[2,3-d][1,2]triazolo[4,3-alpyrimidine-5(1H)-one (11a): Color: Red (from ethanol). Yield: 80%. M.p.: 158-160 °C. FT-IR (KBr, v cm⁻¹): 3200, 3131 (NH), 3050 (CH, aromatic). 1H NMR (300 MHz, DMSO-δ, δ ppm): 5.19 (s, br, 2H, NH), 6.92-8.05 (m, 19H, ArH's). Anal. calcd. for C₂₈H₂₀N₇O₂: C, 68.45; H, 3.35; N, 15.52; S, 5.08. Found: C, 68.33; H, 3.46; N, 15.40; S, 4.99%.

8-Amino-3-acetyl-7-(benzothiazol-2-yl)-5-oxo-1,6-diphenylpyridopyrido[2,3-d][1,2]triazolo[4,3-alpyrimidine-3-carboxamide (11b): Color: Orange (from N,N-dimethylformamide). Yield: 80%. M.p.: 280-281 °C. FT-IR (KBr, v cm⁻¹): 3322, 3224 (NH), 3055 (CH, aromatic), 1725, 1635 (CO). 1H NMR (300 MHz, DMSO-δ, δ ppm): 2.31 (s, 3H, CH₃), 7.12-7.48 (m, 16H, ArH's and NH). MS (El, m/z (%)): 529 (Mʻ, 12.2), 252 (12.2), 240 (6.1), 174 (16.3), 134 (18.4), 57 (100). Anal. calcd. for C₂₈H₂₀N₇O₂S: C, 65.77; H, 3.62; N, 18.51; S, 6.05. Found: C, 65.69; H, 3.71; N, 18.43; S, 6.12%.

8-Amino-3-benzoyl-7-(benzothiazol-2-yl)-1,6-diphenylpyridopyrido[2,3-d][1,2]triazolo[4,3-alpyrimidine-5(1H)-one (11d): Color: Red (from ethanol). Yield: 75%. M.p.: 90-92 °C. FT-IR (KBr, v cm⁻¹): 3479, 3394 (NH), 3050 (CH, aromatic), 1689 (CO), 1593 (C=C). 1H NMR (300 MHz, DMSO-δ, δ ppm): 5.22 (s, br, 2H, NH), 7.12-8.11 (m, 19H, ArH's). Anal. calcd. for C₂₈H₂₀N₇O₂S: C, 69.02; H, 3.52; N, 14.91; S, 4.88. Found: C, 69.29; H, 3.61; N, 14.78; S, 4.93%.

8-Amino-3-acetyl-7-(benzothiazol-2-yl)-5-oxo-1,6-diphenylpyridopyrido[2,3-d][1,2]triazolo[4,3-alpyrimidine (11c): Color: Yellow (from ethanol). Yield: 83%. M.p.: 180-181 °C. FT-IR (KBr, v cm⁻¹): 3300, 3222 (NH), 3038 (CH, aromatic), 11682, 1604 (CO). 1H NMR (300 MHz, DMSO-δ, δ ppm): 2.31 (s, 3H, CH₃), 7.12-7.48 (m, 16H, ArH's and NH). MS (El, m/z (%)): 529 (Mʻ, 12.2), 252 (12.2), 240 (6.1), 174 (16.3), 134 (18.4), 57 (100). Anal. calcd. for C₂₈H₂₀N₇O₂S: C, 65.77; H, 3.62; N, 18.51; S, 6.05. Found: C, 65.69; H, 3.71; N, 18.43; S, 6.12%.

8-Amino-3-acetyl-7-cyano-5-oxo-1,6-diphenylpyridopyrido[2,3-d][1,2]triazolo[4,3-alpyrimidine-3-carboxamide (11e): Color: Yellow (from ethanol). Yield: 75%. M.p.: 180-182 °C. FT-IR (KBr, v cm⁻¹): 3382, 3159, 3109 (NH, NH₃), 3020 (CH, aromatic), 1647 (CO), 1600 (C=C), 1531 (C=C). 1H NMR (300 MHz, DMSO-δ, δ ppm): 6.45 (s, br, 3H, NH, NH₃), 7.12-8.11 (m, 19H, ArH's). Anal. calcd. for C₂₉H₂₁N₇O₃S: C, 67.61; H, 3.66; N, 18.47; S, 5.29. Found: C, 67.21; H, 3.60; N, 18.40; S, 5.20%.

8-Amino-3-acetyl-7-(benzothiazol-2-yl)-5-oxo-1,6-diphenylpyridopyrido[2,3-d][1,2]triazolo[4,3-alpyrimidine-5(1H)-one (12a): Color: Red (from ethanol). Yield: 80%. M.p.: 185-187 °C. FT-IR (KBr, v cm⁻¹): 3425, 3363 (NH), 3062 (CH, aromatic), 1660 (CO). 1H NMR (300 MHz, DMSO-δ, δ ppm): 4.92 (s, br, 2H, NH), 7.00-8.18 (m, 21H, ArH's). Anal. calcd. for C₂₉H₂₁N₇O₃S: C, 69.39; H, 3.52; N, 14.91; S, 4.88. Found: C, 69.29; H, 3.61; N, 14.78; S, 4.93%.
Ethyl 8-amino-7-[(4-phenylthiazol-2-yl)-S-oxo-1,6-diphenyl pyrido[2,3-d][1,2,4]triazolo[4,3-a]pyrimidin-3-carboxylate (12b): Color: Yellow (from N,N-dimethylformamide). Yield: 85%. M.p.: 290-292 °C. FT-IR (KBr, ν, cm⁻¹): 3471, 3394 (NH₂), 3043 (CH, aromatic), 1743, 1697 (C=O), 1600 (C=N). 1H NMR (300 MHz, DMSO-d₆, δ, ppm): 1.21 (t, 3H, J = 7.5 Hz, CH₃), 4.35 (q, 2H, CH₂), 7.22-8.20 (m, 18H, ArH's and NH₂).

8-Amino-3-benzoyl-7-[(4-phenylthiazol-2-yl)-1,6-diphenyl pyrido[2,3-d][1,2,4]triazolo[4,3-a]pyrimidin-5(1H)-one (12c): Color: Red (from ethanol). Yield: 80%. M.p.: 180-182 °C. FT-IR (KBr, v, cm⁻¹): 3471, 3394 (NH₂), 3043 (CH, aromatic), 1697 (C=O), 1600 (C=N). 1H NMR (300 MHz, DMSO-d₆, δ, ppm): 1.21 (t, 3H, J = 7.5 Hz, CH₃), 4.35 (q, 2H, CH₂), 7.22-8.20 (m, 18H, ArH's and NH₂). Anal. calcd. for C₃₂H₂₃N₇O₃S: C, 65.63; H, 3.96; N, 16.74; S, 5.48. Found: C, 65.70; H, 3.88; N, 16.74; S, 5.48.

8-Amino-3-acetyl-7-[(4-phenylthiazol-2-yl)-1,6-diphenyl pyrido[2,3-d][1,2,4]triazolo[4,3-a]pyrimidin-5(1H)-one (12d): Color: Red (from ethanol). Yield: 80%. M.p.: 110-112 °C. FT-IR (KBr, v, cm⁻¹): 3425, 3386 (NH₂), 3062 (CH, aromatic), 1708 (C=O), 1596 (C=N), 1554 (C=C). 1H NMR (300 MHz, DMSO-d₆, δ, ppm): 4.88 (s, br., 2H, NH₂), 7.27-8.30 (m, 21H, ArH's and...
2.2.3. 7-amino-3-(2-benzo furyl)-1-phenyl-[1,2,4]triazolo[4,3-d]pyrimidin-5(1H)-one (13)

A mixture of compound 1 (5 mmol), the appropriate hydrazonyl halides 5a-c (5 mmol) and triethylamine (5 mmol) in chloroform were heated under reflux for 10 hrs. The excess solvent was evaporated and the residue was triturated with ethanol (10 ml). The solid formed was filtered off and crystallized from ethanol to give compound 13 (Scheme 2).

To a solution of 6-aminothiouracil (1), (5 mmol) in methanol (10 ml) and concentrated hydrochloric acid (0.4 ml), compound 14 was added and stirred at room temperature for 4 h, the solid that was obtained was collected by filtration and crystallized from N,N-dimethylformamide to give compound 15 (Scheme 3). Color: Orange. Yield: 75%. M.p.: 215-220 °C. FT-IR (KBr, v, cm⁻¹): 3444, 3321, 3200 (NH), 3058 (CH, aromatic), 1654 (C=O). ¹H NMR (300 MHz, DMSO-d₆, δ ppm): 4.76 (s, 1H, CH₂), 7.24-7.82 (m, 11H, ArHs and pyrazole H₅), 11.95 (s, 2H, 2NH), 14.07 (s, br, 3H, 3NH). ¹³C NMR (75 MHz, DMSO-d₆, δ ppm): 21.65, 100.11, 115.21, 122.64, 124.23, 125.85, 127.35, 127.89, 129.42, 136.472, 137.54, 138.29, 145.11, 155.20, 17298. Anal. calcd. for C₉H₇N₅O₅S: C, 57.70; H, 3.43; N, 19.63; S, 12.84. Found: C, 57.62; H, 3.34; N, 19.53; S, 12.93%.

2.2.4. Alternative synthesis of compounds 10-12

A mixture of the appropriate 13a-7-aminopyrimidin-5-oxo-1,2,4-triazolo[4,3-d]pyrimidine [26] 13 (5 mmol) and the appropriate of arylidine 2a-c (5 mmol) in absolute ethanol (10 ml) containing triethylamine was heated under reflux for 3 h. The reaction mixture was concentrated and cooled. The solid obtained was filtered off, washed with ethanol and recrystallized from a proper solvent to give products identical in all aspects (Mₚ, mixed m.p. and spectra) with the corresponding products obtained by method A (Scheme 2).

2.2.5. 10-(1,3-Diphenyl-1H-pyrazol-4-yl)-2,7-dithioxo-2,5,7,8,9,10-hexahydro-1H,6H-3,7,8,9,10-pentaazaanthracene-4,5-dione (15)

A mixture of compound 15 (5 mmol), the appropriate hydrazonyl halides 5a-c (5 mmol) and triethylamine (5 mmol) in chloroform were heated under reflux for 10 hrs. The excess solvent was evaporated and the residue was triturated with ethanol (10 ml). The solid formed was filtered off and crystallized from a proper solvent to give compound 16a-c, respectively (Scheme 3).

2.2.6. Synthesis of compounds 16a-c

A mixture of compound 15 (5 mmol), the appropriate hydrazonyl halides 5a-c (5 mmol) and triethylamine (5 mmol) in chloroform were heated under reflux for 10 hrs. The excess solvent was evaporated and the residue was triturated with ethanol (10 ml). The solid formed was filtered off and crystallized from a proper solvent to give 16a-c, respectively (Scheme 3).

3.7-Bis-(benzofuran-2-carbonyl)-5-(1,3-diphenyl-1H-pyrazol-4-yl)-1,9-diphenyl-5,11-dihydro-1H,9H-1,2,3a,6a,8,9,10,11,12-nonaaza-dicyclopenta[b]anthracene-4,6-dione (16a): Color: Red (from ethanol). Yield: 75%. M.p.: 202-204 °C. FT-IR (KBr, v, cm⁻¹): 3328 (NH), 3062 (CH, aromatic), 1662 (CO). ¹H NMR (300 MHz, DMSO-d₆, δ ppm): 4.45 (s, 1H, CH), 7.01-8.23 (m, 31H, ArHs). 11.88 (s, br, 1H, NH). Anal. calcd. for C₄₁H₂₃N₉O₆: C, 70.76; H, 3.48; N, 16.30%. Found: C, 70.76; H, 3.39; N, 16.30%.

3,7-Diacetyl-5-(1,3-diphenyl-1H-pyrazol-4-yl)-1,9-diphenyl-5,11-dihydro-1H,9H-1,2,3a,6a,8,9,10,11,12-nonaaza-dicyclopenta[b]anthracene-4,6-dione (16c): Color: Orange (from ethanol). Yield: 83%. M.p.: 268-270 °C. FT-IR (KBr, v, cm⁻¹): 3394 (NH), 3058 (CH, aromatic), 1631 (CO). ¹H NMR (300 MHz, DMSO-d₆, δ ppm): 2.72 (s, 6H, 2CH₃O), 5.12 (s, 1H, CH) 7.12-8.11 (m, 21H, ArHs), 11.87 (s, br, 1H, NH). Anal. calcd. for C₄₃H₂₅N₉O₆: C, 76.10; H, 3.69; N, 19.50. Found: C, 76.19; H, 3.80; N, 19.42.

2.2.7. Synthesis of compound 18a-c

A mixture of compound 17 [27] (5 mmol), the appropriate hydrazonyl halides 5a-c (5 mmol) and triethylamine (5 mmol) in chloroform were heated under reflux for 10 hrs. The excess solvent was evaporated and the residue was triturated with ethanol (10 ml). The solid formed was filtered off and crystallized from a proper solvent to give compound 18a-c, respectively (Scheme 4).

3,7-Bis-(benzofuran-2-carbonyl)-1,9-diphenyl-5,11-dihydro-1H,9H-1,2,3a,6a,8,9,10,11,12-nonaaza-dicyclopenta[b]anthracene-4,6-dione (18a): Color: White (from ethanol). Yield: 70%. M.p.: 158-160 °C. FT-IR (KBr, v, cm⁻¹): 3120 (NH) 1724, 1681 (C=O), 1604 (C=C). ¹H NMR (300 MHz, DMSO-d₆, δ ppm): 3.66 (s, 2H, CH₂), 7.17-8.12 (m, 20H, ArHs), 11.87 (s, br, 1H, NH). Anal. calcd. for C₄₃H₂₅N₉O₆: C, 66.76; H, 3.14; N, 17.09. Found: C, 66.68; H, 3.24; N, 17.12.

4,6-Dioxo-1,9-diphenyl-5,6,9,11-tetrahydro-1H,4H-1,2,3a,6a,8,9,10,11,12-nonaaza-dicyclopenta[b,l]anthracene-3,7-dicarboxylic acid diethyl ester (18b): Color: Yellow (from ethanol). Yield: 70%. M.p.: 138-140 °C. FT-IR (KBr, v, cm⁻¹): 3386 (NH), 1747 (C=O ester), 1681 (C=O), 1600 (C=N). ¹H NMR (300 MHz, DMSO-d₆, δ ppm): 1.14 (t, 6H, J = 7 Hz, 2CH₃), 3.56 (s, 2H, CH₂), 4.13 (q, 4H, J = 7 Hz, 2CH₂), 6.93-7.35 (m, 10H, ArHs), 10.8 (s, 1H, NH). Anal. calcd. for C₄₂H₂₄N₉O₆: C, 58.68; H, 3.91; N, 21.24. Found: C, 58.78; H, 4.00; N, 21.31%.

3,7-Diacyetyl-1,9-diphenyl-5,11-dihydro-1H,9H-1,2,3a,6a,8,9,10,11,12-nonaaza-dicyclopenta[b,l]anthracene-4,6-dione (18c): Color: White (from ethanol). Yield: 68%. M.p.: 200-202 °C. FT-IR (KBr, v, cm⁻¹): 3120 (NH) 1724, 1681(C=O), 1604 (C=N). ¹H NMR (300 MHz, DMSO-d₆, δ ppm): 2.35 (s, 6H, 2CH₃), 3.65 (s, 2H, CH₂), 7.02-7.54 (m, 10H, ArHs), 12.08 (s, 1H, NH).
Anal. calcld. for C_{27}H_{13}N_{10}O_{c} C, 60.79; H, 3.59; N, 23.63. Found: C, 60.70; H, 3.50; N, 23.54%.

2.3. Antimicrobial activity

The tested compounds were dissolved in DMF and prepared in two concentrations; 50 and 100 mg/mL and then 10 μL of each preparation was dropped on disk of 6 mm in diameter and the concentrations became 0.5 and 1.0 mg/mL, respectively. Uniform size filter paper disks (6 mm in diameter) were impregnated by volume (10 μL) from the specific concentration of dissolved compounds and carefully placed on inoculated agar surface. After incubation for 36 hrs at 27 °C in the case of bacteria and for 48 hrs at 24 °C in the case of fungi, inhibition of the organisms which were clearly evident by clear zone surrounding each disk was measured and used to calculate mean of inhibition zone [28].

3. Results and discussion

3.1. Synthesis

Condensation of 6-aminothiouracil (1) with the appropriate amount of benzylidine malononitrile (2a), 2-(benzothiazol-2-yl)-3-phenylacrylonitrile (2b) and 3-phenyl-2-(4-phenylthiazol-2-yl)acrylonitrile (2c) in ethanol containing triethylamine under reflux gave 7-amino-6-substituted 5-phenyl-2,3-dihydro-2-thioxo-pyrido[2,3-d]pyrimidin-4(1H)-one, 4a-c, respectively (Scheme 1). Structures 4a-c were confirmed by elemental analyses, spectral data and chemical transformation.

Thus, treatment of pyrido[2,3-d]pyrimidine derivative 4a with 2-benzofuran-2-yl-n-phenylhydrazonoyl bromide 5a in boiling chloroform containing triethylamine afforded 9-Amino-3-{benzofuran-2-yl-carbonyl]-7-cyano-5-oxo-1,6-diphenyl-1,5-dihydropyrido[2,3-d][1,2,4]triazolo[4,3-a]pyrimidine (10a).

Structure of compound 10a was elucidated via elemental analysis, spectral data and alternative synthesis. Thus, reaction of compound 2a with 7-amino-3-1-benzofuran-2-yl-carbonyl]-1-phenyl[1,2,4]triazolo[4,3-a]pyrimidin-5(1H)-one (13a), which was prepared via reaction of compound 1 with compound 5a in boiling ethanolic triethylamine gave product identical in all aspects (M.p., mixed m.p., and spectra) with compound 10a.

The mechanism outlined in Scheme 2 seems to be the most plausible pathway for the formation of compound 10a from the reaction of compound 4a with compound 5a or nitrite imine 6a, which was prepared in situ by treatment of compound 5a with triethylamine, the reaction involves the initial formation of thiocyanate 7a, which undergoes intermolecular cyclization as soon as it is formed to yield the intermediate 8a or via 1,3-dipolar cycloaddition of nitrite imine 6a to C=S double bond of 4a to give final product compound 10a via elimination of hydrogen sulphide.

Analogously, the appropriate hydrazonoyl halides 5b-e reacted with the appropriate 4a-c in boiling chloroform in presence of catalytic amount of triethylamine gave compound 10b-e, 11a-e and 12a-d, respectively (Scheme 2).

Also, reaction of compound 1 with 1,3-diphenyl-1H-pyrazole-4-carboxaldehyde (14) in methanol containing few drops of hydrochloric acid led to the formation of 10-(1,3-Diphenyl-1H-pyrazol-4-yl)-2,7-dithioxo-2,3,7,8,9,10-hexahydro-1H,6H,1,3,6,8,9-pentaaza-anthracene-4,5-dione (15) (Scheme 4). Structure compound 15 was confirmed by spectral data, elemental analyses and chemical transformation. Thus, compound 15 react with hydrazonoyl halides 5a-e in boiling chloroform to give 16a-c, respectively. 1H NMR spectrum of compound 16b showed signals at 1.07 (1H, J = 7 Hz, CH3), 4.40 (q, 2H, J = 7 Hz CH2), 6.02 (s, 1H, CH9), 6.88-8.08 (m, 10H, ArH’s), 11.27 (s, 1H, NH) ppm.

Moreover, reaction of 2,8-dithioxo-2,3,7,8,9,10-hexahydro-pyrido[2,3-d:6,5-d’]pyrimidine-4,6(1H,5H)-dione (17) [29] with the appropriate hydrazonoyl halides 5a-e were carried out in chloroform under reflux for a long time gave compound 18a-c (Scheme 4). Structures 18 were inferred from their spectral data, elemental analyses and alternative synthesis. Thus 1H NMR spectrum of 18b showed signals at δ = 1.14 (t, 6H, J = 7 Hz, 2CH3), 3.56 (s, 2H, CH2), 4.13 (q, 4H, J = 7 Hz, 2CH2), 6.99-7.35 (m, 10H, ArH’s), 1.07 (s, 1H, NH). Its IR spectrum revealed bands at 3386 (NH) 1747 (CO ester), 1681 (CO), 1600 (C=C). Thus, compound 13b reacted with formaldehyde in presence of hydrochloric acid give product identical in all aspect (M.p., mixed m.p., and spectra) with compound 18b.
3.2. Antimicrobial activity

The tested microorganisms were Gram-positive bacteria: *Staphylococcus Aureus* (ATCC 25923) and *Bacillus Subtilis* (ATCC 6635), Gram-negative bacteria: *Salmonella typhimurium* (ATCC 14028) and *Escherichia coli* (ATCC 25922), Fungus: *Candida Albicans* (ATCC 10231) and *Aspergillus fumigatus*.

In general, (for high and low concentrations) compounds 4a-c, 12a and 18b were capable low inhibition against Gram-positive bacteria *Bacillus Subtilis* and compounds 10b and 11a were capable intermediate inhibition against Gram-negative bacteria *Escherichia coli* whereas compound 4a show intermediate inhibition against yeast and fungi (Table 1). *Staphylococcus Aureus* (ATCC 25923) and *Salmonella typhimurium* (ATCC 14028) are no effect for all synthesized compounds.

4. Conclusion

The present work describes the study of reactions of hydrazonoyl halides towards some pyridodipyrimidine derivatives to give pyridotriazolopyrimidines derivatives in a good yield with some biological activity.

References