Full Paper

Synthesis and biological activity of some new fused thieno[2,3-b] pyridine derivatives; pyridothienopyrimidinones and pyridothienotriazinones

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Abstract
3-Amino-4-aryl-5-ethoxycarbonyl-6-methylthieno[2,3-b]pyridine-2-carboxamides 3a,b were prepared and reacted with triethyl orthoformate to give pyridothienopyrimidinone derivatives 4a,b. The reaction of compound 3b with potassium ethyl xanthate and/or phenyl isothiocyanate produced thioxopyridothienopyrimidinones 5 and 6 respectively. Diazotisation of compounds 3a,b led to the formation of 9-aryl-8-ethoxycarbonyl-7-methylpyrido[3’,2’:4,5]thieno[3,2-d][1,2,3]triazine-4(3H)-ones (7a,b). Compounds 5, 6 and 7a,b underwent some reactions to furnish other new pyridothienopyrimidinones 8, 9a,b and pyridothienotriazinones 10-13a,b. The structural formulas of all newly synthesized compounds were confirmed by elemental and spectral analyses. Also, the biological activity of fifteen compounds as antibacterial and antifungal agents were studied.

Keywords: Thienopyridines, pyridothenopyridines, pyridothienotriazines, Mannich reaction.

1. Introduction
Many thieno[2,3-b]pyridines have been synthesized and investigated in relation with their biological and pharmacological importance [1,2]. Some of them proved to possess antiviral [3-6], antidiabetic [7], antimicrobial [8-10], anti-inflammatory [11], antitumor [12], antiparasitic [13] and neurotropic activities [14]. Also, some pyrido[3’,2’:4,5]thieno[3,2-d]pyrimidines are reported to exhibit antiallergic [15], antiprotocoal [16], antianaphylactic [17,18] and antimicrobial activities [8-10]. Furthermore, a number of pyridothieno triazines have been used as antiprotozoal [16], antitumor [19], antiangiogenic [20] and antimicrobial agents [8]. In view of the above observations, we report herein the synthesis and biological activity of the title compounds which are expected to be biologically active ones owing to incorporation of different pharmacophores.

2. Results and discussion
Our approach to the synthesis of the target compounds started from 3-amino-4-aryl-5-ethoxycarbonyl-6-methylthieno [2,3-b]pyridine-2-carboxamides 3a,b which were prepared from the reaction of ethyl 4-aryl-3-cyano-6-methyl-2-thioxo-
1,2-dihydropyridine-5-carboxylates (1a,b) with chloroa-cetamide according to the reported method [21] (Scheme 1). Condensation of compounds 3a,b with triethyl orthoformate by refluxing in acetic anhydride produced the pyrimidinone derivatives 4a,b. Upon refluxing of 3b with potassium ethyl xanthate in ethanol, ethyl 9-(p-chlorophenyl)-7-methyl-4-oxo-2-thioxo-1,2,3,4-tetrahydropyrido[3′,2′:4,5][3,2-d]pyrimidine-8-carboxylate (5) was obtained. The 3-phenyl analogue 6 was synthesized by reacting 3b with phenyl isothiocyanate in hot pyridine. Treatment of compounds 3a,b in H\textsubscript{2}SO\textsubscript{4}-AcOH mixture with sodium nitrite solution at low temperature resulted in diazotization followed by self coupling to furnish the 1,2,3-triazinones 7a,b (Scheme 2).
The compounds 5, 6 and 7a,b were utilized as precursors for synthesizing other new pyridothienopyrimidinones and pyrido-thienotriazinones. Thus, reaction of thioxopyrimidinone 5 with 2-chloro-methylquinazoline-4(3H)-one and/or N\textsuperscript{4}-chloroacetylthioacetamide in DMF containing sodium acetate, gave ethyl 9-(p-chlorophenyl)-7-methyl-4-oxo-2-(4-oxo-3,4-dihydro-quinazolin-2-yl) methylthio-3,4-dihydropyrido[3’,2’:4,5]thieno[3,2-d]pyrimidine-8-carboxylate (8) and ethyl 2-[(p-aminosulfonylphenyl)-carbamoyl]methylthio-9-(p-chlorophenyl)-7-methyl-4-oxo-3,4-dihydropyrido[3’,2’:4,5]thieno[3,2-d]pyrimidine-8-carboxylate (9a) respectively. Whereas, the reaction of thioxopyrimidinone 6 with N\textsuperscript{4}-chloro-acetylsulphanilamide in an ethanolic sodium hydroxide solution produced ethyl 2-[(p-aminosulfonylphenyl)carbamoyl]methylthio-9-(p-chlorophenyl)-7-methyl-4-oxo-3,4-dihydropyrido[3’,2’:4,5]thieno[3,2-d]pyrimidine-8-carboxylate (9b) in a high yield (Scheme 3). Reaction of compound 7a or 7b with ethyl chloroacetate or chloroacetamidine in DMF containing anhyd. K\textsubscript{2}CO\textsubscript{3} at room temperature gave the N-alkylated triazinones 10 and 11 respectively. When compound 7a was allowed to react with aromatic or heterocyclic amines in the presence of of formaldehyde, the corresponding Mannich bases 12a,b and 13a,b were obtained in high yields (Scheme 4). The structural formulas of all newly synthesized compounds were confirmed by elemental and spectral analyses (cf. experimental part). Among the synthesized compounds, fifteen samples were selected and evaluated for their antimicrobial activities against six strains of bacteria and six strains of fungi. The bioassay results, which are given in tables 1 and 2, revealed that: (i) most of the tested compounds possess mild to strong activity against, at least, one bacterial or fungal strain, (ii) only three compounds (2a, 9a and 9b) showed no activity against all used strains of bacteria and fungi, (iii) Most of the tested compounds possess moderate to very strong inhibition activity against Staphylococcus aureus, (iv) each of triazinone derivatives 7a, 7b and 13b showed mild to moderate activity against all tested strains of bacteria, (v) compounds 1a, 1b and 12b exhibit no activity against all fungal strains used and (vi) Compounds 4b, 5, 6, 7a, 7b and 8 showed partial inhibition zones of 18, 14, 14, 18 and 18 mm., respectively, towards G. candidum

![Scheme 3](http://www.aun.edu.eg)
3. Experimental

All melting points were measured on a Gallen-Kamp melting point apparatus and are uncorrected. IR Spectra were obtained on a Pye-Unicam SP3-100 spectrophotometer using KBr disc technique. $^1$H NMR Spectra were recorded on a Bruker 400 MHz NMR spectrometer (Sohag University) or a Varian EM-390, 90 MHz spectrometer (Assiut University). Elemental analyses were performed on an Elemental Analyser system GmbH VARIO EL V_2.3.1998 CHNS Mode.

3.1. Reaction of compounds 3a,b with triethylthiomercurate; formation of pyridothienopyrimidinones 4a,b; general procedure

A mixture of compound 3a,b (0.005 mol) and triethyl orthoformate (3 ml) in redistilled acetic anhydride (10 ml) was heated under reflux for 4 h. The precipitate that formed while hot was collected by filtration, washed with ethanol and crystallized from DMF to give compounds 4a,b in the form of white needles.

3.1.1. Ethyl 9-(p-methoxyphenyl)-7-methyl-4-oxo-3,4-dihydropyrido[3′,2′:4,5]thieno[3,2-d]pyrimidine-8-carboxylate (4a)

Yield: 80 %, m.p.: 298-299 °C. IR: 3220 (NH), 1731 (C=O, ester), 1659 (C=O, pyrimidinone) cm$^{-1}$. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ = 12.875 (br. s, 1H, NH), 8.03 (s, 1H, CH pyrimidinone), 7.26-7.28 (d, $J = 8.0$ Hz, 2H, Ar-H), 6.98-7.00 (d, $J = 8.0$ Hz, 2H, Ar-H), 4.06-4.08 (q, 2H, OCH$_2$), 3.83 (s, 3H, OCH$_3$), 2.64 (s, 3H, CH$_3$ at C-7), 0.95-0.97 (t, 3H, CH$_3$ of ester). Anal. Calcd. for C$_{20}$H$_{17}$N$_3$O$_4$S (395.43): C, 60.75; H, 4.33; N, 10.63; S, 8.11 %. Found: C, 60.66; H, 4.21; N, 10.41; S, 8.25 %.

3.1.2. Ethyl 9-(p-chlorophenyl)-7-methyl-4-oxo-3,4-dihydropyrido[3′,2′:4,5]thieno[3,2-d]pyrimidine-8-carboxylate (4b)

Yield: 81 %, m.p.: 334-336 °C. IR: 3200 (NH), 1728 (C=O, ester), 1655 (C=O, pyrimidinone) cm$^{-1}$. $^1$H NMR (90 MHz, DMSO-$d_6$): $\delta$ = 12.8 (br. s, 1H, NH), 8.1 (s, 1H, CH pyrimidinone), 7.5-7.9 (d, 4H, Ar-H), 4.0-4.3 (q, 2H, OCH$_2$), 2.6 (s, 3H, CH$_3$ at C-7), 0.9-1.1 (t, 3H, CH$_3$ of ester). Anal. Calcd. for C$_{19}$H$_{15}$ClN$_3$O$_4$S (399.85): C, 57.07; H, 3.53; N, 10.51; S, 8.02 %. Found: C, 57.00; H, 3.61; N, 10.38; S, 7.84 %.

3.2. Ethyl 9-(p-chlorophenyl)-7-methyl-4-oxo-2-thioxo-1,2,3,4-tetrahydropyrido[3′,2′:4,5]thieno[3,2-d]pyrimidine-8-carboxylate (5)

A mixture of compound 3b (1.95 g, 0.005 mol) and ethyl potassium xanthate (1.12 g, 0.007 mol) in absolute ethanol (15 ml) was heated on a water bath under reflux for 6 h. The reaction mixture was cooled, diluted with water (20 ml) and then acidified with dil. HCl. The precipitated solid was collected by filtration, air-dried and crystallized from DMSO to give compound 5. Yield: 87 %, m.p.: 282-283 °C (Lit. m.p.: 281 °C) [22]. IR: 3388 (NH), 1733 (C=O, ester), 1694 (C=O, pyrimidinone) cm$^{-1}$. Anal. Calcd. for C$_{19}$H$_{14}$ClN$_3$O$_2$S$_2$ (431.91): C, 52.84; H, 3.27; N, 9.73; S, 14.85 %. Found: C, 52.93; H, 3.25; N, 9.64; S, 15.00 %.

3.4. Ethyl 9-(p-chlorophenyl)-7-methyl-4-oxo-3-phenyl-2-thioxo-1,2,3,4-tetrahydropyrido[3′,2′:4,5]thieno[3,2-d]pyrimidine-8-carboxylate (6)

A mixture of compound 3b (1.95 g, 0.005 mol) and phenyl isothiocyanate (0.7 ml, 0.007 mol) in absolute ethanol (15 ml) was heated on a water bath for 3 h. The precipitate that formed while hot was collected by filtration, washed with ethanol and recrystallized from DMF to give compound 6. Yield: 87 %, m.p.: 268-270 °C (Lit. m.p.: 267-268 °C) [22]. IR: 3398 (NH), 1733 (C=O, ester), 1697 (C=O, pyrimidinone) cm$^{-1}$. Anal. Calcd. for C$_{20}$H$_{15}$ClN$_3$O$_3$S$_2$ (508.01): C, 59.11; H, 3.57; N, 8.27; S, 12.62 %. Found: C, 59.24; H, 3.50; N, 8.59; S, 12.72 %.
3.5. Diazotisation of compounds 3a,b; formation of triazinone derivatives 7a,b; general procedure

To a chilled mixture of compound 3a,b (0.005 mol) and conc H₂SO₄ (5 ml) in glacial acetic acid (15 ml), 5 ml of sodium nitrite solution (10 %) was added dropwise with stirring during about 10 min. After the completion of addition, stirring was continued for 2 h. The precipitate that formed after dilution with water (10 ml) was collected by filtration and crystallized from DMSO in the form of white crystals.

3.6.1. Ethyl 9-(p-methoxyphenyl)-7-methyl-4-oxo3,4-dihydropyrido[3′,2′:4,5]thieno[3,2-d][1,2,3]triazine-8-carboxylate (7a)

Yield: 80 %, m.p.: 184-185 °C, IR: 3205 (NH), 1724 (C=O, ester), 1671 (C=O, quinazolinone), 1621 (C=N) cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ = 12.55 (br. s, 1H, NH), 7.25-7.27 (d, J = 8.0 Hz, 2H, Ar-H), 6.91-6.93 (d, J = 8.0 Hz, 2H, Ar-H), 4.03-4.06 (q, J = 4.0 Hz, 2H, Ar-H), 3.81 (s, 3H, OCH₃), 2.71 (s, 3H, CH₃ at C-7), 0.96 - 0.98 (t, J = 4.0 Hz, 3H, CH₃ of ester). Anal. Calcd. for C₂₁H₁₈N₂O₃S (366.43): C, 57.57; H, 4.07; N, 14.13; S, 9.30 %. Found: C, 57.44; H, 4.08; N, 14.33; S, 9.72 %.

3.6.2. Ethyl 9-(p-chlorophenyl)-7-methyl-4-oxo3,4-dihydropyrido[3′,2′:4,5]thieno[3,2-d][1,2,3]triazine-8-carboxylate (7b)

Yield: 86 %, m.p.: 201-203 °C, IR: 3203 (NH), 1739 (C=O, ester), 1671 (C=O, triazine) cm⁻¹. ¹H NMR (400 MHz, DMSO-d₆): δ = 12.5 (br. s, 1H, NH), 7.4-7.8 (dd, 4H, Ar-H), 4.0-4.3 (q, 2H, OCH₂), 2.70 (s, 3H, CH₃ at C-7), 0.9 - 1.1 (t, 3H, CH₃ of ester). Anal. Calcd. for C₁₆H₁₃ClN₂O₃S (400.84): C, 53.94; H, 3.27; N, 13.98; S, 8.00 %. Found: C, 54.09; H, 3.21; N, 13.78; S, 0.11 %.

3.7. Reaction of phenylpyrimidinethione 5 with 2-chloromethylquinazoline-4(3H)-one and/or N⁴-chloroacetyl sulphanilamide; formation of compounds 8 and 9a; general procedure

To a mixture of compound 5 (2.16 g, 0.005 mol) and sodium acetate trihydrate (1.0 g, 0.007 mol) in ethanol (25 ml), 2-chloromethylquinazoline-4(3H)-one or N⁴-chloroacetyl sulphanilamide (0.005 mol) was added. The resulting mixture was heated under reflux for 2 h. The precipitate that formed while hot was collected and recrystallized from ethanol to give compounds 8 or 9a respectively.

3.7.1 9-(4-chlorophenyl)-7-methyl-4-oxo-2-(4-oxo-3,4-dihydroquinazolin-2-yl) methylthio3,4-dihydropyrido[3′,2′:4,5]thieno[3,2-d]pyrimidine-8-carboxylate (8)

Yield: 87 %, m.p.: 330-341 °C. IR: 3250 (2 NH), 1717 (C=O, ester), 1647 (C=O, pyrimidinone and quinazolinone), 1621 (C=N) cm⁻¹. ¹H NMR (90 MHz, CDCl₃): δ = 11.6 (br. s, 2H, 2 NH of pyrimidinone and quinazolinone), 7.1- 8.2 (m, 8H, Ar-H), 4.3 (s, 2H, SCH₂), 3.8-4.2 (q, 2H, OCH₂), 2.7 (s, 3H, CH₃at C-7), 0.8 - 1.1 (t, J = 6.0 Hz, 3H, CH₃ of ester). Anal. Calcd. for C₂₈H₂₅ClN₂O₄S₂ (590.07): C, 56.99; H, 3.42; N, 11.87; S, 10.87 %. Found: C, 56.73; H, 3.44; N, 11.80; S, 10.66 %.

3.7.2. Ethyl 9-(4-chlorophenyl)-7-methyl-4-oxo-2-[(p-amino sulfonylphenyl) carbamoyl]methylthio3,4-dihydropyrido[3′,2′:4,5]thieno[3,2-d]pyrimidine-8-carboxylate (9a)

Yield: 80 %, m.p.: 310-311 °C. IR: 3323 (NH), 1721 (C=O, ester), 1649 (C=O, pyrimidinone and anilide) cm⁻¹. ¹H NMR (400 MHz, DMSO-d₆): δ = 13.24 (s, 1H, NH of pyrimidinone), 10.24 (s, 1H, NH of sulphanilamide moiety), 7.79-8.71 (d, J = 8.0 Hz, 2H, Ar-H), 7.71-7.73 (d, J = 8.0 Hz, 2H, Ar-H), 7.44-7.46 (d, J = 8.0 Hz, 2H, Ar-H), 7.35-7.37 (d, J = 8.0 Hz, 2H, Ar-H), 7.20 (s, 2H, SO₂NH₂), 4.01-4.06 (q, J = 6.0 Hz, 2H, OCH₂), 3.41 (s, 2H, SCHR₂), 2.67 (s, 3H, CH₃ at C-7), 0.91-0.94 (t, J = 6.0 Hz, 3H, CH₃ of ester). Anal. Calcd. for C₂₈H₂₅ClN₂O₄S₂ (644.13): C, 50.35; H, 3.44; N, 10.87; S, 14.93 %.

To a solution of compound 6 (1.01 g, 0.002 mol) in an ethanolic sodium hydroxide 5 % (10 ml), N'-chloroacetyl,p-sulphanilamide (0.5 g, 0.002 mol) was added. The reaction mixture was heated under reflux for one hour and then allowed to cool. The precipitate that formed was collected and recrystallized from isopropanol. Yield: 87 %, m.p.: 221-222 °C. IR: 3300 (NH), 1716 (C=O, sulfonamide) cm.

1H NMR (400 MHz, DMSO-d6): δ = 10.22 (s, 1H, NH of sulphanilamide moiety), 7.77-7.79 (d, J = 8.0 Hz, 2H, Ar-H), 7.67-7.69 (d, J = 8.0 Hz, 2H, Ar-H), 7.58 (s, 3H, Ar-H), 7.49-7.51 (d, J = 8.0 Hz, 4H, Ar-H), 7.40-7.42 (d, J = 8.0 Hz, 2H, Ar-H), 7.19 (s, 2H, SO₂NH₂), 4.03-4.08 (q, J = 6.0 Hz, 2H, OCH₂), 3.24 (s, 2H, SCH₂, overlapped with DMSO signal), 3.79 (s, 3H, CH₃ at C-7), 0.93-0.96 (t, J = 6.0 Hz, 3H, CH₃ of ester). Anal. Calcd. for C₃₃H₂₆ClN₅O₅S (720.23): C, 55.03; H, 3.64; N, 9.72; S, 13.35 %. Found: C, 55.18; H, 3.34; N, 9.50; S, 13.37 %.

3.9. Alkylation of triazinones 7a,b, formation of compounds 10 and 11; general procedure

To a mixture of compounds 7a,b (0.005 mol) and ethyl chloroacetate or chloroacetamide (0.005 mol) in DMF (20 ml), anhyd. K₂CO₃ (1.0 g) was added. The reaction mixture was stirred at room temperature for 5 h and then diluted with water. The solid that precipitated was collected and recrystallized from ethanol.

3.9.1. 8-Ethoxycarbonyl-3-ethoxy carbonylmethyl-9-(p-methoxyphenyl)-7-methyl-pyrido[3',2':4,5]thieno[3,2-d][1,2,3]triazine-4(3H)-one (10)

7a with ethyl chlorooacetate following the above general procedure. Yield: 76 %; m.p.: 143-144 °C. IR: 1751 (C=O, non conjugated ester), 1710 (C=O, conjugated ester), 1693 (C=O, triazine). 1H NMR (400 MHz, CDCl₃): δ = 6.92-7.28 (dd, 4H, Ar-H), 5.09 (s, 2H, NCH₂), 4.19 (q, 2H, OCH₂), 4.05 (q, 2H, OCH₂). 3.79 (s, 3H, OCH₃), 2.70 (s, 3H, CH₃ at C-7), 1.19-1.22 (t, 3H, CH₃ of ester group), 0.97-0.99 (t, 3H, CH₃ of ester group). Anal. Calcd. for C₂₃H₂₂N₄O₅S (482.51): C, 57.25; H, 4.60; N, 11.61; S, 6.64 %. Found: C, 57.00; H, 4.53; N, 11.50; S, 7.01 %.

3.9.2. 3-Carbamoylmethyl-9-(p-chlorophenyl)-8-ethoxycarbonyl-7-methylpyrido[3',2':4,5]thieno[3,2-d][1,2,3]triazine-4(3H)-one (11)

It was prepared by reaction of compound 7b with chloroacetamide following the above general procedure. Yield: 81 %; m.p.: 262-264 °C. IR: 3419, 3212 (NH, amide). 1H NMR (400 MHz, DMSO-d6): δ = 7.70 (s, 1H, OH), 7.57-7.59 (d, J = 8 Hz, 2H, Ar-H), 7.45-7.47 (d, J = 8 Hz, 2H, Ar-H), 7.30 (s, 1H, NH), 5.02 (s, 2H, NCH₂), 4.09-4.14 (q, J = 8 Hz, 2H, OCH₂), 2.73 (s, 3H, CH₃ at C-7), 0.97-1.01 (t, J = 8 Hz, 3H, CH₃ of ester group). Anal. Calcd. for C₂₉H₄₆ClN₄O₅S (457.89): C, 52.46; H, 3.52; N, 15.29; S, 7.00 %. Found: C, 52.69; H, 3.38; N, 15.27; S, 7.14 %.

3.10. Reaction of triazinone 7a with aromatic or heterocyclic amines and formaldehyde, formation of Mannich bases 12a,b and 13a,b; general procedure

To a stirred mixture of compound 7a (1.98 g, 0.005 mol), aromatic or heterocyclic amine (0.005 mol) in ethanol (30 ml), formalin solution 37 % (10 ml) was added. The stirring was continued for 4 h. The reaction mixture was then allowed to stand at room temperature overnight. The product that precipitated was collected and recrystallized from proper solvent.

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3.10.1. 8-Ethoxycarbonyl-9-(p-methoxyphenyl)-7-methyl-3-(p-tolylaminomethyl) pyrido[3',2':4,5]thieno[3,2-d][1,2,3]triazine-4(3H)-one (12a)

It was prepared by using p-toluidine in the above general procedure. Yield: 80 %; m.p.: 153-155 °C (EtOH). IR: 3446 (NH), 1730 (C=O, ester), 1689 (C=O, triazinone). Anal. Calcd. for C_{27}H_{25}N_{2}O_{5}S (515.59): C, 58.17; H, 4.81; N, 14.00; S, 6.50 %. Found: C, 58.55; H, 5.47; N, 14.27; S, 6.34 %. 

3.10.2. 3-(p-Chlorophenylaminomethyl)-8-ethoxycarbonyl-9-(p-methoxyphenyl)-7-methylpyrido[3',2':4,5]thieno[3,2-d][1,2,3]triazine-4(3H)-one (12b)

It was prepared by using p-chloroaniline in the above general procedure. Yield: 83 %; m.p.: 167-168 °C (DMSO). IR: 3388 (NH), 1725 (C=O, ester), 1681 (C=O, triazinone). \(^1H\) NMR (90 MHz, CDCl3): \(\delta = 7.0-7.5\) (dd, 4H, Ar-H), 5.4 (s, 2H, NCH_{2}), 4.0-4.3 (q, 2H, OCH_{2}), 3.9 (s, 3H, OCH_{3}), 2.8 (s, 3H, CH_{3} at C-7), 0.9-1.2 (t, 3H, CH_{3} of ester group). Anal. Calcd. for C_{28}H_{22}ClN_{2}O_{5}S (536.00): C, 58.26; H, 4.14; N, 13.07; S, 5.98 %. Found: C, 58.18; H, 4.34; N, 13.13; S, 6.10 %.

3.10.3. 8-Ethoxycarbonyl-9-(p-methoxyphenyl)-7-methyl-3-piperidinomethylpyrido [3',2':4,5]thieno[3,2-d][1,2,3]triazine-4(3H)-one (13a)

It was prepared by using piperidine in the above general procedure. Yield: 78 %; m.p.: 174-175 °C. IR: 2936 (C-H, aliphatic), 1717 (C=O, ester), 1675 (C=O, triazinone). \(^1H\) NMR (90 MHz, CDCl3): \(\delta = 7.0-7.5\) (dd, 4H, Ar-H), 5.4 (s, 2H, NCH_{2}), 4.0-4.3 (q, 2H, OCH_{2}), 3.9 (s, 3H, OCH_{3}), 2.7-2.9 (m, 7H, CH_{2}NCH_{2} and CH_{3} at C-7), 1.3-1.7 (m, 6H, three methylene groups of piperidine ring), 0.9-1.1 (t, 3H, CH_{3} of ester group). Anal.

The antimicrobial activity of fifteen compounds was tested against six bacterial and six fungal strains provided by the Assiut University Mycological Centre (AUMC). These strains were isolated from different sources in Egypt and some of them were involved in human diseases (Staphylococcus aureus, Aspergillus flavus, Candida albicans, Geotrichum candidum, Scopulariopsis brevicaulis and Trichophyton rubrum), plant diseases (Fusarium oxysporum) or frequently reported from contaminated soil, water and food substances (Bacillus cereus, Micrococcus luteus, Escherichia coli, Pseudomonas aeruginosa, Serratia marcescens). To prepare inocula for bioassay, bacterial strains were individually cultured for 48 h in 100 ml conical flasks containing 30 ml nutrient broth medium. Fungi were grown for 7 days in 100 ml conical containing 30 ml Sabouraud's dextrose broth. Bioassay was performed in 10 cm sterile plastic
Petri plates in which microbial suspension (1 ml/plate) and 15 ml appropriate agar medium (15 ml/plate) were poured. Nutrient agar and Sabouraud's dextrose agar were respectively used for bacteria and fungi [23]. After solidification of media, 5 mm diameter cavities were cut in the solidified agar (4 cavities/plate) using sterile cork borer. Organic compounds dissolved in dimethyl sulfoxide (DMSO) at 2 % w/v (=20 mg/ml) were pipette in the cavities (20 ul/cavity). Cultures were then incubated at 28°C for 48 h in case of bacteria and up to 7 days in case of fungi. Results were read as the diameter of inhibition zone around cavities [24].
Table 1: Antibacterial activities of some representative compounds (inhibition zones in mm).

<table>
<thead>
<tr>
<th>Compd. No.</th>
<th>B. cereus</th>
<th>M. luteus</th>
<th>S. aureus</th>
<th>E. Coli</th>
<th>P. aeruginosa</th>
<th>S. marcescens</th>
</tr>
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<tr>
<td>1a</td>
<td>0</td>
<td>0</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<td>0</td>
<td>7</td>
<td>0</td>
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<td>2a</td>
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<td>6</td>
<td>9</td>
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<td>4b</td>
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<td>6</td>
<td>12</td>
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<td>8</td>
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<td>5</td>
<td>6</td>
<td>10</td>
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Control = Chloramphenicol
Table 2: Antifungal activities of some representative compounds (inhibition zones in mm).

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Control = Clotrimazole
p.i. = partial inhibition