Annulation and Evaluation of Antibacterial Activity of the New Fused Tricyclic (5,5,6) Ring System of Pyrazolo[1,5-c]-1,2,4-Triazo[4,3-a]Pyrimidines

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Abstract – A series of the new fused 5-aryl-8-phenyl-2H-pyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine-3-thiones 2 were prepared in excellent yields by the reaction of 5-aryl-7-hydrazino-2-phenylpyrazolo[1,5-c]pyrimidines 1 with carbon disulfide in the presence of potassium hydroxide. The pyrazolotriazolopyrimidinethiones gave with certain electrophiles the respective 6-substituted 3-thiones 4-6 rather than the 7-substituted isomeric structure 7. Oxidation of 2 with sodium nitrite or benzenediazonium chloride afforded the corresponding disulfides 9 or 10 respectively. Moreover, the pyrazolotriazolopyrimidinones 8 were prepared upon reaction with alkaline hydrogen peroxide. All the above compounds were evaluated as antibacterial agents against a variety of microorganisms.

Pyrazolo[1,5-c]pyrimidines and 1,2,4-triazolo[4,3-a]pyrimidines are recurrent as a structure component of biologically important compounds. Several pyrazolo[1,5-c]pyrimidines are known to possess significant hypnotic,1 tranquilizing, fungicidal, insecticidal,2 antitumor3-6 and antibacterial7 activities. Moreover, 1,2,4-triazolo[4,3-a]pyrimidines are known to possess significant antiviral,8-10 antifungal,11-13 antimicrobial,14-16 antibacterial,17 herbicidal,18-24 plant growth regulator,14,25 leishmanicidal,26 nucleic acid antimetabolite,27,28 antitumor,9 antihypertensive29,30 and cardiovascular30-32 activities. In addition to their applications in photography.33-35 In the present study, a new family of pyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidinethiones 2 were synthesized and tested as antibacterial agents.
Reaction of the 5-aryl-7-hydrazino-2-phenylpyrazolo[1,5-c]pyrimidines (1a-d)\textsuperscript{36} with carbon disulfide in the presence of potassium hydroxide followed by acidification gave the respective 5-aryl-8-phenyl-2H-pyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine-3-thiones (2a-d). The infrared spectra of 2 showed characteristic pyrazole and pyrimidine ring bands closed to that reported for a series of 5-aryl-2-phenylpyrazolo[1,5-c]pyrimidine-7(6H)-thiones\textsuperscript{2} as well as thiocarbonyl and NH absorptions of triazole ring. The \textsuperscript{1}H NMR spectra of 2a-d showed a singlet at $\delta$ 7.18-7.21 for the H-6 pyrimidine ring proton and a singlet at $\delta$ 6.86-6.95 for the H-7 pyrazole ring proton. The higher field signal for the H-7 agreed with that reported data for 5-aryl-2-phenylpyrazolo[1,5-c]pyrimidine-7(6H)-thiones.\textsuperscript{2} Moreover, the spectra of 2a,b showed an exchangeable NH proton at $\delta$ 14.07 and an overlapping to this signal for compound 2c,d under the aromatic proton multiplet at $\delta$ 7.14-8.90.

\begin{align*}
\text{Ph} & \quad \text{N} & \quad \text{N} & \quad \text{N} & \quad \text{N} \\
& \quad \text{N} & \quad \text{N} & \quad \text{N} & \quad \text{N} \\
\text{NHNNH}_2 & \quad \text{KO}_2 & \quad \text{Ph} & \quad \text{N} & \quad \text{N} & \quad \text{N} & \quad \text{N} & \quad \text{N} \\
& \quad \text{N} & \quad \text{N} & \quad \text{N} & \quad \text{N} \\
\text{N} & \quad \text{N} & \quad \text{N} & \quad \text{N} & \quad \text{N} \\
\text{Ph} & \quad \text{N} & \quad \text{N} & \quad \text{N} & \quad \text{N} \\
& \quad \text{N} & \quad \text{N} & \quad \text{N} & \quad \text{N} \\
\text{1} & \quad \text{2} & \quad \text{3} \\
4 & \quad \text{X} = \text{Br} \\
5 & \quad \text{X} = \text{I} \\
6 & \quad \text{X} = \text{NO}_2 \\
7 & \quad \text{8} \\
9 & \quad \text{Z} = \text{H} \\
10 & \quad \text{Z} = \text{PhN}=\text{N} \\
\end{align*}

\text{Ar} = \text{C}_{6}\text{H}_{5}(a), \text{p-Me-C}_{6}\text{H}_{4}(b), \text{p-MeO-C}_{6}\text{H}_{4}(c), \text{p-Cl-C}_{6}\text{H}_{4}(d)

\textbf{Scheme 1}
The mass spectra also confirmed the structure of pyrazolotriazolopyrimidinethiones 2 where the spectrum of 2c gave the molecular ion peak at m/z 373 as the base peak, while the p-methylphenyl derivative 2b gave a very intense molecular ion peak at 357 (90%). On the other hand, the spectrum of 2a and 2d gave a moderate intense molecular ion peak at m/z 343 (45%) and 377 (40%) respectively, which reflect the high stability of these molecules. Acetylation of 2a-d with refluxing acetic anhydride yielded the respective 3-acetylthio derivatives 3a-d (Scheme 1). The structure of 3a-d were confirmed by studing their IR spectra which exhibited a carbonyl absorption bands in the range 1730-1741 cm\(^{-1}\) characteristic for S-acetyl rather than N-acetyl derivatives. Their \(^1\)H NMR spectra also showed the presence of a sharp singlet for S-acetyl protons at \(\delta\) 2.44 -2.80. The newly prepared fused pyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine-3-thione rings 2a-d appeared to be an attractive intermediates for the synthesis of a number of substituted derivatives via the reaction with some representative electrophilic reagents, and where there is no reports have been published on the electrophilic substitution reactions of pyrazolotriazolopyrimidine ring system. We are interesting to investigate the reactivity of such heterocyclic ring either at C-6 or C-7 position. Thus, bromination of 2a-d with bromine as well as iodination with iodine monochloride gave the respective 6-bromo 4a-d and 6-iodo 5a-d derivatives respectively. Moreover, nitration of 2a,b with nitric and sulfuric acids in glacial acetic acid afforded the respective 6-nitro derivatives 6a,b. The structures of 6-substituted derivatives 4-6 were confirmed by studying their \(^1\)H NMR spectra which showed the disappearance of the H-6 pyrimidine ring proton signal at \(\delta\) 7.18-7.21.

![Scheme 2](image-url)

\(\text{Ar} = \text{C}_6\text{H}_5(a), p-\text{Me-C}_6\text{H}_4(b), p-\text{MeO-C}_6\text{H}_4(c), p-\text{Cl-C}_6\text{H}_4(d)\)
On the other hand, the structures were confirmed chemically by preparing the 7-substituted isomeric derivatives 7. Since it is known that bromination, iodination, as well as nitration of 2,5-diphenyl-pyrazolo[1,5-c]pyrimidine-7(6H)-thione gave the respective 3-bromo, 3-iodo and 3-nitro derivatives.\(^2\) Bromination of 5-aryl-2-phenylpyrazolo[1,5-c]pyrimidine-7(6H)-thiones (11a-d) with bromine in acetic acid rather than bromine in chloroform\(^2\) led to the formation of the respective 3-bromo derivatives 12a-d (Scheme 2). Refluxing of 12a-d with hydrazine hydrate in ethanolic solution afforded the respective hydrazino derivatives 13a-d which upon reaction with carbon disulfide in the presence of potassium hydroxide, followed by acidification yielded the corresponding 7-bromo derivatives 7a-d. The two isomeric bromo-derivatives 4 and 7 were found to be completely different (TLC, mp and mixed mp, IR, \(^1\)H NMR and MS spectra).

Oxidation of the pyrazolo[1,5-c]-1,2,4-triazolo[4,3-\(a\)]pyrimidine-3-thiones 2a-d with sodium nitrite in glacial acetic acid yielded the corresponding 3,3\'-dithiobis(5-aryl-8-phenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-\(a\)]pyrimidine) (9a-d). On the other hand, reaction of 2a-d with benzendiazonium chloride in the presence of sodium hydroxide gave the respective 3,3\'-dithiobis(5-aryl-6-phenylazo-8-phenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-\(a\)]pyrimidine) (10a-d). The reaction is assumed to proceed by introduction of phenylazo group as well as oxidation of the thiol. Moreover, the reaction of the pyrazolotriazolopyrimidinethiones 2a-d with alkaline hydrogen peroxide led to the formation of the respective pyrazolo[1,5-c]-1,2,4-triazolo[4,3-\(a\)]pyrimidin-3-ones 8a-d. The IR, \(^1\)H NMR and mass spectra confirmed the structure of the above oxidized products. Thirteen pyrazolotriazolopyrimidine derivatives 2,4,5,8-10 were tested for antibacterial activity against some microorganisms. It was shown that, compounds 2c, 4b,c, 5d, 9b were active against Gram negative bacteria at minimum inhibitory concentration (MIC) and 10b,c had no activity towards Gram positive bacteria while the carbonyl derivatives 8b,c had no activity against the both types of bacteria (Table 1). The bispyrazolotriazolopyrimidine dimmers 9b,c showed less reactivity than brominated compounds 4b,c.

**EXPERIMENTAL**

Melting points were determined on a Kofler Block apparatus and are uncorrected. Elemental analyses were carried out in the micro analytical laboratory of the faculty of science, Cairo University. The IR spectra of compounds were recorded on a Fourier Transform infrared 8400 spectrophotometer as potassium bromide pellets and frequencies are reported in cm\(^{-1}\). The \(^1\)H NMR spectra were recorded on a JEOL JNM ECA 500 MHZ and chemical shifts \(\delta\) are in ppm relative to tetramethylsilane as internal standard. Mass spectra were recorded at 70 ev with GCMS-QP 1000 EX. Reactions were routinely followed by thin layer chromatography (TLC) Merck Kiesel gel; 60-F254 precoated plastic plates. The spots were detected by iodine.
5-Aryl-8-phenyl-2H-pyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine-3-thiones (2a-d).

(General Procedure):
A mixture of 1a-d\textsuperscript{16} (0.00332 mol), potassium hydroxide (1.2 g, 0.02143 mol) in water (30 mL) and carbon disulfide (20 mL) in EtOH (100 mL) was heated under reflux for 3 h. The mixture was concentrated, poured onto crushed ice and acidified with diluted hydrochloric acid. The precipitate was filtered off, washed with water several times, dried and recrystallized from EtOH.

5,8-Diphenyl-2H-pyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine-3-thione (2a).
Yield (0.85 g, 75%), mp 171-172 °C; IR: 3427 (NH), 1650 (pyrazole ring C=N), 1500 (triazole ring C=N), 1431 (pyrimidine ring C=C) and 1072 cm\(^{-1}\) (C=S); \(^1\)H NMR (DMSO-\(d_6\)): \(\delta\) = 6.95 (s, 1H, pyrazole-H), 7.21 (s, 1H, pyrimidine-H), 7.31-8.04 (m, 10H, aromatic-H) and 14.07 (s, 1H, exchangeable NH); MS: m/z (%): 345 (4, M\(^+\)2), 344 (13, M\(^+\)), 343 (45, M•+), 342 (30), 260 (2), 128 (15), 127 (14), 103 (13), 102 (23), 78 (12), 77 (100), 51 (45), 50 (26); Anal. Calcd for C\(_{19}\)H\(_{13}\)N\(_5\)S: C, 66.5; H, 3.8; N, 20.4; S, 9.3%. Found: C, 66.4; H, 3.6; N, 20.2; S, 9.0%.

5-p-Methylphenyl-8-phenyl-2H-pyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine-3-thione (2b).
Yield (0.9 g, 79.65%), mp 271-272 °C; IR: 3431 (NH), 1641 (pyrazole ring C=N), 1573 (triazole ring C=N), 1498 (pyrimidine ring C=C) and 1027 cm\(^{-1}\) (C=S); \(^1\)H NMR (DMSO-\(d_6\)): \(\delta\) = 2.34 (s, 3H, CH\(_3\)), 6.91 (s, 1H, pyrazole-H), 7.16-8.05 (m, 9H, aromatic-H), 7.21 (s, 1H, pyrimidine-H) and 14.07 (s, 1H, exchangeable NH); MS: m/z (%): 357 (90, M•+), 356 (34), 315 (36), 314 (100), 300 (13), 299 (30), 222 (16), 196 (16), 195 (24), 194 (22), 77 (11); Anal. Calcd for C\(_{20}\)H\(_{15}\)N\(_5\)S: C, 67.2; H, 4.2; N, 19.6; S, 8.0%. Found: C, 67.3; H, 4.1; N, 19.3; S, 8.6%.

5-p-Methoxyphenyl-8-phenyl-2H-pyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine-3-thione (2c).
Yield (0.9 g, 79.65%), mp 189-190 °C; IR: 3436 (NH), 1645 (pyrazole ring C=N), 1591 (triazole ring C=N), 1510 (pyrimidine ring C=C) and 1022 cm\(^{-1}\) (C=S); \(^1\)H NMR (DMSO-\(d_6\)): \(\delta\) = 3.78 (s, 3H, OCH\(_3\)), 6.91 (s, 1H, pyrazole-H), 7.16-8.05 (m, 9H, aromatic-H), 7.21 (s, 1H, pyrimidine-H) and 14.07 (s, 1H, exchangeable NH); MS: m/z (%): 374 (29, M\(^+\)+1), 373 (100, M•+), 372 (41), 316 (35), 315 (34), 187 (15), 77 (13); Anal. Calcd for C\(_{20}\)H\(_{15}\)N\(_5\)OS: C, 64.3; H, 4.1; N, 18.8; S, 8.6%. Found: C, 64.3; H, 4.0; N, 18.5; S, 8.9%.

5-p-Chlorophenyl-8-phenyl-2H-pyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine-3-thione (2d).
Yield (0.7 g, 61.95%), mp 309-310 °C; IR: 3377 (NH), (pyrazole ring C=N), 1637 (triazole ring C=N), 1596 (pyrimidine ring C=C) and 1010 cm\(^{-1}\) (C=S); \(^1\)H NMR (DMSO-\(d_6\)): \(\delta\) = 6.86 (s, 1H, pyrazole-H), 7.14-8.90 (m, 10H, 9 Aromatic-H + exchangeable NH) and 7.18 (s, 1H, pyrimidine-H); MS: m/z (%): 378 (26, M\(^+\)+1), 377 (40, M\(^+\)), 376 (39), 347 (51), 345 (100), 319 (36), 317 (21), 284 (13), 77 (18); Anal. Calcd for C\(_{19}\)H\(_{12}\)ClN\(_5\)S: C, 60.4; H, 3.2; Cl, 9.4; N, 18.5; S, 8.5%. Found: C, 60.2; H, 3.2; Cl, 9.1; N, 18.2; S, 8.8%.

3-Acetylthio-5-aryl-8-phenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidines (3a-d).
(General Procedure):
A mixture of 2a-d (0.00102 mol) and acetic anhydride (2 mL) was heated under reflux for 1 h. The reaction mixture was cooled and poured onto ice cooled water. The product which separated out, filtered off, washed with water, dried and crystallized from CHCl3/EtOH as pale yellow needles.

3-Acetylthio-5,8-diphenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine (3a).
Yield (0.37 g, 94.9%), mp 243-244 °C; IR: 1730 (C=O), 1666 (pyrazole ring C=N), 1550 (triazole ring C=N) and 1440 cm⁻¹ (pyrimidine ring C=C); ¹H NMR (CDCl₃): δ= 2.80 (s, 3H, CH₃CO), 6.67 (s, 1H, pyrazole-H), 6.90 (s, 1H, pyrimidine-H) and 7.41-8.02 (m, 10H, aromatic-H); MS: m/z (%): 386 (3, M⁺1), 385 (6, M⁺), 345 (6), 344 (10), 343 (43), 342 (30), 285 (25), 129 (12), 127 (12), 126 (13), 104 (13), 103 (15), 99 (12), 89 (13), 77 (100), 50 (29); Anal. Calcd for C₂₁H₁₅N₅OS: C, 65.4; H, 3.9; N, 18.2; S, 8.3%. Found: C, 65.3; H, 3.7; N, 18.1; S, 8.1%.

3-Acetylthio-5-p-methoxyphenyl-8-phenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine (3c).
Yield (0.42 g, 93.3%), mp 259-260 °C; IR: 1733 (C=O), 1666 (pyrazole ring C=N), 1614 (triazole ring C=N) and 1546 cm⁻¹ (pyrimidine ring C=C); ¹H NMR (DMSO-d₆): δ= 2.68 (s, 3H, CH₃CO), 2.80 (s, 3H, CH₂CO), 6.94 (s, 1H, pyrazole-H), 7.26 (s, 1H, pyrimidine-H) and 7.36-8.03 (m, 9H, aromatic-H); MS: m/z (%): 416 (6, M⁺1,),415 (10, M⁺+),375 (12), 374 (34), 373 (100), 372 (47), 316 (36), 315 (61), 271 (6), 77 (12); Anal. Calcd for C₂₂H₁₇N₅OS: C, 63.6; H, 4.1; N, 16.9; S, 7.7%. Found: C, 63.8; H, 4.0; N, 16.6; S, 7.5%.

3-Acetylthio-5-p-chlorophenyl-8-phenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine (3d).
Yield (0.41 g, 93%), mp 271-272 °C; IR: 1741 (C=O), 1668 (pyrazole ring C=N), 1620 (triazole ring C=N) and 1546 cm⁻¹ (pyrimidine ring C=C); ¹H NMR (DMSO-d₆): δ= 2.69 (s, 3H, CH₃CO), 7.07 (s, 1H, pyrazole-H), 7.23 (s, 1H, pyrimidine-H) and 7.49-8.06 (m, 9H, aromatic-H); MS: m/z (%): 421 (3, M⁺+1), 420 (2, M⁺), 419 (7), 381 (3), 380 (10), 379 (44), 378 (43), 377 (100), 375 (31), 319 (40), 82 (88); Anal. Calcd for C₂₁H₁₄ClN₅OS: C, 60.1; H, 3.4; Cl, 8.4; N, 16.7; S, 7.6%. Found: C, 60.0; H, 3.1; Cl, 8.0; N, 16.4; S, 7.2%.

5-Aryl-6-bromo-8-phenyl-2H-pyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine-3-thiones (4a-d).
(General Procedure):
A solution of bromine (0.06 mL, 0.0012 mol) in acetic acid (10 mL) was gradually added to a suspension
of 2a-d (0.00102 mol) in acetic acid (10 mL) with stirring for 3 h at room temperature. The precipitate was filtered off, washed with water dried and crystallized from CHCl3/EtOH in colorless needles.

6-Bromo-5,8-diphenyl-2H-pyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine-3-thione (4a).

Yield (0.4 g, 92.9%), mp 273-274 °C; IR: 3437 (NH), 1643 (pyrazole ring C=N), 1569 (triazole ring C=N), 1508 (pyrimidine ring C=C) and 1027 cm⁻¹ (C=S); MS: m/z (%): 436 (10, M+1), 435 (39, M⁺), 357 (100), 456 (59), 325 (99), 301 (16), 299 (38), 297 (25), 77 (30); Anal. Calcd for C₁₉H₁₂BrN₅S: C, 54.0; H, 2.9; Br, 18.9; N, 16.6; S, 7.6%. Found: C, 54.1; H, 2.8; Br, 18.5; N, 16.3; S, 7.4%.

6-Bromo-5-p-methylphenyl-8-phenyl-2H-pyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine-3-thione (4b).

Yield (0.44 g, 90%), mp 251-252 °C; IR: 3492 (NH), 1633 (pyrazole ring C=N), 1566 (triazole ring C=N), 1554 (pyrimidine ring C=C) and 1029 cm⁻¹ (C=S); ¹H NMR (DMSO-d₆): δ = 2.44 (s, 3H, CH₃), 7.20 (s, 1H, pyrazole-H) and 7.40-9.03 (m, 10H, 9 aromatic -H + exchangeable NH); Anal. Calcd for C₂₀H₁₄BrN₅S: C, 55.1; H, 3.2; Br, 18.3; N, 16.1; S, 7.4%. Found: C, 55.0; H, 3.1; Br, 18.0; N, 16.0; S, 7.1%.

6-Bromo-5-p-methoxyphenyl-8-phenyl-2H-pyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine-3-thione (4c).

Yield (0.43 g, 88.7%), mp 196-197 °C; IR: 3434 (NH), 1637 (pyrazole ring C=N), 1581 (triazole ring C=N), 1510 (pyrimidine ring C=C) and 1020 cm⁻¹ (C=S); ¹H NMR (DMSO-d₆): δ = 3.84 (s, 3H, OCH₃), 7.02 (s, 1H, pyrazole-H) and 7.13-9.03 (m, 10H, 9 aromatic-H + exchangeable NH); Anal. Calcd for C₂₀H₁₄BrN₅OS: C, 53.1; H, 3.1; Br, 17.7; N, 15.5; S, 7.1%. Found: C, 53.2; H, 3.1; Br, 17.4; N, 15.4; S, 6.7%.

6-Bromo-5-p-chlorophenyl-8-phenyl-2H-pyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine-3-thione (4d).

Yield (0.45 g, 93%), mp 237-238 °C; IR: 3488 (NH), 1596 (pyrazole ring C=N), 1490 (triazole ring C=N), 1436 (pyrimidine ring C=C) and 1083 cm⁻¹ (C=S); Anal. Calcd for C₁₉H₁₁BrClN₅S: C, 50.0; H, 2.4; Br, 17.5; Cl, 7.8; N, 15.3; S, 7.0%. Found: C, 49.7; H, 2.4; Br, 17.9; Cl, 7.5; N, 15.2; S, 7.3%.

5-Aryl-6-iodo-8-phenyl-2H-pyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine-3-thiones (5a-d).

(General Procedure):

A solution of iodine monochloride (0.2 g, 0.0012 mol) in acetic acid (10 mL) was gradually added to a suspension of 2a-d (0.00102 mol) in acetic acid (10 mL) with stirring for 3 h at room temperature. The reaction mixture was then poured onto crushed ice and the precipitated product was filtered off, washed with water, dried and crystallized from CHCl₃/EtOH in colorless needles.

5,8-Diphenyl-6-iodo-2H-pyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine-3-thione (5a).

Yield (0.42 g, 87.5%), mp >300 °C; IR: 3504 (NH), 1637 (pyrazole ring C=N), 1564 (triazole ring C=N),
1423 (pyrimidine ring C=C) and 1033 cm⁻¹ (C=S); MS: m/z (%): 467 (4), 466 (4), 449 (5), 414 (5), 343 (28), 286 (13), 171 (18), 129 (17), 102 (26), 77 (100); Anal. Calcd for C₁₉H₁₂IN₅S: C, 48.6; H, 2.6; I, 27.0; N, 14.9; S, 6.8%. Found: C, 48.5; H, 2.4; I, 27.3; N, 14.8; S, 6.6%.

7-Iodo-5-p-methylphenyl-8-phenyl-2H-pyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine-3-thione (5b).
Yield (0.49 g, 90.6%), mp 287-288 °C; IR: 3450 (NH), 1629 (pyrazole ring C=N), 1554 (triazole ring C=N), 1415 (pyrimidine ring C=C) and 1022 cm⁻¹ (C=S); Anal. Calcd for C₂₀H₁₄IN₅S: C, 49.7; H, 2.9; I, 26.3; N, 14.5; S, 6.6%. Found: C, 49.6; H, 2.7; I, 26.0; N, 14.3; S, 6.4%.

6-Iodo-5-p-methoxyphenyl-8-phenyl-2H-pyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine-3-thione (5c).
Yield (0.45 g, 84%), mp 199-200 °C; IR: 3340 (NH), 1635 (pyrazole ring C=N), 1560 (triazole ring C=N), 1444 (pyrimidine ring C=C) and 1020 cm⁻¹ (C=S); Anal. Calcd for C₂₀H₁₄IN₅OS: C, 48.1; H, 2.8; I, 25.4; N, 14.0; S, 6.4%. Found: C, 48.1; H, 2.6; I, 25.2; N, 14.1; S, 6.3%.

5-Chlorophenyl-6-iodo-8-phenyl-2H-pyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine-3-thione (5d).
Yield (0.43 g, 80.52%), mp 301-302 °C; IR: 3512 (NH), 1643 (pyrazole ring C=N), 1571 (triazole ring C=N), 1415 (pyrimidine ring C=C) and 1026 cm⁻¹ (C=S); Anal. Calcd for C₁₉H₁₁ClIN₅S: C, 45.3; H, 2.2; Cl, 7.0; I, 25.2; N, 13.9; S, 6.4%. Found: C, 45.3; H, 2.1; Cl, 7.5; I, 24.8; N, 13.7; S, 6.1%.

5-Aryl-6-nitro-8-phenyl-2H-pyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine-3-thiones (6a,b).
(General Procedure):
A mixture of nitric acid (d 1.41, 1 mL) and sulfuric acid (d 1.84, 1 mL) in glacial acetic acid (10 mL) was gradually added to suspension of 2a,b (0.00102 mol) in glacial acetic acid (10 mL) with stirring for 3 h at room temperature. The reaction mixture was then poured onto cold water with stirring and the reddish brown precipitated solid were filtered off, washed with cold water, dried and crystallized from DMF/EtOH as pale brown needles.

5,8-Diphenyl-6-nitro-2H-pyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine-3-thione (6a).
Yield (0.37 g, 92.5%), mp 181-182 °C; IR: 3407 (NH), 1649 (pyrazole ring C=N), 1556 (triazole ring C=N), 1496 (pyrimidine ring C=C), 1431,1269 (NO₂) and 1072 cm⁻¹ (C=S); ¹H NMR (CDCl₃): δ= 6.94 (s, 1H, pyrazole-H), 7.21-8.09 (m, 10H, aromatic-H) and 14.08 (s, 1H, exchangeable NH); Anal. Calcd for C₁₉H₁₂N₆O₂S: C, 58.8; H, 3.1; N, 21.6; S, 8.3%. Found: C, 58.6; H, 3.1; N, 21.2; S, 8.1%.

5-Aryl-3- bromo-2-phenyl-6H-pyrazolo[1,5-c]pyrimidine-7-thiones (12a-d).
Yield (0.39 g, 86.7%), mp 295-296 °C; IR: 3444 (NH), 1681 (pyrazole ring C=N), 1556 (triazole ring C=N), 1506 (pyrimidine ring C=C), 1419, 1332 (NO₂) and 1026 cm⁻¹ (C=S); ¹H NMR (CDCl₃): δ= 2.40 (s, 3H, CH₃), 6.78 (s, 1H, pyrazole-H) and 7.08-8.68 (m, 10H, 9 aromatic-H + exchangeable NH); Anal. Calcd for C₂₀H₁₄N₆O₂S: C, 59.7; H, 3.5; N, 20.9; S, 8.0%. Found: C, 59.5; H, 3.4; N, 20.7; S, 7.8%.

5-Aryl-3- bromo-2-phenyl-6H-pyrazolo[1,5-c]pyrimidine-7-thiones (12a-d).
(General Procedure):
A solution of bromine (0.3 mL, 0.005 mol) in acetic acid (15 mL) was gradually added to a suspension of 5-aryl-2-phenyl-6H-pyrazolo[1,5-c]pyrimidine-7-thiones 11a-d (0.005 mol) in acetic acid (20 mL) with stirring for 3 h at room temperature. The reaction mixture was then poured onto crushed ice water and the precipitate was filtered off, washed with water, dried and recrystallized from CHCl₃/EtOH in colorless needles.

3-Bromo-2,5-diphenyl-6H-pyrazolo[1,5-c]pyrimidine-7-thione (12a).
Identical to that prepared² from the reaction off 11a with Br₂ / CHCl₃ (TLC, mp and mixed mp and IR).

3-Bromo-5-p-methylphenyl-2-phenyl-6H-pyrazolo[1,5-c]pyrimidine-7-thione (12b).
Yield (0.75 g, 60%), mp 273-274 °C; IR: 3475 (NH), 1595 (pyrazole ring C=N), 1461 (triazole ring C=N), 1427 (pyrimidine ring C=N) and 1024 cm⁻¹ (C=S); ¹H NMR (CDCl₃): δ= 2.28 (s, 3H, CH₃), 3.60 (s, 1H, exchangeable SH), 6.88 (s, 1H, exchangeable NH), 7.36 (s, 1H, pyrimidine-H) and 7.54-8.19 (m, 9H, aromatic-H); MS: m/z (%): 398 (M+3, 11), 397 (M+2, 24), 396 (M+1, 19), 395 (M⁺, 20), 317 (15), 316 (41), 315 (15), 258 (25), 77 (100), 51 (85); Anal Calcd for C₁₉H₁₄BrN₃S: C, 57.6; H, 3.6; Br, 20.2; N, 10.6; S, 8.1%. Found: C, 57.4; H, 3.5; Br, 19.9; N, 10.4; S, 8.3%.

3-Bromo-5-p-methoxyphenyl-2-phenyl-6H-pyrazolo[1,5-c]pyrimidine-7-thione (12c).
Yield (0.7 g, 56.5%), mp 279-280 °C; IR: 3483 (NH), 1589 (pyrazole ring C=N), 1465 (triazole ring C=N), 1425 (pyrimidine ring C=N) and 1022 cm⁻¹ (C=S); Anal Calcd for C₁₉H₁₄BrN₃OS: C, 55.4; H, 3.4; Br, 19.4; N, 10.2; S, 7.8%. Found: C, 55.3; H, 3.2; Br, 19.1; N, 10.5; S, 7.4%.

5-Aryl-3-bromo-2-phenyl-7-hydrazinopyrazolo[1,5-c]pyrimidines (13a-d).
(General Procedure):
A suspension of 12a-d (0.00262 mol) in ethanol (100 mL) was heated under reflux with 99% hydrazine hydrate (10 mL) for 20 h. The product, which separated out was filtered off, washed with EtOH and crystallized from CHCl₃/EtOH as colorless needles.

3-Bromo-2,5-diphenyl-7-hydrazinopyrazolo[1,5-c]pyrimidine (13a).
Yield (0.7 g, 70%), mp 173-174 °C; IR: 3409,3315 (NH₂), 3207 (NH), 1579 (pyrazole ring C=N), 1480 (pyrimidine ring C=N) and 1436 cm⁻¹ (pyrimidine ring C=C); MS: m/z (%): 383 (5, M⁺4), 382 (7, M+3), 381 (8, M+2), 379 (21, M²⁺), 366 (13), 351 (11), 140 (26), 77 (100); Anal. Calcd for C₁₈H₁₄BrN₅: C, 56.7; H, 3.7; Br, 21.0; N, 18.4%. Found: C, 56.6; H, 3.5; Br, 20.6; N, 18.3%.
3-Bromo-7-hydrazino-5-p-methylphenyl-2-phenylpyrazolo[1,5-c]pyrimidine (13b).
Yield (0.8 g, 80%), mp 191-192 °C; IR, 3477 (NH2), 3257 (NH), 1602 (pyrazole ring C=N), 1556 (pyrimidine ring C=N) and 1440 cm⁻¹ (pyrimidine ring C=C); ¹H NMR (CDCl₃): δ= 2.42 (s, 3H, CH₃) and 7.28-8.02 (m, 10H, aromatic-H + pyrimidine-H); MS: m/z (%): 395 (24, M+2), 394 (9, M+1), 393 (29, M⁺), 381 (7), 380 (12), 153 (20), 115 (27), 89 (30), 77 (100); Anal. Calcd for C₁₉H₁₆BrN₅: C, 57.9; H, 4.1; Br, 20.3; N, 17.8%. Found: C, 57.7; H, 4.0; Br, 19.9; N, 17.5%.

3-Bromo-7-hydrazino-5-p-methoxyphenyl-2-phenylpyrazolo[1,5-c]pyrimidine (13c).
Yield (0.76 g, 76%), mp 177-178 °C; IR: 3496, 3425 (NH₂), 3184 (NH), 1606 (pyrazole ring C=N), 1579 (pyrimidine ring C=N) and 1431 cm⁻¹ (pyrimidine ring C=C); ¹H NMR (CDCl₃): δ= 3.88 (s, 3H, OCH₃), 6.99-8.06 (m, 12H, 9 aromatic-H + exchangeable NHNH₂) and 7.18 (s, 1H, pyrimidine-H) MS: m/z (%): 411 (42, M+2), 410 (9, M+1), 409 (51, M⁺), 396 (20), 394 (26), 301(26), 126 (36), 77 (100), 75 (36), 51 (58); Anal. Calcd for C₁₉H₁₆BrN₅S: C, 55.6; H, 3.9; Br, 19.5; N, 17.1; S, 3.9%. Found: C, 55.5; H, 3.9; Br, 19.7; N, 17.0; S, 3.7%.

3-Bromo-7-hydrazino-5-p-chlorophenyl-2-phenylpyrazolo[1,5-c]pyrimidine (13d).
Yield (0.78 g, 78%), mp 209-210 °C; IR: 3415 (NH₂), 3265 (NH), 1571 (pyrazole ring C=N), 1495 (pyrimidine ring C=N) and 1454 cm⁻¹ (pyrimidine ring C=C); Anal. Calcd for C₁₈H₁₃BrClN₅: C, 52.1; H, 3.2; Br, 19.3; Cl, 8.6; N, 16.9%. Found: C, 52.4; H, 3.1; Br, 19.8; Cl, 8.3; N, 16.7%.

5-Aryl-7-bromo-8-phenyl-2H-pyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine-3-thiones (7a-d).
(General Procedure):
A mixture of 13a-d (0.00158 mol), potassium hydroxide (0.3 g. in 30 mL water) and carbon disulfide (10 mL) was heated under reflux in EtOH (100 mL) for 3 h. The reaction mixture was concentrated, poured onto crushed ice and acidified with diluted hydrochloric acid. The precipitated product was filtered off, washed with water and crystallized from CHCl₃/EtOH in colorless needles.

7-Bromo-5,8-diphenyl-2H-pyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine-3-thione (7a).
Yield (0.62 g, 92.5%), mp 247-248 °C; IR: 3310 (NH), 1652 (pyrazole ring C=N), 1585 (triazole ring C=N) and 1122 cm⁻¹ (C=S); Anal. Calcd for C₁₉H₁₂BrN₅S: C, 54.0; H, 2.7; Br, 18.9; N, 16.9; S, 7.6%. Found: C, 54.2; H, 2.6; Br, 18.5; N, 16.5; S, 7.5%.

7-Bromo-5-p-methylphenyl-8-phenyl-2H-pyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine-3-thione (7b).
Yield (0.8 g, 72.73%), mp 301-302 °C; IR: 3301 (NH), 1656 (pyrazole ring C=N), 1600 (triazole ring C=N), 1423 (pyrimidine ring C=C) and 1108 cm⁻¹ (C=S); MS: m/z (%): 438 (8, M+3), 437 (26, M+2), 436 (22, M+1), 435 (27, M⁺), 298 (33), 153 (17), 143 (13), 126 (13), 77 (100); Anal. Calcd for C₂₀H₁₄BrN₅S: C, 55.1; H, 3.2 Br, 18.3; N, 16.1; S 7.4%. Found: C, 54.9; H, 3.0 Br, 18.6; N, 15.7; S 7.7%. 
7-Bromo-5-\(p\)-methoxyphenyl-8-phenyl-2\(H\)-pyrazolo[1,5-\(c\)]-1,2,4-triazolo[4,3-\(a\)]pyrimidine-3-thione (7c).

Yield (0.48 g, 86.4\%), mp 293-294 °C; IR: 3282 (NH), 1654 (pyrazole ring C=N), 1605 (triazole ring C=N), 1431 (pyrimidine ring C=C) and 1125 cm\(^{-1}\) (C=S); \(^1\)H NMR (DMSO-\(d_6\)): \(\delta\) = 3.79 (s, 3H, OCH\(_3\)), 6.67 (s, 1H, pyrimidine-H), 6.92-7.95 (m, 9H, aromatic-H) and 14.17 (s, 1H, exchangeable NH); MS: m/z (%): 453 (41, M+2), 452 (33, M+1), 451 (36, M+), 450 (43), 314 (21), 313 (21), 226 (19), 126 (31), 92 (45), 89 (33), 77 (100); Anal. Calcd for C\(_{20}\)H\(_{14}\)BrN\(_5\)S: C, 53.1; H, 3.1; Br, 17.7; N, 15.5; S, 7.1\%. Found: C, 53.0; H, 3.1; Br, 18.2; N, 15.3; S, 7.3\%.

7-Bromo-5-\(p\)-chlorophenyl-8-phenyl-2\(H\)-pyrazolo[1,5-\(c\)]-1,2,4-triazolo[4,3-\(a\)]pyrimidine-3-thione (7d).

Yield (0.45 g, 81.82\%), mp 293-294 °C; IR: 3313 (NH), 1654 (pyrazole ring C=N), 1590 (triazole ring C=N), 1429 (pyrimidine ring C=C) and 1095 cm\(^{-1}\) (C=S); \(^1\)H NMR (DMSO-\(d_6\)): \(\delta\) = 6.81 (s, 1H, pyrimidine-H), 7.43-7.94 (m, 9 aromatic-H), 14.24 (s, 1H, exchangeable NH); MS: m/z (%): 458 (17, M+3), 457 (40, M+2), 456 (21, M+), 455 (38), 344 (29), 211 (17), 103 (27), 77 (100), 63 (35), 59 (54); Anal. Calcd for C\(_{19}\)H\(_{11}\)BrClN\(_5\)S: C, 50.0; H, 2.4; Br, 17.5; Cl, 7.8; N, 15.3; S, 7.0\%. Found: C, 49.8; H, 2.3; Br, 17.9; Cl, 7.3; N, 15.0; S, 7.5\%.

5-Aryl-8-phenyl-2\(H\)-pyrazolo[1,5-\(c\)]-1,2,4-triazolo[4,3-\(a\)]pyrimidin-3-ones (8a-d).

(General Procedure):
A mixture of 2a-d (0.00102 mol), 30% hydrogen peroxide (4 mL), and 10% sodium hydroxide (18 mL) was heated under reflux on a boiling water bath for 3 h. The resulting solution afforded after adjusting the \(pH\) to 6 by addition of hydrochloric acid. It was filtered off, washed several times with water, dried, and crystallized from EtOH as colorless needles.

5,8-Diphenyl-2\(H\)-pyrazolo[1,5-\(c\)]-1,2,4-triazolo[4,3-\(a\)]pyrimidin-3-one (8a).

Yield (0.28 g, 84.8\%), mp 265-266 °C; IR: 3479 (OH), 3043 (NH), 1620 (C=O), 1577 (pyrazole ring C=N), 1525 (triazole ring C=N) and 1436 cm\(^{-1}\) (pyrimidine ring C=C); \(^1\)H NMR (CDCl\(_3\)): \(\delta\) = 6.93 (s, 1H, pyrazole-H), 6.96 (s, 1H, pyrimidine-H) and 7.38-8.04 (m, 11H, 10 aromatic-H + exchangeable NH); Anal. Calcd for C\(_{19}\)H\(_{13}\)N\(_5\)O: C, 69.7; H, 4.0; N, 21.4\%. Found: C, 69.6; H, 4.1; N, 21.2\%.

5-\(p\)-Methylphenyl-8-phenyl-2\(H\)-pyrazolo[1,5-\(c\)]-1,2,4-triazolo[4,3-\(a\)]pyrimidin-3-one (8b).

Yield (0.35 g, 91.6\%), mp 239-240 °C; IR: 3440 (OH), 3045 (NH), 1633 (C=O), 1612 (pyrazole ring C=N), 1575 (triazole ring C=N) and 1446 cm\(^{-1}\) (pyrimidine ring C=C); \(^1\)H NMR (CDCl\(_3\)): \(\delta\) = 2.47 (s, 3H, CH\(_3\)), 6.80 (s, 1H, pyrazole-H), 6.85-9.28 (m, 10H, 9 aromatic-H + exchangeable NH) and 7.73 (s, 1H, pyrimidine-H); MS: m/z (%): 346 (16), 345 (26), 327 (22), 326 (28), 325 (100), 317 (14), 301 (28), 300 (35), 297 (21), 77 (12); Anal. Calcd for C\(_{20}\)H\(_{15}\)N\(_5\)O: C, 70.4; H, 4.4; N, 20.5\%. Found: C, 70.1; H, 4.3; N, 20.3\%. 
5-\textit{p}-Methoxyphenyl-8-phenyl-2\textit{H}-pyrazolo[1,5-\textit{c}]-1,2,4-triazolo[4,3-\textit{a}]pyrimidin-3-one (8c).

Yield (0.31 g, 81.2\%), mp 211-212 °C; IR: 3440 (OH), 3045 (NH), 1643 (C=O), 1600 (pyrazole ring C=N), 1577 (triazole ring C=N) and 1454 cm\(^{-1}\) (pyrimidine ring C=C); \(^1\)H NMR (CDCl\(_3\)): \(\delta= 3.89\) (s, 3H, OCH\(_3\)), 6.82 (s, 1H, pyrazole-H), 7.01-9.33 (m, 10H, 9 aromatic-H + exchangeable NH) and 7.70 (s, 1H, pyrimidine-H); Anal. Calcd for C\(_{20}\)H\(_{15}\)N\(_5\)O\(_2\): C, 67.2; H, 4.2; N, 19.6%. Found: C, 67.1; H, 4.4; N, 19.9%.

5-\textit{p}-Chlorophenyl-8-phenyl-2\textit{H}-pyrazolo[1,5-\textit{c}]-1,2,4-triazolo[4,3-\textit{a}]pyrimidin-3-one (8d).

Yield (0.33 g, 86.2\%), mp 266-267 °C; IR: 3446 (OH), 3049 (NH), 1608 (C=O), 1581 (pyrazole ring C=N), 1446(triazole ring C=N) and 1406 cm\(^{-1}\) (pyrimidine ring C=C); \(^1\)H NMR (CDCl\(_3\)): \(\delta= 6.85\) (s, 1H, pyrazole-H), 7.44-9.29 (m, 10H, 9 aromatic-H + exchangeable NH) and 7.77 (s, 1H, pyrimidine-H); Anal. Calcd for C\(_{19}\)H\(_{12}\)ClN\(_5\)O: C, 63.1; H, 3.3; Cl, 9.8; N, 19.4%. Found: C, 63.0; H, 3.3; Cl, 10.2; N, 19.2%.

3,3’-Dithiobis(5-aryl-8-phenylpyrazolo[1,5-\textit{c}]-1,2,4-triazolo[4,3-\textit{a}]pyrimidine)s (9a-d).

(General Procedure):

A solution of 5-aryl-8-phenyl-2\textit{H}-pyrazolo[1,5-\textit{c}]-1,2,4-triazolo[4,3-\textit{a}]pyrimidine-3-thiones (2a-d, 0.4 g, 0.00102 mol ) in acetic acid (20 mL) was treated portionwise with 20\% aqueous sodium nitrite (15 mL). The mixture was heated on a boiling water bath with stirring for 1 h, whereby a solid started to separate. The reaction mixture was then diluted with water and the precipitated 3,3’-dithiobis(5-aryl-8-phenylpyrazolo[1,5-\textit{c}]-1,2,4-triazolo[4,3-\textit{a}]pyrimidine)s (11a-d) were filtered, washed with water, dried and crystallized from DMF in colorless needles.

3,3’-Dithiobis(5,8-diphenylpyrazolo[1,5-\textit{c}]-1,2,4-triazolo[4,3-\textit{a}]pyrimidine) (9a).

Yield (0.3 g, 85.7\%), mp 315-316 °C; IR: 1641 (pyrazole ring C=N), 1566 (triazole ring C=N) and 1421 cm\(^{-1}\) (pyrimidine ring C=C); Anal. Calcd for C\(_{38}\)H\(_{24}\)N\(_{10}\)S\(_2\): C, 66.7; H, 3.5; N, 20.5; S, 9.6%. Found: C, 66.9; H, 3.8; N, 20.3; S, 9.0%.

3,3’-Dithiobis(5-\textit{p}-methylphenyl-8-phenylpyrazolo[1,5-\textit{c}]-1,2,4-triazolo[4,3-\textit{a}]pyrimidine) (9b).

Yield (0.31 g, 77.5\%), mp 181-182 °C; IR: 1627 (pyrazole ring C=N), 1579 (triazole ring C=N) and 1421 cm\(^{-1}\) (pyrimidine ring C=C); \(^1\)H NMR (CDCl\(_3\)): \(\delta= 2.41\) (s, 6H, 2CH\(_3\)), 6.81 (s, 2H, 2 pyrazole-H) and 6.90-8.25 (m, 20H, 18 aromatic-H +2 pyrimidine-H); Anal. Calcd for C\(_{40}\)H\(_{28}\)N\(_{10}\)S\(_2\): C, 67.4; H, 3.9; N, 19.7; S, 9.0%. Found: C, 67.3; H, 3.7; N, 19.3; S, 9.3%.

3,3’-Dithiobis(5-\textit{p}-methoxyphenyl-8-phenylpyrazolo[1,5-\textit{c}]-1,2,4-triazolo[4,3-\textit{a}]pyrimidine) (9c).

Yield (0.33 g, 83\%), mp 197-198 °C; IR: 1643 (pyrazole ring C=N), 1591 (triazole ring C=N) and 1450 cm\(^{-1}\) (pyrimidine ring C=C); \(^1\)H NMR (CDCl\(_3\)): \(\delta= 3.87\) (s, 6H, 2OCH\(_3\)), 6.80 (s, 2H, 2 pyrazole-H) and 6.92-8.07 (m, 20H, 18 aromatic-H +2 pyrimidine-H); Anal. Calcd for C\(_{40}\)H\(_{28}\)N\(_{10}\)O\(_2\)S\(_2\): C, 64.5; H, 3.8; N, 18.8; S, 8.6%. Found: C, 64.3; H, 3.6; N, 18.5; S, 8.9%.

3,3’-Dithiobis(5-\textit{p}-chlorophenyl-8-phenylpyrazolo[1,5-\textit{c}]-1,2,4-triazolo[4,3-\textit{a}]pyrimidine) (9d).

Yield (0.3 g, 75\%), mp 167 °C; IR: 1637 (pyrazole ring C=N), 1579 (triazole ring C=N) and 1450 cm\(^{-1}\)
(pyrimidine ring C=C); $^1$H NMR (CDCl$_3$): $\delta$ = 6.82 (s, 2H, 2 pyrazole-H) and 7.07-8.00 (m, 20H, 18 aromatic-H + 2 pyrimidine-H); Anal. Calcd for C$_{38}$H$_{22}$Cl$_2$N$_{10}$S$_2$: C, 60.6; H, 2.9; Cl, 9.4; N, 18.6; S, 8.5%. Found: C, 60.4; H, 2.8; Cl, 8.8; N, 18.2; S, 8.9%.

3,3'-Dithiobis(5-aryl-6-phenylazo-8-phenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine)s (10a-d).

(General Procedure):
An aqueous sodium hydroxide solution (10%, 6 mL) was added to a suspension of 2a-d (0.00102 mol) in EtOH (15 mL). The mixture was cooled to 5 ºC and gradually treated with a solution of benzenediazonium chloride (prepared from 1 mL aniline) with stirring for 3 h. The product was collected by filtration, and crystallized from CHCl$_3$/EtOH in black needles.

3,3'-Dithiobis(6-phenylazo-5,8-diphenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine) (10a).
Yield (0.43 g, 93.5%), mp 141-142 ºC; IR: 1591 (pyrazole ring C=N), 1490 (triazole ring C=N) and 1410 cm$^{-1}$ (pyrimidine ring C=C); $^1$H NMR (CDCl$_3$): $\delta$ = 7.2-8.09 (m, 32H, 30 aromatic-H + 2 pyrazole-H); Anal. Calcd for C$_{50}$H$_{32}$N$_{14}$S$_2$: C, 67.3; H, 3.6; N, 22.0; S, 7.2%. Found: C, 67.2; H, 3.8; N, 21.6; S, 6.7%.

3,3'-Dithiobis(5-p-methylphenyl-8-phenyl-6-phenylazopyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine) (10b).
Yield (0.41 g, 78.8%), mp 203-204 ºC; IR: 1629 (pyrazole ring C=N), 1556 (triazole ring C=N), 1446 cm$^{-1}$ (pyrimidine ring C=C); $^1$H NMR (CDCl$_3$): $\delta$ = 2.41 (s, 6H, 2CH$_3$) and 6.22-8.55 (m, 28 aromatic-H + 2 pyrazole-H); Anal. Calcd for C$_{52}$H$_{36}$N$_{14}$S$_2$: C, 67.8; H, 3.9; N, 21.3; S, 7.0%. Found: C, 68.0; H, 3.7; N, 21.1; S, 6.6%.

3,3'-Dithiobis(5-p-methoxyphenyl-6-phenylazo-8-phenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine) (10c).
Yield (0.46 g, 90.2%), mp 167-168 ºC; IR: 1573 (pyrazole ring C=N), 1510 (triazole ring C=N), 1450 cm$^{-1}$ (pyrimidine ring C=C); $^1$H NMR (CDCl$_3$): $\delta$ = 3.87 (s, 6H, 2OCH$_3$), 6.67 (s, 1H, pyrazole-H) and 6.78-8.00 (m, 28 aromatic-H); Anal. Calcd for C$_{52}$H$_{36}$N$_{14}$O$_2$S$_2$: C, 65.5; H, 3.8; N, 20.6; S, 6.7%. Found: C, 65.4; H, 3.6; N, 20.9; S, 6.4%.

3,3'-Dithiobis(5-p-chlorophenyl-6-phenylazo-8-phenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine) (10d).
Yield (0.44 g, 86.3%), mp 195-196 ºC; IR: 1614 (pyrazole ring C=N), 1550 (triazole ring C=N) and 1446 cm$^{-1}$ (pyrimidine ring C=C); $^1$H NMR (CDCl$_3$): $\delta$ = 6.83 (s, 1H, pyrazoleH) and 7.39-8.08 (m, 28 aromatic H); Anal. Calcd for C$_{50}$H$_{30}$Cl$_2$N$_{10}$S$_2$: C, 62.4; H, 3.1; Cl, 7.4; N, 20.4; S, 6.7%. Found: C, 62.4; H, 3.0; Cl, 7.6; N, 20.1; S, 6.4%.
ANTIBACTERIAL ACTIVITY STUDIES
Thirteen derivatives of pyrazolotriazolopyrimidines were tested for antibacterial activity against some microorganisms; Gram positive aerobic bacteria such as Micrococcus luteus isolated from venous ulcer and Staphylococcus aureus isolated from diabetic foot beside an anaerobic bacteria Peptostococcus isolated from diabetic foot and Gram negative aerobic bacteria such as Klebsiella pneumonia isolated from urine, Proteus mirabilis isolated from diabetic foot and Pseudomonas aeruginosa isolated from diabetic foot. Bio-assays were determined in dimethylsulfoxide as Minimum Inhibitory Concentration (MIC) in concentration of 16, 32, 64, 128, 212 and 256 (µg/mL) (Table 1).

Table 1. Minimum Inhibitory Concentration (µg/mL) of Pyrazolotriazolopyrimidine Derivatives (2c, 4b-d, 5d, 8b,c, 9b-d and 10b-d)

<table>
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<tr>
<th>Compound number</th>
<th>Gram Positive</th>
<th>Gram Negative</th>
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<tr>
<td>2c</td>
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<td>&gt;512</td>
</tr>
<tr>
<td>4b</td>
<td>&gt;512</td>
<td>&gt;512</td>
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<tr>
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REFERENCES
54, 14278c).


