Synthesis and Electrophilic Substitutions of Novel Pyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidines

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Abstract: 5-Aryl-7-hydrazino-2-phenylpyrazolo[1,5-c]pyrimidines 1 were used as precursors for the preparation of a new series of 5-aryl-8-phenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidines 2. The reactions of 2 with certain electrophilic reagents gave the respective 6-substituted derivatives 3-5 rather than the 7-isomeric products. Formylation of the key compounds 1 with ethyl formate yielded the formyl derivatives 6. Furthermore, boiling of compounds 1 with acetic acid afforded 7-acetylhydrazino-5-aryl-2-phenylpyrazolo[1,5-c]pyrimidines 7. Bromination of 7 yielded the dibromo-derivatives 8, while their iodination and nitration gave the monosubstituted derivatives 9 and 10, respectively. Also, treatment of 1 with boiling acetic anhydride yielded the triacetyl derivatives 11. The structure of synthesized products was confirmed by elemental analyses, IR, 1H NMR and MS spectra.

Keywords: pyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidines; synthesis; electrophilic substitution reactions; dehydrative cyclization

1. Introduction

The pyrazolo[1,5-c]pyrimidine ring represents a biologically and synthetically important class of compounds. Many pyrazolo[1,5-c]pyrimidines are known to possess significant hypnotic, tranquilizing, fungicidal, insecticidal and antibacterial activities [1-3]. Also, the coordination of pyrazolo[1,5-c]pyrimidines to transition metal ions such as Cu²⁺ and Ni²⁺ enhances their biological activities [4-7].
In the last few decades, the chemistry of 1,2,4-triazoles and their fused heterocyclic derivatives has received considerable attention owing to their synthetic and effective biological importance. 1,2,4-Triazole moieties have been incorporated into a wide variety of therapeutically interesting drug candidates, e.g., triazolam [8], alprazolam [9], etizolam [10], and furacyn [11], including anti-inflammatory, central nervous system stimulants, sedatives, anti-anxiety compounds, antimicrobial agents [12-15] and antifungal ones such as fluconazole, intraconazole, voriconazole [16,17].

The above mentioned therapeutic activity has prompted the present investigation to synthesize the pyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidines ring system 2 and a new series of 7-acetylhydrazino-5-aryl-2-phenylpyrazolo[1,5-c]pyrimidine derivatives 7.

2. Results and Discussion

Much work from our laboratory has utilized hydrazino heterocycles as raw materials for the synthesis of various types of heterocyclic compounds [18-21]. In the present investigation, the target pyrazolotriazolopyrimidine compounds were synthesized from 5-aryl-7-hydrazino-2-phenylpyrazolo[1,5-c]pyrimidines 1a-d that were prepared via a sequence of reactions from ethyl phenylpropiolate [2,22]. Heating of 1a-d with formic acid under reflux yielded a novel series of 5-aryl-8-phenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidines 2a-d (Scheme 1). The structures of 2a-d were deduced from their spectral analyses. Thus, the $^1$H-NMR spectra revealed the presence of three singlets for the pyrazole ring proton at $\delta_H$ 6.91–7.33 ppm, of the pyrimidine ring proton at $\delta_H$ 7.43–7.44 ppm and of triazole ring proton at $\delta_H$ 8.53–9.00 ppm, in addition to the aromatic ring protons and the absence of NH signals. The MS spectra also showed a molecular ion peak as a base peak that indicated the stability of this ring.

The electrophilic substitution reactions of pyrazolotriazolopyrimidines 2a-d such as bromination with bromine, iodination with iodine monochloride and nitration with nitric and sulfuric acids in glacial acetic acid gave the respective 5-aryl-6-bromo-, 5-aryl-6-iodo- and 5-aryl-6-nitro-8-phenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidines 3a-d, 4a-d and 5a-d. Their $^1$H-NMR spectra revealed the absence of signals due to the pyrimidine ring proton and the presence of a pyrazole ring proton signal at $\delta_H$ 6.81–7.33 ppm and of triazole ring proton at $\delta_H$ 8.53–9.00 ppm, in addition to the aromatic ring protons and the absence of NH signals. The MS spectra also showed a molecular ion peak as a base peak that indicated the stability of this ring.

Treatment of 1a-d with boiling ethyl formate afforded 5-aryl-7-formylhydrazino-2-phenylpyrazolo[1,5-c]pyrimidines 6a-d. Their $^1$H-NMR spectra showed a new characteristic signal at $\delta_H$ 7.98–8.08 ppm corresponding to the formyl proton, in addition to the aromatic ring protons at $\delta_H$ 7.20–7.99 ppm, with other characteristic signals; a singlet for the exchangeable two NH protons which were assigned at $\delta_H$ 4.73–4.80 ppm, a singlet at $\delta_H$ 6.68–6.72 ppm for the pyrazole ring proton and a singlet at $\delta_H$ 7.19–7.29 ppm for the pyrimidine ring proton.
Scheme 1. Synthesis and electrophilic substitution reactions of pyrazolotriazolopyrimidines.

Boiling of hydrazine derivatives 1a-d with acetic acid under reflux afforded 7-acetylhydrazino-5-aryl-2-phenylpyrazolo[1,5-c]pyrimidines 7a-d (Scheme 2). The structures of 7a-d were confirmed by their $^1$H-NMR spectra, which revealed an acetyl group proton singlet at $\delta_H$ 2.04–2.36 ppm, in addition to the characteristic signals of pyrazole and pyrimidine ring protons, two exchangeable NH protons and aromatic ring protons. The mass spectra of 7a-d which showed their molecular ion peaks as a base peak also confirmed the structures.

Next, the electrophilic substitution reaction of 7a-d via bromination with bromine in acetic acid gave the unexpected dibromo derivatives 8a-d rather than the monobromo derivatives. Their $^1$H-NMR spectra showed the absence of the signals of both pyrazole and pyrimidine ring protons and the presence of acetyl group protons, in addition to the other characteristic signals. These unexpected obtained products may be due to the excess bromine added to obtain a homogenous reaction mixture.

Iodination and nitration of 7a-d yielded the expected 5-aryl-2-phenyl-3-substituted-pyrazolo[1,5-c]pyrimidine derivatives 9a-d and 10a-d, respectively. Their $^1$H-NMR spectra revealed the absence of pyrazole ring proton and the presence of pyrimidine ring proton at $\delta_H$ 7.18–7.73 ppm as well as the other characteristic signals.
Scheme 2. Synthesis and electrophilic substitution reactions of 7-acetyl-hydrazinopyrazolopyrimidines.

Furthermore, acetylation of 1a-d with boiling acetic anhydride afforded the triacetyl derivatives 11a-d. Their $^1$H-NMR spectra revealed the absence of the NH protons of the starting hydrazine derivatives and the presence of signals at $\delta_H$ 2.42–2.56 ppm corresponding to the three acetyl groups protons, as well as a singlet at $\delta_H$ 6.87–7.28 ppm for the pyrazole ring proton and a singlet at $\delta_H$ 7.70–8.24 ppm for the pyrimidine ring proton, in addition to the aromatic ring protons at $\delta_H$ 6.98–8.05 ppm. The structures of 11a-d were also confirmed by their MS spectra which showed fragmentation process involving a sequential elimination of two ketene molecules to give the most stable one (M$^+$-2CH$_2$CO) as a base peak.

3. Experimental

3.1. General

Melting points were determined on a Kofler Block and are uncorrected. Elemental analyses were carried out in the Microanalytical Laboratory of the Faculty of Science, Cairo University. The IR
spectra of compounds were recorded on a Bruker Tensor 37 Fourer Transform infrared 8400 spectrophotometer using potassium bromide pellets and frequencies are reported in cm\(^{-1}\). The \(^1\)H- NMR spectra were recorded on a JEOL JNM ECA 500 MHZ instrument and chemical shifts \(\delta_H\) are given in ppm relative to tetramethylsilane used as internal standard. Mass spectra were recorded at 70 ev with a GCMS-QP 1000 EX spectrometer. Reactions were routinely followed by thin layer chromatography (TLC; Merck Kieselgel60-F254 precoated plastic plates). The spots were detected by iodine. 5-Aryl-7-hydrazino-2- phenylpyrazolo[1,5-c]pyrimidines 1 were prepared from the respective acetylenic \(\beta\)-diketones as described earlier [2,22].

3.2. Synthesis of Compounds

3.2.1. 5-Aryl-8-phenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidines 2a-d

A mixture of 5-aryl-7-hydrazino-2-phenylpyrazolo[1,5-c]pyrimidines (1a-d, 1 mmol) and formic acid (10 mL, 99%) was heated under reflux for 10 h. The mixture was evaporated under reduced pressure and the obtained residue was triturated with water, filtered, washed with EtOH and crystallized from EtOH to give the 5-aryl-8-phenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidines 2a-d as colorless needles.

5,8-Diphenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine (2a). Yield 81%, 0.25 g, mp 245–246 °C; IR (\(\nu_{max}\), cm\(^{-1}\)): 1649 (pyrazole ring C=N), 1580 (triazole ring C=N), and 1476 (C=C); \(^1\)H-NMR (CDCl\(_3\), \(\delta_H\) ppm): 6.91 (s, 1H, pyrazole-H), 7.43 (s, 1H, pyrimidine-H), 7.45–7.64 (m, 8H, aromatic-H), 8.05 (d, 2H, aromatic-H) and 8.53 (s, 1H, triazole-H); MS, \(m/z\) (%): 312 (M\(^{+}\)+1, 100), 285 (M\(^{+}\)+CN, 4), 257 (M\(^{+}\)+CN\(_2\), 3), 255 (M\(^{+}\)+CH\(_2\)N\(_3\), 16) and 227 (M\(^{+}\)+CH\(_2\)N\(_5\), 8); Anal. Calc. for C\(_{19}\)H\(_{13}\)N\(_5\) (311.34): C, 73.30; H, 4.21; N, 22.49%, found: C, 73.27; H, 4.22; N, 22.53%.

8-Phenyl-5-p-tolylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine (2b). Yield 76%, 0.25 g, mp 247–248 °C; IR (\(\nu_{max}\), cm\(^{-1}\)): 1643 (pyrazole ring C=N), 1577 (triazole ring C=N), and 1454 (C=C); \(^1\)H NMR (DMSO-d\(_6\), \(\delta_H\) ppm): 2.39 (s, 3H, CH\(_3\)), 7.03 (d, 2H, aromatic-H), 7.26 (s, 1H, pyrazole-H),7.39–7.51 (m, 5H, aromatic-H), 7.44 (s, 1H, pyrimidine-H), 7.65 (d, 2H, aromatic-H) and 8.96 (s, 1H, triazole-H); MS, \(m/z\) (%): 327 (M\(^{+}\)+2, 17), 325 (M\(^{+}\), 100), 297 (M\(^{+}\)+N\(_2\), 24), 282 (M\(^{+}\)+CH\(_2\)N\(_3\), 8),255 (M\(^{+}\)+C\(_2\)H\(_4\)N\(_3\), 7) and 227 (M\(^{+}\)+C\(_2\)H\(_4\)N\(_5\), 10); Anal. Calc. for C\(_{20}\)H\(_{15}\)N\(_5\) (325.37): C, 73.83; H, 4.65;N, 21.52%, found: C, 73.87; H, 4.62; N, 21.55%.

5-(p-Methoxyphenyl)-8-phenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine (2c). Yield 74%, 0.25 g, mp 237–238 °C; IR (\(\nu_{max}\), cm\(^{-1}\)): 1643 (pyrazole ring C=N), 1578 (triazole ring C=N), and 1454 (C=C); \(^1\)H NMR (CDCl\(_3\), \(\delta_H\) ppm): 3.92 (s, 3H, CH\(_3\)), 6.93 (s, 1H, pyrazole-H), 7.10 (d, 2H, aromatic-H), 7.26 (s, 1H, pyrazole-H),7.39–7.51 (m, 5H, aromatic-H), 7.44 (s, 1H, pyrimidine-H), 7.57 (d, 2H, aromatic-H), 8.05 (d, 2H, aromatic-H) and 8.55 (s, 1H, triazole-H); MS, \(m/z\) (%): 343 (M\(^{+}\)+2, 15), 341 (M\(^{+}\), 100), 326 (M\(^{+}\)+CH\(_3\), 3), 313(M\(^{+}\)+N\(_2\), 10), 299 (M\(^{+}\)+CH\(_2\)N\(_2\), 8), 285 (M\(^{+}\)+C\(_2\)H\(_4\)N\(_2\), 2) and 270 (M\(^{+}\)+C\(_2\)H\(_3\)N\(_2\)O, 11); Anal. Calc. for C\(_{20}\)H\(_{15}\)N\(_5\)O (341.37): C, 70.37; H, 4.43; N, 20.52%, found: C, 70.40; H, 4.40; N, 20.55%.
5-(p-Chlorophenyl)-8-phenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine (2d). Yield 71%, 0.25 g, mp 299–300 °C; IR (ν_{max}, cm^{-1}): 1643 (pyrazole ring C=N), 1583 (triazole ring C=N), and 1467 (C=C); ^1H NMR (DMSO-d_6, δ_{H}, ppm): 7.33 (s, 1H, pyrazole-H), 7.43 (s, 1H, pyrimidine-H), 7.44–7.52 (m, 3H, aromatic-H), 7.66 (d, 2H, aromatic-H), 7.79 (d, 2H, aromatic-H), 8.04 (d, 2H, aromatic-H) and 9.00 (s, 1H, triazole-H); MS, m/z (%) = 347 (M^+ + 1, 52), 345 (M^+ - 1, 100), 319 (M^+ - HCN, 8), 317 (M^+ - HN_2, 17), 289 (M^+ - C_2H_5N_2, 6), 282 (M^+ - HClN_2, 13), 255 (M^+ - C_2H_4ClN_2, 16) and 227 (M^+ - C_3H_6ClN_3, 8); Anal. Calc. for C_{19}H_{12}ClN_5 (345.79): C, 66.00; H, 3.50; N, 20.25%, found: C, 59.98; H, 3.50; N, 20.22%.

3.2.2. 5-Aryl-6-bromo-8-phenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidines 3a-d

A solution of bromine (0.06 mL, 1.2 mmol) in acetic acid (10 mL) was gradually added to a suspension of 5-aryl-8-phenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidines 2a-d (1 mmol) in acetic acid (10 mL) with stirring for 3 h at room temperature. The precipitated 5-aryl-6-bromo-8-phenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidines 3a-d were filtered, washed with water, dried and crystallized from EtOH as colorless needles.

6-Bromo-5,8-diphenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine (3a). Yield 75%, 0.30 g, mp 235–236 °C; IR (ν_{max}, cm^{-1}): 1640 (pyrazole ring C=N), 1580 (triazole ring C=N), and 1455 (C=C); ^1H NMR (CDCl_3, δ_{H}, ppm): 6.92 (s, 1H, pyrazole-H), 7.43–7.69 (m, 8H, aromatic-H), 8.14 (d, 2H, aromatic-H) and 8.58 (s, 1H, triazole-H); MS, m/z (%) = 390 (M^+, 100), 362 (M^+ - N_2, 13), 310 (M^+ - Br, 2), 282 (M^+ - BrN_2, 13), 255 (M^+ - CHBrN_3, 12) and 227 (M^+ - CHBrN_5, 6); Anal. Calc. for C_{19}H_{12}BrN_5 (390.24): C, 58.48; H, 3.10; N, 17.95%, found: C, 58.52; H, 3.08; N, 17.90%.

6-Bromo-8-phenyl-5-p-tolylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine (3b). Yield 75%, 0.30 g, mp 215–216 °C; IR (ν_{max}, cm^{-1}): 1636 (pyrazole ring C=N), 1578 (triazole ring C=N), and 1421 (C=C); ^1H NMR (CDCl_3, δ_{H}, ppm): 2.49 (s, 3H, CH_3), 6.90 (s, 1H, pyrazole-H), 7.41–7.57 (m, 7H, aromatic-H), 8.14 (d, 2H, aromatic-H) and 8.60 (s, 1H, triazole-H); MS, m/z (%) = 407 (M^+ + 3, 8), 405 (M^+, 100), 377 (M^+ - HCN, 8), 324 (M^+ - Br, 2), 281 (M^+ - CH_3BrN_2, 6) and 254 (M^+ - C_2H_4BrN_3, 5); Anal. Calc. for C_{20}H_{14}BrN_5 (404.26): C, 59.42; H, 3.49; N, 17.32%, found: C, 59.39; H, 3.45; N, 17.27%.

6-Bromo-5-(p-methoxyphenyl)-8-phenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine (3c). Yield 71%, 0.30 g, mp 213–214 °C; IR (ν_{max}, cm^{-1}): 1632 (pyrazole ring C=N), 1587 (triazole ring C=N), and 1427 (C=C); ^1H NMR (CDCl_3, δ_{H}, ppm): 3.90 (s, 3H, OCH_3), 6.81 (s, 1H, pyrazole-H), 7.09 (d, 2H, aromatic-H), 7.44–7.56 (m, 3H, aromatic-H), 7.59 (d, 2H, aromatic-H), 8.10 (d, 2H, aromatic-H) and 8.57 (s, 1H, triazole-H); MS, m/z (%) = 422 (M^+ + 2, 100), 420 (M^+, 80), 405 (M^+ + 1, 100), 391 (M^+ - HCN, 8), 378 (M^+ - CH_2N_2, 5), 350 (M^+ - C_2H_4N_3, 6), 340 (M^+ - Br, 3), 313 (M^+ - CHBrN_4, 4), 281 (M^+ - CH_3BrN_2O, 5) and 269 (M^+ - C_2H_3BrN_2O, 13); Anal. Calc. for C_{20}H_{14}BrN_5O (420.26): C, 57.16; H, 3.36; N, 16.66%, found: C, 57.20; H, 3.38; N, 16.70%.

6-Bromo-5-(p-chlorophenyl)-8-phenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine (3d). Yield 71%, 0.30 g, mp 238–239 °C; IR (ν_{max}, cm^{-1}): 1637 (pyrazole ring C=N), 1580 (triazole ring C=N),
and 1414 (C=C); ¹H NMR (CDCl₃, δH, ppm): 6.92 (s, 1H, pyrazole-H), 7.47–7.66 (m, 7H, aromatic-H), 8.14 (d, 2H, aromatic-H) and 8.55 (s, 1H, triazole-H); MS, m/z (%) = 429 (M⁺+4, 3), 428 (M⁺+3, 38), 426 (M⁺+1, 100), 424 (M⁺-1, 76), 398 (M⁺-HCN, 11), 317 (M⁺-BrN₂, 8), 289 (M⁺-C₂H₅BrN₂, 8), 281 (M⁺-HBrClN₂, 15), 253 (M⁺-C₂H₂BrClN₂, 10) and 226 (M⁺-C₃H₆BrClN₃, 7); Anal. Calc. for C₁₉H₁₁BrClN₅ (424.68): C, 53.74; H, 2.61; N, 16.49%; found: C, 53.72; H, 2.57; N, 16.50%.

3.2.3. 5-Aryl-6-iodo-8-phenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidines 4a-d

A solution of iodine monochloride (0.2 g, 1.2 mmol) in acetic acid (10 mL) was gradually added to a suspension of 5-aryl-8-phenylpyrazolo[1,5-c]-1,2,4-triazolo[3,4-a]pyrimidines 2a-d (1 mmol) 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 5-aryl-6-iodo-8-phenylpyrazolo[1,5,c]-1,2,4-triazolo[3,4-a]pyrimidines 4a-d were filtered, washed with water, dried and crystallized from EtOH as colorless needles.

6-Iodo-5,8-diphenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine (4a). Yield 91%, 0.40 g, mp 281–282 °C; IR (νmax, cm⁻¹): 1640 (pyrazole ring C=N), 1575 (triazole ring C=N), and 1405 (C=C); ¹H NMR (CDCl₃, δH, ppm): 6.94 (s, 1H, pyrazole-H), 7.50–7.69 (m, 8H, aromatic-H), 8.10 (d, 2H, aromatic-H) and 8.61 (s, 1H, triazole-H); MS, m/z (%) = 437 (M⁺, 100), 409 (M⁺-N₂, 5), 310 (M⁺-I, 7), 282 (M⁺-C₂H₂N₃, 4) and 227 (M⁺-C₃H₅N₃, 8); Anal. Calc. for C₁₉H₁₂IN₅ (437.24): C, 52.19; H, 2.77; N, 15.52%, found: C, 52.17; H, 2.80; N, 15.60%.

6-Iodo-8-phenyl-5-p-tolylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine (4b). Yield 89%, 0.40 g, mp 245–246 °C; IR (νmax, cm⁻¹): 1633 (pyrazole ring C=N), 1576 (triazole ring C=N), and 1416 (C=C); ¹H NMR (CDCl₃, δH, ppm): 2.49 (s, 3H, CH₃), 6.90 (s, 1H, pyrazole-H), 7.41–7.69 (m, 7H, aromatic-H), 8.08 (d, 2H, aromatic-H) and 8.60 (s, 1H, triazole-H); MS, m/z (%) = 453 (M⁺+2, 9), 452 (M⁺+1, 100), 423 (M⁺-N₂, 5), 325 (M⁺+1-I, 12), 296 (M⁺-C₂H₂N₃, 4) and 269 (M⁺-C₃H₅N₃, 8); Anal. Calc. for C₂₀H₁₄IN₅ (451.26): C, 53.23; H, 3.13; N, 15.52%, found: C, 53.27; H, 3.15; N, 15.50%.

6-Iodo-5-(p-methoxyphenyl)-8-phenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine (4c). Yield 85%, 0.40 g, mp 225–226 °C; IR (νmax, cm⁻¹): 1623 (pyrazole ring C=N), 1576 (triazole ring C=N), and 1458 (C=C); ¹H NMR (CDCl₃, δH, ppm): 3.93 (s, 3H, OCH₃), 6.86 (s, 1H, pyrazole-H), 7.12 (d, 2H, aromatic-H), 7.48–7.51 (m, 3H, aromatic-H), 7.61 (d, 2H, aromatic-H), 8.10 (d, 2H, aromatic-H) and 8.61 (s, 1H, triazole-H); MS, m/z (%) = 470 (M⁺+3, 3), 468 (M⁺+1, 100), 439 (M⁺-N₂, 6), 341 (M⁺+1-I, 12), 313 (M⁺-CHIN, 4), 285 (M⁺-CHIN₃, 7), 269 (M⁺-C₂H₂N₂O, 12) and 255 (M⁺-C₂H₂N₃O, 4); Anal. Calc. for C₂₀H₁₄IN₅O (467.26): C, 51.41; H, 3.02; N, 14.99%, found: C, 51.44; H, 3.00; N, 15.02%.

5-(p-Chlorophenyl)-6-iodo-8-phenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine (4d). Yield 85%, 0.40 g, mp 270–271 °C; IR (νmax, cm⁻¹): 1632 (pyrazole ring C=N), 1576 (triazole ring C=N), and 1458 (C=C); ¹H NMR (DMSO-d₆, δH, ppm): 7.02 (s, 1H, pyrazole-H), 7.49–7.54 (m, 3H, aromatic-H), 7.49–7.54 (m, 3H, aromatic-H), 7.61 (d, 2H, aromatic-H) and 8.10 (d, 2H, aromatic-H) and 8.61 (s, 1H, triazole-H); MS, m/z (%) = 470 (M⁺+3, 3), 468 (M⁺+1, 100), 439 (M⁺-N₂, 6), 341 (M⁺+1-I, 12), 313 (M⁺-CHIN, 4), 285 (M⁺-CHIN₃, 7), 269 (M⁺-C₂H₂N₂O, 12) and 255 (M⁺-C₂H₂N₃O, 4); Anal. Calc. for C₂₀H₁₄IN₅O (467.26): C, 51.41; H, 3.02; N, 14.99%, found: C, 51.44; H, 3.00; N, 15.02%.
aromatic-H), 7.65 (d, 2H, aromatic-H), 7.80 (d, 2H, aromatic-H), 7.92 (d, 2H, aromatic-H) and 9.04 (s, 1H, triazole-H); MS, m/z (%) = 475 (M+3, 3), 472 (M+, 100), 443 (M+-HN2, 3), 345 (M+-I, 7), 309 (M+-ClI, 2), 289 (M+-CH2I, 5), 282 (M+-CHCIIN, 8) and 241 (M+-C2H2ClIN3, 9); Anal. Calc. for C19H11ClIN5 (471.68): C, 48.38; H, 2.35; N, 14.85%, found: C, 48.40; H, 2.40; N, 14.90%.

3.2.4. 5-Aryl-6-nitro-8-phenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidines 5a-d

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 a suspension of 5-aryl-8-phenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidines 2a-d (1 mmol) 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 yellow precipitated solids were filtered, washed with cold water, dried and crystallized from EtOH to give the title compounds 5a-d as yellow needles.

6-Nitro-5,8-diphenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine (5a). Yield 83%, 0.30 g, mp 241–242 °C; IR (νmax, cm−1): 1649 (pyrazole ring C=N), 1579 (triazole ring C=N), and 1462 (C=C); 1H NMR (CDCl3, δH, ppm): 6.93 (s, 1H, pyrazole-H), 7.40–7.44 (m, 6H, aromatic-H), 7.62 (d, 2H, aromatic-H); MS, m/z (%) = 356 (M+, 7), 326 (M+-H2N2, 4), 311 (M++1-NO2, 100), 283 (M+-CHN2O2, 27), 271 (M++1-CN3O2, 2) and 255 (M+-CHN4O2, 13); Anal. Calc. for C19H12N6O2 (356.34): C, 64.04; H, 3.39; N, 23.58%, found: C, 64.00; H, 3.40; N, 23.60%.

6-Nitro-8-phenyl-5-p-tolylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine (5b). Yield 81%, 0.30 g, mp 243–244 °C; IR (νmax, cm−1): 1643 (pyrazole ring C=N), 1578 (triazole ring C=N), and 1415 (C=C); 1H NMR (CDCl3, δH, ppm): 2.47 (s, 3H, CH3), 6.90 (s, 1H, pyrazole-H), 7.37–7.45 (m, 5H, aromatic-H), 7.51 (d, 2H, aromatic-H); MS, m/z (%) = 370 (M+, 4), 340 (M+-H2N2, 2), 325 (M++1-NO2, 100), 309 (M+-CH3NO2, 1), 297 (M+-CHN2O2, 22) and 269 (M+-C2H3N3O2, 9); Anal. Calc. for C20H14N6O2 (370.36): C, 64.86; H, 3.81; N, 22.69%, found: C, 64.90; H, 3.80; N, 22.72%.

5-(p-Methoxyphenyl)-6-nitro-8-phenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine (5c). Yield 77%, 0.30 g, mp 250–251 °C; IR (νmax, cm−1): 1637 (pyrazole ring C=N), 1585 (triazole ring C=N), and 1420 (C=C); 1H NMR (CDCl3, δH, ppm): 3.89 (s, 3H, OCH3), 6.97 (s, 1H, pyrazole-H), 7.45–7.47 (m, 3H, aromatic-H), 7.62 (d, 2H, aromatic-H); MS, m/z (%) = 388 (M+2, 15), 387 (M+1, 100), 356 (M+-CH2O, 7), 339 (M+-HNO2, 7), 312 (M+-CH2N2O2, 4), 310 (M+-CH3N2O2, 11), 284 (M+-C2H2N2O2, 5) and 251 (M+-C7H7N2O, 16); Anal. Calc. for C20H14N6O3 (386.36): C, 62.17; H, 3.65; N, 21.75%, found: C, 62.20; H, 3.61; N, 21.73%.

5-(p-Chlorophenyl)-6-nitro-8-phenylpyrazolo[1,5-c]-1,2,4-triazolo[4,3-a]pyrimidine (5d). Yield 77%, 0.30 g, mp 306–307 °C; IR (νmax, cm−1): 1641 (pyrazole ring C=N), 1583 (triazole ring C=N), and 1416 (C=C); 1H NMR (DMSO-d6, δH, ppm): 7.33 (s, 1H, pyrazole-H), 7.43 (t, 1H, aromatic-H), 7.50 (t, 2H, aromatic-H), 7.66 (d, 2H, aromatic-H), 7.79 (d, 2H, aromatic-H), 8.03 (d, 2H, aromatic-H)
and 8.99 (s, 1H, triazole-H); MS, m/z (%) = 391 (M⁺, 3), 349 (M⁺-CH₂N₂, 3), 347 (M⁺-N₂O, 46), 345 (M⁺-NO₂, 100), 317 (M⁺-N₃O₂, 17), 289 (M⁺-C₂H₄N₃O₂, 7), 282 (M⁺-C₆H₅O₂, 15), 254 (M⁺-C₇H₄ClN, 22) and 227 (M⁺-C₇H₃ClN₃, 12); Anal. Calc. for C₁₉H₁₁ClN₆O₂ (390.78): C, 58.40; H, 2.84; N, 21.51%; found: C, 58.44; H, 2.80; N, 21.53%.

3.2.5. 5-Aryl-7-formylhydrazino-2-phenylpyrazolo[1,5-c]pyrimidines 6a-d

A suspension of 5-aryl-7-hydrazino-2-phenylpyrazolo[1,5-c]pyrimidines (1a-d, 1mmol) and ethyl formate (5 mL) was heated under reflux for 3 h. The product which separated upon cooling was filtered, washed with EtOH and crystallized from EtOH to give the title compounds 6a-d as colorless needles.

7-Formylhydrazino-2,5-Diphenylpyrazolo[1,5-c]pyrimidine (6a). Yield 76%, 0.25 g, mp 177–178 °C; IR (ν max, cm⁻¹): 3368 (NH), 1700 (C=O), 1624 (pyrazole ring C=N), 1568 (pyrimidine ring C=N), and 1455 (C=C); ¹H NMR (CDCl₃, δH, ppm): 4.80 (s, 2H, exchangeable 2NH), 6.72 (s, 1H, pyrazole-H), 7.29 (s, 1H, pyrimidine-H), 7.30–7.49 (m, 8H, aromatic -H), 7.98 (d, 2H, aromatic-H) and 8.08 (s, 1H, CHO); MS, m/z (%) = 330 (M⁺+1, 2), 302 (M⁺+1-CO, 100), 286 (M⁺-CHNO, 23), 272 (M⁺-CHN₂O, 81), 257 (M⁺-C₂H₄N₂O₂, 2), 244 (M⁺-C₂H₃N₃O, 17) and 228 (M⁺-C₂H₂N₄O, 6); Anal. Calc. for C₁₉H₁₅N₅O (329.36): C, 69.29; H, 4.59; N, 21.26%, found: C, 69.30; H, 4.62; N, 21.30%.

7-Formylhydrazino-2-phenyl-5-p-tolylpyrazolo[1,5-c]pyrimidine (6b). Yield 71%, 0.25 g, mp 132–133 °C; IR (ν max, cm⁻¹): 3315 (NH), 1701 (C=O), 1610 (pyrazole ring C=N), 1572 (pyrimidine ring C=N), and 1447 (C=C); ¹H NMR (CDCl₃, δH, ppm): 2.42 (s, 3H, CH₃), 4.77 (s, 2H, exchangeable 2NH), 6.70 (s, 1H, pyrazole-H), 7.28 (s, 1H, pyrimidine-H), 7.29-7.49 (m, 7H, aromatic-H), 7.96 (d, 2H, aromatic- H) and 7.98 (s, 1H, CHO); MS, m/z (%) = 344 (M⁺+1, 2), 316 (M⁺+1-CO, 100), 300 (M⁺-CHNO, 33), 286 (M⁺-CHN₂O, 85), 270 (M⁺-C₂H₄N₂O, 4), 259 (M⁺-C₂H₂N₃O, 7) and 227 (M⁺-C₈H₆N, 10); Anal. Calc. for C₂₀H₁₇N₅O (343.38): C, 70.02; H, 5.02; N, 20.44%.

7-Formylhydrazino-5-(p-methoxyphenyl)-2-phenylpyrazolo[1,5-c]pyrimidine (6c). Yield 69%, 0.25 g, mp 157–158 °C; IR (ν max, cm⁻¹): 3265(NH), 1708 (C=O), 1667 (pyrazole ring C=N), 1585 (pyrimidine ring C=N), and 1448 (C=C); ¹H NMR (CDCl₃, δH, ppm): 3.87 (s, 3H, OCH₃), 4.73 (s, 2H, exchangeable 2NH), 6.68 (s, 1H, pyrazole-H), 7.19 (s, 1H, pyrimidine-H), 7.20–7.46 (m, 3H, aromatic-H), 7.95–7.97 (m, 4H, aromatic-H) and 8.00 (s, 1H, CHO); MS, m/z (%) = 361 (M⁺+2, 5), 359 (M⁺, 30), 332 (M⁺+1-CO, 100), 316 (M⁺-CHNO, 23), 302 (M⁺-CHN₂O, 78), 287 (M⁺-C₂H₄N₂O, 12) and 275 (8, M⁺-C₂H₂N₃O); Anal. Calc. for C₂₀H₁₇N₅O₂ (359.38): C, 66.84; H, 4.77; N, 19.49%, found: C, 66.80; H, 4.82; N, 19.50%.

5-(p-Chlorophenyl)-7-formylhydrazino-2-phenylpyrazolo[1,5-c]pyrimidine (6d). Yield 69%, 0.25 g, mp 175–176 °C; IR (ν max, cm⁻¹): 3315 (NH), 1700 (C=O), 1615 (pyrazole ring C=N), 1575 (pyrimidine ring C=N), and 1450 (C=C); ¹H NMR (CDCl₃, δH, ppm): 4.76 (s, 2H, exchangeable 2NH), 6.72 (s, 1H, pyrazole-H), 7.28 (s, 1H, pyrimidine-H), 7.41–7.46 (m, 5H, aromatic-H), 7.95–7.99 (m, 4H, aromatic- H) and 8.00 (s, 1H, CHO); MS, m/z (%) = 361 (M⁺-3, 2.), 335 (M⁺+1-CO, 19), 320
(M$^+$-CHNO, 100), 305 (M$^+$-C$\text{H}_2$N$_2$O, 47), 294 (M$^+$-C$_2$HN$_2$O, 10), 269 (M$^+$-C$_6$H$_6$O, 5) and 242 (M$^+$-C$_7$H$_7$NO, 5); Anal. Calc. for C$_{19}$H$_{14}$ClN$_5$O (363.80): C, 62.73; H, 3.88; N, 19.25%, found: C, 62.70; H, 3.90; N, 19.30%.

3.2.6. 7-Acetylhydrazino-5-aryl-2-phenylpyrazolo[1,5-c]pyrimidines 7a-d

5-Aryl-7-hydrazino-2-phenylpyrazolo[1,5-c]pyrimidines 1a-d (1mmol) and glacial acetic acid (10 mL) was heated at reflux for 3 h. The reaction mixture was poured onto crushed ice and the product which separated was filtered, washed with water, dried and crystallized from EtOH to give the title compounds 7a-d as colorless needles.

7-Acetylhydrazino-2,5-diphenylpyrazolo[1,5-c]pyrimidine (7a). Yield 88%, 0.30 g, mp 217–218 °C; IR ($\nu_{\text{max}}$, cm$^{-1}$): 3150 (NH), 1661 (C=O), 1628 (pyrazole ring C=N), 1568 (pyrimidine ring C=N), and 1459 (C=C); $^1$H NMR (CDCl$_3$, $\delta$H, ppm): 2.21 (s, 3H, COCH$_3$), 6.67 (s, 1H, pyrazole-H), 7.21 (s, 1H, pyrimidine-H), 7.30–7.51 (m, 5H, aromatic-H), 7.84–7.96 (m, 5H, aromatic-H), and 8.01 (s, 1H, exchangeable NH) and 8.48 (s, 1H, exchangeable NHCO); MS, $m/z$ (%) = 343 (M$^+$, 100), 328 (M$^+$-CH$_3$, 1), 301 (M$^+$-COCH$_2$, 59), 286 (M$^+$-NCOCH$_3$, 18) and 243 (M$^+$-C$_3$H$_6$N$_3$O, 11); Anal. Calc. for C$_{20}$H$_{17}$N$_5$O (343.38): C, 69.96; H, 4.99; N, 20.40%, found: C, 70.00; H, 5.02; N, 20.43%.

7-Acetylhydrazino-2-phenyl-5-p-tolylpyrazolo[1,5-c]pyrimidine (7b). Yield 83%, 0.30 g, mp 224–225 °C; IR ($\nu_{\text{max}}$, cm$^{-1}$): 3252 (NH), 1659 (C=O), 1618 (pyrazole ring C=N), 1556 (pyrimidine ring C=N), and 1445 (C=C); $^1$H NMR (CDCl$_3$, $\delta$H, ppm): 2.23 (s, 3H, CH$_3$), 2.36 (s, 3H, COCH$_3$), 6.70 (s, 1H, pyrazole-H), 7.19 (d, 2H, aromatic-H), 7.26 (s, 1H, pyrimidine-H), 7.36–7.48 (m, 3H, aromatic-H), 7.79 (d, 2H, aromatic-H), 7.97 (d, 2H, aromatic-H), 8.14 (s, 1H, exchangeable NH) and 8.31 (s, 1H, exchangeable NHCO); MS, $m/z$ (%) = 358 (M$^+$+1, 100), 315 (M$^+$-COCH$_2$, 63), 300 (M$^+$-NCOCH$_3$, 19), 288 (M$^+$-C$_3$H$_3$NO, 6) and 259 (M$^+$-C$_3$H$_4$N$_3$O, 5); Anal. Calc. for C$_{21}$H$_{19}$N$_5$O (357.41): C, 70.57; H, 5.36; N, 19.59%, found: C, 70.60; H, 5.32; N, 19.55%.

7-Acetylhydrazino-5-p-methoxyphenyl-2-phenylpyrazolo[1,5-c]pyrimidine (7c). Yield 81%, 0.30 g, mp 193–194 °C; IR ($\nu_{\text{max}}$, cm$^{-1}$): 3283 (NH), 1664 (C=O), 1618 (pyrazole ring C=N), 1544 (pyrimidine ring C=N), and 1448 (C=C); $^1$H NMR (CDCl$_3$, $\delta$H, ppm): 2.24 (s, 3H, COCH$_3$), 3.78 (s, 3H, OCH$_3$), 6.63 (s, 1H, pyrazole-H), 6.88 (d, 2H, aromatic-H), 7.07 (s, 1H, pyrimidine-H), 7.36–7.50 (m, 3H, aromatic-H), 7.76 (s, 1H, pyrimidine-H), 8.09 (d, 2H, aromatic-H), 8.09 (d, 2H, aromatic-H), 8.13 (s, 1H, exchangeable NH) and 8.91 (s, 1H, exchangeable NHCO); MS, $m/z$ (%) = 374 (M$^+$+1, 100), 331 (M$^+$-COCH$_2$, 38), 316 (M$^+$-NCOCH$_3$, 16), 302 (M$^+$-NCOCH$_3$, 56), 287 (M$^+$-C$_3$H$_6$N$_2$O, 8) and 259 (M$^+$-C$_3$H$_4$N$_3$O, 19); Anal. Calc. for C$_{21}$H$_{19}$N$_5$O$_2$ (373.41): C, 67.55; H, 5.13; N, 18.76%, found: C, 67.58; H, 5.16; N, 18.80%.

7-Acetylhydrazino-5-p-Chlorophenyl-2-phenylpyrazolo[1,5-c]pyrimidine (7d). Yield 79%, 0.30 g, mp 246–247 °C; IR ($\nu_{\text{max}}$, cm$^{-1}$): 3306 (NH), 1664 (C=O), 1613 (pyrazole ring C=N), 1572 (pyrimidine ring C=N), and 1447 (C=C); $^1$H NMR (DMSO-$d_6$, $\delta$H, ppm): 2.04 (s, 3H, COCH$_3$), 7.08 (s, 1H, pyrazole-H), 7.67 (s, 1H, pyrimidine-H), 7.41–7.52 (m, 5H, aromatic-H), 8.09 (d, 2H, aromatic-H), 9.81 (s, 1H, exchangeable NH) and 10.14 (s, 1H, exchangeable NHCO); MS, $m/z$ (%) = 382 (M$^+$+4,
3.2.7. 7-Acetylhydrazino-5-aryl-3,4-dibromo-2-phenylpyrazolo[1,5-c]pyrimidines 8a-d

A solution of bromine (0.12 mL, 2.4 mmol) in acetic acid (10 mL) was gradually added to a suspension of 7-acetylhydrazino-5-aryl-2-phenylpyrazolo[1,5-c]pyrimidines 7a-d (1 mmol) in acetic acid (10 mL) with stirring for 3 h at room temperature. The precipitated 7-acetylhydrazino-5-aryl-3,4-dibromo-2-phenylpyrazolo[1,5-c]pyrimidines 8a-d were filtered, washed with water, dried and crystallized from EtOH as colorless needles.

7-Acetylhydrazino-3,4-dibromo-2,5-diphenylpyrazolo[1,5-c]pyrimidine (8a). Yield 80%, 0.40 g, mp 229–230 °C; IR (νmax, cm⁻¹): 3451 (NH), 1657 (C=O), 1644 (pyrazole ring C=N), 1560 (pyrimidine ring C=N), and 1439 (C=C); ¹H NMR (CDCl₃, δH, ppm): 2.09 (s, 3H, COCH₃), 7.44–7.53 (m, 6H, aromatic-H), 7.63 (d, 2H, aromatic-H), 7.94 (d, 2H, aromatic-H) and 8.01 (s, 2H, exchangeable NH and exchangeable NHCO); MS, m/z (%) = 505 (M⁺+4, 4), 503 (M⁺+2, 38), 501 (M⁺+, 100), 459 (M⁺+-COCH₂, 80), 444 (M⁺+-NCOCH₃, 14), 429 (M⁺+-NNHCOCH₃, 40), 423 (M⁺++2-Br, 21), 421 (M⁺+-Br, 19) and 341 (M⁺+-Br₂, 2); Anal. Calc. for C₂₀H₁₅Br₂N₅O (501.20): C, 47.96; H, 3.33; N, 13.59%, found: C, 47.50; H, 3.26; N, 13.20%.

7-Acetylhydrazino-3,4-dibromo-2-phenyl-5-p-tolylpyrazolo[1,5-c]pyrimidine (8b). Yield 77%, 0.40 g, mp 212–213 °C; IR (νmax, cm⁻¹): 3280 (NH), 1664 (C=O), 1618 (pyrazole ring C=N), 1562 (pyrimidine ring C=N), and 1439 (C=C); ¹H NMR (CDCl₃, δH, ppm): 2.10 (s, 3H, CH₃), 2.40 (s, 3H, COCH₃), 7.46–7.55 (m, 5H, aromatic-H), 7.86 (d, 2H, aromatic-H), 7.93 (d, 2H, aromatic-H), 8.04 (s, 1H, exchangeable NH) and 8.06 (s, 1H, exchangeable NHCO); MS, m/z (%) = 519 (M⁺+4, 1), 517 (M⁺+2, 15), 515 (M⁺+, 33), 473 (M⁺+COCH₂, 18), 458 (M⁺+NCOCH₃, 2), 444 (M⁺+NNCOCH₃, 7), 442 (M⁺+NNHCOCH₃, 5), 437 (M⁺+2-Br, 100), 435 (M⁺+Br, 84) and 355 (M⁺+Br₂, 1); Anal. Calc. for C₂₁H₁₇Br₂N₅O (515.20): C, 48.96; H, 3.33; N, 13.59%, found: C, 49.00; H, 3.36; N, 13.60%.

7-Acetylhydrazino-5-(p-methoxyphenyl)-3,4-dibromo-2-phenylpyrazolo[1,5-c]-pyrimidine (8c). Yield 75%, 0.40 g, mp 182–183 °C; IR (νmax, cm⁻¹): 3269 (NH), 1668 (C=O), 1612 (pyrazole ring C=N), 1535 (pyrimidine ring C=N), and 1443 (C=C); ¹H NMR (CDCl₃, δH, ppm): 2.47 (s, 3H, COCH₃), 3.79 (s, 3H, OCH₃), 7.48–7.62 (m, 3H, aromatic-H), 7.91 (d, 2H, aromatic-H), 8.04 (d, 2H, aromatic-H), 8.08 (d, 2H, aromatic-H), 10.05 (s, 1H, exchangeable NH) and 10.10 (s, 1H, exchangeable NHCO); MS, m/z (%) = 535(M⁺+4, 1), 533 (M⁺+2, 6), 531 (M⁺+, 10), 489 (M⁺+COCH₂, 6), 475 (M⁺+NCOCH₃, 13), 459 (M⁺+NNHCOCH₃, 23), 453 (M⁺+2-Br, 73), 451 (M⁺+Br, 61) and 370 (M⁺+1-Br₂, 1); Anal. Calc. for C₂₁H₁₇Br₂N₅O₂ (531.20): C, 47.48; H, 3.23; N, 13.18%, found: C, 47.50; H, 3.26; N, 13.20%.

7-Acetylhydrazino-5-(p-chlorophenyl)-3,4-dibromo-2-phenylpyrazolo[1,5-c]-pyrimidine (8d). Yield 74%, 0.40 g, mp 226–227 °C; IR (νmax, cm⁻¹): 3267 (NH), 1664 (C=O), 1620 (pyrazole ring C=N), 1570 (pyrimidine ring C=N), and 1437 (C=C); ¹H NMR (DMSO-d₆, δH, ppm): 2.47 (s, 3H, COCH₃), 7.49–7.57 (m, 5H, aromatic-H), 8.04 (d, 2H, aromatic-H), 8.15 (d, 2H, aromatic-H), 8.15 (d, 2H, aromatic-H), 10.06 (s, 1H,
3.2.8. 7-Acetylhydrazino-5-aryl-3-iodo-2-phenylpyrazolo[1,5-c]pyrimidines 9a-d

A solution of iodine monochloride (0.2 g, 1.2 mmol) in acetic acid (10 mL) was gradually added to a suspension of 7-acetylhydrazino-5-aryl-2-phenylpyrazolo[1,5-c]pyrimidines 7a-d (1 mmol) 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 7-acetylhydrazino-5-aryl-3-iodo-2-phenylpyrazolo[1,5-c]pyrimidines 9a-d were filtered, washed with water, dried and crystallized from EtOH as colorless needles.

7-Acetylhydrazino-3-iodo-2,5-diphenylpyrazolo[1,5-c]pyrimidine (9a). Yield 85%, 0.40 g, mp 229–230 °C; IR (υmax, cm−1): 3433 (NH), 1680 (C=O), 1618 (pyrazole ring C=N), 1549 (pyrimidine ring C=N), and 1438 (C=C); 1H NMR (DMSO-d6, δH, ppm): 2.05 (s, 3H, COCH3), 7.29–7.80 (m, 10H, aromatic-H), 7.48 (s, 1H, pyrimidine-H), and 8.06 (s, 2H, exchangeable NHCO and exchangeable NH); MS, m/z (%) = 469 (M++1, 83), 441 (M+-COCH2, 34), 426 (M+-NCOCH3, 12), 412 (M+-NNCOCH3, 12), 410 (M+-NHNHCOCH3, 1) and 357 (M++1-I, 16); Anal. Calc. for C21H18IN5O (483.30): C, 52.19; H, 3.75; N, 14.49%; found: C, 52.50; H, 3.79; N, 14.52%.

7-Acetylhydrazino-3-iodo-2-phenyl-5-p-tolylpyrazolo[1,5-c]pyrimidine (9b). Yield 83%, 0.40 g, mp 204–205 °C; IR (υmax, cm−1): 3273 (NH), 1661 (C=O), 1610 (pyrazole ring C=N), 1560 (pyrimidine ring C=N), and 1448 (C=C); 1H NMR (CDCl3, δH, ppm): 2.26 (s, 3H, CH3), 2.42 (s, 3H, COCH3), 7.18 (s, 1H, pyrimidine-H), 7.28–7.30 (m, 3H, aromatic-H), 7.49–7.52 (m, 4H, aromatic-H), 7.84 (d, 2H, aromatic-H), 7.97 (s, 1H, exchangeable NH), and 9.28 (s, 2H, exchangeable NHCO and exchangeable NH); MS, m/z (%) = 484 (M++1, 83), 441 (M+-COCH2, 34), 426 (M+-NCOCH3, 12), 412 (M+-NNCOCH3, 12), 410 (M+-NHNHCOCH3, 1) and 357 (M++1-I, 16); Anal. Calc. for C21H18IN5O (493.30): C, 52.19; H, 3.75; N, 14.49%; found: C, 52.50; H, 3.79; N, 14.52%.

7-Acetylhydrazino-3-iodo-5-(p-methoxyphenyl)-2-phenylpyrazolo[1,5-c]-pyrimidine (9c). Yield 80%, 0.40 g, mp 124–125 °C; IR (υmax, cm−1): 3290 (NH), 1711 (C=O), 1610 (pyrazole ring C=N), 1560 (pyrimidine ring C=N), and 1448 (C=C); 1H NMR (CDCl3, δH, ppm): 2.16 (s, 3H, COCH3), 3.87 (s, 3H, OCH3), 6.99–7.49 (m, 7H, aromatic-H), 7.69 (s, 1H, pyrimidine-H), 8.01 (d, 2H, aromatic-H) and 9.28 (s, 2H, exchangeable NH and exchangeable NHCO); MS, m/z (%) = 484 (M++1, 1), 343 (M+-NCOCH2, 3), 373 (M++1-I, 6) and 372 (M+-I, 1); Anal. Calc. for C21H18IN5O2 (493.30): C, 50.52; H, 3.63; N, 14.03%. Found: C, 50.55; H, 3.59; N, 14.06%.

7-Acetylhydrazino-5-(p-chlorophenyl)-3-iodo-2-phenylpyrazolo[1,5-c]pyrimidine (9d). Yield 80%, 0.40 g, mp 207–208 °C; IR (υmax, cm−1): 3273 (NH), 1662 (C=O), 1616 (pyrazole ring C=N), 1566 (pyrimidine ring C=N), and 1439 (C=C); 1H NMR (DMSO-d6, δH, ppm): 2.01 (s, 3H, COCH3), 7.14 (d, 2H, aromatic-H), 7.40 (s, 1H, pyrimidine-H), 7.49–7.54 (m, 3H, aromatic-H), 7.68 (d, 1H, aromatic-H), 7.80 (d, 1H, aromatic-H), 7.98 (d, 2H, aromatic-H), 10.00 (s, 1H, exchangeable NH), and
10.16 (s, 1H, exchangeable NHCO); MS, m/z (%) = 506 (M⁺+2, 45), 504 (M⁺, 100), 463 (M⁺+2-COCH₃, 22), 461 (M⁺-COCH₃, 57), 446 (M⁺-NHCOCH₃, 15), 432 (M⁺ -NNHCOCH₃, 17), 379 (M⁺+2-I, 10) and 377 (M⁺-I, 24); Anal. Calc. for C₂₀H₁₅ClIN₅O (503.72): C, 47.69; H, 3.00; N, 13.90%, found: C, 47.72; H, 2.99; N, 13.92%.

3.2.9. 7-Acetylhydrazino-5-aryl-3-nitro-2-phenylpyrazolo[1,5-c]pyrimidines 10a-d

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 a suspension of 7-acetylhydrazino-5-aryl-2-phenylpyrazolo[1,5-c]pyrimidines 7a-d (1 mmol) 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 yellow precipitated solid was filtered, washed with cold water, dried and crystallized from EtOH to give the title compounds 10a-d as yellow needles.

7-Acetylhydrazino-3-nitro-2,5-diphenylpyrazolo[1,5-c]pyrimidine (10a). Yield 77%, 0.30 g, mp 191–192 ℃; IR (υmax, cm⁻¹): 3436 (NH), 1743 (C=O), 1633 (pyrazole ring C=N), 1551 (pyrimidine ring C=N), and 1462 (C=C); ¹H NMR (CDCl₃, δH, ppm): 1.90 (s, 3H, COCH₃), 7.37 (s, 1H, pyrimidine-H), 7.44–7.68 (m, 6H, aromatic-H), 7.97 (d, 2H, aromatic-H), 8.03 (d, 2H, aromatic-H), 8.34 (s, 1H, exchangeable NH), and 9.26 (s, 1H, exchangeable NHCO); MS, m/z (%) = 389 (M⁺+1, 4), 360 (M⁺-CO, 7), 346 (M⁺-COCH₂, 2), 332 (M⁺-NCOCH₂, 100), 316 (M⁺-NNHCOCH₃, 4), 302 (M⁺-C₃H₆N₂O, 17), 286 (M⁺-C₂H₂N₂O₃, 10) and 258 (M⁺-C₃H₄N₃O₃, 25); Anal. Calc. for C₂₀H₁₆N₆O₃ (388.38): C, 61.85; H, 4.15; N, 21.64%, found: C, 61.89; H, 4.12; N, 21.60%.

7-Acetylhydrazino-3-nitro-2-phenyl-5-p-tolylpyrazolo[1,5-c]pyrimidine (10b). Yield 75%, 0.30 g, mp 194–195 ℃; IR (υmax, cm⁻¹): 3371 (NH), 1745 (C=O), 1601 (pyrazole ring C=N), 1533 (pyrimidine ring C=N), and 1443 (C=C); ¹H NMR (CDCl₃, δH, ppm): 1.96 (s, 3H, CH₃), 2.44 (s, 3H, COCH₃), 7.28–7.71 (m, 10H, aromatic-H and pyrimidine-H) and 8.44 (s, 2H, exchangeable NH and exchangeable NHCO); MS, m/z (%) = 403 (M⁺+1, 2), 402 (M⁺, 3), 401 (M⁺-1, 16), 374 (M⁺-CO, 8) and 346 (M⁺-C₂H₂NO, 6); Anal. Calc. for C₂₁H₁₈N₆O₃ (402.41): C, 62.68; H, 4.51; N, 20.88%, found: C, 62.71; H, 4.50; N, 20.91%.

7-Acetylhydrazino-5-(p-methoxyphenyl)-3-nitro-2-phenylpyrazolo[1,5-c]-pyrimidine (10c). Yield 71%, 0.30 g, mp 132–133 ℃; IR (υmax, cm⁻¹): 3464 (NH), 1747 (C=O), 1696 (pyrazole ring C=N), 1531 (pyrimidine ring C=N), and 1454 (C=C); ¹H NMR (CDCl₃, δH, ppm): 1.81 (s, 3H, COCH₃), 3.89 (s, 3H OCH₃), 7.00–7.71 (m, 10H, aromatic-H and pyrimidine-H) and 8.44 (s, 2H, exchangeable NH and exchangeable NHCO); MS, m/z (%) = 420 (M⁺+2, 1), 358 (M⁺-C₂H₄NO, 1), 334 (M⁺-C₃H₆N₂O, 1) and 300 (M⁺-C₂H₂N₃O₃, 3); Anal. Calc. for C₂₁H₁₈N₆O₄ (418.41): C, 60.28; H, 4.34; N, 20.09%, found: C, 60.31; H, 4.32; N, 20.13%.

7-Acetylhydrazino-5-(p-chlorophenyl)-3-nitro-2-phenylpyrazolo[1,5-c]-pyrimidine (10d). Yield 71%, 0.30 g, mp 174–175 ℃; IR (υmax, cm⁻¹): 3371 (NH), 1749 (C=O), 1597 (pyrazole ring C=N), 1533 (pyrimidine ring C=N), and 1443 (C=C); ¹H NMR (CDCl₃, δH, ppm): 2.13 (s, 3H, COCH₃), 7.34–7.73 (m, 10H, aromatic-H and pyrimidine-H) and 8.45 (s, 2H, exchangeable NH and exchangeable NHCO);
MS, \textit{m/z} (%) = 423 (M$^+$, 1), 381 (M$^+$-COCH$_3$, 1), 366 (M$^+$-NCOCH$_3$, 1), 324 (M$^+$-C$_3$H$_5$N$_3$O, 1) and 300 (M$^+$-C$_6$H$_5$NO$_2$, 2); Anal. Calc. for C$_{20}$H$_{15}$ClN$_6$O$_3$ (422.82): C, 56.81; H, 3.58; N, 19.88%, found: C, 56.77; H, 3.61; N, 19.85%.

3.2.10. 7-Triacetylhydrazino-5-aryl-2-phenylpyrazolo[1,5-c]pyrimidines 11a-d

A suspension of 5-aryl-7-hydrazino-2-phenylpyrazolo[1,5-c]pyrimidines 1a-d (1 mmol) in acetic anhydride (5 mL) was heated under reflux for 1 h and the mixture was cooled and poured onto crushed ice. The product that separated out was filtered off, washed with water and then dried. It was crystallized from EtOH to give the title compounds 11a-d as colorless needles.

7-Triacetylhydrazino-2,5-diphenylpyrazolo[1,5-c]pyrimidine (11a). Yield 83%, 0.35 g, mp 179–180 °C; IR (\textit{\upsilon}_{\text{max}}, \text{cm}^{-1}): 1736 (C=O), 1623 (pyrazole ring C=N), 1542 (pyrimidine ring C=N) and 1458 (C=C); $^1$H NMR (DMSO-$d_6$, \textit{\delta}$_H$, ppm): 2.45 (s, 3H, COCH$_3$), 2.48 (s, 3H, COCH$_3$), 2.50 (s, 3H, COCH$_3$), 7.28 (s, 1H, pyrazole-H), 7.44 (t, 2H, aromatic-H), 7.50 (t, 4H, aromatic-H), 7.99 (d, 2H, aromatic-H), 8.05 (d, 2H, aromatic-H) and 8.24 (s, 1H, pyrimidine-H); MS, \textit{m/z} (%) = 428 (M$^{++}$1, 15), 385 (M$^+$-CH$_2$CO, 15), 343 (M$^+/-$2 CH$_2$CO, 100), 286 (M$^+$-C$_6$H$_5$NO$_2$, 24), 272 (M$^+$-C$_6$H$_6$N$_2$O$_2$, 88) and 270 (M$^+$-C$_6$H$_7$NO$_2$, 26); Anal. Calc. for C$_{24}$H$_{21}$N$_5$O$_3$ (427.46): C, 67.44; H, 4.95; N, 16.38%, found: C, 67.40; H, 5.00; N, 16.40%.

7-Triacetylhydrazino-2-phenyl-5-p-tolylpyrazolo[1,5-c]pyrimidine (11b). Yield 80%, 0.35 g, mp 194–195 °C; IR (\textit{\upsilon}_{\text{max}}, \text{cm}^{-1}): 1726 (C=O), 1622 (pyrazole ring C=N), 1520 (pyrimidine ring C=N) and 1450 (C=C); $^1$H NMR (CDCl$_3$, \textit{\delta}$_H$, ppm): 2.17 (s, 3H, CH$_3$), 2.42 (s, 3H, COCH$_3$), 2.54 (s, 3H, COCH$_3$), 6.90 (s, 1H, pyrazole-H), 7.28 (d, 2H, aromatic-H), 7.42–7.50 (m, 3H, aromatic-H), 7.72 (s, 1H, pyrimidine-H), 7.87 (d, 2H, aromatic-H) and 7.95 (d, 2H, aromatic-H); MS, \textit{m/z} (%) = 443 (M$^{++}$2, 2), 441 (M$^+$, 10), 399 (M$^+$-COCH$_2$, 11), 357 (M$^+/-$2COCH$_2$, 100), 315 (M$^+/-$3COCH$_2$, 44) and 300 (M$^+$-C$_6$H$_7$NO$_3$, 21); Anal. Calc. for C$_{25}$H$_{23}$N$_5$O$_3$ (441.48): C, 68.01; H, 5.25; N, 15.86%, found: C, 68.12; H, 5.22; N, 15.81%.

7-Triacetylhydrazino-5-p-methoxyphenyl-2-phenylpyrazolo[1,5-c]pyrimidine (11c). Yield 76%, 0.35 g, mp 132–133 °C; IR (\textit{\upsilon}_{\text{max}}, \text{cm}^{-1}): 1720 (C=O), 1614 (pyrazole ring C=N), 1510 (pyrimidine ring C=N) and 1448 (C=C); $^1$H NMR (CDCl$_3$, \textit{\delta}$_H$, ppm): 2.53 (s, 9H, 3COCH$_3$), 3.86 (s, 3H, OCH$_3$), 6.87 (s, 1H, pyrazole-H), 6.98 (d, 2H, aromatic-H), 7.41–7.49 (m, 3H, aromatic-H), 7.65 (s, 1H, pyrimidine-H) and 7.91–7.95 (m, 4H, aromatic-H); MS, \textit{m/z} (%) = 459 (M$^{++}$2, 2), 457 (M$^+$, 17), 415 (M$^+$-COCH$_2$, 19), 373 (M$^+/-2$COCH$_2$, 100), 331 (M$^+/-3$COCH$_2$, 39), 316 (M$^+-C_6$H$_7$NO$_3$, 17) and 302 (M$^+-C_7$H$_9$NO$_3$, 41); Anal. Calc. for C$_{25}$H$_{23}$N$_5$O$_4$ (441.48): C, 68.01; H, 5.25; N, 15.31%, found: C, 65.51; H, 5.05; N, 15.28%.

7-Triacetylhydrazino-5-p-chlorophenyl-2-phenylpyrazolo[1,5-c]pyrimidine (11d). Yield 76%, 0.35 g, mp 174–175 °C; IR (\textit{\upsilon}_{\text{max}}, \text{cm}^{-1}): 1722 (C=O), 1614 (pyrazole ring C=N), 1533 (pyrimidine ring C=N), and 1448 (C=C); $^1$H NMR (CDCl$_3$, \textit{\delta}$_H$, ppm): 2.52 (s, 3H, COCH$_3$), 2.56 (s, 6H, 2COCH$_3$), 6.91 (s, 1H, pyrazole-H), 7.41–7.49 (m, 4H, aromatic-H), 7.70 (s, 1H, pyrimidine-H), 7.88 (d, 2H, aromatic-H) and 7.93 (d, 2H, aromatic-H); MS, \textit{m/z} (%) = 464 (M$^{++}$2, 1), 462 (M$^+$, 5), 420 (M$^+$-COCH$_2$, 8), 378
(M\(^+-\)2COCH\(_2\), 58), 336 (M\(^+-\)3COCH\(_2\), 30), 320 (M\(^+-\)C\(_6\)H\(_5\)NO\(_3\), 13) and 306 (M\(^+-\)C\(_6\)H\(_8\)N\(_2\)O\(_3\), 24); Anal. Calc. for C\(_{24}\)H\(_{20}\)ClN\(_5\)O\(_3\) (461.90): C, 62.41; H, 4.36; N, 15.16%, found: C, 62.40; H, 4.32; N, 15.20%.

4. Conclusions

In summary, the strategy for constructing the target compounds started by 5-aryl-7-hydrazino-2-phenylpyrazolo[1,5-c]pyrimidines 1a-d where the hydrazine moiety can be readily heterocyclized with one-carbon inserting agents to give the triazole ring fused to the pyrazolopyrimidine skeleton has been successfully demonstrated.

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*Sample Availability:* Samples of compounds 1-11 are available from the author.

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