Synthesis and Reactions of Some Novel Triazolo-, Azolo-, Tetrazolo-pyridopyrimidine and their Nucleoside Derivatives

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Pyridopyrimidine reacted with aromatic aldehydes afforded the arylhydrazone **2a,b** which could be cyclized into the pyrido[2,3-*d*][1,2,4]triazolo[4,3-*a*]pyrimidine **3a,b**, with formic acid, and carbon disulphide to give pyrido[2,3-*d*][1,2,4]traizolo[4,3-*a*]pyrimidine **4**, **5**. Reaction of **1** with nitrous acid afforded tetrazolo[1,5-*a*]pyrido[2,3-*d*]pyrimidine **6**, which was reduced by zinc dust to give 2-amino-pyrido-[2,3-*d*]pyrimidine **7**. Finally the reaction of 2-hydrazino **1** with D-xylose or D-glucose afforded the acyclic N-nucleoside **8**, **11** which were converted into tetra/penta *O*-acetate acyclic *C*-nucleoside **9**, **12** in acetic anhydride/pyridine. De-acetylation of compounds **9**, **12** afforded *C*-nucleosides **10**, **13**.

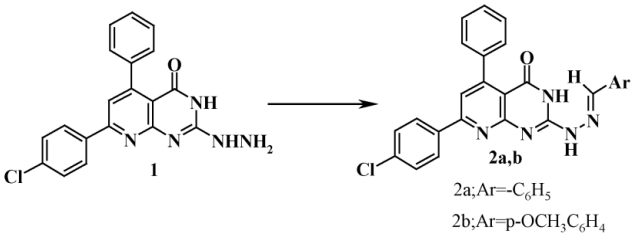
Keywords: Pyridopyrimidine; Azolopyridopyrimidine; C- and N-nucleosides; IR; ^{1}H-NMR and ^{13}C spectra.

INTRODUCTION

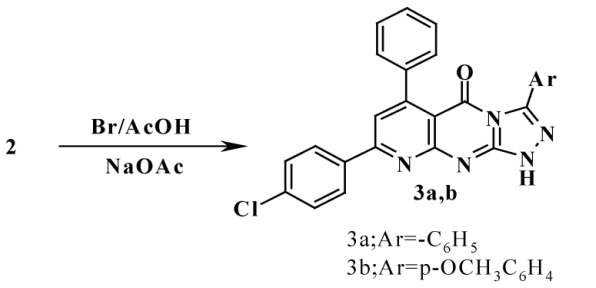
Pyridopyrimidine and their derivatives have exhibited promising biological and pharmacological activities such as antifolate,[1] antibacterial,[2] tyrosine kinas activity,[3] antimicrobial,[4] calcium channel antagonist,[5] antiinflammatory and analgesic activity,[6] antileishmania,[7] tuberculostatic,[8] anti-convulsant,[9] diuretic and potassium-sparing,[10] and anti-aggressive activities.[11] Also, C-nucleosides and acyclic C-nucleosides have shown marked biological activities towards antiviral activities.[12] This encouraged us to become involved in a program directed to the development of syntheses of various new pyridopyrimidines and fused pyridopyrimidines such as azolopyridopyrimidine derivatives and some acyclic C- and N-nucleosides.

RESULTS AND DISCUSSION

The reaction of 2-hydrazino-5-phenyl-7-(4-chloro phenyl)-3*H*,4*H*-pyrido[2,3-*d*]pyrimidine-4-one (**1**)[13] with aromatic aldehyde in boiling dioxane afforded the arylhydrazones **2a,b** which could be cyclized into the 3-aryl-5-phenyl-7-(4-chlorophenyl)-1*H*,4*H*-pyrido[2,3-*d*][1,2,4]-triazolo[4,3-*a*]pyreimidin-5-ones (**3a,b**) when they were treated with catalytic amounts of bromine in glacial acetic acid and anhydrous sodium acetate.



The IR spectrum of **2a** displayed absorption bands at 3330 cm^{-1} (NH) and 1670 cm^{-1} (CO). The ^{1}H-NMR (DMSO-d_6) spectrum of **2a** as an example, showed signals at δ 7.45 (s, 1H, CH, ethylinic proton), δ 7.55-7.65 (m, 10H, phenyl protons), δ 7.75 (m, 4H, phenyl protons), δ 8.05 (s, 1H, CH, pyridinyl proton), δ 11.01 (br. s, 1H, NH, D_2O exchangeable) and δ 11.5 (br. s, 1H, NH, D_2O exchangeable). Moreover, the correct values in elemental analysis, IR, ^{1}H-NMR



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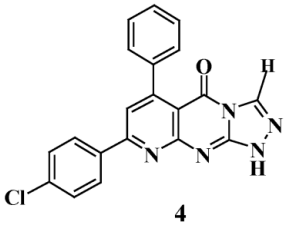
spectra of **3a,b** are in agreement with the assigned structure. It's reported in the literature that the N-3 nitrogen atom and not the N-1 nitrogen atom are involved in the cyclization.[14-17] (Experimental)

Heating under reflux, compound **1** with formic acid resulted in the formation of 6-phenyl-8-(4-chlorophenyl)-1*H*,3*H*-pyrido[2,3-*d*][1,2,4]traizolo[4,3-*a*]pyrimidin-5(5*H*)-one (**4**).



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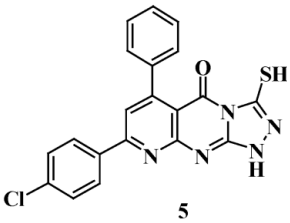

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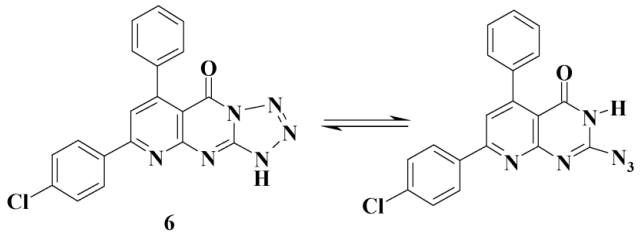
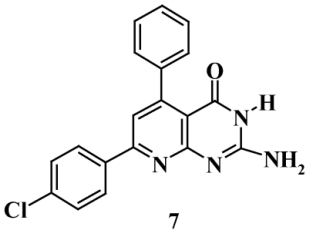
Compound **1** reacted with carbon disulphide in ethanolic potassium hydroxide solution to afford 3-mercapto-6-phenyl-8-(4-chlorophenyl)-1*H*,3*H*-pyrido[2,3-*d*][1,2,4]-traizolo[4,3-*a*]pyrimidin-5(5*H*)-one (**5**), (Experimental). Treatment of compound **1** with nitrous acid at 0 °C led to the formation of 6-phenyl-7-(4-chlorophenyl)-1*H*,5*H*-tetrazolo[1,5-*a*]pyrido[2,3-*d*]pyrimidin-5-one (**6**), which was found in equilibrium with the 2-azido toutomer.



6

The ^{1}H-NMR (DMSO-d_6) spectrum of **6** showed signals at δ 7.38 (m, 5H, phenyl protons), δ 7.45 (m, 4H, phenyl protons), 7.88 (s, 1H, pyridinyl proton) and δ 13.65 (br s, 1H, NH, D_2O exchangeable). The IR spectrum of **6** displayed absorption bands around 3210 (NH), 3022 (CH), 2928 (CH alkyl), 1686 (CO) and a characteristic absorption band for the azido group at 2231 cm^{-1}.



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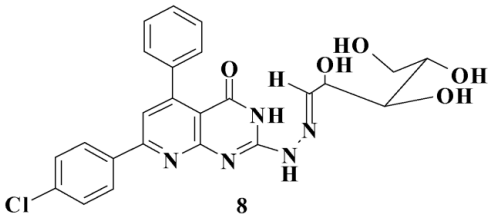
Compound **6** was reduced into 2-amino-5-phenyl-7-(4-chlorophenyl)-3*H*,4*H*-pyrido[2,3-*d*]pyrimidin-4-one **7** by zinc dust and acetic acid. The ^{1}H-NMR (DMSO-d_6) spectrum of **7** showed signals at δ 7.39 (m, 5H, phenyl protons), δ 7.45-7.55 (m, 4H, phenyl protons), δ 7.88 (s, 1H, CH, pyridinyl proton) and δ 10.90 (br. s, 1H, NH, D_2O exchangeable). The IR spectrum of **7** displayed absorption bands at 3420 cm^{-1} (NH_2), 3240 cm^{-1} (NH), 3034 cm^{-1} (CH), 2908 cm^{-1} (CH alkyl) and 1666 cm^{-1} (CO).

Besides the biological activities of the pyridopyrimidine derivatives as described above, acyclic C-nucleosides also act as antivirals and antiherpetices. We report here a simple and convenient method to synthesize new acyclic C- and N-nucleoside derivatives derived from 2-hydrazino-5-phenyl-7-(4-chlorophenyl)-3*H*,6*H*-pyrido[2,3-*d*]pyrimidin-4(4*H*)one (**1**).

Heating under reflux **1** with aldopentose, namely D-xylose in dioxane in the presence of a catalytic amount of pipridine, yielded acyclic N-nucleoside **8**.



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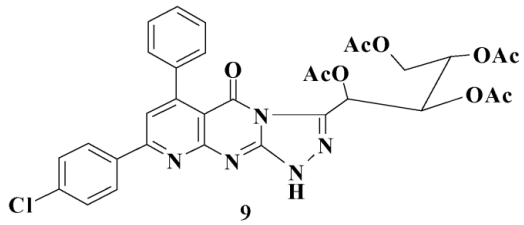
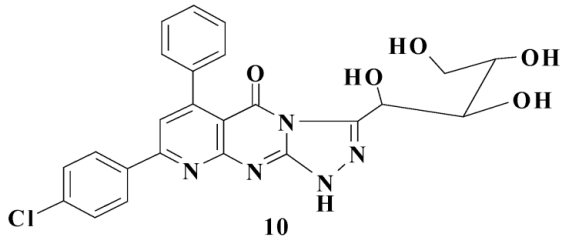


9

The ^{1}H-NMR spectrum of compound **8** showed signals at δ 3.45 (m, 4H, 4OH ,OH-2′-OH-5′, D_2O exchangeable), δ 4.25 (m, 1H, H-4′), δ 4.35 (m, 2H, CH_2, H-5′), δ 4.60 (m, 1H, H-3′), δ 5.65 (m, 1H, H-2′), δ 7.25 (m, 1H, H-1′), δ 7.45 (m, 5H, phenyl protons), δ 7.65 (m, 4H, phenyl protons), δ 7.90 (s, 1H, CH, pyridinyl proton), δ 11.20 (br. s, 1H, NH, D_2O exchangeable) and δ 11.40 (br. s, 1H, NH, D_2O exchangeable). Its IR spectrum displayed absorption bands at 3460-3455 cm^{-1} (broad OH), 3250 cm^{-1} (NH), 3026 cm^{-1} (CH), 2924 cm^{-1} (CH alkyl) and 1667 cm^{-1} (CO).

The acyclic N-nucleoside **8** was stirred at room temperature in acetic anhydride/pyridine mixture (1:1) to afford the corresponding protected tetra *O*-acetate acyclic *C*-nucleoside **9**. The ^{1}H-NMR spectrum of compound **9** showed signals at δ 1.65 (s, 3H, OCH_3), δ 1.85 (s, 3H, OCH_3), δ 2.00 (s, 3H, OCH_3), δ 2.15 (s, 3H, OCH_3), δ 5.25 (m, 1H, H-3′), δ 5.35 (m, 2H, CH_2, H-4′), δ 5.55 (m, 1H, H-2′), δ 5.75 (m, 1H, H-1′), δ 7.40-7.55 (m, 5H, phenyl protons), δ 7.85 (m, 4H, phenyl protons), δ 7.90 (s, 1H, 1H, CH, pyridinyl proton) and δ 11.40 (br. s, 1H, NH, D_2O exchangeable). Its IR spectrum displayed absorption bands at 3300 cm^{-1} (NH), 3025 cm^{-1} (CH), 2900 cm^{-1} (CH alkyl), 1740-1760 cm^{-1} (ester carbonyl) and 1700 cm^{-1} (CO).

De-acetylation of **9** could be achieved by treatment with methanolic sodium methoxide solution to give the de-protected acyclic *C*-nucleoside **10**.



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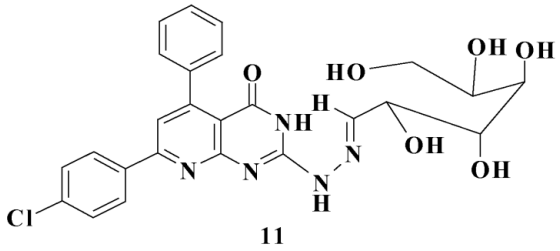
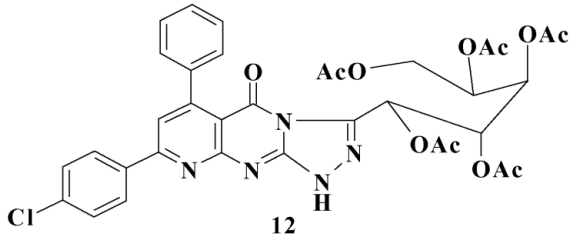
Also, heating under reflux **1** with aldohexoses, namely *D*-glucose in dioxane in the presence of a catalytic amount of pipridine, yielded acyclic *N*-nucleoside **11**.



11

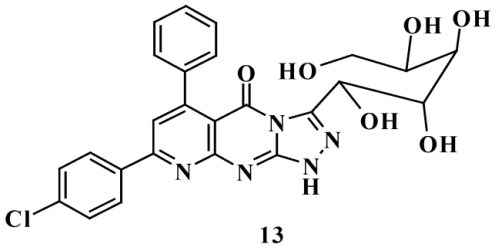


12

The ^{1}H-NMR spectrum of compound **11** showed signals at δ 3.60 (m, 5H, 5OH, OH-2′-OH-6′, D_2O exchangeable), δ 3.70 (m, 1H, H-5′), δ 4.35 (m, 2H, H-6′), δ 4.40 (m, 1H, H-4′), δ 4.60 (m, 1H, H-3′), δ 5.35 (m, 1H, H-2′), δ 6.15 (d, 1H, H-1′), δ 7.55-7.65 (m, 5H, phenyl protons), δ 7.70-7.75 (m, 4H, aryl protons), δ 8.20 (s, 1H, CH, pyridinyl proton), δ 11.05 (brs, 1H, NH, D_2O exchangeable) and δ 11.25 (brs, 1H, NH, D_2O exchangeable). Its IR spectrum displayed absorption bands at 3265 cm^{-1} (NH), 3224 cm^{-1} (NH), 3030 cm^{-1} (CH), 2920 cm^{-1} (CH alkyl) and 1670 cm^{-1} (CO).

On the other hand, acetylation of compound **11** with an acetic anhydride/pyridine mixture (1:1) at room temperature afforded the protected penta *O*-acetylated acyclic *C*-nucleoside **12**. The ^{1}H-NMR spectrum of compound **12** showed signals at δ 1.85 (s, 3H, OCH_3), δ 1.95 (s, 3H, OCH_3), δ 2.00 (s, 3H, OCH_3), δ 2.15 (s, 3H, OCH_3), δ 2.40 (s, 3H, OCH_3), δ 4.85 (m, 1H, H-4′), δ 5.45 (m, 1H, H-3′), δ 5.55 (m, 2H, CH_2, H -5′), δ 5.65 (m, 1H, H-2′), δ 5.70 (m, 1H, H-1′), δ 6.85 (m, 5H, phenyl protons), δ 7.65 (m, 4H, phenyl protons), δ 8.00 (s, 1H, CH, pyridinyl proton) and δ 11.45 (br s, 1H, HN, D_2O exchangeable). Its IR spectrum displayed absorption band at 3230 cm^{-1} (NH), 3030 cm^{-1} (CH), 2920 cm^{-1} (CH alkyl), 1745-1715 cm^{-1} (ester carbonyl) and 1685 cm^{-1} (CO).

De-protection of the acyclic *C*-nucleoside could be achieved when it was stirred in methanolic sodium methoxide solution at room temperature to give the acyclic *C*-nucleoside **13**. The structure of **13** was confirmed by spectral and elemental analysis. (Experimental)



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EXPERIMENTAL

Solid compounds were re-crystallized to constant melting points and dried in vacuum in a drying pistol containing sodium hydroxide. All melting points are uncorrected and were taken in open capillaries on a Gallenkamp apparatus. Micro analyses were carried out at the Micro Analytical Unit of the National Research Centre and Fac-

ulty of Science, Cairo University. IR spectra were carried out on an FT/IR 300 E Jasco using KBr discs. ^{1}H-NMR spectra were measured in DMSO or $CDCl_3$, using a Joel Ex. 270 NMR spectrometer. Signals were measured with reference to TMS as an internal standard. The mass spectra were recorded on a Finnigan SSQ 7000 spectrometer. All reactions were followed up by TLC using $CHCl_3$/MeOH (9:1, v/v) and/or ethyl acetate/benzene (7:3) and detected under a UV lamp.

2-Hydrazino-5-phenyl-7-(4-chlorophenyl)-3*H*,6*H*-pyrido[2,3-*d*]pyrimidin-4(4*H*)one (1)

A mixture of 7-(4-chlorophenyl)-2-methylthio-5-phenyl-3*H*,4*H*-pyrido[2,3-*d*]pyrimidin-4-one (3.80 g, 0.01 mole) and hydrazine hydrate (99-100%) (11.40 mL, 0.03 mole) in dioxane (20 mL) and ethanol (10 mL) was heated under reflux for five hours. The solid that separated upon cooling the reaction mixture was filteredoff and recrystallized from dioxane (45 mL) to yield the title compound as pale yellow crystals (2.3 g, 63%), mp. 313-2 °C. [$C_{19}H_{14}N_5OCl$] (363.80) Required: C, 62.73%; H, 3.88%; N, 19.25. Found: C, 62.41%; H, 3.54%; N, 19.11%. IR (KBr) cm^{-1}: 3330 (NH_2), 3225 (NH), 3020 (CH) and 1666 (CO). ^{1}H-NMR (DMSO-d_6) δ ppm: 7.30-7.40 (m, 5H, phenyl protons), 7.45-7.55 (m, 4H, phenyl protons), 8.05 (s, 1H, CH) and 8.75 (br s, 1H, NH, D_2O exchangeable). MS (EI+Q1MS LMR UP LR): 363.8 (M^+) 100%.

2-(Arylmethylenehydrazone)-5-phenyl-7-(4-chlorophenyl)-3*H*,4*H*-pyrido[2,3-*d*]pyrimidin-4-one (2a,b)
General procedure

A mixture of compound **1** (3.63 g, 0.01 mole), the appropriate aromatic aldehyde (0.01 mole), dioxane (30 mL) and a catalytic amount of piperidine was heated under reflux for six hours. The reaction mixture was allowed to cool to room temperature and then it was poured into water (100 mL). The formed precipitate was filteredoff, washed with water, dried and recrystallized from the proper solvent to yield **2a,b.**

2-(Phenylmethylenehydrazone)-7-(4-chlorophenyl)-3*H*,4*H*-pyrido[2,3-*d*]pyrimidin-4-one (2a)

From compound **1** and benzaldehyde (1.06 g, 0.01 mole). The product was recrystallized from dioxane (35 mL) to yield the title compound as shining yellow crystals (3.07 g, 68%); m.p. 287-2 °C. [$C_{26}H_{18}N_5ClO$] (541.91). Require: C, 69.10%; H, 4.01%; N, 15.50%. Found: C, 68.60%; H, 3.78%; N, 15.10%. ^{13}C-NMR (DMSO-d_6) δ ppm: 65.92 (CH), 131.03, 132.41, 134.60, 134.06, 134.12, 137.61, 138.22, 139.43, 138.18, 138.61, 138.83, 139.13, 139.24, 140.77, 142.15, 142.40, 146.76, 147.88, 150.13, 162.05, 163.05, 165.60, and 166.00, 166.18 (Pyridopyrimidone carbon atoms and aromatic carbon atoms) and 167.81 (CO). MS (EI + Q1MS LMR UP LR): 451.9 (M^+) 100%.

2-(4-Methoxyphenylmethylenehydrazone)-5-phenyl-7-(4-chlorophenyl)-3*H*,4*H*-pyrido[2,3-*d*]pyrimidin-4-one (2b)

From compound **1** and 4-methoxybenzaldehyde (1.36 g, 0.01 mole). The product was recrystallized from dioxane (35 mL) to yield the title compound as orange crystals (3.40 g, 71%); m.p. > 300 °C. [$C_{27}H_{20}N_5ClO_2$] (481.94) Required: C, 67.29%; H 4.18%; N, 14.53%. Found: C, 67.01%; H, 3.78%; N, 14.34%. IR (KBr) cm^{-1}: 3222 (NH), 3020 (CH), 2928 (CH alkyl) and 1672 (CO). ^{1}H-NMR (DMSO-d_6) δ ppm: 3.80 (s, 3H, OCH_3), 6.95-7.25 (m, 5H, phenyl protons), 7.40-7.55 (m, 4H, phenyl protons),7.65 (s, 1H, CH, ethylenic proton), 7.70-7.80 (m, 4H, aromatic protons), 8.00 (s, 1H, CH, pyridinyl proton), 11.15 (br. s, 1H, NH, D_2O exchangeable) and 11.55 (br. s, 1H, NH, D_2O exchangeable). ^{13}C-NMR (DMSO-d_6) δ ppm: 54.61 (OCH_3), 66.71 (CH), 129.71, 131.33, 131.62, 133.92, 135.51, 137.11,137.73, 138.32, 139.14, 139.84, 138.61, 138.83, 139.13, 139.24, 140.77, 142.15, 142.40, 146.76, 147.88, 151.11, 162.11, 163.04, 165.31, and 166.08, 166.27 (Pyridopyrimidone carbon atoms and aromatic carbon atoms) and 167.92 (CO). MS (EI + Q1MS LMR UP LR): 481.9 (M^+) 100%.

3-Aryl-5-phenyl-7-(4-chlorophenyl)-1*H*,4*H*-pyrido[2,3-*d*][1,2,4]triazolo[4,3-*a*]pyrimidin-5-one (3a,b)
General Procedure

A mixture of either of **3a** (4.51 g, 0.01 mol) or **3b** (4.81 g, 0.01 mol) with 2 g anhydrous sodium acetate, bromine (2.44 g, 0.01 mol) and glacial acetic acid (25 mL) was heated on a water bath at 80 °C for about 8 hours (under TLC control). The reaction mixture was poured onto water

and the formed solid was collected by filtration and crystallized from the proper solvent to give 3**a,b**.

3,5-Diphenyl-7-(4-chlorophenyl)-1*H*,4*H*-pyrido[2,3-*d*][1,2,4]triazolo[4,3-*a*]pyrimidin-5-one (3a)

Compound **3a** was obtained in 60% yield; m.p. 304 °C; [$C_{26}H_{16}N_5ClO$] (449.90); Required: C, 69.41%; H 3.58%; N, 15.56%. Found: C, 69.10%; H 3.33%; N, 15.14%. IR (KBr) cm^{-1}: 3225 (NH), 3030 (CH), and 1700 (CO). ^{1}H-NMR (DMSO-d_6) δ ppm: 7.25-7.35 (m, 10H, aromatic protons), 7.45-7.55 (m, 4H, aromatic protons), 7.80 (s, 1H, CH, pyridinyl proton) and 11.25 (br. s, 1H, NH, D_2O exchangeable). MS (EI + Q1MS LMR UP LR): 449.90 (M^+) 100%.

8-(4-Chlorophenyl)-3-(4-methoxyphenyl)-1*H*,5*H*-pyrido[2,3-*d*][1,2,4]triazolo[4,3-*a*]pyremidin-5-one (3b)

Compound **3b** was obtained in 63% yield; m.p. 317 °C; [$C_{27}H_{18}N_5ClO_2$] (479.92); Required: C, 67.57%; H 3.77%; N, 14.59%. Found: C, 67.24%; H 3.61%; N, 14.13%. IR (KBr) cm^{-1}: 3256 (NH), 3020 (CH aromatic), 2928 (CH alkyl) and 1685 (CO). ^{1}H-NMR (DMSO-d_6) δ ppm: 3.80 (s, 3H, OCH_3), 7.25-7.37 (m, 5H, phenyl protons), 7.40-7.55 (m, 4H, phenyl protons), 7.60-6.70 (m, 4H, aromatic protons), 7.80 (s, 1H, CH, pyridinyl proton) and 11.25 (br. s, 1H, NH, D_2O exchangeable). MS (EI + Q1MS LMR UP LR): 479.92 (M^+) 100%.

6-Phenyl-8-(4-chlorophenyl)-1*H*,3*H*-pyrido[2,3-*d*][1,2,4]-traizolo[4,3-*a*]pyrimidin-5(5*H*)-one (4)

A mixture of compound **1** (3.63 g, 0.01 mole), formic acid (1 mL) and a catalytic amount of concentrated hydrochloric acid solution was heated under reflux for five hours. The reaction mixture was allowed to cool to room temperature, then poured into water (100 mL). The formed solid was collected by filtration, washed with ethanol (20 mL), dried and crystallized from dioxane (35 mL) to yield the title compound as colorless crystals (1.42 g, 61%), m.p. 281-82 °C and crystallized from acetic acid to yield the title product as pale yellow crystals (2.50 g, 67%), mp. 239-41 °C. [$C_9H_{11}N_5SO$] (233.27); Required: C, 46.34%; H, 5.03%; N, 13.75%. Found: C, 45.81%; H, 3.10%; N, 13.45%. IR (KBr) cm^{-1}: 3211 (NH), 3022 (CH), 2890 (CH alkyl) and 1680 (CO). ^{1}H-NMR (DMSO-d_6) δ ppm: 7.15 (s, 1H, triazolo proton), 7.56 (m, 5H, phenyl protons), 7.73 (m, 4H, phenyl protons), 7.90 (s, 1H, pyridinyl proton) and 9.66 (br. s, 1H, NH, D_2O exchangeable). MS (EI + Q1 MS LMR UP LR): 373.79 (M^+) 100%.

3-Mercapto-1,6,7,8-tetrahydrocyclopentanothieno[2,3-*d*][1,2,4]traizolo[4,3-*a*]pyrimidin-5(5*H*)-one (5)

To a warmed ethanolic sodium hydroxide solution (prepared by dissolving sodium hydroxide (0.40 g, 0.01 mole) in ethanol (50 mL), compound **1** (3.63 g, 0.01 mole) and carbon disulphide (10 mL) were added. The mixture was heated on a water bath at 80 °C under reflux for eight hours, then allowed to cool to room temperature, poured into water (100 mL), and neutralized by dilute acetic acid. The formed precipitate was filteredoff, dried and crystallized from dioxane (30 mL) to yield the title product as a pale yellow powder (1.70 g, 64%), m.p. > 300 °C. [$C_{10}H_8N_4S_2O$] (264.31); Required: C, 45.44%; H, 3.05%; N, 21.19%. Found: C, 45.10%; H, 3.30%; N, 20.82%. IR (KBr) cm^{-1}; 3100 (broad NH), 3010 (CH), 2920 (CH alkyl) and 1690 (CO) ^{1}H-NMR (DMSO-d_6) δ ppm: 1.43 (s, 1H, SH), 7.30 (m, 5H, phenyl protons), 7.35-7.42 (m, 2H, phenyl protons), 7.64-7.70 (m, 2H, phenyl protons), 7.95 (s, 1H, CH, pyridinyl proton) and 12.60 (br. s, 1H, NH, D_2O exchangeable). ^{13}C-NMR (DMSO-d_6) δ ppm: 128.76, 130.33, 131.00, 133.14, 134.60, 134.06, 134.12, 137.61, 139.24, 144.11, 144.26, 147.06, 151.33, 162.05, 163.05, 165.60, and 166.00, 166.18 (Pyridopyrimidone carbon atoms, triazol carbon atom and aromatic carbon atoms) and 166.13 (CO). MS (EI + Q1 MS LMR UP LR): 373.79 (M^+) 100%.

7-(4-Chlorophenyl)-6-phenyl-1*H*,5*H*-tetraazolo[1,5-*a*]-pyrido[2,3-*d*]pyrimidin-5-one (6)

To an ice-cold solution of compound **1** (3.63 g, 0.01 mole) in acetic acid (15 mL) was added dropwise, a solution of sodium nitrite (prepared by dissolving sodium nitrite (1.70 g, 0.015 mole) in the least amount of water) in an icebath at -5 °C. The reagent mixture was allowed to stand overnight at room temperature, and then it was poured into water (100 mL). The solid so-precipitated was filteredoff and recrystallized from acetic acid to yield the title compound as yellow crystals (2.50g, 67%), m.p.301-2 °C.

$[C_{19}H_{11}N_6OCl]$ (374.78); Required: C, 60.89%; H, 2.95%; N, 22.42%. Found: C, 60.64%; H, 2.88%; N, 22.01%. MS (EI + Q1 MS LMR UP LR): 374.7 (M^+) 100%.

2-Amino-5-phenyl-7-(4-chlorophenyl)-3*H*,4*H*-pyrido-[2,3-*d*]pyrimidin-4-one (7)

To a well-stirred solution of compound **6** (3.74. g, 0.01 mole) in glacial acetic acid (40 mL) was added portionwise activated zinc dust (5.00 g) at room temperature over a period of 30 minutes. Stirring was continued for an additional three hours. Thereafter, the reaction mixture was heated on a water bath (80-90 °C) for three hours. The progress of reduction was monitored by TLC. After allowing the reaction mixture to cool to room temperature, it was poured into cold water to (100 mL). The insoluble solid, which separated, was filtered, washed with water and dried. The crude solid was extracted with hot benzene and the solid obtained after removal of benzene under reduced pressure was crystallized from acetic acid to yield the title product as yellow crystals (2.14 g, 61.5%), m.p. 243-45 °C. $[C_{19}H_{13}N_4OCl]$ (348.78), Required: C, 65.43%; H, 3.75%; N, 16.06%. Found: C, 65.03%; H, 3.60%; N, 15.71%. MS (EI + Q1 MS LMR UP LR): 348.7 (M^+) 100%.

2-Glycosylhydrazino-5-phenyl-7-(4-chlorophenyl)-3*H*,6*H*-pyrido[2,3-*d*]pyrimidin-4-one (8, 11)
General Procedure

A mixture of compound **1** (3.63 g, 0.01 mole) and the appropriate monosaccharide (0.01 mole), dioxane (30 mL), ethanol (10 mL) and catalytic amounts of piperidine was stirred under reflux for eight hours. The reaction mixture was allowed to cool to room temperature. The precipitate so-formed was filteredoff, washed with ethanol and recrystallized from dioxane (30 mL) to afford the title compounds.

2-Xylosylhydrazino-5-phenyl-7-(4-chlorophenyl)-3*H*,6*H*-pyrido[2,3-*d*]pyrimidin-4-one (8)

From compound **1** and D-xylose (1.50 g, 0.01 mole). The product was recrystallized from dioxane (35 mL) to yield the title compound as yellow powder (3.20 g, 64.60%); m.p. 283-2 °C. $[C_{24}H_{22}N_5O_5]$ (495.91); Required: C, 58.12%; H, 4.47%; N, 14.12%. Found: C, 58.00%; H, 4.11%; N, 13.34%.

2-Glucosylhydrazino-5-phenyl-7-(4-chlorophenyl)-3*H*,6*H*-pyrido[2,3-*d*]pyrimidin-4-one (11)

A mixture of compound **1** and D-glucose (1.80 g, 0.01 mole), dioxane (30 mL), ethanol (10 mL) and catalytic amounts of piperidine was stirred under reflux for eight hours. The reaction mixture was allowed to cool to room temperature. The precipitate so-formed was filteredoff, washed with ethanol and recrystallized from dioxane (35 mL) to afford the title compound as yellow crystals (3.34, 63%); m.p. 281-2 °C $[C_{25}H_{24}N_5O_6\,Cl]$ (525.95); Required: C, 57.09%; H, 4.59%; N, 13.31%. Found: C, 56.48%; H, 4.38%; N, 12.76%.

3-(O-Acetylglycosyl)-6-phenyl-8-(4-chlorophenyl)-1*H*,7*H*-pyrido[2,3-*d*][1,2,4]triazolo[4,3-*a*] pyrimidin-5(5*H*)-one (9, 12)
General Procedure

A solution of compounds **8** or compounds **11** (0.01 mole) in a mixture of acetic anhydride-pyridine (20 mL: 20 mL) was stirred at room temperature overnight, then it was poured into water. The reaction mixture was then extracted with chloroform several times and after the removal of chloroform under reduced pressure, the formed crystals were recrystallized from the proper solvent to produce **9** or **12**.

3-(1′,2′,3′,4′-O-tetraacetylxylosyl)-6-phenyl-8-(4-chlorophenyl)-1*H*,7*H*-pyrido[2,3-*d*][1,2,4]triazolo[4,5-*a*]pyrimidine-5(5*H*)-one (9)

From compound **8** (4.95 g, 0.01 mole). The product was recrystallized from methanol (30 mL) to afford the title compound as golden yellow crystals (3.26 g, 66%); m.p. 156-2 °C. $[C_{32}H_{20}N_5O_9]$ (662.05). Required: C, 58.05%; H, 4.26%; N, 10.57%. Found: C, 57.51%; H, 3.81%; N, 10.12%.

3-(1′,2′,3′,4′,5′-O-pentaacetylglucosyl)-6-phenyl-8-(4-chlorophenyl)-1*H*,7*H*-pyrido[2,3-*d*][1,2,4]triazolo[4,3-*a*]pyrimidin-5(5*H*)-one (12)

From compound **11** (5.25 g, 0.01 mole). The product was recrystallized from methanol (35 mL) to yield the title compound as yellow crystals (4.38 g, 65%); m.p. 161-2 °C. $[C_{30}H_{34}N_5O_{11}Cl]$ (676.08). Required: C, 53.30%; H, 5.11%; N, 10.36%. Found: C, 53.01%; H, 4.93%; N,10%. ^{13}C-

NMR ($CDCl_3$) δ ppm : 20.00, 20.30, 20.50, 20.80, and 23.30 (CH_3), 29.60 (CH_2), 66.70, 67.00, 67.40 and 69.10 (CH), 137.30, 137.60, 138.00, 138.40, 138.30, 138.60, 139.00, 139.30, 139.80, 141.61, 142.73, 143.00, 145.11, 145.31, 147.10, 153.40, 155.00, 155.66, and 157.15 (Pyridopyrimidone carbon atoms, triazol carbon atoms and aromatic carbon atoms) and 168.36, 168.70, 168.90, 170.00, 170.30 and 171.10 (CO).

3-Glycosyl-6-phenyl-8-(4-chlorophenyl)-1*H*,7*H*-pyrido-[2,3-*d*][1,2,4]triazolo[4,3-*a*]pyrimidin-5(5*H*)-one (10, 13) General procedure

A solution of methanolic sodium methoxide (prepared by dissolving sodium metal (0.23 g, 0.01 mole) in absolute methanol (25 mL)) was added to either compounds **9** (0.01 mole) or compounds **12** (0.01 mole). The reaction mixture was allowed to stire for eight hours, and then neutralized with hydrochloric acid solution (neutralization takes place under pH control). The excess methanol was removed under reduced pressure, whereby a solid was precipitated. The precipitate so-formed was filteredoff, washed with cold water, dried and recrystallized from the proper solvent to produce the title compounds in good yield.

3-Xylosyl-6-phenyl-8-(4-chlorophenyl)-1*H*,7*H*-pyrido-[2,3-*d*][1,2,4]triazolo[4,3-*a*]pyrimidin-5(5*H*)-one (10)

From compound **9** (6.62 g, 0.01 mole). The product was recrystallized from dioxane (40 mL) to yield the title compound as yellow powder (2.35 g, 47.50%); m.p. 248-2 °C. [$C_{24}H_{20}N_5O_5Cl$] (493.9); Required: C, 58.36%; H, 4.08%; N, 14.17%. Found: C, 58.14%; H, 3.84%; N, 13.77%.

3-Glucosyl-6-phenyl-8-(4-chlorophenyl)-1*H*,7*H*-pyrido-[2,3-*d*][1,2,4]triazolo[4,3-*a*]pyrimidin-5(5*H*)-one (13)

From compound **12** (6.76 g, 0.01 mole). The product was recrystallized from dioxane (40 mL) to yield the title compound as yellow powder (2.70 g, 51.50%); m.p. 251-2 °C. [$C_{25}H_{23}N_5O_6Cl_]$ (524.94). Required: C, 57.18%; H, 4.42%; N, 13.34%. Found: C, 56.47%; H, 4.12%; N, 1.55%. IR (KBr) cm^{-1}: 3460- 3449 (broad OH), 3245 (NH), 3025 (CH), 2920 (CH alkyl), 1700 (CO). ^{1}H-NMR (DMSO-d_6) δ ppm: 3.85 (m, 5H, 5OH, D_2O exchangeable),4.00 (m, 1H, H-2′), 4.30 (m, 1H, H-3′), 4.45 (m, 2H, H-5′, H-5′′), 4.50 (m, 1H, H-4′), 4.65 (m, 1H, H-1′), 7.20 (brs, 1H, NH, D_2O exchangeable), 7.35 (m, 5H, phenyl protons), 7.40 (m, 2H, phenyl protons), 7.55 (m, 2H, phenyl protons) and 7.85 (s, 1H, CH, pyridinyl proton). ^{13}C-NMR (DMSO-d_6) δ ppm: 26.60 (CH_2), 60.05, 63.71, 64.43 and 66.30 (CH), 134.60, 137.11, 137.22, 138.00, 138.18, 138.61, 138.83, 139.13, 139.24, 139.33, 139.91, 142.40, 144.31, 144.55, 144.60, 144.72, 146.00, 151.42, and 157.64 (Pyridopyriidone carbon atoms, triazol carbon atoms and aromatic carbon atoms) and 167.69 (CO).

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