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# Synthesis and reactions of some novel triazolo-, azolo-, tetrazolo-pyridopyrimidine and their nucleoside derivatives

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## ABSTRACT

Pyridopyrimidine react with aldehyde afforded the arylhydrazone **(2a,b)** which could be cyclized into the pyrido[2,3-d][1,2,4]triazolo[4,3-a]pyreimidine **(3a,b)**, and with formic acid, acetic acid and carbondisulphide to give pyrido[2,3-d][1,2,4]traizolo[4,3-a]-yrimidine **(4**,**5)**. Reaction of **(1)** with nitrous acid afforded tetrazolo[1,5-a]pyrido[2,3-d]-yrimidine **(6)**, which was reduced by zinic dust to give 2-amino-pyrido[2,3-d]pyrimidine **7**. Finally the reaction of 2-hydrazino **1** with D-zyloxe 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. Deactylation of compounds **(9**,**12)** afforded C-nucleosides **(10**,**13)**.



## KEYWORDS

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

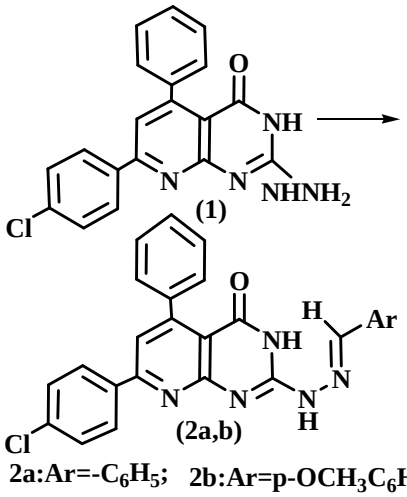
## INTRODUCTION

Pyridopyrimidine and their derivatives have exhibit promising biological and pharmacological activities such as antifolate[1], antibacterial[2], tyrosine kinase activity[3], antimacrobial[4], calcium channel antagonists[5], anti-inflamatory and analgesic activity[6], Anti-leishmamia[7], tuberculostalic[8], anti-convulsants[9], diuretic and potassium-spring[10] and anti-aggressive activities[11]. Also, C-nucleosides and acyclic C-nucleosides showed marked bioglical activities against antiviral activities[12]. This promoted us to involve 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.

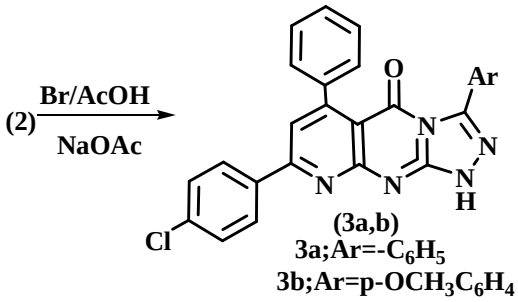
## RESULTS AND DISCUSSION

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

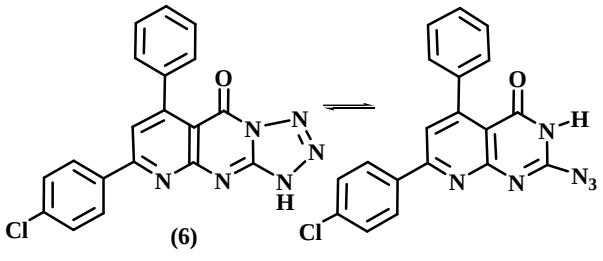
The IR spectrum of **(2a)** displayed absorption bands at 3330cm$^{-1}$ (NH) and 1670cm$^{-1}$ (CO). The $^{1}$H-NMR (DMSO-$d_6$) spectrum of **(2a)** as an example, showed signals at δ 7.45 (s, 1H, CH, ethylinic proton), δ 7.55-7.65 (m, 10H, phenyl protons), δ 7.75 (m, 4H, phenyl



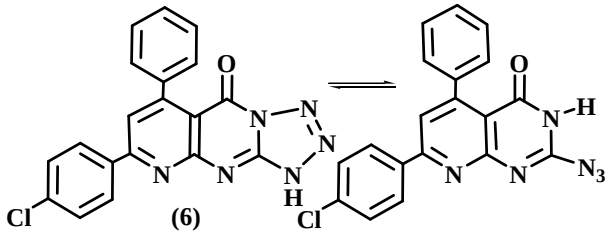

protons), δ 8.05(s, 1H, CH, pyridinyl proton), 11.01 (br. s, 1H, NH, $D_2O$ exchangeable) and δ 11.5 (br . s, 1H, NH, $D_2O$ exchangeable). Beside the correct values in elemental analysis, IR, $^1$H-NMR spectra of **(3a,b)** are in agreement with the assigned structure. It's reported in the literature that N-3 nitrogen atom and not N-1 nitrogen atom involved in the cyclization[14-17].



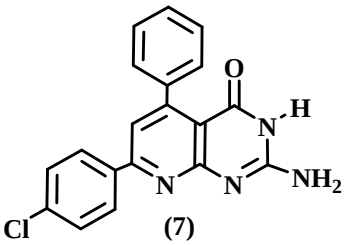

Heating under reflux, compound **(1)** with formic acid resulted in the formation of 6–phenyl-8-(4-chlorophenyl)-1H,3H-pyrido[2,3-d][1,2,4]traizolo [4,3-a]pyrimidin-5(5H)-one **(4)**.




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




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 an absorption bands around 3210 (NH), 3022 (CH), 2928 (CH alkyl), 1686 (CO) and characteristic absorption band for azido group at 2231cm$^{-1}$.

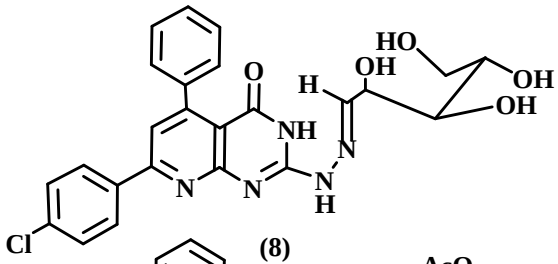



Compound **(6)** was reduced into 2-amino-5-phenyl-7-(4-chlorophenyl)-3H,4H-pyrido[2,3-d]pyrimidin -4-one **(7)** by zinc dust and acetic acid . The $^1$H-NMR (DMSO-$d_6$) spectrum of **(7)** showed signals at δ 7.39 (m, 5H, phenyl protons), δ 7.45-7.55 (m, 4H, phenyl protons), δ 7.88 (s, 1H, CH, pyridinyl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

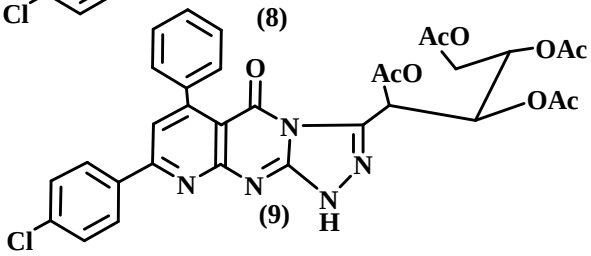
Beside the biological activities of the pyridopyrimidine derivatives as described above also, acyclic C-nucleosides act as antiviral and antiherpetices activities. We reported here a simple and convenient method to synthesis a new acyclic C- and N- nucleoside derivatives derived from 2-hydrazino-5-phenyl-7-(4-

chlorophenyl)-3H,6H-pyrido[2,3-d]pyrimidin-4(4H) one **(1)**.

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



**(8)**

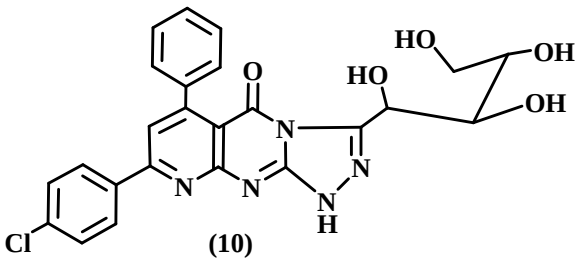


**(9)**

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- 3455cm$^{-1}$ (broad OH), 3250cm$^{-1}$ (NH), 3026cm$^{-1}$(CH), 2924 cm$^{-1}$ (CH alkyl) and 1667cm$^{-1}$ (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 δ1.65 (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 δ11.40 (br. s, 1H, NH, $D_2O$ exchangeable). Its IR spectrum displayed absorption bands at 3300cm$^{-1}$(NH), 3025cm$^{-1}$(CH), 2900cm$^{-1}$ (CH alkyl), 1740-1760cm$^{-1}$ (ester carbonyl) and 1700cm$^{-1}$ (CO).

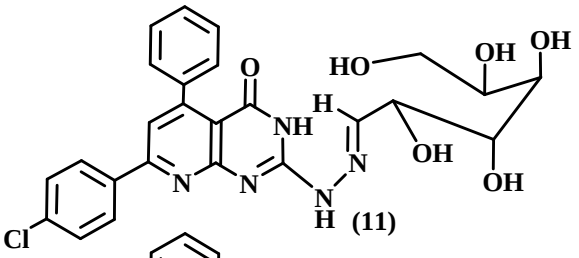
Deacetylation of **(9)** could achieve by treatment with



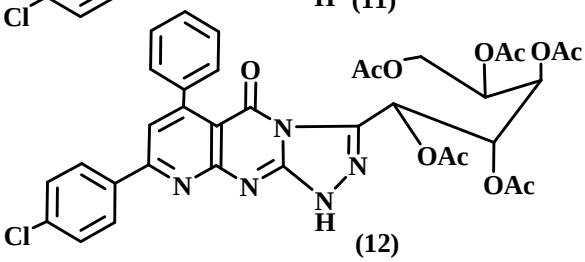
**(10)**

ethanolic sodium methoxide solution to give the deprotected acyclic C-nucleoside **(10)**.

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



**(11)**



**(12)**

The $^1$H-NMR spectrum of compound **(11)**, showed signals at 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′), 4.40 (m,1H, H-4′), δ 4.60 (m, 1H, H-3′), 5.35 (m, 1H, H-2′), δ 6.15 (d, 1H, H-1′), δ 7.55-7.65 (m, 5H, phenyl protons + s,1H, pyridinyl protone), 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 δ11.25 (brs, 1H, NH, $D_2O$ exchangeable). Its IR spectrum displayed absorption bands atcm$^{-1}$ 3265 (NH), cm$^{-1}$, 3224 (NH), cm$^{-1}$, 3030 (CH), cm$^{-1}$, 2920 (CH alkyl) and 1670cm$^{-1}$ (CO).

On the other hand acetylation of compound **(11)** with 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, $OCH_3$), δ1.95 (s, 3H, $OCH_3$), δ 2.00 (s, 3H, $OCH_3$), δ 2.15 (s,

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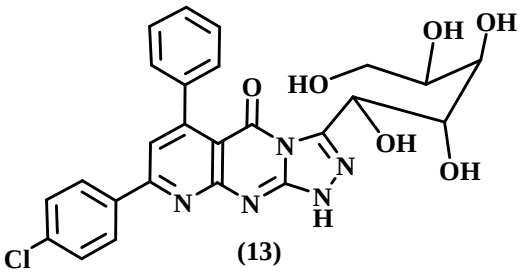


(13)

3H, $OCH_3$), δ2.40 (s, 3H, $OCH_3$), δ 4.85 (m, 1H, H-4′), δ 5.45 (m, 1H, H-3′), δ5.55 (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).

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

## EXPERIMENTAL

Solid compounds were re-crystallized to constant melting points and dried in vacuum in drying pistol containing sodium hydroxide. All melting points are uncorrected and were taken in open capillaries on a Gallen Kamp Apparatus. Micro analyses were carried out at the Micro analytical unite National Research Centre and Faculty of Science, Cairo University. IR spectra were carried out on FT/IR 300 E Jasco using KBr discs. $^1$H-NMR spectra were measured in DMSO or $CDCl_3$, using Joel Ex. 270 NMR spectrometer. Signals were measured with reference to TMS as an internal standard. The Mass spectra were recorded on 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 UV Lamp.

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

A mixture of 7-(4-chlorophenyl)-2-methylthio-5-phenyl-3H,4H-pyrido[2,3-d]pyrimidin-4-one (3.80g, 0.01mole) and hydrazine hydrate (99-100%) (11.40ml, 0.03 mole) in dioxane (20ml) and ethanol (10ml) was heated under reflux for five hours. The solid that separated upon cooling the reaction mixture was filtered-off and re-crystallized from dioxane (45ml) to yield the title compound as pall yellow crystals (2.3g, 63%), mp. 313-2°C. [$C_{19}H_{14}N5OCl$] (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-chlorophenly)-3H, 4H-pyrido[2,3-dpyrimidin--4-one(2a,b)

### General procedure

A mixture of compound **(1)** (3.63g, 0.01mole), the appropriate aromatic aldehyde (0.01 mole), dioxane (30ml) 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 (100ml). The formed precipitate was filtered-off, washed with water, dried and re-crystallized from proper solvent to yield**(2a,b)**.

### 2-(Phenylmethylenehydrazone)-7-(4-chlorophenly) -3H,4H-pyrido[2,3-dpyrimidin-4-one(2a)

From compound **(1)** and benzaldehyde(1.06g, 0.01mole). The product was re-crystallized from dioxane (35ml) to yield the title compound as a shining yellow crystals (3.07g, 68%); m.p. 287-2$^0$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%. IR (KBr)$cm^{-1}$: 3330 (NH), 3037 (CH), 2926 (CH alkyl) and 1670 (CO). $^1$H-NMR (DMSO-$d_6$) δ ppm: 7.45 (s, 1H, CH, ethylinic proton), 7.55-7.65 (m, 10H, phenyl protons), 7.75 (m, 4H, aromatic protons), 8.05 (s, 1H, CH, pyridinyl proton), 11.01 (br. s, 1H, NH, $D_2O$ exchangeable) and 11.50 (br. s, 1H, NH, $D_2O$ exchangeable). MS (EI + Q1MS LMR UP LR): 451.9 ($M^+$) 100%.

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

From compound **(1)** and 4-methoxybenzaldehyde (1.36g, 0.01mole). The product was re-crystallized from dioxane(35ml) to yield the title compound as orange crystals(3.40g, 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)$cm^{-1}$: 3345($NH_2$), 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). MS (EI + Q1MS LMR UP LR): 481.9 ($M^+$) 100%.

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

**General procedure**

A mixture of either of **(3a)** (4.51, 0.01mol) or 3b (4.81g, 0.01mol) with 2g anhydrous sodium acetate, bromine (2.44g, 0.01) and glacial acetic acid (25ml) was heated on water bath at 80ºC 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 proper solvent to give **(3a,b)**.

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

Compound **(3a)** was obtained in 60% yield; m.p.304ºC; [$C_{26}H_{16}N_5ClO$] (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)-1H, 5H-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)-1H,3H-pyrido[2,3-d][1,2,4]traizolo[4,3-a]pyrimidin-5(5H)-one(4)**

A mixture of compound **(1)** (3.63g, 0.01mole), formic acid (1ml) 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, poured into water (100ml). The formed solid was collected by filtration, washed with ethanol (20ml), dried and crystallized from dioxane (35ml) to yield the title compound as a colorless crystals (1.42g, 61%), m.p. 281-82ºC and crystallized from acetic acid to yield the title product as a pale yellow crystals (2.50g, 67%), mp. 239-41ºC. [$C_9H_{11}N_5SO$] (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(5H)-one(5)**

To a warmed ethanolic sodium hydroxide solution (prepared by dissolving sodium hydroxide (0.40g, 0.01mole) in ethanol (50ml), compound **(1)** (3.63g, 0.01mole) and carbon disulphide (10ml) was added. The mixture was heated on a water bath at 80ºC under reflux for eight hours, then it allow to cool to room temperature, poured into water (100ml), neutralized by dilute acetic acid. The formed precipitate was filtered – off, dried and crystallized from dioxin (30ml) to yield the title product as a pale yellow powder (1.70g, 64%), m.p.> 300ºC. [$C_{10}H_8N_4S_2O$] (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). MS (EI + Q1 MS LMR UP LR): 373.79 ($M^+$) 100%.

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

To an ice-cold solution of compound **(1)** (3.63g, 0.01mole) in acetic acid (15ml) was added drop wisely, a solution of sodium nitrite (prepared by dissolving sodium nitrite (1.70g, 0.015 mole) in the least amount of water) in an ice-path at -5$^0$C. The reagent mixture was allowed to stand over night at room temperature, and then it was poured into water (100ml). The solid so-precipitated was filtered–off and re-crystallized from acetic acid to yield the title compound as a yellow crystals (2.50g, 67%), m.p.301-2$^0$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%. IR (KBr) $cm^{-1}$: 3210 (NH), 3022 (CH), 2928 (CH alkyl) and 1686 (CO). $^1$H-NMR (DMSO-$d_6$) δ ppm: 7.38 (m, 5H, phenyl protons), 7.45 (m, 4H, phenyl protons), 7.88(s, 1H, pyridinyl proton) and 13.65 (br. s, 1H, NH, $D_2O$ exchangeable). MS (EI + Q1 MS LMR UP LR): 374.7 ($M^+$) 100%.

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

To a well stirred solution of compound **(6)** (3.74g, 0.01mole) in glacial acetic acid (40ml) was added portion wise activated zinc dust (5.00g) at room temperature over a period of 30 minuets. Stirring was continued for additional three hours. Therefore, the reaction mixture was heated on a water bath (80-90$^0$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(100ml). 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 a yellow crystals (2.14g, 61.5%), m.p. 243-45$^o$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%. IR (KBr)$cm^{-1}$: 3420 ($NH_2$), 3240 (NH), 3034 (CH), 2908 (CH alkyl) and 1666(CO). $^1$H-NMR (DMSO-$d_6$) δ ppm: 7.39 (m, 5H, phenyl protons), 7.45-7.55 (m, 4H, phenyl protons), 7.88 (s, 1H, CH, pyridinyl proton), 8.25 (br. s, 2H, $NH_2$, $D_2O$ exchangeable) and 10.90 (br. s, 1H, NH, $D_2O$ exchangeable). MS (EI + Q1 MS LMR UP LR): 348.7 ($M^+$) 100%.

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

**General procedure**

A mixture of compound **(1)** (3.63g, 0.01mole) and the appropriate monosaccharide (0.01mole), dioxane (30ml), ethanol (10ml) and a 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 filtered-off, wash with ethanol and recrystallized from dioxane (30ml) to afford the title compounds.

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

From compound **(1)** and D-xylose(1.50g, 0.01 mole). The product was re-crystallized from dioxane (35 ml) to yield the title compound as yellow powder (3.20g, 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%. IR (KBr)$cm^{-1}$: 3460- 3455 (broad OH), 3250 (NH), 3026 (CH), 2924 (CH alkyl) and 1667 (CO). $^1$H-NMR (DMSO-$d_6$) δ ppm : 3.45 (m, 4H, 4OH,OH-2′-OH-5′, $D_2O$ exchangeable), 4.25 (m, 1H, H-4′), 4.35 (m, 2H, $CH_2$,H-5′), 4.60 (m, 1H, H-3‘), 5.65 (m, 1H, H-2′), 7.25 (m, 1H, H-1‘), 7.45 (m, 5H, phenyl protons), 7.65 (m, 4H, phenyl protons), 7.90 (s, 1H, CH, pyridinyl proton), 11.20 (br. s, 1H, NH, $D_2O$ exchangeable) and 11.40 (br. s, 1H, NH, $D_2O$ exchangeable).

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

A mixture of compound **(1)** and D-glucose (1.80g, 0.01mole), dioxane (30ml), ethanol (10ml) and a 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 filtered-off, wash with ethanol and re-crystallized from daioxane (35ml) to afford the title compound as yellow crystals (3.34,63%);m.p.281-2ºC [$C_{25}H_{24}N_5O_6$ Cl] (525.95); Required: C, 57.09%; H, 4.59%; N, 13.31%. Found: C, 56.48%; H, 4.38%; N, 12.76%. IR (KBr)$cm^{-1}$: 3450- 3445 (broad OH), 3265 (NH), 3224 (NH), 3030 (CH), 2920 (CH alkyl) and 1670(CO). $^1$H-NMR (DMSO-$d_6$) δ ppm : 3.60 (m, 5H, 5OH, OH-2′-OH-6′, $D_2O$ exchangeable), 3.70 (m, 1H, H-5′), 4.35 (m,2H, $CH_2$, H-6′,H-6′′), 4.40 (m, 1H, H-4′), 4.60(m, 1H, H-3′), 5.35 (m, 1H, H-2′), 6.95 (m, 5H, phenyl protons), 7 .75 (m, 1H, H-1‘), 7.90 (m, 4H, aromatic protons), 8 .20 (s, 1H, CH, pyridinyl proton), 11.05 (br. s, 1H, NH, $D_2O$ exchangeable) and 11.25 (br. s, 1H, NH, $D_2O$ exchangeable).

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

**General procedure**

A solution of compounds **(8)** or compounds **(11)** (0.01mole) in a mixture of acetic anhydride-pyridine (20ml:20ml) was stirred at room temperature for over night them 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 re-crystallized from the proper solvent to produce **(9)** or **(12)**.

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

From compound **(8)** (4.95g, 0.01mole).The product was re-crystallized from methanol (30 ml) to afford the title compound as golden yellow crystals (3.26g, 66%); m.p. 15 6-2°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%. IR (KBr)$cm^{-1}$: 3300 (NH), 3025 (CH), 2900 (CH alkyl), 1740-1760 (ester carbonyl) and 1700 (CO). $^1$H-NMR ($CDCl_3$) δ ppm : 1.65 (s, 3H, $OCH_3$), 1.85 (s, 3H, $OCH_3$), 2.00 (s, 3H,$OCH_3$), 2.15 (s, 3H, $OCH_3$), 5.25 (m, 1H, H-3‘), 5.35 (m, 2H, $CH_2$,H-4‘), 5.55 (m, 1H, H-2‘), 5.75 (m, 1H, H-1‘), 7.40-7.55 (m,5H, phenyl protons), 7.85 (m, 4H, phenyl protons), 7.90 (s, 1H, CH , pyridinyl proton) and 11.40 (br. s, 1H, NH, $D_2O$ exchangeable) .

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

From compound **(11)** (5.25g, 0.01mole).The product was re-crystallized from methanol (35ml) to yield the title compound as yellow crystals (4.38g, 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%. IR (KBr)$cm^{-1}$: 3230 (NH), 3030 (CH), 2920 (CH alkyl), 1745-1715 (ester carbonyl) and 1685 (CO). $^1$H-NMR ($CDCl_3$) δ ppm : 1.85 (s, 3H, $OCH_3$), 1.95 (s, 3H, $OCH_3$), 2.00 (s, 3H, $OCH_3$), 2.15 (s, 3H, $OCH_3$), 2.40 (s, 3H, $OCH_3$), 4.85 (m, 1H, H-4′), 5.45 (m, 1H, H-3′), 5.55 (m, 2H, $CH_2$, H-5′), 5.65 (m, 1H, H-2′), 5.70 (m, 1H, H-1′), 6.85 (m, 5H, phenyl protons), 7.65 (m, 4H, aromatic protons), 8.00 (s, 1H, CH, pyridinyl proton) and 11.45 (br. s, 1H, HN, $D_2O$ exchangeable). $^{13}$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 (Pyridopyriidone 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)-1H,7H-pyrido[2,3-d][1,2,4]triazolo[4,3-a] pyrimidin-5(5H)-one(10,13)**

**General procedure**

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

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

From compound **(9)** (6.62g, 0.01mole).The product was re-crystallized from dioxane (40ml) to yield the title compound as yellow powder (2.35g, 47.50%); m.p.248-2°C. [$C_{24}H_{20}N_5O_5Cl$] (493.9); Require: C, 58.36%; H, 4.08%; N, 14.17%. Found: C, 58.14%; H, 3.84%; N, 13.77%.IR (KBr)$cm^{-1}$: 3460- 3455 (broad OH), 3255 (NH), 3026 (CH), 2922 (CH alkyl) and 1717 (CO). $^1$H-NMR (DMSO-$d_6$) δ ppm : 3.80 (m, 1H, H-2′), 3.90 (m, 4H, 4OH, $D_2O$ exchangeable), 4.20 (m, 1H, H-3′), 4.55 (m, 2H, H-4′: H-4′′), 4.65 (m,1H, H-1′), 7.40 (m, 5H, phenyl protons), 7.75 (m, 4H, phenyl protons),7.80 (s,1H,CH, pyridinyl proton) and 9.95 (br. s, 1H, NH, $D_2O$ exchangeable).

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

From compound **(12)** (6.76g, 0.01 mole).The product was re-crystallized from dioxane (40 ml) to yield the title compound as yellow powder (2.70 g, 51.50%); m.p.251-2°C. [$C_{25}H_{23}N_5O_6Cl_1$] (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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