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Research Article

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Synthesis of some *N*-Acyclic Pyrazolopyrimidine Nucleosides and Pyrazolotriazolopyrimidines

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Abstract Pyrazolo[3,4-*d*]pyrimidin-4-one derivative **1** was used as a key compound for the preparation of some *N*-acyclic nucleosides of pyrazolo[3,4-*d*]pyrimidines **2-5**. Also, the synthesis and structure characterization of pyrazolo[3,4-*d*]pyrimidin-6-yl-hydrazine derivative **6** was reported as a key compound for the preparation of pyrazolotriazolopyrimidine derivatives **7-9** under different suitable reaction conditions. Cyclization of the hydrazone derivatives **10** and **11** with acetic anhydride, in pyridine, gave the corresponding *O*-acetylated sugar hydrazone derivatives **12** and **13** instead of the cyclized form of pyrazolotriazolopyrimidine derivatives. The prepared compounds are expected to possess notable pharmacological applications.

Keywords Pyrazoles, Pyrazolopyrimidines, Pyrazolotriazolopyrimidines, Acyclic nucleosides.

Introduction

Pyrazolo[3,4-*d*]pyrimidine derivatives have been found to possess considerable attention due to their applications and pharmacological activities, [1] not only as antimicrobial, [2,3] antifungal, [4] herbicidal, [5] anti-inflammatory and analgesic, [6] antitubercular, [7] hyperuricemia, [8] cardiovascular agents, [9] antitumor, [10-14] antiviral, [15-17] anticoccidial, [18] antiamoebic, [19] antileishmanial, [20] radioprotectant, [21] and corrosion inhibitors for carbon steel, [22] but also they are important as starting materials for the synthesis of other fused heterocyclic systems. One of the most important fused pyrazolopyrimidine moieties is pyrazolotriazolopyrimidine derivatives which possess notable chemical and pharmacological activities. [2, 12, 24-26]. Moreover, the binding of pyrazolopyrimidines with acyclic sugar moiety, forming the corresponding nucleosides, attracted the attention of many researchers because of their high potential to exhibit chemotherapeutic activity [14,15,18,22]. Based on the above mentioned research results and in continuation of our research program on pyrazolopyrimidine and pyrazolotriazolopyrimidine systems [23, 27] the goal of this study is to synthesize and characterize the structure of novel pyrazolopyrimidine and pyrazolotriazolopyrimidine derivatives with expected notable pharmacological applications.

Experimental

All melting points were uncorrected and measured using Electro-Thermal IA 9100 apparatus (Shimadzu, Japan). Infrared spectra were recorded as potassium bromide pellets on a Perkin-Elmer 1650 spectrophotometer (Perkin-Elmer, Norwalk, CT, USA). ^{1}H NMR and ^{13}C NMR spectra were determined on a Jeol-Ex-400 NMR spectrometer (JEOL, Tokyo, Japan) and chemical shifts were expressed as part per million; (δ values, ppm) against TMS as internal reference. Mass spectra were recorded on VG 2AM-3F mass spectrometer (Thermo Electron Corporation, USA). Microanalyses were operated using Mario El Mentar apparatus, Organic Micro analytical Unit. Follow up of the reactions and checking the purity of the compounds was made by TLC on silica gel-precoated aluminum sheets (Type 60 F254; Merck, Darmstadt, Germany). Column chromatography was performed on Silica gel 60 (particle size 0.06–0.20 mm; Merck). Compounds **1** was prepared according to reported method [14].

General procedure for the Synthesis of compounds **2-5***:*

To 0.01 mol of compound **1** in 20 mL DMF was added 0.01 NaH, and the reaction mixture was stirred for 2h. To this reaction mixture, an equivalent amount (0.01 mol) of either 2-chloroethyl methyl ether, chloroacetaldehyde dimethyl-acetal, 2-chloroethanol or 2-(2-chloroethoxy)-ethanol was added respectively and the reaction mixture was stirred at 50-60 ^{o}C for 3-5 h. The reaction mixture was monitored with TLC till reaction was completed, then the reaction mixture was poured onto crushed ice then extracted with diethyl ether. After evaporation under reduced pressure, the residues were purified on silica gel column using chloroform: methanol (9:1) as an eluent to give compounds **2-5,** respectively.

5-(Methoxyethyl)-6-(methylthio)-1-(9-methyl-5,6-dihydronaphtho[1',2':4,5]thieno[2,3-d]pyrimidin-11-yl)-1,5-dihydro-4H-pyrazolo[3,4-d]pyrimidin-4-one **2**

Buff powder; (Yield 49%); m.p. 195-196^{o}C;IR (KBr) υ cm^{-1}: 1659 (N-C=O); ^{1}H NMR (DMSO-d_6) δ ppm: 2.25 (s, 3H, S-CH_3), 2.50 (s, 3H, CH_3), 2.77-2.89 (m, 4H, 2CH_2), 3.55 (s, 3H, -O-CH_3), 3.85 (m, 2H, N-CH_2), 4.16 (m, 2H, -CH_2-O-), 7.20-7.30 (m, 4H, 3Ar-H+90pyrazole-H), 7.88 (d, 1H, *J*=8 Hz, Ar-H); MS, *m/z* (%): 490.00 (M^+, 100.00), 476.00 (M^+-[CH_3], 14.32), 445.00 (M^+-[CH_2-O-CH_3], 17.80), 449.00 (75), 430.00 (M^+-[CH_2-CH_2-O-CH_3], 18.86), 63.00 (56.04); Anal. Calcd. for $C_{24}H_{22}N_6O_2S_2$ (490.60) (%): C, 58.76; H, 4.52; N, 17.13; S, 13.07. Found (%): C, 58.63; H, 4.72; N, 17.04; S, 13.18.

5-(2,2-Dimethoxyethyl)-6-(methylthio)-1-(9-methyl-5,6-dihydronaphtho[1',2':4,5]thieno[2,3-d]pyrimidin-11-yl)-1,5-dihydro-4H-pyrazolo[3,4-d]pyrimidin-4-one **3**

Brown powder; (Yield 49%); m.p.207-209^{o}C; IR (KBr) υ cm^{-1}: 1606(-N-C=O); ^{1}H NMR (DMSO-d_6) δ ppm: 2.23 (s, 3H, S-CH_3), 2.51 (s, 3H, CH_3), 2.88-2.96 (2m, 4H, 2CH_2), 3.37 (s, 6H, 2-O-CH_3), 3.80 (d, 2H, N-CH_2), 4.45 (t, 1H, N-CH_2-CH), 7.16-7.28 (2m, 4H, 3Ar-H+H-pyrazole), 8.41 (d, 1H, *J*=7.4 Hz, Ar-H); MS, *m/z* (%): 521.50 (M^++1, 1.61), 520.50 (M^+, 41.25), 505.50 (M^+-[CH_3], 84.45), 489.55 (M^+-[OCH_3], 70.25), 458.40 (M^+-(OCH_3)$_2$, 28.50), 384.35 (26.44), 269.25 (46.87), 251.25 (51.65), 64.00 (100.00); Anal. Calcd. for $C_{25}H_{24}N_6O_3S_2$ (520.62) (%): C, 57.67; H, 4.65; N, 16.14; S, 12.32. Found (%): C, 57.58; H, 4.54; N, 16.27; S, 12.47.

5-(2-Hydroxyethyl)-6-(methylthio)-1-(9-methyl-5,6-dihydronaphtho[1',2':4,5]thieno[2,3-d]pyrimidin-11-yl)-1,5-dihydro-4H-pyrazolo[3,4-d]pyrimidin-4-one **4**

Brown oil; (Yield 54%); IR υ cm^{-1}: 3418 (OH broad), 1596 (-N-C=O); ^{1}H NMR (DMSO-d_6) δ ppm: 2.20 (s, 3H, S-CH_3), 2.46 (s, 3H, CH_3), 2.74-2.89 (2m, 4H, 2CH_2), 3.90-4.25 (m, 4H, N-CH_2-CH_2), 5.00 (br, 1H, OH, D_2O exchangeable), 7.20-7.28 (2m, 4H, 3Ar-H+H-pyrazole), 7.88 (d, 1H, *J*=8 *Hz*, Ar-H); MS, *m/z* (%):476 (M^+, 31.50), 445.40 (M^+-[CH_2OH], 24.00), 384.35 (72.00), 368.35 (100.00), 251.20 (11.23), 225.20 (10.97); Anal. Calcd. for $C_{23}H_{20}N_6O_2S_2$ (476.57) (%): C, 57.96; H, 4.23; N, 17.63; S, 13.46. Found (%): C, 57.84; H, 4.42; N, 17.54; S, 13.61.

5-[2-(2-Hydroxyethoxy)ethyl]-6-(methylthio)-1-(9-methyl-5,6-dihydronaphtho[1',2':4,5]thieno[2,3-d]pyrimidin-11-yl)-1,5-dihydro-4H-pyrazolo[3,4-d]pyrimidin-4-one **5**

Pale brown powder; (Yield 61%); m.p. 183-185^{o}C; IR (KBr) υ cm^{-1}: 3376 (OH broad), 1604 (N-C=O); ^{1}H NMR (DMSO-d_6) δ ppm: 2.15 (s, 3H, S-CH_3), 2.38 (s, 3H, CH_3), 2.64-2.90 (2m, 4H, 2CH_2), 3.90 (m, 2H, N-CH_2), 4.33-4.4.61 (2m, 6H, -CH_2-O-CH_2-CH_2-OH), 5.25 (br, 1H, OH, D_2O exchangeable), 7.20-7.39 (2m, 4H, 3Ar-H+H3-pyrazole), 8.40 (d, 1H, *J*=7.5 *Hz*, Ar-H); MS, *m/z* (%): 520.50 (M^+, 28.82), 431.40 (M^+-[$(CH_2)_2OCH_2CH_3$], 2.26), 250.15 (18.07), 85.15 (100); Anal. Calcd. for $C_{25}H_{24}N_6O_3S_2$ (520.62) (%): C, 57.67; H, 4.65; N, 16.14; S, 12.32. Found (%): C, 57.76; H, 4.75; N, 16.01; S, 12.47.

1-(9-Methyl-5,6-dihydronaphtho[1',2':4,5]thieno[2,3-d]pyrimidin-11-yl)-1H-pyrazolo[3,4-d]pyrimidin-6-yl-hydrazine-4-one **6**

To a solution of compound **1** (0.01 mol), in dry ethanol (30 mL), hydrazine hydrate (0.01 mol 99%) was added and the reaction mixture was heated under reflux for 3 h. The reaction mixture was poured onto crushed ice and the deposited solid was filtered off, washed several times with water, dried and recrystallized from ethanol to give compound **6**. Pale yellow crystals; (Yield 81%); m.p. 301-303^{o}C; IR (KBr) υ cm^{-1}: 3428 (-NH), 3261, 3211 (-NH_2), 1690 (C=O), 1561 (C=N); ^{1}H NMR (DMSO-d_6) δ ppm: 2.51 (s, 3H, CH_3), 2.82-2.92 (2m, 4H, 2CH_2), 4.00 (br, 2H, NH, D_2O exchangeable), 7.15-7.28 (2m, 4H, 3Ar-H+ H3-pyrazole), 8.40 (s, 1H, NH,D_2O exchangeable), 8.42 (d, 1H, *J* = 8 *Hz*, Ar-H), 12.41 (s, 2H, NH_2,D_2O exchangeable); MS, *m/z* (%): 419.00 (M^++3, 49.31), 418.00 (M^++3, 56.94), 417.00 (M^++1, 38.19), 416.00 (M^+, 41.67), 399.00 (M^+-(NH_2+H^+), 37.50), 69.00 (100.00); Anal. Calcd. for $C_{20}H_{16}N_8OS$ (416.64) (%): C, 57.68; H, 3.87; N, 26.91; S, 7.70. Found (%): C, 57.80; H, 4.07; N, 27.02; S, 7.54.

8-(9-Methyl-5,6-dihydronaphtho-[1',2':4,5]thieno[2,3-d]pyrimidin-11-yl)-1,8-dihydro-5H-pyrazolo[3,4-d][1,2,4]triazolo[4,3-a]pyrimidin-5-one **7**

A solution of compound **6** (2.5 mmol) in 30 mL formic acid was refluxed for 10 h. The reaction mixture was poured onto crushed ice and the formed precipitate was filtered off, washed with water, dried and recrystallized from ethanol to give the title compound **7**. Grey powder, (Yield 71%); m.p. 301-303^{o}C; IR (KBr) υ cm^{-1}: 3429 (NH), 1613 (N-C=O), 1512 (C=N); ^{1}H NMR (DMSO-d_6) δ ppm: 2.37 (s, 3H, CH_3), 2.82-3.09 (2m, 4H, 2CH_2), 7.15-7.39 (m, 4H, 3 Ar-H+H-pyrazole), 8.38 (d, 1H, *J*=8 Hz, Ar-H), 8.76 (s, 1H, H-triazole), 12.45 (s, 1H, NH-triazole, D_2O exchangeable); ^{13}C NMR (DMSO-d_6) δ ppm: 20.54 (CH_3), 23.37 (CH_2), 28.90 (CH_2), 126.20-154.81 (17 sp^2-C), 158.10 (C=O); MS, *m/z* (%): 426.30 (M^+, 6.20), 384.30 (M^+-NH-N=CH, 4.27), 330.30 (8.40), 316.30 (4.20), 279.00 (13.64), 267.10 (100.00), 251.10 (8.95);Anal. Calcd. for $C_{21}H_{14}N_8OS$ (426.45) (%): C, 59.14; H, 3.31; N, 26.28; S, 7.52. Found (%): C, 59.06; H, 3.42; N, 26.39; S, 7.40.

3-Methyl-8-(9-methyl-5,6-dihydro-naphtho[1',2':4,5]thieno[2,3-d]pyrimidin-11-yl)-1,8-dihydro-5H-pyrazolo[3,4-d][1,2,4]triazolo[4,3-a]-pyrimidin-5-one **8**

A solution of compound **6** (2.5 mmol), glacial acetic acid 20 mL and acetic anhydride 20 mL, was heated under reflux for 7 h. The formed precipitate was filtered off and washed several times with hot water, dried and recrystallized from ethanol/dioxane to give compound **8**. Pale white powder; (Yield 78%); m.p. 283-285^{o}C; IR (KBr) υ cm^{-1}: 3440 (NH), 1659 (N-C=O), 1592 (C=N); ^{1}H NMR (DMSO-d_6) δ ppm: 2.38 (s, 3H, CH_3), 2.51 (s, 3H, CH_3), 2.82-23.05 (m, 4H, 2CH_2), 7.16-7.39 (m, 4H, 3 Ar-H+H-pyrazole), 8.45 (d, 1H, *J*=7.6 *Hz*,Ar-H), 12.45 (s, 1H, NH-triazole, D_2O exchangeable); ^{13}C NMR (DMSO-d_6) δ ppm: 20.55 (CH_3), 22.14 (CH_3), 23.69 (CH_2), 29.25 (CH_2), 118.31-158.13 (176 sp^2-C), 164.63 (C=O); MS, *m/z* (%): 441.00 (M^++1, 18.79), 440.00 (M^+, 21.52), 182.05 (87.58), 111.05 (100.00);Anal. Calcd. for $C_{22}H_{16}N_8OS$ (440.48) (%): C, 59.99; H, 3.66; N, 25.44; S, 7.28. Found (%): C, 59.87; H, 3.77; N, 25.24; S, 7.42.

8-(9-Methyl-5,6-dihydronaphtho-[1',2':4,5]thieno[2,3-d]pyrimidin-11-yl)-1,8-dihydro-5H-pyrazolo [3,4-d][1,2,4]triazolo[4,3-a]pyrimidin-3-thiol-5-one **9**

A mixture of compound **6** (2.5 mmol) and carbon disulfide 10 mL in alcoholic potassium hydroxide solution (2.5 mmol, 0.14 g) in 30 mL ethyl alcohol, was heated on water bath (60^{o}C) for 7 h. The reaction mixture was poured

onto crushed ice and the formed precipitate was filtered off, washed several times with hot water, dried and recrystallized from ethanol/dioxane to give the title compound **8**. Pale white powder; (Yield 77%); m.p. 310-312^{o}C; IR (KBr) υ cm^{-1}: 3437 (NH), 1659 (C=O), 1593 (C=N); ^{1}H NMR (DMSO-d_6) δ ppm: 2.33 (s, 1H, SH), 2.46 (s, 3H, CH_3), 2.46-3.52 (m, 4H, $2CH_2$), 6.95-7.23 (2m, 4H, 3Ar-H+ H-pyrazole), 7.41 (d, 1H, *J*=8 *Hz*, Ar-H), 9.53 (s, 1H, NH, D_2O exchangeable); MS, *m/z* (%): 458.15 (M^+, 50), 384.20 (40), 268.10 (100.00); Anal. Calcd. for $C_{21}H_{14}N_8OS_2$ (458.52) (%): C, 55.01; H, 3.08; N, 24.44; S, 13.99. Found (%): C, 55.45; H, 3.11; N, 24.27; S, 13.89.

*General procedure for the synthesis of **10** and **11***

A mixture of compound **6** (2.5 mmol), *D*-glucose (2.5 mmol), or *D*-ribose (2.5 mmol) in ethanol (30 ml), and a catalytic amount of glacial acetic acid (3 drops) was heated on water bath (70^{o}C) for 2 h. The formed precipitate was filtered while hot, washed with water several times, air dried and recrystallized from ethanol/dioxane to give compounds **10** and **11**, respectively.

D-Glucose N-1-(9-methyl-5,6-dihydronaphtho-[1',2':4,5]thieno[2,3-d]pyrimidin-11-yl)-4-oxo-4,5-dihydro-1H-pyrazolo[3,4-d]pyrimidin-6-yl-hydrazone **10**

Pale brown powder; (Yield 72%); m.p. 201-203^{o}C; IR (KBr) υ cm^{-1}: 3408 (NH), 3418 (broad, OH), 1614 (N-C=O); ^{1}H NMR (DMSO-d_6) δ ppm: 2.34 (s, 3H, CH_3), 2.83-2.88 (m, 4H, $2CH_2$), 3.00-3.34 (m, 4H, CHOH), 3.79 (m, 2H, CH_2OH), 4.35 (s, 1H, CH_2OH, D_2O exchangeable), 4.75-5.05 (m, 2H, 2OH, D_2O exchangeable), 5.35 (m, 2H, 2OH, D_2O exchangeable), 7.14-7.38 (m, 4H, 3Ar-H+92yrazolo-H), 8.36 (d, 1H, *J*=8 *Hz*, Ar-H), 8.72 (s, 1H, N=C-H), 9.35 (br, 1H, NH, D_2O exchangeable), 12.40 (s, 1H, NH, D_2O exchangeable); MS, *m/z* (%):578.50 (M^+, 55.85), 561.50 (M^+-[OH], 69.82), 545.40 (65.09) 411.20 (82.84), 316.20 (72.19), 303.30 (100.00), 251.15 (28.40); Anal. Calcd. for $C_{26}H_{26}N_8O_6S$ (578.60) (%): C, 53.97; H, 4.53; N, 19.37; S, 5.54. Found (%): C, 53.84; H, 4.64; N, 19.18; S, 5.67.

*D-Ribose N-1-(9-methyl-5,6-dihydronaphtho[1',2':4,5]-thieno[2,3-d]pyrimidin-11-yl)-4-oxo-4,5-dihydro-1H-pyrazolo[3,4-d]pyrimidin-6-yl-hydrazone **11***

Grey powder, (Yield 69%); m.p. 189-191^{o}C; IR (KBr) υ cm^{-1}: 3418 (broad NH+OH), 1624 (N-C=O); ^{1}H NMR (DMSO-d_6) δ ppm: 2.34 (s, 3H, CH_3), 2.83-3.13 (m, 4H, $2CH_2$), 3.18-3.33 (m, 3H, CHOH), 3.68 (m, 2H, CH_2OH), 4.09 (s, 1H, CH_2OH, D_2O exchangeable), 4.80-5.00 (m, 2H, 2OH, D_2O exchangeable), 5.23 (s, 1H, OH, D_2O exchangeable), 7.14-7.56 (2m, 4H, 3Ar-H+92yrazolo-H), 8.37 (d, 1H, *J*=8 *Hz*, Ar-H), 8.76 (s, 1H, N=C-H), 10.36 (br, 1H, NH, D_2O exchangeable), 12.40 (s, 1H, NH, D_2O exchangeable);MS, *m/z* (%): 548.50 (M^+, 20.55), 370.30 (21.13), 251.20 (12.46), 163.10 ([NH-N=C-$(CHOH)_3CH_2OH$], 30.72); Anal. Calcd. for $C_{25}H_{24}N_8O_5S$ (548.75) (%): C, 54.74; H, 4.41; N, 20.43; S, 5.85. Found (%): C, 54.89; H, 4.53; N, 20.30; S, 5.96.

*General procedure for the synthesis of compounds **12** and **13***

Compounds **10** or **11** (2.5 mmol) were stirred at room temperature in a mixture of pyridine/acetic anhydride (5:15 mL) for 3 and 4 h, respectively. The reaction mixtures were poured onto crushed ice with stirring and the solids that precipitated were collected by filtration, washed with water, dried and recrystallized from dioxane/ethanol to give compounds **12** and **13** respectively.

*2,3,4,5,6-Penta-O-acetyl-aldehydo-D-glucose-N-1-(9-methyl-5,6-dihydro-naphtha[1',2':4,5]thieno[2,3-d]pyrimidin-11-yl)-4-oxo-4,5-dihydro-1H-pyrazolo[3,4-d]pyrimidin-6-yl-hydrazone **12***

Pale brown powder; (Yield 54%); m.p. 208-210^{o}C; IR (KBr) υ cm^{-1}: 3316 (NH), 1725 (O=C-CH_3), 1620 (N-C=O), 1512 (C=N); ^{1}H NMR (DMSO-d_6) δ ppm: 2.05-2.20 (m, 9H, 3 Oac), 2.37 (s, 3H, CH_3), 2.44-2.60 (m, 6H, 2 Oac), 2.85-2.934 (m, 4H, $2CH_2$), 4.05-4.23 (m, 2H, CH_2Oac), 4.65-5.01 (m, 4H, 4CHOAc), 7.14-7.27 (m, 4H, 3Ar-H+92yrazolo-H), 7.65 (s, 1H, N=C-H), 8.40 (d, 1H, *J*=7.5 *Hz*,Ar-H), 9.40 (br, 1H, NH, D_2O exchangeable), 12.40 (s, 1H, NH, D_2O exchangeable); MS, *m/z* (%): 789.20 (M^++1, 11.71), 269.10 (23.17), 268.10 (100.00); Anal. Calcd.

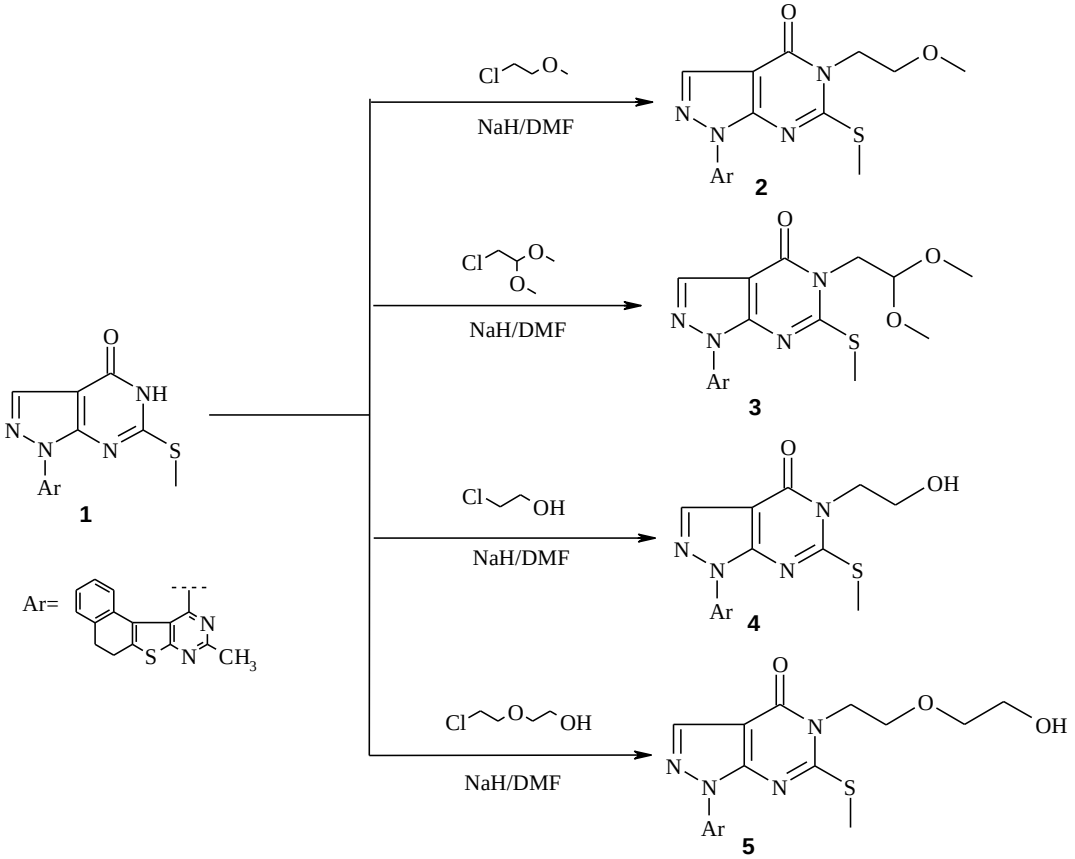
for $C_{36}H_{36}N_8O_{11}S$ (788.78) (%): C, 54.82; H, 4.60; N, 14.21; S, 4.07. Found (%): C, 54.79; H, 4.63; N, 14.23; S, 4.10.

2,3,4,5-Tetra-O-acetyl-D-ribose-N-1-(9-methyl-5,6-dihydro-naphtha[1',2':4,5]thieno[2,3-d]pyrimidin-11-yl)-4-oxo-4,5-dihydro-1H-pyrazolo[3,4-d]pyrimidin-6-yl-hydrazone ***13***

Pale white powder, (Yield 49%); m.p. 195-198^{o}C; IR (KBr) υ cm^{-1}: 3433 (NH), 1725 (O=C-CH_3), 1658.48 (N-C=O), 1532.17 (C=N); ^{1}H NMR (DMSO-d_6) δ ppm: 1.91-2.2 (m, 6H, 2 Oac), 2.31 (s, 3H, CH_3), 2.40-2.67 (m, 6H, 2 Oac), 2.83-2.91 (m, 4H, $2CH_2$), 4.15-4.40 (m, 2H, CH_2Oac), 4.93-5.35 (m, 3H, 3CHOAc), 7.14-7.27 (m, 4H, 3Ar-H+93yrazolo-H), 7.60 (s, 1H, N=CH), 8.43 (d, 1H, *J*=8 *Hz*, Ar-H), 9.21 (br, 1H, NH, D_2O exchangeable), 12.38 (s, 1H, NH, D_2O exchangeable); MS, *m/z* (%): 718.20 (M^++2, 12.68), 716.20 (M^+, 20.49), 701.20 (M^+-CH_3, 2.20), 657.20 (M^+-$OCOCH_3$, 13.90), 427.20 (M^+-sugar residue, 5.37) 80.15 (100.00); Anal. Calcd. for $C_{33}H_{32}N_8O_9S$ (716.72) (%): C, 55.30; H, 4.50; N, 15.63; S, 4.47. Found (%): C, 55.98; H, 4.54; N, 15.60; S, 4.44.

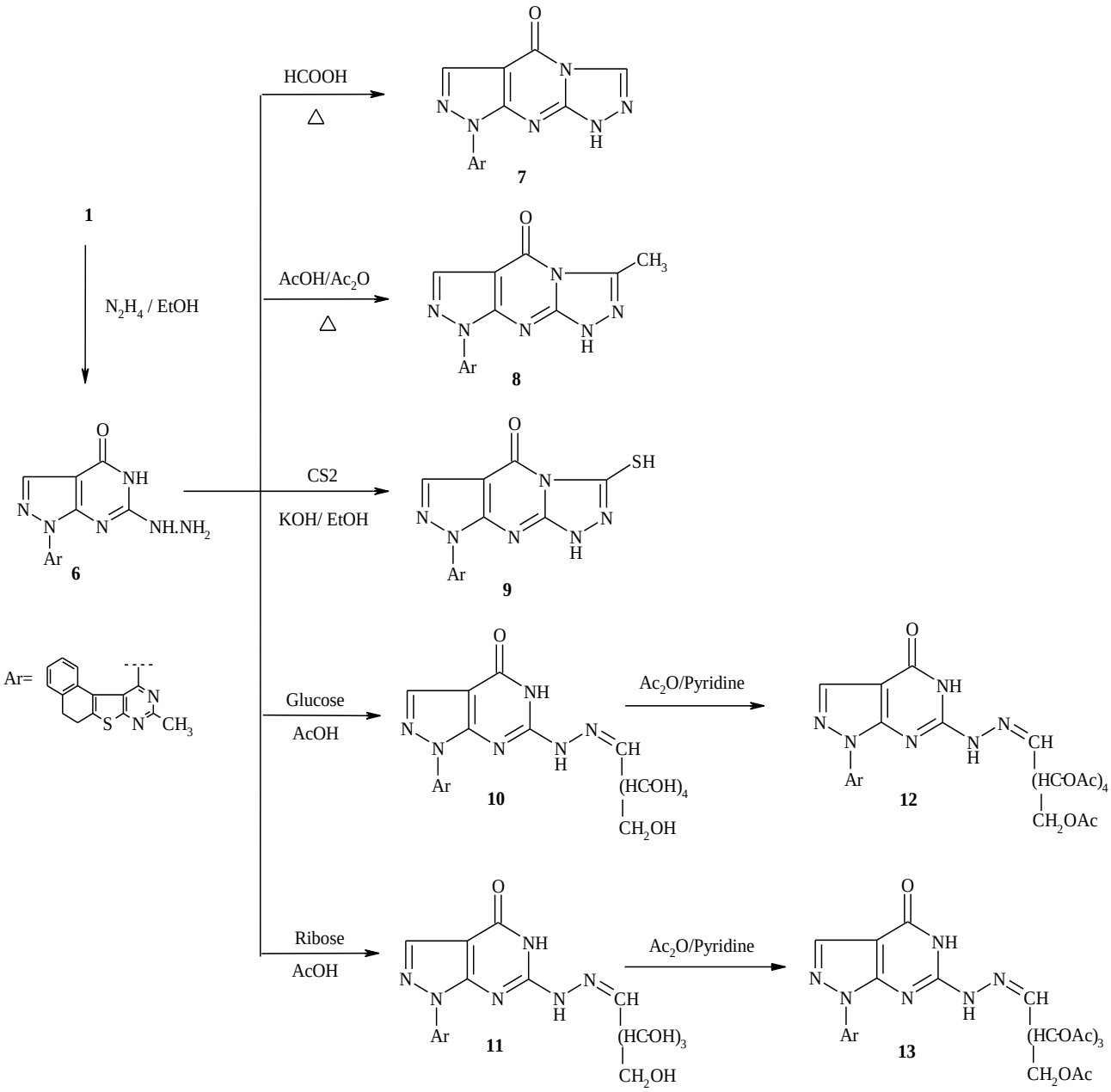
Result and Discussion

6-Methylthio-1-(9-methyl-5,6-dihydronaphtho-[1',2':4,5]thieno[2,3-*d*]pyrimidin-11-yl)-1*H*-pyrazolo-[3,4-*d*]pyrimidin-4-one (**1**) [14] was prepared as the key compound for this study and for further syntheses of other fused heterocyclic compounds. Thus, when compound **1** was treated with 2-chloroethyl methyl ether, chloracetaldehydedimethylacetal, 2-chloroethanol and 2-(2-chloroethoxy)ethanol, it afforded the corresponding *N*-acyclic nucleoside derivatives**2-5**, respectively (Scheme 1). The IR spectra of the latter compounds revealed the presence of the C=O absorption band and the absence of the N-H absorption band for each compound, and the ^{1}H NMR spectra indicated the absence of the NH signals and the presence of hydroxyethyl, dimethoxyethyl, methoxyethyl and hydroxymethoxy ethyl signals, respectively (*cf*. experimental).



Scheme 1

*Scheme 1: Synthesis of compounds **2-5***



Scheme 2

*Scheme 2: Synthesis of compounds **6-13***

Hydrazinolysis of compound **1**, in ethanol, gave the corresponding 1-(5,6-dihydronaphtho-[1',2':4,5]thieno[2,3-*d*]pyrimidin-11-yl)-1*H*-pyrazolo[3,4-*d*]-pyrimidin-6-yl-hydrazine-4-one **(6)** (Scheme 2). The ^{1}H NMR spectrum of compound **6** gave signals for NH, NH_2, exchangeable with D_2O.

When compound **6** was treated with formic acid or glacial acetic acid and acetic anhydride, it gave pyrazolo[3,4-*d*][1,2,4]triazolo[4,3-*a*]pyrimidin-5-onederivatives **7** and **8**, respectively. The ^{1}H NMR spectra of compound **8**

showed singlet signal at δ 2.38 ppm for the extra methyl group and singlet signal at δ 12.45 ppm, D_2O exchangeable, corresponding to the NH-triazole group.

While, on treatment compound **6** with carbon disulfide in alcoholic potassium hydroxide solution, it gave 8-(9-methyl-5,6-dihydronaphtho[1',2':4,5]thieno[2,3-*d*]-pyrimidin-11-yl)-1,8-dihydro-5*H*-pyrazolo[3,4-*d*][1,2,4]-triazolo[4,3-*a*]pyrimidin-3-thiol-5-one **9** (Scheme 2). The ^{1}H NMR spectrum of compound **9** showed the presence of singlet signal at δ 2.33 ppm corresponding to the –SH proton.

Furthermore, treatment of compound **6** with either *D*-glucose or *D*-ribose in presence of a catalytic amount of glacial acetic acid gave the corresponding hydrazone derivatives**10** or **11**, respectively. IR spectrum of compound **10** revealed absorption bands at υ 3408 and 3418 cm^{-1}corresponding to NH and OH groups.

Acetylation of the hydrazone derivatives **10** or **11** with acetic anhydride in pyridine gave the corresponding *O*-acetylated sugar derivatives **12** and **13**, instead of the cyclized form of pyrazolotriazolopyrimidines. The ^{1}H NMR spectra of derivatives **12** and **13** showed the presence of -OAc groups and two exchangeable –NH, as well as the presence of signals corresponding to at δ 7.65 and 7.60 ppm, respectively (Scheme 2).

Conclusion

The synthesis and structure characterization of some *N*-acyclic nucleosides of pyrazolo[3,4-*d*]pyrimidines, pyrazolo[4,3-i][1,2,4]triazolo[4,3-*c*]pyrimidine derivatives, and *C*-acyclic nucleosides of pyrazolo[3,4-*d*]pyrimidine derivatives were prepared. The prepared compounds are expected to possess notable pharmacological applications.

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