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New Synthesis of C- and N-Acyclic Nucleosides from 2-Hydrazinothienopyrimidone Derivatives

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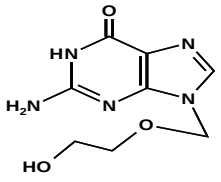
ACYCLIC N-nucleosides are prepared by heating under reflux 2-hydrazinocyclopentenothienopyrimidone 1 with aldopentoses in dioxane to give the corresponding acyclic N-nucleosides 2 and 3, which cyclized on stirring at room temperature in acetic anhydride/pyridine mixture to afford the corresponding protected tetra O-acetate C-nucleosides 4 and 5, respectively. De-acetylation of compound 4 and 5 afforded the free acyclic C-nucleosides 6 and 7, respectively. On the other hand, acyclic N-nucleosides 8 and 10 were obtained on treatment of 1 with aldohexoses in the same manner. The protected penta O-acetyl C-nucleosides 11-13 were obtained when stirred compounds 8-10 with acetic anhydride/pyridine mixture at room temperature. De-protection afforded the free acyclic C-nucleosides 14-16, respectively.

Keywords: 2-Hydrazinocyclopentenothienopyrimidone, Acyclic N-nucleosides, O-acetyl C-nucleosides and Acyclic C-nucleosides.

Since 1957, when pseudouridine [5-(β-D-ribofuranosyl)uracil] was isolated from yeast DNA[(1)], the chemistry and biochemistry of naturally occurring and non- biogenic C-nucleosides has become a field of broad interest [(2,3-8)].

On the other hand, the discovery of 9-[(2-hydroxyethoxy)-methyl]guanine (acyclovir, ACV, zovirax^{R}) which acts as antiherpetic drug and posses antiviral activity in cells infected with herpes simplex virus type I (HSV-I), but is essentially nontoxic to uninfected host cells.



ACV I

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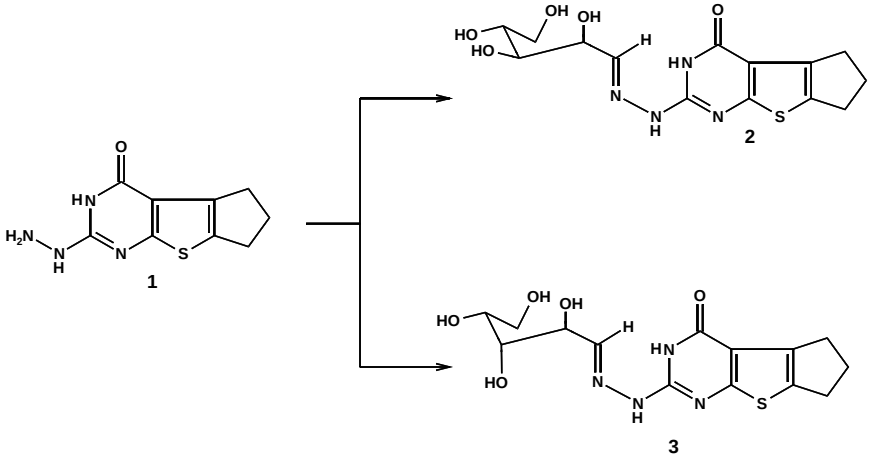
Recently, acyclic nucleosides of the HEPT type 1-[(2-hydroxy) methyl]-6-(phenylthio) thymine have shown high selectivity toward HIV-I[9].

These discoveries had led to extensive efforts to synthesize other acyclic analogues of the natural nucleoside[10-23] and evaluated their biological activity.

We reported here a simple and convenient method to synthesize a series of new acyclic C- & N-nucleosides derivatives, starting with 2-hydrazino-thienocyclopentenopyrimidone derivative 1 [24].

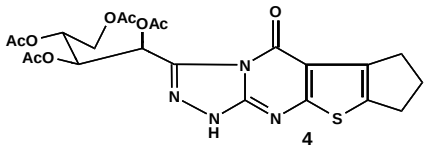
Results and Discussion

Heating under reflux 1 with aldopentoses namely D-arabinose and D-xylose in dioxane in presence of catalytic amounts of piperidine yielded the corresponding acyclic N-nucleosides 2 and 3.



The ^{1}H-NMR spectrum (DMSO-d_6) of compound 3 as an example, showed signals at δ 2.30 ppm (m, 2H, CH_2), δ 2.85 (m, 4H, 2 CH_2), δ 3.50 – 5.00 (m, 4 OH, D_2O exchangeable, OH-2', OH-3', OH-4' and OH-5'), δ 4.25 (q, 1H, J=6.0 Hz, H-4'), δ 4.45 (m, 2H, H_2-5''), δ 4.65 (d, 1H, J=5.0 Hz, H-3'), 5.85 (dd, 1H, J=7.5 Hz, H-2'), δ 7.45 (d, 1H, J=4.0 Hz, H-1') and δ 11.40 (br. s, 1H, NH, D_2O exchangeable). Its IR spectrum displayed absorption bands at 3420 cm^{-1} (broad OH), 3250 (NH), 2929 (CH alkyl) and 1667 (CO).

The acyclic N-nucleosides 2 and 3 were stirred at room temperature in acetic anhydride / pyridine mixture (1:1) to afford the corresponding protected tetra O-acetate C-nucleosides 4 and 5 , respectively.



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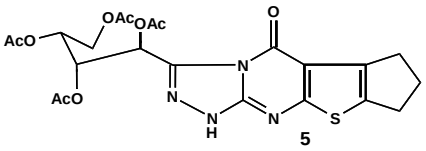

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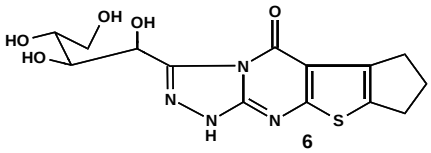
The ^{1}H-NMR spectrum ($CDCl_3$) of compound 5 as an example, showed signals at δ 1.65 ppm (s, 1H, triazolo proton), δ 1.95 (s, 3H, CH_3), δ 2.05 (s, 3H, CH_3), δ 2.10 (s, 3H, CH_3), δ 2.15 (s, 3H, CH_3), δ 2.35 (m, 2H, CH_2), δ 2.85 (m, 4H, $2CH_2$), δ 5.25 (m, 1H, H-3'), δ 5.40 (m, 2H, H_2-4'), δ 5.65 (m, 1H, H-2') and 5.95 (m, 1H, H-1'). Also, its ^{13}C-NMR spectrum ($CDCl_3$) confirmed the given formula (see Experimental).

De-acetylating of 4 and 5 could be achieved by treatment with methanolic sodium methoxide solution to give the deprotected acyclic C-nucleosides 6 and 7, respectively.



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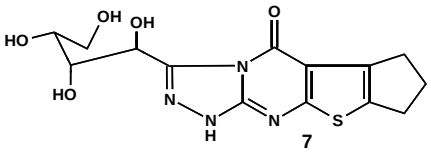

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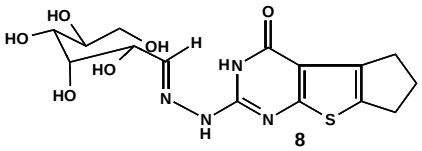
^{1}H-NMR, ^{13}C-NMR and IR spectra of 6 and 7 gave data which support assigned formulae (see Experimental).

Also, we extend our work to apply on aldohexoses namely D-glucose, D-galactose and D-mannose. Thus, heating under reflux in boiling dioxane and in the presence of catalytic amounts of piperidine, yielded the corresponding acyclic N-nucleosides 8, 9 and 10.



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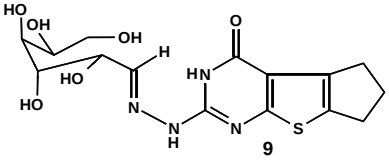

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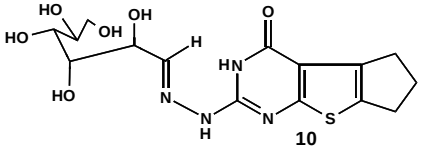

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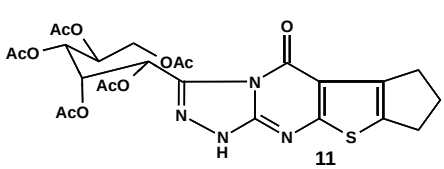
The ^{1}H-NMR spectrum (DMSO-d_6) of 8, as an example, showed signals at δ 2.35 ppm. (m, 2H, CH_2), δ 2.85 (m, 4H, $2CH_2$), δ 3.55 (m, 5H, 5 OH, D_2O exchangeable OH-2'-OH-6'), δ 3.75 (m, 1H, H-5`), δ 4.30 (m, 2H, H-6`, H-6``), δ 4.45 (m, 1H, H-4`), δ 4.60 (m, 1H, H-3`), δ 5.40 (m, 1H, H-2`), δ 7.50 (m, 1H, H-1`), δ 11.30 (br. s, 1H, NH, D_2O exchangeable) and δ 11.40 (br. s, 1H, NH, D_2O exchangeable). Its ^{13}C-NMR, DEPT spectra are in agreement with the assignment formula (see Experimental).

On the other hand, acetylation of compounds 8-10 with acetic anhydride – pyridine mixture (1:1), at room temperature afforded the protected penta O-acetyl C-nucleosides 11, 12 and 13.



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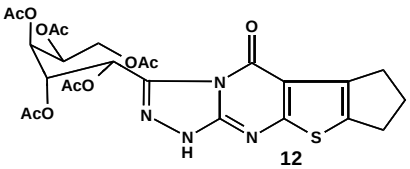

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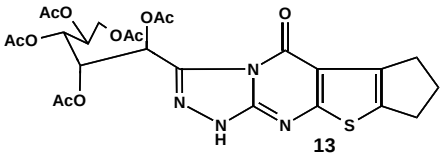

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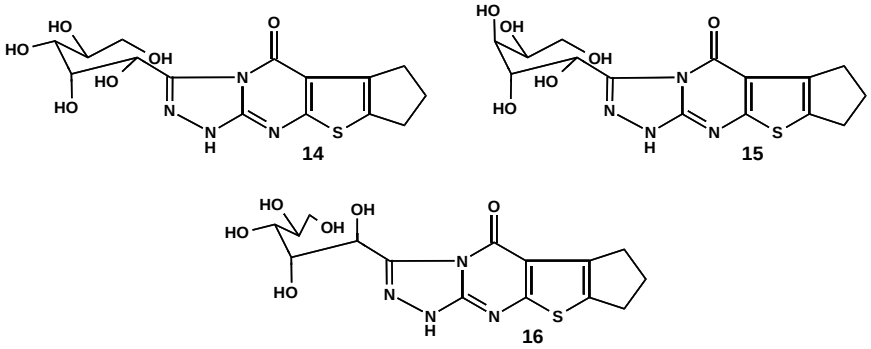
The ^{1}H-NMR spectrum ($CDCl_3$) of compound 11, as an example, showed signals at δ 1.85 ppm (s, 3H, CH_3), δ 1.95 (s, 3H, CH_3), δ 2.05 (s, 3H, CH_3), δ 2.15 (s, 3H, CH_3), δ 2.40 (s, 3H, CH_3), δ 2.45 (m, 2H, CH_2), δ 2.75 (m, 4H, $2CH_2$), δ 4.75 (m, 1H, H-4`), δ 5.30 (d, 1H, J = 10.8 Hz, H-3`), δ 5.45 (m, 2H, H_2- 5`), δ 5.55 (s, 1H, H-2`) and δ 5.70 (s, 1H, H-1`). Beside ^{1}H-NMR data, its ^{13}C-NMR, DEPT spectra are in agreement with the assignment formula (see Experimental).

De-protection of the acyclic C-nucleosides 11-13 could be achieved when they were stirred in methanolic sodium methoxide solution at room temperature to give the acyclic C-nucleosides 14, 15 and 16, respectively.



Formulae 14-16 are confirmed with spectral and elemental data (see Experimental).

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-d_6 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.

General procedure

Preparations of 2-Glycosylhydrazino-3,5,6,7-tetrahydrocyclopentenothieno [2,3-d] pyrimidine-4(4H)-one 2,3 and 8-10.

A mixture of 2-Hydrazino-3,5,6,7-tetrahydrocyclopentenothieno-[2,3-d]pyrimidin-4(4H) one (1) (2.22 g, 10 mmole) and the appropriate monosaccharide (10 m mole), dioxane (30 ml), ethanol (10 ml) and a catalytic amounts of piperidine was stirred under reflux for 8 hr. The reaction mixture was allowed to cool to room temperature. The precipitate so-formed was filtered-off, washed with ethanol and re-crystallized from proper solvent to afford the title compounds.

2-Arabinosylhydrazino-3,5,6,7-tetrahydrocyclopentenothieno[2,3-d] pyrimidin- 4 (4H)-one (2)

A mixture of compound 1 (2.22 g, 10 mmole) and D-arabinose (1.50 g, 10 mmol). The product was re-crystallized from dioxane (30 ml) to yield the title compound as yellow powder (2.55g, 72%); mp. 240-42°C. [$C_{18}H_{18}N_4S_2$] (354.4). Required: C, 47.44%; H, 5.12%; N, 15.81%. Found: C, 47.41%; H, 5.00%; N, 15.72%. IR (Potassium bromide) cm^{-1}: 3230 (NH), 2880 (CH alkyl) and 1680

(CH alkyl). ^{1}H-NMR (DMSO-d_6) δ ppm: 2.30 (m, 2H, CH_2), 2.85 (m, 4H, $2CHB_2$), 3.70 (m, 4H, 4OH, D_2O exchangeable, OH-2`-OH-5`), 4.35 (m, 1H, H-3`), 4.45 (m, 1H, H-4`), 4.60 (m, 2H, H_2-5`), 5.10 (dd, 1H, J=7.50 Hz, H-2`), 7.45 (d, 1H, 7.50Hz, H-1`), 11.25 (br s, 1H, NH, D_2O exchangeable) and 11.45 (br s, 1H, NH, D_2O exchangeable).

2-Xylosylhydrazino-3,5, 6, 7-tetrahydrocyclopentenothieno[2,3-d] pyrimidin-4(4H)-one (3)

A mixture of compound 1 (2.22 g, 10 mmole) and D-xylose (1.50 g, 10 mmole). The product was re-crystallized from dioxane (30 ml) to yield the title compound as yellow powder (2.47 g, 70%); mp. 233-35°C. [$C_{14B}H_{18}N_4SO_5$] (354.4).Required: C, 47.45%; H, 5.12%; N, 15.81%. Found: C, 46.97%; H, 4.88%; N, 15.65%. IR (Potassium bromide) cm^{-1}: 3250 (NH), 2929 (CH alkyl) and 1667 (CO). ^{1}H-NMR (DMSO-d_6) δ ppm: 2.30 (m, 2H, CH_2), 2.85 (m, 4H, $2CH_2$), 3.50 (m, 4H, 4OH, D_2O exchangeable, OH-2`-OH-5`), 4.25 (q, 1H, J = 6Hz, H-4`), 4.45 (m, 2H, H_2-5``), 4.65 (d, 1H, J = 5Hz, H-3`), 5.85 (dd, 1H, J=7.5Hz, H-2`), 7.45 (d, 1H, J = 4Hz, H-1`), 11.20 (br s, 1H, NH, D_2O exchangeable) and 11.40 (br s, 1H, NH, D_2O exchangeable).

2-Glucosylhydrazino-3,5,6,7-tetrahydrocyclopentenothieno[2,3-d]pyrimidin-4 (H)-one (8)

A mixture from compound 1 (2.22g, 10 mmole) and D-glucose (1.80g,10 mmol). The product was re-crystallized from dioxane (30 ml) to yield the title compound as yellow crystals (2.60 g, 68%); mp. 250-51°C. [$C_{15}H_{20}N_4SO_6$] (384.4). Required: C, 46.86%; H, 5.24%; N, 14.57%. Found: C, 47.00%; H, 5.11%; N, 14.51%. IR (Potassium bromide) cm^{-1}: 3222 (NH), 2900 (CH alkyl) and 1680 (CO). ^{1}H-NMR (DMSO-d_6) δ ppm: 2.35 (m, 2H, CH_2), 2.85 (m, 4H, CH_2), 3.55 (m, 5H, 5OH, D_2O exchangeable OH-2`-OH-6`), 3.75 (m, 1H, H-5`), 4.30 (m, 2H, H-6`, H-6``), 4.45 (m, 1H, H-4`), 4.60 (m, 1H, H-3`), 5.40 (m, 1H, H-2`), 7.50 (m, 1H, H-1`), 11.30 (br s, 1H, NH, D_2O exchangeable). and 11.40 (br s, 1H, NH, D_2O exchangeable). ^{13}C-NMR (DMSO-d_6) δ ppm: 27.9, 28.2, 28.6 and 28.9 (CH_2); 67.8, 68.3, 69.1 and 69.4 (CH); 138.6, 138.8, 139.1, 139.6, 140.4 and 141.8 (Thienopyrimidone carbon atoms and glucose C-1` carbon atom) and 167.7 (CO).

2-Galactosylhydrazino-3,5,6,7-tetrahydrocyclopentenothieno[2,3-d] pyrimidine-4(4H)-one (9)

A mixture from compound 1 (2.22 g, 10 mmole) and D-galactose (1.80 g, 10 mmole). The product was re-crystallized from dioxane (30 ml) to yield the title compound as a pale yellow powder (2.72 g, 71%); mp. 233-34°C. [$C_{15}H_{20}N_4SO_6$] (384.4). Required: C, 46.86%; H, 5.24%; N, 14.57%. Found: C, 47.30%; H, 4.95%; N, 14.55%. IR (Potassium bromide) cm^{-1}: 3247 (CH alkyl) and 1678 (CO). ^{1}H-NMR (DMSO-d_6) δ ppm: 2.35 (m, 2H, CH_2), 2.75 (m, 4H, $2CH_2$), 3.75 (m, 5H, 5OH, D_2O exchangeable OH-2`-OH-6`), 4.20 (m, 2H, H_2-6`), 4.50 (m, 3H, H-3`-H-5`), 5.10 (d, 1H, J = 7.5Hz, H-2`), 7.40 (4H, CH, H-1`), 11.25 (br. s, 1H, NH, D_2O exchangeable) and 11.40 (br. s, 1H, NH, D_2O exchangeable).

2-Mannosylhydrazino-3,5,6,7- tetrahydrocyclopentenothieno [2,3-d] pyrimidin-4(4H)-one (10)

From compound 1 (2.22 g, 10 mmole) and D-mannose (1.80 g, 10 mmole). The product was re-crystallized from dioxane to yield the title compound as yellow powder (2.70 g, 70%); mp. 246-47°C. [$C_{15}H_{20}N_4SO_6$] (384.4). Required: C, 46.86%; H, 5.24%; N, 14.57%. Found: C, 46.63%; H, 5.01%; N, 14.33%. IR (Potassium bromide) cm^{-1}: 3274 (NH), 2910 (CH alkyl) and 1700 (CO). ^{1}H-NMR (DMSO-d_6) δ ppm: 2.30 (m, 2H, CH_2), 2.75 (m, 4H, $2CH_2$), 3.60 (m, 5H, 5OH, D_2O exchangeable OH-2`-OH-6`), 4.25 (m, 1H, CH, H-3`), 4.35 (m, 2H, $CH_2$, $H_2$-6`), 4.50 (m, 2H, 2CH, H-3` and H-4`), 5.20 (dd, 1H, CH, J=7.5Hz, H-2`), 7.65 (d, 1H, J=7.5Hz, H-1`), 11.30 (br s, 1H, NH, D_2O exchangeable) and 11.45 (br. s, 1H, NH, D_2O exchangeable).

General procedure

Preparations of 3-(O-Acetylglycosyl)-1,6,7,8-tetrahydrocyclopentenothieno-[2, 3-d] [1, 2, 4] triazolo [4, 3-4]pyrimidin-5(5H)-one. 4, 5 and 11-13

A solution of compounds 2, 3 or compounds 8-10 (10 mmole) in a mixture of acetic anhydride-pyridine (20 ml: 20 ml) was stirred at room temperature for over night 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 was re-crystallized from the proper solvent to produce 4,5 or 11-13.

3-(2`,3`,4`,5`-O-Tetracetylarabinosyl)-3,6,7,8-tetrahydrocyclopenteno thieno [2,3-d] [1,2,4] triazol [4,3-a] pyrimidin-5(5H)-one (4)

From compound 2 (3.54 g, 10 mmole). The product was re-crystallized from methanol (35 ml) to yield the title product as reddish brown crystals (3.20, 60%); m.p. 149-50°C. IR (Potassium bromide) cm^{-1}: 2918 (CH alkyl), 1755-1720, 1670 (CO). 1.80, (s, 1H, triazol proton) ^{1}H-NMR (DMSO-d_6) δ ppm: 2.00 (s, 3H, CH_3), 2.15 (s, 3H, CH_3), 2.20 (s, 3H, CH_3), 2.5 (s, 3H, CH_3), 2.45 (m, 2H, CH_2), 3.01 (m, 4H, $2CH_2$), 4.40 (m, 2H, H_2-4`), 5.20 (m, 1H, H-3`), 5.51 (m, 1H, H-2`), 5.45 (m, 1H, H-1`), 7.35 (br s, 1H, NH, D_2O exchangeable). ^{13}C-NMR (CDCl3) δ ppm: 20.0, 20.1, 20.3 and 20.4 (CH_3), 23.4, 27.6, 28.6, 28.6 and 29.3 (CH_2), 62.5, 67.7, 67.9 and 68.6 (CH), 139.3, 139.7, 145.4, 154.1 and 155.0 (thienopyrimidone carbon atoms) and 169.5, 169.6, 169.8, 170.4 and 170.5 (CO).

3-(1`,2`,3`,4`-O-Tetraacetylxylosyl)-3,6,7,8-tetrahydrocyclopentenothieno[2,3-d] [1,2,4] triazolo [4,5-a] pyrimidin-5(5H)-one (5)

From compound 3 (3.54g, 10 mmole). The product was re-crystallized from methanol (30 ml) to afford the title compound as golden yellow crystals (3.18 g, 61%); mp. 145-46°C. [$C_{22}H_{24}N_4SO_9$] (520.5). Required: C, 50.76%; H, 4.64%; N, 10.76%. Found: C, 50.77%; H, 4.56%; N, 10.80%. IR (Potassium bromide) cm^{-1}: 2900 (CH alkyl), 1740-1760, 1680 (CO). ^{1P}H-NMR ($CDCl_3$) δ ppm: 1.65 (s, 1H, CH, triazolo proton), 1.95 (s, 3H, CHB_3), 2.05 (s, 3H, CH_3), 2.10 (s, 3H, CH_3),

2.15 (s, 3H, CH_3), 2.35 (m, 2H, CH_2), 2.85 (m, 4H, $2CH_2$), 5.25 (m, 1H, H-3`), 5.40 (m, 2H, $H_2$ - 4`, 5.65 (m, 1H, H-2`). and 5.95 (m, 1H, H-1`).^{13}C-NMR (CDCl3) δ ppm: 20.2, 20.3, 20.5 and 20.7 (CH_3), 28.1, 29.2, 30.0 and 31.0 (CH_2), 67.1, 68.2, 69.6 and 73.2 (CH), 139.2, 139.5, 140.3, 140.9 and 141.8 (thieno pyrimidone carbon atoms) and 169.6, 169.7, 169.8, 169.9 and 170.0 (CO).

3- (1`,2`,3`,4`,5`- O- pentaacetylglucosyl)-3,6,7,8-tetrahydrocyclopenteno thieno [2,3-d] [1,2,4-] triazolo [4,5-a] pyrimidin-5(5H)-one (11)

From compound 8 (3,84 g, 10 mmole). The product was re-crystallized from methanol (35 ml) to yield the title compound as yellow crystals (3.73 g, 63%); mp. 153-54°C. [$C_{25}H_{28}N_4SO_{11}$] (592.6). Required: C, 50.67%; H, 4.76%; N, 9.46%. Found: C, 50.46%; H, 4.65%; N, 9.50%. IR (Potassium bromide) cm^{-1}: 1920 (CH alkyl), 1760-1740 (ester carbonyl) and 1677 (CO). ^{1}H-NMR ($CDCl_3$) δ ppm: 1.85 (s, 3H, CH_3), 1.95 (s, 3H, CH_3), 2.05 (s, 3H, CH_3), 2.15 (5, 3H, CH_3), 2.40 (s, 3H, CHB_3), 2.45 (m, 2H, CH_{2B}), 2.75 (m, 4H, $2CH_2$), 4.75 (m, 1H, H-4`), 5.30 (d, 1H, J=10.8 Hz, H-3`), 5.45 (m, 2H, H_2-5`), 5.55 (s, 1H, H-2`) and 5.70 (s, 1H, H-1`). ^{13}C-NMR ($CDCl_3$) δ ppm: 20.0, 20.5, 20.6, 20.9 and 23.5 (CH_3), 25.3, 27.6, 29.3 and 30.0 (CH_2), 67.2, 67.4, 68.4 and 70.9 (CH), 138.0, 139.3, 141.6, 148.3, 155.1 and 156.0 (thienopyrimidone carbon atoms and triazol carbon atom) and 168.0, 1168.3, 168.7, 169.4, 169.4, 170.3 and 171.0 (CO).

3-(1`,2`,3`,4`,5`-O-pentacetylgalactosyl)-3,6,7,8-tetrahydrocyclopenteno-thieno-[2,3-d][1,2,4]triazolo [4.5-a]pyrimidin-5(5H)-one (12)

From compound 9 (3.89 g, 10 mmole). The product was re-crystallized from methanol (30 ml) to yield the title product as yellow crystals (3.60 g, 61%); mp. 156-57°C. [$C_{25}H_{28}N_4SO_{11}$] (522.6). Required: C, 50.67%; H, 4.76%; N, 9.46%. Found: C, 50.71%; H, 4.56%; N, 9.44%. IR (Potassium bromide) cm^{-1}: 2895(CH alkyl), 1745-1720, (ester carbonyls) and 1688 (CO). ^{1}H-NMR ($CDCl_3$) δ ppm: 1.80 (s, 3H, CH_3), 1.95 (s, 3H, CH_3), 2.05 (s, 3H, CH_3), 2.10 (s, 3H, CH_3), 2.30 (5, 3H, CH_3), 2.35 (m, 2H, CH_2), 2.80 (m, 4H, $2CH_2$), 4.76 (m, 1H, H-4`), 5.10 (m, 1H, H-1`), 5.30 5.50 (m, 2H, H_2-5`), 5.55 (d, 1H, J=7.50Hz, H-3`), 5.70 (d, 1H, J=7.50Hz, H-2`) and 7.25 (br s, 1H, NH, D_2O exchangeable).

3-(1`,2`,3`,4`,5-O-Pentacetylmannosyl)3,6,7,8-tetrahydrocyclopenteno[2,3-d] [1,2,4] triazolo [4,5-a] pyrimidin-5(5H)-one (13)

From compound 10 (3.84 g, 10 mmole). The product was re-crystallized from methanol (30 ml) to produce the title compound as yellow crystals (3.70 g, 62%); mp. 146-48°C. [$C_{25}H_{28}N_4SO_{11}$] (592.6). Required: C, 50.67%; H, 4.76%; N, 9.46%. Found: C, 50.67%; H, 4.77%; N, 9.45%. IR (Potassium bromide) cm^{-1}: 2900 (CH alkyl), 1740-1720, (ester carbonyls) and 1700 (CO). ^{1}H-NMR ($CDCl_3$) δ ppm: 1.80 (s, 3H, CH_3), 1.90 (s, 3H, CH_3), 1.95 (s, 3H, CH_3), 2.00 (s, 3H, CH_3), 2.15 (s, 3H, CH_3), 2.30 (m, 2H, CH_2), 2.85 (m, 4H, $2CH_2$), 5.25 (m, 1H, H-4`), 5.35 (m, 2H, $H_2$-5`), 5.40 (d, 1H, H-3`), 5.50 (d, 1H, H-2`), 5.65 (m, 1H, H-1`) and 7.45 (br. s, 1H, NH, D_2O exchangeable).

General procedure

Preparations of 3-Glycosyl-3,6,7,8-tetrahydrocyclopentenothieno[2,3-d] [1,2,4] triazolo[4,5-a]pyrimidin-5(5H)-one 6, 7 and 14-16

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 4,5 (10 mmole) or compounds 11-13 (10 mmole). The reaction mixture was allowed to stirr for 8 hr, 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.

3-Arabenosyl-3,6,7,8-tetrahydrocyclopentenothieno [2,3-d] [1,2,4] triazolo [4,5-a] pyrimidin-5(5H)-one (6)

From compound 4 (5.20 g, 10 mmole). The product was re-crystallized from dioxane (20 ml) to yield the title products as pale yellow powder (1.80 g; 51%); mp. 250-52°C. [$C_{14}H_{17}N_4SO_5$] (352.4). Required: C, 47.71%; H, 4.58%; N, 15.90%. Found: C, 47.65%; H, 4.55%; N, 16.10%. IR (Potassium bromide) cm^1: 3450 (broad OH), 2925 (CH alkyl) and 1688 (CO). ^{1}H-NMR (DMSO-d_6) δ ppm: 2.35 (m, 2H, CH_2), 2.85 (m, 4H, CHB_2), 4.45 (m, 4H, 4OH,D_2O exchangeable, OH-1′-OH-4′), 4.65 (m, 1H, H-3′), 4.90 (m, 2H, H_2-4′), 5.10 (m, 1H, H-2′) 5.80 (m, 1H, H-1′) and 8.15 (br. s, 1H, NH, D_2O exchangeable). ^{13}C-NMR (DMSO-d_6) δ pm: 27.5, 28.6, 30.1 and 30.2 (CH_2), 63.1, 68.9, 69.8 and 70.0 (CH of the sugar moiety and the triazol carbon atom), 112.0, 130.7, 139.0, 148.2 and 150.0 (thienopyrimidone carbon atoms) and 158.0 (CO).

3-Xylosyl-3,6,7,8-tetrahydrocyclopentenothieno [2,3-d] [1,2,4] triazolo [4,3-a] pyri- midin-5(5H)-one (7)

From compound 5 (5.20 g, 10 mmole). The product was re-crystallized from dioxane (20 ml) to yield the title products as yellow powder (1.87 g; 53%); mp. 244-46°C. [$C_{14}H_{17}N_4SO_5$] (352.4). Required: C, 47.71%; H, 4.58%; N, 15.90%. Found: C, 47.67%; H, 4.55%; N, 15.78%. IR (Potassium bromide) cm^{-1}: 3450 (broad OH), 2935 (CH alkyl) and 1678 (CO). ^{1}H-NMR (DMSO-d_6) δ ppm.: 2.25 (m, 2H, CH_2), 2.55 (d, 1H, J=13Hz, CH of the triazol ring), 2.95 (m, 4H, $2CH_2$), 4.10 (m, 4H, 4OH, D_2O exchangeable), 4.35 (dd, 1H, J=10.8 Hz, H-3`), 5.25 (m, 1H, H-1`) and 8.25 (brs, 1H, NH, D_2O exchangeable). ^{13}C-NMR (DMSO-d_6) δ pm: 27.5, 28.6, 30.1 and 30.2 (CH_2), 63.1, 68.9, 69.8 and 70.0 (CH of the sugar moity and the triazol carbon atom), 112.0, 130.7, 139.0, 148.2 and 150.0 (thienopyrimidone carbon atoms) and 158.0 (CO).

3-Glucosyl-3,6,7,8-tetrahydrocyclopentenothieno[2,3-d][1,2,4] triazolo [4,5-a] pyri-midin-5(5H)-one (14)

From compound 11 (5.92g, 10 mmole). The product was re-crystallized from dioxane (30 ml) to yield the title compound as yellow powder (1.87 g, 49%); mp 253-55°C. [$C_{15}H_{18}N_4SO_6$] (382.4). Required: C, 47.11%; H, 4.74%; N, 14.65%.

Found: C, 47.00%; H, 4.68%; N, 14.66%. IR (Potassium bromide) cm^{-1}: 3460, 3440 (OH), 3265 (NH), 2920 (CH alkyl) and 1670 (CO). ^{1}H-NMR (DMSO-d_6) δ ppm: 2.35 (m, 2H, CH_2), 2.85 (m, 4H, $2CH_2$), 3.10 (m, 5H, 5OH, D_2O exchangeable), 3.35 (m, 1H, H-3`), 3.65 (m, 2H, H-5`, H-5``), 4.20 (m, 1H, H-2`), 4.65 (m, 1H, H-1`) and 9.95 (br s, 1H, NH, D_2O exchangeable).

3-Glalctosyl-3,6,7,8-tetrahydrocyclopentenothieno[2,3-d][1,2,4] triazolo-[4,5-a] pyrimidin-5(5H)-one (15)

From compound 12 (5.92g, 10 mmole). The product was re-crystallized from dioxane (35 ml) to yield the title compound as pale yellow powder (1.95 g, 51%); m.p 261-63°C. [$C_{15}H_{18}N_4SO_6$] (382.4). Required: C, 47.11%; H, 4.74%; N, 14.65%. Found: C, 47.13%; H, 4.73%; N, 14.55%. IR (Potassium bromide) cm^{-1}: 3420, 3400 (OH), 3250 (NH), 2930 (CH alkyl) and 1677 (CO). ^{1}H-NMR (DMSO-d_6) δ ppm: 2.35 (m, 2H, CH_2), 2.70 (m, 4H, $2CH_2$), 3.65 (m, 5H, 5OH, D_2O exchangeable, OH-1`-OH-5`), 4.35 (m, 2H, CH_2, H_2-5`), 4.55 (m, 3H, 3CH, H-2`-H-4`), 5.25 (m, 1H, CH, H-1`) and 11.05 (br. s, 1H, NH, D_2O exchangeable). ^{13}C-NMR (DMSO-d_6) δ ppm: 27.4, 27.6 and 28.9 (CH_2), 62.6, 67.0, 67.9 and 69.5 (CH), 103.0, 112.4, 131.2, 131.6, 133.7 and 139.1 (thienopyrimidone carbon atoms and triazol carbon atom) and 157.4 (CO).

3-Mannosyl-3,6,7,8-tetrahydrocyclopentenothieno[2,3-d][1,2,4] triazolo [4,5-a] pyri-midin-5(5H)-one (16)

From compound 13 (5.92 g, 10 mmole). The product was re-crystallized from dioxane (30 ml) to afford the title compound as yellow powder (1.90 g, 50%); mp 258-60°C. [$C_{15}H_{18}NB_4SO_6$] (382.4). Required: C, 47.11%; H, 4.74%; N, 14.65%. Found: C, 47.07%; H, 4.65%; N, 14.67%. IR (Potassium bromide) cm^{-1}: 3430, 3420 (OH), 3240 (NH), 2890 (CH alkyl) and 1660 (CO). ^{1}H-NMR (DMSO-d_6) δ ppm: 2.30 (m, 2H, CH_2), 2.80 (m, 4H, $2CH_2$), 3.45 (m, 5H, 5OH, D_2O exchangeable, H-1`-H-5`), 3.80 (m, 1H, CH, H,2`), 4.15 (m, 2H, 2CH, $CH_2$, $H_2$-5`), 4.25 (m, 1H, CH, H-4`) 4.35 (m, 1H, CH, H-3`), 4.55 (m, 1H, CH, H-1`) and 9.95 (br. s, 1H, NH, $DBBB_{2BBB}O$ exchangeable). ^{13}C-NMR (DMSO-d6) δ ppm: 27.0, 27.4, 28.1 and 28.9 (CH_2), 63.9, 69.5, 69.7 and 70.9 (CH), 112.6, 130.7, 139.0, 148.6, 150.0 and 158.0 (thienopyrimidone carbon atoms and triazolo ring carbon atom) and 170.9 (CO).

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تشييد ك- و ن-نيوكليسيدات جديدة من مشتقات ٢-هيدرازين ثينوبيريميدين

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قسم الكيمياء الضوئية (وحدة كيمياء المركبات الغير متجانسة الحلقة) المركز القومى للبحوث – الدقى – القاهرة – مصر .

ن-نيوكليسيدات الغير محاوقة تحضر عن طرق التسخين الشديد حتى الغليان لمركب ٢-هيدرازينوسيكلوبينتينوثيينوبيريويدون ١ مع السكريات الألدهيدية الخماسية أو السداسية فى وجود مذيب الداى أوكسا ن و بإضافة بعض النقاط من محفز الببيريدين ليعطى المشتقات٢و٣و٨و٩و١٠على التوالى. و تم حلوقة المشتقات السابقة وذلك بتفاعلها مع مخلوط انهيدريد الخليك و البيريدين بنسبة ١:١ عند درجة حرارة الغرفة لنحصل على مشتقات الخلات الرباعية و الخماسية ٤و٥و١١و١٢و١٣ على التوالى. و قد تم بعد ذلك الحصول على ك- نيوكوسيدات المحررة ١٥،١٤،٧،٦و١٦ .