Synthesis of Some Biologically Active Pyrazoles and *C*-Nucleosides

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Abstract

(5,6-Dihydronaphtho[1′,2′:4,5]thieno[2,3-*d*]pyrimidin-11-yl)-hydrazine (**1**) was used as a precursor for preparation of some novel 1-(5,6-dihydronaphtho[1′,2′:4,5]thieno[2,3-*d*]pyrimidin-11-yl)-pyrazole derivatives **2-7**. Also, some acyclic and cyclic *C*-nucleosides **8** and **10-12** were prepared by treating compound **1** with aldoses. Some of the prepared products showed potent antimicrobial activity.

Key words: Thieno[2,3-*d*]pyrimidine, pyrazole, aldoses, *C*-nucleosides

Introduction

Substituted pyrimidines, in general, have received a great biological interest,[1] in particular 4-hydrazinopyrimidine derivatives, which were tested for their bactericidal and fungicidal activity.[2,3] On the other hand, condensation of the appropriate heterocyclic hydrazinopyrimidine derivatives with monosacharides give the corresponding sugar hydrazones, which upon cyclization gives the corresponding acyclo *C*-nucleosides.[4-8] Actually, some *C*-nucleosides were shown to exhibit prominent and versatile biological activities,[9,10] and many of their derivatives have been synthesized recently as potential antimicrobial[5] and antiviral agents.[11] So, many reports[12-17] have recently appeared dealing with this class of nucleosides. However, to the best of our knowledge, *C*-nucleosides of thieno[2,3-*d*]pyrimidines are not known.

In continuation of our previous work on the synthesis of biologically active pyrazoles,[18,19] fused pyrimidines,[19-21] and different nucleoside derivatives,[21,22] we aimed to incorporate a fused pyrimidine moiety into the 1-position of the pyrazole ring system to obtain new compounds which are expected to possess notable chemical and biological activities.
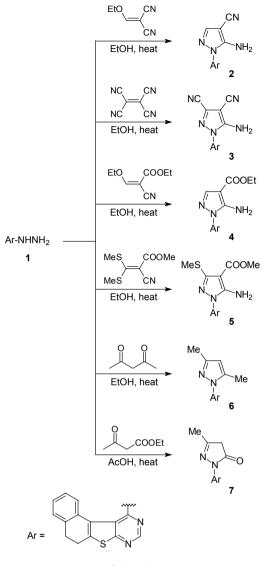
Results and Discussion

In this investigation, compound **1**[20] was dissolved in ethanol and refluxed with ethoxymethylenema lononitrile, tetracyanoethylene, bis(methylthio)-methylenemalononitrile, or ethyl(ethoxymethylene)-cyanoacetate to afford the corresponding substituted

pyrazole derivatives **2–5**, respectively (Scheme 1). The structures of the latter compounds were confirmed on the basis of their elemental analysis and spectral data (cf. Experimental). The IR spectra of compounds **2** and **3** showed absorption bands characteristic for NH_2 and $C\equiv N$ groups, while those of compounds **4** and **5** revealed absorption bands characteristic for NH_2 and $C=O$. Also, the ^1H NMR spectra showed signals at δ = 6.75, 6.80, 6.80 and 6.90 ppm due to NH_2 (exchangeable with D_2O) for compounds **2–5**, respectively. The MS gave the molecular ion peaks at m/z (%) = 342 (100), 367 (89), 389 (100), and 421 (100) for compounds **2–5**, respectively.

Similarly, when compound **1** was refluxed with acetylacetone or ethyl acetoacetate, the pyrazole derivatives **6** and **7** were obtained, respectively (Scheme 1). The ^1H NMR spectra of the latter compounds showed signals at δ = 1.80 ppm and 2.40 ppm ($2CH_3$) for compound **6** and at δ = 2.70 ppm (CH_3), 3.40 ppm (CH_2) for compound **7**, while the IR spectrum of compound **7** revealed the presence of $C=O$ group. The MS, gave the molecular ion peaks at m/z (%) = 332 (78) and 306 (M^+-CO, 70), for compounds **6** and **7**, respectively.

The hydrazone derivatives **8a,b** were prepared by reacting compound **1** with some monosacharides: namely, D-glucose or D-ribose in the presence of catalytic amounts of glacial acetic acid. The products revealed absorption bands for (OH+NH), and (C=N) in IR spectra and their ^1H NMR spectra showed the presence of the sugar protons, NH, and azo-methine (C<u>H</u>=N) (cf. Experimental). Cyclization of hydrazones or *O*-acetylated hydrazones in different conditions were intensively reported.[4-8] However, our attempt to cyclize

Scheme 1

the hydrazone **8a**, by heating in dimethylformamide in the presence of glacial acetic acid, failed and gave an unexpected product assigned the structure of 8,9-dihydronaphtho[1′,2′:4,5]thieno[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (**9**).[20] The formation of compound **9** might have taken place *via* hydrolysis of the hydrazone **8** producing (*in situ*) the hydrazinopyrimidine **1**, which then cyclized with dimethylformamide in refluxing glacial acetic acid.

Acetylation of the hydrazone derivatives **8a,b** with acetic anhydride at room temperature gave the *O*-acetylated sugar derivatives **10a,b**. The IR spectra of the latter compounds revealed the absence of hydroxyl groups and showed absorption bands due to NH and C=O groups. The ^{1}H NMR spectra showed the presence of OAc groups and one exchangeable NH, while the ^{13}C NMR spectra revealed the presence of

acetoxy groups (cf. Experimental). Oxidative cyclization of compounds **10a,b** using bromine/acetic acid,[4,14,23] afforded the *O*-acetylated cyclic *C*-nucleosides **11a,b** (Scheme 2). The absence of NH as well as the azomethine (C$\underline{\text{H}}$=N) in ^{1}H NMR spectra confirmed their structures (cf. Experimental).

Deprotection of **11a,b** using ammonium hydroxide solution in methanol,[4] gave the target free cyclic *C*-nucleosides **12a,b**. The structures of the aforementioned compounds were confirmed on the basis of their spectral data (cf. Experimental). The IR spectra revealed absorption bands due to (OH), and (C=N); while their ^{1}H NMR spectra showed signals of the alditol protons congregated with the solvent absorption[4–8] and the presence of hydroxyl groups (D$_2$O exchangeable) (cf. Experimental).
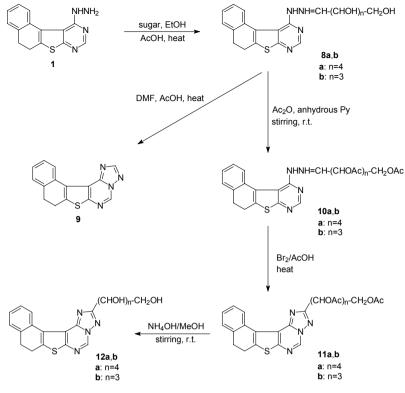
In general, The Dimroth type rearrangement of *S*-triazolopyrimidines was intensively discussed and verified with X-ray diffraction by Rashad *et al*.[20] So, the triazolo[1,5-*c*]pyrimidine derivatives **9**, **11a,b** and **12a,b**, were obtained directly *via* Dimroth type rearrangement of their triazolo[4,3-*c*]pyrimidine derivatives.

Antimicrobial activity

The in vitro antimicrobial activity of the synthesized compounds was investigated against several pathogenic representative Gram- positive bacteria (*Bacillus Subtilis),* Gram- negative bacteria (*Escherichia Coli), Fungi (Aspergillus Niger)* and Yeast *(Candida Albicans)*. All microorganisms used were obtained from the culture collection of the Department of Natural and Microbial Products, National Research Centre, Dokki, Cairo, Egypt.

Method [24–26]

The cap-assay method containing (g/L): peptone 6, yeast extract 3, meat extract 1.5, glucose 1 and agar 20 were used. The medium was sterilized and divided while hot (50–60 °C) in 15 mL portions among sterile petri-dishes of 9 cm diameter. One mL of the spore suspension of each microorganism was spread all over the surface of the cold solid medium placed in the petri-dish. Each of the tested compounds (0.5 g) was dissolved in 5 mL of dimethylformamide. An amount of 0.1 mL of test solution was placed on watman paper disc of 9 mm diameter and the solvent was left to evaporate. These saturated discs were placed carefully on the surface of the inoculated solid medium; each petri-dish contains at least 3 discs. The petri-dishes were incubated at 5 °C for an hour to permit good diffusion and then transferred to an incubator of 85 °C overnight, then examined. The results were then recorded by measuring the inhibition zone diameters.

Scheme 2

Results

As shown in Table 1, the antimicrobial effect of the tested compounds was evaluated by measuring the zone diameters and they results were compared with those of well known drugs (standards). Among the tested compounds, it was noticed that β-enaminoesters **4** and **5** demonstrated inhibitory activity more than β-enaminonitriles **2** and **3**. On the other hand, the non-acetylated sugar derivatives **8a,b** and **12a,b** showed more significant antimicrobial activity than those of acetylated sugar derivatives **10a,b** and **11a,b**. Also, non-acetylated sugar triazolo derivatives **12a,b** showed more significant antimicrobial activity than those of acetylated sugar triazolo derivatives **11a,b**. In general, the target free cyclic *C*-nucleosides **12a,b** showed more significant antimicrobial activity than some known drugs (standards).

Experimental

All melting points are uncorrected and measured using Electro-thermal IA 9100 apparatus, Shimadzu (Japan). IR spectra were recorded as potassium bromide pellets on a Perkin-Elmer 1650 spectrophotometer, National Research Centre, Cairo, Egypt. ^{1}H NMR and ^{13}C NMR spectra were determined on a Jeol-Ex-300 NMR spectrometer and chemical shifts were expressed as part per million; ppm (δ values) against

Table 1. The antimicrobial activity of the newly synthesized compounds.

Tested Compounds & Standers (μg/mL- Lot. No., Bioanalyse)	Inhibition Zone (mm)			
	Microorganism			
	Bacteria		Fungi	Yeast
	Gram-negative	Gram-positive		
	Escherichia Coli.	Bacillus Subtilis	Aspergillus Niger	Candida Albicans
Streptomycin (10–30225)	+++	+++	+	+++
Fusidic Acid (10–30301)	–	–	+++	+++
Amoxicillin (25–30730)	++	–	–	–
Ampicillin (10–30731)	++	–	–	–
2	–	+	+	–
3	–	+	–	–
4	++	+	+	+
5	++	++	+	+
6	+	+	–	+
7	+	+	+	+
8a	++	+	+	+
8b	++	+	+	+
10a	+	+	–	–
10b	+	+	–	–
11a	++	+	+	+
11b	++	+	+	+
12a	+++	++	++	++
12b	+++	++	++	++

+ + + Highly sensitive (21–25 mm); + + Fairly sensitive (16–20 mm); + Slightly sensitive (15–10 mm); – Not sensitive.

TMS as internal reference (Faculty of Science, Cairo University, Cairo, Egypt). Mass spectra were recorded on EI + Q1 MSLMR UPLR, National Research Centre, Cairo, Egypt. Microanalyses were operated using Mario Elmentar apparatus, Organic Microanalysis Unit, National Research Centre, Cairo, Egypt and the results were within the accepted range (± 0.40) of the calculated values. Column Chromatography was performed on (Merck) Silica gel 60 (particle size 0.06–0.20 mm).

Preparation of compounds 2–5. General procedure: To a solution of compound **1** (1 mmol, 2.68 g) in (20 mL) anhydrous ethanol, ethoxymethylene-malononitrile, tetracyanoethylene, ethyl-(ethoxymethylene)-cyanoacetate, or methyl bis(methylthio)-ethoxymethylene cyanoacetate (1 mmol) was added and the reaction mixtures were refluxed for 2–4 h, respectively. The products, which separated on cooling, were collected by filtration and recrystallized from ethanol to give compounds **2–5**.

5-Amino-1-(5,6-dihydronaphtho[1′,2′:4,5]thieno-[2,3-*d*]pyrimidin-11-yl)-1*H*-pyrazole-4-carbonitrile (2). 2 h, yield 95%, mp 270–272 °C. Anal. calcd for $C_{18}H_{12}N_6S$: C 70.15, H 4.12, N 16.36. Found: C 70.27, H 4.24, N 16.11. IR ν 3407, 3200 (NH$_2$), 2209 (CN) cm^{-1}. ^{1}H NMR (DMSO-d$_6$) δ 2.9–3.1 (m, 4H, 2CH$_2$), 6.4–7.3 (m, 6H, 4Ar-H and NH$_2$, D$_2$O exchangeable), 7.6 (s, 1H, C$_3$-H), 9.10 (s, 1H, C$_2$-H). EIMS *m/z* (%): 344 (M$^+$, 100). ^{13}C NMR (DMSO-d$_6$) δ 24.9 (C-5`), 29.3 (C-6`), 109 (CN), 126.3-129.7 (Ar-C), 134 (C-4) 130.3 (C-11a`), 135.4 (C-11b`), 138 (C-3) 140.9 (C-6a`), 149.7 (C-7a`), 154 (C-5), 159.5 (C-9`), 162.7 (C-11`).

5-Amino-1-(5,6-dihydronaphtho[1′,2′:4,5]thieno [2,3-*d*]pyrimidin-11-yl)-1*H*-pyrazole-3,4-dicarbonitrile (3). 4 h, yield 65%, mp 216–218 °C. Anal. calcd for $C_{19}H_{11}N_7S$: C 68.65, H 3.57 N, 19.06. Found: C 68.47, H 3.64, N 19.11. IR ν 3407, 3200 (NH$_2$), 2219 (CN) cm^{-1}. ^{1}H NMR (DMSO-d$_6$) δ 2.8–2.9 (m, 4H, 2CH$_2$), 6.43 7.3 (m, 6H, 4Ar-H and NH$_2$, D$_2$O exchangeable), 9.1 (s, 1H, C$_2$-H). EIMS *m/z* (%): 369 (M$^+$, 18). ^{13}C NMR (DMSO-d$_6$) δ 25.4 (C-5`), 29.8 (C-6`), 102 (CN), 110.4 (CN), 126.3-162.7 (Ar-C).

5-Amino-1-(5,6-dihydronaphtho[1′,2′:4,5]thieno [2,3-*d*]pyrimidin-11-yl)-1*H*-pyrazole-4-carboxylic acid ethyl ester (4). 3 h, yield 90%, mp 200–202 °C. Anal. calcd for $C_{20}H_{17}N_5O_2S$: C 67.85, H 4.92, N 10.79, S 8.23. Found: C 68.1, H 4.94, N 10.71, S 8.15. IR ν 3464, 3354 (NH$_2$), 1685 (CO) cm^{-1}. ^{1}H NMR (DMSO-d$_6$) δ 1.3 (t, *J* = 6.9 Hz, 3H, CH$_3$), 2.9–3.1 (m, 4H, 2CH$_2$), 4.2 (q, *J = 7.5 Hz*, 2H, CH$_2$), 6.4–7.3 (m, 6H, 4Ar-H and NH$_2$, D$_2$O exchangeable), 7.4 (s, 1H, C$_3$-H), 9.1 (s, 1H, C$_2$-H). EIMS *m/z* (%): 391 (M$^+$, 100). ^{13}C NMR (DMSO-d$_6$)

δ 15.2 (CH$_3$), 24.9 (C-5`), 29.3 (C-6`), 58.5 (OCH$_2$), 126.3-162.7 (Ar-C), 158 (CO).

5-Amino-3-methylthio-1-(5,6-dihydronaphtho-[1′,2′:4,5]thieno[2,3-*d*]pyrimidin-11-yl)-1*H*-pyrazole--4-carboxylic acid methyl ester (5). 3 h, yield 90%, mp 220–222 °C. Anal. calcd for $C_{20}H_{17}N_5O_2S_2$: C 56.72, H 4.05, N 16.54, S 15.14. Found: C 56.67, H 4.15, N 16.34, S 15.20. IR ν 3460, 3346 (NH$_2$), 1685 (CO) cm^{-1}. ^{1}H NMR (DMSO-d$_6$) δ 1.5 (s, 3H, CH$_3$), 2.8–3.1 (m, 4H, 2CH$_2$), 3.8 (s, 3H, SCH$_3$), 6.4–7.3 (m, 6H, 4Ar-H and NH$_2$, D$_2$O exchangeable), 9.0 (s, 1H, C$_2$-H). EIMS *m/z* (%): 423 (M$^+$, 100). ^{13}C NMR (DMSO-d$_6$) δ 18.5 (SCH$_3$), 23.9 (C-5`), 29.3 (C-6`), 50.2 (OCH$_3$), 126.3-162.7 (Ar-C), 160.8 (CO).

11-(3,5-Dimethyl-pyrazol-1-yl)-5,6-dihydronaphtho-[1′,2′:4,5]thieno[2,3-*d*]pyrimidine (6). To a solution of compound **1** (2.68 g, 1 mmol) in ethanol (20 mL), acetylacetone (1 mmol) was added and the reaction mixture was refluxed for 10 h. The solvent was then removed under reduced pressure and the residue was recrystallized from ethanol to give compound **6**. Yield 70%, mp 130–132 °C. Anal. calcd for $C_{19}H_{16}N_4S$: C 68.65, H 4.85, N 16.85, S 9.65. Found: C 68.47, H 4.94, N 16.71, S 9.61. ^{1}H NMR (DMSO-d$_6$) δ 1.8 (s, 3H, CH$_3$), 2.4 (s, 3H, CH$_3$), 2.9–3.0 (m, 4H, 2CH$_2$), 6.1 (s, 1H, C$_4$-H), 6.7–7.3 (m, 4H, Ar-H), 9.0 (s, 1H, C$_2$-H). EIMS *m/z* (%): 332 (M$^+$, 78). ^{13}C NMR (DMSO-d$_6$) δ 15.2 (CH$_3$), 18.5 (CH$_3$), 23.9 (C-5`), 29.3 (C-6`), 116.4-162.9. (Ar-C).

5-Methyl-2-(5,6-dihydronaphtho[1′,2′:4,5]thieno-[2,3-*d*]pyrimidin-11-yl)-2,4-dihydro-pyrazol-3-one (7). To a solution of compound **1** (2.68 g, 1 mmol) in glacial acetic acid (20 mL), ethyl acetoacetate (1 mmol) was added and the reaction mixture was refluxed for 6 h. The solvent was then removed under reduced pressure and the obtained product was recrystallized from ethanol to give compound **7**. Yield 70%, mp 140–142 °C. Anal. calcd for $C_{18}H_{14}N_4OS$: C 64.65, H 4.22, N 16.75, S 9.59. Found: C 64.56, H 4.24, N 16.71, S 10.12. IR ν 1690 (CO) cm^{-1}, ^{1}H NMR (DMSO-d$_6$) δ 2.7 (s, 3H, CH$_3$), 2.9–3.4 (m, 6H, 3CH$_2$), 7.2–9.1 (m, 4H, Ar-H), 9.5 (s, 1H, C$_2$-H). EIMS *m/z* (%): 306 (M$^+$-CO, 64). ^{13}C NMR (DMSO-d$_6$) δ 19.2 (CH$_3$), 23.9 (C-5`), 29.4 (C-6`), 35.2 (CH$_2$) 126.5-160.7 (Ar-C), 154 (CO).

Aldose *N*-(5,6-dihydronaphtho[1′,2′:4,5]thieno-[2,3-*d*]pyrimidin-11-yl)hydrazones (8a,b). General procedure: A mixture of compound **1** (2.68 g, 1 mmol), D-glucose (1.8 g, 1 mmol), or D-ribose (1.4 g, 1 mmol), ethanol (30 mL), and a catalytic amount of glacial acetic acid (3 drops) was heated at 80 °C for 2 h. The formed precipitate was filtered off, dried and recrystallized from ethanol to give compounds **8a,b**.

D-Glucose *N*-(5,6-dihydronaphtho[1′,2′:4,5]thieno-[2,3-*d*]pyrimidin-11-yl)hydrazone (8a). Yield 60%, mp 170–172 °C. Anal. calcd for $C_{20}H_{22}N_4O_5S$: C 55.80, H 5.15, N 13.01, S 7.45. Found: C 55.67, H 5.24, N 13.11, S 7.5. IR ν 3353–3220 (broad, OH+NH) cm⁻¹, ¹H NMR (DMSO-d_6) δ 2.8–3.0 (m, 4H, $2CH_2$), 3.2–3.6 (protons of the alditol congregated with the solvent absorption), 3.7–3.8 (m, 2H, CH_2OH), 4.4–5.1 (m, 5H, 5OH, D_2O exchangeable), 7.0–7.4 (m, 5H, Ar-H and NH, D_2O exchangeable), 8.3 (s, 1H, N=CH), 8.50 (s, 1H, C_2-H). ¹³C-NMR (DMSO-d_6) δ 23.6 (C-5), 29.6 (C-6), 61.2-73.2 (C-alditol), 126.3-162.9 (Ar-C+ N=CH).

D-Ribose *N*-(5,6-dihydronaphtho[1′,2′:4,5]thieno-[2,3-*d*]pyrimidin-11-yl)hydrazone (8b). Yield 55%, mp 150-152 °C. Anal. calcd for $C_{19}H_{20}N_4O_4S$: C 56.99, H 5.03, N 13.99, S 8.01. Found: C 57.17, H 5.14, N 13.81, S 8.12. IR ν 3440–3220 (broad, OH+NH). ¹H NMR (DMSO-d_6) δ 2.8–3.0 (m, 4H, $2CH_2$), 3.3–3.5 (protons of the alditol congregated with the solvent absorption), 3.6–3.7 (m, 2H, CH_2OH), 4.2–5.9 (m, 4H, 4OH, D_2O exchangeable), 7.1–7.4 (m, 5H, Ar-H and NH, D_2O exchangeable), 8.3 (s, 1H, N=CH), 8.5 (s, 1H, C_2-H). ¹³C-NMR (DMSO-d_6) δ 23.5 (C-5), 29.6 (C-6), 61.1-73.2 (C-alditol), 126.3-162.7 (Ar-C+ N=CH).

8,9-Dihydronaphtho[1′,2′:4,5]thieno[3,2-*e*] [1,2,4]triazolo[1,5-*c*]pyrimidine (9).

Compound **8a** (1 mmol) in dimethylformamide (20 mL), and glacial acetic acid (1 mL) was heated under reflux for 2 h, cooled, poured into water with stirring. The precipitated solid was collected by filtration, washed with water, dried, and recrystallized from ethanol to give compound **9** in 54% yield. Compound **9** was identical in all respects (physical and spectral data) with that obtained previously.[20]

Per-*O*-acetyl-D-aldose *N*-(5,6-dihydronaphtho-[1′,2′:4,5]thieno[2,3-*d*]pyrimidin-11-yl)hydrazones (10a,b). General procedure: A solution of compounds **8a,b** (1 mmol) in a mixture of acetic anhydride (10 mL) and anhydrous pyridine (10 mL) was stirred at room temperature for 8 h. The reaction mixture was poured into ice-water with stirring and the solids that precipitated were collected by filtration, washed with water, dried and recrystallized from ethanol to give compounds **10a,b**.

2,3,4,5,6-Penta-*O*-acetyl-D-glucose *N*-(5,6-dihydronaphtho[1′,2′:4,5]thieno[2,3-*d*]pyrimidin-11-yl)hydrazone (10a). Yield 73%, mp 99–101 °C. IR ν 3325 (NH), 1751 (OAc). ¹H NMR (CDCl₃) δ 1.8–2.1 (m, 15H, 5OAc), 2.8–3.1 (m, 6H, 3CH₂), 4.2–5.5 (m, 4H, 4CHOAc), 7.0–7.4 (m, 5H, Ar-H and NH, D_2O exchangeable), 8.5 (s, 1H, N=CH), 8.9 (s, 1H, C_2-H).

¹³C-NMR (DMSO-d_6) δ 20.5-21.1 (5CH₃), 23.9 (C-5), 29.3 (C-6), 61.3-71.8 (C-alditol), 126.3-166.9 (Ar-C+N=CH), 168.9-172.2 (5C=O).

2,3,4,5-Tetra-*O*-acetyl-D-ribose *N*-(5,6-dihydronaphtho[1′,2′:4,5]thieno[2,3-*d*]pyrimidin-11-yl)hydrazone (10b). Yield 65%, mp 92–93 °C. IR ν 3435 (NH), 1747 (OAc). ¹H NMR (CDCl₃) δ 1.9–2.1 (m, 12H, 4OAc), 2.8–3.1 (m, 6H, 3CH₂), 4.1–5.2 (m, 3H, 3CHOAc), 7.0–7.4 (m, 5H, Ar-H and NH, D_2O exchangeable), 8.5 (s, 1H, N=CH), 8.9 (s, 1H, C_2-H). ¹³C-NMR (DMSO-d_6) δ 20.3-21.0 (4CH₃), 23.8 (C-5), 29.3 (C-6), 61.2-71.7 (C-alditol), 126.2-166.9 (Ar-C+N=CH), 168.9-172.3 (4CO).

(1S)-Per-*O*-acetyl-1-*C*-(8,9-dihydronaphtho-[1′,2′:4,5]thieno[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-2-yl)polyols (11a,b). General procedure: Compounds **10a,b** (1 mmol), in glacial acetic acid (20 mL), bromine (1 mmol) in glacial acetic acid (5 mL), was added dropwise at room temperature. The reaction mixtures were heated under reflux for 1 h, cooled, poured into water with stirring. The solids that precipitated were collected by filtration, washed with water, dried, and recrystallized from ethanol to give compounds **11a,b**.

(1*S*)-1,2,3,4,5-Penta-*O*-acetyl-1-*C*-(8,9-dihydro-naphtho[1′,2′:4,5]thieno[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-2-yl)-D-arabinitol (11a). Yield 70%, mp 161–162 °C. IR ν 1748 (OAc), 1602 (C=N). ¹H NMR (CDCl₃) δ 1.9–2.2 (m, 15H, 5OAc), 2.8–3.1 (m, 6H, 3CH₂), 4.2–5.5 (m, 4H, 4CHOAc), 7.1–7.4 (m, 4H, Ar-H), 8.9 (s, 1H, C_2-H). ¹³C-NMR (DMSO-d_6) δ 21.4-22.2 (5CH₃), 23.9 (C-5), 29.6 (C-6), 62.5-74.6 (C-alditol), 126.2-162.4 (Ar-C), 171-172.1 (5CO).

(1*S*)-1,2,3,4-Tetra-*O*-acetyl-1-*C*-(8,9-dihydro-naphtho[1′,2′:4,5]thieno[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-2-yl)-D-erithritol (11b). Yield 65%, mp 150–152 °C. IR ν 1745 (OAc), 1605 (C=N). ¹H NMR (CDCl₃) δ 1.8–2.1 (m, 12H, 4OAc), 2.8–3.1 (m, 6H, 3CH₂), 4.2–5.2 (m, 3H, 3CHOAc), 7.1–7.4 (m, 4H, Ar-H), 8.9 (s, 1H, C_2-H).

(1*S*)-1-*C*-(8,9-Dihydronaphtho[1′,2′:4,5]thieno-[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-2-yl)polyols (12a,b).

General procedure: To a solution of compounds **11a,b** (1 mmol) in anhydrous methanol (20 mL), ammonium hydroxide solution (5 mL, 35%) was added, then the reaction mixtures were stirred at room temperature for 2 and 3 h, respectively. The reaction mixtures were evaporated under reduced pressure at 40 °C and the residues were purified on silica gel column

using chloroform:methanol (4:1) as an eluent to give products **12a,b**.

(1*S*)-1-*C*-(8,9-Dihydronaphtho[1′,2′:4,5]thieno-[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-2-yl)-D-arabinitol (12a). Yield 60%, mp 190–192 °C. Anal. calcd for $C_{20}H_{20}N_4O_5S$: C, 56.07, H 4.70, N 13.08, S 7.48. Found: C 56.27, H 4.64, N 13.11, S 7.35. IR ν 3442–3320 (broad, OH), ^{1}H NMR (DMSO-d_6): δ 2.8–3.0 (m, 4H, 2CH$_2$), 3.3–3.6 (protons of the alditol congregated with the solvent absorption), 3.7–3.9 (m, 2H, *CH₂*OH), 4.3–5.2 (m, 5H, 5OH, D$_2$O exchangeable), 7.1–7.4 (m, 4H, Ar-H), 8.5 (s, 1H, C$_2$-H). ^{13}C NMR (DMSO-d_6) δ 23.9 (C-5), 29.6 (C-6), 61.6-72.2 (C-alditol), 126.4-162.8 (Ar-C).

(1*S*)-1-*C*-(8,9-Dihydronaphtho[1′,2′:4,5]thieno-[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-2-yl)-D-erithritol (12b). Yield 59%, mp 184–186 °C. Anal. calcd for $C_{19}H_{18}N_4O_4S$: C 57.28, H 4.55, N 14.06, S 8.05. Found: C 57.20, H 4.34, N 14.11, S 8.10. IR ν 3440–3320 (broad, OH), ^{1}H NMR (DMSO-d_6) δ 2.8–3.1 (m, 4H, 2CH$_2$), 3.2–3.6 (the protons of the alditol congregated with the solvent absorption), 3.9–5.1 (m, 4H, 4OH, D$_2$O exchangeable), 7.1–7.4 (m, 4H, Ar-H), 8.5 (s, 1H, C$_2$-H).

Conclusion

Evaluation of the new compounds established that ß-enaminoesters of pyrazole ring system **4** and **5** demonstrated inhibitory activity more than ß-enaminonitriles **2** and **3**. On the other hand, the non-acetylated sugar derivatives of thienopyrimidines or triazolopyrimidines **8a,b** and **12a,b** showed more significant antimicrobial activity than those of acetylated sugar derivatives **10a,b** and **11a,b**. In general, the target free cyclic *C*-nucleosides **12a,b** showed more significant antimicrobial activity than some known drugs (standards).

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Povzetek

Iz (5,6-dihidronafto[1′,2′:4,5]tieno[2,3-*d*]pirimidin-11-il)-hidrazina (**1**) smo pripravili nove derivate 1-(5,6-dihidronafto[1′,2′:4,5]tieno[2,3-*d*]pirimidin-11-il)-pirazola **2-7**. Z reakcijo spojine **1** z aldozami smo pripravili aciklične in ciklične *C*-nukelozide **8** in **10-12**. Nekatere pripravljene spojine kažejo močno protimikrobno delovanje.