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NON-NATURAL NUCLEOSIDES BASED ON 1,2,4-TRIAZOLO[1,5-*a*]PYRIMIDIN-7-ONES

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Abstract – Two methods for synthesis of new nucleosides bearing 6-phenyl-1,2,4-triazolo[1,5-*a*]pyrimidin-7-ones as a base have been developed. The first one includes Vorbrüggen glycosylation reaction. The second method, which is effective for synthesis of acyclic nucleosides, is based on the condensation between sodium salts of 6-phenyl-1,2,4-triazolo [1,5-*a*]pyrimidin-7-ones and 4-bromobuthyl acetate or (*Z*)-4-bromobut-2-en-1-yl acetate.

INTRODUCTION

In recent years there has been a continuing interest in nucleoside analogs in which a base residue is modified to provide structures with a variety of altered properties. Biological properties of base-modified nucleosides have found application as antiviral tools against *herpes simplex virus* (HSV), *varicella-zoster virus* (VZV), *cytomegalovirus*, *hepatitis B virus* (HBV) and *human immunodeficiency virus* (HIV);[1,2] in the study on the base-to-base interaction in DNA;[3] as well as in DNA-probe technology.[4,5] Bicyclic pyrimidine nucleosides have shown considerable potential as antiviral agents.[6,7] The fused pyrimidine base-modified nucleosides are of particular interest. Thus, imidazo[1,2-*c*]pyrimidin-5-one derivatives **1a-d** have demonstrated anti-HBV[8,9] and anti-HIV activities.[10] Pyrrolo[2,3-*d*]pyrimidones **2a**,**b** were reported as promising fluorescent cytidine and deoxycytidine analogs for study of DNA structure[11] (Figure 1).

Herein we report a synthesis of modified nucleosides based on NH-heterocycles **3a-c** which have [1,5-*a*] type of fusion of the azole and azine rings. These structures are of interest as analogs of bicyclic pyrimidine nucleosides with sugar fragment attached to pyrimidine part. On the other hand,

1,2,4-triazolo[1,5-*a*]pyrimidin-7-ones with *β*-D-ribofuranose fragment in azole ring are considered as purine nucleoside analogs possessing bridgehead nitrogen atom.[12,13]

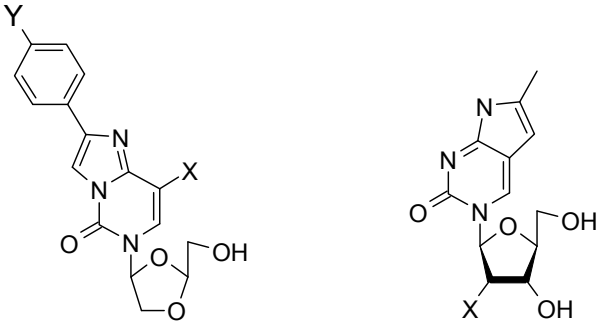
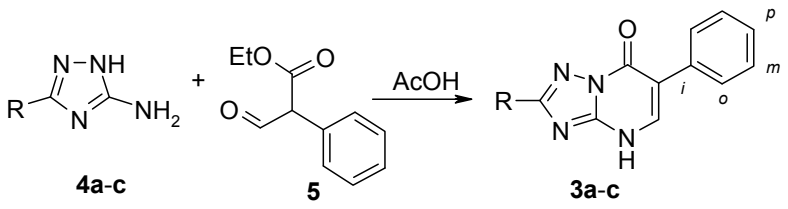


Figure 1. Nucleosides based on azolopyrimidines

Also, the choice of compound **3a-c** as bases for synthesis of nucleosides was due to the fact that 6-nitro-1,2,4-triazolo[1,5-*a*]pyrimidines showed activity against *cowpox virus*.[14] In addition, 6-arylazolo[1,5-*a*]pyrimidin-7-ones were reported as inhibitor replication of *hepatitis C virus* (HCV).[15]

RESULTS AND DISCUSSION

For synthesis of 6-phenyl-1,2,4-triazolo[1,5-*a*]pyrimidin-7-one **3a** and its 2-substituted derivatives **3b**,**c** we used the interaction of 5-amino-1,2,4-triazoles **4a-c** with ethyl α-formylphenylacetate **5**. Yields of the compounds **3a-c** were 70-80% (Scheme 1).

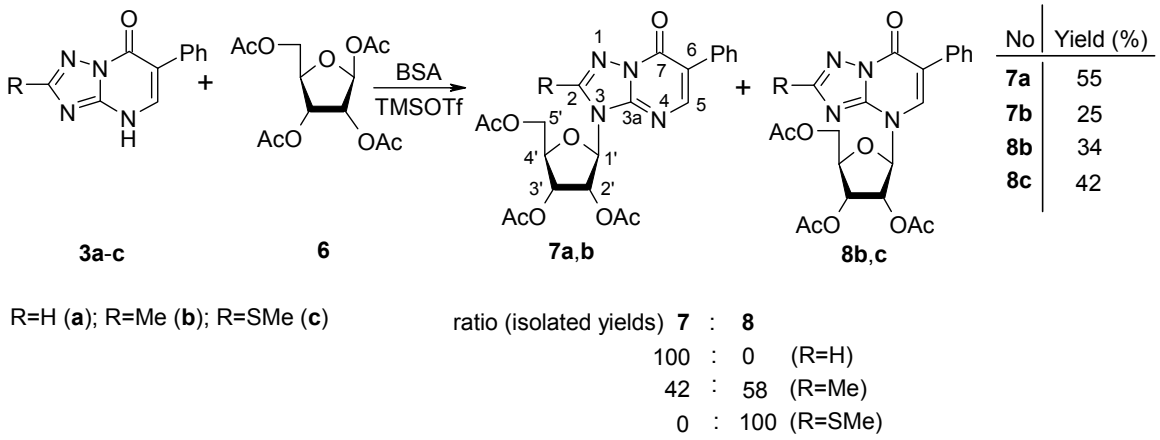


No	Yield (%)
3a	70
3b	74
3c	80

Scheme 1

The Vorbrüggen-type glycosylation procedure is an important nucleoside-forming methodology.[16] This approach involves the interaction of ribose tetraacetate (or benzoate) with the appropriate silylated base in the presence of Lewis acids. Earlier we reported that Vorbrüggen one-step method[17,18] was effective for ribosylation of 1,2,4-triazolo[5,1-*c*][1,2,4]triazin-7-ones.[19] Herein, we discuss application of this method for synthesis of nucleosides based on another heterocyclic system 1,2,4-triazolo[1,5-*a*]pyrimidin-7-ones. Treatment of NH-heterocycles **3a-c** with *N*,*O*-bis(trimethylsilyl)acetamide (BSA) and trimethylsilyl trifluoromethanesulfonate (TMSOTf) followed by addition of 1,2,3,4-tetra-*O*-acetyl-*β*-D-ribofuranose **6**

gave compounds **7a**,**b** and **8b**,**c** (Scheme 2). In all cases the coupling was completed within 15 min at ambient temperature.

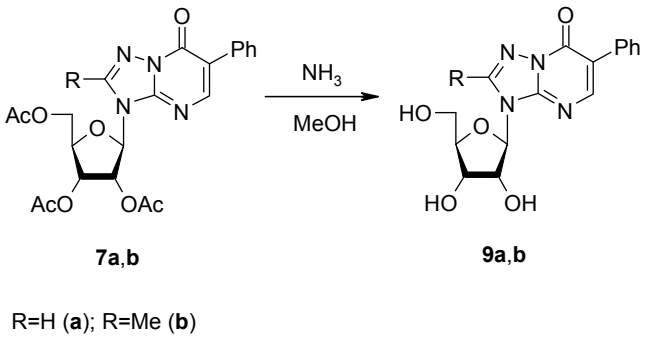


No	Yield (%)
7a	55
7b	25
8b	34
8c	42

Scheme 2

Use of pyrimidine derivative **3a** led to compound **7a**, being a glycosylation product of azole fragment. Ribosylation of 2-methylthio-1,2,4-triazolo[1,5-*a*]pyrimidine **3c** gave product **8c** containing sugar in azine part as a single the coupling product. In case of 2-methylated compound **3b** we obtained a mixture of isomers (**7b** and **8b)** which were successfully separated by column chromatography. Obviously, position of the glycosylation depends on substituent at the azole ring. Bulky substituent (Me < SMe) shifts the ratio **7** : **8** towards product of glycosylation at the azine fragment.

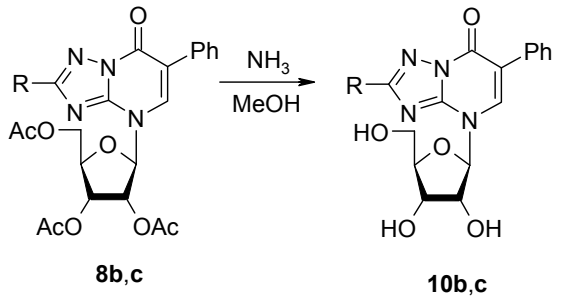
Treatment of **7a**,**b** with methanolic ammonia at 0 ºC for several hours afforded 3-*β*-D-ribofuranosyl-1,2,4-triazolo[1,5-*a*]pyrimidin-7-ones **9a**,**b**, analogs of purine nucleosides (Scheme 3).



No	Yield (%)
9a	60
9b	40

Scheme 3

Removal of protecting groups in compounds **8b**,**c** was carried out in the same conditions to give the corresponding bicyclic analogs of pyrimidine nucleosides **10b**,**c** in 48-59% yields (Scheme 4).



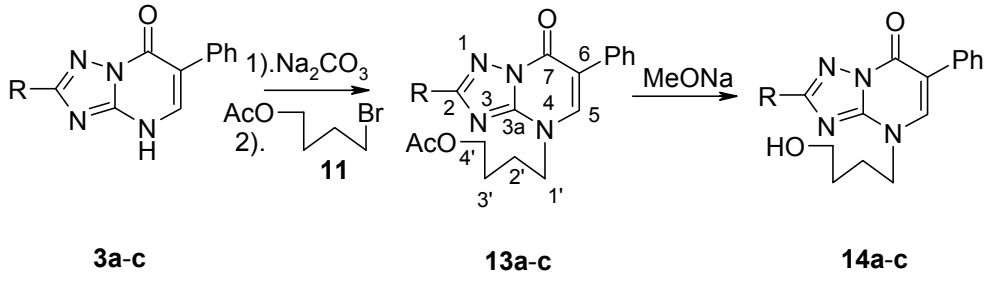
No	Yield (%)
10a	59
10c	48

R=Me (**b**); R=SMe (**c**)

Scheme 4

Reactions of sodium or mercury salts of purines and pyrimidines with halogen derivatives of sugars provide an alternative nucleoside-forming methodology.[20-22] Previously reported conditions for alkylation of 1,2,4-triazolo[1,5-*a*]pyrimidin-7-ones sodium salts by iodomethane[23] have found to be effective for the synthesis of acyclic nucleosides based on heterocycles **3a-c**. We alkylated **3a-c** with 4-bromobutyl acetate **11** and (*Z*)-4-bromobut-2-enyl acetate **12**. In all cases the alkylation proceeded at the N4-atom of azine ring without any influence of substituents at the azole ring. Obviously, in *anions* of azoloazines **3a-c**, which are formed under basic conditions, nitrogen atom of the azine ring is more nucleophilic in S_N2 substitution of bromide in **11** and **12**. Contrary that the Vorbrüggen glycosylation of **3a-c**, which is S_N1 reaction, key stage is interaction of bulky acyloxonium cation bridge involving the C1-C2 bond of the sugar ring with *neutral* trimethylsilylated derivatives of 1,2,4-triazolo[1,5-*a*]pyrimidin-7-ones. In this case position of glycosilation depends on steric hindrances caused by substituent in the azole ring.

Treatment of **3a-c** with 4-bromobutyl acetate **11** in the presence of sodium carbonate in DMF resulted in acetyl derivatives **13a-c** in 60-80% yields (Scheme 5).



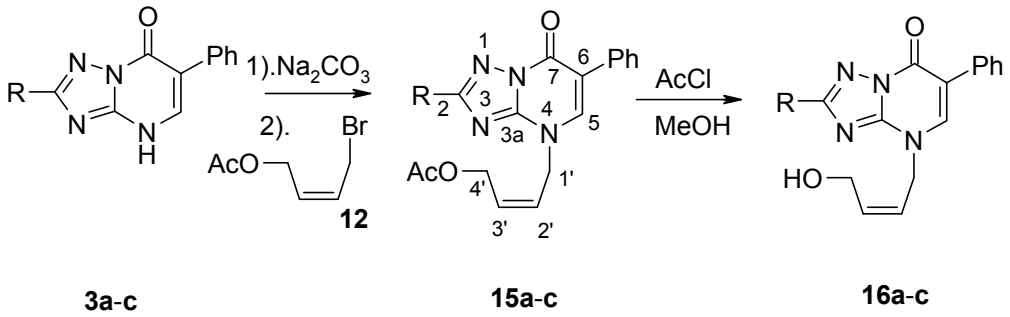
No	Yield (%)
13a	60
13b	76
13c	80
14a	60
14b	50
14c	57

R=H (**a**); R=Me (**b**); R=SMe (**c**)

Scheme 5

The deacylation of compounds **13a-c** with sodium methoxide afforded 4-(4-hydroxybutyl)-1,2,4-triazolo[1,5-*a*]pyrimidin-7-ones **14a-c.**

The same conditions were used for reaction of NH-heterocycles **3a-c** with (*Z*)-4-bromobut-2-en-1-yl acetate (**12**) (Scheme 6). Removal of protection group in compounds **15a-c** was carried out in HCl saturated methanol solution prepared by addition acetyl chloride to methanol. Triazolopyrimidines **16a-c** were obtained in 30-40% yields.



No	Yield (%)
15a	51
15b	40
15c	37
16a	30
16b	40
16c	32

R=H (**a**); R=Me (**b**); R=SMe (**c**)

Scheme 6

Purine derivatives containing *N*-hydroxybutyl fragment have been considered as «Acyclovir» analogs[24] which possess antiviral activity against HSV in cells.[25] Acyclic nucleosides containing (*Z*)-4-hydroxybutenyl group in alkyl moiety based on adenine and 3-deazaadenine are analogs of «Neplanocin A» and described as potential inhibitors of *S*-adenosylhomocysteine hydrolase.[26,27]

The signals in both ^{1}H- and ^{13}C- NMR spectra of compounds **3a-c**, **7a**,**b**, **8b**,**c**, **9a**,**b**, **10b**,**c**, **13a-c**, **14a-c**, **15a-c**, **16a-c** were assigned using 2D ^{13}C-^{1}H gHSQC and gHMBC experiments. The position of sugar fragment in **7a**,**b** and **9b**,**c** was evident from the observed cross-peaks of H1' signals with C3a and C2 in HMBC spectra. In the case of compounds **8b**,**c** and **10b**,**c** the presence of ribofuranose ring at N4-atom was proved by correlation peaks of H1' with C5 and C3a in HMBC spectra. Also, 2D gHMBC experiments allowed determining the position of attachment of N-alkyl substitutes in pyrimidines **13a-c**, **14a-c**, **15a-c** and **16a-c**. We observed cross-peaks of both C3a and C5 signals with signals of protons of N-CH_2 fragment that unambiguously confirmed attachment of alkyl substitute at azine part.

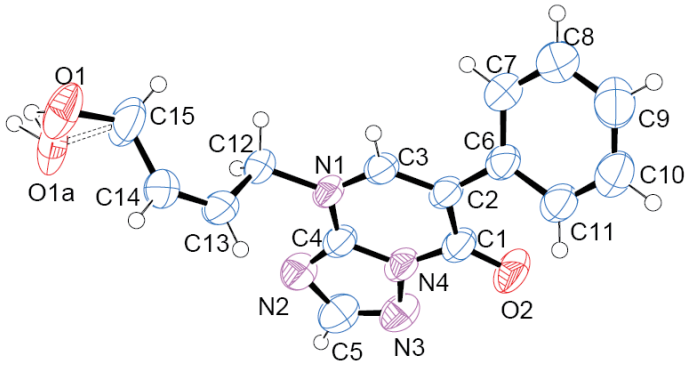


Figure 2. ORTEP drawing of **16a**

The anomeric configuration of **7a**,**b**, **8b**,**c**, **9a**,**b** and **10b**,**c** was assigned as β on the basis of correlation peak between of H1' and H4' in 2D ^{1}H-^{1}H gNOESY spectra. The coupling constant (11 Hz) between protons of –CH=CH– fragment corresponded to the (*Z*)-configuration of *N*-butenyl moiety in compounds **15a-c** and **16a-c**. These results were in a good agreement with the data of X-ray diffraction analysis of **16a** (Figure 2) whose single crystal was obtained by recrystallization from 2-propanol. In the crystal the triazole and pyrimidine rings formed a virtually planar bicyclic system un-conjugated with phenyl substituent. The C7C6C2C3 torsion angle is 33.3º. The geometric parameters of 1,2,4-triazolo[1,5-*a*]pyrimidine **16a** had standard values.[28,29]

In conclusion, we have developed two methods for synthesis of non-natural nucleosides based on 6-phenyl-1,2,4-triazolo[1,5-*a*]pyrimidin-7-ones. The first way is based on the Vorbrüggen glycosylation procedure. It has been shown by the example of ribosylation that this process can be nonselective. Use of this method makes it possible to obtain nucleoside analogs of both purines and pyrimidines. Another way which was effective for the synthesis of acyclic nucleosides involves the reaction of sodium salt of 6-phenyl-1,2,4-triazolo[1,5-*a*]pyrimidin-7-ones with 4-bromobuthyl acetate **11** or (*Z*)-4-bromobut-2-enyl acetate **12**. We have found that this method leads only to products of azine fragment alkylation.

Preliminary study of the biological activity of acyclic nucleosides **14a-c** has shown their low activity against influenza virus A (culture H3N2).

EXPERIMENTAL

The ^{1}H-NMR (400 MHz), ^{13}C-NMR (100 MHz) and ^{13}C- and ^{1}H- 2D NMR spectra were measured on a Bruker AVANCE II (400 MHz) spectrometer. Chemical shifts are given in δ values (ppm) using TMS as the internal standard. The IR spectra were recorded using a Perkin Elmer Spectrum One B Fourier-transform infrared spectrometer equipped with a diffuse reflection attachment. Elementary combustion analyses were performed using a Perkin Elmer PE 2400 series II CHNS/O analyzer. All reaction were monitored by TCL employing 0.25 mm silica gel plates (Merck 60F 254). The column chromatography was performed on silica gel Alfa Aesar (Avocado Research Chemical Ltd, Silica gel 60, 0.035–0.070 mm (220–440 mesh)).

Trimethylsilyl trifluoromethanesulfonate (TMSOTf), *N*,*O*-bis-(trimethylsilyl)acetamide (BSA), 1,2,3,4-tetra-*O*-acetyl-β-D-ribofuranose and 5-amino-1,2,4-triazoles **4a,c** were purchased from Aldrich.

3-Methyl-5-amino-1,2,4-triazole 4b was prepared according to the procedure described earlier.[30]

Ethyl α-formylphenylacetate (5) was prepared according to the procedure described earlier.[31]

6-Phenyl-1,2,4-triazolo[1,5-*a*]pyrimidin-7-ones (3a-c). 5-Amino-1,2,4-triazole **(4a-b)** (11.90 mmol) was dissolved in acetic acid (4 mL), ethyl α-formylphenylacetate **(5)** (2.28 g, 11.90 mmol) was added, and the mixture was refluxed for 1 h. After cooling, the precipitate formed was filtered off and dried.

3a: 1.76 g; 70%; mp 311 ºC; ^{1}H-NMR (DMSO-d_6) δ 7.33 (m, 1H, C$_p$-H), 7.40 (m, 2H, C$_m$-H), 7.65 (m, 2H, C$_o$-H), 8.21 (s, 1H, C5-H), 8.21 (s, 1H, C2-H), 13.21-13.88 (br.s, 1H, NH); ^{13}C-NMR (DMSO-d_6) δ 111.82 (C6), 127.35 (C*p*), 128.21 (C*m*), 128.67 (C*o*), 133.35 (C*i*), 138.79 (C5), 150.11 (C3a), 152.29 (C2), 155.74 (C7); IR 3096, 3007, 2884, 1673 (C=O), 1634, 1591, 1470, 1278, 1180, 1137, 766, 684, 639 cm^{-1}; Anal. Calcd for $C_{11}H_8N_4O$: C, 62.26; H, 3.80; N, 26.40%. Found: C, 62.10; H, 4.00; N, 26.57%.

3b: 1.99 g; 74%; mp > 320 ºC; ^{1}H-NMR (DMSO-d_6) δ 2.38 (s, 3H, CH$_3$), 7.32 (dd, *J*= 7.5 Hz, 1H, C$_p$-H), 7.40 (dd, *J*= 7.5 Hz, 2H, C$_m$-H), 7.64 (d, *J*= 7.5 Hz, 2H, C$_o$-H), 8.13 (s, 1H, C5-H), 12.3-13.71 (br.s, 1H, NH); ^{13}C-NMR (DMSO-d_6) δ 14.13 (CH$_3$), 111.88 (C6), 127.20 (C*p*), 128.13 (C*m*), 128.56 (C*o*), 133.51 (C*i*), 138.85 (C5), 150.29 (C3a), 155.29 (C7), 160.74 (C2); IR 3007, 2863, 2763, 1668 (C=O), 1640, 1596, 1287, 775, 693, 630 cm^{-1}; Anal. Calcd for $C_{12}H_{10}N_4O$: C, 63.71; H, 4.46; N, 24.76%. Found: C, 64.01; H, 4.24; N, 24.55%.

3c: 2.47 g; 80%; mp > 320 ºC; ^{1}H-NMR (DMSO-d_6) δ 2.61 (s, 3H, SCH$_3$), 7.33 (m, 1H, C$_p$-H), 7.40 (m, 2H, C$_m$-H), 7.63 (m, 2H, C$_o$-H), 8.14 (s, 1H, C5-H), 13.00-14.00 (br.s, 1H, NH); ^{13}C-NMR (DMSO-d_6) δ 14.13 (SCH$_3$), 111.88 (C6), 127.20 (C*p*), 128.13 (C*m*), 128.56 (C*o*), 133.51 (C*i*), 138.85 (C5), 150.29 (C-3a), 155.29 (C2), 160.74 (C7); IR 3070, 2955, 2836, 2774, 1668 (C=O), 1632, 1586, 1503, 1273, 1204, 1157, 773, 729, 695, 652 cm^{-1}; Anal. Calcd for $C_{12}H_{10}N_4OS$: C, 55.80; H, 3.90; N, 21.69%. Found: C, 55.84; H, 4.02; N, 21.38%.

3-(2,3,5-Tri-*O*-acetyl-β-D-ribofuranosyl)-6-phenyl-1,2,4-triazolo[1,5-*a*]pyrimidin-7-one (7a). *N,O*-Bis(trimethylsilyl)acetamide (BSA) (0.86 mL, 0.71 g, 3.54 mmol), trimethylsilyl trifluoromethanesulfonate (TMSOTf) (0.70 mL, 0.85 g, 3.78 mmol) and 1,2,3,5-tetra-*O*-acetyl-β-D-ribofuranose **(6)** (0.75 g, 2.36 mmol) were added to a solution of compound **3a** (0.5 g, 2.36 mmol) in MeCN (40 mL). The obtained suspension was stirred at ambient temperature for 15 min, diluted with 10 mL of MeCN with a few drops of water and neutralized with $NaHCO_3$. The resulting suspension was filtered. The filtrate was concentrated *in vacuo*. Recrystallization of the residue from 2-propanol gave **7a**. Yield 0.610 g; 55%; mp 115 ºC; $[\alpha]^{20}_D$ -20.70(*c* 0.68, MeCN); ^{1}H-NMR (CD_3COCD_3) δ 2.04 (s, 3H, CH$_3$), 2.08 (s, 3H, CH$_3$), 2.11 (s, 3H, CH$_3$), 4.44 (m, 2H, C5'-H$_2$), 4.52 (dt, *J*= 3.6 and 5.2 Hz, 1H, C4'-H), 5.71 (dd, *J*= 5.1 and 5.6 Hz, 1H, C3'-H), 6.08 (dd, *J*= 4.8 and 5.6 Hz, 1H, C2'-H), 6.23 (d, *J*= 4.7 Hz, 1H, C1'-H), 7.32 (m, 1H, C$_p$-H), 7.41 (m, 2H, C$_m$-H), 7.75 (m, 2H, C$_o$-H), 8.21 (s, 1H, C5-H), 8.88 (s, 1H, C2-H); ^{13}C-NMR (CD_3COCD_3) δ 20.42 (CH$_3$), 20.53 (CH$_3$), 20.77 (CH$_3$), 63.70 (C5'), 71.16 (C3'), 73.53 (C2'), 81.66 (C4'), 87.97 (C1'), 118.68 (C6), 128.03 (C*p*), 129.05 (C*o*), 129.40 (C*m*), 135.59 (C*i*), 141.77 (C2), 148.54 (C3a), 152.14 (C5), 155.73 (C7), 170.03 (C=O), 170.10 (C=O), 170.78 (C=O); IR 1752 (C=O), 1692 (C=O), 1600, 1538, 1228, 1209, 1160, 798 cm^{-1}; Anal.

Calcd for $C_{22}H_{22}N_4O_8$: C, 56.17; H, 4.71; N, 11.91%. Found: C, 56.43; H, 4.35; N, 11.68%.

***N*-(2,3,5-Tri-*O*-acetyl-β-D-ribofuranosyl)-2-methyl-6-phenyl-1,2,4-triazolo[1,5-*a*]pyrimidin-7-ones (7b) and (8b).** *N*,*O*-Bis(trimethylsilyl)acetamide (BSA) (0.86 mL, 0.71 g, 3.54 mmol), trimethylsilyl trifluoromethanesulfonate (TMSOTf) (0.70 mL, 0.85 g, 3.78 mmol) and 1,2,3,5-tetra-*O*-acetyl-β-D-ribofuranose **(6)** (0.75 g, 2.36 mmol) were added to a solution of compound **3b** (0.533 g, 2.36 mmol) in MeCN (40 mL). The obtained suspension was stirred at ambient temperature for 15 min, diluted with 10 mL of MeCN with a few drops of water and neutralized with $NaHCO_3$. The resulting suspension was filtered. The filtrate was concentrated *in vacuo*. The usual column chromatography of the residue gave compound **7b** as the first-eluted component (eluent: hexane - EtOAc (4:1)), and compound **8b** as the second-eluted component (eluent: EtOAc (100%)).

7b: 0.285 g, 25% ; mp 87 ºC; $[\alpha]^{20}_D$ -15.71 (*c* 0.91, MeCN); ^{1}H-NMR ($CDCl_3$) δ 2.06 (s, 3H, CH_3), 2.12 (s, 3H, CH_3), 2.16 (s, 3H, CH_3), 2.63 (s, 3H, CH_3), 4.33 (dd, *J*= 11.5 and 5.9 Hz, 1H, C5'-Ha), 4.49 (dd, *J*= 11.5 and 3.1 Hz, 1H, C5'-Hb), 4.43 (m, 1H, C4'-H), 5.78 (m, 2H, C1'-H and C3'-H), 6.14 (dd, *J*= 4.5 and 5.9 Hz, 1H, C2'-H), 7.34 (m, 1H, C_p-H), 7.42 (m, 2H, C_m-H), 7.67 (m, 2H, C_o-H), 8.10 (s, 1H, C5-H); ^{13}C-NMR ($CDCl_3$) δ 11.70 (CH_3), 20.60 (CH_3), 20.62 (CH_3), 20.83 (CH_3), 62.99 (C5'), 70.42 (C3'), 72.05 (C2'), 80.45 (C4'), 87.27 (C1'), 119.32 (C6), 127.73 (C*p*), 128.60 (C*o*), 128.68 (C*m*), 133.89 (C*i*), 147.49 (C3a), 150.29 (C2), 151.02 (C5), 155.29 (C7), 169.67 (C=O), 169.92 (C=O), 170.54 (C=O); IR 1744 (C=O), 1687 (C=O), 1596, 1535, 1224, 1046, 1024, 738 cm^{-1}; Anal. Calcd for $C_{23}H_{24}N_4O_8$: C, 57.02; H, 4.99; N, 11.56%. Found: C, 57.15; H, 5.03; N, 11.55%.

8b: 0.388 g, 34%, ; mp 77 ºC; $[\alpha]^{20}_D$ -53.04 (*c* 1.04, MeCN); ^{1}H-NMR (CD_3COCD_3) δ 1.93 (s, 3H, CH_3), 2.04 (s, 3H, CH_3), 2.12 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 4.45 (dd, *J*= 2.8 and 3.7 Hz, 2H, C5'-H_2), 4.50 (dt, *J*= 4.0 and 4.1 Hz, 1H, C4'-H), 5.64 (dd, *J*= 4.6 and 5.9 Hz, 1H, C3'-H), 5.93 (dd, *J*= 5.9 Hz, 1H, C2'-H), 6.37 (d, *J*= 5.0 Hz, 1H, C1'-H), 7.38 (dd, *J*= 7.2 Hz, 1H, C_p-H), 7.43 (dd, *J*= 7.2 Hz, 2H, C_m-H), 7.65 (dd, *J*= 7.2 Hz, 2H, C_o-H), 8.24 (s, 1H, C5-H); ^{13}C-NMR (CD_3COCD_3) δ 14.59 (CH_3), 20.34 (CH_3), 20.52 (CH_3), 20.61 (CH_3), 63.78 (C5'), 71.05 (C3'), 73.44 (C2'), 81.57 (C4'), 92.64 (C1'), 115.41 (C6), 128.76 (C*p*), 129.16 (C*m*), 129.74 (C*o*), 134.09 (C-*i*), 136.89 (C-5), 150.88 (C-3a), 155.43 (C-7), 162.47 (C-2), 170.04 (C=O), 170.11 (C=O), 170.61 (C=O); IR 1746 (C=O), 1701 (C=O), 1582, 1217, 1095, 1043, 725 cm^{-1}; Anal. Calcd for $C_{23}H_{24}N_4O_8$: C, 57.02; H, 4.99; N, 11.56%. Found: C, 57.18; H, 4.82; N, 11.56%.

4-(2,3,5-Tri-*O*-acetyl-β-D-ribofuranosyl)-2-methylthio-6-phenyl-1,2,4-triazolo[1,5-*a*]pyrimidin-7-one (8c). *N*,*O*-Bis(trimethylsilyl)acetamide (BSA) (0.86 mL, 0.71 g, 3.54 mmol), trimethylsilyl trifluoromethanesulfonate (TMSOTf) (0.70 mL, 0.85 g, 3.78 mmol) and 1,2,3,5-tetra-*O*-acetyl-β-D-ribofuranose **(6)** (0.75 g, 2.36 mmol) were added to a solution of compound **3c** (0.509 g, 2.36 mmol) in MeCN (40 mL). The obtained suspension was stirred at ambient temperature for

15 min, diluted with 10 mL of MeCN with a few drops of water and neutralized with $NaHCO_3$. The resulting suspension was filtered. The filtrate was concentrated *in vacuo*. The product **8c** was isolated by column chromatography using EtOAc as eluent. Yield 0.511 g, 42%, mp 173 ºC ; $[\alpha]^{20}_D$ -38.36 (*c* 1.00, MeCN); ^{1}H-NMR ($CDCl_3$) δ 1.91 (s, 3H, CH_3), 2.10 (s, 3H, CH_3), 2.15 (s, 3H, CH_3), 2.71 (s, 3H, CH_3), 4.39 (d, *J*= 3.0 Hz, 2H, C5'-H_2), 4.46 (dt, *J*= 3.3 and 3.7 Hz, 1H, C4'-H), 5.49 (dd, *J*= 4.4. and 5.7 Hz, 1H, C3'-H), 5.66 (dd, *J*= 5.6 Hz, 1H, C2'-H), 6.26 (d, *J*= 5.6 Hz, 1H, C1'-H), 7.37 (m, 1H, C_p-H), 7.43 (m, 2H, C_m-H), 7.58 (m, 2H, C_o-H), 7.80 (s, 1H, C5-H); ^{13}C-NMR ($CDCl_3$) δ 14.28 (CH_3), 20.52 (CH_3), 20.63 (CH_3), 20.67 (CH_3), 63.12 (C5'), 70.38 (C3'), 72.80 (C2'), 80.86 (C4'), 90.88 (C1'), 116.29 (C6), 128.88 (C*p*, C*o* and C*m*), 132.32 (C*i*), 133.72 (C5), 150.14 (C3a), 154.08 (C7), 165.60 (C2), 169.63 (C=O), 169.73 (C=O), 170.19 (C=O); IR 1747 (C=O), 1695 (C=O), 1579, 1227, 1211, 1099, 1061, 771, 699 cm^{-1}; Anal. Calcd for $C_{23}H_{24}N_4O_8S$: C, 53.48; H, 4.68; N, 10.85%. Found: C, 53.64; H, 4.79; N, 10.63%.

***N*-(*β*-D-Ribofuranosyl)-6-phenyl-1,2,4-triazolo[1,5-*a*]pyrimidin-7-ones (9a,b) and 10(b,c).** Compound **(7a,b, 8b,c)** (0.38 mmol) was dissolved in MeOH (30 mL) saturated with ammonia (at 0 ºC). The resulting solution was left at 0 ºC for 5 h and evaporated to dryness. The product was isolated by column chromatography using EtOAc as eluent.

9a: 0.0784 g; 60%; mp 156 ºC; $[\alpha]^{20}_D$ -34.34 (*c* 0.62, MeCN); ^{1}H-NMR (CD_3COCD_3) δ 3.79 (dd, *J*= 2.5 and 12.4 Hz, 1H, C5'-Ha), 3.82 (dd, *J*= 2.5 and 12.3 Hz, 1H, C5'-Hb), 4.20 (m, 1H, C4'-H), 4.47 (br. s, 1H, OH), 4.49 (dd, *J*=4.5 Hz, 1H, C3'-H), 4.83 (dd, *J*= 4.6 Hz, 1H, C2'-H), 4.92 (br. s, 2H, OH), 6.01 (d, *J*= 4.5 Hz, 1H, C1'-H), 7.31 (m, 1H, C_p-H), 7.42 (m, 2H, C_m-H), 7.75 (m, 2H, C_o-H), 8.18 (s, 1H, C5-H), 8.99 (s, 1H, C2-H); ^{13}C-NMR (CD_3COCD_3) δ 62.26 (C5'), 71.44 (C3'), 75.17 (C2'), 87.56 (C4'), 90.89 (C1'), 118.15 (C6), 127.94 (C*p*), 129.00 (C*o*), 129.36 (C*m*), 135.63 (C*i*), 141.98 (C2), 148.69 (C3a), 151.89 (C5), 155.81 (C7); IR 3430 (OH), 3107, 1676 (C=O), 1597, 1540, 1066, 1024, 783 cm^{-1}; Anal. Calcd for $C_{16}H_{16}N_4O_5 \cdot H_2O$: C, 53.04; H, 5.01; N, 15.46%. Found: C, 52.73; H, 4.96; N, 15.44%.

9b: 0.054 g; 40%; mp 233 ºC; $[\alpha]^{20}_D$ -56.33 (*c* 0.43, MeCN); ^{1}H-NMR (DMSO-d_6) δ 2.63 (s, 3H, CH_3), 3.55 (m, 2H, C5'-H_2) 3.97 (br.s, 1H, C4'-H), 4.21 (br.s, 1H, C3'-H), 4.86 (dd, *J*= 6.1 and 11.2 Hz, 1H, C2'-H), 5.15 (t, *J*= 5.6 Hz, 1H, OH), 5.30 (d, *J*= 4.6 Hz, 1H, OH), 5.50 (d, *J*= 5.8 Hz, 1H, OH), 5.79 (d, *J*= 6.2 Hz, 1H, C1'-H), 7.32 (dd, *J*= 7.4 Hz, 1H, C_p-H), 7.41 (dd, *J*= 7.4 Hz, 2H, C_m-H), 7.69 (d, *J*= 7.4 Hz, 2H, C_o-H), 8.19 (s, 1H, C5-H); ^{13}C-NMR (DMSO-d_6) δ 11.83 (CH_3), 61.45 (C5'), 70.17 (C3'), 71.12 (C2'), 86.44 (C-4'), 88.71 (C1'), 117.47 (C6), 127.11 (C*p*), 128.21 (C*o* and C*m*), 134.18 (C*i*), 148.19 (C3a), 150.71 (C5), 151.49 (C2), 155.38 (C7); IR 3278 (OH), 3219, 2851, 1672 (C=O), 1585, 1573, 1106, 1074, 1024, 782 cm^{-1}; Anal. Calcd for $C_{17}H_{18}N_4O_5$: C, 56.98; H, 5.06; N, 15.63%. Found: C, 57.12; H, 5.04; N, 15.91%.

10b: 0.0803 g; 59%; mp 227 ºC; $[\alpha]^{20}_D$ -37.85 (*c* 0.25, MeCN); ^{1}H-NMR (DMSO-d_6) δ 2.41 (s, 3H, CH_3),

3.62 (m, 1H, C5'-Ha), 3.66 (m, 1H, C5'-Hb), 4.01 (m, 1H, C4'-H), 4.16 (dd, *J*= 10.0 and 5.0 Hz, 1H, C3'-H), 4.38 (dd, *J*= 4.6 and 9.1 Hz, 1H, C2'-H), 5.18 (d, *J*= 5.6 Hz, 1H, OH), 5.39 (t, *J*= 4.5 Hz, 1H, OH), 5.60 (d, *J*= 5.4 Hz, 1H, OH), 6.05 (d, *J*= 3.9 Hz, 1H, C1'-H), 7.34 (dd, *J*= 7.2 Hz, 1H, C_p-H), 7.45 (dd, *J*= 7.2 Hz, 2H, C_m-H), 7.65 (d, *J*= 7.2 Hz, 2H, C_o-H), 8.76 (s, 1H, C5-H); ^{13}C-NMR (DMSO-d_6) δ 14.33 (CH_3), 59.92 (C5'), 69.11 (C3'), 74.03 (C2'), 85.16 (C4'), 92.73 (C1'), 112.74 (C6), 127.52 (C*p*), 128.50 (C*m*), 128.53 (C*o*), 133.11 (C*i*), 136.08 (C5), 149.74 (C3a), 154.65 (C7), 161.26 (C2); IR 3285 (OH), 1712 (C=O), 1693 (C=O), 1577, 1432, 1334, 1086, 1067, 1045, 777 cm^{-1}; Anal. Calcd for $C_{17}H_{18}N_4O_5$: C, 56.98; H, 5.06; N, 15.63%. Found: C, 56.69; H, 5.12; N, 15.32%.

10c: 0.078 g; 48%; mp 184 ºC; $[\alpha]^{20}_D$ -22.00 (*c* 0.30, MeCN); ^{1}H-NMR (DMSO-d_6) δ 2.64 (s, 3H, CH_3), 3.62 (m, 1H, C5'-Ha), 3.66 (m, 1H, C5'-Hb), 3.99 (dt, *J*= 5.4 and 2.7 Hz, 1H, C4'-H), 4.15 (dd, *J*= 10.5 and 5.4 Hz, 1H, C3'-H), 4.36 (dd, *J*= 8.9 and 4.1 Hz, 1H, C2'-H), 5.18 (d, *J*= 5.6 Hz, 1H, OH), 5.35 (t, *J*= 4.5 Hz, 1H, OH), 5.63 (d, *J*= 5.4 Hz, 1H, OH), 6.00 (d, *J*= 3.7 Hz, 1H, C1'-H), 7.36 (dd, *J*= 7.4 Hz, 1H, C_p-H), 7.43 (dd, *J*= 7.4 Hz, 2H, C_m-H), 7.65 (d, *J*= 7.4 Hz, 2H, C_o-H), 8.75 (s, 1H, C5-H); ^{13}C-NMR (DMSO-d_6) δ 13.55 (CH_3), 59.80 (C5'), 68.98 (C3'), 74.09 (C2'), 85.07 (C4'), 92.69 (C1'), 113.07 (C6), 127.60 (C*p*), 128.32 (C*m*), 128.49 (C*o*), 133.03 (C*i*), 135.62 (C5), 150.20 (C3a), 153.99 (C7), 163.53 (C2); IR 3262 (OH), 1687 (C=O), 1577, 1468, 1271, 1086, 776, 695 cm^{-1}; Anal. Calcd for $C_{17}H_{18}N_4O_5S{\cdot}2H_2O$: C, 47.88; H, 5.20; N, 13.14%. Found: C, 47.89; H, 5.08; N, 13.21%.

4-Bromobutyl acetate (11)[32] and **(*Z*)-4-bromobut-2-enyl acetate (12)**[33] were synthesized according to procedures described earlier.

4-(4-Acetoxybutyl)-6-phenyl-1,2,4-triazolo[1,5-*a*]pyrimidin-7-ones (13a-c). A suspension of 6-phenyl-1,2,4-triazolo[1,5-*a*]pyrimidin-7-one **(3a-c)** (9.40 mmol) in a 17% aqueous Na_2CO_3 solution (5 mL) was stirred at ambient temperature for 0.5 h. The precipitate was filtered off, dried, and dissolved in DMF (10 mL). 4-Bromobutyl acetate **(11)** (1.79 g, 9.20 mmol) was added to the reaction solution. The reaction mixture was heated at 100 ºC for 2 h and then cooled. Water (200 mL) was added to the mixture, and the precipitate was filtered off and crystallized from 2-propanol.

13a: 1.838 g; 60%; mp 146 ºC; ^{1}H-NMR (DMSO-d_6) δ 1.64 (m, 2H, C3'H_2), 1.90 (m, 2H, C2'H_2), 1.98 (s, 3H, CH_3), 4.02 (t, *J*= 6.5 Hz, 2H, C4'H_2), 4.28 (t, *J*= 7.2 Hz, 2H, C1'H_2), 7.35 (dd, *J*= 7.5 Hz, 1H, C_p-H), 7.45 (dd, *J*= 7.5 Hz, 2H, C_m-H), 7.67 (d, *J*= 7.5 Hz, 2H, C_o-H), 8.44 (s, 1H, C5-H); ^{13}C-NMR (DMSO-d_6) δ 20.71 (CH_3), 24.84 (C2'), 25.03 (C3'), 51.05 (C1'), 63.34 (C4'), 112.09 (C6), 127.53 (C*p*), 128.24 (C*m*), 128.61 (C*o*), 133.04 (C*i*), 141.63 (C5), 150.33 (C2), 152.32 (C3a), 155.08 (C7), 170.42 (C=O).; IR 1726 (C=O), 1671 (C=O), 1569, 1359, 1233, 1163, 1036, 781, 694 cm^{-1}; Anal. Calcd for $C_{17}H_{18}N_4O_3$: C, 62.57; H, 5.56; N, 17.17%. Found: C, 62.55; H, 5.52; N, 17.18%.

13b: 2.429 g; 76%; mp 137 ºC; ^{1}H-NMR (DMSO-d_6) δ 1.63 (m, 2H, C3'H_2), 1.89 (m, 2H, C2'H_2), 2.00 (s,

3H, CH_3), 2.40 (s, 3H, CH_3), 4.04 (t, *J*= 7.2 Hz, 2H, C4'H_2), 4.23 (t, *J*= 7.2 Hz, 2H, C1'H_2), 7.33 (m, 1H, C_p-H), 7.43 (m, 2H, C_m-H), 7.66 (m, 2H, C_o-H), 8.37 (s, 1H, C5-H); ^{13}C-NMR (DMSO-d_6) δ 14.81 (CH_3), 21.15 (CH_3), 25.27 (C2'), 25.45 (C3'), 51.41 (C1'), 63.80 (C4'), 112.44 (C6), 127.89 (C*p*), 128.65 (C*m*), 128.99 (C*o*), 133.56 (C*i*), 141.48 (C5), 150.94 (C3a), 155.17 (C7), 161.85 (C2), 170.86 (C=O); IR 1724 (C=O), 1691 (C=O), 1580, 1536, 1427, 1247, 1230, 1047, 780, 697 cm^{-1}; Anal. Calcd for $C_{18}H_{20}N_4O_3$: C, 63.52; H, 5.92; N, 16.46%. Found: C, 63.53; H, 5.87; N, 16.55%.

13c: 2.797 g; 80%; mp 140 ºC; ^{1}H-NMR (DMSO-d_6) δ 1.62 (m, 2H, C3'H_2), 1.88 (m, 2H, C2'H_2), 1.99 (s, 3H, CH_3), 2.65 (s, 3H, CH_3), 4.05 (t, *J*= 6.6 Hz, 2H, C4'H_2), 4.24 (t, *J*= 7.2 Hz, 2H, C1'H_2), 7.35 (dd, *J*= 7.2 Hz, 1H, C_p-H), 7.40 (dd, *J*= 7.2 Hz, 2H, C_m-H), 7.64 (d, *J*= 7.2 Hz, 2H, C_o-H), 8.30 (s, 1H, C5-H); ^{13}C-NMR (DMSO-d_6) δ 13.50 (CH_3), 20.72 (CH_3), 24.73 (C2'), 24.97 (C3'), 50.97 (C1'), 63.34 (C4'), 112.43 (C6), 127.56 (C*p*), 128.25 (C*m*), 128.55 (C*o*), 133.00 (C*i*), 140.74 (C5), 150.99 (C3a), 154.06 (C7), 163.60 (C2), 170.42 (C=O); IR 1733 (C=O), 1669 (C=O), 1564, 1453, 1268, 1222, 1041, 777, 731, 688 cm^{-1}; Anal. Calcd for $C_{18}H_{20}N_4O_3S$: C, 58.05; H, 5.41; N, 15.04%. Found: C, 57.86; H, 5.42; N, 15.92%.

4-(4-Hydroxybutyl)-6-phenyl-1,2,4-triazolo[1,5-*a*]pyrimidin-7-ones (14a-c). Compound **(13a-c)** (3.00 mmol) was added to a solution, which was prepared from sodium (0.07 g, 3.04 mmol) and MeOH (30 mL). The reaction mixture was refluxed for 0.5 h, cooled, neutralized with acetic acid and concentrated *in vacuo*. The product was isolated by column chromatography using EtOAc as eluent.

14a: 0.511 g; 60%; mp 145 ºC; ^{1}H-NMR (DMSO-d_6) δ 1.47 (m, 2H, C3'H_2), 1.89 (m, 2H, C2'H_2), 3.42 (dt, *J*= 5.5 and 5.6 Hz, 2H, C4'H_2), 4.28 (t, *J*= 7.0 Hz, 2H, C1'H_2), 4.48 (t, *J*= 4.8 Hz, 1H, OH), 7.35 (dd, *J*= 7.4 Hz, 1H, C_p-H), 7.44 (dd, *J*= 7.4 Hz, 2H, C_m-H), 7.66 (dd, *J*= 7.4 Hz, 2H, C_o-H), 8.31 (s, 1H, C2-H), 8.45 (s, 1H, C5-H); ^{13}C-NMR (DMSO-d_6) δ 25.11 (C2'), 29.22 (C3'), 51.47 (C1'), 60.22 (C4'), 111.98 (C6), 127.52 (C*p*), 128.25 (C*m*), 128.62 (C*o*), 133.03 (C*i*), 141.71 (C5), 150.30 (C3a), 152.36 (C2), 155.06 (C7); IR 3466 (OH), 1665 (C=O), 1570, 1394, 1283, 1173, 1156, 1038, 1014, 783, 707, 649 cm^{-1}; Anal. Calcd for $C_{15}H_{16}N_4O_2$: C, 63.37; H, 5.67; N, 19.71%. Found: C, 63.01; H, 5.91; N, 19.50%.

14b: 0.447 g; 50%; mp 157 ºC; ^{1}H-NMR (DMSO-d_6) δ 1.46 (m, 2H, C3'H_2), 1.88 (m, 2H, C2'H_2), 2.40 (s, 3H, CH_3), 3.43 (dt, *J*= 6.3 and 5.4 Hz, 2H, C4'H_2), 4.23 (t, *J*= 7.2 Hz, 2H, C1'H_2), 4.48 (t, *J*= 5.2 Hz, 1H, OH), 7.33 (dd, *J*= 7.2 Hz, 1H, C_p-H), 7.44 (dd, *J*= 7.2 Hz, 2H, C_m-H), 7.66 (dd, *J*= 7.2 Hz, 2H, C_o-H), 8.36 (s, 1H, C5-H); ^{13}C-NMR (DMSO-d_6) δ 14.39 (CH_3), 25.13 (C2'), 29.23 (C3'), 51.40 (C1'), 60.23 (C4'), 111.92 (C6), 127.44 (C*p*), 128.18 (C*m*), 128.55 (C*o*), 133.12 (C*i*), 141.08 (C5), 150.49 (C3a), 154.72 (C7), 161.46 (C2); IR 3466 (OH),1668 (C=O), 1577, 1409, 1325, 1282, 1049, 783, 712, 694 cm^{-1}; Anal. Calcd for $C_{16}H_{18}N_4O_2$: C, 64.41; H, 6.08; N, 18.78%. Found: C, 64.38; H, 5.98; N, 18.86%.

14c: 0.564 g; 57%; mp 184 ºC; ^{1}H-NMR (DMSO-d_6) δ 1.46 (m, 2H, C3'H_2), 1.88 (m, 2H, C2'H_2), 2.63 (s,

3H, CH_3), 3.43 (dt, *J*= 6.0 and 5.5 Hz, 2H, C4'H_2), 4.23 (t, *J*= 6.8 Hz, 2H, C1'H_2), 4.48 (t, *J*= 5.0 Hz, 1H, OH), 7.33 (dd, *J*= 7.4 Hz, 1H, C$_p$-H), 7.44 (dd, *J*= 7.4 Hz, 2H, C$_m$-H), 7.66 (dd, *J*= 7.4 Hz, 2H, C$_o$-H), 8.35 (s, 1H, C5-H); ^{13}C-NMR (DMSO-d_6) δ 13.52 (CH_3), 25.02 (C2'), 29.18 (C3'), 51.41 (C1'), 60.24 (C4'), 112.34 (C6), 127.54 (C*p*), 128.25 (C*m*), 128.55 (C*o*), 132.99 (C*i*), 140.77 (C5), 150.97 (C3a), 154.04 (C7), 163.64 (C2); IR 3474 (OH), 3029, 1663 (C=O), 1573, 1443, 1269, 1248, 1041, 963, 773, 699 cm^{-1}; Anal. Calcd for $C_{16}H_{18}N_4O_2S$: C, 58.16; H, 5.49; N, 16.96%. Found: C, 58.45; H, 5.50; N, 17.00%.

4-(4-Acetoxybut-2-enyl)-6-phenyl-1,2,4-triazolo[1,5-*a*]pyrimidin-7-ones (15a-c). A suspension of 6-phenyl-1,2,4-triazolo[1,5-*a*]pyrimidin-7-one **(3a-c)** (9.40 mmol) in a 17% aqueous Na_2CO_3 solution (5 mL) was stirred at ambient temperature for 0.5 h. The precipitate was filtered off, dried, and dissolved in DMF (10 mL). (*Z*)-4-Bromobut-2-enyl acetate (**12**) (1.77 g, 9.20 mmol) was added to the reaction solution. The reaction mixture was heated at 100 ºC for 2 h and cooled. Then water (200 mL) was added, and the precipitate was filtered off and crystallized from 2-propanol.

15a: 1.553 g; 51%; mp 136 ºC; ^{1}H-NMR (DMSO-d_6) δ 2.04 (s, 3H, CH_3), 4.83 (d, *J*= 6.3 Hz, 2H, C4'H_2), 4.24 (t, *J*= 6.8 Hz, 2H, C1'H_2), 5.79 (dtt, *J*= 11.0 and 6.6 and 1.5 Hz, 1H, C2'H), 5.90 (dtt, *J*= 11.0 and 6.9 and 1.3 Hz, 1H, C3'H), 7.37 (m, 1H, C$_p$-H), 7.44 (m, 2H, C$_m$-H), 7.67 (m, 2H, C$_o$-H), 8.32 (s, 1H, C2-H), 8.41 (s, 1H, C5-H); ^{13}C-NMR (DMSO-d_6) δ 20.69 (CH_3), 48.18 (C1'), 59.88 (C4'), 112.36 (C6), 126.97 (C3'), 127.61 (C*p*), 128.30 (C*m*), 128.58 (C*o*), 128.99 (C2'), 132.98 (C*i*), 141.33 (C5), 150.20 (C3a), 152.37 (C2), 155.06 (C7), 170.34 (C=O); IR 1737 (C=O), 1668 (C=O), 1566, 1218, 1166, 1020, 959, 777, 710, 691 cm^{-1}; Anal. Calcd for $C_{17}H_{16}N_4O_3$: C, 62.95; H, 4.97; N, 17.27%. Found: C, 62.75; H, 4.96; N, 17.15%.

15b: 1.271 g; 40%; mp 147 ºC; ^{1}H-NMR (DMSO-d_6) δ 2.03 (s, 3H, CH_3), 2.40 (s, 3H, CH_3), 4.81 (d, *J*= 6.5 Hz, 2H, C4'H_2), 4.24 (t, *J*= 6.5 Hz, 2H, C1'H_2), 5.78 (dtt, *J*= 11.0 and 6.5 and 1.5 Hz, 1H, C2'H), 5.88 (dtt, *J*= 11.0 and 6.5 and 1.5 Hz, 1H, C3'H), 7.34 (dd, *J*= 7.3 Hz, 1H, C$_p$-H), 7.43 (dd, *J*= 7.3 Hz, 2H, C$_m$-H), 7.65 (d, *J*= 7.3 Hz, 2H, C$_o$-H), 8.33 (s, 1H, C5-H); ^{13}C-NMR (DMSO-d_6) δ 14.37 (CH_3), 20.68 (CH_3), 48.08 (C1'), 59.89 (C4'), 112.29 (C6), 126.99 (C3'), 127.53 (C*p*), 128.56 (C*m*), 128.51 (C*o*), 128.94 (C2'), 133.06 (C*i*), 140.69 (C5), 150.39 (C3a), 154.69 (C7), 161.44 (C2), 170.31 (C=O); IR ; Anal. Calcd for $C_{18}H_{18}N_4O_3$: C, 63.89; H, 5.36; N, 16.56%. Found: C, 63.71; H, 5.44; N, 16.46%.

15c: 1.287 g; 37%; mp 114 ºC; ^{1}H-NMR (DMSO-d_6) δ 2.04 (s, 3H, CH_3), 2.62 (s, 3H, CH_3), 4.81 (d, *J*= 6.2 Hz, 2H, C4'H_2), 4.24 (t, *J*= 6.6 Hz, 2H, C1'H_2), 5.78 (dtt, *J*= 11.0 and 6.4 and 1.3 Hz, 1H, C2'H), 5.88 (dtt, *J*= 11.0 and 6.4 and 1.3 Hz, 1H, C3'H), 7.34 (m, 1H, C$_p$-H), 7.43 (m, 2H, C$_m$-H), 7.65 (m, 2H, C$_o$-H), 8.32 (s, 1H, C5-H); ^{13}C-NMR (DMSO-d_6) δ 13.50 (CH_3), 20.68 (CH_3), 48.12 (C1'), 59.89 (C4'), 112.69 (C6), 126.75 (C3'), 127.61 (C*p*), 128.27 (C*m*), 128.48 (C*o*), 129.09 (C2'), 132.92 (C*i*), 140.38 (C5),

150.78 (C3a), 154.01 (C7), 163.66 (C2), 170.31 (C=O); IR 1730 (C=O), 1689 (C=O), 1578, 1452, 1254, 1228, 1210, 1025, 774, 694 cm^{-1}; Anal. Calcd for $C_{18}H_{18}N_4O_3S$: C, 58.36; H, 4.90; N, 15.12%. Found: C, 58.30; H, 4.79; N, 15.10%.

4-(4-Hydroxybut-2-enyl)-6-phenyl-1,2,4-triazolo[1,5-*a*]pyrimidin-7-ones (16a-c). Acetyl chloride (1 mL) was added dropwise to MeOH (30 mL). Then compound **(15a-c)** (1.5 mmol) was added to the resulting solution. The reaction mixture was kept at ambient temperature for 4 h and neutralized with anhydrous sodium acetate. The solvent was evaporated *in vacuo*. The product (**16a-c**) was isolated from the residue by silica gel column chromatography using the ethyl acetate as the eluent.

16a: 0.127 g; 30%; mp 129 ºC; ^{1}H-NMR (DMSO-d_6) δ 4.22 (ddd, *J*= 6.8 and 6.0 and 1.5 Hz, 2H, C4'H_2), 4.92 (t, *J*= 5.6 Hz, 1H, OH), 4.94 (d, *J*= 6.8 Hz, 2H, C1'H_2), 5.70 (dtt, *J*= 11.0 and 6.9 and 1.5 Hz, 1H, C2'H), 5.80 (dtt, *J*= 11.0 and 6.0 and 1.3 Hz, 1H, C3'H), 7.36 (m, 1H, C_p-H), 7.45 (m, 2H, C_m-H), 7.65 (m, 2H, C_o-H), 8.32 (s, 1H, C2-H), 8.38 (s, 1H, C5-H); ^{13}C-NMR (DMSO-d_6) δ 48.28 (C1'), 57.12 (C4'), 112.32 (C6), 123.01 (C2'), 128.29 (C*p*), 128.32 (C*m*), 128.63 (C*o*), 133.00 (C*i*), 135.69 (C3'), 141.25 (C5), 150.23 (C3a), 152.35 (C2), 155.04 (C7); IR 3367 (OH), 2960, 2922, 2852, 1665 (C=O), 1568, 1258, 1156, 1023, 780, 697, 646 cm^{-1}; Anal. Calcd for $C_{15}H_{14}N_4O_2$: C, 63.82; H, 5.00; N, 19.85%. Found: C, 63.50; H, 5.01; N, 19.55%.

16b: 0.178 g; 40%; mp 146 ºC; ^{1}H-NMR (DMSO-d_6) δ 2.40 (s, 3H, CH_3), 4.21 (dd, *J*= 5.4 Hz, 2H, C4'H_2), 4.90 (m, 3H, C1'H_2, and OH), 5.66 (dtt, *J*= 11.0 and 6.8 and 1.5 Hz, 1H, C2'H), 5.80 (dtt, *J*= 11.0 and 6.0 and 1.3 Hz, 1H, C3'H), 7.35 (m, 1H, C_p-H), 7.45 (m, 2H, C_m-H), 7.65 (m, 2H, C_o-H), 8.30 (s, 1H, C5-H); ^{13}C-NMR (DMSO-d_6) δ 14.39 (CH_3), 48.21 (C1'), 57.11 (C4'), 112.23 (C6), 123.12 (C2'), 127.54 (C*p*), 128.28 (C*m*), 128.56 (C*o*), 133.09 (C*i*), 135.59 (C3'), 140.64 (C5), 150.44 (C3a), 154.70 (C7), 161.44 (C2); IR 3455 (OH), 1662 (C=O), 1575, 1427, 1300, 1266, 1016, 911, 777, 698 cm^{-1}; Anal. Calcd for $C_{16}H_{16}N_4O_2$: C, 64.85; H, 5.44; N, 18.91%. Found: C, 64.45; H, 5.46; N, 18.71%.

16c: 0.157 g; 32%; mp 144 ºC; ^{1}H-NMR (DMSO-d_6) δ 2.69 (s, 3H, CH_3), 4.21 (dd, *J*= 5.5 Hz, 2H, C4'H_2), 4.93 (m, 3H, C1'H_2, and OH), 5.72 (dtt, *J*= 11.0 and 6.8 and 1.5 Hz, 1H, C2'H), 5.86 (dtt, *J*= 11.0 and 6.0 and 1.3 Hz, 1H, C3'H), 7.42 (m, 1H, C_p-H), 7.50 (m, 2H, C_m-H), 7.70 (m, 2H, C_o-H), 8.35 (s, 1H, C5-H); ^{13}C-NMR (DMSO-d_6) δ 13.52 (CH_3), 48.25 (C1'), 57.12 (C4'), 112.65 (C6), 122.90 (C2'), 127.62 (C*p*), 128.53 (C*m*), 128.56 (C*o*), 132.96 (C*i*), 135.75 (C3'), 140.33 (C5), 150.87 (C3a), 154.02 (C7), 163.64 (C2); IR 3413 (OH), 2961, 1686 (C=O), 1275, 1258, 1079, 1048, 696, 625 cm^{-1}; Anal. Calcd for $C_{16}H_{16}N_4O_2S$: C, 58.52; H, 4.91; N, 17.06%. Found: C, 58.45; H, 4.90; N, 17.27%.

X-Ray crystal data of 16a was carried out on an automated Xcalibur 3 CCD diffractometer**.** $C_{15}H_{14}N_4O_2$, M=282.30, monoclinic, P2(1)/c, a = 8.850(3), b = 13.1842(18), c = 11.7078(16) Å, U = 1366.0(6) $Å^3$, Z = 4 $D_{calc.}$=1.373 g/cm^3, μ(Mo-Kα)=0.095 cm^3, 2782 reflections ($2\theta \leq$ 26.38), R_1 (I>2.00σ(I)) 0.0397, wR_2

($I>2.00\sigma(I)$) 0.0906, CCDC reference number – 742061.

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