Synthesis of acyclic nucleosides based on 1,2,4-triazolo[3,2-*c*][1,2,4]triazin-7-ones*

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A new class of acyclic nucleosides based on 6-phenyl-1,2,4-triazolo[3,2-*c*][1,2,4]triazin-7-ones was synthesized and structurally characterized for the first time.

Key words: acyclic nucleosides, antiviral drugs, 1,2,4-triazolo[3,2-*c*][1,2,4]triazin-7-ones, alkylation, deacylation.

Anomalous nucleosides belong to a group of compounds most widely used as antiviral medications. Their activity is manifested in different steps of a pathogenic process, from infection of normal cells to persistence and reproduction of virions. The structures of antiviral anomalous nucleosides should reproduce or mimic the most substantial structural elements of natural nucleosides that provide the resistance of organisms to viral infections.

The design of such nucleosides is generally based on the modification of one of the constituents of natural compounds, *viz.*, the furanose ring or a nucleic base.[1] For example, acyclic nucleosides 9-(2-hydroxyethoxymethyl)-guanine (Acyclovir)[2] or 9-[4-hydroxy-3-(hydroxymethyl)-butyl]guanine (Penciclovir)[3] are considered as structural analogs of guanosine, in which the cyclic ribose residue is replaced by an aliphatic chain bearing oxygen-containing groups. These compounds have found use as antiherpetic drugs, as well as for the inhibition of cytomegaloviruses. Ribavirin (1-β-D-ribofuranosyl-1,2,4-triazole-3-carboxamide), which is a medication used for the treatment of influenza A and B viruses and hepatitis B and C viruses,[1,4] can be cited as an example of the design of antiviral drugs by modifying a heterocyclic base. The usefulness of the concept of structural analogies in the search for new antiviral medications was demonstrated by the synthesis of anomalous nucleosides modified at both the heterocyclic moiety and the carbohydrate residue. Thus tricyclic analogs of Acyclovir (3-[(2-hydroxyethoxy)methyl]-9-oxoimidazo[1,2-*a*]purine derivatives) showing significant antiherpetic activity were synthesized;[5,6] Acyclovir and Ganciclovir analogs containing the substituted pyrimidine moiety are active against HIV[7,8] and hepatitis B viruses.[9,10] Various acyclic nucleosides based on 2,3-dihydrofuro[2,3-*d*]pyrimidin-2-ones proved to be efficient against the Herpes simplex virus and the human immunodeficiency virus.[11]

In the present study, we performed the synthesis of anomalous nucleosides based on 2-R-6-phenyl-1,2,4-triazolo[3,2-*c*][1,2,4]triazin-7-ones (**1a—c**) containing acyclic fragments with the terminal hydroxy group at the N(4) atom. Hence, we synthesized nucleosides, which are anomalous in both the aglycone and glycoside moieties. The choice of 1,2,4-triazolo[3,2-*c*][1,2,4]triazin-7-ones (**1a—c**) as bases was determined, on the one hand, by the structural similarity with purines and, on the other hand, by the fact that representatives of this class of compounds exhibited antiviral activity.[12,13]

The fusion of heterocycles **1a—c** with an excess of (2-acetoxyethoxy)methyl acetate (**2**) at 150 °C in the presence of $ZnCl_2$ regioselectively affords 4-(2-acetoxyethoxy)methyl-6-phenyl-1,2,4-triazolo[3,2-*c*][1,2,4]-triazin-7-ones **3a—c**. The deacetylation of compounds **3a—c** gives derivatives **4a—c** containing the *N*-(2-hydroxyethoxy)methyl fragment present in the antiviral medication Acyclovir. The yields of compounds **4a—c** were 30—46% (Scheme 1).

* Dedicated to Professor A. F. Pozharskii on the occasion of his 70th birthday.

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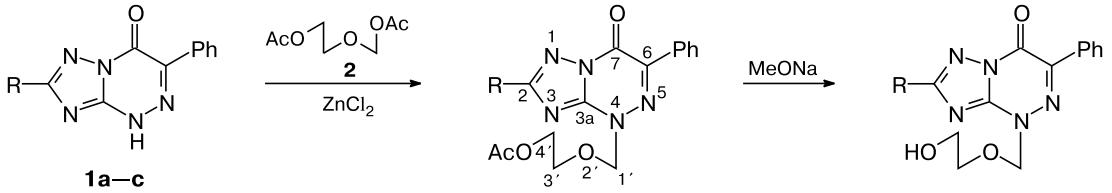
Scheme 1



1a—c **3a—c** **4a—c**

1, 3, 4: R = H (**a**), Me (**b**), SMe (**c**)

We used the ability of 1,2,4-triazolo[3,2-*c*][1,2,4]-triazin-7-ones (**1a—c**) to react with iodo- and bromoalkanes under basic conditions[14,15] to synthesize *N*(4)-hydroxyalkyl derivatives of nucleosides. We alkylated heterocyclic compounds **1a—c** with 4-bromobutyl acetate (**5**) and 4-bromobut-2-enyl acetate (**6**) in DMF in the presence of sodium carbonate (Scheme 2).

It is known that acyclic nucleosides synthesized with the use of compound **5** are structural analogs of Acyclovir.[16] Purine derivatives with the 4-hydroxybutenyl substituent show significant antiherpetic activity in cell cultures.[17] Acyclic nucleosides based on adenine and 3-deazaadenine containing the (*Z*)-4-hydroxybutenyl group in the alkyl moiety are analogs of Neplanocin A and were described as potential inhibitors of S-adenosylhomocysteine hydrolase.[18,19]

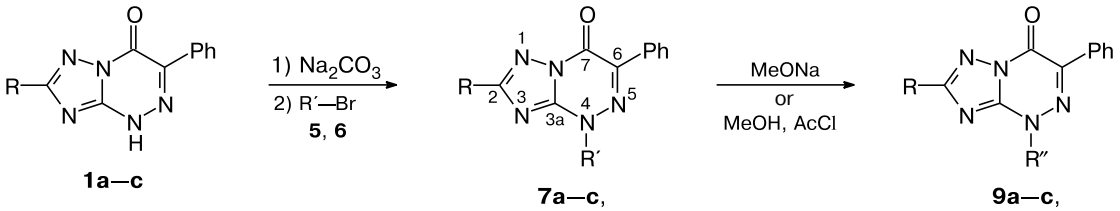
The deacylation of compounds **7a—c** with sodium methoxide afforded nucleosides **9a—c** in 62—74% yields. Hydroxy derivatives **10a—c** were prepared from compounds **8a—c** by acid-catalyzed methanolysis.

The alkylation of heterocyclic compounds **1a—c** with chloroethyl acetate (**11**) was carried out in the presence of cesium carbonate in DMF; compounds **12a—c** were obtained in 29—38% yields (Scheme 3). In the presence of potassium or sodium carbonate, no alkylation of heterocyclic compounds **1a—c** with chloroethyl acetate **11** took place.

It should be noted that this is the first example of alkylation of 1,2,4-triazolo[3,2-*c*][1,2,4]triazin-7-ones with chloro derivatives.

The treatment of acyl derivatives **12a—c** with sodium methoxide afforded *N*-hydroxyethyltriazolotriazines **13a—c**.

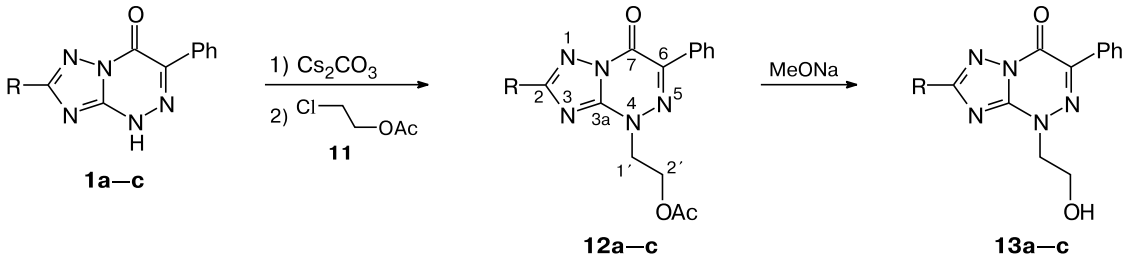
Scheme 2



1a—c **7a—c**, **8a—c** **9a—c**, **10a—c**

1, 7—10: R = H (**a**), Me (**b**), SMe (**c**)
5, 7: R′ = $C(1')H_2—C(2')H_2—C(3')H_2—C(4')H_2—OAc$
6, 8: R′ = $C(1')H_2—C(2')H=C(3')H—C(4')H_2—OAc$
9: R″ = $CH_2—CH_2—CH_2—CH_2—OH$
10: R″ = $CH_2—CH=CH—CH_2—OH$

Scheme 3



1a—c **12a—c** **13a—c**

1, 12, 13: R = H (**a**), Me (**b**), SMe (**c**)

In the IR spectra of compounds **3a—c**, **7a—c**, **8a—c**, and **12a—c**, two strong absorption bands at 1688—1745 cm^{-1} are assigned to stretching vibrations of the carbonyl group of the heterocycle and the acetyl group. In the spectra of compounds **4a—c**, **9a—c**, **10a—c**, and **13a—c**, the presence of the only band of the carbonyl group at 1680—1715 cm^{-1} and the appearance of the OH absorption band at 3320—3530 cm^{-1} confirm the removal of the *O*-acetyl group.

The ^1H NMR spectra of compounds **3a—c**, **4a—c**, **7a—c**, **8a—c**, **9a—c**, **10a—c**, **12a—c**, and **13a—c** show signals for the corresponding alkyl and heterocyclic moieties. The appearance of a signal for the hydroxy group in the ^1H NMR spectra of compounds **4a—c**, **9a—c**, **10a—c**, and **13a—c**, which was assigned based on NMR experiments following deuterium exchange with CF_3COOD, also confirmed the removal of the acetyl group. The coupling constant (11 Hz) between the protons of the —CH=CH— fragment corresponds to the *cis* configuration[20] of the butenyl substituent in compounds **8a—c** and **10a—c**.

The determination of the positions of the *N*-alkyl substituents and the assignment of the signals in the ^1H and ^{13}C NMR spectra of nucleosides were performed by 2D NMR correlation experiments (2D COSY, HSQC, and HMBC). The positions of the alkyl moieties in compounds **7a,c** and **12a** were determined by the analysis of the fine structure of the signal for the bridgehead atom C(3a) in the coupled $^{13}C—^1H$ NMR spectra. Thus the ^{13}C NMR spectra of compounds **7a** and **12a** contain signals for C(3a) at δ 151.13 and 151.32, respectively, as doublets of triplets. The presence of the methylthio group in the 1,2,4-triazole ring of compound **7c** results in a reduction in the multiplicity of the signal for the atom C(3a) at δ 151.71 to a triplet. The presence of the triplet components in the signals for the atoms C(3a) in the coupled $^{13}C—^1H$ NMR spectra of compounds **7a,c** and **12a** confirms the introduction of the alkyl moieties into the triazine ring.

In all cases, the alkylation of 6-phenyl-1,2,4-triazolo-[3,2-*c*][1,2,4]triazin-7-ones (**1a—c**) proceeds at the N(4) atom of the triazine ring. This conclusion is confirmed by the X-ray diffraction data for 4-(4-hydroxybutyl)-2-methyl-6-phenyl-1,2,4-triazolo[3,2-*c*][1,2,4]triazin-7-one (**9b**) and 4-(4-hydroxybut-2-enyl)-6-phenyl-1,2,4-triazolo[3,2-*c*][1,2,4]triazin-7-one (**10a**) (Figs 1 and 2, respectively; Tables 1 and 2). In the crystals of compounds **9b** and **10a**, the triazole and triazine rings form a virtually planar bicyclic system, which is not conjugated with the phenyl substituent. In heterocyclic compounds **9b** and **10a**, the dihedral angles between the planes of the triazine and benzene rings are 37.4° and 31.9°, respectively. The geometric parameters of triazolo[3,2-*c*][1,2,4]-triazines **9b** and **10a** have standard values.[15,21] In addition, the X-ray diffraction data for compound **10a** unambiguously confirm the *cis* configuration of the *N*-alkyl moiety.

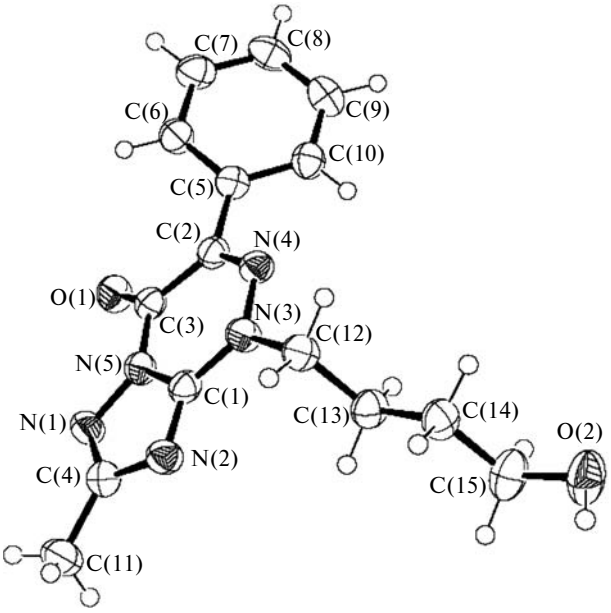


Fig. 1. Molecular structure of compound **9b**.

Table 1. Selected bond lengths (*d*) and bond angles (ω) in molecule **9b**

Bond	*d*/Å	Angle	ω/deg
O(1)—C(3)	1.207(2)	C(2)—N(4)—N(3)	120.2(1)
N(4)—C(2)	1.305(2)	C(1)—N(5)—N(1)	108.7(1)
N(4)—N(3)	1.358(2)	C(1)—N(5)—C(3)	125.0(1)
N(5)—C(1)	1.358(2)	N(1)—N(5)—C(3)	126.2(11)
N(5)—N(1)	1.380(2)	C(1)—N(3)—N(4)	120.8(1)
N(5)—C(3)	1.397(2)	C(1)—N(3)—C(12)	122.0(1)
N(3)—C(1)	1.352(2)	N(4)—N(3)—C(12)	117.0(1)
N(3)—C(12)	1.468(2)	C(1)—N(2)—C(4)	101.9(1)
N(2)—C(1)	1.312(2)	N(2)—C(1)—N(3)	129.0(1)
N(2)—C(4)	1.377(2)	N(2)—C(1)—N(5)	111.6(1)
C(2)—C(5)	1.477(2)	N(3)—C(1)—N(5)	119.4(1)
C(2)—C(3)	1.487(2)	N(4)—C(2)—C(5)	115.6(1)
O(2)—C(15)	1.418(2)	N(4)—C(2)—C(3)	124.2(1)
C(5)—C(6)	1.389(2)	C(5)—C(2)—C(3)	120.3(1)
C(5)—C(10)	1.395(2)	O(1)—C(3)—N(5)	122.7(1)
C(12)—C(13)	1.510(2)	O(1)—C(3)—C(2)	127.0(1)
N(1)—C(4)	1.321(2)	N(5)—C(3)—C(2)	110.3(1)
C(14)—C(15)	1.507(2)	C(6)—C(5)—C(2)	121.6(1)
C(14)—C(13)	1.522(2)	C(10)—C(5)—(C2)	119.9(1)
		N(3)—C(12)—C(13)	112.4(1)
		C(4)—N(1)—N(5)	101.9(1)
		C(15)—C(14)—C(13)	111.5(1)
		C(12)—C(13)—C(14)	112.5(1)
		N(1)—C(4)—N(2)	115.9(1)
		N(1)—C(4)—C(11)	123.1(1)
		N(2)—C(4)—C(11)	121.0(1)
		O(2)—C(15)—C(14)	113.8(2)

To summarize, we synthesized a new class of acyclic nucleosides based on 2-substituted 6-phenyl-1,2,4-triazolo[3,2-*c*][1,2,4]triazin-7-ones.

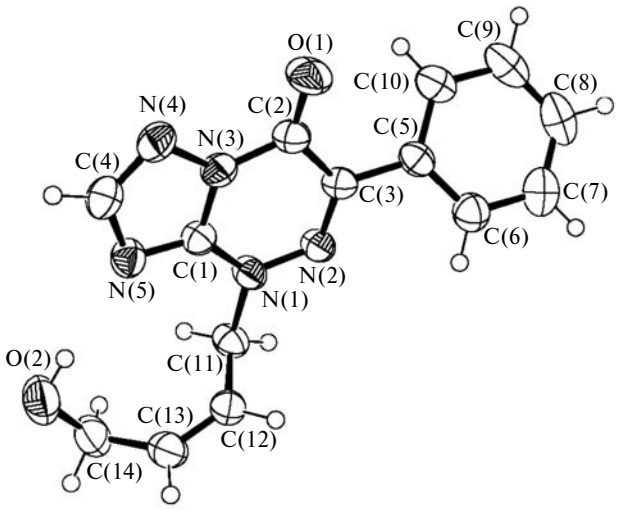


Fig. 2. Molecular structure of compound **10a**.

Table 2. Selected bond lengths (*d*) and bond angles (ω) in molecule **10a**

Bond	*d*/Å	Angle	ω/deg
O(1)—C(2)	1.211(1)	C(1)—N(3)—N(4)	109.15(10)
N(3)—C(1)	1.363(1)	C(1)—N(3)—C(2)	124.91(10)
N(3)—N(4)	1.379(1)	N(4)—N(3)—C(2)	125.79(9)
N(3)—C(2)	1.394(2)	C(1)—N(5)—C(4)	101.27(10)
N(5)—C(1)	1.315(2)	C(3)—N(2)—N(1)	120.67(10)
N(5)—C(4)	1.370(2)	N(2)—N(1)—C(1)	121.12(9)
N(2)—C(3)	1.308(1)	N(2)—N(1)—C(11)	117.57(9)
N(2)—N(1)	1.342(1)	C(1)—N(1)—C(11)	121.30(10)
N(1)—C(1)	1.3503(2)	N(5)—C(1)—N(1)	130.01(11)
C(11)—C(12)	1.490(2)	N(5)—C(1)—N(3)	111.19(10)
N(4)—C(4)	1.312(2)	N(1)—C(1)—N(3)	118.80(11)
C(12)—C(13)	1.315(2)	N(2)—C(3)—C(2)	123.73(11)
C(13)—C(14)	1.493(2)	N(2)—C(3)—C(5)	116.14(10)
C(5)—C(6)	1.392(2)	C(2)—C(3)—C(5)	120.11(10)
C(5)—C(10)	1.394(2)	O(1)—C(2)—N(3)	121.84(11)
C(10)—C(9)	1.389(2)	O(1)—C(2)—C(3)	127.44(12)
C(9)—C(8)	1.375(2)	N(3)—C(2)—C(3)	110.68(9)
C(14)—O(2)	1.422(18)	N(1)—C(11)—C(12)	110.74(10)
C(6)—C(7)	1.378(2)	C(4)—N(4)—N(3)	101.02(10)
C(8)—C(7)	1.373(2)	N(4)—C(4)—N(5)	117.36(11)
		C(13)—C(12)—C(11)	125.57(13)
		C(6)—C(5)—C(3)	119.75(11)
		C(10)—C(5)—C(3)	121.69(12)
		O(2)—C(14)—C(13)	111.33(12)

Experimental

The ^{1}H NMR spectra were recorded on Bruker WM-250 and Bruker DRX-400 instruments in DMSO-d_6 with Me_4Si as the internal standard. The 2D NMR correlation experiments were performed and the ^{13}C NMR spectra (100 MHz) were recorded on a Bruker DRX-400 spectrometer in DMSO-d_6.

The IR spectra were measured on a Perkin Elmer Spectrum One B Fourier-transform infrared spectrometer equipped with a diffuse reflection attachment.

Column chromatography was performed on silica gel Alfa Aesar (Avocado Research Chemical Ltd, Silica gel 60, 0.035—0.070 vv (220—440 mesh)).

X-ray diffraction study of compounds 9b and 10a was carried out on an automated Xcalibur 3 diffractometer equipped with a CCD detector (ω/2θ-scanning technique, Mo-K_α radiation, graphite monochromator) according to a standard procedure.

Both structures were solved by direct methods and refined by the least-squares method using the SHELXS-97[22] and SHELXL-97[23] program packages with anisotropic displacement parameters (isotropic displacement parameters for H atoms). Absorption corrections were not applied because of the low absorption coefficients.

The geometric characteristics of compounds **9b** and **10a** are listed in Tables 1 and 2, respectively. The X-ray data collection and refinement statistics are given in Table 3.

6-Phenyl-2-R-1,2,4-triazolo[3,2-*c*][1,2,4]triazin-7-ones (1a—c) were synthesized according to a procedure described earlier.[24]

(2-Acetoxyethoxy)methyl acetate (2) was synthesized according to a procedure described earlier.[25]

4-(2-Acetoxyethoxymethyl)-6-phenyl-2-R-1,2,4-triazolo-[3,2-*c*][1,2,4]triazin-7-ones (3a—c). Catalytic amounts of anhydrous $ZnCl_2$ were added to mixtures of (2-acetoxyethoxy)-methyl acetate (**2**) (1.23 g, 7.04 mmol) and 6-phenyl-2-R-1,2,4-triazolo[3,2-*c*][1,2,4]triazin-7-one (**1a—c**) (2.30 mmol). The reaction mixtures were kept at 150 °C for 0.5 h and the reaction products were isolated by silica gel column chromatography using the ethyl acetate—hexane system (2 : 1) as the eluent.

4-(2-Acetoxyethoxymethyl)-6-phenyl-1,2,4-triazolo[3,2-*c*]-[1,2,4]triazin-7-one (3a, R = H). The yield was 61%, m.p. 94 °C. ^{1}H NMR (400 MHz), δ: 1.97 (s, 3 H, OAc); 3.91 (m, 2 H, H(3′)); 4.14 (m, 2 H, H(4′)); 5.78 (s, 2 H, H(1′)); 7.51—7.55 (m, 3 H, H_m, H_p); 8.00 (m, 2 H, H_o); 8.46 (s, 1 H, H(2)). ^{13}C NMR (100 MHz), δ: 20.57 (CO—$\underline{C}H_3$); 62.78 (C(4′)); 67.63 (C(3′)); 82.58 (C(1′)); 128.23 (C_m); 128.65 (C_o); 129.84 (C_p); 131.96 (C_{ipso}); 139.82 (C(6)); 149.17 (C(7)); 151.35 (C(3a)); 153.20 (C(2)); 170.25 ($\underline{C}O$—CH_3). Found (%): C, 54.78; H, 4.51; N, 21.36. $C_{15}H_{15}N_5O_4$. Calculated (%): C, 54.71; H, 4.56; N, 21.27. IR, ν/cm^{-1}: 1740, 1710 (C=O).

4-(2-Acetoxyethoxymethyl)-2-methyl-6-phenyl-1,2,4-tri-azolo[3,2-*c*][1,2,4]triazin-7-one (3b, R = Me). The yield was 65%, m.p. 82 °C. ^{1}H NMR (400 MHz), δ: 1.97 (s, 3 H, OAc); 2.46 (s, 3 H, C(2)—Me); 3.89 (m, 2 H, H(3′)); 4.13 (m, 2 H, H(4′)); 5.73 (s, 2 H, H(1′)); 7.50—7.54 (m, 3 H, H_m, H_p); 7.99 (m, 2 H, H_o). ^{13}C NMR (100 MHz), δ: 14.27 (C(2)—$\underline{Me}$); 20.57 (CO—$\underline{C}H_3$); 62.80 (C(4′)); 67.56 (C(3′)); 82.53 (C(1′)); 128.21 (C_m); 128.62 (C_o); 129.80 (C_p); 132.04 (C_{ipso}); 139.78 (C(6)); 148.68 (C(7)); 151.53 (C(3a)); 162.71 (C(2)); 170.27 ($\underline{C}O$—CH_3). Found (%): C, 55.94; H, 4.88; N, 20.64. $C_{16}H_{17}N_5O_4$. Calculated (%): C, 55.98; H, 4.96; N, 20.41. IR, ν/cm^{-1}: 1735, 1715 (C=O).

4-(2-Acetoxyethoxymethyl)-2-methylthio-6-phenyl-1,2,4-tri-azolo[3,2-*c*][1,2,4]triazin-7-one (3c, R = SMe). The yield was 50%, m.p. 123 °C. ^{1}H NMR (400 MHz), δ: 1.98 (s, 3 H, OAc); 2.67 (s, 3 H, SMe); 3.89 (m, 2 H, H(3′)); 4.14 (m, 2 H, H(4′)), 5.70 (s, 2 H, H(1′)); 7.51—7.54 (m, 3 H, H_m, H_p); 7.99 (m, 2 H, H_o). ^{13}C NMR (100 MHz), δ: 13.51 (SMe); 20.57 (CO—$\underline{C}H_3$); 62.76 (C(4′)); 67.58 (C(3′)); 82.52 (C(1′)); 128.23 (C_m); 128.61 (C_o); 129.90 (C_p); 131.93 (C_{ipso}); 140.23 (C(6)); 147.85 (C(7)); 151.89 (C(3a)); 165.50 (C(2)); 170.22 ($\underline{C}O$—CH_3). Found (%):

Table 3. Crystallographic data and the X-ray data collection and refinement statistics

Parameter	**9b**	**10a**
Molecular formula	$C_{15}H_{17}N_5O_2$	$C_{14}H_{13}N_5O_2$
Molecular weight	299.34	283.29
T/K	295(2)	295(2)
Crystal system	Triclinic	Monoclinic
Space group	$P\bar{1}$	$P2(1)/n$
a/Å	8.6817(10)	7.8396(6)
b/Å	9.0154(12)	6.7342(5)
c/Å	10.2608(16)	25.3722(12)
α/deg	115.948(12)	90.00
β/deg	91.466(14)	90.313(5)
γ/deg	99.687(10)	90.00
Z	2	4
λ/Å	0.71073	0.71073
V/Å^3	707.37(17)	1339.47(16)
Ranges of *hkl* indices	$-10 \le h \le 10$	$-10 \le h \le 9$
	$-11 \le k \le 11$	$-8 \le k \le 8$
	$-12 \le l \le 12$	$-33 \le l \le 33$
d_{calc}/g cm^{-3}	1.405	1.405
μ/mm^{-1}	0.098	0.099
θ-Scan range/deg	3.08—26.37	2.72—28.31
Number of measured/independent reflections	9159/2861	13115/3306
Number of reflections with $I > 2\sigma(I)$	1914	2229
R_1 ($I > 2\sigma(I)$)	0.0356	0.0400
wR_2 (based on all reflections)	0.0908	0.1171
Number of refined parameters	267	211
GOOF	1.000	1.000
Residual electron density/Å^{-3} (min/max)	−0.185/0.169	−0.186/0.215

C, 51.18; H, 4.46; N, 18.18. $C_{16}H_{17}N_5O_4S$. Calculated (%): C, 51.20; H, 4.53; N, 18.66. IR, ν/cm^{-1}: 1715, 1736 (C=O).

4-(2-Hydroxyethoxymethyl)-6-phenyl-2-R-1,2,4-triazolo-[3,2-*c*][1,2,4]triazin-7-ones (4a—c). The corresponding 4-(2-acetoxyethoxymethyl)-6-phenyl-2-R-1,2,4-triazolo-[3,2-*c*][1,2,4]triazin-7-one (**3a—c**) (3.00 mmol) was added to a solution of MeONa, which was prepared from sodium metal (0.07 g, 3.04 mmol), in anhydrous MeOH (20 mL). The reaction mixture was refluxed for 1 h, cooled, and neutralized with acetic acid. The solvent was evaporated *in vacuo*. The reaction product was isolated by silica gel column chromatography using the ethyl acetate—hexane system (7 : 1) as the eluent.

Compound 4a (R = H). The yield was 46%, m.p. 88 °C. ^{1}H NMR (250 MHz), δ: 3.52 (q, 2 H, H(4′), J = 5.2 Hz); 3.76 (t, 2 H, H(3′), J = 5.2 Hz); 4.42 (t, 1 H, OH, J = 5.2 Hz); 5.77 (s, 2 H, (H1′)); 7.47—7.50 (m, 3 H, H_m, H_p); 8.04 (m, 2 H, H_o), 8.28 (s, 1 H, H(2)). Found (%): C, 54.35; H, 4.44; N, 24.54. $C_{13}H_{13}N_5O_3$. Calculated (%): C, 54.35; H, 4.53; N, 24.39. IR, ν/cm^{-1}: 1695 (CO), 3501 (OH).

Compound 4b (R = Me). The yield was 37%, m.p. 125 °C. ^{1}H NMR (250 MHz), δ: 2.48 (s, 3 H, C(2)—Me); 3.52 (q, 2 H, H(4′), J = 5.1 Hz); 3.74 (t, 2 H, H(3′), J = 5.1 Hz); 4.42 (t, 1 H, OH, J = 5.1 Hz); 5.72 (s, 2 H, H(1′)); 7.44—7.49 (m, 3 H, H_m, H_p); 8.03 (m, 2 H, H_o). Found (%): C, 55.80; H, 4.86; N, 23.21. $C_{14}H_{15}N_5O_3$. Calculated (%): C, 55.81; H, 4.98; N, 23.26. IR, ν/cm^{-1}: 1692 (CO), 3490 (OH).

Compound 4c (R = SMe). The yield was 30%, m.p. 142 °C. ^{1}H NMR (250 MHz), δ: 2.68 (s, 3 H, SMe), 3.53 (q, 2 H, H(4′), J = 5.2 Hz); 3.75 (t, 2 H, H(3′), J = 5.2 Hz); 4.41 (t, 1H, OH, J = 5.2 Hz); 5.70 (s, 2 H, H(1′)); 7.44—7.50 (m, 3 H, H_m, H_p); 8.03 (m, 2 H, H_o). Found (%): C, 50.43; H, 4.34; N, 20.96. $C_{14}H_{15}N_5O_3S$. Calculated (%): C, 50.45; H, 4.51; N, 21.02. IR, ν/cm^{-1}: 1690 (CO), 3475 (OH).

4-Bromobutyl acetate (5)[26] and **(Z)-4-bromobut-2-enyl acetate (6)**[27] were synthesized according to procedures described earlier.

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

Compound 7a (R = H). The yield was 40%, m.p. 74 °C. ^{1}H NMR (400 MHz), δ: 1.71 (m, 2 H, H(3′)); 1.98 (m, 2 H, H(2′)), 1.99 (s, 3 H, OAc); 4.05 (t, 2 H, H(4′) J = 6.5 Hz); 4.44 (t, 2 H, H(1′), J = 6.9 Hz); 7.47—7.54 (m, 3 H, H_m, H_p); 8.02 (m, 2 H, H_o); 8.44 (s, 1 H, H(2)). Coupled ^{1}H—^{13}C NMR (100 MHz), δ: 20.63 (q, CO—$\underline{C}H_3$, ^1J = 129.2 Hz), 24.20 (tm, C(2′), ^1J = 128.2 Hz); 24.93 (tm, C(3′), ^1J = 127.0 Hz); 53.50 (tt, C(1′), ^1J = 142.7 Hz, ^2J = 4.1 Hz); 63.23 (tt, C(4′), ^1J = 147.1 Hz, ^2J = 4.1 Hz); 128.16 (dm, C_m, ^1J = 160.6 Hz); 128.43 (dm, C_o, ^1J = 162.4 Hz); 129.54 (dt, C_p, J = 161.3 and 7.4 Hz); 132.33 (t, C_{ipso}, J = 7.2 Hz); 138.84 (t, C(6), ^3J = 3.7 Hz); 149.12 (s,

C(7)); 151.13 (dt, C(3a), ^3J = 9.3 and 2.7 Hz); 153.24 (d, C(2), ^1J = 210.8 Hz); 170.30 (qt, CO—CH_3, ^2J = 6.6 Hz, ^3J = 3.3 Hz). Found (%): C, 58.08; H, 5.12; N, 21.36. $C_{16}H_{17}N_5O_3$. Calculated (%): C, 58.71; H, 5.20; N, 21.41. IR, ν/cm^{-1}: 1729, 1704 (C=O).

Compound 7b (R = Me). The yield was 50%, m.p. 78 °C. ^{1}H NMR (400 MHz), δ: 1.70 (m, 2 H, H(3′)); 1.96 (m, 2 H, H(2′)); 1.99 (s, 3 H, OAc); 2.45 (s, 3 H, C(2)—Me); 4.05 (t, 2 H, H(4′), J = 6.5 Hz); 4.40 (t, 2 H, H(1′), J = 6.9 Hz); 7.47—7.53 (m, 3 H, H_m, H_p); 8.01 (m, 2 H, H_o). ^{13}C NMR (100 MHz), δ: 14.30 (C(2)—Me); 20.66 (CO—CH_3); 24.20 (C(2′); 24.94 (C(3′)); 53.44 (C(1′)); 63.27 (C(4′)); 128.16 (C_m); 128.41 (C_o); 129.51 (C_p); 132.42 (C_{ipso}); 138.82 (C(6)); 148.65 (C(7)); 151.35 (C(3a)); 162.73 (C(2)); 170.33 (CO—CH_3). Found (%): C, 59.88; H, 5.63; N, 20.65. $C_{17}H_{19}N_5O_3$. Calculated (%): C, 59.82; H, 5.57; N, 20.53. IR, ν/cm^{-1}: 1733, 1702 (C=O).

Compound 7c (R = SMe). The yield was 75%, m.p. 110 °C. ^{1}H NMR (400 MHz), δ: 1.70 (m, 2 H, H(3′)); 1.95 (m, 2 H, H(2′)); 1.99 (s, 3 H, OAc); 2.66 (s, 3 H, SMe), 4.05 (t, 2 H, H(4′), J = 6.4 Hz); 4.37 (t, 2 H, H(1′), J = 7.0 Hz); 7.47—7.54 (m, 3 H, H_m, H_p); 8.01 (m, 2 H, H_o). ^{1}H—^{13}C NMR (100 MHz), δ: 13.49 (q, SMe, ^1J = 142.5 Hz), 20.66 (q, CO—CH_3, ^1J = 129.2 Hz); 24.11 (tm, C(2′), ^1J = 127.8 Hz); 24.89 (tm, C(3′), ^1J = 126.8 Hz); 53.40 (tt, C(1′), ^1J = 142.8 Hz, J = 4.0 Hz), 63.26 (tt, C(4′), ^1J = 147.1 Hz, J = 4.1 Hz), 128.19 (dm, C_m, ^1J = 161.5 Hz); 128.42 (ddd, C_o, J = 161.9, 7.4, and 5.7 Hz); 129.64 (dt, C_p, J = 161.8 and 7.4 Hz); 132.30 (m, C_{ipso}); 139.34 (t, C(6), ^3J = 3.8 Hz); 147.84 (s, C(7)); 151.71 (t, C(3a), ^3J = 2.8 Hz); 165.48 (q, C(2), ^3J = 4.8 Hz); 170.33 (qt, CO—CH_3, J = 6.6 and 3.4 Hz). Found (%): C, 54.62; H, 4.76; N, 18.90. $C_{17}H_{19}N_5O_3S$. Calculated (%): C, 54.69; H, 5.09; N, 18.77. IR, ν/cm^{-1}: 1700, 1688 (C=O).

4-(4-Acetoxybut-2-enyl)-2-R-6-phenyl-1,2,4-triazolo-[3,2-*c*][1,2,4]triazin-7-ones (8a—c). A suspension of 6-phenyl-2-R-1,2,4-triazolo[3,2-*c*][1,2,4]triazin-7-one (**1a—c**) (9.40 mmol) in a 17% aqueous Na_2CO_3 solution (6 mL) was stirred at room temperature for 0.5 h. The precipitate was filtered off, dried, and dissolved in DMF (10 mL). (*Z*)-4-Bromobut-2-enyl acetate (**6**) (1.77 g, 9.20 mmol) was added to the reaction solution. The reaction mixture was heated at 100 °C for 2 h and cooled. Then water (200 mL) was added, and the precipitate was filtered off and crystallized from isopropyl alcohol.

Compound 8a (R = H). The yield was 30%, m.p. 83 °C. ^{1}H NMR (400 MHz), δ: 2.04 (s, 3 H, OAc); 4.82 (dd, 2 H, H(4′), ^3J = 6.5 Hz, ^4J = 1.3 Hz); 5.16 (dd, 2 H, H(1′), ^3J = 6.5 Hz, ^4J = 1.2 Hz); 5.85 (dtt, 1 H, H(2′), ^3J = 11.0 Hz, ^3J = 6.5 Hz, ^4J = 1.3 Hz); 5.94 (dtt, 1 H, H(3′), ^3J = 11.0 Hz, ^3J = 6.5 Hz, ^4J = 1.2 Hz); 7.49—7.54 (m, 3 H, H_m, H_p); 8.01 (m, 2 H, H_o); 8.45 (s, 1 H, H(2)). ^{13}C NMR (100 MHz), δ: 20.63 (CO—CH_3), 50.88 (C(1′)), 59.80 (C(4′)), 126.42 (C(2′)), 128.21 (C_m), 128.45 (C_o), 129.10 (C(3′)), 129.66 (C_p), 132.22 (C_{ipso}), 139.15 (C(6)), 149.12 (C(7)), 150.94 (C(3a)), 153.29 (C(2)), 170.19 (CO—CH_3). Found (%): C, 59.09; H, 4.45; N, 21.65. $C_{16}H_{15}N_5O_3$. Calculated (%): C, 59.08; H, 4.62; N, 21.54. IR, ν/cm^{-1}: 1713, 1745 (C=O).

Compound 8b (R = Me). The yield was 60%, m.p. 70 °C. ^{1}H NMR (400 MHz), δ: 2.04 (s, 3 H, OAc); 2.45 (s, 3 H, C(2)—Me); 4.81 (dd, 2 H, H(4′), ^3J = 6.5 Hz, ^4J = 1.3 Hz); 5.11 (dd, 2 H, H(1′), ^3J = 6.6 Hz, ^4J = 1.3 Hz); 5.84 (dtt, 1 H, H(2′), ^3J = 11.0 Hz, ^3J = 6.6 Hz, ^4J = 1.3 Hz); 5.93 (dtt, 1 H, H(3′), ^3J = 11.0 Hz, ^3J = 6.5 Hz, ^4J = 1.3 Hz); 7.48—7.51 (m, 3 H, H_m, H_p); 8.00 (m, 2 H, H_o). ^{13}C NMR (100 MHz), δ: 14.30 (C(2)—Me); 20.62 (CO—CH_3); 50.79 (C(1′)), 59.81 (C(4′)), 126.47 (C(2′)), 128.17 (C_m), 128.40 (C_o), 129.03 (C(3′)), 129.60 (C_p), 132.29 (C_{ipso}), 139.10 (C(6)), 148.60 (C(7)), 151.15 (C(3a)), 162.78 (C(2)), 170.17 (CO—CH_3). Found (%): C, 60.08; H, 5.03; N, 20.84. $C_{17}H_{17}N_5O_3$. Calculated (%): C, 60.18; H, 5.01; N, 20.65. IR, ν/cm^{-1}: 1714, 1740 (C=O).

Compound 8c (R = SMe). The yield was 67%, m.p. 104 °C. ^{1}H NMR (400 MHz), δ: 2.04 (s, 3H, OAc); 2.66 (s, 3 H, SMe); 4.81 (dd, 2 H, H(4′), ^3J = 6.5 Hz, ^4J = 1.3 Hz); 5.08 (dd, 2 H, H(1′), ^3J = 6.5 Hz, ^4J = 1.1 Hz); 5.81 (dtt, 1 H, H(2′), ^3J = 11.0 Hz, ^3J = 6.5 Hz, ^4J = 1. Hz1); 5.92 (dtt, 1 H, H(3′), ^3J = 11.0 Hz, ^3J = 6.5 Hz, ^4J = 1.3 Hz); 7.48—7.52 (m, 3 H, H_m, H_p); 8.00 (m, 2 H, H_o). ^{13}C NMR (100 MHz), δ: 13.50 (SMe); 20.62 (CO—CH_3); 50.79 (C(1′)); 59.81 (C(4′)); 126.25 (C(2′)); 128.20 (C_m); 128.40 (C_o); 129.16 (C(3′)); 129.72 (C_p); 132.16 (C_{ipso}); 139.60 (C(6)); 147.79 (C(7)); 151.45 (C(3a)); 165.55 (C(2)); 170.16 (CO—CH_3). Found (%): C, 54.89; H, 4.49; N, 18.88. $C_{17}H_{17}N_5O_3S$. Calculated (%): C, 54.98; H, 4.58; N, 18.87. IR, ν/cm^{-1}: 1728, 1692 (C=O).

4-(4-Hydroxybutyl)-2-R-6-phenyl-1,2,4-triazolo[3,2-*c*]-[1,2,4]triazin-7-ones (9a—c). 4-(4-Acetoxybutyl)-1,2,4-triazolo-[3,2-*c*][1,2,4]triazin-7-one (**7a—c**) (3.00 mmol) was added to a solution of MeONa, which was prepared from sodium metal (0.07 g, 3.04 mmol)) in anhydrous MeOH (20 mL). The reaction mixture was refluxed for 1 h, cooled, and neutralized with acetic acid. The solvent was evaporated *in vacuo*. Reaction products **9a—c** were isolated from the residue by silica gel column chromatography using the ethyl acetate—hexane system (2 : 1) as the eluent.

Compound 9a (R = H). The yield was 74%, m.p. 87 °C. ^{1}H NMR (250 MHz), δ: 1.56 (m, 2 H, H(3′)); 2.02 (m, 2 H, H(2′)); 3.47 (q, 2 H, H(4′), J = 5.7 Hz); 4.21 (t, 1 H, OH, J = 5.1 Hz); 4.45 (t, 2 H, H(1′), J = 7.0 Hz); 7.43—7.48 (m, 3 H, H_m, H_p), 8.04 (m, 2 H, H_o), 8.26 (s, 1 H, H(2)). Found (%): C, 58.94; H, 5.43; N, 24.57. $C_{14}H_{15}N_5O_2$. Calculated (%): C, 58.95; H, 5.26; N, 24.56. IR, ν/cm^{-1}: 1696 (CO), 3548 (OH).

Compound 9b (R = Me). The yield was 70%, m.p. 166 °C. ^{1}H NMR (400 MHz), δ: 1.53 (m, 2 H, H(3′)); 1.95 (m, 2 H, H(2′)); 2.45 (s, 3 H, C(2)—Me); 3.44 (td, 2 H, H(4′), J = 6.1 and 5.1 Hz); 4.38 (t, 2 H, H(1′), J = 7.2 Hz); 4.45 (t, 1 H, OH, J = 5.1 Hz); 7.46—7.53 (m, 3 H, H_m, H_p), 8.01 (m, 2 H, H_o). Found (%) C, 60.27; H, 5.62; N, 23.42. $C_{15}H_{17}N_5O_2$. Calculated (%) C, 60.20; H, 5.69; N, 23.41. IR, ν/cm^{-1}: 1715 (CO), 3408 (OH).

Compound 9c (R = SMe). The yield was 62%, m.p. 134 °C. ^{1}H NMR (250 MHz), δ: 1.56 (m, 2 H, H(3′)); 2.00 (m, 2 H, H(2′)); 2.67 (s, 3 H, SMe); 3.47 (q, 2 H, H(4′), J = 5.5 Hz); 4.20 (t, 1 H, OH, J = 5.1 Hz); 4.38 (t, 2 H, H(1′) , J = 7.2 Hz), 7.42—7.48 (m, 3 H, H_m, H_p), 8.02 (m, 2 H, H_o). Found (%): C, 54.37; H, 5.14; N, 21.35. $C_{15}H_{17}N_5O_2S$. Calculated (%): C, 54.38; H, 5.14; N, 21.15. IR, ν/cm^{-1}: 1686 (CO), 3523 (OH).

4-(4-Hydroxybut-2-enyl)-2-R-6-phenyl-1,2,4-triazolo-[3,2-*c*][1,2,4]triazin-7-ones (10a—c). Acetyl chloride (1 mL) was added dropwise to MeOH (30 mL). Then 4-(4-acetoxybut-2-enyl)-2-R-6-phenyl-1,2,4-triazolo[3,2-*c*][1,2,4]triazin-7-one (**8a—c**) (1.5 mmol) was added to the reaction solution. The reaction mixture was kept at room temperature for 4 h and neutralized with anhydrous sodium acetate. The solvent was evaporated *in vacuo*. The reaction products (**10a—c**) were iso-

lated from the residue by silica gel column chromatography using the ethyl acetate—hexane system (4 : 1) as the eluent.

Compound 10a (R = H). The yield was 41%, m.p. 112 °C. ^{1}H NMR (400 MHz), δ: 4.23 (ddd, 2 H, H(4′), ^3J = 5.8 and 5.4 Hz, ^4J = 1.2 Hz); 4.87 (t, 1 H, OH, ^3J = 5.4 Hz); 5.11 (dd, 2 H, H(1′), ^3J = 6.5 Hz, ^4J = 1.2 Hz); 5.72 (dtt, 1 H, H(2′), ^3J = 11.0 and 6.5 Hz, ^4J = 1.4 Hz); 5.82 (dtt, 1 H, H(3′), ^3J = 11.0 and 5.8 Hz, ^4J = 1.2 Hz); 7.48—7.54 (m, 3 H, H_m, H_p); 8.01 (m, 2 H, H_o); 8.45 (s, 1H, H(2)). ^{13}C NMR (100 MHz), δ: 51.18 (C(1′)), 57.33 (C4′), 122.35 (C(2′)), 128.21 (C_m), 128.46 (C_o), 129.61 (C_p), 132.82 (C_{ipso}), 135.54 (C(3′)), 139.06 (C(6)), 149.12 (C(7)), 150.93 (C(3a)), 153.28 (C(2)). Found (%): C, 59.30; H, 4.54; N, 24.71. $C_{14}H_{13}N_5O_2$. Calculated (%): C, 59.36; H, 4.59; N, 24.73. IR, ν/cm^{-1}: 1700 (CO), 3368 (OH).

Compound 10b (R = Me). The yield was 70%, m.p. 125 °C. ^{1}H NMR (400 MHz), δ: 2.45 (s, 3 H, C(2)—Me); 4.21 (ddd, 2 H, H(4′), ^3J = 5.8 Hz, 5.3, ^4J = 1.5 Hz); 4.88 (t, 1 H, OH, ^3J = 5.3 Hz); 5.07 (dd, 2 H, H(1′), ^3J = 6.5 Hz, ^4J = 1.4 Hz); 5.71 (dtt, 1 H, H(2′), ^3J = 11.1 Hz, 6.5, ^4J = 1.5 Hz); 5.82 (dtt, 1 H, H(3′), ^3J = 11.1 and 5.8 Hz, ^4J = 1.4 Hz); 7.46—7.53 (m, 3 H, H_m, H_p); 8.00 (m, 2 H, H_o). ^{13}C NMR (100 MHz), δ: 14.33 (C(2)—Me), 51.13 (C(1′)), 57.36 (C(4′)), 122.44 (C(2′)); 128.20 (C_m); 128.43 (C_o); 129.59 (C_p); 132.36 (C_{ipso}); 135.45 (C3′); 139.04 (C(6)); 148.63 (C(7)); 151.17 (C(3a)); 162.79 (C(2)). Found (%): C, 60.53; H, 5.05; N, 23.51. $C_{15}H_{15}N_5O_2$. Calculated (%): C, 60.61; H, 5.05; N, 23.57. IR, ν/cm^{-1}: 1698 (CO), 3329 (OH).

Compound 10c (R = SMe). The yield was 45%, m.p. 146 °C. ^{1}H NMR (400 MHz), δ: 2.66 (s, 3 H, SMe); 4.21 (ddd, 2 H, H(4′), ^3J = 5.8 Hz, 5.3, ^4J = 1.6 Hz); 4.86 (t, 1 H, OH, ^3J = 5.3 Hz); 5.04 (dd, 2 H, H(1′), ^3J = 6.5 Hz, ^4J = 1.3 Hz); 5.70 (dtt, 1 H, H(2′), ^3J = 11.1 Hz, 6.5, ^4J = 1.6 Hz); 5.82 (dtt, 1 H, H(3)′, ^3J = 11.1 and 5.8 Hz, ^4J = 1.4 Hz); 7.49—7.52 (m, 3 H, H_m, H_p); 8.00 (m, 2H, H_o). ^{13}C NMR (100 MHz), δ: 13.51 (SMe); 51.10 (C(1′)); 57.34 (C(4′)); 122.24 (C(2′)); 128.21 (C_m); 128.42 (C_o); 129.69 (C_p); 132.24 (C_{ipso}); 135.55 (C(3′)); 139.53 (C(6)); 147.81 (C(7)); 151.49 (C(3a)); 165.52 (C(2)). Found (%): C, 54.56; H, 4.50; N, 21.02. $C_{15}H_{15}N_5O_2S$. Calculated (%): C, 54.71; H, 4.56; N, 21.28. IR, ν/cm^{-1}: 1698 (CO), 3492 (OH).

2-Chloroethyl acetate (11) was synthesized according to a procedure described earlier.[28]

4-(2-Acetoxyethyl)-2-R-6-phenyl-1,2,4-triazolo[3,2-*c*]-[1,2,4]triazin-7-ones (12a—c). 6-Phenyl-2-R-1,2,4-triazolo-[3,2-*c*][1,2,4]triazin-7-one (**1a—c**) (5.50 mmol) was added to a solution of cesium carbonate (0.98 g, 3.00 mmol) in water (3 mL). The suspension was stirred for 0.5 h and filtered. The precipitate was dried and dissolved in DMF (10 mL). Chloroethyl acetate (**11**) (0.67 g, 5.5 mmol) was added to the solution. The reaction mixture was heated at 100 °C for 5 h and cooled. Then cold water (250 mL) was added. The precipitate was filtered off and crystallized from isopropyl alcohol.

Compound 12a (R = H). The yield was 29%, m.p. 97 °C. ^{1}H NMR (400 MHz), δ: 1.92 (s, 3 H, OAc); 4.53 (t, 2 H, H(2′), J = 5.3 Hz); 4.68 (t, 2 H, H(1′), J = 5.3 Hz); 7.50—7.55 (m, 3 H, H_m, H_p); 8.02 (m, 2 H, H_o); 8.46 (s, 1 H, H(2)). Coupled ^{1}H—^{13}C NMR (100 MHz), δ: 20.49 (q, CO—$\underline{C}H_3$, ^1J = 129.6 Hz); 52.93 (tt, C(1′), ^1J = 144.8 Hz, ^2J = 2.6 Hz); 60.66 (tt, C(2′), ^1J = 151.0 Hz, ^2J = 2.8 Hz); 128.22 (dm, C_m, ^1J = 161.1 Hz); 128.46 (dm, C_o, ^1J = 162.2 Hz); 129.71 (dt, C_p, J = 161.6 and 7.3 Hz); 132.09 (t, C_{ipso}, J = 7.5 Hz); 139.19 (t, C(6), ^3J = 3.8 Hz); 149.00 (s, C(7)); 151.32 (dt, C(3a), ^3J = 9.2 and 2.8 Hz); 153.32 (d, C(2), ^1J = 211.1 Hz); 170.27 (qt, $\underline{C}O—CH_3$, ^2J = 6.8 Hz, ^3J = 3.4 Hz). Found (%): C, 56.07; H, 4.28; N, 23.66. $C_{14}H_{13}N_5O_3$. Calculated (%): C, 56.18; H, 4.38; N, 23.40. IR, ν/cm^{-1}: 1736, 1710 (C=O).

Compound 12b (R = Me). The yield was 29%, m.p. 108 °C. ^{1}H NMR (400 MHz), δ: 1.92 (s, 3 H, OAc); 2.46 (s, 3 H, C(2)—Me); 4.51 (t, 2 H, H(2′), J = 5.3 Hz); 4.63 (t, 2 H, H(1′), J = 5.3 Hz); 7.49—7.53 (m, 3 H, H_m, H_p); 8.01 (m, 2 H, H_o). ^{13}C NMR (100 MHz), δ: 14.27 (C(2)—Me); 20.52 (CO—$\underline{C}H_3$); 52.89 (C(1′)); 60.67 (C(2′)); 128.22 (C_m); 128.44 (C_o); 129.68 (C_p); 132.18 (C_{ipso}); 139.17 (C(6)); 148.53 (C(7)); 151.53 (C(3a)); 162.86 (C(2)); 170.31 ($\underline{C}O—CH_3$). Found (%): C, 57.51; H, 4.68; N, 22.49. $C_{15}H_{15}N_5O_3$. Calculated (%): C, 57.50; H, 4.83; N, 22.35. IR, ν/cm^{-1}: 1739, 1706 (C=O).

Compound 12c (R = SMe). The yield was 38%, m.p. 142 °C. ^{1}H NMR (400 MHz), δ: 1.93 (s, 3 H, OAc); 2.66 (s, 3 H, SMe); 4.50 (t, 2 H, H(2′), J = 5.3 Hz); 4.60 (t, 2 H, H(1′), J = 5.3 Hz); 7.50—7.54 (m, 3 H, H_m, H_p); 8.00 (m, 2 H, H_o). ^{13}C NMR (100 MHz), δ: 13.50 (SMe); 20.52 (CO—$\underline{C}H_3$); 52.85 (C(1′)); 60.62 (C(2′)); 128.25 (C_m); 128.45 (C_o); 129.80 (C_p); 132.06 (C_{ipso}); 139.69 (C(6)); 147.70 (C(7)), 151.88 (C(3a)); 165.64 (C(2)); 170.30 ($\underline{C}O—CH_3$). Found (%): C, 52.01; H, 4.15; N, 20.52. $C_{15}H_{15}N_5O_3S$. Calculated (%): C, 52.17; H, 4.35; N, 20.29. IR, ν/cm^{-1}: 1732, 1706 (C=O).

4-(2-Hydroxyethyl)-2-R-6-phenyl-1,2,4-triazolo[3,2-*c*]-[1,2,4]triazin-7-ones (13a—c). 4-(2-Acetoxyethyl)-2-R-6-phenyl-1,2,4-triazolo[3,2-*c*][1,2,4]triazin-7-one (**12a—c**) (3.00 mmol) was added to a solution of MeONa, which was prepared from sodium metal (0.07 g, 3.00 mmol), in anhydrous MeOH (20 mL). The reaction mixture was refluxed for 1 h, cooled, and neutralized with acetic acid. The solvent was evaporated *in vacuo*. The reaction products (**13a—c**) were isolated from the residue by column chromatography using the ethyl acetate—hexane system (3 : 1) as the eluent.

Compound 13a (R = H). The yield was 41%, m.p. 145 °C. ^{1}H NMR (250 MHz), δ: 3.93 (q, 2 H, H(2′), J = 5.6 Hz); 4.49 (t, 2 H, H(1′), J = 5.3 Hz), 4.65 (t, 1 H, OH, J = 6.4 Hz), 7.44—7.49 (m, 3 H, H_m, H_p), 8.05 (m, 2 H, H_o), 8.26 (s, 1 H, H(2)). Found (%): C, 55.99; H, 4.21; N, 27.44. $C_{12}H_{11}N_5O_2$. Calculated (%): C, 56.03; H, 4.31; N, 27.22. IR, ν/cm^{-1}: 1692 (CO), 3485 (OH).

Compound 13b (R = Me). The yield was 35%, m.p. 151 °C. ^{1}H NMR (250 MHz), δ: 2.47 (s, 3 H, C(2)—Me); 3.92 (q, 2 H, H(2′), J = 5.7 Hz); 4.44 (t, 2 H, H(1′), J = 5.3 Hz); 4.67 (t, 1 H, OH, J = 6.4 Hz); 7.43—7.48 (m, 3 H, H_m, H_p); 8.04 (m, 2 H, H_o). Found (%): C, 57.60; H, 4.76; N, 26.01. $C_{13}H_{13}N_5O_2$. Calculated (%): C, 57.56; H, 4.83; N, 25.82. IR, ν/cm^{-1}: 1686 (CO), 3467 (OH).

Compound 13c (R = SMe). The yield was 34%, m.p. 176 °C. ^{1}H NMR (250 MHz), δ: 2.68 (s, 3 H, SMe); 3.91 (q, 2 H, H(2′), J = 5.6 Hz); 4.42 (t, 2 H, H(1′), J = 5.3 Hz); 4.66 (t, 1 H, OH, J = 6.4 Hz); 7.43—7.49 (m, 3 H, H_m, H_p); 8.04 (m, 2 H, H_o). Found (%): C, 51.67; H, 4.17; N, 23.05. $C_{13}H_{13}N_5O_2S$. Calculated (%): C, 51.47; H, 4.32; N, 23.09. IR, ν/cm^{-1}: 1695 (CO), 3491 (OH).

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