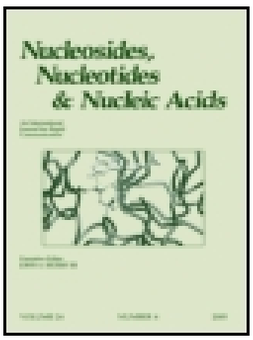

Nucleosides, Nucleotides and Nucleic Acids

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Synthesis and Antimicrobial Screening of Novel Thioglycosides and Acyclonucleoside Analogs Carrying 1,2,3-Triazole and 1,3,4-Oxadiazole Moieties

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ABSTRACT

The solvent-free 1,3-dipolar cycloaddition reaction of dimethylacetylene dicarboxylate (**1**) with 2-chlorophenyl azide (**2**) afforded 1,2,3-triazole diester **3** that upon hydrazinolysis, furnished the corresponding bis-acid hydrazide **4**. The treatment of compound **4** with carbon disulfide in a refluxing potassium hydroxide solution furnished the desired bis-1,3,4-oxadiazole-2-thione **5** tethered to a 1,2,3-triazole moiety. The respective SOx-glycosides **9–11** were obtained by glycosylation of bis-oxadiazole **5** with 2,3,4,6-tetra-O-acetyl-α-d-glucopyranosyl bromide (**6**), 2,3,4,6-tetra-O-acetyl-α-d-galactopyranosyl bromide (**7**), and 2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-α-d-glucopyranosyl chloride (**8**) in dry acetone in the presence of Et_3N, which acted as a base. However, alkylation of **5** with halogeno-alkanol **12** or **13**, chloroglycerol **14**, bromoethers **20** or **21**, and epichlohydrin **22** in the presence of K_2CO_3 in DMF yielded the corresponding acyclonucleoside analogs **16–18** and **23–25**. The isopropylidenes **19** and acetyl derivatives **26–28** of the products were also prepared. The newly synthesized compounds were characterized by ^{1}H NMR, ^{13}C NMR, 2D NMR, and mass spectra. The compounds were screened for their antibacterial and antifungal activities. A number of the tested compounds exhibited significant antimicrobial activity compared to the reference drugs.

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KEYWORDS
1,2,3-Triazoles; 1,3,4-oxadiazoles; thioglycosides; acyclonucleoside analogs; antimicrobial activity

Introduction

Considerable attention has been devoted to the synthesis and biological activity of thioglycosides.[1] In particular, glycosylthioheterocycles were recently extensively employed as glycosyl donors in glycosidation reactions and as potential therapeutics and enzyme inhibitors.[2–5] The interest in the chemotherapeutical properties of acyclonucleoside analogs has steadily increased since the discovery of acyclovir.[6] The

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design of novel acyclonucleoside analogs, such as HBG,[7] DHPG, iso-NDG,[8–11] penciclovir[7] and its oral form famiciclovir, has commanded the world-wide attention of many researchers due to their potential antiviral activity.[7,12] However, five-membered heterocycles with three heteroatoms, such as 1,2,3-triazoles and 1,3,4-oxadiazoles, were reported to exhibit various pharmacological activities including antimicrobial, anticancer, anti-inflammatory and antiviral properties.[13–15] In our ongoing interest in the synthesis of thioglycoside-based heterocycles[16,17] and acyclonucleoside analogs[18,19] based on recent interest in glycosylsulfanyl bearing nitrogen containing heterocyles and their acyclonucleoside analogs, we report the synthesis of novel 1,2,3-triazole system based 1,3,4-oxadiazole thioglycosides and their acyclic analogs, as well as the evaluation of their antimicrobial activity.

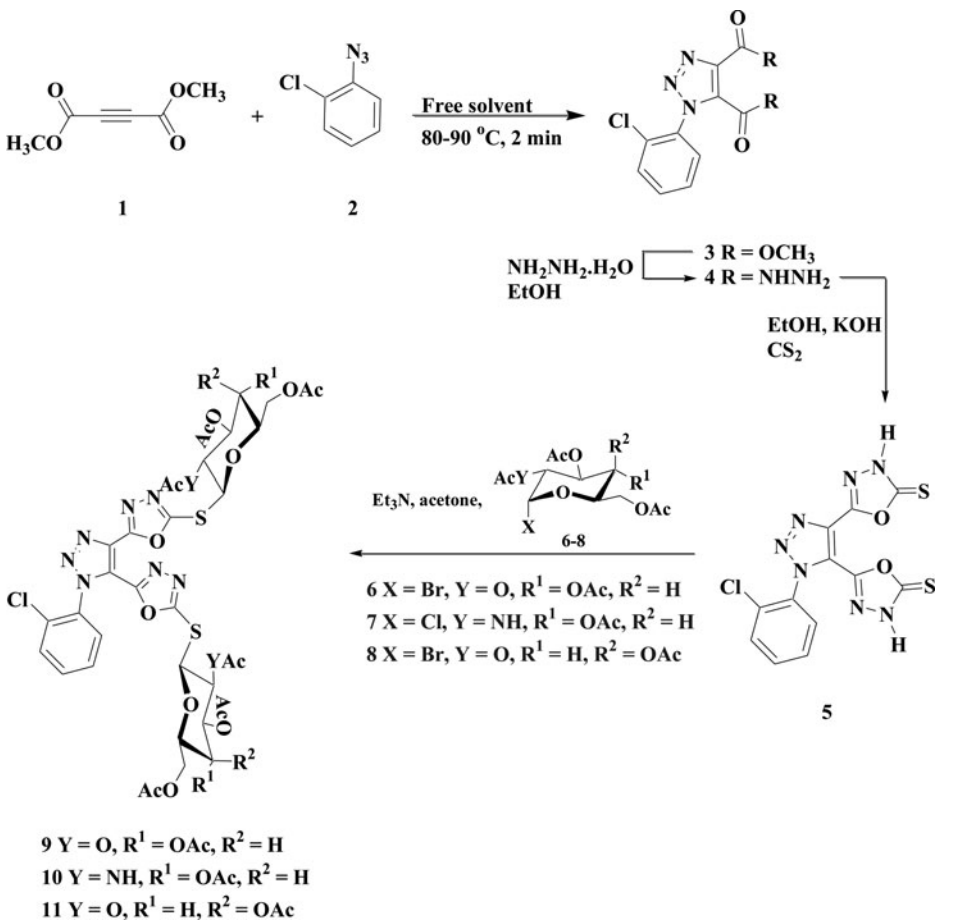
Results and discussion

Chemistry

The 1,3-dipolar cycloaddition reaction of dimethylacetylene dicarboxylate **1** with 2-chloroazidobenzene **2** under solvent-free conditions at 80–90°C afforded the corresponding 1,2,3-triazole diester **3** in 96% yield within two minutes (Scheme 1). The synthesis of compound **3** has been previously reported by Bouasla et al.[20] using the same 1,3-dipolar cycloaddition in the presence of dichloromethane as solvent, under both conventional and microwave methods. The reaction required regular stirring for nine days to afford 62% yield, while under MWI 80% yield was obtained after 10 minutes. The aryl azide was prepared *via* the diazotization of *p*-chloroaniline in the presence of a sodium nitrite solution in acidic media followed by addition of sodium azide according to a previously reported protocol.[21] This optimized method constitutes an efficient eco-friendly method for the synthesis of aromatic 1,2,3-triazoles in quantitative yields in a very short period of time with a simple purification workup.

The ^{1}H NMR spectrum of compound **3** displayed two characteristic singlets at 3.84 and 3.88 ppm corresponding to the two nonequivalent methoxy groups and four aromatic protons for di-substituted benzene between 7.64 and 7.87 ppm. However, the ^{13}C NMR spectrum displayed no signals in the sp-carbon regions, which confirmed the success of the cycloaddition reaction. In addition, two additional signals appeared at 158.50 and 159.79 ppm, which were characteristic of the two ester carbonyl carbons (C=O).

The treatment of 1,2,3-triazole bis-ester **3** with hydrazine hydrate in refluxing ethanol afforded the expected bis-acid hydrazide **4** in excellent yield (90%) *via* a nucleophilic acyl substitution reaction (Scheme 1). The ^{1}H NMR of compound **4** indicated the disappearance of the two methoxy groups below 4 ppm and the appearance of two new broad singlets at 4.70 and 10.61, which were attributed to the NH_2 and NH groups, respectively. However, the ^{13}C NMR spectrum also confirmed the success of the hydrazinolysis reaction based on the disappearance of the two methoxy signals from their chemical shift regions and the upfield shifting of



Scheme 1.

the two carbonyls from the ester moieties (158.50 and 159.79 ppm) to the amide moieties (156.33 and 157.81 ppm).

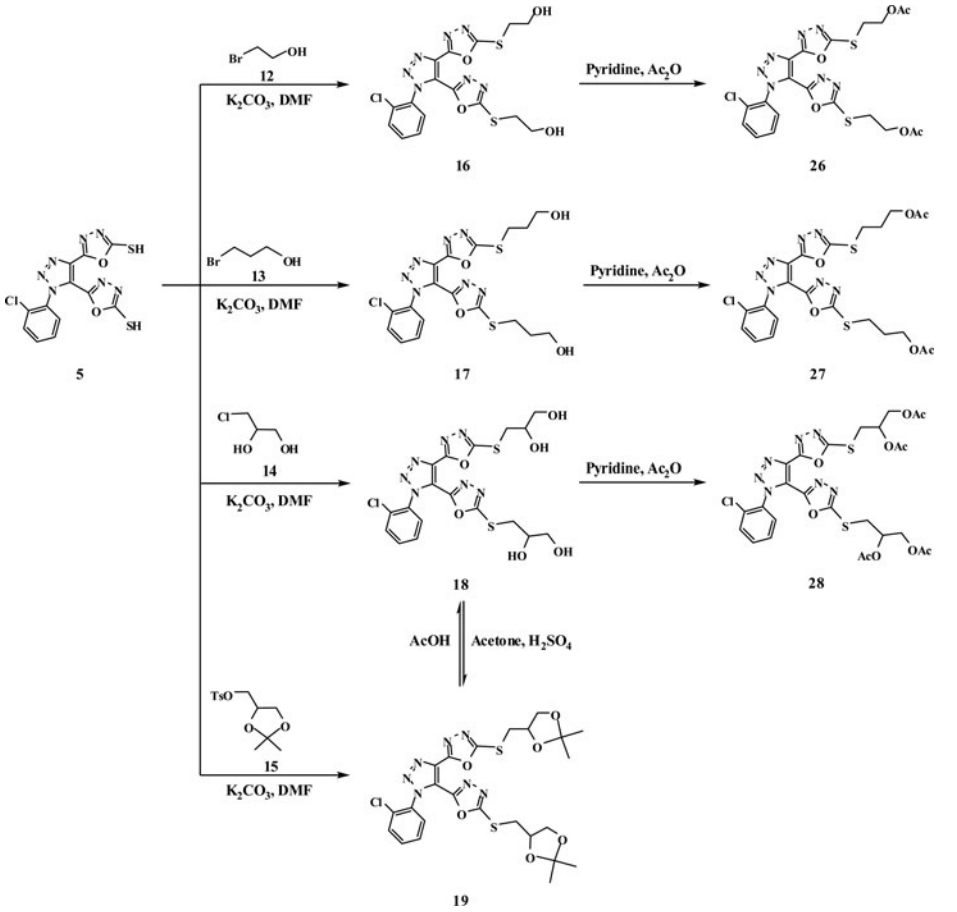
The thermal condensation of bis-acid hydrazide **4** with carbon disulfide in the presence of potassium hydroxide in ethanol yielded the desired bis-1,3,4-oxadiazole-2-thione **5** tethered to the 1,2,3-triazole nucleus in 84% yield (Scheme 1). The ^{1}H NMR analysis indicated that the two broad singlets at 12.10 and 15.01 ppm corresponded to the unsymmetrical NH's of the thione isomer. The ^{13}C NMR spectrum confirmed the formation of the oxadiazole ring in its thione form based on the appearance of two nonequivalent C=S peaks at 177.82 and 177.94 ppm.

Thioglycosilation was carried out through the coupling of **5** with two equivalents of 2,3,4,6-tetra-*O*-acetyl-α-d-glucopyranosylbromide (**6**), 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-d-glucopyranosyl chloride (**7**) and 2,3,4,6-tetra-*O*-acetyl-α-d-galactopyranosylbromide (**8**) in the presence of triethylamine as the base and acetone as the solvent to yield the corresponding bis-(SOx-glycosides) **9–11** in 82–90% (Scheme 1).

The structures of the synthesized thioglycosides have been confirmed based on their ^{1}H and ^{13}C NMR spectra. Therefore, the ^{1}H NMR spectra of **9–11** indicated

the disappearance of the NH protons of their precursor **5** and the appearance of signals at δ_H 1.81–2.20 ppm belonging to the eight methyl acetate group (OAc), which confirmed the presence of two glycosyl residues. The heteromultiple bond correlation from the ^{1}H-^{1}H DQFCOSY and ^{1}H-^{13}C HMQC experiments also facilitated the spectral assignment of the sugar protons and carbons. Therefore, the anomeric protons of **9–11** were assigned as two doublets at 5.49–5.47 ppm for H_{1a} and 5.62–6.00 ppm for H_{1b} with coupling constant values of $J_{1',2'} = 9.9–10.2$ Hz, confirming the presence of two glycosyl residues in the β-configuration (see experimental part).

The alkylation of bis-1,3,4-oxadiazole **5** with 2.2 equivalents of bromoethanol (**12**), chloropropanol (**13**), 2,3-dihydroxy-1-chloropropane (**14**) or the protected derivative 2,3-*O*-isopropylidene-1-*O*-(*p*-tolylsulfonyl)-glycerol (**15**) in the presence of the DMF solvent and potassium carbonate, which acted as the deprotonating basic catalyst, afforded the corresponding S-acyclic analogs **16–19** in 81–88% yield. In addition, isopropylidenation of bis-glycerol **18** with acetone in sulfuric acid afforded the corresponding protected acyclonucleoside analog **19** whose deprotection in refluxing 70% acetic acid yielded compound **18** in 78% yield (Scheme 2).

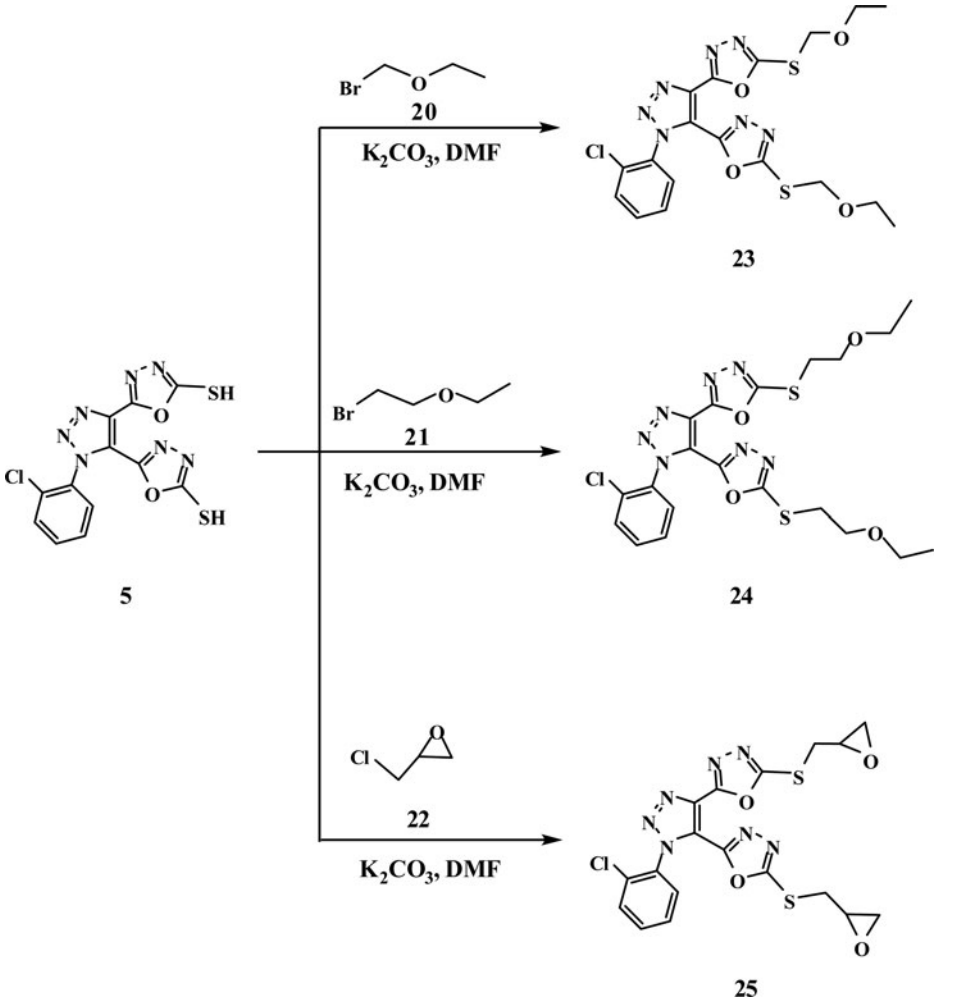


Scheme 2.

The structures of the S-acyclonucleoside analogs **16–18** were confirmed by the presence of characteristic absorption bands at 3267–3414 cm^{-1} corresponding to the OH of the acyclic side chains. The ^{1}H NMR spectrum of compound **16** displayed two characteristic triplets at δ_H 5.03 and 5.07 ppm due to the two OH protons in addition to two triplets at δ_H 3.31 and 4.19 ppm for the two unsymmetrical SCH_2 groups. In addition, the ^{13}C NMR spectrum of compound **16** displays these nonequivalent SCH_2 carbons at δ_C 36.40 and 51.60 ppm. In the ^{1}H NMR spectrum of compound **18**, the presence of four characteristic singlets between δ_H 4.79 and 5.15 ppm, which correspond to the four OH protons, confirmed the incorporation of two glycerol side chains. The success of the isopropylidenation reaction of compound **18** has been confirmed by ^{1}H NMR analysis where the appearance of four characteristic singlets in the upper field region at δ_H 1.35–1.44 ppm corresponded to the four methyl groups on the two dioxalane rings. The peaks corresponding to the same methyl groups were observed at δ_C 22.63–29.70 ppm in the ^{13}C NMR spectrum. However, when compound **5** was treated with alkylating agents, such as bromoethylmethylether (**20**), bromoethylethylether (**21**), and epichlorohydrin (**22**), using the same procedure, thioether acyclonucleoside analogs **23**, **24**, and S-methyloxirane **25** were obtained in 93% yields (Scheme 3).

The structure of compound **23** has been deduced by ^{1}H NMR analysis, which revealed the presence of two triplets at $\delta_H = 3.40$ and 4.29 ppm and two singlets at $\delta_H = 3.25$ and 3.27 ppm that are characteristic of two SCH_2 and two OCH_3 groups, respectively. The ^{13}C NMR spectrum displayed signals at $\delta_C =$ 33.09 and 48.64 ppm, which are characteristic of the two nonequivalent SCH_2 carbons. The ^{1}H NMR spectrum of **25** displayed a multiplet signal at δ_H 5.88–5.97 ppm for the two CHO groups of the two epoxypropyl moieties in addition to the two triplets at δ_H 3.76 and 4.94 ppm corresponding to the diastereotropic protons of the two S-CH_2 groups. The treatment of hydroxylated acyclic nucleoside analogs **16–18** with acetic anhydride in pyridine at 0°C afforded their acetylated analogs **26–28**. The disappearance of the OH protons in the ^{1}H NMR spectra of compounds **26–28** and the appearance of characteristic singlet peaks in the down field region at δ_H 2.00–2.70 ppm were due to the methyl acetate protons, confirming the success of the acetylation reaction. Their ^{13}C NMR spectra confirmed the presence of acetate groups based on the appearance of characteristic signals at δ_C 20.65–21.81 ppm and 170.37–172.05 ppm due to the CH_3 and (C=O) groups, respectively.

The appearance of protons and carbons of glycopyranosyl moieties and acyclic side chains in different chemical shifts confirmed the nonequivalence of the two oxadiazoles rings. This could presumably be due to the restricted rotation around the C=C bond of the 1,2,3-triazole ring which could generates different steric rearrangements of the two oxadiazoles in the geometric cis and trans isomers. Moreover, the anisotropic effect generated by the 2-chlorophenyl ring also affects the chemical shifts of all protons and carbons.



Scheme 3.

Antibacterial and antifungal activity

Both microbial studies were assessed by minimum inhibitory concentration (MIC) using the broth dilution method.[22–24] Data for the preliminary antimicrobial activities expressed as MIC values are summarized in Table 1. Most of the tested compounds exhibited high inhibition activities at MIC values of 4–31.25 μg/ml. Dimethyl 1-(2-chlorophenyl)-1*H*-1,2,3-triazole-4,5-dicarboxylate (**3**) exhibited good antibacterial activity against all Gram positive bacteria at a MIC value of 16 μg/ml. The evaluation of the antimicrobial activity of bis-acid hydrazide **4** and bis-oxadiazole **5** revealed that these compounds are more effective against Gram-positive bacterial strains and fungal species at a MIC of 4–16 μg/ml. However, all of the synthesized thioglycosides (Sox-glycosides) exhibit antibacterial activity against all of the bacterial strains at MIC values of 4–16 μg/ml and a loss of activity against the tested fungal species. In general, the highest antibacterial activity was exhibited by the hydroxylated acyclonucleoside analogs **16–18** against all of

Table 1. Antimicrobial activity expressed as MIC (μg/mL).

	Gram-Positive Organisms[a]			Gram-Negative Organisms[b]			Fungi [c]	
Compounds	*Sp*	*Bs*	*Sa*	*Pa*	*Ec*	*Kp*	*Af*	*Ca*
3	16	16	16	31.25	31.25	31.25	125	250
4	8	4	4	31.25	31.25	31.25	16	16
5	16	16	16	31.25	31.25	31.25	8	4
9	8	16	4	8	4	8	62.5	62.5
10	8	16	8	8	8	16	62.5	125
11	4	16	4	8	4	16	62.5	125
16	4	8	8	8	8	8	16	16
17	8	8	4	8	4	8	16	16
18	4	4	4	8	4	8	16	16
19	16	31.25	16	62.5	62.5	62.5	125	62.5
23	62.5	62.5	62.5	31.25	31.25	31.25	16	16
24	125	62.5	62.5	31.25	31.25	31.25	16	16
25	62.5	62.5	62.5	31.25	31.25	31.25	16	16
26	31.25	31.25	31.25	62.5	62.5	62.5	16	31.25
27	31.25	31.25	31.25	62.5	125	62.5	31.25	16
28	31.25	31.25	31.25	31.25	62.5	31.25	31.25	16
Ciprofloxacin	≤5	≤1	≤5	≤5	≤1	≤1	—	—
Fluconazole	—	—	—	—	—	—	≤1	≤1

Notes: [a]: Gram-positive bacteria: *Streptococcus pneumonia* (RCMB 010010, Sp), *Bacillus subtilis* (RCMB 010067, Bs), *Staphylococcus aureus* (RCMB 010025, Sa); [b]: Gram-negative bacteria: *Pseudomonas aeuroginosa* (RCMB 010043, Pa), *Escherichia coli* (RCMB 010052, Ec), *Klebsiella pneumonia* (RCMB 010058, Kp); [c]: yeasts: *Aspergillus fumigatus* (RCMB 02568, Af), *Candida albicans* (RCMB 05036, Ca).

bacterial strains at MIC values of 4–8 μg/ml, and compounds **19, 23–28** exhibited weak antibacterial activities at lower concentrations. Antifungal screening revealed that all of the acyclonucleoside analogs **16–19** and **23–28** exhibited moderate antifungal inhibition against all of the fungal species at MIC values of 16–31.25 μg/ml. Therefore, the antimicrobial activity and structure activity relationship indicated that the cyclization of bis-acid hydrazide **4** to the corresponding oxadiazole derivative **5** resulted in higher inhibition activities against Gram-positive bacterial strains and fungal species. In addition, the incorporation of cyclic sugar moieties to the oxadiazole ring via a thioglycosidic linkage resulted in higher antibacterial activity. However, antimicrobial screening confirmed that the acyclic nucleoside analogs with free hydroxyl groups exhibited improved activity compared to the corresponding ethers, isopropylidene or acetylated analogs against all of the bacterial strains, indicating the influence of the free hydroxyl groups in the acyclic side chains.

Conclusion

This study reports the synthesis and characterization of novel thioglycosides and acyclonucleoside analogs carrying 1,2,3-triazole and 1,3,4-oxadiazole moieties in one scaffold, as potential antimicrobial agents. The antimicrobial screening showed that some of the synthesized compounds displayed significant antimicrobial activity.

Experimental

General. The melting points were determined on a Melt-temp apparatus and are uncorrected. TLC was performed on Merck silica gel 60 F254, and the spots were

visualized by UV light absorption and/or treatment with a solution of 10% H_2SO_4 in aqueous methanol followed by heating. The IR spectra were measured using potassium bromide pellets on a Perkin-Elmer 1430 series FT-IR spectrometer. The ^{1}H NMR spectra were recorded on an Avance Bruker NMR spectrometer at 400–600 MHz, and the ^{13}C NMR spectra were recorded on the same instrument at 100–150 MHz with TMS as the internal standard. The 2D ^{1}H-^{1}H DQFCOSY and ^{1}H-^{13}C HMQC experiments were also recoded. Elemental analyses were performed using an elementary analyzer system (i.e., GmbH-vario EL III Element Analyzer). The LC-MS spectra were measured by HPLC-MS (Ion trap) from scientific thermo.

General procedure for the synthesis of dimethyl 1-(2-chlorophenyl)-1*H*-1,2,3-triazole-4,5-dicarboxylate (3). Dimethyl acetylenedicarboxylate (2.13 g, 15 mmol) and 1-azido-2-chlorobenzene (3.06 g, 20 mmol) were heated to 80–90°C for 2 minutes. The reaction mixture was cooled, and then, ether was added to precipitate the product. The solid was filtered and washed with ether to give **3** in 96% yield (from EtOH), mp: 113–114°C. FT-IR ($\sqrt{}_{max}$, KBr/cm^{-1}): 1564 (C=C), 1729 (C=O), 2930–2985 (CH_3), 3074 (C-H Ar). ^{1}H NMR (400 MHz, DMSO-d_6), δ_H 3.84 (3H, s, OCH_3), 3.88 (3H, s, OCH_3), 7.46–7.63 (m, 2 H, Ar-H), 7.73–7.86 (m, 2 H, Ar-H). ^{13}C NMR (100 MHz, DMSO-d_6)), δ_C 52.80 (OCH_3), 53.89 (OCH_3), 122.43, 122.52, 124.09, 128.77, 134.67, 136.16, 153.90, 156.40 (Ar-C), 158.50, 159.79 (C=O). Anal. Calcd. for $C_{12}H_{10}ClN_3O_4$: C, 48.75; H, 3.41; N, 14.21. Found: C, 48.60; H, 3.56; N, 14.08. MS (ESI) *m/z*: 296.03 $[M+H]^+$.

General procedure for the synthesis of 1-(2-chlorophenyl)-1*H*-1,2,3-triazole-4,5-dicarbohydrazide (4). A mixture of compound **3** (6 g, 20 mmol) and hydrazine hydrate (2 g, 40 mmol) in ethanol (50 mL) was heated under reflux for 5 hours. After cooling, ethanol was removed under reduced pressure to give **4** in 92% yield (from EtOH), mp: 278–279°C. FT-IR ($\sqrt{}_{max}$, KBr/cm^{-1}): 1570 (C=C), 1684 (C=O), 3062 (C–H Ar), 3250–3387 (NH, NH_2). ^{1}H NMR (400 MHz, DMSO-d_6), δ_H 4.70 (4H, br s, **NH_2**), 7.41–7.58 (m, 2 H, Ar-H), 7.66–7.80 (m, 2 H, Ar-H), 10.61 (2H, br s, NH). ^{13}C NMR (100 MHz, DMSO-d_6), δ_C 123.24, 123.03, 124.54, 128.70, 134.83, 137.14, 153.22, 155.06 (Ar-C), 156.33, 157.81 (C=O). Anal. Calcd. for $C_{10}H_{10}ClN_7O_2$: C, 40.62; H, 3.41; N, 33.16. Found: C, 40.53; H, 3.52; N, 33.32. MS (ESI) *m/z*: 296.06 $[M+H]^+$.

General procedure for the synthesis of 5,5′-(1-(2-chlorophenyl)-1*H*-1,2,3-triazole-4,5-diyl)bis(1,3,4-oxadiazole-2(3*H*)-thione) (5). To a solution of acid hydrazide **4** (0.327g, 1 mmol) in ethanol (20 ml), potassium hydroxide (0.12 g, 2.2 mmol) in water (5 ml) and carbon disulfide (0.76 g, 10 mmol) were added. The reaction mixture was heated under reflux for 6 hr. The mixture was cooled, diluted with cold water (10 ml) and acidified with dilute HCl. The resulting precipitate was collected by filtration, washed with water, and recrystallized to give the desired compound **5** in 84% yield (from EtOH) as yellow needles. mp: 244–245°C. FT-IR ($\sqrt{}_{max}$, KBr/cm^{-1}): 1296 (C=S), 1557 (C=C), 1626 (C=N), 3082 (C–H Ar), 3297–3328 (NH). ^{1}H NMR (600 MHz, DMSO-d_6), δ_H 7.56–7.70 (m, 2 H, Ar-H), 7.79–7.89 (m, 2 H, Ar-H), 12.10 (0.5H, br s, NH), 15.02 (1.5H, br s, NH). ^{13}C NMR (150 MHz,

DMSO-d_6), δ_C 123.62, 123.92, 124.92, 129.26, 135.37, 138.02, 154.71, 155.28 (Ar-C), 177.82, 177.94 (C=S). Anal. Calcd. for $C_{12}H_6ClN_7O_2S_2$: C, 37.95; H, 1.59; N, 25.82. Found: C, 37.76; H, 1.43; N, 25.60. MS (ESI) *m/z*: 379.94 $[M+H]^+$.

General procedure for the synthesis of thioglycosides (SOx-glycosides) 9–11. To a stirred solution of compound **5** (0.379 g, 1 mmol) and triethylamine (0.22 g, 2.2 mmol) in dry acetone (25 ml), the appropriate glycosyl halide (2,3,4,6-tetra-*O*-acetyl-α-d-glucopyranosylbromide (**6**), 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-d-glucopyranosyl chloride (**7**) and 2,3,4,6-tetra-*O*-acetyl-α-d-galactopyranosylbromide (**8**)) (2.2 mmol) was added portion wise followed by stirring overnight. The reaction mixture was filtered, washed with acetone, evaporated under reduced pressure, and recrystallized from ethanol to afforded Sox-glycosides **9–11**.

2,2′-(5,5′-(1-(2-Chlorophenyl)-1*H*-1,2,3-triazole-4,5-diyl)bis(1,3,4-oxadiazole-5,2-diyl))bis-(sulfanediyl)bis(2,3,4,6-tetra-*O*-acetyl-β-D-thioglucopyranoside) (9). This compound was obtained as colorless crystals in 88% yield (from EtOH). $\mathbf{R}_f$: 0.35 (ethylacetate/*n*-hexane 2:1); mp: 197–198°C; FT-IR ($\sqrt{}_{max}$, KBr/cm^{-1}): 1551 (C=C), 1614 (C=N), 1732 (C=O), 3048 (C–H Ar). ^{1}H NMR (600 MHz, $CDCl_3$), δ_H 1.89, 1.98, 2.01, 2.02, 2.05, 2.06, 2.09, 2.11 (8s, 24 H, 8 OAc), 3.90–3.97 (m, 1 H, H-5a), 4.02–4.07 (m, 1 H, H-5b), 4.19 (dd, 1 H, $J_{6,5}$ = 3.6 Hz, J_{gem} = 12.4 Hz, H-6a), 4.24 (dd, 1 H, $J_{6,5}$ = 3.6 Hz, J_{gem} = 12.4 Hz, H-6b), 4.27 (dd, 1 H, $J_{6,5}$ = 6.9 Hz, J_{gem} = 12.4 Hz, H-6′a), 4.35 (dd, 1 H, $J_{6',5}$ = 6.9 Hz, J_{gem} = 12.4 Hz, H-6′b), 5.10 (dd, 1 H, $J_{4,3}$ = 9.3 Hz, $J_{4,5}$ = 10.2 Hz, H-4a), 5.17 (dd, 1 H, $J_{2,1}$ = 10.2 Hz, $J_{2,3}$ = 9.3 Hz, H-2a), 5.25 (dd, 1 H, $J_{4,3}$ = 9.3 Hz, $J_{4,5}$ = 10.2 Hz, H-4b), 5.36 (t, 1 H, $J_{3,2}$ = $J_{3,4}$ = 9.3 Hz, H-3a), 5.39 (t, 1 H, $J_{3,2}$ = 9.6 Hz, $J_{3,4}$ = 9.3 Hz, H-3b), 5.64 (d, 1 H, $J_{1,2}$ = 10.2 Hz, H-1a), 5.69 (d, 1 H, $J_{1,2}$ = 9.9 Hz, H-1b), 5.86 (t, 1 H, $J_{2,1}$ = 9.9 Hz, $J_{2,3}$ = 9.6 Hz, H-2b), 7.32–7.40 (m, 2 H, Ar-H), 7.76–7.83 (m, 2 H, Ar-H). ^{13}C NMR (150 MHz, $CDCl_3$), δ_C 20.66, 20.75, 20.79, 21.32 (*C*H_3CO), 62.68 (C-6b), 63.24 (C-6a), 66.60 (C-4b), 68.81 (C-4a), 69.85 (C-2a), 71.17 (C-2b), 72.77 (C-3a), 73.42 (C-3b), 75.60 (C-5b), 77.90 (C-5a), 83.62 (C-1a), 84.70 (C-1b), 121.35, 122.90, 123.62, 128.86, 135.30, 135.84, 150.94, 157.21 (Ar-C), 167.50, 168.73, 169.84, 170.14, 170.70, 170.94, 171.70 (CH$_3$*C*O). Anal. Calcd. for $C_{40}H_{42}ClN_7O_{20}S_2$: C, 46.24; H, 4.07; N, 9.42. Found: C, 46.35; H, 3.99; N, 9.31. MS (ESI) *m/z*: 1040.22 $[M+H]^+$.

2,2′-(5,5′-(1-(2-Chlorophenyl)-1*H*-1,2,3-triazole-4,5-diyl)bis(1,3,4-oxadiazole-5,2-diyl))bis-(sulfanediyl)bis(2-acetamido-2-deoxy-3,4,6-tri-*O*-acetyl-β-D-glucopyranoside) (10). This compound was obtained as colorless crystals in 85% yield (from EtOH). $\mathbf{R}_f$: 0.28 (ethylacetate/*n*-hexane 4:1); mp: 221–222°C. FT-IR ($\sqrt{}_{max}$, KBr/cm^{-1}): 1562 (C=C), 1619 (C=N), 1727 (C=O), 3072 (C–H Ar). ^{1}H NMR (600 MHz, $CDCl_3$), δ_H 1.85, 1.90, 1.97, 1.99, 2.01, 2.04, 2.05 (7s, 24 H, 2 NAc, 6 OAc), 3.73–3.99 (m, 1 H, H-5a), 3.91–3.98 (m, 1 H, H-5b), 4.07 (dd, 1 H, $J_{6,5}$ = 3.6 Hz, J_{gem} = 12.9 Hz, H-6a), 4.21 (dd, 1 H, $J_{6,5}$ = 3.6 Hz, J_{gem} = 12.9 Hz, H-6b), 4.26 (dd, 1 H, $J_{6',5}$ = 6.7 Hz, J_{gem} = 12.9 Hz, H-6′a), 4.28 (dd, 1 H, $J_{6,5}$ = 6.7 Hz, J_{gem} = 12.9 Hz, H-6′b), 4.34 (ddd, 1 H, $J_{2,1}$ = 10.2 Hz, $J_{2,3}$ = 9.6 Hz, $J_{2,NH}$ = 7.9 Hz, H-2a), 4.54 (ddd, 1 H, $J_{2,1}$ = 10.2 Hz, $J_{2,3}$ = 9.9 Hz, $J_{2,NH}$

= 7.9 Hz, H-2b), 5.11 (t, 1 H, $J_{4,3} = J_{4,5} = 9.6$ Hz, H-4a), 5.25 (t, 1 H, $J_{3,2} = J_{3,4} = 9.6$ Hz, H-3a), 5.45 (dd, 1 H, $J_{3,2} = 9.9$ Hz, $J_{3,4} = 9.6$ Hz, H-3b), 5.49 (d, 1 H, $J_{1,2} = 10.2$ Hz, H-1a), 5.69 (dd, 1 H, $J_{4,3} = 9.6$ Hz, $J_{4,5} = 9.9$ Hz, H-4b), 6.00 (d, 1 H, $J_{1,2} = 10.2$ Hz, H-1b), 6.55 (d, 1 H, $J_{NH,2} = 7.9$ Hz, NHAc), 7.38–7.47 (m, 2 H, Ar-H), 7.60–7.65 (m, 1 H, Ar-H), 7.72 (d, 1 H, $J_{NH,2} = 7.9$ Hz, NHAc), 7.81–7.87 (m, 1 H, Ar-H). ^{13}C NMR (150 MHz, $CDCl_3$), δ_C = 20.45, 20.65, 20.77, 20.87 (CH_3CO), 52.78 (C-2a), 53.90 (C-2b), 62.74 (C-6a), 63.85 (C-6b), 67.19 (C-4b), 68.36 (C-4a), 70.64 (C-3b), 73.93 (C-3′a), 74.23 (C-5b), 75.87 (C-5a), 84.70 (C-1a), 85.07 (C-1′b), 121.96, 123.08, 123.81, 128.31, 136.22, 136.72, 150.31, 157.64 (Ar-C), 169.47, 169.87, 170.44, 170.94, 171.33, 171.48, 171.76, 172.05 (CH_3CO). Anal. Calcd. for $C_{40}H_{44}ClN_9O_{18}S_2$: C, 46.27; H, 4.27; N, 12.14. Found: C, 46.39; H, 4.42; N, 12.30. MS (ESI) *m/z*: 1038.15 $[M+H]^+$.

2,2′-(5,5′-(1-(2-Chlorophenyl)-1*H*-1,2,3-triazole-4,5-diyl)bis (1,3,4-oxadiazole-5,2-diyl))bis-(sulfanediyl)bis(2,3,4,6-tetra-*O*-acetyl-*β*-D-thiogalactopyranoside) (11). This compound was obtained as colorless crystals in 90% yield (from EtOH). $\mathbf{R}_f$: 0.43 (ethylacetate/*n*-hexane 2:1); mp: 170–171°C. FT-IR ($\sqrt{}_{max}$, KBr/cm^{-1}): 1566 (C=C), 1631 (C=N), 1739 (C=O), 3051 (C–H Ar). ^{1}H NMR (600 MHz, $CDCl_3$), δ_H 1.81, 1.87, 1.92, 1.96, 1.99, 2.03, 2.10, 2.20 (8s, 24 H, 8 OAc), 4.03–4.11 (m, 6 H, H-5a, H-5b, H-6a, H-6b, H-6a, H-6b), 5.11 (dd, 1 H, $J_{3,2} = 9.6$ Hz, $J_{3,4} = 4.2$ Hz, H-3b), 5.15 (dd, 1 H, $J_{3,2} = 9.2$ Hz, $J_{3,4} = 4.2$ Hz, H-3a), 5.48 (dd, 1 H, $J_{2,1} = 10.2$ Hz, $J_{2,3} = 9.2$ Hz, H-2a), 5.51 (d, 1 H, $J_{4,3} = 4.2$ Hz, H-4a), 5.57 (d, 1 H, $J_{4,3} = 4.2$ Hz, H-4b), 5.62 (d, 1 H, $J_{1,2} = 9.9$ Hz, H-1b), 5.74 (d, 1 H, $J_{1,2} = 10.2$ Hz, H-1a), 5.90 (dd, 1 H, $J_{2,1} = 9.9$ Hz, $J_{2,3} = 9.6$ Hz, H-2b), 7.33–7.39 (m, 2 H, Ar-H), 7.72–7.80 (m, 2 H, Ar-H). ^{13}C NMR (150 MHz, $CDCl_3$), δ_C 20.65, 20.75, 20.79, 21.02, 21.42 (CH_3CO), 62.47 (C-6a), 62.93 (C-6b), 66.92 (C-2a), 67.32 (C-2b), 68.72 (C-4a, C-4b), 71.84 (C-3a), 72.96 (C-3b), 73.04 (C-5a), 76.24 (C-5b), 84.82 (C-1a), 86.56 (C-1b), 121.48, 122.61, 123.80, 126.31, 126.85, 127.08, 135.62, 136.07 (Ar-C), 167.02, 168.32, 169.77, 170.24, 170.46, 171.85 (CH_3CO). Anal. Calcd. for $C_{40}H_{42}ClN_7O_{20}S_2$: C, 46.24; H, 4.07; N, 9.42. Found: C, 46.39; H, 3.93; N, 9.56. MS (ESI) *m/z*: 1040.14 $[M+H]^+$.

General procedure for the synthesis of acyclonucleoside analogs 16–19. A solution of compound **5** (0.379 m, 1 mmol) in dry DMF (15 ml) and potassium carbonate (0.30 g, 2.2 mmol) was stirred for two hours, and then, the appropriate alkylating agent **12–15, 20–22** (2.2 mmol) was added. The stirring was continued overnight. The reaction mixture was poured onto crushed ice, and the obtained product was washed with water, dried, and recrystallized from ethanol to yield the corresponding acyclonucleoside analog.

2,2′-(5,5′-(1-(2-Chlorophenyl)-1*H*-1,2,3-triazole-4,5-diyl)bis (1,3,4-oxadiazole-5,2-diyl))bis-(sulfanediyl)diethanol (16). This compound was obtained in 88% yield (from EtOH) as colorless crystals. mp: 172–173°C. FT-IR ($\sqrt{}_{max}$, KBr/cm^{-1}): 1572 (C=C), 1609 (C=N), 3026 (C–H Ar), 3267–3370 (OH). ^{1}H NMR (600 MHz, DMSO-d_6), δ_H 3.31 (t, 2 H, $J = 6.0$ Hz, SCH_2), 3.69–3.72 (q, 2 H, CH_2O), 3.77–3.80 (q, 2 H, CH_2O), 4.19 (t, 2 H, $J = 6.0$ Hz, SCH_2), 5.03 (t, 1 H, $J = 6.0$ Hz, OH), 5.07 (t, 1 H, $J = 6.0$ Hz, OH), 7.43–7.87 (m, 4 H, Ar-H).

^{13}C NMR (150 MHz, DMSO-d_6), δ_C 36.40 (SCH_2), 51.60 (SCH_2), 59.72 (CH_2O), 60.36 (CH_2O), 127.60, 130.21, 130.93, 131.00, 131.58, 131.92, 152.98, 159.47 (Ar-C, C=N). Anal. Calcd. for $C_{16}H_{14}ClN_7O_4S_2$: C, 41.07; H, 3.02; N, 20.95. Found: C, 40.88; H, 3.19; N, 20.74. MS (ESI) *m/z*: 468.07 $[M+H]^+$.

2,2′-(5,5′-(1-(2-Chlorophenyl)-1*H*-1,2,3-triazole-4,5-diyl)bis(1,3,4-oxadiazole-5,2-diyl))bis-(sulfanediyl)dipropanol (17). This compound was obtained in 86% yield (from EtOH) as colorless crystals. mp: 190–191°C. FT-IR ($\sqrt{}_{max}$, KBr/cm^{-1}): 1561 (C=C), 1595 (C=N), 3072 (C–H Ar), 3284–3350 (OH). ^{1}H NMR (600 MHz, DMSO-d_6), δ_H 1.84–1.87 (m, 2 H, $CH_2\underline{C}H_2CH_2$), 1.93–1.96 (m, 2 H, $CH_2\underline{C}H_2CH_2$), 3.28 (t, 2 H, J = 6.0 Hz, SCH_2), 3.47 (t, 2 H, J = 6.0 Hz, CH_2O), 3.52 (t, 2 H, J = 6.0 Hz, CH_2O), 4.18 (t, 2 H, J = 6.0 Hz, SCH_2), 4.60 (bs, 2 H, 2 × OH), 7.44–7.84 (m, 4 H, Ar-H). ^{13}C NMR (150 MHz, DMSO-d_6), δ_C 30.38 ($CH_2\underline{C}H_2CH_2$), 32.61 ($CH_2\underline{C}H_2CH_2$), 32.71 (SCH_2), 45.99 (SCH_2), 58.04 (CH_2O), 59.44 (CH_2O), 127.63, 130.24, 130.96, 131.57, 131.95, 152.11, 159.47 (Ar-C, C=N). Anal. Calcd. for $C_{18}H_{18}ClN_7O_4S_2$: C, 43.59; H, 3.66; N, 19.77. Found: C, 43.73; H, 3.52; N, 20.03. MS (ESI) *m/z*: 496.01 $[M+H]^+$.

3,3′-(5,5′-(1-(2-Chlorophenyl)-1*H*-1,2,3-triazole-4,5-diyl)bis(1,3,4-oxadiazole-5,2-diyl))bis-(sulfanediyl)dipropane-1,2-diol (18). This compound was obtained in 81% yield (from EtOH) as white solid. mp: 274–275°C. FT-IR ($\sqrt{}_{max}$, KBr/cm^{-1}): 1562 (C=C), 1605 (C=N), 3042 (C–H Ar), 3267–3414 (OH). ^{1}H NMR (600 MHz, DMSO-d_6), δ_H 3.19 (dd, 1 H, J = 6.0 Hz, J = 8.1 Hz, SCH_2), 3.30–3.46 (m, 5 H, SCH_2, 2 × CH_2O), 3.60–3.69 (m, 1 H, CHO), 3.77–3.83 (m, 1 H, CHO), 4.10 (dd, 1 H, J = 7.8 Hz, J = 12.9 Hz, SCH_2), 4.30 (dd, 1 H, J = 6.0 Hz, J = 12.0 Hz, SCH_2), 4.79 (s, 1 H, OH), 4.89 (s, 1 H, OH), 5.08 (s, 1 H, OH), 5.15 (s, 1 H, OH), 7.51–8.02 (m, 4 H, Ar-H). ^{13}C NMR (150 MHz, DMSO-d_6), δ_c 36.41 (SCH_2), 64.96 (CH_2O), 71.01 (HC-O), 127.90, 130.95, 131.66, 131.91, 132.07, 156.11, 156.50 (Ar-C, C=N). Anal. Calcd. for $C_{18}H_{18}ClN_7O_6S_2$: C, 40.95; H, 3.44; N, 18.57. Found: C, 41.12; H, 3.27; N, 18.73. MS (ESI) *m/z*: 528.06 $[M+H]^+$.

5,5′-(1-(2-Chlorophenyl)-1*H*-1,2,3-triazole-4,5-diyl)bis(2-((2,2-dimethyl-1,3-dioxolan-4-yl)- methylthio)-1,3,4-oxadiazole) (19). This compound was obtained in 85% yield (from EtOH) as white solid. mp: 188–189°C. FT-IR ($\sqrt{}_{max}$, KBr/cm^{-1}): 1577 (C=C), 1615 (C=N), 3026 (C–H Ar). ^{1}H NMR (600 MHz, $CDCl_3$), δ_H 1.35, 1.39, 1.41, 1.44 (4s, 12 H, 4 × CH_3), 3.49 (dd, 2 H, J = 6.0 Hz, J = 11.7 Hz, SCH_2), 3.82 (dd, 1 H, J = 7.8 Hz, J = 10.5 Hz, CH_2O), 4.13 (dd, 1 H, J = 7.8 Hz, J = 10.5 Hz, CH_2O), 4.16–4.20 (m, 2 H, 2 × CH_2O), 4.22–4.30 (m, 2 H, SCH_2), 4.53–4.60 (m, 2 H, 2 × CHO), 7.44–7.88 (m, 4 H, Ar-H).^{13}C NMR (150 MHz, $CDCl_3$), δ_C 22.63, 23.80, 28.56, 29.70 (4 × Me), 38.07 (SCH_2), 51.44 (SCH_2), 68.89 (CH_2O), 70.05 (CH_2O), 76.94 (CHO), 77.19 (CHO), 127.09, 130.77, 131.52, 131.18, 132.70, 153.27, 159.56 (Ar-C, C=N). Anal. Calcd. for $C_{24}H_{26}ClN_7O_6S_2$: C, 47.40; H, 4.31; N, 16.12. Found: C, 47.25; H, 4.19; N, 16.29. MS (ESI) *m/z*: 608.14 $[M+H]^+$.

5,5′-(1-(2-Chlorophenyl)-1*H*-1,2,3-triazole-4,5-diyl)bis(2-(2-methoxyethylthio)-1,3,4-oxadiazole) (23). This compound was obtained in 90% yield (from EtOH) as colorless crystals. mp: 139–140°C. FT-IR ($\sqrt{}_{max}$, KBr/cm^{-1}):

1576 (C=C), 1613 (C=N), 3064 (CH-Ar). ^{1}H NMR (600 MHz, DMSO-d_6), δ_H 3.25 (s, 3 H, OCH_3), 3.27 (s, 3 H, OCH_3), 3.40 (t, 2 H, J = 6.0 Hz, SCH_2), 3.64 (t, 2 H, J = 6.0 Hz, CH_2O), 3.74 (t, 2 H, J = 6.0 Hz, CH_2O), 4.29 (t, 2 H, J = 6.0 Hz, SCH_2), 7.43–7.85 (m, 4 H, Ar-H). ^{13}C NMR (150 MHz, DMSO-d_6), δ_C 33.09 (SCH_2), 48.64 (SCH_2), 58.33 (OCH_3), 58.57 (OCH_3), 70.05 (CH_2O), 70.67 (CH_2O), 127.65, 130.09, 131.02, 131.55, 131.93, 152.78, 159.61 (Ar-C, C=N). Anal. Calcd. for $C_{18}H_{18}ClN_7O_4S_2$: C, 43.59; H, 3.66; N, 19.77. Found: C, 43.70; H, 3.79; N, 19.93. MS (ESI) *m/z*: 496.11 $[M+H]^+$.

5,5′-(1-(2-Chlorophenyl)-1*H*-1,2,3-triazole-4,5-diyl)bis(2-(2-ethoxyethylthio)-1,3,4-oxadiazole) (24). This compound was obtained in 91% yield (from EtOH) as colorless crystals. mp: 152–153°C. FT-IR ($\sqrt{}_{max}$, KBr/cm^{-1}): 1551 (C=C), 1610 (C=N), 3084 (CH-Ar). ^{1}H NMR (600 MHz, DMSO-d_6), δ_H 1.09 (t, 3 H, J = 6.0 Hz, CH_3), 1.16 (t, 3 H, J = 6.0 Hz, CH_3), 3.33 (t, 2 H, J = 6.0 Hz, SCH_2), 3.39–3.46 (m, 4 H, CH_2CH_3), 3.68 (t, 2 H, J = 6.0 Hz, CH_2O), 3.84 (t, 2 H, J = 6.0 Hz, CH_2O), 4.33 (t, 2 H, J = 6.0 Hz, SCH_2), 7.40–7.87 (m, 4 H, Ar-H). ^{13}C NMR (150 MHz, DMSO-d_6), δ_C 14.98 (CH_3), 15.47 (CH_3), 31.77 (SCH_2), 48.90 (SCH_2), 65.56 (CH_2CH_3), 67.34 (CH_2CH_3), 70.34 (CH_2O), 71.51 (CH_2O), 127.87, 130.56, 131.46, 131.94, 132.22, 153.41, 159.51 (Ar-C, C=N). Anal. Calcd. for $C_{20}H_{22}ClN_7O_4S_2$: C, 45.84; H, 4.23; N, 18.71. Found: C, 45.69; H, 4.16; N, 18.90. MS (ESI) *m/z*: 524.11 $[M+H]^+$.

5,5′-(1-(2-Chlorophenyl)-1H-1,2,3-triazole-4,5-diyl)bis(2-(oxiran-2-ylmethylthio)-1,3,4-oxadiazole) (25). This compound was obtained in 93% yield (from EtOH) as yellow crystals. mp 198–199°C. FT-IR ($\sqrt{}_{max}$, KBr/cm^{-1}): 1580 (C=C), 1620 (C=N), 3078 (C–H Ar). ^{1}H NMR (600 MHz, DMSO-d_6), δ_H 3.76 (d, 2 H, J = 6.0 Hz, SCH_2), 4.94 (d, 2 H, J = 6.0 Hz, SCH_2), 5.02, 5.08 (2dd, 2 H, J = 3.0 Hz, J = 15.9 Hz, CH_2O), 5.16, 5.26 (2dd, 2 H, J = 3 Hz, J = 11.7 Hz, CH_2O), 5.88–5.97 (m, 2 H, 2 × CHO), 7.50–8.07 (m, 4 H, Ar-H). ^{13}C NMR (150 MHz, DMSO-d_6), δ_c 38.22 (SCH_2), 66.41 (CH_2O), 73.79 (HC-O), 126.44, 132.41, 132.70, 132.97, 133.48, 156.38, 157.82 (Ar-C, C=N). Anal. Calcd. for $C_{18}H_{14}ClN_7O_4S_2$: C, 43.95; H, 2.87; N, 19.93. Found: C, 44.19; H, 2.76; N, 20.10. MS (ESI) *m/z*: 492.06 $[M+H]^+$.

General procedure for the synthesis of acetylated bis(acyclonucleoside) analogs 26–28. To a cold solution of **16, 17**, or **18** (1 mmol) in dry pyridine (5 ml), acetic anhydride (7 ml) was added, and the reaction mixture was maintained overnight at room temperature. Next, the mixture was poured into ice-cold water. The crude product was filtered and crystallized from ethanol.

2,2′-(5,5′-(1-(2-Chlorophenyl)-1*H*-1,2,3-triazole-4,5-diyl)bis(1,3,4-oxadiazole-5,2-diyl))bis- (sulfanediyl)bis(ethane-2,1-diyl)diacetate (26). This compound was obtained in 91% yield (from $CHCl_3$) as colorless plates. mp: 121–122°C. FT-IR ($\sqrt{}_{max}$, KBr/cm^{-1}): 1571 (C=C), 1598 (C=N), 1734 (C=O), 3063 (C–H Ar). ^{1}H NMR (400 MHz, $CDCl_3$), δ_H 2.00, 2.02 (2s, 6 H, 2 × CH_3), 3.48 (t, 2 H, J = 8.0 Hz, SCH_2), 4.35–4.43 (m, 6 H, NCH_2, 2 × CH_2O), 7.26–7.83 (m, 4 H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$), δ_c 20.86 (2 × CH_3), 32.32 (SCH_2), 47.78 (NCH_2), 62.02, 62.74 (2 × CH_2O), 126.74, 129.77, 130.23, 130.74, 131.31,

132.76, 152.15, 160.69 (Ar-C, C=N), 170.63, 170.73 (2 × C=O). Anal. Calcd. for $C_{20}H_{18}ClN_7O_6S_2$: C, 43.52; H, 3.29; N, 17.76. Found: C, 43.70; H, 3.39; N, 17.62. MS (ESI) *m/z*: 552.01 $[M+H]^+$.

2,2′-(5,5′-(1-(2-Chlorophenyl)-1*H*-1,2,3-triazole-4,5-diyl)bis(1,3,4-oxadiazole-5,2-diyl))bis- (sulfanediyl)bis(propane-3,1-diyl)diacetate (27). This compound was obtained in 90% (from EtOH) yield as colorless plates. mp: 106–107°C. FT-IR ($\sqrt{}_{max}$, KBr/cm^{-1}): 1547 (C=C), 1593 (C=N), 1724 (C=O), 3081 (C–H Ar). ^{1}H NMR (400 MHz, $CDCl_3$), δ_H 2.06, 2.10 (2s, 6 H, 2 × CH_3), 2.02–2.06 (m, 2 H, $CH_2CH_2CH_2$), 3.39 (t, 2 H, J = 8.0 Hz, SCH_2), 4.18 (t, 2 H, J = 8.0 Hz, NCH_2), 4.33 (t, 4 H, 2 × CH_2O), 7.35–7.80 (m, 4 H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$), δ_c 20.65, 21.81 (2 × CH_3), 32.08 (SCH_2), 46.94 (NCH_2), 62.35, 62.67 (2 × CH_2O), 126.90, 129.26, 130.64, 131.85, 132.10, 132.63, 152.67, 159.46 (Ar-C, C=N), 170.57, 171.82 (2 × C=O). Anal. Calcd. for $C_{22}H_{22}ClN_7O_6S_2$: C, 45.55; H, 3.82; N, 16.90. Found: C, 45.69; H, 3.94; N, 17.04. MS (ESI) *m/z*: 580.01 $[M+H]^+$.

(((1-(2-Chlorophenyl)-1*H*-1,2,3-triazole-4,5-diyl)bis(1,3,4-oxadiazole-5,2-diyl))bis-(sulfanediyl))bis(propane-3,1,2-triyl)tetraacetate (28). This compound was obtained in 87% yield (from $CHCl_3$) as colorless plates. FT-IR ($\sqrt{}_{max}$, KBr/cm^{-1}): 1567 (C=C), 1605 (C=N), 1738 (C=O), 3092 (C–H Ar). ^{1}H NMR (400 MHz, $CDCl_3$), δ_H 2.01, 2.05, 2.06, 2.09 (4s, 12 H, 4 × CH_3), 3.49 (dd, 2 H, J = 4.0 Hz, J = 8.0 Hz, SCH_2), 4.31 (dd, 2 H, J = 4.0 Hz, J = 8.0 Hz, NCH_2), 4.49–4.56 (m, 4 H, 2 × CH_2O), 5.52–5.58 (m, 2 H, 2 × CHO), 7.38–7.85 (m, 4 H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$), δ_c 20.66, 21.24, 21.53 (3 × CH_3), 33.68 (SCH_2), 48.07 (NCH_2), 65.80, 66.24 (2 × CH_2O), 72.77, 73.61 (2 × CHO), 126.56, 129.79, 131.35, 131.65, 132.66, 132.97, 152.19, 158.80 (Ar-C, C=N), 170.37, 171.34, 172.05 (3 × C=O). Anal. Calcd. for $C_{26}H_{26}ClN_7O_{10}S_2$: C, 44.86; H, 3.76; N, 17.16. Found: C, 44.98; H, 3.82; N, 17.04. MS (ESI) *m/z*: 696.12 $[M+H]^+$.

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