

Copper-catalyzed Synthesis and Antimicrobial Activity of Disubstituted 1,2,3-Triazoles Starting from 1-Propargyluracils and Ethyl (4-Azido-1,2,3-trihydroxybutyl)furan-3-carboxylate

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1,3-Dipolar cycloaddition reactions of 1-propargyluracils **2a–h** with the azido derivative **3** afforded the corresponding 1,2,3-triazoles **4a–h**. Hydrazinolysis of the esters **4a–h** gave the corresponding acid hydrazides **5a–h**. Reaction of **5a–h** with carbon disulfide in ethanol afforded **6a–h**. The antimicrobial activity of compounds **4–6** was determined.

Key words: 1,3-Dipolar Cycloaddition, 1,2,3-Triazoles, 1,3,4-Oxadiazoles, Antimicrobial Activity

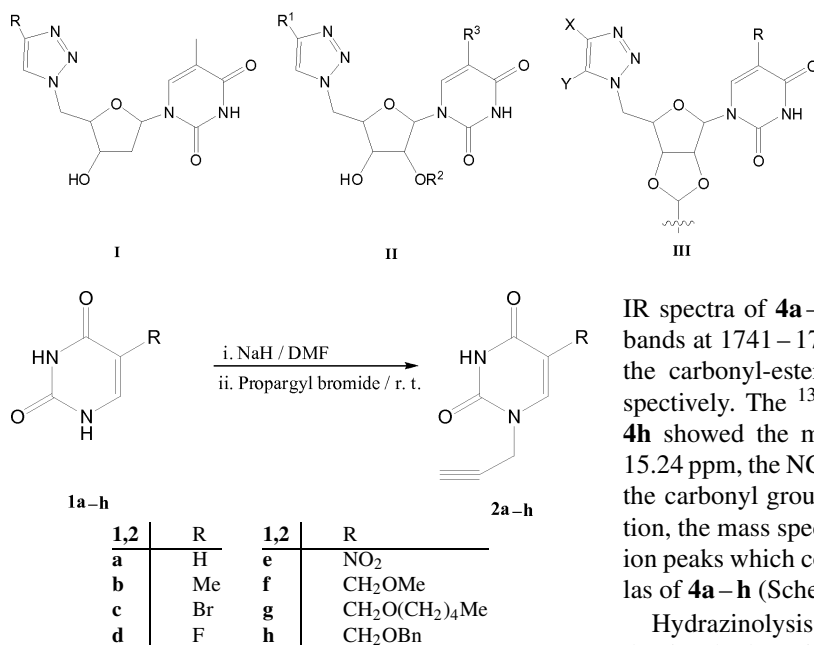
Introduction

The reaction of azides and alkynes yielding 1,2,3-triazoles is the most popular Huisgen 1,3-dipolar cycloaddition [1–3] and has found widespread application, *e. g.*, in combinatorial drug research and drug discovery processes [4–7]. The application of azide-alkyne cycloaddition as a common strategy to assemble ligands in the construction of multivalent structures as an important principle used to increase weak interactions to biologically relevant levels has been reported [8–10]. Furthermore, 1,3-dipolar cycloaddition reactions have long been popular in the generation of carbohydrate mimetics [11] with thermally induced Huisgen azide-alkyne cross-coupling [12] being used for the synthesis of *N*-glycosyl triazoles [13]. Triazole-substituted sugars have also been explored as potential monovalent and multivalent galectin ligands [14, 15] and for the investigation of substrate recognition and inhibition of glycosyltransferases [16, 17]. The 1,2,3-triazole nucleus is found in a large number of compounds with agrochemical and pharmaceutical uses [18], and shows activities, such as anti-HIV [19] anti-microbial [20], antibacterial [21], and antitumor [22] properties and has also found many applications in chemical industries [23]. Recently Zhou *et al.* [24] have reported the synthesis of 1,2,3-triazole-substituted thymidines **I** which are found to be antiviral. Synthesis of triazole-linked heterocycle nucleoside conjugates **II** was documented by Kosiova *et al.* [25].

These materials have wide applications as fluorescent probes and signaling units. Solid-phase synthesis of 1,2,3-triazolyl-uridines **III** from 5'-azidouridine and monosubstituted and carboxy-substituted alkyne components was reported by Eppele *et al.* [26] (Fig. 1). On the other hand, 1,3,4-oxadiazoles represent an important class of compounds which possess a broad spectrum of biological activity in both agrochemicals and pharmaceuticals, such as antibacterial [27], antimicrobial [28], insecticidal [29], herbicidal, fungicidal [30], anti-inflammatory [31], hypoglycaemic [32], hypotension [33] characteristics, antiviral [34], and anti-tumor [35]. Consequently, and as a part of our ongoing program aiming at the synthesis of new antimicrobial agents [36–39], we hypothesized that newly synthesized compounds containing a 1,2,3-triazolyl moiety linked through a trihydroxyalkyl chain of a substituted furan (carbohydrate mimics) to a 1,3,4-oxadiazolyl moiety can be expected to have enhanced biological activities as antimicrobial agents.

Results and Discussion

The coupling reaction of uracils **1a–h** with propargyl bromide was carried out as described in the literature for **2a, b** at r. t. in DMF in the presence of sodium hydride to afford 1-propargyluracils **2a–h** in 75–85 % yields (Scheme 1). The analytical data of **2a** and **b** are in agreement with those described in the literature [40]. The structure of **2c–h** was based on their spec-



Scheme 1. Synthesis of 1-propargyluracils.

tral data (IR, ¹H, ¹³C NMR and mass spectra) as well as elemental analyses. The ¹H NMR spectra showed a singlet peak at $\delta = 3.07$ – 3.22 ppm corresponding to the $\text{HC}\equiv\text{C}$ proton in addition to a singlet at $\delta = 3.92$ – 3.99 ppm for NCH_2 .

The recent advent of the Cu-catalyzed azide-alkyne cycloaddition [41], one of the most reliable click reactions [42], has enabled practical and efficient preparation of 1,4-disubstituted 1,2,3-triazoles from an unprecedented range of substrates. Thus, when the alkynes **2a–h** were treated with ethyl 5-(4-azido-1,2,3-trihydroxybutyl)furan-3-carboxylate (**3**) in *t*BuOH at 0 °C in the presence of 2,6-lutidine and a catalytic amount of CuI, the corresponding 1,2,3-triazoles **4a–h** were obtained in 85–94 % yield. It is believed that the starting point of the catalytic cycle for the copper-catalyzed Huisgen reaction is considered to be the formation of a Cu-acetylide complex [43, 44] which precludes alkynes as cycloaddition partners to give the 5-cuprated 1,4-disubstituted 1,2,3-triazole intermediate [45]. In general, no significant difference of reactivity was observed when reacting 1-propargyluracils **2a–h** with the azide **3** at the reaction times of 10–12 h for all derivatives, and no significant differences in yields were observed.

The structures of the 1,2,3-triazoles **4a–h** were confirmed by their spectral and analytical data. Thus, the

Fig. 1. 1,2,3-Triazoles linked to carbohydrate mimics.

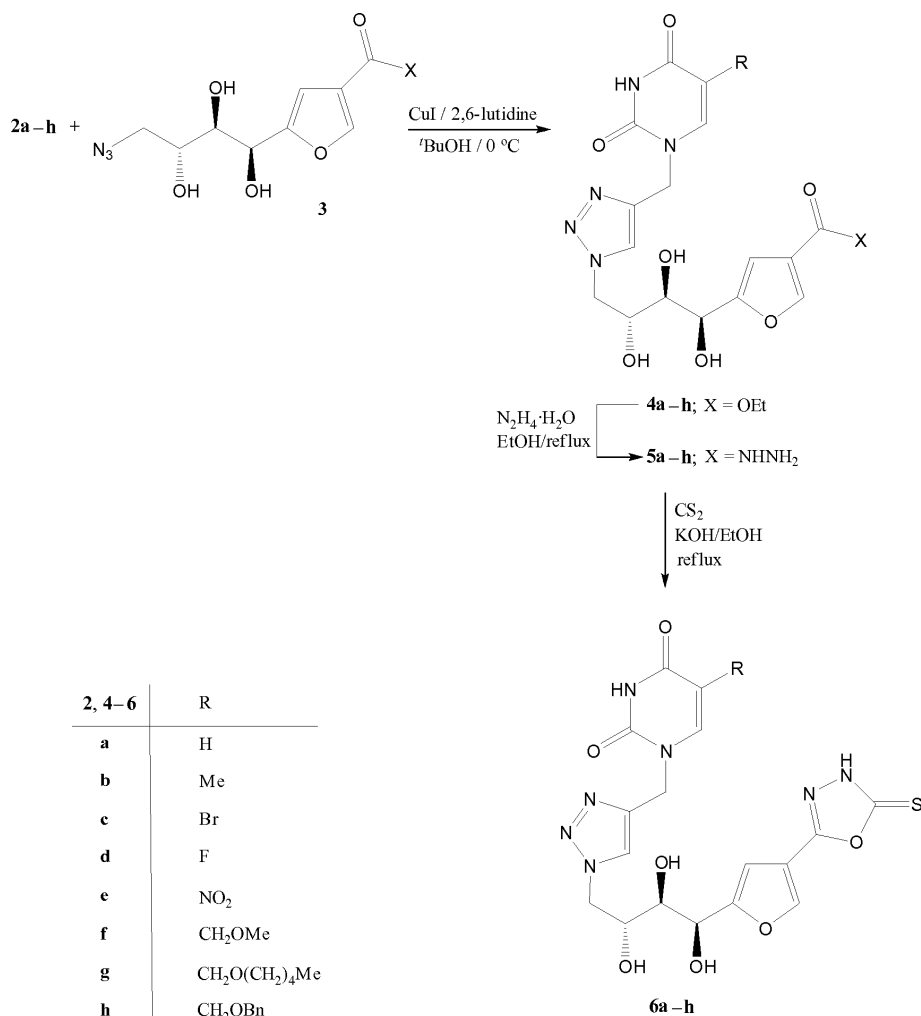
IR spectra of **4a–h** showed characteristic absorption bands at 1741 – 1735 cm^{-1} and 1676 – 1672 cm^{-1} for the carbonyl-ester and carbonyl-amid functions, respectively. The ¹³C NMR spectra of **4a**, **4b**, **4d** and **4h** showed the methyl group signal at $\delta = 15.20$ – 15.24 ppm, the NCH_2 signals at 46.95 – 52.84 ppm and the carbonyl groups at 164.21 – 164.25 ppm. In addition, the mass spectra showed signals of the molecular ion peaks which corresponded to the molecular formulas of **4a–h** (Scheme 2).

Hydrazinolysis of **4a–h** by treatment with hydrazine hydrate in ethanol at reflux temperature afforded the corresponding hydrazides **5a–h** in 84–91 % yields. The IR spectra of the products showed absorption bands at 1676 – 1682 cm^{-1} for carbonyl groups in addition to NH bands at 3362 – 3370 cm^{-1} . The ¹H NMR spectra revealed the disappearance of the ethyl signals, and instead signals appeared which correspond to NH_2 and NH groups (Scheme 2).

When the hydrazide derivatives **5a–h** were reacted with carbon disulfide in the presence of potassium hydroxide in ethanol at reflux temperature, the corresponding 1,3,4-oxadiazole derivatives **6a–h** were afforded in 80–91 % yields. The ¹³C NMR spectra of **6a**, **6b**, **6e** and **6f** showed a characteristic signal which corresponds to $\text{C}=\text{S}$ (Scheme 2).

Antimicrobial activity

The antimicrobial activity of compounds **4–6** was evaluated against the three microorganisms *Bacillus subtilis* (ATCC 6633) (Gram-positive), *Pseudomonas aeruginosa* (ATCC 27853) (Gram-negative), and *Streptomyces* species (Actinomycetes). Each of the test compounds and standards were dissolved in 12.5 % DMSO at concentrations of 500 $\mu\text{g/mL}$. Further dilutions of the compounds and standards in the test medium were prepared at the required quantities. Bacteria strains were supplied from the Botany Department, Faculty of Science, Menoufia University, Shebin El-Koam, Egypt. The bacterial strains were main-



Scheme 2. Synthesis of 1,2,3-triazoles.

tained on MHA (Mueller–Hinton agar) medium (Oxoid Chemical Co., UK) for 24 h at 37 °C. The medium was molten on a water bath, inoculated with 0.5 mL of the culture of the specific microorganism and poured into sterile Petri dishes to form a layer of about 3–4 mm thickness. The layer was allowed to cool and harden. With the aid of a cork-borer, cups of about 10 mm diameter were produced [46]. The activities were evaluated using MHA medium (17.5 g casein hydrolysate, 1.5 g soluble starch, 1000 mL beef extract). A stock solution of each compound (500 µg/mL) in DMSO was prepared, and graded quantities of the test compounds were incorporated in specified quantity of sterilized liquid MH medium. Different concentrations of the test compounds in DMF were placed separately in cups in the agar medium. All plates were incubated

at 37 °C overnight. The inhibition zones were measured after 24 h. The minimum inhibitory concentration (MIC) was defined as the intercept of the grave of logarithm concentrations *versus* the diameter of the inhibition zones [47].

The values of minimal inhibitory concentrations (MICs) of the tested compounds are presented in Table 1. The results of the antimicrobial activity test revealed that **5d**, **6d** and **6f** showed the highest activity against *B. subtilis* with MIC values of 75 µg mL⁻¹ followed by compounds **5f**, **6c**, **6d** and **6h**. Compounds **6d** and **6g** showed the highest inhibition activity against *P. aeruginosa*, whereas **5h**, **6f** and **6h** were the most active among the series of tested compounds against *Streptomyces* species with MIC values of 75 µg mL⁻¹. The results also revealed that

Table 1. Minimum inhibitory concentration (MIC in $\mu\text{g mL}^{-1}$) of the title compounds. The negative control DMSO showed no activity.

Compound	<i>Bacillus subtilis</i> (Gram-positive)	<i>Pseudomonas aeruginosa</i> (Gram-negative)	<i>Streptomyces</i> species (Actinomycetes)
4a	— ^a	— ^a	500
4b	500	250	— ^a
4c	250	500	500
4d	125	250	100
4e	500	— ^a	250
4f	250	125	250
4g	125	125	125
4h	250	125	125
5a	250	500	250
5b	250	125	250
5c	125	250	125
5d	100	125	100
5e	250	500	125
5f	75	125	125
5g	100	125	100
5h	125	125	75
6a	125	125	100
6b	125	100	125
6c	100	125	100
6d	75	75	100
6e	250	250	125
6f	75	100	75
6g	100	75	100
6h	100	100	75
Penicillin	31	46	33

^a Totally inactive (MIC > 500 $\mu\text{g mL}^{-1}$).

some compounds showed little or no activity against the microorganisms (Table 1).

From the structure-activity relationship it is clear that compounds containing the 1,2,3-triazolyl moiety linked through a trihydroxy alkyl chain of a substituted furyl ring (carbohydrate mimics) to a 1,3,4-oxadiazolyl moiety showed higher activity than the corresponding furyl-substituted esters or hydrazide derivatives. Furthermore, substitution at the 5-position in the uracil ring with a fluorine atom enhances the antimicrobial activity especially against *B. subtilis* and *P. aeruginosa*, whereas the activity was reduced when the 5-position was substituted with other groups. Moreover, substitution at the 5-position with a methoxy methyl group resulted in higher antimicrobial activity especially against *B. subtilis* and *P. Streptomyces*.

Experimental Section

All solvents were dried by standard methods. Melting points were determined with a Kofler block apparatus and are uncorrected. IR spectra were recorded with a Perkin-Elmer Model 1720 FTIR spectrometer. Specific rotations are given

for dimethylsulfoxide solutions. ^1H NMR spectra were determined with a Bruker AC-250 FT spectrometer. The chemical shifts in ppm are expressed on the δ scale using tetramethylsilane as internal standard. Coupling constants are given in Hz. Mass spectra were recorded on an AEIMS 30 spectrometer. TLC was performed on Merck silica gel 60-F254 pre-coated plastic plates. Microanalyses were performed in the unit of microanalysis at Tokyo University (Japan). Antimicrobial activity of the synthesized compounds was examined at the Botany Department, Faculty of Science, Menoufia University, Shebin El-Koam, Egypt.

General procedure for the preparation of 1-propargyluracils 2a–h

A mixture of an uracil derivative **1a–h** (10 mmol), sodium hydride (0.288 g, 12 mmol), and dry DMF (20 mL) was stirred at r. t. for 15 min at 0 °C, and the mixture was stirred overnight at r. t. After filtration, the solvent was removed *in vacuo*, and the residue was chromatographed on a silica gel column, using 0.5 % MeOH in CH_2Cl_2 to afford the propargylated products **2a–h** in 75–85 % yield.

5-Bromo-1-(prop-2-ynyl)pyrimidine-2,4(1H,3H)-dione (2c)

Yellow powder; m. p. 188–190 °C; yield: 1.74 g (76 %). – IR (KBr): $\nu = 1668$ (C=O), 3367 cm^{-1} (NH). – ^1H NMR ([D₆]DMSO): $\delta = 3.11$ (s, 1H, $\text{HC}\equiv\text{C}$ -), 3.98 (s, 2H, NCH_2), 8.11 (s, 1H, 6-H), 9.96 (brs, 1H, NH). – ^{13}C NMR ([D₆]DMSO): $\delta = 35.80$ (CH_2), 76.65 ($\text{HC}\equiv\text{C}$), 81.25 ($\text{HC}\equiv\text{C}$), 104.18 (C-5), 149.50 (C-6), 153.68 (C-2), 158.88 (C-4). – MS (EI, 70 eV): m/z (%) = 228/230 (82) [$\text{M}]^+$. – $\text{C}_7\text{H}_5\text{BrN}_2\text{O}_2$ (229.03): calcd. C 36.71, H 2.20, N 12.23; found C 36.60, H 2.13, N 12.09.

5-Fluoro-1-(prop-2-ynyl)pyrimidine-2,4(1H,3H)-dione (2d)

Colorless powder; m. p. 169–171 °C; yield: 1.22 g (73 %). – IR (KBr): $\nu = 1670$ (C=O), 3359 cm^{-1} (NH). – ^1H NMR ([D₆]DMSO): $\delta = 3.07$ (s, 1H, $\text{HC}\equiv\text{C}$ -), 3.95 (s, 2H, NCH_2), 8.07 (s, 1H, 6-H), 9.93 (brs, 1H, NH). – MS (EI, 70 eV): m/z (%) = 168 (75) [$\text{M}]^+$. – $\text{C}_7\text{H}_5\text{FN}_2\text{O}_2$ (168.13): calcd. C 50.01, H 3.00, N 16.66; found C 49.79, H 2.85, N 16.45.

5-Nitro-1-(prop-2-ynyl)pyrimidine-2,4(1H,3H)-dione (2e)

Pale-yellow powder; m. p. 197–199 °C; yield: 1.46 g (75 %). – IR (KBr): $\nu = 1672$ (C=O), 3369 cm^{-1} (NH). – ^1H NMR ([D₆]DMSO): $\delta = 3.22$ (s, 1H, $\text{HC}\equiv\text{C}$ -), 3.97 (s, 2H, NCH_2), 9.80 (s, 1H, 6-H), 9.90 (brs, 1H, NH). – MS (EI, 70 eV): m/z (%) = 195 (63) [$\text{M}]^+$. – $\text{C}_7\text{H}_5\text{N}_3\text{O}_4$ (195.13): calcd. C 43.09, H 2.58, N 21.53; found C 42.88, H 2.41, N 21.34.

5-Methoxymethyl-1-(prop-2-ynyl)pyrimidine-2,4(1H,3H)-dione (2f)

Colorless powder; m.p. 155–157 °C; yield: 1.53 g (79 %). – IR (KBr): ν = 1667 (C=O), 3365 cm^{-1} (NH). – ^1H NMR ([D₆]DMSO): δ = 3.16 (s, 1H, HC≡C-), 3.39 (s, 3H, OCH₃), 3.99 (s, 2H, NCH₂), 4.12 (s, 2H, OCH₂), 7.89 (s, 1H, 6-H), 9.88 (brs, 1H, NH). – ^{13}C NMR ([D₆]DMSO): δ = 35.72 (CH₂), 58.24 (OCH₃), 63.28 (CH₂), 76.89 (HC≡C), 81.80 (HC≡C), 111.18 (C-5), 148.58 (C-2), 153.68 (C-6), 160.88 (C-4). – MS (EI, 70 eV): m/z (%) = 194 (73) [M]⁺. – C₉H₁₀N₂O₃ (194.19): calcd. C 55.67, H 5.19, N 14.43; found C 55.51, H 5.13, N 14.37.

5-Pentyloxymethyl-1-(prop-2-ynyl)pyrimidine-2,4(1H,3H)-dione (2g)

Colorless powder; m.p. 148–150 °C; yield: 2.07 g (83 %). – IR (KBr): ν = 1670 (C=O), 3368 cm^{-1} (NH). – ^1H NMR ([D₆]DMSO): δ = 0.94 (t, 3H, J = 5.5 Hz, CH₃), 1.33–1.55 (m, 6H, 3CH₂), 3.16 (s, 1H, HC≡C-), 3.36 (t, 2H, J = 5.6 Hz, OCH₂), 3.92 (s, 2H, NCH₂), 4.16 (s, 2H, OCH₂), 7.83 (s, 1H, 6-H), 9.79 (brs, 1H, NH). – MS (EI, 70 eV): m/z (%) = 250 (80) [M]⁺. – C₁₃H₁₈N₂O₃ (250.29): calcd. C 62.38, H 7.25, N 11.19; found C 62.23, H 7.12, N 11.07.

5-Benzyloxymethyl-1-(prop-2-ynyl)pyrimidine-2,4(1H,3H)-dione (2h)

Colorless powder; m.p. 181–183 °C; yield: 2.29 g (85 %). – IR (KBr): ν = 1675 (C=O), 3359 cm^{-1} (NH). – ^1H NMR ([D₆]DMSO): δ = 3.12 (s, 1H, HC≡C-), 3.98 (s, 2H, NCH₂), 4.13 (s, 2H, OCH₂), 4.86 (s, 2H, OCH₂), 7.33–7.48 (m, 5H, Ar-H), 7.79 (s, 1H, 6-H), 9.82 (brs, 1H, NH). – ^{13}C NMR ([D₆]DMSO): δ = 35.85 (CH₂), 61.10, 61.28 (2 CH₂), 76.85 (HC≡C), 81.82 (HC≡C), 111.21 (C-5), 116.60, 120.37, 127.56, 151.15, 153.46, 155.07 (Ar-C, C-2, C-6), 160.82 (C-4). – MS (EI, 70 eV): m/z (%) = 270 (80) [M]⁺. – C₁₅H₁₄N₂O₃ (270.28): calcd. C 66.66, H 5.22, N 10.36; found C 66.51, H 5.18, N 10.21.

General procedure for the synthesis of 5-substituted ethyl 5-((1S,2R,3R)-4-{4-[(2,4-dioxo-3,4-dihydropyrimidin-1(2H)yl)methyl]-1H-1,2,3-triazol-1-yl}-1,2,3-trihydroxybutyl)furan-3-carboxylates 4a–h

A solution of an alkyne **2a–h** (5 mmol), the respective azide **3** (4 mmol), 2,6-lutidine (5 mmol), and CuI (0.4 mmol) in *t*BuOH (10 mL) was stirred for 10–12 h at 0 °C. The solvent was evaporated under reduced pressure, and the residue was purified by silica gel column chromatography using 0.3 % MeOH in CH₂Cl₂ to afford the corresponding 1,2,3-triazole derivatives **4a–h**.

Ethyl 5-((1S,2R,3R)-4-{4-[(2,4-dioxo-3,4-dihydropyrimidin-1(2H)yl)methyl]-1H-1,2,3-triazol-1-yl}-1,2,3-trihydroxybutyl)furan-3-carboxylate (4a)

Colorless powder; m.p. 260–262 °C; yield: 3.87 g (89 %). – $[\alpha]_D$: +40. – IR (KBr): ν = 1669 (C=O), 1735 (C=O), 3358 (NH), 3475 cm^{-1} (OH). – ^1H NMR ([D₆]DMSO): δ = 1.30 (t, 3H, J = 5.2 Hz, CH₃CH₂), 3.30 (m, 1H, CH), 3.58 (brs, 3H, 3 OH), 3.71 (m, 1H, CH), 3.79, 4.00 (2d, 2H, J = 4.0 Hz, NCH₂), 4.32 (q, 2H, J = 5.2 Hz, CH₃CH₂), 4.51 (s, 2H, NCH₂), 4.83 (m, 1H, CH), 5.79 (d, 1H, J = 6.5 Hz, 5-H), 6.75 (s, 1H, 4-H furan), 7.65 (s, 1H, 5-H triazole), 7.83 (s, 1H, 2-H furan), 9.66 (d, 1H, J = 6.5 Hz, 6-H), 9.92 (brs, 1H, NH). – ^{13}C NMR ([D₆]DMSO): δ = 15.20 (CH₃), 47.75, 52.84 (2 NCH₂), 60.42 (CH₂), 62.15 (OCH₂), 74.24, 75.12, 76.18 (3 CH), 104.22, 112.52, 116.68, 120.37, 123.24, 127.59, 136.71, 147.29, 150.18, 154.41, 155.36 (Ar-C, C-2, C-5, C-6), 160.14 (C-4), 164.24 (C=O). – MS (EI, 70 eV): m/z (%) = 435 (43) [M]⁺. – C₁₈H₂₁N₅O₈ (435.39): calcd. C 49.66, H 4.86, N 16.09; found C 49.45, H 4.65, N 15.88.

Ethyl 5-((1S,2R,3R)-4-{4-[(5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)yl)methyl]-1H-1,2,3-triazol-1-yl}-1,2,3-trihydroxybutyl)furan-3-carboxylate (4b)

Colorless powder; m.p. 231–233 °C; yield: 4.19 g (92 %). – $[\alpha]_D$: +6.9. – IR (KBr): ν = 1667 (C=O), 1738 (C=O), 3360 (NH), 3477 cm^{-1} (OH). – ^1H NMR ([D₆]DMSO): δ = 1.23 (t, 3H, J = 5.2 Hz, CH₃CH₂), 2.45 (s, 3H, CH₃), 3.27 (m, 1H, CH), 3.58 (brs, 3H, 3 OH), 3.71 (m, 1H, CH), 3.83, 4.03 (2d, 2H, J = 4.0 Hz, NCH₂), 4.29 (q, 2H, J = 5.2 Hz, CH₃CH₂), 4.56 (s, 2H, NCH₂), 4.78 (m, 1H, CH), 6.83 (s, 1H, 4-H furan), 7.63 (s, 1H, 6-H), 7.67 (s, 1H, 5-H triazole), 7.79 (s, 1H, 2-H furan), 9.98 (brs, 1H, NH). – ^{13}C NMR ([D₆]DMSO): δ = 14.88 (CH₃), 15.24 (CH₃), 47.71, 53.28 (2 NCH₂), 60.45 (CH₂), 62.32 (OCH₂), 74.21, 75.32, 76.20 (3 CH), 104.31, 112.55, 116.49, 120.35, 123.24, 127.51, 136.70, 147.33, 150.52, 154.92, 155.80 (Ar-C, C-2, C-5, C-6), 160.35 (C-4), 164.25 (C=O). – MS (EI, 70 eV): m/z (%) = 449 (32) [M]⁺. – C₁₉H₂₃N₅O₈ (449.41): calcd. C 50.78, H 5.16, N 15.58; found C 50.59, H 5.03, N 15.43.

Ethyl 5-((1S,2R,3R)-4-{4-[(5-bromo-2,4-dioxo-3,4-dihydropyrimidin-1(2H)yl)methyl]-1H-1,2,3-triazol-1-yl}-1,2,3-trihydroxybutyl)furan-3-carboxylate (4c)

Yellow powder; m.p. 288–290 °C; yield: 4.52 g (88 %). – $[\alpha]_D$: +0.3. – IR (KBr): ν = 1668 (C=O), 1737 (C=O), 3364 (NH), 3472 cm^{-1} (OH). – ^1H NMR ([D₆]DMSO): δ = 1.27 (t, 3H, J = 5.2 Hz, CH₃CH₂), 3.33 (m, 1H, CH), 3.58 (brs, 3H, 3 OH), 3.70 (m, 1H, CH), 3.75, 4.03 (2d, 2H, J = 4.0 Hz, NCH₂), 4.38 (q, 2H, J = 5.2 Hz, CH₃CH₂), 4.49 (s, 2H, NCH₂), 4.80 (m, 1H, CH), 6.78 (s, 1H, 4-H furan), 7.59 (s,

1H, 5-H triazole), 7.80 (s, 1H, 2-H furan), 8.11 (s, 1H, 6-H), 9.88 (brs, 1H, NH). – MS (EI, 70 eV): m/z (%) = 513/515 (22) $[M]^+$. – $C_{18}H_{20}BrN_5O_8$ (514.28): calcd. C 42.04, H 3.92, N 13.62; found C 41.89, H 3.83, N 13.56.

Ethyl 5-[(1S,2R,3R)-4-{4-[(5-flouro-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)methyl]-1H-1,2,3-triazol-1-yl}-1,2,3-trihydroxybutyl]furan-3-carboxylate (4d)

Colorless powder; m.p. 270–272 °C; yield: 3.94 g (87 %). – $[\alpha]_D$: +13. – IR (KBr): ν = 1668 (C=O), 1735 (C=O), 3363 (NH), 3477 cm^{-1} (OH). – 1H NMR ($[D_6]DMSO$): δ = 1.33 (t, 3H, J = 5.2 Hz, CH_3CH_2), 3.27 (m, 1H, CH), 3.54 (brs, 3H, 3 OH), 3.66 (m, 1H, CH), 3.81, 4.07 (2d, 2H, J = 4.0 Hz, NCH_2), 4.36 (q, 2H, J = 5.2 Hz, CH_3CH_2), 4.48 (s, 2H, NCH_2), 4.87 (m, 1H, CH), 6.70 (s, 1H, 4-H furan), 7.71 (s, 1H, 5-H triazole), 7.87 (s, 1H, 2-H furan), 8.05 (s, 1H, 6-H), 9.81 (brs, 1H, NH). – ^{13}C NMR ($[D_6]DMSO$): δ = 15.22 (CH_3), 47.68, 53.50 (2 NCH_2), 60.51 (CH_2), 62.18 (OCH_2), 74.33, 75.94, 76.87 (3 CH), 104.30, 112.52, 116.65, 120.40, 123.24, 127.62, 136.83, 147.48, 150.19, 154.41, 155.31 (Ar-C, C-2, C-5, C-6), 159.18 (C-4), 164.24 (C=O). – MS (EI, 70 eV): m/z (%) = 453 (28) $[M]^+$. – $C_{18}H_{20}FN_5O_8$ (453.38): calcd. C 47.68, H 4.45, N 15.45; found C 47.51, H 4.29, N 15.31. *Ethyl*

5-[(1S,2R,3R)-4-{4-[(5-nitro-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)methyl]-1H-1,2,3-triazol-1-yl}-1,2,3-trihydroxybutyl]furan-3-carboxylate (4e)

Pale-yellow powder; m.p. 266–268 °C; yield: 4.08 g (85 %). – $[\alpha]_D$: +12.7. – IR (KBr): ν = 1672 (C=O), 1740 (C=O), 3368 (NH), 3479 cm^{-1} (OH). – 1H NMR ($[D_6]DMSO$): δ = 1.23 (t, 3H, J = 5.2 Hz, CH_3CH_2), 3.25 (m, 1H, CH), 3.49 (brs, 3H, 3 OH), 3.66 (m, 1H, CH), 3.70, 3.98 (2d, 2H, J = 4.0 Hz, NCH_2), 4.39 (q, 2H, J = 5.2 Hz, CH_3CH_2), 4.56 (s, 2H, NCH_2), 4.87 (m, 1H, CH), 6.71 (s, 1H, 4-H furan), 7.60 (s, 1H, 5-H triazole), 7.85 (s, 1H, 2-H furan), 9.80 (s, 1H, 6-H), 9.99 (brs, 1H, NH). – MS (EI, 70 eV): m/z (%) = 480 (32) $[M]^+$. – $C_{18}H_{20}N_6O_{10}$ (480.39): calcd. C 45.00, H 4.20, N 17.49; found C 44.81, H 4.07, N 17.36.

Ethyl 5-[(1S,2R,3R)-4-{4-[(5-methoxymethyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)methyl]-1H-1,2,3-triazol-1-yl}-1,2,3-trihydroxybutyl]furan-3-carboxylate (4f)

Colorless powder; m.p. 239–241 °C; yield: 4.45 g (93 %). – $[\alpha]_D$: +43. – IR (KBr): ν = 1669 (C=O), 1739 (C=O), 3368 (NH), 3475 cm^{-1} (OH). – 1H NMR ($[D_6]DMSO$): δ = 1.28 (t, 3H, J = 5.2 Hz, CH_3CH_2), 3.25 (m, 1H, CH), 3.40 (s, 3H, OCH_3), 3.56 (brs, 3H, 3 OH), 3.78 (m, 1H, CH), 3.70–4.08 (m, 4H, NCH_2 , OCH_2), 4.44 (q, 2H, J = 5.2 Hz, CH_3CH_2), 4.50 (s, 2H, NCH_2), 4.80 (m, 1H,

CH), 6.74 (s, 1H, 4-H furan), 7.68 (s, 1H, 5-H triazole), 7.70 (s, 1H, 6-H), 7.87 (s, 1H, 2-H furan), 9.80 (brs, 1H, NH). – MS (EI, 70 eV): m/z (%) = 479 (12) $[M]^+$. – $C_{20}H_{25}N_5O_9$ (479.44): calcd. C 50.10, H 5.26, N 14.61; found C 50.03, H 5.13, N 14.55.

Ethyl 5-[(1S,2R,3R)-4-{4-[(5-pentoxymethyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)methyl]-1H-1,2,3-triazol-1-yl}-1,2,3-trihydroxybutyl]furan-3-carboxylate (4g)

Colorless powder; m.p. 215–217 °C; yield: 4.92 g (92 %). – $[\alpha]_D$: +21. – IR (KBr): ν = 1668 (C=O), 1740 (C=O), 3368 (NH), 3474 cm^{-1} (OH). – 1H NMR ($[D_6]DMSO$): δ = 0.90 (t, 3H, J = 5.5 Hz, CH_3), 1.23–1.50 (m, 8H, 3 CH_2 , CH_3CH_2), 3.30–3.40 (m, 3H, CH, OCH_2), 3.58 (brs, 3H, 3 OH), 3.77 (m, 1H, CH), 3.78–4.09 (m, 4H, NCH_2 , OCH_2), 4.39 (q, 2H, J = 5.2 Hz, CH_3CH_2), 4.47 (s, 2H, NCH_2), 4.88 (m, 1H, CH), 6.71 (s, 1H, 4-H furan), 7.60 (s, 1H, 5-H triazole), 7.71 (s, 1H, 6-H), 7.86 (s, 1H, 2-H furan), 9.90 (brs, 1H, NH). – MS (EI, 70 eV): m/z (%) = 535 (11) $[M]^+$. – $C_{24}H_{33}N_5O_9$ (535.55): calcd. C 53.82, H 6.21, N 13.08; found C 53.67, H 6.11, N 13.01.

Ethyl 5-[(1S,2R,3R)-4-{4-[(5-benzyloxymethyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)methyl]-1H-1,2,3-triazol-1-yl}-1,2,3-trihydroxybutyl]furan-3-carboxylate (4h)

Colorless powder; m.p. 227–229 °C; yield: 5.21 g (94 %). – $[\alpha]_D$: +34.1. – IR (KBr): ν = 1670 (C=O), 1741 (C=O), 3368 (NH), 3479 cm^{-1} (OH). – 1H NMR ($[D_6]DMSO$): δ = 1.27 (t, 3H, J = 5.2 Hz, CH_3CH_2), 3.30 (m, 1H, CH), 3.57 (brs, 3H, 3 OH), 3.70 (m, 1H, CH), 3.80–4.09 (m, 4H, NCH_2 , OCH_2), 4.37 (q, 2H, J = 5.2 Hz, CH_3CH_2), 4.58 (s, 2H, NCH_2), 4.79–4.85 (m, 3H, CH, OCH_2), 6.73 (s, 1H, 4-H furan), 7.38–7.50 (m, 5H, Ar-H), 7.64 (s, 1H, 5-H triazole), 7.73 (s, 1H, 6-H), 7.80 (s, 1H, 2-H furan), 9.81 (brs, 1H, NH). – ^{13}C NMR ($[D_6]DMSO$): δ = 15.27 (CH_3), 46.95, 53.32 (2 NCH_2), 60.12, 60.24, 61.38 (3 CH_2), 74.39, 75.18, 76.77 (3 CH), 102.21, 104.48, 120.59, 124.53, 136.76, 146.37, 150.24, 151.87, 155.43 (Ar-C, C-2, C-5, C-6), 160.05 (C-4), 164.21 (C=O). – MS (EI, 70 eV): m/z (%) = 555 (17) $[M]^+$. – $C_{26}H_{29}N_5O_9$ (555.54): calcd. C 56.21, H 5.26, N 12.61; found C 56.11, H 5.12, N 12.44.

General procedure for the synthesis of 5-substituted 5-[(1S,2R,3R)-4-{4-[(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)methyl]-1H-1,2,3-triazol-1-yl}-1,2,3-trihydroxybutyl]furan-3-carbohydrazides 5a–h

To a solution of an ethyl ester **4a–h** (10 mmol) in EtOH (15 mL) was added hydrazine hydrate (0.5 g, 10 mmol), and the reaction mixture was heated under reflux for 4–5 h. The volume of the solvent was reduced under vacuum, and the precipitated solid was filtered, washed with cold ethanol and recrystallized from ethanol to afford the hydrazides **5a–h**.

5-*[(1S,2R,3R)-4-{4-[(2,4-Dioxo-3,4-dihydropyrimidin-1(2H)-yl)methyl]-1H-1,2,3-triazol-1-yl}-1,2,3-trihydroxybutyl]furan-3-carbohydrazide (5a)*

Colorless powder; m.p. 312–314 °C; yield: 3.91 g (90 %). – $[\alpha]_D$: +21. – IR (KBr): ν = 1680 (C=O), 3367 (NH), 3480 cm^{-1} (OH). – ^1H NMR ($[\text{D}_6]\text{DMSO}$): δ = 3.32 (m, 1H, CH), 3.57 (brs, 3H, 3 OH), 3.75 (m, 1H, CH), 3.82, 4.02 (2d, 2H, J = 4.0 Hz, NCH_2), 4.50 (s, 2H, NCH_2), 4.85 (m, 1H, CH), 5.76 (brs, 2H, NH_2), 5.81 (d, 1H, J = 6.5 Hz, 5-H), 6.77 (s, 1H, 4-H furan), 7.67 (s, 1H, 5-H triazole), 7.85 (s, 1H, 2-H furan), 8.98 (brs, 1H, NH), 9.68 (d, 1H, J = 6.5 Hz, 6-H), 9.91 (brs, 1H, NH). – ^{13}C NMR ($[\text{D}_6]\text{DMSO}$): δ = 47.82, 52.29 (2 NCH_2), 74.29, 75.15, 77.10 (3 CH), 103.28, 104.37, 121.82, 123.27, 127.71, 136.70, 137.66, 147.25, 151.19, 155.42 (Ar-C, C-2, C-5, C-6), 160.18 (C-4), 165.20 (C=O). – MS (EI, 70 eV): m/z (%) = 422 (35) $[\text{M}+1]^+$.

5-*[(1S,2R,3R)-4-{4-[(5-Methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)methyl]-1H-1,2,3-triazol-1-yl}-1,2,3-trihydroxybutyl]furan-3-carbohydrazide (5b)*

Colorless powder; m.p. 280–282 °C; yield: 4.09 g (91 %). – $[\alpha]_D$: +7.8. – IR (KBr): ν = 1678 (C=O), 3370 (NH), 3475 cm^{-1} (OH). – ^1H NMR ($[\text{D}_6]\text{DMSO}$): δ = 2.32 (s, 3H, CH_3), 3.29 (m, 1H, CH), 3.56 (brs, 3H, 3 OH), 3.72 (m, 1H, CH), 3.82, 4.05 (2d, 2H, J = 4.0 Hz, NCH_2), 4.59 (s, 2H, NCH_2), 4.80 (m, 1H, CH), 5.77 (brs, 2H, NH_2), 6.85 (s, 1H, 4-H furan), 7.66 (s, 1H, 6-H), 7.69 (s, 1H, 5-H triazole), 7.84 (s, 1H, 2-H furan), 8.96 (brs, 1H, NH), 9.94 (brs, 1H, NH). – MS (EI, 70 eV): m/z (%) = 436 (24) $[\text{M}+1]^+$.

5-*[(1S,2R,3R)-4-{4-[(5-Bromo-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)methyl]-1H-1,2,3-triazol-1-yl}-1,2,3-trihydroxybutyl]furan-3-carbohydrazide (5c)*

Colorless powder; m.p. 322–324 °C; yield: 4.57 g (89 %). – $[\alpha]_D$: +0.1. – IR (KBr): ν = 1682 (C=O), 3368 (NH), 3477 cm^{-1} (OH). – ^1H NMR ($[\text{D}_6]\text{DMSO}$): δ = 3.34 (m, 1H, CH), 3.58 (brs, 3H, 3 OH), 3.71 (m, 1H, CH), 3.77, 4.04 (2d, 2H, J = 4.0 Hz, NCH_2), 4.50 (s, 2H, NCH_2), 4.82 (m, 1H, CH), 5.84 (brs, 2H, NH_2), 6.77 (s, 1H, 4-H furan), 7.70 (s, 1H, 5-H triazole), 7.84 (s, 1H, 2-H furan), 8.14 (s, 1H, 6-H), 9.02 (brs, 1H, NH), 9.90 (brs, 1H, NH). – ^{13}C NMR ($[\text{D}_6]\text{DMSO}$): δ = 47.74, 53.87 (2 NCH_2), 74.27, 75.14, 76.21 (3 CH), 103.26, 106.15, 121.40, 123.37, 136.72, 137.69, 145.31, 151.23, 154.38 (Ar-C, C-2, C-5, C-6), 157.20 (C-4), 165.29 (C=O). – MS (EI, 70 eV): m/z (%) = 500/502 (16) $[\text{M}+1]^+$.

5-*[(1S,2R,3R)-4-{4-[(5-Fluoro-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)methyl]-1H-1,2,3-triazol-1-yl}-1,2,3-trihydroxybutyl]furan-3-carbohydrazide (5d)*

Colorless powder; m.p. 293–295 °C; yield: 4.08 g (90 %). – $[\alpha]_D$: +17. – IR (KBr): ν = 1677 (C=O), 3369

(NH), 3473 cm^{-1} (OH). – ^1H NMR ($[\text{D}_6]\text{DMSO}$): δ = 3.29 (m, 1H, CH), 3.52 (brs, 3H, 3 OH), 3.63 (m, 1H, CH), 3.82, 4.11 (2d, 2H, J = 4.0 Hz, NCH_2), 4.49 (s, 2H, NCH_2), 4.92 (m, 1H, CH), 5.82 (brs, 2H, NH_2), 6.74 (s, 1H, 4-H furan), 7.75 (s, 1H, 5-H triazole), 7.88 (s, 1H, 2-H furan), 8.04 (s, 1H, 6-H), 8.96 (brs, 1H, NH), 9.80 (brs, 1H, NH). – MS (EI, 70 eV): m/z (%) = 440 (22) $[\text{M}+1]^+$.

5-*[(1S,2R,3R)-4-{4-[(5-Nitro-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)methyl]-1H-1,2,3-triazol-1-yl}-1,2,3-trihydroxybutyl]furan-3-carbohydrazide (5e)*

Colorless powder; m.p. 273–275 °C; yield: 4.08 g (85 %). – $[\alpha]_D$: +10. – IR (KBr): ν = 1681 (C=O), 3370 (NH), 3478 cm^{-1} (OH). – ^1H NMR ($[\text{D}_6]\text{DMSO}$): δ = 3.28 (m, 1H, CH), 3.48 (brs, 3H, 3 OH), 3.64 (m, 1H, CH), 3.73, 4.05 (2d, 2H, J = 4.0 Hz, NCH_2), 4.58 (s, 2H, NCH_2), 4.86 (m, 1H, CH), 5.80 (brs, 2H, NH_2), 6.70 (s, 1H, 4-H furan), 7.62 (s, 1H, 5-H triazole), 7.88 (s, 1H, 2-H furan), 9.11 (brs, 1H, NH), 9.89 (s, 1H, 6-H), 10.02 (brs, 1H, NH). – MS (EI, 70 eV): m/z (%) = 467 (32) $[\text{M}+1]^+$.

5-*[(1S,2R,3R)-4-{4-[(5-Methoxymethyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)methyl]-1H-1,2,3-triazol-1-yl}-1,2,3-trihydroxybutyl]furan-3-carbohydrazide (5f)*

Colorless powder; m.p. 267–269 °C; yield: 4.16 g (87 %). – $[\alpha]_D$: +37. – IR (KBr): ν = 1680 (C=O), 3368 (NH), 3480 cm^{-1} (OH). – ^1H NMR ($[\text{D}_6]\text{DMSO}$): δ = 3.24 (m, 1H, CH), 3.42 (s, 3H, OCH_3), 3.55 (brs, 3H, 3 OH), 3.78 (m, 1H, CH), 3.72–4.11 (m, 4H, NCH_2 , OCH_2), 4.48 (s, 2H, NCH_2), 4.78 (m, 1H, CH), 5.78 (brs, 2H, NH_2), 6.70 (s, 1H, 4-H furan), 7.69 (s, 1H, 5-H triazole), 7.71 (s, 1H, 6-H), 7.86 (s, 1H, 2-H furan), 9.05 (brs, 1H, NH), 9.85 (brs, 1H, NH). – ^{13}C NMR ($[\text{D}_6]\text{DMSO}$): δ = 47.68, 53.75 (2 NCH_2), 57.35 (OCH_3), 63.32 (OCH_2), 74.25, 75.16, 76.24 (3 CH), 106.26, 112.20, 121.39, 123.26, 136.75, 137.69, 145.21, 151.20, 155.31 (Ar-C, C-2, C-5, C-6), 160.14 (C-4), 166.20 (C=O) pm. – MS (EI, 70 eV): m/z (%) = 466 (18) $[\text{M}+1]^+$.

5-*[(1S,2R,3R)-4-{4-[(5-Pentoxymethyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)methyl]-1H-1,2,3-triazol-1-yl}-1,2,3-trihydroxybutyl]furan-3-carbohydrazide (5g)*

Colorless powder; m.p. 239–241 °C; yield: 4.62 g (84 %). – $[\alpha]_D$: +17. – IR (KBr): ν = 1676 (C=O), 3362 (NH), 3478 cm^{-1} (OH). – ^1H NMR ($[\text{D}_6]\text{DMSO}$): δ = 1.22–1.50 (m, 9H, 3 CH_2 , CH_3CH_2), 3.31–3.42 (m, 3H, CH, OCH_2), 3.58 (brs, 3H, 3 OH), 3.74 (m, 1H, CH), 3.78–4.10 (m, 4H, NCH_2 , OCH_2), 4.48 (s, 2H, NCH_2), 4.86 (m, 1H, CH), 5.80 (brs, 2H, NH_2), 6.77 (s, 1H, 4-H furan), 7.72 (s, 1H, 5-H triazole), 7.78 (s, 1H, 6-H), 7.88 (s, 1H, 2-H furan), 9.02 (brs, 1H, NH), 9.94 (brs, 1H, NH). – ^{13}C

NMR ([D₆]DMSO): δ = 16.24 (CH₃), 26.18, 31.88, 36.15 (3 CH₂), 47.71, 53.77 (2 NCH₂), 63.42, 67.62 (2 OCH₂), 74.28, 75.18, 76.25 (3 CH), 106.26, 112.22, 121.42, 123.26, 136.77, 137.70, 145.24, 151.21, 155.42 (Ar-C, C-2, C-5, C-6), 160.18 (C-4), 166.21 (C=O) pm. – MS (EI, 70 eV): m/z (%) = 522 (21) [M+1]⁺.

5-*{[1S,2R,3R]-4-[4-[(5-Benzoyloxymethyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)methyl]-1H-1,2,3-triazol-1-yl]-1,2,3-trihydroxybutyl}furan-3-carbohydrazide (5h)*

Colorless powder; m.p. 241–243 °C; yield: 4.65 g (86 %). – $[\alpha]_D$: +29. – IR (KBr): ν = 1677 (C=O), 3365 (NH), 3477 cm⁻¹ (OH). – ¹H NMR ([D₆]DMSO): δ = 3.28 (m, 1H, CH), 3.54 (brs, 3H, 3 OH), 3.67 (m, 1H, CH), 3.77–4.08 (m, 4H, NCH₂, OCH₂), 4.55 (s, 2H, NCH₂), 4.60–4.87 (m, 3H, CH, OCH₂), 5.76 (brs, 2H, NH₂), 6.71 (s, 1H, 4-H furan), 7.36–7.47 (m, 5H, Ar-H), 7.62 (s, 1H, 5-H triazole), 7.70 (s, 1H, 6-H), 7.79 (s, 1H, 2-H furan), 8.97 (brs, 1H, NH), 9.80 (brs, 1H, NH). – ¹³C NMR ([D₆]DMSO): δ = 47.28, 53.98 (2 NCH₂), 68.05, 68.37 (2 OCH₂), 74.28, 75.19, 77.10 (3 CH), 106.28, 121.39, 123.24, 126.68, 127.39, 129.70, 131.16, 132.46, 136.40, 137.63, 139.11, 151.19, 155.41 (Ar-C, C-2, C-5, C-6), 160.18 (C-4), 164.28 (C=O). – MS (EI, 70 eV): m/z (%) = 542 (15) [M+1]⁺.

General procedure for the synthesis of 5-substituted 1-{[1-((2R,3R,4S)-4-[4-(5-mercapto-1,3,4-oxadiazol-2-yl)furan-2-yl]-2,3,4-trihydroxybutyl)-1H-1,2,3-triazol-4-yl]methyl}pyrimidine-2,4(1H,3H)-diones 6a–h**

A mixture of a hydrazide **5a–h** (10 mmol) and carbon disulfide (0.6 mL, 10 mmol) was added to a solution of KOH (0.56 g, 10 mmol) in a mixture of water and ethanol (1 : 4) (50 mL). The reaction mixture was refluxed for 4 h. After evaporation under reduced pressure, a solid was obtained, which was dissolved in water (50 mL) and acidified with conc. HCl. The precipitate was filtered off, washed with H₂O, and recrystallized from ethanol to afford the corresponding 1,3,4-oxadiazoles **6a–h**.

1-*{[1-((2R,3R,4S)-4-[4-(5-thioxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)furan-2-yl]-2,3,4-trihydroxybutyl)-1H-1,2,3-triazol-4-yl]methyl}pyrimidine-2,4(1H,3H)-dione (6a)*

Pale-yellow powder; m.p. 333–335 °C; yield: 4.07 g (88 %). – $[\alpha]_D$: +26.7. – IR (KBr): ν = 1669 (C=O), 3360 (NH), 3479 cm⁻¹ (OH). – ¹H NMR ([D₆]DMSO): δ = 3.33 (m, 1H, CH), 3.60 (brs, 3H, 3 OH), 3.75 (m, 1H, CH), 3.71, 4.02 (2d, 2H, J = 4.0 Hz, NCH₂), 4.48 (s, 2H, NCH₂), 4.80 (m, 1H, CH), 5.77 (d, 1H, J = 6.5 Hz, 5-H), 6.55 (s, 1H, 4-H furan), 7.64 (s, 1H, 5-H triazole), 7.73 (s, 1H, 2-H furan), 8.55 (d, 1H, J = 6.5 Hz, 6-H), 10.00 (brs, 1H, NH), 13.05 (brs, 1H, NH). – ¹³C NMR ([D₆]DMSO): δ = 47.92,

53.18 (2 NCH₂), 74.47, 75.28, 76.20 (3 CH), 102.25, 104.31, 112.30, 123.98, 136.70, 142.28, 148.12, 151.19, 152.67, 154.38 (Ar-C, C-2, C-5, C-6), 160.14 (C-4), 172.24 (C=S). – MS (EI, 70 eV): m/z (%) = 463 (15) [M]⁺. – C₁₇H₁₇N₇O₇S (463.42): calcd. C 44.06, H 3.70, N 21.16; found C 43.89, H 3.57, N 21.07.

5-Methyl-1-*{[1-((2R,3R,4S)-4-[4-(5-thioxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)furan-2-yl]-2,3,4-trihydroxybutyl)-1H-1,2,3-triazol-4-yl]methyl}pyrimidine-2,4(1H,3H)-dione (6b)*

Pale-yellow powder; m.p. 305–307 °C; yield: 4.24 g (89 %). – $[\alpha]_D$: +5.2. – IR (KBr): ν = 1668 (C=O), 3364 (NH), 3478 cm⁻¹ (OH). – ¹H NMR ([D₆]DMSO): δ = 2.45 (s, 1H, CH₃), 3.28 (m, 1H, CH), 3.66 (brs, 3H, 3 OH), 3.70 (m, 1H, CH), 3.78, 4.00 (2d, 2H, J = 4.0 Hz, NCH₂), 4.53 (s, 2H, NCH₂), 4.88 (m, 1H, CH), 6.48 (s, 1H, 4-H furan), 7.60 (s, 1H, 5-H triazole), 7.68 (s, 2H, 2-H furan, 6-H), 10.03 (brs, 1H, NH), 13.00 (brs, 1H, NH). – ¹³C NMR ([D₆]DMSO): δ = 15.12 (CH₃), 47.72, 53.28 (2 NCH₂), 74.28, 76.12, 77.14 (3 CH), 102.21, 108.23, 112.42, 123.78, 136.70, 141.24, 145.27, 151.31, 152.49, 154.52 (Ar-C, C-2, C-5, C-6), 160.18 (C-4), 172.34 (C=S). – MS (EI, 70 eV): m/z (%) = 477 (23) [M]⁺. – C₁₈H₁₉N₇O₇S (477.45): calcd. C 45.28, H 4.01, N 20.54; found C 45.14, H 3.88, N 20.33.

5-Bromo-1-*{[1-((2R,3R,4S)-4-[4-(5-thioxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)furan-2-yl]-2,3,4-trihydroxybutyl)-1H-1,2,3-triazol-4-yl]methyl}pyrimidine-2,4(1H,3H)-dione (6c)*

Yellow powder; m.p. 341–343 °C; yield: 4.87 g (90 %). – $[\alpha]_D$: +0.7. – IR (KBr): ν = 1667 (C=O), 3365 (NH), 3479 cm⁻¹ (OH). – ¹H NMR ([D₆]DMSO): δ = 3.26 (m, 1H, CH), 3.61 (brs, 3H, 3 OH), 3.69 (m, 1H, CH), 3.77, 4.00 (2d, 2H, J = 4.0 Hz, NCH₂), 4.51 (s, 2H, NCH₂), 4.75 (m, 1H, CH), 6.45 (s, 1H, 4-H furan), 7.60 (s, 1H, 5-H triazole), 7.70 (s, 1H, 2-H furan), 8.08 (s, 1H, 6-H), 9.90 (brs, 1H, NH), 12.93 (brs, 1H, NH). – MS (EI, 70 eV): m/z (%) = 541/543 (17) [M]⁺. – C₁₇H₁₆BrN₇O₇S (542.32): calcd. C 37.65, H 2.97, N 18.08; found C 37.51, H 2.78, N 17.79.

5-Fluoro-1-*{[1-((2R,3R,4S)-4-[4-(5-thioxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)furan-2-yl]-2,3,4-trihydroxybutyl)-1H-1,2,3-triazol-4-yl]methyl}pyrimidine-2,4(1H,3H)-dione (6d)*

Pale-yellow powder; m.p. 315–317 °C; yield: 3.84 g (80 %). – $[\alpha]_D$: +23. – IR (KBr): ν = 1670 (C=O), 3368 (NH), 3477 cm⁻¹ (OH). – ¹H NMR ([D₆]DMSO): δ = 3.30 (m, 1H, CH), 3.55 (brs, 3H, 3 OH), 3.69 (m, 1H, CH), 3.76, 4.00 (2d, 2H, J = 4.0 Hz, NCH₂), 4.49 (s, 2H, NCH₂), 4.85 (m, 1H, CH), 6.59 (s, 1H, 4-H furan), 7.68 (s, 1H, 5-H tri-

azole), 7.78 (s, 1H, 2-H furan), 8.00 (s, 1H, 6-H), 9.88 (brs, 1H, NH), 13.02 (brs, 1H, NH). – MS (EI, 70 eV): m/z (%) = 481 (23) $[M]^+$. – $C_{17}H_{16}FN_7O_7S$ (481.42): calcd. C 42.41, H 3.35, N 20.37; found C 42.33, H 3.23, N 20.11.

5-Nitro-1- $\{1-[(2R,3R,4S)-4-[4-(5-thioxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)furan-2-yl]-2,3,4-trihydroxybutyl]-1H-1,2,3-triazol-4-yl\}methyl\}$ pyrimidine-2,4(1H,3H)-dione (6e**)**

Yellow powder; m. p. 294–296 °C; yield: 4.06 g (80 %). – $[\alpha]_D$: +20.1. – IR (KBr): ν = 1667 (C=O), 3364 (NH), 3480 cm^{-1} (OH). – 1H NMR ($[D_6]DMSO$): δ = 3.27 (m, 1H, CH), 3.63 (brs, 3H, 3 OH), 3.69 (m, 1H, CH), 3.77, 4.01 (2d, 2H, J = 4.0 Hz, NCH_2), 4.53 (s, 2H, NCH_2), 4.77 (m, 1H, CH), 6.53 (s, 1H, 4-H furan), 7.59 (s, 1H, 5-H triazole), 7.69 (s, 1H, 2-H furan), 8.85 (s, 1H, 6-H), 9.94 (brs, 1H, NH), 13.00 (brs, 1H, NH). – ^{13}C NMR ($[D_6]DMSO$): δ = 48.12, 53.24 (2 NCH_2), 74.32, 75.15, 76.30 (3 CH), 103.34, 114.32, 123.28, 130.89, 137.22, 142.25, 147.28, 152.19, 153.48, 154.12, 155.46 (Ar-C, C-2, C-4, C-5, C-6), 172.42 (C=S). – MS (EI, 70 eV): m/z (%) = 508 (17) $[M]^+$. – $C_{17}H_{16}N_8O_9S$ (508.42): calcd. C 40.16, H 3.17, N 22.04; found C 40.00, H 3.05, N 21.88.

5-Methoxymethyl-1- $\{1-[(2R,3R,4S)-4-[4-(5-thioxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)furan-2-yl]-2,3,4-trihydroxybutyl]-1H-1,2,3-triazol-4-yl\}methyl\}$ pyrimidine-2,4(1H,3H)-dione (6f**)**

Pale-yellow powder; m. p. 280–282 °C; yield: 4.25 g (84 %). – $[\alpha]_D$: +29.7. – IR (KBr): ν = 1669 (C=O), 3368 (NH), 3477 cm^{-1} (OH). – 1H NMR ($[D_6]DMSO$): δ = 3.28–3.37 (m, 3H, CH, OCH_3), 3.62 (brs, 3H, 3 OH), 3.73 (m, 1H, CH), 3.71–4.02 (m, 4H, NCH_2 , OCH_2), 4.53 (s, 2H, NCH_2), 4.85 (m, 1H, CH), 6.54 (s, 1H, 4-H furan), 7.60 (s, 1H, 5-H triazole), 7.77 (s, 2H, 2-H furan, H-6), 9.89 (brs, 1H, NH), 12.95 (brs, 1H, NH). – ^{13}C NMR ($[D_6]DMSO$): δ = 47.79, 53.87 (2 NCH_2), 57.32 (OCH_3), 62.80 (OCH_2),

74.25, 75.14, 76.86 (3 CH), 101.24, 112.14, 114.38, 124.18, 137.24, 142.20, 147.25, 151.10, 152.70, 154.82 (Ar-C, C-2, C-5, C-6), 159.84 (C-4), 172.22 (C=S). – MS (EI, 70 eV): m/z (%) = 507 (25) $[M]^+$. – $C_{19}H_{21}N_7O_8S$ (507.48): calcd. C 44.97, H 4.17, N 19.32; found C 44.83, H 4.09, N 19.12.

5-Pentoxymethyl-1- $\{1-[(2R,3R,4S)-4-[4-(5-thioxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)furan-2-yl]-2,3,4-trihydroxybutyl]-1H-1,2,3-triazol-4-yl\}methyl\}$ pyrimidine-2,4(1H,3H)-dione (6g**)**

Pale-yellow powder; m. p. 266–268 °C; yield: 5.01 g (89 %). – $[\alpha]_D$: +36.2. – IR (KBr): ν = 1670 (C=O), 3369 (NH), 3479 cm^{-1} (OH). – 1H NMR ($[D_6]DMSO$): δ = 0.91 (t, 3H, J = 5.5 Hz, CH_3), 1.29–1.48 (m, 6H, 3 CH_2), 3.30–3.38 (m, 3H, CH, OCH_2), 3.58 (brs, 3H, 3 OH), 3.69 (m, 1H, CH), 3.75–4.05 (m, 4H, NCH_2 , OCH_2), 4.54 (s, 2H, NCH_2), 4.84 (m, 1H, CH), 6.55 (s, 1H, 4-H furan), 7.60 (s, 1H, 5-H triazole), 7.77 (s, 2H, 2-H furan, 6-H), 10.02 (brs, 1H, NH), 13.06 (brs, 1H, NH). – MS (EI, 70 eV): m/z (%) = 563 (19) $[M]^+$. – $C_{23}H_{29}N_7O_8S$ (563.58): calcd. C 49.02, H 5.19, N 17.40; found C 48.82, H 5.00, N 17.27.

5-Benzoyloxymethyl-1- $\{1-[(2R,3R,4S)-4-[4-(5-thioxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)furan-2-yl]-2,3,4-trihydroxybutyl]-1H-1,2,3-triazol-4-yl\}methyl\}$ pyrimidine-2,4(1H,3H)-dione (6h**)**

Pale-yellow powder; m. p. 277–279 °C; yield: 5.30 g (91 %). – $[\alpha]_D$: +25.8. – IR (KBr): ν = 1671 (C=O), 3365 (NH), 3476 cm^{-1} (OH). – 1H NMR ($[D_6]DMSO$): δ = 3.30 (m, 1H, CH), 3.63 (brs, 3H, 3 OH), 3.73 (m, 1H, CH), 3.76–4.04 (m, 4H, NCH_2 , OCH_2), 4.49 (s, 2H, NCH_2), 4.77 (m, 1H, CH), 6.57 (s, 1H, 4-H furan), 7.69 (s, 1H, 5-H triazole), 7.77 (s, 2H, 2-H furan, 6-H), 10.00 (brs, 1H, NH), 13.00 (brs, 1H, NH). – MS (EI, 70 eV): m/z (%) = 583 (42) $[M]^+$. – $C_{25}H_{25}N_7O_8S$ (583.57): calcd. C 51.45, H 4.32, N 16.80; found C 51.23, H 4.17, N 16.66.

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