Click reaction of 3-propargyl-4*H*-pyrano[2,3-*d*]pyrimidines and peracetylated D-glucopyaranosyl azide under microwave-assisted conditions

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Abstract. Some D-glucose-conjugated 1*H*-1,2,3-triazoles having 4*H*-pyrano[2,3-*d*]pyrimidines had been synthesized. Click chemistry between *N*-propargyl-4*H*-pyrano[2,3-*d*]pyrimidines and peracetylated D-glucopyaranosyl azide was performed using CuI@Montmorillonite clays as a catalyst under microwave-assisted conditions. Gram-positive antibacterial activity of these 1*H*-1,2,3-triazoles was probed using minimum inhibitory concentration. These compounds have screened their antibacterial activity. The detailed structure-activity relationship (SAR) *in vitro* and *in silico* studies were performed.

Keywords: D-glucose; 1*H*-1,2,3-triazoles; 4*H*-pyrano[2,3-*d*]pyrimidines; microwave-assisted; propargyl derivatives.

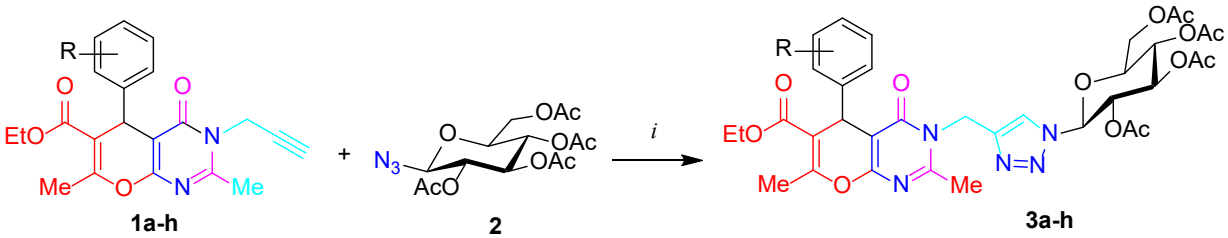
1. Introduction

Pyrano[2,3-*d*]pyrimidine ring is an unsaturated heterocyclic system, consisted of two six member heterocyclic rings, pyran and pyrimidine, fused together. This heterocyclic ring moiety brings many biological activities of interest, such as anticancer [1], antitubercular [2], antifungal [3], and antioxidant [4] activity. Therefore, its derivatives have obtained interest in medicinal chemistry and the synthesis of these derivatives has been carried out widely. The field of 1,2,3-triazole chemistry (click chemistry) was introduced in the 2000s and is growing rapidly, both in terms of syntheses (catalysts and reaction conditions) and of biological activity explorations [5]. In addition, click chemistry is widely employed for drug development and diverse chemical-biology applications [6], as well as for macromolecular syntheses [7]. 1*H*-1,2,3-Triazoles are an important class of nitrogen-containing heterocyclic compounds in organic and medicinal chemistry [8]. These compounds have diverse interesting pharmacological properties, such as anticancer [9], antifungal [10], antibacterial [11] antitubercular [12], and anti-HIV [13], activities, etc.

In this paper, we reported herein the synthesis of substituted 4*H*-pyrano[2,3-*d*]pyrimidines bearing propargyl unit and its click chemistry. We further evaluated the *in vitro* inhibitory activity of synthesized 1*H*-1,2,3-triazole-tethered 4*H*-pyrano[2,3-*d*]pyrimidines and D-glucose conjugates having the antibacterial activity.

2. Results and discussion

The target molecules, 1*H*-1,2,3-triazoles **3a-g**, were synthesized by click chemistry of *N*-propargyl derivatives **1a-g** of 4*H*-pyrano[2,3-*d*]pyrimidines with 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl azide **2** (Scheme 3). The processes were performed under CuAAC conditions, using CuI@Montmorillonite clays. The reaction was performed by microwave irradiation. The corresponding 1*H*-1,2,3-triazoles **3a-g** were abtained with the yields of 64−94% (Scheme 1).



Scheme 1. Click chemistry of *N*-propargyl 3,5-dihydro-4*H*-pyrano[2,3-*d*]pyrimidines (**1a-g**) Reaction conditions: CuI@Montmorillonite (2 mol%)/DIPEA, *t*-BuOH/H_2O, microwave irradiation, 20 min.

All synthesized glucose-conjugated 1*H*-1,2,3-triazoles **8a-8s** were evaluated their biological activity of against some bacteria, such as *Bacillus subtilis*, *Staphylococcus aureus*, *Staphylococcus epidermidis* (Gram-positive bacteria). Ciprofloxacin and methicillin were used as reference drugs for Gram-positive bacteria, and vancomycin for Gram-negative bacteria. Their MIC values were as follows: ciprofloxacin, 3.125 μg/mL (for Gram-positive bacteria), 1.56 μg/mL (for Gram-negative bacteria); vancomycin: 0.78−3.12 μg/mL (for Gram-positive bacteria). Methicillin had almost no inhibitory activity against all tested bacteria (with MIC values of 400 μg/mL). The results in Table 1 showed that almost all novel hybrid molecule of 4*H*-pyrano[2,3-*d*]pyrimidine−1*H*-1,2,3-triazole exhibited remarkable antibacterial activity against the tested bacteria. Their activities were comparable to the MIC values of the references drugs. Some compounds had strong inhibitory effect on both Gram-positive and Gram-negative bacteria with MIC values of 0.78−3.125 μg/mL, such as compounds **3b**, **3c**, and **3g**. Especially, compound **3g** having 4-dimethylamino groups on 5-phenyl of 4*H*-pyrano[2,3-*d*]pyrimidine ring had strong inhibition to two tested Gram-positive bacteria with MIC values of 1.56, 1.56, and 3.125 μg/mL against *B. subtilis*, *S. aureus*, and *S. epidermidis*, respectively. Compounds **8b**, **8c**, and **8g**inhibited bacterium *B. subtilis*, whereas only compound **8g** exhibited medium inhibition against bacterium *S. epidermidis*. Compounds **8c** and **8g** expressed the good to excellent inhibitory activity against *S. aureus* with MIC = 3.125 and 1.56 μg/mL.

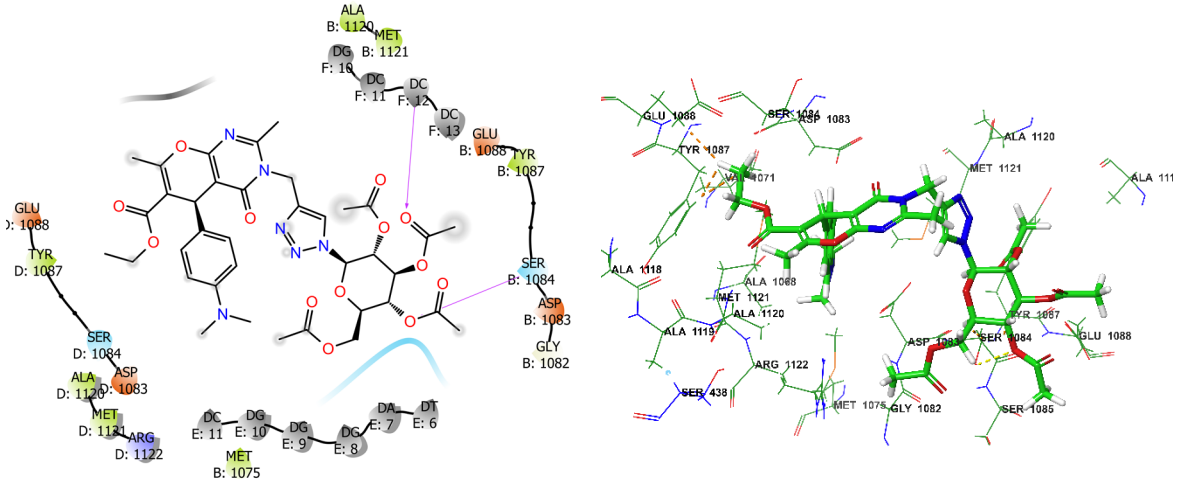
From Table 1, we realized that the synthesized D-glucose-conjugated 1*H*-1,2,3-triazole hybrid compounds with 4*H*-pyrano[2,3-*d*]pyrimidine exhibited good antibacterial activity, in particular against Gram-positive bacterium *Bacillus subtilis*. The best active compound **8g** was selected for molecular docking study. Crystal structure of two enzymes, including *S. aureus* Gyrase complexed with GSK299423 and DNA was retrieved from the RCSB Protein Data Bank (https://www.rcsb.org/structure/2XCS, PDB ID: 2XCS). These structures were solved by

X-ray crystallography at 2.10 Å resolution. The molecular docking was accomplished and analyzed via the Glide v. 7.8 (Maestro, v. 11.5: Schrödinger, LLC, New York, NY, USA). The receptor grid was located in the center based on the active site of the protein, using the receptor grid generation tool. The ligands were flexibly docked in grid box using Monte Carlo-based simulation algorithm and a high throughput virtual screening (HTVS) method without any constraints was employed that generated binding poses based on energy.

Table 7 Antibacterial activity of glucose-conjugated 1*H*-1,2,3-triazoles **3a-g**

Entry	R	Gram-positive bacteria/MIC (μg/mL)		
		B. subtilis	*S. aureus*	*S. epidermidis*
3a	H	50	25	50
3b	4-NO_2	1.56	25	50
3c	4-Cl	1.56	3.125	25
3d	4-Br	12.5	100	12.5
3e	4-OH	50	12.5	200
3f	4-OMe	12.5	6.25	100
3g	4-NMe_2	1.56	1.56	3.125
	Ciprofloxacin	3.125	3.125	3.125
	Vancomycin	1.56	1.56	0.78
	Methicillin	400	400	400

The most active compound **6g** was docked into the empty binding site of this enzyme shown in Fig. 1. The figures revealed the disposition of protein side-chains and DNA that formed the drug binding pockets.



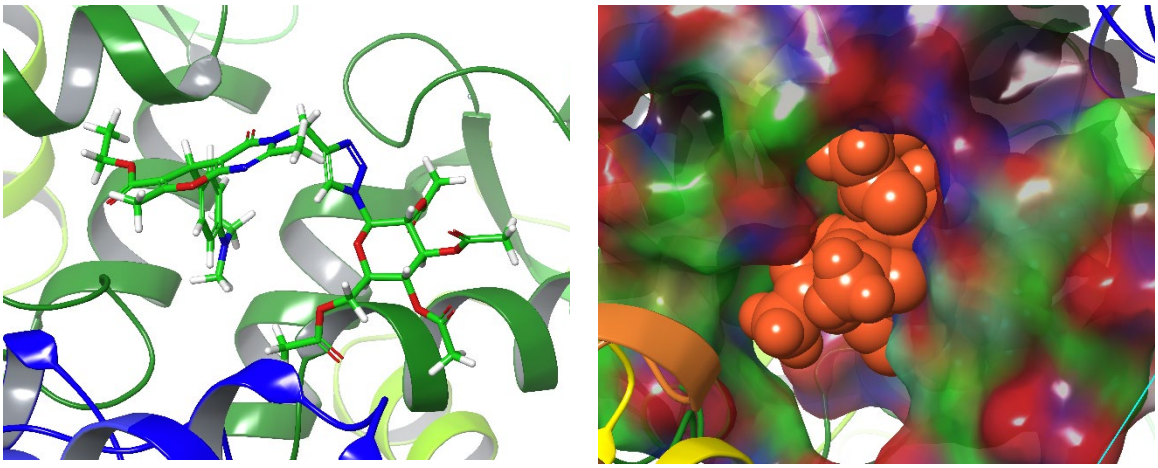


Figure 1. Interacting mode of compound **3g** (colored elements) without and with helix form in the active region surrounded in DNA Gyrase active site. Two-dimensional diagram (top) in ligand interaction of compound **3g** in DNA Gyrase active site showed active ligand-receptor interactions. The pocket on this enzyme was shown by electrostatic potential surface (bottom).

3. Conclusions

Ultrasound-assisted synthetic method was efficient and convenient method for synthesis of a series of *N*-propargyl-4*H*-pyrano[2,3-*d*]pyrimidines. Click chemistry between these *N*-propargyl derivatives and peracetylated D-glucopyaranosyl azide was performed using CuI@Montmorillonite as a catalyst in absolute ethanol. Gram-positive and Gram-negative antibacterial activity as well as antifungal activity of these 1*H*-1,2,3-triazoles was probed using minimum inhibitory concentration. Anti-MRSA activity of these compounds also was screened against some MRSA types. Obtained results showed that they displayed significant inhibition *in vitro* against almost of tested bacteria and fungi. Induced fit docking study was performed to observe binding efficiency and steric interactions of the lead compound **3g**. Molecular docking results showed that compound **8g** is compatible with the active site of *S. aureus* DNA Gyrase 2XCS with six hydrogen bonding interaction and two π-π stacking interaction, which suggested that the tested compounds inhibited the synthesis of this enzyme in *S. aureus*.

4. Experimental

Melting points were determined by open capillary method on STUART SMP3 (BIBBY STERILIN, UK). The IR spectra were recorded on FT-IR Affinity-1S Spectrometer (Shimadzu, Japan) in KBr pellet. The ^{1}H NMR spectra were recorded at 500 MHz (on Avance AV500 Spectrometer, Bruker, Germany) and at 600 MHz (on AvanceNEO Spectrometer, Bruker, Germany), and ^{13}C NMR spectra at 125 and 160 MHz, respectively, using DMSO-d_6 as solvent and TMS as an internal standard. ESI-mass spectra were recorded on LC-MS LTQ Orbitrap XL (Thermo Fisher Scientific Inc., USA) in methanol/dichloromethane or methanol using ESI method. The analytical thin-layer chromatography (TLC) was performed on silica gel 60WF$_{254}$ No. 5715 aluminium sheets (Merck, Germany) with toluene : ethyl acetate (1:1 by volume) as solvent system, and spots were visualized directly due to own colour of corresponding isatins. All chemical reagents in high purity (reagent grade for organic synthesis) were purchased from the Merck Chemical Company.

General procedure for synthesis of ethyl 3-(1-((2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl))-1H-1,2,3-triazol-4-yl)methyl-2,7-dimethyl-5-(R-phenyl)-4-oxo-3,5-dihydro-4H-pyrano[2,3-d]pyrimidin-6-carboxylates

Reaction mixture consisted of 2-amino-4-phenyl-7-propargyloxy-4*H*-chromene-3-carbonitrile **1a-g** (1 mmol, 302 mg) and azide **2** (1 mmol, 373 mg) in absolute ethanol (2 mL). Amount of used catalyst CuI@Montmorillonite clays (0.02 mmol, 3.99 mg) was added. The reaction mixture was irradiated under microwave-assisted condition for 20 min. Then, the reaction mixture was cooled to room temperature, toluene (with half a volume) was added, the reaction mixture was heated to boiling, and the solid copper catalysts were filtered out. The filtrate was left to stand overnight, and the product separated was filtered and crystallized from solvent mixture of 96% ethanol and toluene (ratio of 2:1 by volumes) to yield the compound **3a-g**.

*4.1. 1H-1,2,3-Triazole (**3a**)*

White solids, from **1a** (R = H, 0.5 mmol, 0.182 g). Yield: 94%. M.p. 131−133°C. ^{1}H NMR, δ (ppm): 8.34 (s, 1H, Ha), 7.27−7.24 (m, 4H, H-2′, H-3′, H-5′, H-6′), 7.16 (m, 1H, H-4′), 6.32−6.29 (m, 1H, H-1″), 5.61−5.58 (m, 1H, H-3″), 5.57−5.52 (m, 1H, H-2″), 5.34−5.25 (m, 1H, N-CH_2-triazol), 5.19-5.16 (m, 1H, H-4″), 5.07-5.01 (m, 1H, N-CH_2-triazol), 4.85 (s, 1H, H-5), 4.37−4.36 (m, 1H, H-5″), 4.14−4.10 (m, 2H, H-6″a & H-6″b), 4.06−4.01 (m, 2H, COO**CH_2**CH_3), 2.59 (s, 3H, 2-CH_3), 2.42 (s, 3H, 7-CH_3), 2.04, 2.01, 1.98, 1.77 (4×3H, 2″-, 3″-, 4″- & 6″-CO**CH_3**), 1.12 (s, 3H, OCH_2**CH_3**). ^{13}C NMR, δ (ppm): 170.5, 170.0, 170.0, 168.9 (2″-, 3″-, 4″- & 6″-**CO**CH_3), 166.0 (6-**CO**OEt), 161.3 (C-4), 160.0 (C-2), 158.8 (C-8a), 158.6 (C-7), 144.2 (C-4′), 143.2 (C-b), 128.6 (C-1′), 128.5 (C-2′ & C-6′), 127.2 (C-3′ & C-5′), 123.3 (C-a), 108.4 (C-6), 100.8 (C-4a), 84.4 (C-1″), 73.8 (C-5″), 72.4 (C-2″), 70.8 (C-3″), 68.0 (C-4″), 62.3 (C-6″), 60.7 (6-CO_2**CH_2**CH_3), 39.9 (N-CH_2-triazol), 37.0 (C-5), 23.0 (2-CH_3), 21.0, 20.8, 20.7, 20.3 (2″-, 3″-, 4″- & 6″-CO**CH_3**), 18.8 (7-CH_3), 14.3 (6-CO_2CH_2**CH_3**). ESI-MS: cald. for $C_{35}H_{39}N_5O_{13}$ = 737.25, found *m/z* 760.46 (100%) $[M+Na]^+$.

*4.2. 1H-1,2,3-Triazole (**3b**)*

Pale yellow solids, from **1b** (R = 4-NO_2, 0.5 mmol, 0.205 g). Yield: 73%. M.p. 158−159°C. ^{1}H NMR, δ (ppm): 8.36 (s, 1H, H-a), 8.15 (d, *J* = 8.5 Hz, 2H, H-3′ & H-5′), 7.48 (d, *J* = 8.5 Hz, 2H, H-2′ & H-6′), 6.31−6.29 (m, 1H, H-1″), 5.58−5.56 (m, 1H, H-3″), 5.55−5.52 (m, 1H, H-2″), 5.33−5.24 (m, 1H, N-CH_2-triazol), 5.19−5.15 (m, 1H, H-4″), 5.07−5.04 (m, 1H, N-CH_2-triazol), 4.98 (s, 1H, H-5), 4.37−4.35 (m, 1H, H-5″), 4.14−4.06 (m, 2H, H-6″a & H-6″b), 4.04−3.99 (m, 2H, 6-CO_2**CH_2**CH_3), 2.61 (s, 3H, 2-CH_3), 2,46 (s, 3H, 7-CH_3), 2.04, 2.01, 1.98, 1.75 (4×3H, 2″-, 3″-, 4″- & 6″-CO**CH_3**), 1.09 (s, 3H, 6-CO_2CH_2**CH_3**). ^{13}C NMR, δ (ppm): 170.5, 170.0, 169.8, 168.9 (2″-, 3″-, 4″- & 6″-**CO**CH_3), 165.9 (6-**CO**OEt), 161.3 (C-4), 160.2 (C-2), 159.7 (C-8a), 158.8 (C-7), 152.7 (C-1′), 146.9 (C-4′), 142.9 (C-b), 129.0 (C-2′ & C-6′), 124.3 (C-3′ & C-5′), 123.3 (C-a), 107.2 (C-6), 99.9 (C-4a), 84.4 (C-1″), 73.7 (C-5″), 72.4 (C-2″), 70.8 (C-3″), 68.0 (C-4″), 62.3 (C-6″), 60.9 (6-CO_2**CH_2**CH_3), 40.1 (N-CH_2-triazol), 37.2 (C-5), 23.1 (2-CH_3), 21.0, 20.9, 20.7, 20.3 (2″-, 3″-, 4″- & 6″-CO**CH_3**), 19.0 (7-CH_3), 14.2 (6-CO_2CH_2**CH_3**).

*4.3. 1H-1,2,3-Triazole (**3c**)*

White solids, from **1c** (R = 4-Cl, 0.5 mmol, 0.199 g). Yield: 74%. M.p. 105−107°C. ^{1}H NMR, δ (ppm): 8.36 (s, 1H, H-a), 7.33 (d, *J* = 8.5 Hz, 2H, H-3′ & H-5′), 7.26 (d, *J* = 8.5 Hz, 2H, H-2′ & H-6′), 6.33−6.29 (m, 1H, H-1″), 5.63−5.57 (m, 1H, H-3″), 5.56−5.52 (m, 1H, H-2″), 5.34−5.26 (m, 1H, N-CH_2-triazol), 5.20−5.15 (m, 1H, H-4″), 5.07−5.02 (m, 1H, N-CH_2-

triazol), 4.84 (s, 1H, H-5, 4.37−4.36 (m, 1H, H-5″), 4.15−4.10 (m, 2H, H-6″a & H-6″b), 4,07−4,01 (m, 2H, 6-CO_2**CH_2**CH_3), 2.60 (s, 3H, 2-CH_3), 2.42 (s 3H, 7-CH_3), 2.04, 2.01, 1.98 1.77 (4×3H, 2″-, 3″-, 4″- & 6″-CO**CH_3**), 1.20−1.10 (m, 3H, OCH_2**CH_3**). ^{13}C NMR, δ (ppm): 170.5, 170.0, 169.8, 168.9 (2″-, 3″-, 4″- & 6″-**C**OCH_3), 165.8 (6-**C**OOEt), 161.3 (C-4), 160.2 (C-2), 159.0 (C-8a), 158.8 (C-7), 143.1 (C-4′), 142.9 (C-b), 131.8 (C-1′), 130.4 (C-2′ & C-6′), 128.6 & 128.5 (C-3′ & C-5′), 123.4 (C-a), 107.2 (C-6), 99.8 (C-4a), 84.4 (C-1″), 73.7 (C-5″), 72.4 (C-2″), 70.8 (C-3″), 68.0 (C-4″), 62.3 (C-6″), 60.9 (6-CO_2**CH_2**CH_3), 40.1 (N-CH_2-triazol), 37.3 (C-5), 23.1 (2-CH_3), 21.0, 20.9, 20.7, 20.3 (2″-, 3″-, 4″- & 6″-CO**CH_3**), 19.0 (7-CH_3), 14.2 (6-CO_2CH_2**CH_3**). ESI-MS: cald. for $C_{35}H_{38}ClN_5O_{13}$ = 771.22/773.21, found *m/z* (771.36, 43%), $[M]^+$, 770.29 (100%)/772.34 (44%), $[M-H]^-$.

*4.4. 1H-1,2,3-Triazole (**3d**)*

White solids, from **1d** (R = 4-Br, 0.5 mmol, 0.221 g). Yield: 77%. M.p. 105−107°C. ^{1}H NMR, δ (ppm): 8.36 (s, 1H, H-a), 7.44 (d, *J* = 8.5 Hz, 2H, H-3′ & H-5′), 7.16 (d, *J* = 8.5 Hz, 2H, H-2′ & H-6′), 6.33−6.32 (m, 1H, H-1″), 5.64−5.59 (m, 1H, H-3″), 5.56−5.51 (m, 1H, H-2″), 5.34−5.22 (m, 1H, N-CH_2-triazol), 5.19−5.15 (m, 1H, H-4″), 5.05−5.03 (m, 1H, N-CH_2-triazol), 4.77 (s, 1H, H-5), 4,36−4,34 (m, 1H, H-5″), 4.14−4.09 (m, 2H, H-6″a & H-6″b), 4.06−4.02 (m, 2H, 6-CO_2**CH_2**CH_3), 2.57 (s, 3H, 2-CH_3), 2.42 (s, 3H, 7-CH_3), 2.04, 2.01, 1.96, 1.75 (4×3H, 2″-, 3″-, 4″- & 6″-CO**CH_3**), 1.22–1.12 (m, 3H, 6-CO_2CH_2**CH_3**). ^{13}C NMR, δ (ppm): 170.5, 170.2, 169.8, 168.9 (2″-, 3″-, 4″- & 6″-**C**OCH_3), 166.9 (6-**C**OOEt), 163.1 (C-4), 160.2 (C-2), 158.2 (C-8a), 153.8 (C-7), 142.9 (C-b), 141.2 (C-1′), 132.1 (C-3′ & C-5′), 128.7 (C-2′ & C-6′), 121.8 (C-4′), 123.4 (C-a), 107.3 (C-6), 99.8 (C-4a), 84.5 (C-1″), 73.8 (C-5″), 72.4 (C-2″), 70.8 (C-3″), 68.0 (C-4″), 62.3 (C-6″), 60.9 (6-CO_2**CH_2**CH_3), 40.1 (N-CH_2-triazol), 37.5 (C-5), 23.1 (2-CH_3), 21.0, 20.9, 20.7, 20.3 (2″-, 3″-, 4″- & 6″-CO**CH_3**), 19.0 (7-CH_3), 14.2 (6-CO_2CH_2**CH_3**). ESI-MS: cald. for $C_{35}H_{38}BrN_5O_{13}$ = 815.16/817.16, found *m/z* 814.22 (100%)/816.23 (95%) $[M-H]^-$.

*4.5. 1H-1,2,3-Triazole (**3e**)*

White solids, from **1e** (R = 4-OH, 0.5 mmol, 0.190 g). Yield: 84%. M.p. 197−199°C. ^{1}H NMR, δ (ppm): 9.76 (s, 1H, 4-OH), 8.36 (s, 1H, H-a), 6.96 (d, *J* = 8.5 Hz, 2H, H-3′ & H-5′), 6.58 (d, *J* = 8.5 Hz, 2H, H-2′ & H-6′), 6.33−6,31 (m, 1H, H-1″), 5.65−5.58 (m, 1H, H-3″), 5.57−5.51 (m, 1H, H-2″), 5.34−5.20 (m, 1H, N-CH_2-triazol), 5.19−5.15 (m, 1H, H-4″), 5.05−5.01 (m, 1H, N-CH_2-triazol), 4.79 (s, 1H, H-5), 4,36−4,34 (m, 1H, H-5″), 4.14−4.09 (m, 2H, H-6″a & H-6″b), 4.06−4.01 (m, 2H, 6-CO_2**CH_2**CH_3), 3.69 (s, 3H, 4′-O**CH_3**), 2.59 (s, 3H, 7-CH_3), 2.40 (s, 3H, 2-CH_3), 2.03, 2.01, 1.96, 1.77 (4×3H, 2″-, 3″-, 4″- & 6″-CO**CH_3**), 1.20–1.12 (m, 3H, 6-CO_2CH_2**CH_3**). ^{13}C NMR, δ (ppm): 170.4, 170.3, 170.2, 169.8 (2″-, 3″-, 4″- & 6″-**C**OCH_3), 167.2 (6-**C**OOEt), 163.3 (C-4), 160.5 (C-2), 158.2 (C-8a), 156.5 (C-4′), 153.8 (C-7), 143.2 (C-b), 134.3 (C-1′), 129.2 (C-2′ & C-6′), 123.3 (C-a), 119.6 (C-3′ & C-5′), 108.5 (C-6), 100.8 (C-4a), 84.3 (C-1″), 73.7 (C-5″), 72.4 (C-2″), 70.6 (C-3″), 68.0 (C-4″), 62.3 (C-6″), 60.7 (6-CO_2**CH_2**CH_3), 41.7 (N-CH_2-triazol), 36.6 (C-5), 31.0 [**C**H$(CH_3)_2$], 24.2 [CH**$(CH_3)_2$**], 23.0 (2-CH_3), 21.0, 20.9, 20.7, 20.3 (2″-, 3″-, 4″- & 6″-CO**CH_3**), 18.8 (7-CH_3), 14.4 (6-CO_2CH_2**CH_3**). ESI-MS: cald. for $C_{35}H_{39}N_5O_{14}$ = 753.25, found *m/z* 776.31 (100%) $[M+Na]^+$.

*4.6. 1H-1,2,3-Triazole (**3f**)*

White solids, from **1f** (R = 4-OMe, 0.5 mmol, 0.197 g). Yield: 84%. M.p. 97−99°C. ^{1}H NMR, δ (ppm): 8.37 (s, 1H, H-a), 7.13 (d, *J* = 8.5 Hz, 2H, H-3′ & H-5′), 6.82 (d, *J* = 8.5 Hz, 2H, H-2′ & H-6′), 6.33−6,31 (m, 1H, H-1″), 5.65−5.58 (m, 1H, H-3″), 5.57−5.51 (m, 1H, H-2″), 5.34−5.20 (m, 1H, N-CH_2-triazol), 5.19−5.15 (m, 1H, H-4″), 5.05−5.01 (m, 1H, N-CH_2-

triazol), 4.79 (s, 1H, H-5), 4,36−4,34 (m, 1H, H-5″), 4.14−4.09 (m, 2H, H-6″a & H-6″b), 4.06−4.01 (m, 2H, 6-CO_2**CH_2**CH_3), 3.69 (s, 3H, 4′-O**CH_3**), 2.59 (s, 3H, 7-CH_3), 2.40 (s, 3H, 2-CH_3), 2.03, 2.01, 1.96, 1.77 (4×3H, 2″-, 3″-, 4″- & 6″-CO**CH_3**), 1.20–1.12 (m, 3H, 6-CO_2CH_2**CH_3**). ^{13}C NMR, δ (ppm): 170.8, 170.5, 170.0, 168.9 (2″-, 3″-, 4″- & 6″-**CO**CH_3), 166.1 (6-**CO**OEt), 161.3 (C-4), 159.8 (C-2), 158.7 (C-8a), 158.1 (C-7), 143.2 (C-4′), 143.0 (C-b), 136.3 (C-1′), 129.5 (C-2′ & C-6′), 123.3 (C-a), 114.0 (C-3′ & C-5′), 108.6 (C-6), 101.0 (C-4a), 84.4 (C-1″), 73.8 (C-5″), 72.5 (C-2″), 70.8 (C-3″), 68.0 (C-4″), 62.3 (C-6″), 60.7 (6-CO_2**CH_2**CH_3), 55.4 (4′-OCH_3), 41.8 (N-CH_2-triazol), 36.2 (C-5), 23.0 (2-CH_3), 21.2, 21.0, 20.7, 20.3 (2″-, 3″-, 4″- & 6″-CO**CH_3**), 18.8 (7-CH_3), 14.6 (6-CO_2CH_2**CH_3**). ESI-MS: cald. for $C_{36}H_{41}N_5O_{14}$ = 767.27, found *m/z* 790.37 (100%) $[M+Na]^+$.

*4.7. 1H-1,2,3-Triazole (**3g**)*

Ivory solids, from **6r** (R = 4-NMe_2, 0.5 mmol, 0.205 g). Yield: 85%. M.p. 127−129°C. ^{1}H NMR, δ (ppm): 8.36 (s, 1H, H-a), 7.08 (d, *J* = 7.5, 2H, H-2′ & H-6′), 6.58 (d, *J* = 7.5, 2H, H-3′ & H-5′), 6.30−6,27 (m, 1H, H-1″), 5.59 (d, *J* = 12.0 Hz, 1H, N-CH_2-triazol), 5.58−5.54 (m, 2H, H-2″ & H-3″), 5.46 (d, *J* = 12.0 Hz, 1H, N-CH_2-triazol), 5.19−5.17 (m, 1H, H-4″), 5.10 (s, 1H, H-5), 4,37−4,33 (m, 1H, H-5″), 4.20−4.16 (m, 1H, H-6″a), H-6″b), 4.06−4.01 (m, 2H, 6-CO_2**CH_2**CH_3), 3.69 (s, 3H, 4′-O**CH_3**), 2.59 (s, 3H, 7-CH_3), 2.40 (s, 3H, 2-CH_3), 2.03, 2.01, 1.96, 1.77 (4×3H, 2″-, 3″-, 4″- & 6″-CO**CH_3**), 1.20–1.12 (m, 3H, 6-CO_2CH_2**CH_3**). ^{13}C NMR, δ (ppm): 170.4, 170.3, 170.1, 169.8 (2″-, 3″-, 4″- & 6″-**CO**CH_3), 167.6 (6-**CO**OEt), 163.4 (C-4), 160.9 (C-2), 158.1 (C-8a), 153.7 (C-7), 151.4 (C-4′), 143.0 (C-b), 131.7 (C-1′), 127.9 (C-2′ & C-6′), 123.3 (C-a), 112.0 (C-3′ & C-5′), 108.6 (C-6), 101.0 (C-4a), 84.4 (C-1″), 73.8 (C-5″), 72.5 (C-2″), 70.8 (C-3″), 68.0 (C-4″), 62.3 (C-6″), 60.7 (6-CO_2**CH_2**CH_3), 55.4 (4′-OCH_3), 41.8 (N-CH_2-triazol), 40.3 [4′-$N(CH_3)_2$], 36.2 (C-5), 23.0 (2-CH_3), 21.2, 21.0, 20.7, 20.3 (2″-, 3″-, 4″- & 6″-CO**CH_3**), 18.8 (7-CH_3), 14.6 (6-CO_2CH_2**CH_3**). ESI-MS: cald. for $C_{37}H_{44}N_6O_{13}$ = 780.30, found *m/z* 803.35 (100%) $[M+Na]^+$.

Acknowledgements. This research is funded by Vietnam National Foundation for Science and Technology Development (NAFOSTED) under Grant Number 104.01-2020.01.

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