



Expeditious preparation of triazole-linked glycolipids via microwave accelerated click chemistry and their electrochemical and biological assessments

Shao-Xing Song^a, Hai-Lin Zhang^a, Chol-Guk Kim^a, Li Sheng^b, Xiao-Peng He^{c,d,*}, Yi-Tao Long^a, Jia Li^{b,*}, Guo-Rong Chen^{a,*}

^a Key Laboratory for Advanced Materials and Institute of Fine Chemicals, School of Chemistry and Molecular Engineering, East China University of Science and Technology, Shanghai 200237, PR China

^b National Center for Drug Screening, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai 201203, PR China

^c Department of Pharmaceutical Engineering, School of Pharmacy, East China University of Science and Technology, Shanghai 200237, PR China

^d PPSM, ENS Cachan, CNRS, 61 av. President Wilson, F-94230 Cachan, France

ARTICLE INFO

Article history:

Received 6 July 2010

Received in revised form 27 September 2010

Accepted 15 October 2010

Available online 18 November 2010

Keywords:

Glycolipid derivatives

Microwave-assisted click chemistry

EIS measurement

Gold surface adsorption

Cytotoxicity

ABSTRACT

A series of triazole-linked ester-type glycolipids were efficiently prepared via a two-step sequence involving microwave accelerated 'click' chemistry and debenzylolation. All carbon chain length varied *O*-alkynyl fatty esters used to couple with 1-azido-tetra-*O*-benzyl- β -D-glucoside showed excellent tolerance to the microwave-assisted 1,3-dipolar cycloaddition (click reaction), forming the unique cycloadducts in almost quantitative yields of 92.9–99.0% within a quarter. The desired glycolipids were then readily afforded via the successive hydrogenolysis promoted by PdCl₂/H₂. Their adsorption competence on gold electrode were evaluated through EIS (electrochemical impedance spectroscopy) measurement and the resulting structure–activity relationship (SAR) was discussed. In addition, the cytotoxicity of this triazolyl glycolipid class on HeLa (cervix cancer) cell line was identified by MTT assay.

© 2010 Elsevier Ltd. All rights reserved.

1. Introduction

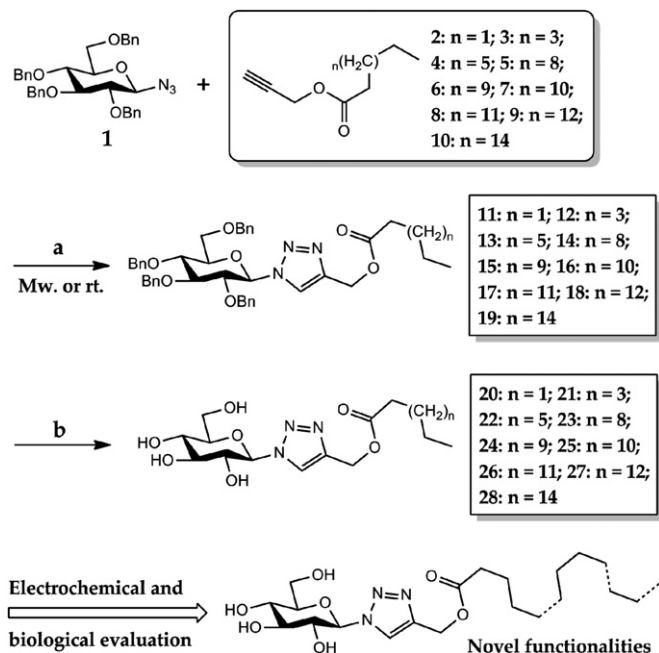
Glycolipids represent a class of crucial glycoconjugate structure in which the naturally occurring carbohydrates and lipids are covalently coupled. They constitute animal or plant membranes and are of considerable biological and physiochemical interest.¹ The identification of α -GalCer (α -galactosyl ceramide) as CD1d (an autoimmunity-related protein) binding ligands well exemplified the qualification of natural glycolipids as cell surface associated antigens.² In addition, some glycolipid derivatives have also been developed as ion-pairing agents for oral drug delivery,³ cell adhesion mediators⁴ as well as potential anticancer agents toward the inhibition of cell proliferation^{5–7} due to their lipophilic feature. Besides their compelling biological versatility, the amphiphilic glycolipids have simultaneously proven practical as non-ionic surfactants that are environmentally friendly due to the low toxic and highly biocompatible nature of carbohydrates.⁸ Consequently, the efficient preparation of such multifunctional glycoconjugate series is of great interest.

The incorporation of 'click' chemistry⁹ with microwave irradiation that may tremendously enhance the reaction rate¹⁰ has recently become a laboratorial preference toward the construction of combinatorial compound libraries.^{11b} A plethora of investigations were reported on the click chemistry-based carbohydrate research¹¹ fulfilled under either conventional or microwave-assisted conditions.¹² However, research on the preparation of synthetic triazolyl glycolipid derivatives as well as their potential functions^{6,13} was still in its infancy. Loganathan and co-workers first described a general method for the synthesis of ether-type glycolipid derivatives via 1,3-dipolar cycloaddition.^{13a} A very recent report by Krausz and co-workers also revealed the interesting physiochemical property of several fatty acid-contained triazolyl glycolipids.^{13b} Enlightened by such innovative and promising work, we envisioned to synthesize a series of ester-type glycolipid derivatives via click chemistry while their newly explored functions were also reported.

Notably, former relevant studies were mainly devoted to the change of the hydrophilic carbohydrate moieties toward the diversification of glycolipid derivatives synthesized, whereas only a limited scope of hydrophobic lipid chain was employed. As shown in Scheme 1, we particularly emphasized in this study the impact of length variation of lipid chain toward the reaction tolerance as well

* Corresponding authors. Tel.: +86 021 64253016; fax: +86 021 64252758; e-mail addresses: 020060205@ecust.edu.cn (X.-P. He), jli@mail.shcnc.ac.cn (J. Li), mrs_guorongchen@ecust.edu.cn (G.-R. Chen).

as related functions of the formed glycolipids. Nine fatty acids (with carbon numbers of 5, 7, 9, 12, 13, 14, 15, 16, and 18, respectively) were utilized as starting materials to prepare various lipid alkynes for achieving the click reaction with the 1-azido-tetra-*O*-benzyl- β -D-glucosyl donor (**1**, Scheme 1). Microwave irradiation was introduced into this key step for evaluating whether the corresponding reactivity would be enhanced. Parallel click reactions were also conducted under conventional condition (stirring at rt) and the comparable results were discussed.



Scheme 1. Synthetic route of triazole-linked glycolipids, reagents and conditions: (a) VcNa (0.4 equiv)/CuSO₄·5H₂O (0.2 equiv) under Mw. or VcNa (6 equiv)/CuSO₄·5H₂O (3 equiv) at rt in CH₂Cl₂/H₂O; (b) PdCl₂/H₂ in MeOH.

Furthermore, two brand new functions of this specific triazolyl glycolipid class were disclosed by our further analysis via electrochemistry and MTT assay. First, it is well documented that triazole derivatives could form protecting film on metal surface for corrosion inhibition.¹⁴ We have thus performed EIS measurement on gold electrode coated by the triazolyl glycolipids for the modeling study of their initial adsorption competence. The resulting SAR in an interesting carbon chain length-dependent manner was sequentially elucidated. Next, the cytotoxicity of this triazolyl glycolipid class on HeLa (cervix cancer) cell line was identified by MTT assay.

2. Result and discussion

2.1. Synthesis

As shown in Scheme 1, the known azido glucoside **1**¹⁵ was employed as the glycodonor for coupling with various terminal *O*-alkynes. Commercially available valeric, heptylic, pelargonic, lauric, tridecanoic, myristic, pentadecanoic, palmitic and stearic acids have been previously converted to the corresponding *O*-alkynyl fatty esters (**2**–**10**) in the presence of 1.5 equiv K₂CO₃ and 1.5 equiv propargyl bromide in dry DMF.^{16a}

With azide and alkyne materials ready, the Cu(I)-catalyzed 1,3-dipolar cycloaddition (click reaction) via microwave irradiation was then attempted. Initially, the azido glucoside (**1**) and different *O*-alkynes (**2**–**10**) were dissolved in CH₂Cl₂/H₂O (1:1, v/v), followed by the addition of catalytic amount of sodium ascorbate (0.4 equiv)

and CuSO₄·5H₂O (0.2 equiv). The mixture was then transferred to the microwave oven (YL8023B1, Yalian Company) at 55 °C for a ramp time of 2 min and hold time of 12 min with vigorous stirring. TLC monitoring (by spraying with 6 N H₂SO₄ and charring at 300 °C) indicated that all starting materials had been fully converted in this 14-min pattern to the unique crude products, which were successively purified by extraction and column chromatography. To our surprise, all carbon chain length varied *O*-alkynyl fatty esters have proven tolerable toward the microwave-assisted click reaction, affording the desired products **11**–**19** in excellent yields of 92.9–99.0% (Table 1).

Table 1
Click products (**11**–**19**) and debenzylated glycolipids (**20**–**28**) yielded via Scheme 1

Compd	Yield (%) ^a	Yield (%) ^b	Compd	Yield (%)
11	92.9	97.1	20	90.5
12	97.7	94.7	21	92.5
13	99.0	93.5	22	83.7
14	96.6	98.8	23	66.1
15	96.5	96.9	24	84.4
16	98.3	96.7	25	72.3
17	96.1	95.7	26	90.6
18	96.6	94.5	27	75.1
19	98.3	95.2	28	85.5

^a This is fulfilled under microwave irradiation within 14 min.

^b This is fulfilled by stirring under rt within 6 h.

Next, for validating the predominance of the microwave-assisted click chemistry, we performed the same reaction under conventional condition. Such result was listed in Table 1. Clearly, all click reactions stirring at room temperature was much more sluggish, which required approximately 6 h (consecutive monitoring by TLC every 30 min for the first 1 h and every 1 h for the rest 5 h) for complete conversion. In addition, compared with the microwave-assisted reactions, excessive catalyst loading (VcNa from 0.4 equiv to 6 equiv, CuSO₄·5H₂O from 0.2 equiv to 3 equiv) was required toward those accomplished conventionally within such timeframe for retaining the final yields (93.5–98.8%). The experimental outcome above described has thus demonstrated the introduction of microwave irradiation into the present case desirable for tremendously accelerating the reaction rate and enhancing the reactivity. This may alternatively represent a facile methodology toward the expeditious preparation of the triazolyl glycolipid series.

Eventually, the afforded click products (**11**–**19**) were debenzylated with careful manipulation (see experimental Section 4.2.) under a PdCl₂/H₂ promoted^{16b} system (Scheme 1), which gave the desired alcohols (**20**–**28**) in moderate-to-good yields of 66.1–92.5% (Table 1).

2.2. Electrochemical measurement

Numerous lipid chain-containing organic compounds were identified as corrosion inhibitors, which may economically and practically reduce corrosive attack on metals.^{17,18} However, most of the currently reported inhibitors suffer from their environmentally toxic nature and are thereby limited for further industrialization.¹⁹ Glycolipids represent a class of highly biocompatible substances with extremely low toxicity and fast biodegradation. They were proposed as green surfactants⁵ and the physiochemical property of several triazole-linked glycolipids was revealed recently.^{13b} In addition, triazole derivatives have also been evaluated as potent anticorrosion agents due to their *N*-heterocyclic nature.¹⁴ Prompted by such compelling evidence, we tended to investigate the adsorption competence of our triazolyl glycolipids on metals. EIS measurement on gold electrode was employed as the preliminary analysis model involving various chain length varied samples (**20**–**28**).

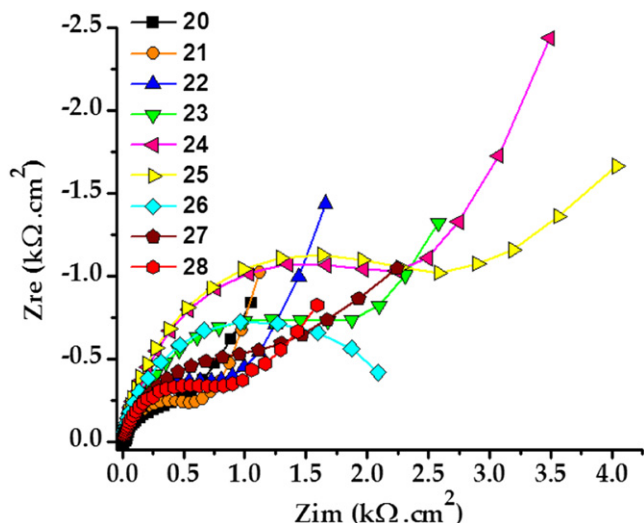


Fig. 1. Electrochemical impedance spectra measured on glycolipid film covered electrode.

The self-assembled films were formed on pretreated gold electrode after 2-h immersing in 2 mM triazolyl glycolipid solution in CH_2Cl_2 . EIS measurements were carried out in 10–100 mHz frequency range at a modified Randle's model (Fig. 2, where R_s is the solution resistance between the working electrode and reference electrode; Q is the constant-phase elements; W is the Warburg impedance) disturbed with amplitude of 5 mV controlled by electrochemical software ZSimpWin. The values of charge transfer resistance (R_{ct}) were obtained from the impedance measurement and the surface coverage (θ) and inhibition efficiency ($P\%$) can be calculated by following formulas:

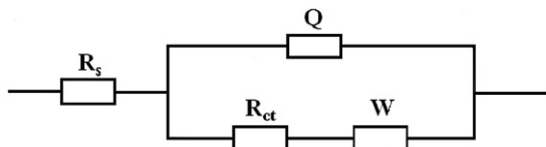


Fig. 2. Equivalent circuit for the impedance spectra.

$$(1 - \theta) = \frac{R_{ct}^0}{R} \quad (1)$$

$$P\% = \frac{v_{corr}^0 - v_{corr}}{v_{corr}^0} \times 100 = \frac{R_{ct} - R_{ct}^0}{R_{ct}} \times 100 \quad (2)$$

where R_{ct} and R_{ct}^0 are the charge transfer values with and without film, respectively, for gold electrode.

Nyquist diagram of gold electrode in the presence and absence of triazolyl glycolipids was shown in Fig. 1 and Fig. S1 (see Supplementary data), respectively. Obviously, as listed in Table 2, the values of R_{ct} gradually increased when the carbon number of alkyl group on triazole ring gradually prolonged from C_5 to C_{13} , which then tended to decrease when the chain continuously extended (from C_{14} to C_{18}). An obvious increase of R_{ct} value ($\Delta R_{ct} = 1.181 \text{ k}\Omega \text{ cm}^2$) was observed by comparing **23** (C_{12}) with **22** (C_9) whereas a fairly regular decrease was occurred from **25** (C_{13}) to **28** (C_{18}) with ΔR_{ct} values being 0.415 (C_{14} – C_{13}), 0.603 (C_{15} – C_{14}), 0.545 (C_{16} – C_{15}), 0.343 (C_{18} – C_{16}) $\text{k}\Omega \text{ cm}^2$, respectively. This experimental phenomenon showed that the chain length preference of the protecting film attached to gold electrode was maximum 13 carbon atoms on fatty acid while further chain elongation rendered deleterious impact.

In addition, such unique SAR was further elaborated by the calculated surface coverage (θ) as well as inhibition efficiency (P)

Table 2

The surface coverage (θ) and inhibition efficiency (P) of different films covered gold electrodes

Compd	Alkyl	R_{ct} ($\text{k}\Omega \text{ cm}^2$)	ΔR_{ct} ($\text{k}\Omega \text{ cm}^2$) ^b	$1 - \theta$ ^c	P (%) ^d
—	—	0.063 ^a	—	—	—
20	C_5	0.260	+0.197	0.241	75.9
21	C_7	0.587	+0.327	0.107	89.3
22	C_9	0.885	+0.298	0.071	92.9
23	C_{12}	2.066	+1.181	0.031	96.9
24	C_{13}	2.675	+0.609	0.024	97.6
25	C_{14}	2.260	−0.415	0.028	97.2
26	C_{15}	1.657	−0.603	0.038	96.2
27	C_{16}	1.112	−0.545	0.057	94.3
28	C_{18}	0.769	−0.343	0.082	91.8

^a This is the R_{ct} value without films (see Fig. S1).

^b This is the R_{ct} difference between the present entry and the last entry.

^c This is calculated via formula (1).

^d This is calculated via formula (2).

according to formulas (1) and (2), respectively (Table 2). As reflected in Fig. 3 triazolyl glycolipids with carbon numbers of 12, 13, and 14 on fatty acid possessed the most promising inhibition efficiencies of 96.9, 97.6, 97.2% (at a compound concentration of $2 \times 10^{-3} \text{ M}$ in CH_2Cl_2) with **24** (C_{13}) being most privileged. However, such variant (P) slightly but gradually lowered when the chain length continued to prolong (**26**: 96.2%, **27**: 94.3%, **28**: 91.8%).

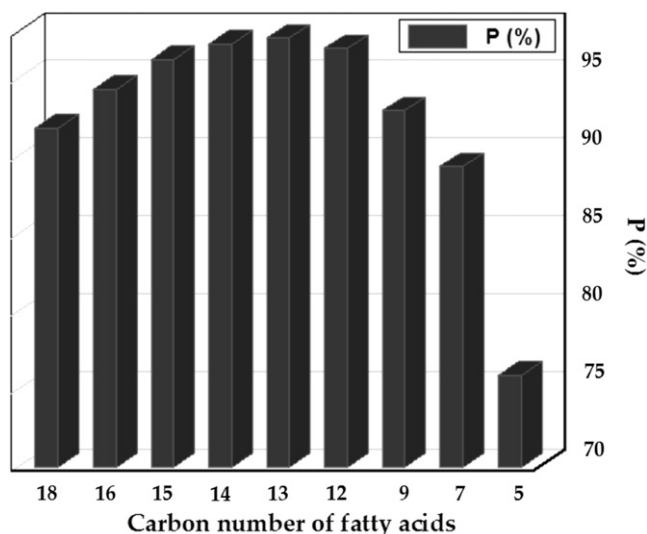


Fig. 3. Variation of the inhibition effect as a function of alkyl chain length.

Our preliminary result yielded by EIS measurement has demonstrated the promising adsorption competence of this new triazolyl glycolipid class on metal surface, which adopted a chain length-dependent manner. This may potentially provide valuable information toward the development of glycolipid-based green corrosion inhibitors.

2.3. Biological assay

Since glycolipids have previously been purposed as potential anticancer agents possibly by inhibiting the cell proliferation process,⁴ we evaluated preliminarily the cytotoxicity of compounds **20–28** on HeLa cell (cervix cancer) line by MTT assay.

As shown in Fig. 4, HeLa cells were treated with indicated concentrations of various glycolipids (**20–28**) and the cell viability was then determined by MTT assay and was expressed as mean of three separate experiments. The IC_{50} values of glycolipids **23–28** (with inhibition >50% at compound concentration of 200 $\mu\text{g/mL}$)

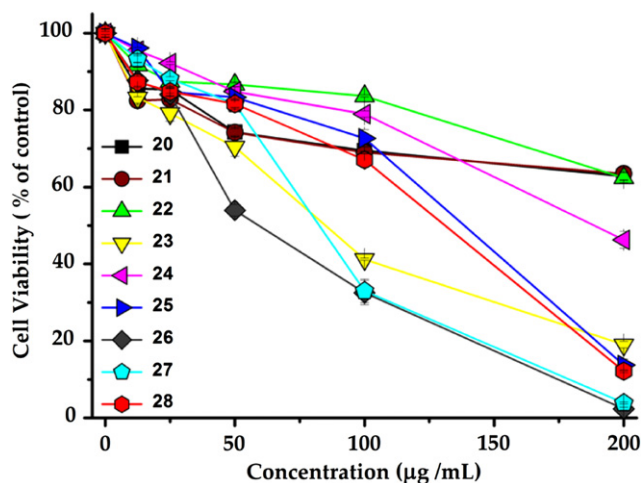


Fig. 4. Effects of the various glycolipids on the viability of HeLa cells.

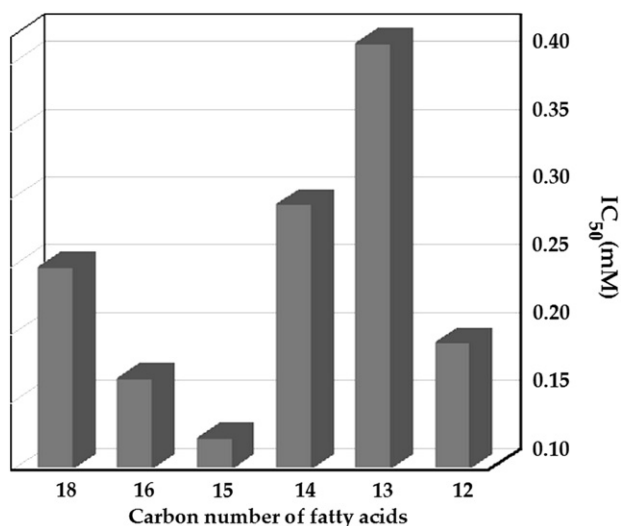


Fig. 5. IC₅₀ value of bioactive glycolipids.

were then evaluated according to the cell viability curve.²⁰ This result was illustrated in Fig. 5.

Evidently, the IC₅₀ values moderately increased from 0.191 (C₁₂, compound **23**) to 0.412 mM (C₁₃, compound **24**), which then gradually decreased till 0.121 mM (C₁₅, compound **26**). However, small increases in IC₅₀ values were sequentially observed when the chain length continuously prolonged (0.165–0.247 mM from C₁₆ to C₁₈). Such tendency indicated that compound **26** with an alkyl chain length of 15 carbon atoms was preferential toward inhibition of HeLa cell line among the triazolyl glycolipids synthesized.

Indeed, triazole-contained glycolipids have been evaluated as immunostimulating agents,^{2c} whereas rare studies were then revealed in relation with their potential biological profiles. Therefore, our MTT assay performed has shown another biological activity of triazole-linked glycolipids, which would furnish better understanding toward the intrinsic therapeutic values of this specific compound class.

3. Conclusion

In summary, we have efficiently prepared a series of novel triazole-linked ester-type glycolipids via microwave accelerated click

chemistry in almost quantitative yields within only a quarter. Such synthetic shortcut may represent a facile methodology toward the preparation of this specific glycolipid class. Two brand new functions of these newly constructed glycolipids have been sequentially disclosed. EIS measurement indicated the potent adsorption competence of this compound series on gold surface in a carbon chain length-dependent manner, which would provide new insights toward the development of triazolyl glycolipid-based green corrosion inhibitors. In addition, the following MTT assay showed the cytotoxicity of the synthesized compounds on HeLa cell line howbeit with moderate inhibitory activities. Further study including the construction of new glycolipid derivatives of this kind as well as their physicochemical and biological assessments is currently underway.

4. Experimental section

All purchased chemicals and reagents are of high commercially available grade. Solvents were purified by standard procedures. ¹H and ¹³C NMR spectrum were recorded on a Bruker AM-400 spectrometer in CDCl₃ or D₂O solutions using tetramethylsilane as the internal standard (chemical shifts in δ parts per million). Microwave-assisted reactions were performed in a Yalian (YL8023B1) system at 55 °C with a ramp time of 2 min and hold time of 12 min. All reactions were monitored by TLC (thin-layer chromatography) with detection by UV or by spraying with 6 N H₂SO₄ and charring at 300 °C. Optical rotations were measured using a Perkin–Elmer 241 polarimeter at room temperature and a 10-cm 1-mL cell. High resolution mass spectra (HRMS) were recorded on an MA1212 instrument using standard conditions (ESI, 70 eV). Electrochemical experiments were carried out by using an IM6 system (ZAHNER, Germany) controlled with analysis software (ZSimpWin).

4.1. General procedure for the click reaction

Microwave-assisted pattern: To a well-stirred biphasic solution of sugar azide (1 equiv) and alkynyl carboxylic ester (2 equiv) in CH₂Cl₂ (4 mL) and H₂O (4 mL), were added CuSO₄·5H₂O (0.2 equiv) and sodium ascorbate (0.4 equiv) successively. The mixture was then transferred to the microwave oven at 55 °C for a ramp time of 2 min and hold time of 12 min. Upon completion, the resulting mixture was diluted with CH₂Cl₂ (10 mL), washed with brine (2×9 mL), dried over MgSO₄ and concentrated under reduced pressure. The crude residue was purified by column chromatography (for conventional pattern, see Supplementary data).

4.1.1. Tetra-O-benzyl- β -D-pyranoglucosyl triazolyl pentanoate (11**).** From **2** (30.7 mg, 0.22 mmol) and **1** (62 mg, 0.11 mmol), column chromatography (petroleum ether/EtOAc, 6:1 to 4:1) afforded **11** as a white ceraceous solid (71.9 mg, 92.9%). TLC: R_f =0.20 (petroleum ether/EtOAc, 4:1); [α]_D²⁵ −0.17 (c 0.1, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): δ =7.68 (s, 1H), 7.35–7.27 (m, 13H), 7.23–7.15 (m, 5H), 6.94–6.92 (m, 2H), 5.57 (d, J =9.3 Hz, 1H), 5.20 (dd, J =12.8 Hz, 16.4 Hz, 2H), 4.91 (dd, J =11.0, 12.8 Hz, 2H), 4.85 (d, J =10.8 Hz, 1H), 4.60 (d, J =10.8 Hz, 1H), 4.55 (d, J =12.0 Hz, 1H), 4.49 (d, J =12.3 Hz, 1H), 4.49 (d, J =10.8 Hz, 1H), 4.07 (d, J =10.8 Hz, 1H), 4.02 (t, J =8.9 Hz, 1H), 3.82 (m, 2H), 3.73–3.67 (m, 3H), 2.30 (t, J =7.5 Hz, 2H), 1.57 (m, 2H), 1.30 (m, 2H), 0.87 (t, J =7.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ =173.3, 143.0, 138.0, 137.6, 137.5, 136.8, 128.3, 128.2, 128.1, 128.0, 127.8, 127.7, 127.6, 127.6, 127.5, 127.4, 123.0, 87.3, 85.2, 80.6, 77.9, 77.1, 75.5, 75.0, 74.7, 73.3, 68.2, 57.1, 33.6, 26.6, 22.0, 13.5; HRESIMS: calcd for C₄₂H₄₇N₃O₇+H: 706.3492; found: 706.3488.

4.1.2. Tetra-O-benzyl- β -D-pyranoglucosyl triazolyl heptanoate (12**).** From **3** (51.3 mg, 0.31 mmol) and **1** (86.3 mg, 0.15 mmol), column chromatography (petroleum ether/EtOAc, 6:1 to 4:1) afforded **12** as

a colorless ceraceous solid (109.4 mg, 97.7%). TLC: R_f =0.27 (petroleum ether/EtOAc, 4:1); $[\alpha]_D^{25}$ –19.5 (c 0.2, CH_2Cl_2); ^1H NMR (400 MHz, CDCl_3): δ =7.68 (s, 1H), 7.34–7.28 (m, 13H), 7.23–7.16 (m, 5H), 6.94–6.92 (m, 2H), 5.57 (d, J =9.0 Hz, 1H), 5.20 (dd, J =12.8, 16.8 Hz, 2H), 4.92 (dd, J =11.2, 12.8 Hz, 2H), 4.85 (d, J =10.8 Hz, 1H), 4.60 (d, J =10.8 Hz, 1H), 4.55 (d, J =12.3 Hz, 1H), 4.49 (d, J =12.5 Hz, 1H), 4.49 (d, J =10.8 Hz, 1H), 4.07 (d, J =10.5 Hz, 1H), 4.02 (t, J =8.9 Hz, 1H), 3.82 (m, 2H), 3.73–3.67 (m, 3H), 2.29 (t, J =7.5 Hz, 2H), 1.58 (m, 2H), 1.31–1.20 (br m, 6H), 0.86 (t, J =6.9 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ =173.4, 143.0, 138.0, 137.6, 137.6, 136.8, 128.3, 128.3, 128.2, 128.1, 127.8, 127.8, 127.7, 127.6, 127.6, 127.5, 123.0, 87.4, 85.3, 80.6, 77.9, 77.1, 75.6, 75.0, 74.7, 73.4, 68.2, 57.2, 33.9, 31.2, 28.6, 24.6, 22.3, 13.9; HRESIMS: calcd for $\text{C}_{44}\text{H}_{51}\text{N}_3\text{O}_7+\text{H}$: 734.3085; found: 734.3082.

4.1.3. Tetra-*O*-benzyl- β -D-pyranoglucosyl triazolyl nonanoate (13**).** From **4** (41.9 mg, 0.21 mmol) and **1** (60.4 mg, 0.11 mmol), column chromatography (petroleum ether/EtOAc, 6:1 to 4:1) afforded **13** as a white ceraceous solid (80.6 mg, 99.0%). TLC: R_f =0.34 (petroleum ether/EtOAc, 4:1); $[\alpha]_D^{25}$ –15.1 (c 0.07, CH_2Cl_2); ^1H NMR (400 MHz, CDCl_3): δ =7.68 (s, 1H), 7.34–7.27 (m, 13H), 7.22–7.16 (m, 5H), 6.94–6.92 (m, 2H), 5.57 (d, J =9.0 Hz, 1H), 5.20 (dd, J =12.8 Hz, 16.8 Hz, 2H), 4.92 (dd, J =11.2, 12.8 Hz, 2H), 4.85 (d, J =10.5 Hz, 1H), 4.60 (d, J =10.5 Hz, 1H), 4.55 (d, J =12.0 Hz, 1H), 4.49 (d, J =12.5 Hz, 1H), 4.49 (d, J =10.5 Hz, 1H), 4.07 (d, J =10.5 Hz, 1H), 4.02 (t, J =8.8 Hz, 1H), 3.82 (m, 2H), 3.73–3.68 (m, 3H), 2.29 (t, J =7.5 Hz, 2H), 1.58 (m, 2H), 1.30–1.24 (br m, 10H), 0.87 (t, J =6.9 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ =173.4, 143.0, 137.9, 137.6, 137.5, 136.8, 128.3, 128.3, 128.2, 128.1, 127.8, 127.8, 127.7, 127.7, 127.6, 127.5, 123.1, 87.3, 85.3, 80.5, 77.9, 77.0, 75.6, 75.0, 74.7, 73.3, 68.1, 57.2, 33.9, 31.6, 29.0, 28.9, 28.9, 24.6, 22.5, 14.0; HRESIMS: calcd for $\text{C}_{46}\text{H}_{55}\text{N}_3\text{O}_7+\text{Na}$: 784.3938; found: 784.3941.

4.1.4. Tetra-*O*-benzyl- β -D-pyranoglucosyl triazolyl dodecanoate (14**).** From **5** (42.9 mg, 0.18 mmol) and **1** (51.0 mg, 0.09 mmol), column chromatography (petroleum ether/EtOAc, 6:1 to 4:1) afforded **14** as a white ceraceous solid (70.0 mg, 96.6%). TLC: R_f =0.29 (petroleum ether/EtOAc, 4:1); $[\alpha]_D^{25}$ –42.4 (c 0.2, CH_2Cl_2); ^1H NMR (400 MHz, CDCl_3): δ =7.68 (s, 1H), 7.34–7.27 (m, 13H), 7.22–7.16 (m, 5H), 6.94–6.92 (m, 2H), 5.57 (d, J =9.0 Hz, 1H), 5.20 (dd, J =12.8, 16.4 Hz, 2H), 4.92 (dd, J =11.0, 12.8 Hz, 2H), 4.85 (d, J =10.8 Hz, 1H), 4.60 (d, J =10.8 Hz, 1H), 4.55 (d, J =12.0 Hz, 1H), 4.49 (d, J =12.8 Hz, 1H), 4.49 (d, J =10.5 Hz, 1H), 4.07 (d, J =10.8 Hz, 1H), 4.02 (t, J =8.8 Hz, 1H), 3.82 (m, 2H), 3.73–3.67 (br m, 3H), 2.29 (t, J =7.5 Hz, 2H), 1.58 (br m, 2H), 1.32–1.24 (br m, 16H), 0.88 (t, J =6.8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ =173.4, 143.0, 138.0, 137.6, 136.8, 128.3, 128.3, 128.2, 128.1, 127.8, 127.7, 127.6, 127.5, 123.0, 87.4, 85.3, 80.6, 77.9, 77.1, 75.6, 75.0, 74.7, 73.4, 68.2, 57.2, 33.9, 31.7, 29.4, 29.3, 29.2, 29.1, 29.0, 24.7, 22.5, 14.0; HRESIMS: calcd for $\text{C}_{49}\text{H}_{61}\text{N}_3\text{O}_7+\text{H}$: 804.4588; found: 804.4583.

4.1.5. Tetra-*O*-benzyl- β -D-pyranoglucosyl triazolyl tridecanoate (15**).** From **6** (41.9 mg, 0.17 mmol) and **1** (47 mg, 0.08 mmol), column chromatography (petroleum ether/EtOAc, 6:1 to 4:1) afforded **15** as a white ceraceous solid (65.6 mg, 96.5%). TLC: R_f =0.35 (petroleum ether/EtOAc, 4:1); $[\alpha]_D^{25}$ –19.4 (c 0.1, CH_2Cl_2); ^1H NMR (400 MHz, CDCl_3): δ =7.68 (s, 1H), 7.34–7.28 (m, 13H), 7.21–7.15 (m, 5H), 6.94–6.92 (m, 2H), 5.57 (d, J =9.0 Hz, 1H), 5.20 (dd, J =12.9, 16.8 Hz, 2H), 4.92 (dd, J =11.3, 12.8 Hz, 2H), 4.85 (d, J =10.8 Hz, 1H), 4.60 (d, J =10.8 Hz, 1H), 4.55 (d, J =12.0 Hz, 1H), 4.49 (d, J =12.3 Hz, 2H), 4.07 (d, J =10.5 Hz, 1H), 4.02 (t, J =8.8 Hz, 1H), 3.82 (m, 2H), 3.72–3.68 (br m, 3H), 2.29 (t, J =7.7 Hz, 2H), 1.57 (br m, 2H), 1.32–1.24 (br m, 18H), 0.88 (t, J =6.8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ =173.5, 143.1, 138.0, 137.6, 137.6, 136.8, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.7, 127.7, 127.6, 127.5, 123.0, 87.4, 85.3, 80.6, 77.9, 77.1, 75.6, 75.0, 74.8, 73.4, 68.2, 57.2, 34.0, 31.8, 29.6, 29.5, 29.5, 29.3, 29.2, 29.1, 29.0, 24.7, 22.6, 14.0; HRESIMS: calcd for $\text{C}_{51}\text{H}_{65}\text{N}_3\text{O}_7+\text{Na}$: 854.4720; found: 854.4719.

14.0; HRESIMS: calcd for $\text{C}_{50}\text{H}_{63}\text{N}_3\text{O}_7+\text{Na}$: 840.4564; found: 840.4560.

4.1.6. Tetra-*O*-benzyl- β -D-pyranoglucosyl triazolyl tetradecanoate (16**).** From **7** (48.1 mg, 0.18 mmol) and **1** (51.1 mg, 0.09 mmol), column chromatography (petroleum ether/EtOAc, 6:1 to 4:1) afforded **16** as a white ceraceous solid (73.9 mg, 98.3%). TLC: R_f =0.29 (petroleum ether/EtOAc, 4:1); $[\alpha]_D^{25}$ –20.4 (c 0.1, CH_2Cl_2); ^1H NMR (400 MHz, CDCl_3): δ =7.68 (s, 1H), 7.34–7.27 (m, 13H), 7.22–7.16 (m, 5H), 6.94–6.92 (m, 2H), 5.57 (d, J =9.0 Hz, 1H), 5.20 (dd, J =12.8, 16.4 Hz, 2H), 4.91 (dd, J =11.2, 12.8 Hz, 2H), 4.85 (d, J =10.8 Hz, 1H), 4.60 (d, J =10.8 Hz, 1H), 4.55 (d, J =12.3 Hz, 1H), 4.49 (d, J =12.5 Hz, 1H), 4.49 (d, J =10.5 Hz, 1H), 4.07 (d, J =10.5 Hz, 1H), 4.02 (t, J =8.8 Hz, 1H), 3.82 (m, 2H), 3.73–3.67 (br m, 3H), 2.29 (t, J =7.5 Hz, 2H), 1.58 (br m, 2H), 1.30–1.24 (br m, 20H), 0.88 (t, J =6.8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ =173.4, 143.1, 138.0, 137.6, 137.6, 136.8, 128.3, 128.3, 128.2, 128.1, 127.9, 127.8, 127.7, 127.7, 127.6, 127.6, 123.0, 87.4, 85.3, 80.6, 78.0, 77.1, 75.6, 75.1, 74.8, 73.4, 68.2, 57.2, 34.0, 31.8, 29.5, 29.5, 29.5, 29.3, 29.2, 29.1, 29.0, 24.7, 22.6, 14.0; HRESIMS: calcd for $\text{C}_{51}\text{H}_{65}\text{N}_3\text{O}_7+\text{Na}$: 854.4720; found: 854.4719.

4.1.7. Tetra-*O*-benzyl- β -D-pyranoglucosyl triazolyl pentadecanoate (17**).** From **8** (49.8 mg, 0.18 mmol) and **1** (50.2 mg, 0.09 mmol), column chromatography (petroleum ether/EtOAc, 6:1 to 4:1) afforded **17** as a white ceraceous solid (72.2 mg, 96.1%). TLC: R_f =0.35 (petroleum ether/EtOAc, 4:1); $[\alpha]_D^{25}$ +20.0 (c 0.1, CH_2Cl_2); ^1H NMR (400 MHz, CDCl_3): δ =7.68 (s, 1H), 7.34–7.28 (m, 13H), 7.22–7.14 (m, 5H), 6.93–6.91 (m, 2H), 5.57 (d, J =9.0 Hz, 1H), 5.20 (dd, J =12.8 Hz, 16.8 Hz, 2H), 4.92 (dd, J =11.0 Hz, 12.8 Hz, 2H), 4.85 (d, J =10.5 Hz, 1H), 4.59 (d, J =10.8 Hz, 1H), 4.55 (d, J =12.0 Hz, 1H), 4.49 (d, J =10.8 Hz, 2H), 4.07 (d, J =10.8 Hz, 1H), 4.03 (t, J =8.9 Hz, 1H), 3.82 (m, 2H), 3.71–3.68 (br m, 3H), 2.28 (t, J =7.7 Hz, 2H), 1.57 (br m, 2H), 1.33–1.28 (br m, 2H), 1.24 (d, J =5.3 Hz, 20H), 0.88 (t, J =6.9 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ =173.5, 143.0, 138.0, 137.6, 137.5, 136.8, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.7, 127.7, 127.6, 123.1, 87.3, 85.3, 80.5, 77.9, 77.0, 75.6, 75.1, 74.8, 73.4, 68.1, 57.2, 34.0, 31.8, 29.6, 29.6, 29.5, 29.5, 29.3, 29.2, 29.1, 29.0, 24.7, 22.6, 14.0; HRESIMS: $\text{C}_{52}\text{H}_{67}\text{N}_3\text{O}_7+\text{Na}$: calcd for 868.4877; found: 868.4876.

4.1.8. Tetra-*O*-benzyl- β -D-pyranoglucosyl triazolyl palmitate (18**).** From compound **9** (46.8 mg, 0.16 mmol) and **1** (45 mg, 0.08 mmol), column chromatography (petroleum ether/EtOAc, 8:1 to 4:1) afforded **18** as a white ceraceous solid (66.1 mg, 96.6%). TLC: R_f =0.31 (petroleum ether/EtOAc, 4:1); $[\alpha]_D^{25}$ –8.0 (c 0.2, CH_2Cl_2); ^1H NMR (400 MHz, CDCl_3): δ =7.68 (s, 1H), 7.36–7.28 (m, 13H), 7.21–7.15 (m, 5H), 6.94–6.91 (m, 2H), 5.57 (d, J =9.0 Hz, 1H), 5.20 (dd, J =12.9, 16.4 Hz, 2H), 4.92 (dd, J =11.3, 12.8 Hz, 2H), 4.85 (d, J =10.8 Hz, 1H), 4.60 (d, J =10.8 Hz, 1H), 4.55 (d, J =12.0 Hz, 1H), 4.49 (d, J =12.3 Hz, 2H), 4.07 (d, J =10.5 Hz, 1H), 4.02 (t, J =8.8 Hz, 1H), 3.82 (m, 2H), 3.72–3.68 (br m, 3H), 2.28 (t, J =7.5 Hz, 2H), 1.57 (br m, 2H), 1.32–1.28 (br m, 2H), 1.25 (d, J =6.3 Hz, 22H), 0.88 (t, J =6.7 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ =173.4, 143.0, 138.0, 137.6, 137.6, 136.8, 128.3, 128.3, 128.2, 128.1, 127.8, 127.8, 127.7, 127.7, 127.6, 127.5, 123.0, 87.4, 85.3, 80.6, 77.9, 77.1, 75.6, 75.0, 74.8, 73.4, 68.2, 57.2, 34.0, 31.8, 29.6, 29.5, 29.5, 29.3, 29.2, 29.1, 29.0, 24.7, 22.6, 14.0; HRESIMS: $\text{C}_{53}\text{H}_{69}\text{N}_3\text{O}_7+\text{Na}$: calcd for 882.5033; found: 882.5037.

4.1.9. Tetra-*O*-benzyl- β -D-pyranoglucosyl triazolyl stearate (19**).** From compound **10** (69.6 mg, 0.22 mmol) and **1** (61 mg, 0.11 mmol), column chromatography (petroleum ether/EtOAc, 10:1 to 4:1) afforded **19** as a white ceraceous solid (94.1 mg, 98.3%). TLC: R_f =0.30 (petroleum ether/EtOAc, 4:1); $[\alpha]_D^{25}$ –9.21 (c 0.2, CH_2Cl_2); ^1H NMR (400 MHz, CDCl_3): δ =7.68 (s, 1H), 7.33–7.28 (m, 13H), 7.21–7.16 (m, 5H), 6.94–6.92 (m, 2H), 5.57 (d, J =9.0 Hz, 1H), 5.20 (dd, J =12.8 Hz, 16.4 Hz, 2H), 4.92 (dd, J =11.3, 13.0 Hz, 2H), 4.85 (d, J =10.8 Hz, 1H), 4.60 (d, J =10.8 Hz, 1H), 4.55 (d, J =12.0 Hz, 1H), 4.49 (d, J =12.3 Hz, 2H), 4.07 (d, J =10.5 Hz, 1H), 4.03 (t, J =8.9 Hz, 1H), 3.82 (m, 2H),

3.72–3.68 (br m, 3H), 2.29 (t, $J=7.7$ Hz, 2H), 1.58 (br m, 2H), 1.34–1.28 (br m, 2H), 1.25 (d, $J=6.3$ Hz, 26H), 0.88 (t, $J=6.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): $\delta=173.5, 143.1, 138.0, 137.6, 137.6, 136.8, 128.4, 128.3, 128.3, 128.1, 127.9, 127.9, 127.7, 127.7, 127.6, 123.1, 87.4, 85.4, 80.6, 78.0, 77.1, 75.7, 75.1, 74.8, 73.4, 68.2, 57.3, 34.0, 31.8, 29.6, 29.6, 29.5, 29.4, 29.3, 29.1, 29.0, 24.7, 22.6, 14.1$; HRESIMS: $\text{C}_{55}\text{H}_{73}\text{N}_3\text{O}_7+\text{Na}$: calcd for 910.5346; found: 910.5341.

4.2. General procedure for the debenzoylation

To a solution of benzylated glycolipids in MeOH (8–16 mL) was added PdCl_2 (0.5 equiv), stirring vigorously under hydrogen atmosphere for 20 min. After which, the hydrogen gas was released rapidly and the system was refilled with H_2 again. This manipulation was repeated thrice. The resulting mixture was then filtered and concentrated under reduced pressure to give the crude residue, which was purified by column chromatography.

4.2.1. β -D-Pyranoglucosyl triazolyl heptanoate (20). From **11** (311 mg, 0.441 mmol), column chromatography (EtOAc/EtOH, 12:1 to 6:1) afforded **20** as a colorless solid (137.7 mg, 90.5%). TLC: $R_f=0.42$ (EtOAc/MeOH, 4:1); $[\alpha]_D^{25}-1.93$ (c 0.30, CH_3OH); ^1H NMR (400 MHz, CDCl_3): $\delta=8.10$ (s, 1H), 5.61 (d, $J=9.3$ Hz, 1H), 5.08 (s, 2H), 3.91 (t, $J=8.9$ Hz, 1H), 3.77–3.72 (m, 1H), 3.70–3.65 (m, 1H), 3.63–3.54 (m, 3H), 2.24 (t, $J=7.5$ Hz, 2H), 1.46 (m, 2H), 1.20 (m, 2H), 0.78 (t, $J=7.3$ Hz, 3H); ^{13}C NMR (100 MHz, $\text{CDCl}_3+\text{CD}_3\text{OD}$): $\delta=173.9, 142.6, 124.3, 87.6, 78.8, 76.4, 72.3, 68.8, 60.7, 56.9, 33.5, 26.6, 21.9, 13.4$; HRESIMS: calcd for: $\text{C}_{14}\text{H}_{23}\text{N}_3\text{O}_7+\text{H}$: 346.1614; found: 346.1616.

4.2.2. β -D-Pyranoglucosyl triazolyl pentanoate (21). From compound **12** (304 mg, 0.414 mmol), column chromatography (EtOAc/EtOH, 12:1 to 8:1) afforded **21** as a colorless solid (143.1 mg, 92.5%). TLC: $R_f=0.48$ (EtOAc/MeOH, 4:1); $[\alpha]_D^{25}-2.36$ (c 0.3, CH_3OH); ^1H NMR (400 MHz, CDCl_3): $\delta=8.01$ (s, 1H), 5.56 (d, $J=8.8$ Hz, 1H), 5.07 (s, 2H), 3.90 (t, $J=8.2$ Hz, 1H), 3.77–3.67 (m, 2H), 3.64–3.56 (m, 3H), 2.23 (t, $J=7.4$ Hz, 2H), 1.51 (m, 2H), 1.20 (br s, 6H), 0.80 (t, $J=6.5$ Hz, 3H); ^{13}C NMR (100 MHz, $\text{CDCl}_3+\text{CD}_3\text{OD}$): $\delta=174.0, 142.6, 124.4, 87.6, 78.9, 76.3, 72.3, 68.8, 60.7, 56.9, 33.9, 31.2, 28.6, 24.5, 22.3, 13.8$; HRESIMS: calcd for: $\text{C}_{16}\text{H}_{27}\text{N}_3\text{O}_7+\text{H}$: 374.1927; found: 374.1925.

4.2.3. β -D-Pyranoglucosyl triazolyl nonanoate (22). From compound **13** (165 mg, 0.216 mmol), column chromatography (EtOAc/EtOH, 12:1 to 8:1) afforded **22** as a colorless solid (83.7 mg, 96.5%). TLC: $R_f=0.67$ (EtOAc/MeOH, 4:1); $[\alpha]_D^{25}-0.90$ (c 0.3, CH_3OH); ^1H NMR (400 MHz, CDCl_3): $\delta=8.00$ (s, 1H), 5.56 (d, $J=8.3$ Hz, 1H), 5.03 (s, 2H), 3.97 (t, $J=8.2$ Hz, 1H), 3.74–3.67 (br m, 2H), 3.62–3.55 (br m, 3H), 2.24 (t, $J=7.0$ Hz, 2H), 1.53 (br m, 2H), 1.23 (br s, 10H), 0.85 (t, $J=6.8$ Hz, 3H); ^{13}C NMR (100 MHz, $\text{CDCl}_3+\text{CD}_3\text{OD}$): $\delta=173.9, 142.7, 124.7, 87.6, 78.8, 76.3, 72.4, 68.8, 60.7, 57.0, 33.9, 31.8, 29.2, 29.1, 24.7, 22.6, 14.0$; HRESIMS: calcd for: $\text{C}_{18}\text{H}_{31}\text{N}_3\text{O}_7+\text{H}$: 402.2240; found: 402.2241.

4.2.4. β -D-Pyranoglucosyl triazolyl dodecanoate (23). From compound **14** (286 mg, 0.356 mmol), column chromatography (EtOAc/EtOH, 12:1 to 8:1) afforded **23** as a colorless solid (104.3 mg, 66.1%). TLC: $R_f=0.65$ (EtOAc/MeOH, 4:1); $[\alpha]_D^{25}-0.78$ (c 0.2, CH_3OH); ^1H NMR (400 MHz, CDCl_3): $\delta=7.99$ (s, 1H), 5.55 (d, $J=9.0$ Hz, 1H), 5.03 (s, 2H), 3.92 (t, $J=8.9$ Hz, 1H), 3.75–3.66 (br m, 2H), 3.66–3.59 (br m, 2H), 3.54 (br s, 1H), 2.24 (t, $J=7.5$ Hz, 2H), 1.53 (br m, 2H), 1.24 (br s, 16H), 0.86 (t, $J=6.7$ Hz, 3H); ^{13}C NMR (100 MHz, $\text{CDCl}_3+\text{CD}_3\text{OD}$): $\delta=173.9, 142.4, 124.1, 87.6, 78.9, 76.4, 72.3, 68.7, 60.7, 56.8, 33.8, 31.7, 29.4, 29.2, 29.1, 29.1, 28.9, 24.5, 22.4, 13.8$; HRESIMS: calcd for $\text{C}_{21}\text{H}_{37}\text{N}_3\text{O}_7+\text{H}$: 444.2710; found: 444.2703.

4.2.5. β -D-Pyranoglucosyl triazolyl tridecanoate (24). From compound **15** (164 mg, 0.201 mmol), column chromatography (EtOAc/

EtOH, 12:1 to 8:1) afforded **24** as a white solid (77.6 mg, 84.4%). TLC: $R_f=0.63$ (EtOAc/MeOH, 4:1); $[\alpha]_D^{25}-6.57$ (c 0.4, CH_3OH); ^1H NMR (400 MHz, CDCl_3): $\delta=7.98$ (s, 1H), 5.56 (d, $J=9.0$ Hz, 1H), 5.05 (s, 2H), 3.95 (t, $J=8.3$ Hz, 1H), 3.77–3.71 (br m, 2H), 3.70–3.65 (br m, 2H), 3.56 (br s, 1H), 2.25 (t, $J=7.7$ Hz, 2H), 1.54 (br m, 2H), 1.24 (br s, 18H), 0.87 (t, $J=6.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): $\delta=173.9, 142.7, 124.7, 87.6, 78.8, 76.4, 72.3, 68.7, 60.7, 56.9, 33.9, 31.9, 29.7, 29.7, 29.6, 29.5, 29.3, 29.2, 24.7, 22.6, 14.0$; HRESIMS: calcd for: $\text{C}_{22}\text{H}_{39}\text{N}_3\text{O}_7+\text{H}$: 458.2866; found: 458.2861.

4.2.6. β -D-Pyranoglucosyl triazolyl tetradecanoate (25). From compound **16** (273 mg, 0.328 mmol), column chromatography (EtOAc/EtOH, 12:1 to 8:1) afforded **25** as a white solid (111.8 mg, 72.3%). TLC: $R_f=0.60$ (EtOAc/MeOH, 4:1); $[\alpha]_D^{25}-3.01$ (c 0.3, CH_3OH); ^1H NMR (400 MHz, CDCl_3): $\delta=7.98$ (s, 1H), 5.55 (d, $J=8.8$ Hz, 1H), 5.04 (s, 2H), 3.93 (t, $J=8.8$ Hz, 1H), 3.75–3.67 (br m, 2H), 3.66–3.59 (br m, 2H), 3.55 (br s, 1H), 2.24 (t, $J=7.5$ Hz, 2H), 1.54 (br m, 2H), 1.24 (br s, 20H), 0.87 (t, $J=6.8$ Hz, 3H); ^{13}C NMR (100 MHz, $\text{CDCl}_3+\text{CD}_3\text{OD}$): $\delta=173.9, 142.5, 124.1, 87.6, 78.9, 76.4, 72.3, 68.7, 60.7, 56.9, 33.8, 31.7, 29.5, 29.5, 29.5, 29.3, 29.2, 29.1, 29.0, 24.6, 22.5, 13.9$; HRESIMS: calcd for: $\text{C}_{23}\text{H}_{41}\text{N}_3\text{O}_7+\text{H}$: 472.3023; found: 472.3020.

4.2.7. β -D-Pyranoglucosyl triazolyl tetradecanoate (26). From compound **17** (303 mg, 0.359 mmol), column chromatography (EtOAc/EtOH, 12:1 to 8:1) afforded **26** as a white solid (157.8 mg, 90.6%). TLC: $R_f=0.51$ (EtOAc/MeOH, 4:1); $[\alpha]_D^{25}-2.0$ (c 0.3, CH_3OH); ^1H NMR (400 MHz, CDCl_3): $\delta=7.98$ (s, 1H), 5.55 (d, $J=8.8$ Hz, 1H), 5.04 (s, 2H), 3.93 (t, $J=8.7$ Hz, 1H), 3.73–3.68 (br m, 2H), 3.67–3.60 (br m, 2H), 3.55 (br s, 1H), 2.25 (t, $J=7.5$ Hz, 2H), 1.54 (br m, 2H), 1.24 (br s, 22H), 0.87 (t, $J=6.9$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): $\delta=173.8, 142.6, 124.6, 87.6, 78.8, 76.4, 72.3, 68.7, 60.8, 56.9, 33.9, 31.9, 29.1, 29.6, 29.6, 29.5, 29.3, 29.1, 29.0, 24.7, 22.6, 14.0$; HRESIMS: calcd for: $\text{C}_{24}\text{H}_{43}\text{N}_3\text{O}_7+\text{H}$: 486.3179; found: 486.3177.

4.2.8. β -D-Pyranoglucosyl triazolyl palmitate (27). From compound **18** (251 mg, 0.292 mmol), column chromatography (EtOAc/EtOH, 12:1 to 8:1) afforded **27** as a white solid (109.5 mg, 75.1%). TLC: $R_f=0.59$ (EtOAc/MeOH, 4:1); $[\alpha]_D^{25}-18.8$ (c 0.1, CH_3OH); ^1H NMR (400 MHz, CDCl_3): $\delta=7.98$ (s, 1H), 5.55 (d, $J=9.0$ Hz, 1H), 5.04 (s, 2H), 3.93 (t, $J=8.5$ Hz, 1H), 3.75–3.68 (br m, 2H), 3.66–3.60 (br m, 2H), 3.55 (br s, 1H), 2.24 (t, $J=7.5$ Hz, 2H), 1.54 (br m, 2H), 1.24 (br s, 24H), 0.87 (t, $J=6.5$ Hz, 3H); ^{13}C NMR (100 MHz, $\text{CDCl}_3+\text{CD}_3\text{OD}$): $\delta=173.9, 142.7, 124.7, 87.6, 78.7, 76.3, 72.3, 68.6, 60.6, 56.9, 34.0, 31.9, 29.7, 29.7, 29.4, 29.2, 29.1, 24.7, 22.7, 14.1$; HRESIMS: calcd for: $\text{C}_{25}\text{H}_{45}\text{N}_3\text{O}_7+\text{H}$: 500.3336; found: 500.3333.

4.2.9. β -D-Pyranoglucosyl triazolyl stearate (28). From compound **19** (255 mg, 0.287 mmol), column chromatography (EtOAc/EtOH, 12:1 to 8:1) afforded **28** as a white solid (129.4 mg, 85.5%). TLC: $R_f=0.57$ (EtOAc/MeOH, 4:1); $[\alpha]_D^{25}-1.90$ (c 0.1, CH_3OH); ^1H NMR (400 MHz, CDCl_3): $\delta=7.94$ (s, 1H), 5.56 (d, $J=9.0$ Hz, 1H), 5.06 (s, 2H), 4.06 (t, $J=8.5$ Hz, 1H), 3.80–3.71 (br m, 4H), 3.59 (br s, 1H), 2.25 (t, $J=7.5$ Hz, 2H), 1.55 (br m, 2H), 1.25 (br s, 28H), 0.88 (t, $J=6.8$ Hz, 3H); ^{13}C NMR (100 MHz, $\text{CDCl}_3+\text{CD}_3\text{OD}$): $\delta=173.9, 142.6, 124.0, 87.8, 79.0, 77.2, 72.4, 68.9, 61.0, 56.9, 33.9, 31.7, 29.5, 29.5, 29.4, 29.3, 29.2, 29.1, 29.0, 24.6, 22.5, 13.9$; HRESIMS: calcd for: $\text{C}_{27}\text{H}_{49}\text{N}_3\text{O}_7+\text{H}$: 528.3649; found: 528.3646.

4.3. EIS measurement

The gold electrode (1.0 mm radius) was polished first mechanically with alumina powder slurry (0.3 down to 0.05) on a polish cloth, sonicated in water baths for 5 min to remove any physically adsorbed species, then electrochemically by cycling the electrode potential from 0.0 to +1.6 V versus SCE in 0.5 M H_2SO_4 until reproducible cyclic voltammograms were obtained. The electrode

was sequentially rinsed with double-distilled water rapidly, followed by rinsing with absolute ethanol as soon as possible and immersed in 2 mM triazolyl glycolipid solutions in CH_2Cl_2 for 2 h to form self-assembled film. After completion of the film formation, the electrodes were taken out rinsed with absolute ethanol and double-distilled water.

Electrochemical experiments were performed in a three electrode electrochemical cell of 20 mL. A platinum wire (about 3 cm) was used as the counter electrode. A saturated calomel electrode (SCE) was used as a reference electrode. All potentials were measured against the SCE. For the EIS measurements, a sine wave potential with 5 mV amplitude superimposed on formal potential versus reference electrode was applied. A wide frequency range from 10 kHz to 100 mHz was scanned, and the impedances were recorded. Analysis of the EIS data was performed using ZSimpWin software. A modified Randles' model (Fig. 2) was used to explain the EIS spectra obtained. All EIS measurements were carried out in 1 mM $\text{K}_3(\text{Fe}(\text{CN})_6)$ +0.1 M KCl solution at room temperature.

4.4. MTT assessment

Hela cells were seeded into 96-well microculture plates and allowed to adhere for 8 h. After cells were exposed to compounds at concentrations from 200 to 0.01 μM for 48 h, medium was aspirated and replenished with complete medium. IC_{50} was evaluated by MTT tetrazolium dye assay.²⁰ Each experiment was performed three times.

Acknowledgements

This project was supported by National Natural Science Foundation of China (Grant No. 20876045), National Science & Technology Major Project of China 'Key New Drug Creation and Manufacturing Program' (No. 2009ZX09302-001), Shanghai Science and Technology Community (No. 10410702700, 08DZ2291300 and 09DZ2291200), and Chinese Academy of Sciences (No. KSCX2-YW-R-168). X.-P. He also gratefully acknowledges the French Embassy for the financial support of a co-tutored doctoral program as well as his French advisor Prof. J. Xie (ENS Cachan).

Supplementary data

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tet.2010.10.033.

References and notes

- Hakomori, S. *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 225–232.
- (a) Tsuji, M. *Cell. Mol. Life Sci.* **2006**, *63*, 1889–1898; (b) Wu, D.; Fujio, M.; Wong, C. H. *Bioorg. Med. Chem.* **2008**, *16*, 1073–1083; (c) Lee, T.; Cho, M.; Ko, S.-Y.; Yoon, H.-J.; Baek, D. J.; Cho, W.-J.; Kang, C.-Y.; Kim, S. J. *Med. Chem.* **2007**, *50*, 585–589.
- Falconer, R. A.; Toth, I. *Bioorg. Med. Chem.* **2007**, *15*, 7012–7020.
- Vogel, J.; Bendas, G.; Bakowsky, U.; Hummel, G.; Schmidt, R. R.; Ketmann, U.; Rothe, U. *Biochim. Biophys. Acta* **1998**, *1372*, 205–215.
- Adams, S.; Kaufmann, F. *Chem. Phys. Lipids* **1991**, *59*, 255–262.
- Jung, M.; Lee, Y.; Moon, H.-I.; Jung, Y.; Jung, H.; Oh, M. *Eur. J. Med. Chem.* **2009**, *44*, 3120–3129.
- Kuriyama, I.; Musumi, K.; Yonezawa, Y.; Takemura, M.; Maeda, N.; Iijima, H.; Hada, T.; Yoshida, H.; Mizushima, Y. *J. Nutr. Biochem.* **2005**, *16*, 594–601.
- (a) de Almeida, M. V.; Hyaric, M. L. *Mini-Rev. Org. Chem.* **2005**, *2*, 283–297; (b) Thiesen, P. H.; Rosenfeld, H.; Konidala, P.; Garamus, V. M.; He, L.; Prange, A.; Niemeyer, B. J. *Biotechnol.* **2006**, *124*, 284–301.
- (a) Kolb, H. C.; Finn, M. G.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2001**, *40*, 2004–2021; (b) Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 2596–2599.
- Caddick, S.; Fitzmaurice, R. *Tetrahedron* **2009**, *65*, 3325–3355.
- For late reviews, see: (a) Jewett, J. C.; Bertozzi, C. R. *Chem. Soc. Rev.* **2010**, *39*, 1272–1279; (b) Kappe, C. O.; Van der Eycken, E. *Chem. Soc. Rev.* **2010**, *39*, 1280–1290; (c) El-Sagheer, A. H.; Brown, T. *Chem. Soc. Rev.* **2010**, *39*, 1388–1405.
- (a) Amblard, F.; Cho, J. H.; Schinazi, R. F. *Chem. Rev.* **2009**, *109*, 4207–4220; (b) Appukkuttan, P.; Dehaen, W.; Fokin, V. V.; der Eycken, E. V. *Org. Lett.* **2004**, *6*, 4223–4225.
- (a) Paul, K. J. V.; Loganathan, D. *Tetrahedron Lett.* **2008**, *49*, 6356–6359; (b) Neto, V.; Granet, R.; Krausz, P. *Tetrahedron* **2010**, *66*, 4633–4646; (c) Broggi, J.; Joubert, N.; Dóez-González, S.; Berteina-Raboin, S.; Zevaco, T.; Nolan, S. P.; Agrofoglio, L. A. *Tetrahedron* **2009**, *65*, 1162–1170; (d) Baron, A.; Blériot, Y.; Sollogoub, M.; Vauzeilles, B. *Org. Biomol. Chem.* **2008**, *6*, 1898–1901.
- (a) Bentiss, F.; Lebrini, M.; Vezin, H.; Lagrenee, M. *Mater. Chem. Phys.* **2004**, *87*, 18–23; (b) Zhang, S.; Tao, Z.; Li, W.; Hou, B. *Appl. Surf. Sci.* **2009**, *255*, 6757–6763; (c) Tao, Z.; Zhang, S.; Li, W.; Hou, B. *Corros. Sci.* **2009**, *51*, 2588–2595.
- Soli, E. D.; Manoso, A. S.; Patterson, M. C.; DeShong, P. J. *Org. Chem.* **1999**, *64*, 3171–3177.
- (a) Masaki, Y.; Tanaka, N.; Miura, T. *Chem. Lett.* **1997**, 55–56; (b) Qu, F.; Hong, J. H.; Du, J.; Newton, M. G.; Chu, C. K. *Tetrahedron* **1999**, *55*, 9073–9088.
- (a) Stupnisek-Lisae, E.; Kasunic, D.; Vorkapic-Furac, J. *Corrosion* **1995**, *51*, 767–772; (b) Quraishi, M. A.; Jamal, D. *Mater. Chem. Phys.* **2001**, *71*, 202–205; (c) Quraishi, M. A.; Jamal, D. *J. Am. Oil Chem. Soc.* **2000**, *77*, 1107–1111.
- Cetin, M.; Yildirim, A. *Corros. Sci.* **2008**, *50*, 155–165.
- Raja, P. B.; Sethuraman, M. G. *Mater. Lett.* **2007**, *62*, 113–116.
- Kuroda, M.; Mimaki, Y.; Sashida, Y.; Hirano, T.; Oka, K.; Dobashi, A.; Li, H.; Harada, N. *Tetrahedron* **1997**, *53*, 11549–11562.