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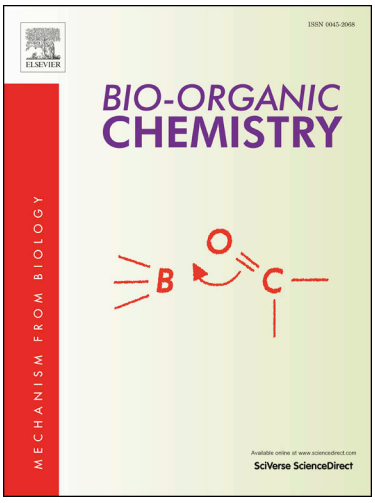

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Semi-synthesis of C28-modified triterpene acid derivatives from maslinic acid or corosolic acid as potential α-glucosidase inhibitors

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Abstract

Combining two bioactive moieties by covalent bond into a novel single hybrid biological entity in view of the principle of active splicing, twenty-two C28-modified derivatives of pentacyclic dihydroxytriterpene carboxylic acids with saturated nitrogen heterocycle segments (i.e. 1-deoxynojirimycin or piperazines) have been synthesized. The inhibitory activities of all final target compounds on α-glucosidase were evaluated *in vitro*. The results of α-glucosidase inhibition assay indicate that some derivatives (e.g. **4b**: IC_{50} = 1468.4 μM; **12b**: IC_{50} = 499.6 μM **12c**: IC_{50} = 768.5 μM, **13c**: IC_{50} = 819.2 μM) show superior inhibitory activity in α-glucosidase than that of the precursor maslinic acid (IC_{50} = 2540.6 μM) or corosolic acid (IC_{50} = 1363.7 μM), in which compound **12b** (IC_{50} = 499.6 μM) possesses stronger inhibitory activity than that of acarbose (IC_{50} = 606 μM). In addition, the result of enzyme kinetics study reveals that the inhibitory mechanism

of the compound 12b is non-competitive inhibition and the inhibition constant K_i is 570 μM. The binding interaction between compounds with α-glucosidase are predicted by molecular docking simulation.

Key words: Maslinic acid; Corosolic acid; 1-Deoxynojirimycin; Piperazine; α-Glucosidase inhibitory activity.

1. Introduction

As one of the major problems threaten the health of human being, diabetes mellitus is a metabolic disease characterized by elevated blood sugar which causing by insulin secretion defect and impaired biological function, or both [1]. Diabetes can be roughly divided into type 1 and type 2, and almost over 90% of patients suffer from type 2 diabetes in clinical treatment [2]. Many serious complications that usually aroused from type 2 diabetes, such as blurred vision [3], renal failure [4], nerve damage [5] and cardiovascular disorders [6]. Currently, the effective strategies to cure type 2 diabetes are including oral hypoglycemic agents and insulin therapy, or a combination of both. Meantime, a healthy diet and proper exercise as supplementary therapy are necessary [7, 8]. As one of hypoglycemic drugs, inhibitors of α-glucosidase play a crucial role of decreasing the postprandial blood glucose. The disaccharides and oligosaccharides from the diet cannot be converted to monosaccharides due to the α-glucosidase activity is suppressed effectually [9]. Thus, it is essential to regard α-glucosidase as an important target protein to treat type 2 diabetes and it also encourages many scientists to develop new α-glucosidase inhibitors constantly. In recent years, researches of α-glucosidase inhibitors primarily focused on plant extracts and synthetic organic compounds. The natural compounds including 1-deoxynojirimycin (**1-DNJ**) [10], polysaccharides [11] and polyphenols [12] extracted from plants all showed different degrees of inhibitory activity on α-glucosidase. In the other hand, α-glucosidase inhibitors can be obtained from chemical synthesis,

such as benzotriazole derivatives [13], heterocyclic candidates [14], piperidine derivatives [15], oxazolxanthone derivatives [16] and indolcarbohydrazones [17] have been studied and found continuously. All the aforementioned α-glucosidase inhibitors are expected to be the potential therapeutics to regulate blood glucose levels in the body. Meanwhile, conventional α-glucosidase inhibitors (e.g. acarbose, voglibose and miglitol) usually lead some side effects on human body during treatment, such as diarrhea, bellyache, flatulence and so on [18, 19]. Therefore, it is necessary to develop α-glucosidase inhibitors with high activity and low toxicity as potential drugs for the treatment of type 2 diabetes in clinical.

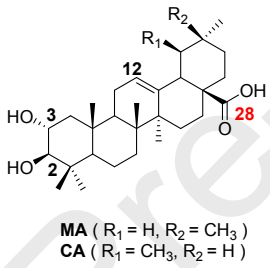


Fig. 1. The structure of maslinic acid and corosolic acid.

Natural products have been the most important sources for developing new drugs because of their wide range of resources and high safety. Maslinic acid (**MA**) and corosolic acid (**CA**) are a class of naturally pentacyclic dihydroxytriterpene carboxylic acids distributed widely in *Olive*, *Lagerstroemia speciose* and other plants [20-22] (Fig. 1). To obtain a great quantity of the **MA** and **CA**, the method of plant extraction is complicated and costly, however, and have been not commercialized yet. Hence, the low-cost and efficient chemical synthesis of **MA** and **CA** become an alternative method, using commercial oleanolic acid and ursolic acid as raw materials, respectively [23, 24]. Studies have exhibited that **MA** and **CA** play a positive act in lowing blood sugar [25, 26], but the application of them in clinical as therapeutic drugs is extremely limited by their poor solubility and low bioavailability which are caused by the rigid skeleton. To improve the

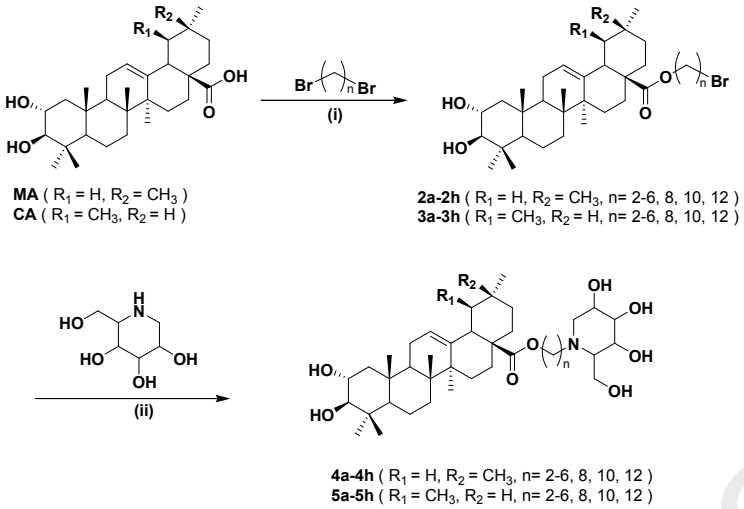
solubility and bioactivity of pentacyclic triterpenic acids, a large number of researchers made great efforts to modify the hydrophobic backbone through either introducing cyclodextrins [27, 28], monosaccharide, disaccharide, oligosaccharide [29] and amino acid [30] into their parent compounds or salifying [31]. As a sugar analog, **1-DNJ** has both the characteristics of saturated nitrogen heterocycles and sugar where the oxygen atom is substituted by nitrogen on the pyran ring, mainly obtained from plant extraction and microbial fermentation. It has been demonstrated that **1-DNJ** is a highly potent α-glucosidase inhibitor causing side effects towards human body scarcely [32]. Therefore, the introduction of **1-DNJ** into parent compounds might be improved the bioactivity and further play the effect of synergistic hypoglycemia. Meanwhile, piperazines are typical saturated nitrogen heterocyclic compounds which are often introduced into drug molecules as synergistic groups, thus beneficial to improve the pharmacokinetics properties, regulate acid-base balance parameters and lipid-water partition coefficient of drugs [33-35]. In addition, it can also improve the biological activity of drug molecules by forming hydrogen bonds or ionic bonds with the target protein [36]. Zhao introduced piperazine into the C-10 site of dihydroartemisinin by ether formation or esterification, and the results showed that all derivatives provided a better growth inhibitory effect than dihydroartemisinin in human leukemia HL-60 cells, mouse lymphoma P388 and adriamycin resistant P388/Adr [37]. Here, taking all the facts into account, the first series of **MA** (or **CA**) derivatives are synthesized, according to the principle of active splicing, by utilizing α, ω-bromoalkanes as linkers to combine **MA** (or **CA**) with **1-DNJ**. Subsequently, the measurement of inhibitory activity of the **MA** (or **CA**)-**1-DNJ** derivatives towards α-glucosidase, does not fully achieve the desired effects for improving the hypoglycemic activity of the lead compounds. Consequently, piperazines are chosen to couple with **MA** (or **CA**) at C-28 site directly to prepare

the second series of compounds, and the α-glucosidase inhibitory activity indicates that some products possess superior inhibition rate than that of the precursor **MA** (or **CA**) as well as acarbose. In the end, after evaluating the α-glucosidase inhibition activities of all **MA** (or **CA**) derivatives, the preliminary structure-activity relationship and inhibitory mechanism of the compounds have been discussed.

2. Results and discussion

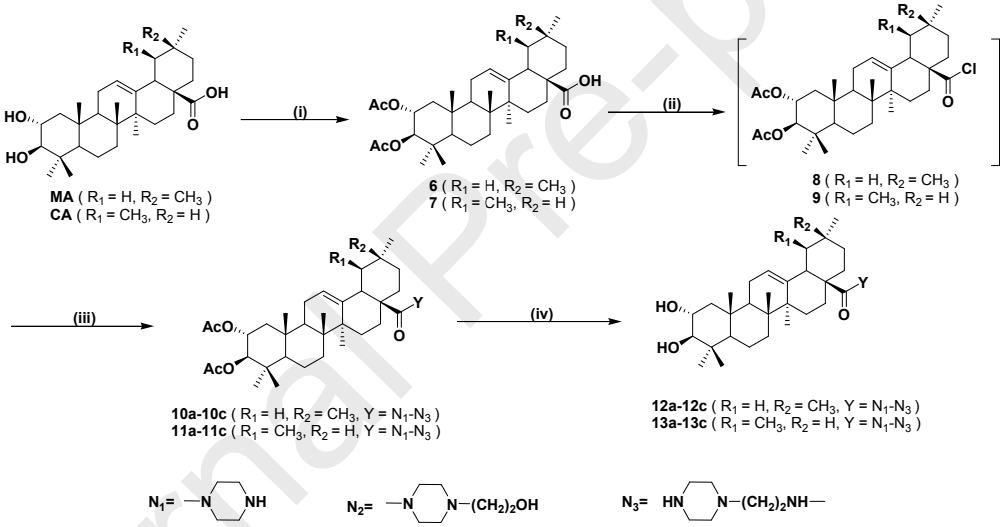
2.1. Chemistry

The highly efficient α-glucosidase inhibitor **1-DNJ** was introduced at the C-28 position of **MA** (or **CA**) by an esterification and a nucleophilic substitution reaction [38, 39], as shown in Scheme 1. **MA** (or **CA**) was first reacted with α, ω-bromoalkanes to generate a series of compounds **2a**–**2h** (or **3a**–**3h**) in the presence of anhydrous potassium carbonate, and then treated with **1-DNJ** *via* nucleophilic substitution reaction to prepare **MA** (or **CA**)**-DNJ** conjugates. As outlined in Scheme 2, **MA** (or **CA**) was acetylated by acetic anhydride to obtain white solid **6** (or **7**), which then converted into the intermediates **10a**–**10c** (or **11a**–**11c**) by reaction with oxalyl chloride and piperazines at the presence of triethylamine. Hydrolysis of **10a**–**10c** (or **11a**–**11c**) in 4N solution of sodium hydroxide got the final compounds **12a**–**12c** (or **13a**–**13c**). The structure of all target derivatives was characterized by $^{1}H/^{13}C$ NMR and HRMS.



Scheme 1. Synthesis of pentacyclic dihydroxyterpene carboxylic acid derivatives **4a**–**4h** (**5a**–**5h**).

Reagents and conditions: (i) K_2CO_3, DMF, rt, 24h; (ii) K_2CO_3, KI, N_2, DMF, 50°C, 24h.



Scheme 2. Synthesis of pentacyclic dihydroxyterpene carboxylic acid derivatives **12a**–**12c** (**13a**–**13c**). Reagents and conditions: (i) acetic anhydride, Py, rt, 20h; (ii) oxalyl chloride, Et_3N, DCM, 0°C–25°C, 24h; (iii) Et_3N, DCM, piperazines, 0°C–25°C, 3h; (iv) 4N NaOH, CH_3OH/THF, 25°C, 1h.

2.2. Bioactivity

In order to investigate the inhibitory effect of the synthesized compounds on α-glucosidase, all final products dissolving in DMSO were performed inhibition experiments *in vitro*. As the results

listed in Table 1, most of the compounds exhibit a certain inhibitory activity against α-glucosidase. Among the first series of triterpenic acid-**DNJ** derivatives (**4a**–**4h**, **5a**–**5h**), compound **4a** (IC_{50} = 2041.4 μM), **4b** (IC_{50} = 1468.4 μM), **4c** (IC_{50} = 1718.4 μM) and **5a** (IC_{50} = 1257.3 μM) featuring the linker of alkyl chain (2–4 carbon atoms) are show lower IC_{50} than those of their leading compound **MA** (IC_{50} = 2540.6 μM) and **CA** (IC_{50} = 1363.7 μM), respectively. However, with the longer hydrophobic carbon chain (4–8 carbon atoms) embedding the molecular structure, the inhibitory activity of the derivatives is lower than that of the parent compound **MA** or **CA**, such as **4d** (IC_{50} = 3660.4 μM), **4f** (IC_{50} = 3068.4 μM), **5b** (IC_{50} = 1554.4 μM), **5c** (IC_{50} = 1841.4 μM), **5d** (IC_{50} = 1381.8 μM) and **5f** (IC_{50} = 1741.2 μM). Meanwhile, the solubility in the measurement system is significantly dropped when the carbon chains of the derivatives contain 10 or 12 carbon atoms (e.g. **4h**, **4f**, **5h**, **5f**), and the inhibition rate measured at a low concentration is less than the precursors. Consequently, no alternative solvent system is suitable to determine the IC_{50} values of these compounds. The introduction of **1-DNJ** in the **MA** (or **CA**) structure elevates the solubility of derivatives significantly in comparison with the triterpene acids. Regrettably, the inhibitory activity of most derivatives coupling **1-DNJ** is not enhanced compared to **MA** (or **CA**). The α-glucosidase inhibitory activities of the products demonstrate that the carbon chain lengths of the linker between triterpenic acid and **1-DNJ** play a vital role in the hypoglycemic activity of the derivatives. It is obvious that the inhibitory effect of derivatives with short linkers against α-glucosidase is superior to that of the compounds containing overlong linkers. In addition, it is interesting that most of the **CA** derivatives provide better inhibitory effects than those of **MA** analogues (e.g. **5a** *vs* **4a**, **5d** *vs* **4d**, **5f** *vs* **4f**). Pentacyclic dihydroxytriterpene carboxylic acid coupling with piperazines (i.e. **12a**–**12c**, **13a**–**13c**) belong to the second series of derivatives. The piperazine segment of

compounds with one free hydroxyl (**12b**: IC_{50} = 499.6 μM, **13b**: IC_{50} = 660.7 μM) and amino groups (**12c**: IC_{50} = 768.5 μM, **13c**: IC_{50} = 819.2 μM) present higher inhibition activity notably than that of **MA** (IC_{50} = 2540.6 μM) and **CA** (IC_{50} = 1363.7 μM). It is worthy note that the hypoglycemic activity of compound **12b** is superior to acarbose (IC_{50} = 606 μM). The results demonstrate that a free hydroxyl or an amino group in piperazine as a substructure in the pentacyclic triterpene acids derivatives can enhance the α-glucosidase inhibition activity of the modified compounds (e.g. **12b** *vs* **12a**, **12c** *vs* **12a**, **13b** *vs* **13a**, **13c** *vs* **13a**). Besides, **MA** derivatives perform better bioactive than that of **CA** counterparts on inhibition of α-glucosidase (e.g. **12b** *vs* **13b**, **12c** *vs* **13c**).

Table 1 IC_{50} values (μM) of the derivatives for the inhibition of α-glucosidase.

Products number	IC_{50}[a]	Products number	IC_{50}[a]
4a	2041.4 ± 20.2	**5a**	1257.3 ± 13.5
4b	1468.4 ± 17.1	**5b**	1554.4 ±13
4c	1718.4 ± 8.4	**5c**	1841.4 ± 20.4
4d	3660.4 ± 74	**5d**	1381.8 ± 30
4e	[b]NI	**5e**	[b]NI
4f	3068.4 ± 2.8	**5f**	1741.2 ± 15.3
4g	[c]/	**5g**	[c]/
4h	[c]/	**5h**	[c]/
12a	[b]NI	**13a**	[b]NI
12b	499.6 ± 2.3	**13b**	660.7 ± 13.5
12c	768.5 ± 12.3	**13c**	819.2 ± 14.7
Acarbose	606 ± 11	**1-DNJ**	142.2 ± 3.6
MA	2540.6 ± 68	**CA**	1363.7 ± 0.7

[a] Values are the mean of four experiments.

[b] NI = NO Inhibition.

[c] The derivatives cannot dissolved in the solvent system of measurement.

Kinetics study was employed to explore the inhibitory mechanism of compounds on α-glucosidase. Given the inhibitory similarity of the derivatives on α-glucosidase, the highly active compound **12b** is chosen as a representative for enzyme kinetics analysis. As shown in Fig. 2, the increasing of inhibitor concentrations results in different slopes of the straight lines in the case of certain substrate concentration. All the lines approximately intersect at one point on the −x axis,

which define that the enzyme kinetics inhibitory mechanism of compound **12b** belongs to the typical non-competitive inhibition. Furthermore, the secondary plot of the slop versus various concentrations of inhibitor **12b** to give an estimate inhibition constant, K_i = 570 μM (Fig. 3).

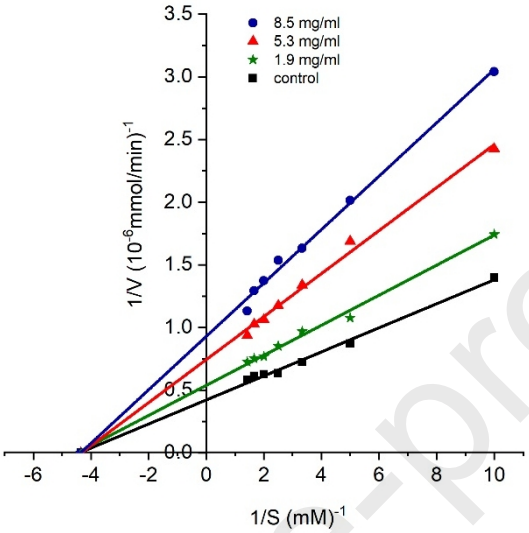


Fig. 2. Lineweaver-Burk plot of **12b**.

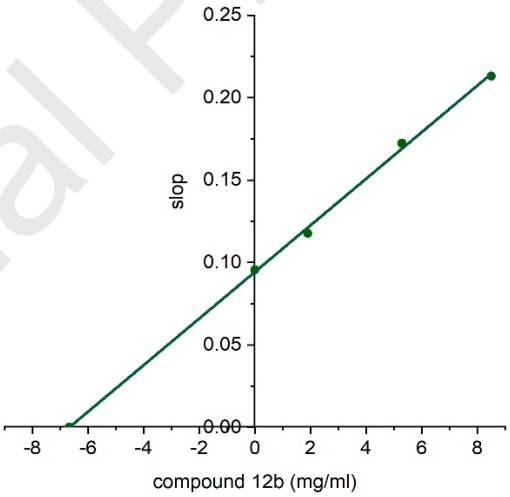


Fig. 3. The secondary plot between slop and concentrations of compound **12b**.

2.3. Docking analysis

To shed light on the varied measurement results of the triterpene acids and their derivatives on α-glucosidase inhibition activity, molecular docking simulation was performed to analyze the binding mode of the compounds with the protein receptor. The more active compounds (**4b**, **5a**, **12b**

and **1-DNJ**) and parent compounds were selected as the donators simultaneously. The molecule docking results (Table 2) show that compounds **4b**, **5a** and **12b** possess lower interaction energy than the precursors, which indicate that the active compounds are binding closely with receptor of α-glucosidase. Therefore, it means that their inhibitory activities higher than those of precursors. As shown in Fig. 4, compound **12b** establishes three hydrogen bonds through carbonyl and hydroxyl group with the binding site residues Tyr464, Asn449 and Ser465, and forms hydrophobic interactions with His447 and Tyr464 residues. The **1-DNJ** segment of compound **4b** constructs five hydrogen bonds with residues including Ser465 (2), Asn449 (2) and Asp450, and the other entity forms hydrophobic interactions with His447 and Tyr464 residues. As to compound **5a** establishes hydrogen bonding interactions with His447 and Asp450 residues *via* hydroxyl group, and forms hydrophobic interactions with Val333 and Tyr464 residues. Precursor **MA** only forms hydrophobic interactions with His447 and Tyr464 residues, and **CA** builds only one hydrogen bond through carboxyl with the binding site Arg15 residue and forms hydrophobic interactions with His447 residue. The free hydroxyl groups of **1-DNJ** construct five hydrogen bonds with the residues Asp450 (2), Ile448, Asp446 and His447. In view of these facts, it can be suggested that the synergistic modification of **MA** and **CA** increase the hydrogen bonding interactions between derivatives and the receptor protein, which probably the principal reason that the inhibitory activity of derivatives on α-glucosidase is superior to their parents. Fortunately, the docking results are good consistent with the activities tested *in vitro*. Besides, the hydroxyl groups in the molecules strengthen the interactions with target protein and play an important role in improving the bioactivity. Therefore, it is expected to be the potential α-glucosidase inhibitors *via* incorporate the active moieties of **1-DNJ** and piperazines to the molecular framework of **MA** and **CA**.

Table 2 The docking results of **12b**, **4b**, **5a**, **CA**, **MA** and **1-DNJ**.

Compound	– CDOCKER INTERACTION ENERGY (kcal/mol)
12b	39.2597
4b	47.4599
5a	43.4789
CA	30.5992
MA	30.3889
1-DNJ	23.7343

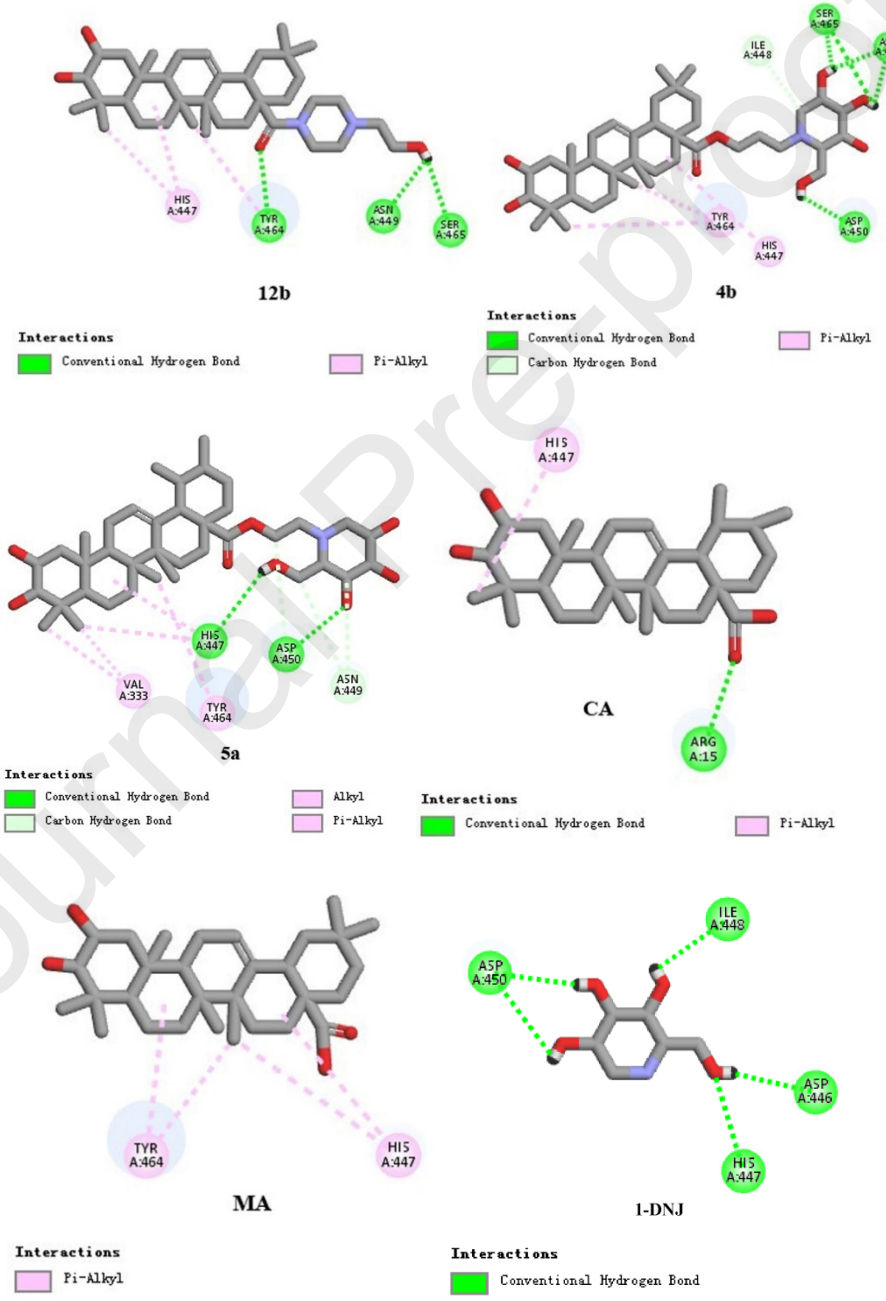


Fig. 4. The diagram of molecular docking between the compound **12b**, **4b**, **5a**, **MA**, **CA**, **1-DNJ**

and α-glucosidase.

3. Conclusion

In summary, based on the principle of active splicing, a total of 22 pentacyclic tricarboxylic acid-saturated nitrogen heterocycle compounds have been synthesized, and the α-glucosidase inhibition activity of the synthesized compounds was performed *in vitro*. Among of the pentacyclic tricarboxylic acid-piperazine derivatives, the inhibitory activity of the **MA** derivatives is higher than that of the **CA** counterparts, wherein the inhibitory activity of the compound **12b** (IC_{50} = 499.6 μM) on α-glucosidase is stronger than that of acarbose (IC_{50} = 606 μM) and **MA**. Triterpenic acid-**1-DNJ** conjugates such as **4a**, **4b**, **4c** and **5a** are exhibited lower IC_{50} than their leading compound **MA** and **CA**, respectively. The derivatives of **CA** obtain better inhibitory effects than that of **MA** analogues (e.g. **CA** *vs* **MA**, **5a** *vs* **4a**, **5d** *vs* **4d**, **5f** *vs* **4f**), but the inhibition of **5b** and **5c** is slightly weaker than that of **4b** and **4c**, respectively. Nevertheless, it is fortunate that most of the second series derivatives containing piperazine unit have superior α-glucosidase inhibition activities with respect to the precursors. Molecular docking simulation further manifests that the increased bioactivity of the derivatives is attributed to the introduction of active groups (i.e. **1-DNJ** and piperazines) into the **MA** (or **CA**) which enhances the hydrogen bond interaction between the compounds and α-glucosidase. Moreover, the result of kinetics study indicates that the inhibition mechanism of the derivatives is non-competitive inhibition.

4. Experimental section

All of the chemicals and solvents were purchased from commercial vendors and were not further purified unless otherwise stated. The described reactions were monitored by Thin layer chromatography (TLC) using silica gel GF_{254} plates, which were visualized by heating the TLC

plates sprayed with 5% sulfuric acid in ethanol. The compounds were purified by column chromatography on silica gel (200-300 mesh) with petroleum ether and ethyl acetate or dichloromethane and methanol as eluent. ^{1}H and ^{13}C NMR spectra were taken on a Bruker spectrometer at 400 MHz (^{1}H NMR), 100 MHz (^{13}C NMR) using $CDCl_3$ or DMSO-d_6 as solvents, and chemical shifts (δ) were reported in ppm, coupling constants (J) were presented in hertz. High resolution mass spectrometry (HRMS) were acquired from Finnigan MAT 95 XP mass spectrometer. α-Glucosidase (CAS: 9001-42-7) derived from *Saccharomyces cerevisiae* was purchased from Sigma. Acarbose and 4-nitrophenyl-α-D-glucopyranoside were obtained from Aladdin.

*4.1. Synthesis of **MA** and **CA***

MA and **CA** were prepared by previous methods in the literature[23, 24].

*4.2. Synthesis of **MA/CA-1-DNJ** derivatives*

*4.2.1. 28-(2-Bromoethyl) maslinic acid ester (**2a**)*

MA (534 mg, 1.13 mmol) and anhydrous potassium carbonate (468 mg, 3.39 mmol) were resolved in waterless DMF (10 mL), and the mixture was stirred for 30 minutes at room temperature, then dripped 1, 2-dibromoethane (1.5 mL). When TLC analyzed that **MA** was consumed completely, quenched the reaction by water and extracted with ethyl acetate. The upper layer was added anhydrous Na_2SO_4 to absorbing water, then filtrated and evaporated to dryness. The residue was purified by column chromatography on silica gel to obtain **2a** as a white flake solid. Yield 83%, mp: 175 °C–176 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.30 (t, J = 8 Hz, 1H), 4.26–4.37 (m, 2H), 3.65–3.72 (m, 1H), 3.48 (t, J = 12 Hz, 2H), 2.98 (d, J = 12 Hz, 1H), 2.22–2.27 (m, 1H), 1.90–1.98 (m, 3H), 1.64–1.73 (m, 4H), 1.53–1.59 (m, 4H), 1.34–1.46 (m, 4H), 1.18–1.31 (m, 6H), 1.13 (s, 3H), 1.02 (s, 3H), 0.97 (s, 3H), 0.90 (d, J = 12 Hz, 6H), 0.82 (s, 3H), 0.73 (s, 3H). ^{13}C NMR (100 MHz,

$CDCl_3$): δ 176.81, 143.05, 121.97, 83.43, 68.45, 63.16, 54.81, 47.10, 46.36, 45.94, 45.30, 41.26, 40.77, 38.97, 38.68, 37.80, 33.37, 32.58, 32.15, 31.96, 30.20, 28.51, 28.13, 27.16, 25.39, 23.09, 23.00, 22.44, 17.86, 16.60, 16.26, 16.13. HRMS (ESI, *m/z*): $[M + Na]^+$ Calcd for $C_{32}H_{51}BrNaO_4$: 601.2863; found: 601.2863.

*4.2.2. 28-(3-Bromopropyl) maslinic acid ester (**2b**)*

Compound **2b** was a white flake solid prepared from **MA** and 1,3-dibromopropane by using the same method established for **2a**. Yield 90%, mp: 134 °C–136 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 5.27 (t, *J* = 8 Hz, 1H), 4.13–4.17 (m, 2H), 3.65–3.72 (m, 1H), 3.45 (t, *J* = 12 Hz, 2H), 2.98 (d, *J* = 12 Hz, 1H), 2.12–2.18 (m, 2H), 1.89–1.99 (m, 5H), 1.59–1.70 (m, 6H), 1.16–1.52 (m, 10H), 1.13 (s, 3H), 1.02 (s, 3H), 0.97 (s, 3H), 0.90 (d, *J* = 8 Hz, 6H), 0.82 (s, 3H), 0.73 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.99, 143.31, 121.84, 83.44, 68.44, 61.35, 54.82, 47.11, 46.31, 45.94, 45.30, 41.29, 40.89, 38.94, 38.68, 37.81, 33.35, 32.57, 32.16, 32.00, 31.30, 30.19, 28.99, 28.13, 27.11, 25.41, 23.11, 23.03, 22.54, 17.85, 16.69, 16.24, 16.11. HRMS (ESI, *m/z*): $[M + K]^+$ Calcd for $C_{33}H_{53}BrKO_4$: 631.2759; found: 631.2759.

*4.2.3. 28-(4-Bromobutyl) maslinic acid ester (**2c**)*

Compound **2c** was a white flake solid prepared from **MA** and 1,4-dibromobutane by using the same method established for **2a**. Yield 88%, mp: 130 °C–131 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 5.29 (s, 1H), 4.04 (s, 2H), 3.65–3.72 (m,1H), 3.43 (s, 2H), 2.84–3.00 (m, 1H), 2.19–2.25 (m, 2H), 1.92–1.97 (m, 6H), 1.52–1.77 (m, 10H), 1.25–1.36 (m, 3H), 1.13 (s, 4H), 0.82–1.03 (m, 18H), 0.72 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.21, 143.32, 121.79, 83.40, 68.43, 62.72, 54.79, 47.08, 46.22, 45.88, 45.33, 41.25, 40.79, 38.91, 38.68, 37.80, 33.36, 32.59, 32.12, 32.01, 30.21, 29.05, 28.13, 27.09, 26.86, 25.42, 23.12, 22.98, 22.50, 17.84, 16.62, 16.27, 16.11. HRMS (ESI, *m/z*): [M

+ K]$^+$ Calcd for $C_{34}H_{55}BrKO_4$: 645.2915; found: 645.2916.

*4.2.4. 28-(5-Bromoamyl) maslinic acid ester (**2d**)*

Compound **2d** was a white flake solid prepared from **MA** and 1,5-dibromopentane by using the same method established for **2a**. Yield 84%, mp: 137 °C–138 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.27 (t, *J* = 8 Hz, 1H), 4.00–4.04 (m, 2H), 3.65–3.71 (m, 1H), 3.39 (t, *J* = 12 Hz, 2H), 2.98 (d, *J* = 8 Hz, 1H), 2.23–2.27 (m, 2H),1.95–1.99 (m, 2H), 1.86–1.92 (m, 4H), 1.64–1.69 (m, 4H), 1.59–1.62 (m, 4H), 1.51–1.55 (m, 4H), 1.36–1.46 (m, 4H), 1.25–1.33 (m, 4H), 1.16–1.20 (m, 2H), 1.12 (s, 3H), 0.97 (s, 3H), 0.89 (d, *J* = 12 Hz, 6H), 0.81 (s, 3H), 0.72 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.26, 143.39, 121.71, 83.43, 68.44, 63.35, 54.81, 47.11, 46.21, 45.92, 45.38, 41.26, 40.80, 38.93, 38.68, 37.81, 33.40, 33.00, 32.60, 32.15, 32.02, 31.79, 30.22, 28.14, 27.33, 27.12, 25.41, 24.31, 23.13, 23.01, 22.51, 17.86, 16.59, 16.27, 16.12. HRMS (ESI, *m/z*): [M + H]$^+$ Calcd for $C_{35}H_{58}BrO_4$: 621.3513; found: 621.3513.

*4.2.5. 28-(6-Bromohexyl) maslinic acid ester (**2e**)*

Compound **2e** was a white flake solid prepared from **MA** and 1,6-dibromohexane by using the same method established for **2a**. Yield 87%, mp: 176 °C–178 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.26 (t, *J* = 8 Hz, 1H), 3.99–4.02 (m, 2H), 3.66–3.71 (m, 1H), 3.38 (t, *J* = 16 Hz, 2H), 2.98–3.01 (m, 1H), 2.18–2.24 (m, 1H), 1.95–1.99 (m, 2H), 1.83–1.92 (m, 5H), 1.58–1.69 (m, 9H), 1.43–1.52 (m, 6H), 1.36–1.40 (m, 2H), 1.27–1.33 (m, 2H), 1.16–1.20 (m, 2H), 1.12 (s, 3H), 1.02 (s, 3H), 0.97 (s, 3H), 0.89 (d, *J* = 12 Hz, 6H), 0.81 (s, 3H), 0.72 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.28, 143.37, 121.67, 83.34, 68.40, 63.53, 54.79, 47.07, 46.17, 45.90, 45.36, 41.24, 40.78, 38.90, 38.70, 37.77, 33.39, 33.14, 32.61, 32.18, 32.00, 30.21, 28.15, 27.96, 27.28, 27.09, 25.41, 24.80, 23.13, 22.99, 22.50, 17.85, 16.59, 16.30, 16.11. HRMS (ESI, *m/z*): [M + H]$^+$ Calcd for $C_{36}H_{60}BrO_4$:

635.3670; found: 635.3671.

*4.2.6. 28-(8-Bromooctyl) maslinic acid ester (**2f**)*

Compound **2f** was a white flake solid prepared from **MA** and 1,8-dibromooctane by using the same method established for **2a**. Yield 85%, mp: 156 °C–158 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.26 (t, *J* = 8 Hz, 1H), 3.96–4.03 (m, 2H), 3.65–3.71 (m, 1H), 3.38 (t, *J* = 12 Hz, 2H), 2.98 (d, *J* = 8 Hz, 1H), 2.23–2.29 (m, 1H), 1.83–1.99 (m, 7H), 1.59–1.72 (m, 9H), 1.39–1.52 (m, 5H), 1.25–1.32 (m, 10H), 1.16–1.20 (m, 1H), 1.12 (s, 1H), 1.02 (s, 1H), 0.97 (s,1H), 0.89 (d, *J* = 12 Hz, 6H), 0.81 (s, 3H), 0.72 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.28, 143.39, 121.66, 83.39, 68.42, 63.71, 54.80, 47.09, 46.16, 45.91, 45.38, 41.24, 40.78, 38.92, 38.68, 37.79, 33.40, 32.61, 32.28, 32.15, 31.99, 30.21, 28.51, 28.21, 28.13, 28.07, 27.59, 27.10, 25.47, 25.40, 23.12, 22.99, 22.50, 17.86, 16.58, 16.27, 16.11. HRMS (ESI, *m/z*): $[M - H]^-$ Calcd for $C_{38}H_{62}BrO_4$: 661.3837; found: 661.3815.

*4.2.7. 28-(10-Bromodecyl) maslinic acid ester (**2g**)*

Compound **2g** was a white flake solid prepared from **MA** and 1,10-dibromodecane by using the same method established for **2a**. Yield 86%, mp: 123 °C–125 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.26 (t, *J* = 8 Hz, 1H), 3.98–4.02 (m, 2H), 3.65–3.71 (m, 1H), 3.38 (t, *J* = 16 Hz, 1H), 2.98 (d, *J* = 12 Hz, 1H), 2.22–2.27 (m, 1H), 1.81–1.99 (m, 7H), 1.55–1.69 (m, 8H), 1.36–1.52 (m, 7H), 1.29–1.33 (m, 12H), 1.16–1.20 (m, 2H), 1.12 (s, 3H), 1.02 (s, 3H), 0.97 (s, 3H), 0.89 (d, *J* = 12 Hz, 6H), 0.82 (s, 3H), 0.72 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.31, 143.40, 121.65, 83.38, 68.42, 63.77, 54.78, 47.09, 46.15, 45.89, 45.37, 41.23, 40.77, 38.90, 38.68, 37.78, 33.50, 33.40, 32.62, 32.32, 32.14, 31.98, 30.22, 28.98, 28.87, 28.67, 28.27, 28.12, 27.67, 27.09, 25.56, 25.41, 23.13, 22.99, 22.49, 17.85, 16.58, 16.29, 16.11. HRMS (ESI, *m/z*): $[M + H]^+$ Calcd for $C_{40}H_{68}BrO_4$: 691.4296; found: 691.4285.

*4.2.8. 28-(12-Bromododecyl) maslinic acid ester (**2h**)*

Compound **2h** was a white flake solid prepared from **MA** and 1,12-dibromododecane by using the same method established for **2a**. Yield 83%, mp: 119 °C–120 °C. ^{1}H NMR (400 MHz, $CDCl_3$) : δ 5.26 (t, *J* = 8 Hz, 1H), 3.98–4.03 (m, 2H), 3.66–3.72 (m, 1H), 3.39 (t, *J* = 12 Hz, 2H), 2.99 (d, *J* = 8 Hz, 1H), 1.83–2.00 (m, 6H), 1.57–1.69 (m, 9H), 1.36–1.52 (m, 7H), 1.25–1.33 (m, 18H), 1.16–1.20 (m, 1H), 1.13 (s, 3H), 1.03 (s, 3H), 0.97 (s, 3H), 0.90 (d, *J* = 8 Hz, 6H), 0.82 (s, 3H), 0.72 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.32, 143.39, 121.65, 83.36, 68.41, 63.80, 54.78, 47.08, 46.15, 45.89, 45.37, 41.23, 40.76, 38.90, 38.69, 37.77, 33.54, 33.40, 32.63, 32.34, 32.13, 31.98, 30.22, 29.05, 28.71, 28.29, 28.13, 27.69, 27.09, 25.57, 25.41, 23.13, 22.98, 22.48, 17.86, 16.57, 16.30, 16.10. HRMS (ESI, *m/z*): $[M + K]^+$ Calcd for $C_{42}H_{71}BrKO_4$: 757.4167; found: 757.4203.

*4.2.9. 28-(2-Bromoethyl) corosolic acid ester (**3a**)*

Compound **3a** was a white foamy solid prepared from **CA** and 1,2-dibromoethane by using the same method established for **2a**. Yield 90%, mp: 103 °C–104 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.26 (t, *J* = 8 Hz, 1H), 4.28–4.32 (m, 2H), 3.66–3.71 (m, 1H), 3.46 (t, *J* = 12 Hz, 2H), 2.98 (d, *J* = 8 Hz, 1H), 2.22 (d, *J* = 12 Hz, 1H), 1.92–2.01 (m, 4H), 1.75–1.82 (m, 1H), 1.68–1.71 (m, 2H), 1.48–1.63 (m, 4H), 1.25–1.41 (m, 7H), 1.08 (s, 3H), 0.93–1.02 (m, 9H), 0.81–0.86 (m, 6H), 0.75 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.65, 137.47, 125.15, 83.28, 68.40, 63.20, 54.79, 52.27, 47.74, 46.99, 46.19, 41.61, 39.15, 38.74, 38.55, 38.34, 37.69, 36.18, 32.44, 30.14, 28.53, 28.21, 27.46, 23.63, 23.07, 22.89, 20.68, 17.84, 16.67, 16.51, 16.39, 16.26. HRMS (ESI, *m/z*): $[M + Na]^+$ Calcd for $C_{32}H_{51}BrNaO_4$: 601.2863; found: 601.2863.

*4.2.10. 28-(2-Bromopropyl) corosolic acid ester (**3b**)*

Compound **3b** was a white foamy solid prepared from **CA** and 1,3-dibromopropane by using

the same method established for **2a**. Yield 88%, mp: 104 °C–105 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.23 (t, *J* = 8 Hz, 1H), 4.05–4.19 (m, 2H), 3.66–3.72 (m, 1H), 3.44 (t, *J* = 16 Hz, 2H), 2.98 (d, *J* = 12 Hz, 1H), 2.11–2.25 (m, 5H), 1.93–2.03 (m, 4H), 1.73–1.81 (m, 1H), 1.65–1.69 (m, 3H), 1.47–1.64 (m, 5H), 1.25–1.42 (m, 5H), 1.08 (s, 3H), 1.03 (s, 3H), 0.99 (s, 3H), 0.93 (d, *J* = 8 Hz, 3H), 0.84 (d, *J* = 8 Hz, 3H), 0.82 (s, 3H), 0.76 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.84, 137.87, 124.93, 83.43, 68.46, 61.33, 54.79, 52.40, 47.69, 47.03, 46.13, 41.65, 39.12, 38.67, 38.57, 38.38, 37.73, 36.24, 32.44, 31.29, 30.13, 29.12, 28.16, 27.41, 23.73, 23.09, 22.92, 20.66, 17.81, 16.76, 16.51, 16.30, 16.25. HRMS (ESI, *m/z*): $[M + H]^+$ Calcd for $C_{33}H_{54}BrO_4$: 593.3200; found: 593.3200.

*4.2.11. 28-(4-Bromobutyl) corosolic acid ester (**3c**)*

Compound **3c** was a white foamy solid prepared from **CA** and 1,4-dibromobutane by using the same method established for **2a**. Yield 86%, mp: 78 °C–79 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.23 (t, *J* = 8 Hz, 1H), 3.95–4.07 (m, 2H), 3.66–3.72 (m, 1H), 3.40 (t, *J* = 16 Hz, 1H), 2.98 (d, *J* = 8 Hz, 1H), 2.20 (d, *J* = 12 Hz, 1H), 1.90–2.02 (m, 7H), 1.60–1.79 (m, 7H), 1.46–1.58 (m, 5H), 1.25–1.41 (m, 5H), 1.07 (s, 3H), 1.02 (s, 3H), 0.98 (s, 3H), 0.93 (d, *J* = 4 Hz, 3H), 0.82 (t, *J* = 16 Hz, 6H), 0.74 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.04, 137.82, 124.90, 83.41, 68.45, 62.70, 54.79, 52.33, 48.08, 47.01, 46.11, 41.49, 39.12, 38.67, 38.58, 38.37, 37.73, 36.25, 32.55, 32.44, 30.15, 29.02, 28.17, 27.41, 26.83, 23.70, 23.08, 22.86, 20.68, 17.81, 16.68, 16.52, 16.31, 16.26. HRMS (ESI, *m/z*): $[M + H]^+$ Calcd for $C_{34}H_{56}BrO_4$: 607.3357; found: 607.3357.

*4.2.12. 28-(5-Bromoamyl) corosolic acid ester (**3d**)*

Compound **3d** was a white foamy solid prepared from **CA** and 1,5-dibromopentane by using the same method established for **2a**. Yield 85%, mp: 84 °C–85 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ

5.23 (t, *J* = 8 Hz, 1H), 3.98 (t, *J* = 8 Hz, 2H), 3.66–3.72 (m, 1H), 3.39 (t, *J* = 16 Hz, 2H), 2.98 (d, *J* = 12 Hz, 1H), 2.21 (d, *J* = 12 Hz, 2H), 1.86–2.02 (m, 7H), 1.73–1.81 (m, 2H)，1.57–1.68 (m, 7H), 1.47–1.55 (m, 6H), 1.30–1.41 (m, 4H), 1.25 (s, 1H), 1.07 (s, 3H), 1.02 (s, 3H), 0.98 (s, 3H), 0.93 (d, *J* = 4 Hz, 3H), 0.82 (t, *J* = 12 Hz, 3H), 0.74 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.05, 137.84, 124.85, 83.46, 68.48, 63.32, 54.80, 52.35, 47.58, 47.03, 46.16, 41.64, 39.15, 38.59, 38.38, 37.74, 36.25, 32.95, 32.46, 31.79, 30.18, 29.20, 28.16, 27.45, 27.29, 24.31, 23.71, 23.06, 22.89, 20.67, 17.82, 16.66, 16.52, 16.27. HRMS (ESI, *m/z*): $[M + H]^+$ Calcd for $C_{35}H_{58}BrO_4$: 621.3513; found: 621.3513.

*4.2.13. 28-(6-Bromohexyl) corosolic acid ester (**3e**)*

Compound **3e** was a white foamy solid prepared from **CA** and 1,6-dibromohexane by using the same method established for **2a**. Yield 88%, mp: 79 °C–80 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.24 (t, *J* = 8 Hz, 1H), 3.96–4.00 (m, 2H), 3.66–3.72 (m, 1H), 3.42 (t, *J* = 12 Hz, 2H), 3.01 (d, *J* = 12 Hz, 1H), 2.17–2.26 (m, 3H), 1.98–2.02 (m, 2H), 1.92–1.95 (m, 2H), 1.84–1,88 (m, 2H), 1.76–1.81 (m, 1H), 1.68 (s, 3H), 1.57–1.64 (m, 4H), 1.46–1.55 (m, 6H), 1.30–1.39 (m, 6H), 1.07 (s, 3H), 1.02 (s, 3H), 0.98 (s, 3H), 0.94 (d, *J* = 4 Hz, 3H), 0.86 (t, *J* = 16 Hz, 6H), 0.74 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.58, 138.34, 125.31, 83.92, 68.96, 64.01, 55.31, 52.86, 48.07, 47.53, 46.65, 42.14, 39.64, 39.17, 39.08, 38.88, 38.23, 36.74, 33.60, 32.97, 32.66, 30.68, 28.66, 28.43, 27.94, 27.79, 25.30, 24.21, 23.55, 23.37, 21.16, 18.32, 17.17, 17.01, 16.80, 16.74. HRMS (ESI, *m/z*): $[M + K]^+$ Calcd for $C_{36}H_{59}BrKO_4$: 673.3228; found: 673.3223.

*4.2.14. 28-(8-Bromooctyl) corosolic acid ester (**3f**)*

Compound **3f** was a white foamy solid prepared from **CA** and 1,8-dibromooctane by using the same method established for **2a**. Yield 84%, mp: 73 °C–74 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.23

(s, 1H), 3.95–4.00 (m, 2H), 3.67–3.72 (m, 1H), 3.38 (t, *J* = 16 Hz, 2H), 2.98 (d, *J* = 12 Hz, 1H), 2.21–2.24 (d, *J* = 12 Hz, 1H), 1.77–2.02 (m, 8H), 1.43–1.69 (m, 15H), 1.32 (s, 9H), 1.02 (d, *J* = 20 Hz, 6H), 0.94 (d, *J* = 16 Hz, 6H), 0.82 (t, *J* = 12 Hz, 6H), 0.74 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.15, 137.82, 124.82, 83.41, 68.47, 63.72, 54.81, 52.35, 47.55, 47.04, 46.16, 41.63, 39.14, 38.68, 38.60, 38.39, 37.74, 36.24, 33.42, 32.48, 32.28, 30.21, 28.54, 28.20, 28.05, 27.61, 27.45, 25.49, 23.72, 23.08, 22.88, 20.71, 17.84, 16.67, 16.55, 16.34, 16.28. HRMS (ESI, *m/z*): $[M + Na]^+$ Calcd for $C_{38}H_{63}BrNaO_4$: 685.3802; found: 685.3806.

*4.2.15. 28-(10-Bromodecyl) corosolic acid ester (**3g**)*

Compound **3g** was a white foamy solid prepared from **CA** and 1,10-dibromodecane by using the same method established for **2a**. Yield 82%, mp: 71 °C–72 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.23 (t, *J* = 8 Hz, 1H), 3.94–4.00 (m, 2H), 3.66–3.72 (m, 1H), 3.39 (t, *J* = 12 Hz, 2H), 2.98 (d, *J* = 12 Hz, 1H), 2.21 (d, *J* = 12 Hz, 1H), 1.92–2.02 (m, 4H), 1.81–1.87 (m, 2H), 1.74–1.78 (m, 1H), 1.38–1.68 (m, 15H), 1.29–1.35 (m, 14H), 1.07 (s, 3H), 1.03 (s, 3H), 0.98 (s, 3H), 0.94 (s, 3H), 0.82 (t, *J* = 16 Hz, 6H), 0.74 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.31, 137.82, 124.80, 83.43, 68.47, 63.78, 54.79, 52.33, 47.54, 47.02, 46.14, 41.62, 39.12, 38.66, 38.59, 38.38, 37.73, 36.23, 33.51, 32.46, 32.33, 30.20, 28.96, 28.88, 28.68, 28.26, 28.16, 28.08, 27.68, 27.43, 25.57, 23.70, 23.07, 22.86, 20.70, 17.83, 16.66, 16.54, 16.32, 16.26. HRMS (ESI, *m/z*): $[M + K]^+$ Calcd for $C_{40}H_{67}BrKO_4$: 729.3854; found: 729.3855.

*4.2.16. 28-(12-Bromododecyl) corosolic acid ester (**3h**)*

Compound **3h** (yield 81%) was a white foamy solid prepared from **CA** and 1,12-dibromododecane by using the same method established for **2a**. Yield 81%, mp: 65 °C–66 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.21 (t, *J* = 8 Hz, 1H), 3.94–3.99 (m, 2H), 3.66–3.71 (m, 1H), 3.38 (t,

J = 12 Hz, 2H), 2.97 (d, *J* = 8 Hz, 1H), 2.59–2.65 (m, 1H), 2.20 (d, *J* = 12 Hz, 1H), 1.91–2.01 (m, 5H), 1.76–1.85 (m, 4H), 1.41–1.67 (m, 14H), 1.26–1.31 (m, 16H), 1.01 (d, *J* = 20 Hz, 6H), 0.93 (d, *J* = 16 Hz, 6H), 0.80 (t, *J* = 20 Hz, 6H), 0.73 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.16, 137.81, 124.81, 83.38, 68.44, 63.81, 54.79, 52.32, 47.53, 47.02, 46.14, 41.61, 39.12, 38.69, 38.59, 38.38, 37.72, 36.22, 33.53, 32.46, 32.34, 30.20, 29.05, 28.72, 28.29, 28.18, 28.08, 27.69, 27.43, 25.58, 23.70, 23.07, 22.87, 20.71, 17.83, 16.65, 16.54, 16.34, 16.24. HRMS (ESI, *m/z*): $[M + K]^+$ Calcd for $C_{42}H_{71}BrKO_4$: 757.4167; found: 757.4160.

*4.2.17. 28-[2-(1-Deoxynojirimycin)-ethyl] maslinic acid ester (**4a**)*

To a solution of compound **2a** (1.27 g, 2.19 mmol) anhydrous K_2CO_3 (251 mg, 6.57 mmol) and 1-deoxynojirimycin (714 mg, 4.38 mmol) in dry DMF (15 mL) which was stirred for 15 minutes, then added potassium iodide (2.18 g, 12.74 mmol) in a nitrogen atmosphere and left standing overnight at 50 °C. The reaction was quenched by 1 N HCl, diluted with water and ethyl acetate, and combined organic layer was dried over anhydrous Na_2SO_4, concentrated and dried in vacuo. The crude product was chromatographed on silica gel to give a white solid **4a**. Yield 52%, mp: 173 °C–174 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.19 (s, 1H), 4.76–4.78 (m, 2H), 4.70 (s, 1H), 4.40 (s, 1H), 4.32 (s, 1H), 4.25 (s, 1H), 4.07–4.10 (m, 1H), 3.87-3.90 (m, 1H), 3.77–3.80 (m, 1H), 3.51–3.54 (m, 1H), 3.16–3.20 (m, 1H), 2.89–2.99 (m, 3H), 2.73–2.79 (m, 3H), 2.04–2.11 (m, 2H), 1.90–1.97 (m, 1H), 1.82–1.85 (m, 1H), 1.72–1.75 (m, 1H), 1.56–1.64 (m, 3H), 1.48–1.52 (m, 2H), 1.32–1.41 (m, 5H), 1.23 (s, 3H), 1.07 (s, 3H), 0.90 (d, J = 16 Hz, 12H), 0.68 (s, 3H), 0.63 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 177.23, 143.99, 122.48, 82.81, 79.69, 71.30, 69.90, 67.70, 66.92, 61.98, 59.98, 58.16, 55.31, 50.72, 47.62, 47.36, 46.47, 46.04, 41.76, 41.31, 38.19, 33.76, 33.33, 32.77, 32.55, 31.49, 30.91, 29.34, 27.66, 26.27, 23.96, 23.54, 23.09, 22.60, 18.58, 17.65, 17.26,

16.84. HRMS (ESI, *m/z*): $[M + K]^+$ Calcd for $C_{38}H_{63}NKO_8$: 700.4185; found: 700.4185.

*4.2.18. 28-[3-(1-Deoxynojirimycin)-propyl] maslinic acid ester (**4b**)*

Compound **4b** was a white solid prepared from **2b** and **1-DNJ** by using the same method established for **4a**. Yield 50%, mp: 186 °C–187 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.18 (s, 1H), 4.85–4.91 (m, 2H), 4.43 (d, *J* = 20 Hz, 2H), 3.94 (t, *J* = 12 Hz, 2H), 3.69–3.72 (m, 1H), 3.56–3.58 (m, 1H), 3.06–3.08 (m, 1H), 2.94–2.97 (m, 1H), 2.71–2.78 (m, 4H), 1.91–1.95 (m, 1H), 1.80–1.83 (m, 2H), 1.66–1.75 (m, 7H), 1.58–1.61 (m, 2H), 1.49–1.51 (m, 3H), 1.39–1.42 (m, 2H), 1.28–1.31 (m, 2H), 1.21 (s, 3H), 1.07(s, 3H), 0.90 (t, *J* = 16 Hz, 12H), 0.68 (s, 3H), 0.63 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 177.19, 144.15, 122.40, 82.89, 79.41, 70.94, 69.55, 67.79, 67.29, 62.90, 59.25, 57.15, 55.37, 49.51, 47.67, 47.42, 46.62, 46.08, 41.91, 41.52, 38.23, 33.86, 33.38, 32.90, 32.65, 30.97, 29.42, 27.73, 26.24, 24.54, 23.97, 23.64, 23.21, 18.63, 17.74, 17.36, 16.90. HRMS (ESI, *m/z*): $[M + H]^+$ Calcd for $C_{39}H_{66}NO_8$: 676.4783; found: 676.4783.

*4.2.19. 28-[4-(1-Deoxynojirimycin)-butyl] maslinic acid ester (**4c**)*

Compound **4c** was a white solid prepared from **2c** and **1-DNJ** by using the same method established for **4a**. Yield 50%, mp: 186 °C–187 °C. Yield 52%, mp: 155 °C–156 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.18 (s, 1H), 4.65–4.70 (m, 2H), 4.31 (d, *J* = 32 Hz, 2H), 3.90–3.96 (m, 2H), 3.69–3.71 (m, 1H), 3.54–3.58 (m, 1H), 3.04–3.07 (m, 1H), 2.92–2.94 (m, 1H), 2.72–2.79 (m, 4H), 1.94–1.98 (m, 2H), 1.82–1.83 (m, 2H), 1.73–1.77(m, 2H), 1.55–1.62 (m, 5H), 1.48–1.52 (m, 7H), 1.40–1.43 (m, 3H), 1.28–1.32 (m, 2H), 1.23(s, 2H), 1.08 (s, 3H), 0.91(t, J = 20 Hz, 12H), 0.69 (s, 3H), 0.64 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 177.18, 144.14, 122.42, 82.88, 79.69, 71.18, 69.80, 67.78, 67.12, 64.31, 59.46, 57.24, 55.37, 52.23, 47.67, 47.43, 46.64, 46.07, 41.92, 41.52, 38.24, 33.85, 33.36, 32.93, 32.75, 30.98, 29.41, 27.68, 26.84, 26.25, 23.95, 23.64, 23.20, 21.62,

18.63, 17.72, 17.37, 16.91. HRMS (ESI, *m/z*): $[M + H]^+$ Calcd for $C_{40}H_{68}NO_8$: 690.4939; found: 690.4940.

*4.2.20. 28-[5-(1-Deoxynojirimycin)-amyl] maslinic acid ester (**4d**)*

Compound **4d** was a white solid prepared from **2d** and **1-DNJ** by using the same method established for **4a**. Yield 50%, mp: 131 °C–132 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.18 (s, 1H), 4.66–4.72 (m, 2H), 4.27–4.37 (m, 2H), 3.91–3.93 (m, 2H), 3.69–3.72 (m, 1H), 3.51–3.55 (m, 2H), 3.18–3.21 (m, 1H), 3.01–3.04 (m, 1H), 2.88–2.92 (m, 2H), 2.78–2.80 (m, 1H), 2.72–2.86 (m, 2H), 1.93–1.97 (m, 3H), 1.83–1.81 (m, 2H), 1.73–1.75 (m, 1H), 1.59–1.62 (m, 2H), 1.52–1.55 (m, 4H), 1.48–1.50 (m, 2H), 1.38–1.40 (m, 7H), 1.29–1.32 (m, 2H), 1.23 (s, 2H), 1.08 (s, 3H), 0.91 (t, *J* = 20 Hz, 12H), 0.69 (s, 3H), 0.64 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 177.05, 143.98, 122.29, 82.72, 79.58, 71.18, 69.77, 67.62, 67.21, 64.14, 59.66, 57.26, 55.23, 52.51, 47.51, 47.31, 46.50, 45.91, 41.76, 41.39, 38.10, 33.68, 33.23, 32.78, 32.60, 30.85, 29.27, 28.54, 27.52, 27.11, 26.11, 24.62, 24.04, 23.82, 23.51, 23.04, 18.50, 17.59, 17.25, 16.78. HRMS (ESI, *m/z*): $[M + H]^+$ Calcd for $C_{41}H_{70}NO_8$: 704.5096; found: 704.5096.

*4.2.21. 28-[6-(1-Deoxynojirimycin)-hexyl] maslinic acid ester (**4e**)*

Compound **4e** was a white solid prepared from **2e** and **1-DNJ** by using the same method established for **4a**. Yield 45%, mp: 158 °C–159 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.18 (s, 1H), 4.67–4.72 (m, 2H), 4.27–4.37 (m, 2H), 3.90–3.94 (m, 2H), 3.68–3.70 (m, 1H), 3.53–3.56 (m, 1H), 3.19–3.21 (m, 1H), 3.01–3.05 (m, 1H), 2.88–2.92 (m, 1H), 2.76–2.80 (m, 2H), 2.71–2.74 (m, 1H), 1.91–1.97 (m, 3H), 1.81–1.83 (m, 2H), 1.72–1.76 (m, 1H), 1.58–1.65 (m, 3H), 1.48–1.54 (m, 6H), 1.29–1.42 (m, 11H), 1.18–1.22 (m, 3H), 1.08 (s, 3H), 0.91 (t, *J* = 20 Hz, 12H), 0.69 (s, 3H), 0.64 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 177.19, 144.15, 122.41, 82.87, 79.71, 71.27, 69.89,

67.77, 67.23, 64.25, 59.53, 57.38, 55.38, 52.66, 47.65, 47.45, 46.65, 46.06, 41.91, 41.53, 38.24, 33.83, 33.36, 32.94, 32.75, 30.98, 29.41, 28.72, 27.67, 27.18, 26.24, 26.18, 25.08, 23.94, 23.65, 23.18, 18.64, 17.71, 17.38, 16.91. HRMS (ESI, *m/z*): $[M + H]^+$ Calcd for $C_{42}H_{72}NO_8$: 718.5252; found: 718.5252.

*4.2.22. 28-[8-(1-Deoxynojirimycin)-octyl] maslinic acid ester (**4f**)*

Compound **4f** was a white solid prepared from **2f** and **1-DNJ** by using the same method established for **4a**. Yield 47%, mp: 134 °C–135 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.17 (s, 1H), 4.69–4.73 (m, 2H), 4.28–4.37 (m, 2H), 3.90–3.94 (m, 2H), 3.67–3.71 (m, 1H), 3.54–3.57 (m, 1H), 3.02–3.05 (m, 1H), 2.88–2.93 (m, 1H), 2.71–2.80 (m, 4H), 1.91–1.97 (m, 3H), 1.81–1.83 (m, 2H), 1.72–1.76 (m, 1H), 1.58–1.62 (m, 1H), 1.49–1.55 (m, 6H), 1.41–1.44 (m, 2H), 1.35–1.38 (m, 3H), 1.28–1.32 (m, 3H), 1.24 (m, 9H), 1.15-1.19 (m, 3H), 1.08 (s, 3H), 0.91 (t, J = 20.0 Hz, 12H), 0.69 (s, 3H), 0.64 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 177.04, 144.04, 122.27, 82.74, 79.54, 71.14, 69.75, 67.63, 67.09, 64.12, 59.43, 57.24, 55.24, 52.62, 47.51, 47.32, 46.51, 45.93, 41.78, 41.40, 38.11, 33.71, 33.22, 32.80, 32.62, 31.43, 30.84, 29.51, 29.27, 29.10, 28.56, 27.53, 27.42, 26.11, 26.03, 24.96, 23.80, 23.51, 23.06, 22.53, 18.51, 17.58, 17.24, 16.74, 14.41. HRMS (ESI, *m/z*): $[M + H]^+$ Calcd for $C_{44}H_{76}NO_8$: 746.5565; found: 746.5565.

*4.2.23. 28-[10-(1-Deoxynojirimycin)-decyl] maslinic acid ester (**4g**)*

Compound **4g** was a white solid prepared from **2g** and **1-DNJ** by using the same method established for **4a**. Yield 50%, mp: 122 °C–123 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.17 (s, 1H), 4.70–4.74 (m, 2H), 4.29–4.38 (m, 2H), 3.89–3.96 (m, 2H), 3.67–3.70 (m, 1H), 3.55–3.57 (m, 1H), 3.03–3.05 (m, 1H), 2.90–2.93 (m, 1H), 2.71–2.80 (m. 4H), 1.91–1.97 (m, 1H), 1.81–1.83 (m, 1H), 1.71–1.75 (m, 2H), 1.58–1.65 (m, 4H), 1.50–1.55 (m, 6H), 1.38–1.43 (m, 5H), 1.30–1.32 (m, 4H),

1.23 (s, 8H), 1.15–1.18 (m, 3H), 1.08 (s, 3H), 0.90 (t, J = 12 Hz, 12H), 0.69 (s, 3H), 0.64 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 177.16, 144.18, 122.39, 82.87, 79.65, 71.25, 69.85, 67.76, 67.18, 64.23, 59.51, 57.31, 55.35, 52.74, 47.63, 47.43, 46.64, 46.06, 41.91, 41.52, 38.23, 33.84, 33.35, 32.92, 32.75, 30.97, 29.67, 29.40, 29.17, 28.69, 27.66, 26.24, 26.17, 25.07, 23.93, 23.64, 23.18, 18.64, 17.71, 17.37, 16.87. HRMS (ESI, *m/z*): $[M + Na]^+$ Calcd for $C_{46}H_{79}NNaO_8$: 796.5698; found: 796.5699.

4.2.24. 28-[12-(1-Deoxynojirimycin)-dodecyl] maslinic acid ester (4h)

Compound **4h** was a white solid prepared from **2h** and **1-DNJ** by using the same method established for **4a**. Yield 54%, mp: 125 °C–126 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.17 (s, 1H), 4.65–4.71 (m, 2H), 4.28–4.38 (m, 2H), 3.88–3.95 (m, 2H), 3.68–3.70 (m, 1H), 3.53–3.56 (m, 1H), 3.01–3.06 (m, 1H), 2.88–2.92 (m, 1H), 2.71–2.80 (m, 4H), 1.91–1.97 (m, 2H), 1.81–1.83 (m, 2H), 1.71–1.75 (m, 2H), 1.59–1.65 (m, 3H), 1.49–1.55 (m, 6H), 1.41–1.44 (m, 2H), 1.35–1.38 (m, 3H), 1.29–1.32 (m, 5H), 1.23 (s, 16H), 1.09 (s, 3H), 0.91 (d, J = 20.0 Hz, 12H), 0.69 (s, 3H), 0.64 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 177.15, 144.18, 122.39, 82.87, 79.70, 71.29, 69.88, 67.76, 67.19, 64.22, 59.54, 57.41, 55.34, 52.73, 47.63, 47.42, 46.64, 46.07, 41.90, 41.52, 38.23, 33.85, 33.36, 32.92, 32.75, 31.56, 30.96, 29.78, 29.72, 29.62, 29.39, 29.16, 28.68, 27.68, 26.23, 26.16, 25.09, 23.92, 23.64, 23.19, 22.66, 18.64, 17.68, 17.37, 16.87, 14.53. HRMS (ESI, *m/z*): $[M + Na]^+$ Calcd for $C_{48}H_{83}NNaO_8$: 824.6011; found: 824.6011.

*4.2.25. 28-[2-(1-Deoxynojirimycin)-ethyl] corosolic acid ester (**5a**)*

Compound **5a** was a white solid prepared from **3a** and **1-DNJ** by using the same method established for **4a**. Yield 43%, mp: 161 °C–162 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.17 (s, 1H), 4.67–4.72 (m, 1H), 4.37–4.38 (m, 1H), 4.21–4.27 (m, 2H), 4.00–4.03 (m, 1H), 3.88–3.91 (m, 1H),

3.75–3.79 (m, 1H), 3.51–3.53 (m, 1H), 3.16–3.18 (m, 1H), 2.89–2.99 (m, 4H), 2.78–2.82 (m, 1H), 2.71–2.74 (m, 1H), 2.09–2.14 (m, 2H), 2.03–2.06 (m, 1H), 1.94–1.97 (m, 1H), 1.85–1.87 (m, 1H), 1.71–1.79 (m, 1H), 1.54–1.57 (m, 2H), 1.43–1.49 (m, 4H), 1.28–1.33 (m, 3H), 1.03 (s, 3H), 0.91 (s, 9H), 0.81 (d, J = 4 Hz, 3H), 0.69 (d, J = 12 Hz, 6H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 176.97, 138.51, 125.57, 82.91, 79.73, 71.39, 69.94, 67.78, 67.02, 61.96, 60.07, 58.37, 55.36, 53.01, 50.78, 47.89, 47.68, 47.60, 42.23, 39.08, 38.94, 38.17, 36.79, 33.16, 30.67, 29.43, 28.05, 24.37, 23.97, 23.56, 22.65, 21.57, 18.61, 17.76, 17.55, 17.37, 17.02. HRMS (ESI, *m/z*): $[M + H]^+$ Calcd for $C_{38}H_{64}NO_8$: 662.4626; found: 662.4627.

*4.2.26. 28-[3-(1-Deoxynojirimycin)-propyl] corosolic acid ester (**5b**)*

Compound **5b** was a white solid prepared from **3b** and **1-DNJ** by using the same method established for **4a**. Yield 42%, mp: 188 °C–189 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.16 (s, 1H), 4.74–4.71 (m, 2H), 4.38 (s, 1H), 4,27 (s, 1H), 3.87–3.93 (m, 2H), 3.71 (d, J = 8 Hz, 1H), 3.51-3.55 (m, 1H), 3.19–3.22 (m, 1H), 3.00–3.05 (m, 1H), 2.72–2.93 (m, 4H), 2.13 (d, J = 8 Hz, 1H), 1.76–1.96 (m, 6H), 1.23–1.68 (m, 16H), 1.03 (s, 3H), 0.90 (s, 9H), 0.81 (s, 3H), 0.66 (d, J = 8 Hz, 6H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 175.72, 137.41, 124.25, 81.69, 78.46, 70.90, 68.64, 66.58, 66.14, 61.73, 58.52, 56.22, 54.16, 51.89, 48.21, 46.78, 46.48, 46.40, 41.08, 37.83, 37.76, 36.96, 35.64, 32.02, 29.50, 28.24, 26.84, 23.51, 23.21, 22.71, 22.39, 20.39, 17.41, 16.57, 16.33, 16.22, 15.83. HRMS (ESI, *m/z*): $[M + K]^+$ Calcd for $C_{39}H_{65}NKO_8$: 714.4342; found: 714.4342.

*4.2.27. 28-[4-(1-Deoxynojirimycin)-butyl] corosolic acid ester (**5c**)*

Compound **5c** was a white solid prepared from **3c** and **1-DNJ** by using the same method established for **4a**. Yield 54%, mp: 154 °C–155 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.15 (s, 1H), 4.72–4.80 (m, 2H), 4.41 (s, 1H), 4.31 (s, 1H), 3.90 (s, 2H), 3.69–3.72 (m, 1H), 3.53–3.57 (m, 1H),

3.20–3.24 (m, 1H), 3.02–3.06 (m, 1H), 2.91–2.94 (m, 1H), 2.72–2.81 (m, 3H), 2.12 (d, *J* = 12 Hz, 1H), 1.69–2.00 (m, 8H), 1.45–1.57 (m, 13H), 1.30–1.35 (m, 3H), 1.23 (s, 3H), 0.81 (t, *J* = 36 Hz, 12H), 0.66 (d, *J* = 12 Hz, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 176.31, 137.95, 124.84, 82.24, 79.05, 70.52, 69.19, 67.13, 66.58, 63.69, 58.78, 56.59, 54.71, 52.45, 51.62, 47.36, 46.99, 46.96, 41.63, 38.41, 38.32, 37.50, 36.29, 32.59, 30.93, 30.05, 28.81, 27.36, 26.15, 23.76, 23.28, 22.96, 22.04, 20.97, 17.95, 17.16, 16.92, 16.77, 16.40, 13.93. HRMS (ESI, *m/z*): $[M + H]^+$ Calcd for $C_{40}H_{68}NO_8$: 690.4939; found: 690.4940.

*4.2.28. 28-[5-(1-Deoxynojirimycin)-amyl] corosolic acid ester (**5d**)*

Compound **5d** was a white solid prepared from **3d** and **1-DNJ** by using the same method established for **4a**. Yield 55%, mp: 135 °C–136 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.15 (s, 1H), 4.71–4.78 (m, 1H), 4.37 (d, J = 44 Hz, 2H), 3.89–3.90 (m, 2H), 3.70–3.72 (m, 1H), 3.55–3.59 (m, 1H), 3.04–3.07 (m, 1H), 2.90–2.95 (m, 1H), 2.72–2.83 (m, 3H), 2.12–2.15 (m, 1H), 1.93–2.00 (m, 2H), 1.86 (s, 2H), 1.76–1.79 (m, 1H), 1.69–1.71 (m, 1H), 1.43–1.53 (m, 12H), 1.22–1.31 (m, 6H), 1.03 (s, 3H), 0.9 (s, 9H), 0.81 (s, 3H), 0.69 (d, J = 12.0 Hz, 6H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 176.83, 138.45, 125.34, 82.71, 79.62, 70.97, 69.91, 67.60, 67.07, 64.14, 59.39, 57.08, 55.20, 52.94, 52.45, 47.86, 47.54, 47.41, 42.12, 38.92, 38.30, 38.00, 36.79, 33.08, 30.52, 29.30, 28.46, 27.83, 24.24, 23.98, 23.78, 23.45, 21.47, 18.46, 17.66, 17.42, 17.29, 16.91. HRMS (ESI, *m/z*): $[M + K]^+$ Calcd for $C_{41}H_{69}NKO_8$: 726.4915; found: 726.4915.

*4.2.29. 28-[6-(1-Deoxynojirimycin)-hexyl] corosolic acid ester (**5e**)*

Compound **5e** was a white solid prepared from **3e** and **1-DNJ** by using the same method established for **4a**. Yield 53%, mp: 137 °C–138 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.15 (s, 1H), 4.69–4.75 (m, 2H), 4.26–4.38 (m, 2H), 3.86–3.91 (m, 2H), 3.68–3.71 (m, 1H), 3.54–3.57 (m, 1H),

3.03–3.07 (m, 1H), 2.88–2.92 (m, 1H), 2.72–2.82 (m, 4H), 2.12–2.15 (m, 1H), 1.95–1.99 (m, 3H), 1.84–1.87 (m, 2H), 1.76–1.80 (m, 2H), 1.69–1.70 (m, 1H), 1.48–1.53 (m, 7H), 1.41–1.45 (m, 3H), 1.28–1.33 (m, 6H), 1.22–1.25 (m, 3H), 1.03 (s, 3H), 0.91 (s, 3H), 0.82 (d, J = 8.0 Hz, 3H), 0.69 (d, J = 12.0 Hz, 6H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 176.95, 138.63, 125.47, 82.89, 79.69, 71.23, 69.85, 67.78, 67.23, 64.25, 59.50, 57.33, 55.37, 53.10, 52.66, 48.02, 47.67, 47.58, 42.29, 39.07, 38.96, 38.16, 36.94, 33.25, 30.68, 29.44, 28.70, 27.99, 27.19, 26.17, 25.00, 24.40, 23.91, 23.59, 21.59, 18.61, 17.77, 17.53, 17.43, 17.03. HRMS (ESI, *m/z*): $[M + H]^+$ Calcd for $C_{42}H_{72}NO_8$: 718.5252; found: 718.5252.

*4.2.30. 28-[8-(1-Deoxynojirimycin)-octyl] corosolic acid ester (**5f**)*

Compound **5f** was a white solid prepared from **3f** and **1-DNJ** by using the same method established for **4a**. Yield 51%, mp: 120 °C–121 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.10 (s, 1H), 4.63–4.68 (m, 2H), 4.53 (s, 1H), 4.24 (s, 1H), 4.08–4.12 (m, 1H), 3.81–3.88 (m, 2H), 3.64 (d, J = 12 Hz, 1H), 3.48–3.52 (m, 1H), 3.13–3.17 (m, 1H), 2.95–3.01 (m, 1H), 2.84–2.88 (m, 1H), 2.67–2.77 (m, 3H), 2.08 (d, J = 12 Hz, 1H), 1.62–1.96 (m, 8H), 1.37–1.94 (m, 9H), 1.15–1.31 (m, 15H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 175.72, 137.42, 124.24, 81.65, 78.43, 69.98, 68.62, 66.54, 65.98, 63.05, 58.20, 56.11, 54.14, 51.87, 51.54, 46.80, 46.44, 46.35, 41.06, 37.87, 37.76, 36.93, 35.73, 32.03, 29.48, 28.44, 28.22, 28.08, 27.47, 26.77, 26.40, 24.98, 23.80, 23.19, 22.71, 22.36, 20.39, 17.40, 16.58, 16.34, 16.20, 15.79. HRMS (ESI, *m/z*): $[M + K]^+$ Calcd for $C_{44}H_{75}NKO_8$: 784.5124; found: 784.5125.

*4.2.31. 28-[10-(1-Deoxynojirimycin)-decyl] corosolic acid ester (**5g**)*

Compound **5g** was a white solid prepared from **3g** and **1-DNJ** by using the same method established for **4a**. Yield 55%, mp: 131 °C–132 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.14 (s, 1H),

4.67–4.73 (m, 2H), 4.38 (d, *J* = 4 Hz, 1H), 4.27–4.30 (m, 1H), 3.86–3.91 (m, 2H), 3.67–3.70 (m, 1H), 3.53–3.57 (m, 1H), 3.19–3.22 (m, 1H), 3.01–3.06 (m, 1H), 2.89–2.92 (m, 1H), 2.71–2.81 (m, 3H), 2.12 (d, *J* = 12 Hz, 1H), 1.83–1.99 (m, 5H), 1.67–1.79 (m, 3H), 1.41–1.56 (m, 11H), 1.29–1.36 (m, 7H), 1.24 (s, 10H), 1.03 (s, 3H), 0.89 (d, *J* = 8 Hz, 9H), 0.80 (d, *J* = 8 Hz, 3H), 0.66 (d, *J* = 12 Hz, 6H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 175.69, 137.42, 124.24, 81.67, 78.43, 69.99, 68.61, 66.55, 65.94, 63.03, 58.20, 56.11, 54.13, 51.87, 51.54, 46.79, 46.43, 46.35, 41.05, 37.88, 37.76, 36.94, 35.73, 32.03, 30.37, 29.49, 28.51, 28.22, 28.02, 27.47, 26.78, 26.50, 24.99, 23.82, 23.79, 23.19, 22.70, 22.36, 21.48, 20.39, 17.41, 16.56, 16.33, 16.20, 15.79, 13.36. HRMS (ESI, *m/z*): [M + Na]$^+$ Calcd for $C_{46}H_{79}NNaO_8$: 796.5698; found: 796.5699.

*4.2.32. 28-[12-(1-Deoxynojirimycin)-dodecyl] corosolic acid ester (**5h**)*

Compound **5h** was a white solid prepared from **3h** and **1-DNJ** by using the same method established for **4a**. Yield 45%, mp: 120 °C–121 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.14 (s, 1H), 4.71–4.76 (m, 2H), 4.40 (s, 1H), 4.19–4.29 (m, 1H), 3.88 (s, 2H), 3.67 (d, *J* = 12 Hz, 1H), 3.54–3.57 (m, 1H), 3.19–3.23 (m, 1H), 3.04–3.08 (m, 1H), 2.90–2.93 (m, 1H), 2.71–2.82 (m, 3H), 2.13 (d, *J* = 8 Hz, 1H), 1.67–1.97 (m, 9H), 1.41–1.55 (m, 11H), 1.30–1.36 (m, 7H), 1.23 (s, 13H), 1.03 (s, 3H), 0.90 (s, 9H), 0.81 (s, 3H), 0.66 (d, *J* = 8 Hz, 6H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 176.24, 137.99, 124.82, 82.26, 78.98, 70.54, 69.14, 67.14, 66.51, 63.59, 58.70, 56.62, 54.70, 52.45, 52.10, 47.37, 46.94, 41.64, 38.46, 38.35, 37.52, 36.31, 32.61, 30.08, 29.10, 29.04, 28.78, 28.57, 28.03, 27.37, 27.05, 25.55, 24.41, 23.78, 23.27, 22.94, 20.94, 17.99, 17.10, 16.88, 16.78, 16.36. HRMS (ESI, *m/z*): [M + Na]$^+$ Calcd for $C_{48}H_{83}NNaO_8$: 824.6011; found: 824.6011.

*4.3. Synthesis of **MA/CA**-piperazines derivatives*

*4.3.1. 2α, 3β-Diacetoxy-ole-12-en-28-oic acid (**6**)*

To a suspension of **MA** (or **CA**) (731.8 mg, 1.55 mmol) in dry Pyridine (10 mL) being cooled to 0 °C was added acetic anhydride (5 mL) dropwise. The reaction was stirred at room temperature overnight. After the reaction was completed, the mixture was extracted with water and dichloromethane, and the organic layer dried with anhydrous sodium sulfate. The solvent was removed under reduced pressure after filtration, and the purification of crude product on silica gel column chromatography using petroleum ether/ethyl acetate (v:v) = 10:1 to give **6** (or **7**) as a white solid (yield 90%) . NMR data as reported in the literature[30].

*4.3.2. N-(2α, 3β-Diacetoxy-ole-12-en-28-aminocarbonyl) piperazine (**10a**)*

Compound **6** (136.6 mg, 0.25 mmol) was dissolved in waterless DCM (5 mL), then triethylamine (0.05 mL) and oxalyl chloride (0.21 mL) were added slowly to the mixture under the ice bath. After 12 h, removing the solvent by using rotary evaporator and dry DCM (5×10 mL) was diluted to the residue for bring out excess oxalyl chloride, then concentrated in vacuum to obtain compound **8** which was directly added to the next step without further operation.

A solution of piperazine (138 mg, 1.06 mmol) and triethylamine (0.1 mL) in DCM was dropwise added 2α, 3β-Diacetoxy-ole-12-en-28 acyl chloride **8** (305.2 mg, 0.53 mmol) dissolved in anhydrous dichloromethane at 0 °C, then the reaction was refluxed 2 h and allowed to cool to room temperature. The reaction mixture was poured into water and extracted with dichloromethane, and the organic layer was dried by anhydrous Na_2SO_4, concentrated under reduced pressure. Purification by silica gel column chromatography (dichloromethane: methanol = 8:1) to obtain a white solid **10a**. Yield 65%, mp: 211 °C–212 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.24 (s, 1H), 5.05–5.11 (m, 1H), 4.74 (d, *J* = 12.0 Hz, 1H), 3.77–3.82 (m, 4H), 2.98a–3.05 (m, 4H), 2.08–2.16 (m, 1H), 2.04 (s, 3H), 1.97 (s, 3H), 1.80–1.85 (m, 1H), 1.55–1.70 (m, 7H), 1.37–1.48 (m, 2H), 1.32–1.38 (m, 2H), 1.25–1.30 (m,

5H), 1.14–1.20 (m, 3H), 1.11 (s, 3H), 1.03 (s, 3H), 0.94–0.98 (m, 1H), 0.91 (d, *J* = 8.0 Hz, 12H), 0.69 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.95, 170.76, 170.41, 144.84, 121.08, 80.70, 70.00, 54.99, 47.70, 47.38, 46.53, 46.39, 46.11, 43.88, 43.55, 41.86, 39.33, 39.19, 38.20, 34.00, 33.01, 32.64, 31.52, 30.35, 29.89, 28.40, 27.88, 25.88, 24.05, 23.44, 22.72, 21.06, 20.83, 18.20, 17.57, 16.86, 16.40, 14.04. HRMS (ESI, *m/z*): $[M + K]^+$ Calcd for $C_{38}H_{60}N_2KO_5$: 603.4134; found: 603.4134.

*4.3.3. [N-(2α, 3β-Diacetoxy-ole-12-en-28-aminocarbonyl)-N'-(2-hydroxyethyl)] piperazine (**10b**)*

Compound **10b** was a white solid prepared from intermediates **8** and N-(2-Hydroxyethyl) piperazine by using the same method established for **10a**. Yield 60%, mp: 197 °C–198 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.23 (s, 1H), 5.05–5.11 (m, 1H), 4.74 (d, *J* = 12.0 Hz, 1H), 3.61–3.65 (m, 6H), 3.04–3.08 (m, 1H), 2.55 (t, *J* = 8.0 Hz, 2H), 2.44–2.49 (m, 3H), 2.04 (s, 3H), 1.96 (s, 3H), 1.78–1.85 (m, 1H), 1.25–1.69 (m, 17H), 1.14–1.19 (m, 2H), 1.11 (s, 3H), 1.03 (s, 3H), 0.91 (d, *J* = 12.0 Hz, 12H), 0.71 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.94, 170.76, 170.40, 144.78, 121.10, 80.68, 70.00, 59.36, 57.77, 54.98, 53.11, 47.69, 47.38, 46.35, 45.34, 43.88, 41.85, 39.33, 39.18, 38.20, 34.01, 33.01, 32.64, 31.52, 30.35, 29.96, 28.40, 27.86, 25.88, 24.04, 23.44, 22.73, 22.59, 21.06, 20.83, 18.21, 17.57, 16.88, 16.41, 14.04. HRMS (ESI, *m/z*): $[M + Na]^+$ Calcd for $C_{40}H_{64}N_2NaO_6$: 691.4656; found: 691.4651.

*4.3.4. N-[2-(2α, 3β-Diacetoxy-ole-12-en-28-aminocarbonyl)] ethyl piperazine (**10c**)*

Compound **10c** was a white solid prepared from intermediates **8** and N-Aminoethylpiperazine by using the same method established for **10a**. Yield 67%, mp: 160 °C–161 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.20 (s, 1H), 5.31 (s, 1H), 5.03–5.10 (m, 1H), 4.74 (d, *J* = 12.0 Hz, 1H), 3.40–3.45 (m, 1H), 3.21 (s, 5H), 2.75–2.80 (m, 3H), 2.47–2.54 (m, 3H), 2.04 (s, 3H), 1.96 (s, 3H), 1.87–1.90 (m,

1H), 1.69–1.75 (m, 1H), 1.61–1.64 (m, 3H), 1.43–1.55(m, 7H), 1.17–1.39 (m, 9H), 1.13 (s, 3H), 1.02 (s, 3H), 0.88 (s, 12H), 0.72 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.76, 170.71, 170.48, 144.79, 122.08, 80.47, 69.96, 56.81, 54.78, 54.01, 47.42, 46.75, 46.28, 46.10, 43.83, 42.23, 42.02, 39.39, 39.30, 39.03, 38.07, 35.59, 34.12, 32.93, 32.64, 32.14, 30.66, 28.37, 27.24, 25.64, 23.60, 23.54, 23.45, 21.04, 20.80, 18.14, 17.55, 16.82, 16.40, 14.03. HRMS (ESI, m/z): $[M + H]^+$ Calcd for $C_{40}H_{66}N_3O_5$: 668.4997; found: 668.4999.

*4.3.5. N-(2α, 3β-Diacetoxy-urs-12-en-28-aminocarbonyl) piperazine (**11a**)*

Compound **11a** was a white solid prepared from intermediates **9** and piperazine by using the same method established for **10a**. Yield 67%, mp: 191 °C–192 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.20 (s, 1H), 5.05–5.12 (m, 1H), 4.74 (d, *J* = 8.0 Hz, 1H), 3.61 (s, 4H), 2.86 (s, 4H), 2.59 (s, 1H), 2.04 (s, 3H), 1.96 (s, 3H), 1.89–1.92 (m, 1H), 1.71–1.74 (m, 1H), 1.24–1.58 (m, 19H), 1.05 (d, *J* = 4.0 Hz, 6H), 0.93 (d, *J* = 4.0 Hz, 3H), 0.89 (d, *J* = 4.0 Hz, 6H), 0.85 (d, *J* = 4.0 Hz, 3H), 0.73 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.20, 170.72, 170.37, 138.73,124.74, 80.67, 70.01, 54.93, 48.44, 47.55, 46.36, 45.90, 44.07, 42.14, 39.47, 39.31, 38.68, 38.08, 34.19, 32.81, 31.50, 30.47, 28.42, 28.13, 23.66, 23.35, 22.57, 21.18, 21.02, 20.81, 18.15, 17.62, 17.34, 16.47, 14.03. HRMS (ESI, m/z): $[M + K]^+$ Calcd for $C_{38}H_{60}N_2KO_5$: 603.4134; found: 603.4135.

*4.3.6. [N-(2α, 3β-Diacetoxy-urs-12-en-28-aminocarbonyl)-N'-(2-hydroxyethyl)] piperazine (**11b**)*

Compound **11b** was a white solid prepared from intermediates **9** and N-(2-Hydroxyethyl) piperazine by using the same method established for **10a**. Yield 62%, mp: 227 °C–228 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.20 (s, 1H), 5.06–5.12 (m, 1H), 4.75(d, *J* = 12.0 Hz, 1H), 3.64 (t, *J* = 12.0 Hz, 4H), 2.55 (t, *J* = 8.0 Hz, 3H), 2.46 (s, 5H), 2.04 (s, 3H), 1.96 (s, 3H), 1.89–1.92 (m, 2H), 1.72–1.76 (m, 2H), 1.24–1.58 (m, 17H), 1.06 (d, *J* = 4 Hz, 3H), 0.94 (d, *J* = 8 Hz, 3H), 0.89 (s, 6H),

0.86 (d, J = 8 Hz, 3H), 0.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.75, 170.32, 169.98, 138.27, 124.29, 80.22, 69.58, 58.93, 57.32, 54.45, 52.56, 47.98, 47.08, 44.92, 43.60, 41.68, 38.99, 38.85, 38.22, 37.62, 33.77, 32.35, 30.01, 29.15, 27.96, 27.65, 23.22, 22.88, 20.71, 20.56, 20.35, 17.70,17.15,16.86, 16.37, 16.02. HRMS (ESI, m/z): $[M + H]^+$ Calcd for $C_{40}H_{65}N_2O_6$: 669.4837, found: 669.4837.

*4.3.7. N-[2-(2α, 3β-Diacetoxy-urs-12-en-28-aminocarbonyl)] ethyl piperazine (**11c**)*

Compound **11c** was a white solid prepared from intermediates **9** and N-Aminoethylpiperazine by using the same method established for **10a**. Yield 66%, mp: 154 °C–155 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.18 (s, 1H), 5.24 (s, 1H), 5.04–5.10 (m, 1H), 4.75 (d, J = 12.0 Hz, 1H), 3.39–3.44 (m, 1H), 3.19 (s, 5H), 2.70–2.78 (m, 4H), 2.52 (t, J = 8.0 Hz, 2H), 2.04 (s, 3H), 1.96 (s, 3H), 1.85 (t, J = 24.0 Hz, 3H), 1.68–1.72 (m, 1H), 1.57–1.61 (m, 2H), 1.38–1.52 (m, 7H), 1.28–1.31 (m, 2H), 1.24 (s, 2H), 1.07 (d, J = 16.0 Hz, 5H), 0.94 (s, 3H), 0.89 (t, J = 20.0 Hz, 15H), 0.74 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.72, 170.72, 170.49, 139.6, 124.97, 80.51, 70.02, 56.96, 54.81, 54.06, 53.93, 47.73, 47.43, 46.11, 44.06, 42.48, 39.71, 39.59, 39.32, 39.08, 38.04, 37.31, 35.61, 32.52, 30.87, 28.43, 27.77, 24.73, 23.47, 23.21, 21.17, 21.05, 20.83, 18.14, 17.63, 17.24, 16.85, 16.54, 14.04. HRMS (ESI, m/z): $[M + H]^+$ Calcd for $C_{40}H_{66}N_3O_5$: 668.4997; found: 668.5026.

*4.3.8. N-(2α, 3β-Dihydroxy-ole-12-en-28-aminocarbonyl) piperazine (**12a**)*

To a slurry of **10a** (172.5 mg, 0.26 mmol) in tetrahydrofuran/methanol (2:3, 10 mL) in the presence of 4N sodium hydroxide solution (0.65 mL) which was stirred at 25 °C for 1 h. After TLC monitored the starting material was disappeared completely, DCM was diluted to the mixture and washed with water, 1 N HCl was added to adjust pH to 7.0. The combined organic layer was dried over anhydrous Na_2SO_4, filtrated and concentrated in vacuum. The crude product was eluted with

dichloromethane/methanol (v:v) = 20:1 on silica gel column chromatography to give a white powder **12a**. Yield 57%, mp: 276 °C–277 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.26 (s, 1H), 3.65–3.70 (m, 1H), 3.60 (s, 3H), 3.09 (d, *J* = 12.0 Hz, 1H), 3.00 (d, *J* = 12.0 Hz, 1H), 2.80–2.86 (m, 4H), 2.10 (s, 4H), 1.94–1.99 (m, 2H), 1.84–1.89 (m, 1H), 1.66–1.71 (m, 4H), 1.57–1.61 (m, 1H), 1.51–1.54 (m, 1H), 1.33–1.44(m, 3H), 1.28–1.32 (m, 1H), 1.25(s, 3H), 1.19 (s, 1H), 1.13 (s, 3H), 1.02 (s, 3H), 0.97 (s, 3H), 0.92 (s, 3H), 0.89 (s, 3H), 0.81 (s, 3H), 0.73 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.01, 144.82, 121.32, 83.92, 68.95, 55.40, 47.78, 47.40, 46.68, 46.42, 46.20, 43.56, 41.89, 39.22, 39.13, 38.38, 34.02, 33.03, 32.77, 30.37, 29.92, 29.65, 28.59, 27.91, 25.98, 24.08, 23.44, 22.77, 18.32, 16.96, 16.69, 16.60, 14.04. HRMS (ESI, *m/z*): $[M + H]^+$ Calcd for $C_{34}H_{57}N_2O_3$: 541.4364; found: 541.4362.

*4.3.9. [N-(2α, 3β-Dihydroxy-ole-12-en-28-aminocarbonyl)-N'-(2-hydroxyethyl)] piperazine (**12b**)*

Compound **12b** was a white solid prepared from hydrolysis of **10b** by using the method established for **12a**. Yield 62%, mp: 210 °C–211 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.25 (s, 1H), 3.62–3.68 (m, 6H), 3.04–3.08 (m, 1H), 3.0 (d, *J* = 12.0 Hz, 1H), 2.56 (t, *J* = 8.0 Hz, 2H), 2.45–2.50 (m, 4H), 2.06–2.14 (m, 1H), 1.88–1.98 (m, 2H), 1.56–1.70 (m, 6H), 1.29–1.54 (m, 6H), 1.25 (s, 2H), 1.19 (d, *J* = 12.0 Hz, 1H), 1.12 (s, 2H), 1.07 (s, 1H), 0.96 (s, 3H), 0.92 (s, 3H), 0.89 (d, *J* = 8.0 Hz, 6H), 0.81 (s, 3H), 0.71 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.09, 144.65, 121.40, 83.74, 68.82, 59.49, 57.80, 55.38, 53.13, 47.72, 47.40, 46.41, 46.34, 45.27, 43.51, 41.85, 39.19, 39.15, 38.31, 33.98, 33.01, 32.75, 31.51, 30.34, 29.98, 28.63, 27.87, 25.98, 24.06, 23.43, 22.57, 18.33, 16.94, 16.76, 16.60, 14.04. HRMS (ESI, m/z): $[M + K]^+$ Calcd for $C_{36}H_{60}N_2KO_4$: 623.4185; found: 623.4186.

*4.3.10. N-[2-(2α, 3β-Dihydroxy-ole-12-en-28-aminocarbonyl)] ethyl piperazine (**12c**)*

Compound **12c** was a white solid prepared from hydrolysis of **10c** by using the method established for **12a**. Yield 66%, mp: 158 °C–159 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.47 (s, 1H), 5.37 (s, 1H), 3.65–3.71 (m, 1H), 3.39–3.45 (m, 1H), 3.13–3.19 (m, 1H), 2.98–3.04 (m, 5H), 2.48–2.55 (m, 6H), 1.95–1.98 (m, 4H), 1.64–1.75 (m, 5H), 1.51-1.56 (m, 3H), 1.35–1.43 (m, 4H), 1.25 (s, 5H), 1.15 (s, 3H), 1.02 (s, 3H), 0.96 (s, 3H), 0.90 (s, 6H), 0.81 (s, 3H), 0.74 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.94, 144.84, 122.35, 83.84, 68.78, 56.81, 55.18, 53.27, 47.51, 46.37, 46.33, 45.64, 42.27, 42.07, 39.43, 39.16, 38.22, 35.65, 34.14, 32.95, 32.68, 32.27, 31.54, 30.69, 29.65, 28.59, 27.27, 25.74, 23.61, 23.49, 18.29, 16.97, 16.71, 16.63. HRMS (ESI, m/z): $[M + K]^+$ Calcd for $C_{36}H_{61}N_3KO_3$: 622.4345; found: 622.4349.

*4.3.11. N-(2α, 3β- Dihydroxy-urs-12-en-28-aminocarbonyl) piperazine (**13a**)*

Compound **13a** was a white solid prepared from hydrolysis of **11a** by using the method established for **12a**. Yield 64%, mp: 275 °C–276 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.21 (s, 1H), 3.64–3.71 (m, 1H), 3.57 (s, 4H), 2.99 (d, J = 8.0 Hz, 1H), 2.82 (s, 4H), 2.41–2.43 (m, 1H), 2.22 (s, 2H), 1.94–2.01 (m, 4H), 1.73–1.76 (m, 1H), 1.46–1.57 (m, 7H), 1.29–1.38 (m, 5H), 1.24 (s, 1H), 1.07 (s, 3H), 1.02 (s, 3H), 0.97 (s, 3H), 0.94 (d, J = 8.0 Hz, 3H), 0.87 (d, J = 8.0 Hz, 3H), 0.81 (s, 3H), 0.74 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.31, 138.73, 124.99, 83.84, 68.88, 55.36, 48.45, 47.62, 46.65, 46.08, 42.17, 39.51, 39.14, 38.72, 38.26, 34.22, 32.92, 30.50, 29.64, 28.65, 28.17, 23.36, 21.21, 18.29, 17.38, 16.91, 16.77, 16.69, 14.04. HRMS (ESI, m/z): $[M + K]^+$ Calcd for $C_{34}H_{56}N_2KO_3$: 579.3923; found: 579.3920.

*4.3.12. [N-(2α, 3β-Dihydroxy-urs-12-en-28-aminocarbonyl)-N'-(2-hydroxyethyl)] piperazine (**13b**)*

Compound **13b** was a white solid prepared from hydrolysis of **11b** by using the method established for **12a**. Yield 64%, mp: 184 °C–185 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.21 (s, 1H),

3.68–3,71 (m, 1H), 3.65(t, J = 8 Hz, 4H), 3.0 (d, *J* = 8.0 Hz, 1H), 2.58 (t, *J* = 12.0 Hz, 2H), 2.49 (s, 3H), 2.29–2.32 (m, 2H), 2.11–2.16 (m, 1H), 1.94–2.01 (m, 3H), 1.76 (d, *J* = 16.0 Hz, 2H), 1.44–1.58 (m, 5H), 1.29–1.41 (m, 6H), 1.25 (s, 2H), 1.07 (s, 3H), 1.02 (s, 3H), 0.97 (s, 3H), 0.94 (d, *J* = 4.0 Hz, 3H), 0.89 (t, *J* = 16.0 Hz, 6H), 0.81 (s, 3H), 0.73 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.34, 138.68, 125.02, 83.77, 68.85, 59.49, 57.75, 55.34, 53.05, 48.48, 47.58, 46.62, 45.27, 42.15, 39.49, 39.15, 38.72, 38.23, 34.28, 32.94, 30.48, 29.63, 28.67, 28.14, 23.81, 23.35, 21.20, 18.30, 17.37, 16.92, 16.80, 16.70,14.05. HRMS (ESI, m/z): $[M + H]^+$ Calcd for $C_{36}H_{61}N_2O_4$: 585.4626; found: 585.4626.

*4.3.13. N-[2-(2α, 3β- Dihydroxy-urs-12-en-28-aminocarbonyl)] ethyl piperazine (**13c**)*

Compound **13c** was a white solid prepared from hydrolysis of **11c** by using the method established for **12a**. Yield 64%, mp: 173 °C–174 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.39 (s, 1H), 5.30 (s, 1H), 3.66–3.71 (m, 1H), 3.36–3.41 (m, 1H), 3.28 (s, 4H), 3.14–3.19 (m, 1H), 3.07 (s, 4H), 3.00 (d, *J* = 8.0 Hz, 1H), 2.56 (s, 2H), 2.47 (s, 2H), 1.92–2.01 (m, 4H), 1.83–1.87 (m, 2H), 1.72–1.76 (m, 1H), 1.58–1.62 (m, 2H), 1.47–1.51 (m, 3H), 1.40–1.43 (m, 2H), 1.28–1.31 (m, 2H), 1.24 (s, 3H), 1.08 (s, 3H), 1.02 (s, 3H), 0.96 (d, *J* = 4.0 Hz, 3H), 0.87 (d, *J* = 4.0 Hz, 3H), 0.80 (s, 3H), 0.75 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.95, 139.58, 125.26, 83.64, 68.65, 56.91, 55.20, 53.88, 53.57, 47.73, 47.45, 46.63, 45.75, 42.47, 39.71, 39.59, 39.19, 39.05, 38.13, 37.29, 35.69, 32.63, 31.51, 30.85, 28.69, 27.77, 24.75, 23.45, 23.27, 21.17, 18.27, 17.27, 16.95, 16.84, 16.74, 14.04. HRMS (ESI, m/z): $[M + H]^+$ Calcd for $C_{36}H_{62}N_3O_3$: 584.4786; found: 584.4785.

4.4. In vitro α-glucosidase inhibition assay

The inhibition test on α-glucosidase of the compounds were performed on the methods reported in the literature and adjusted slightly [40, 41]. The specific procedure was as follows: 10 μL of 1

U/mL α-glucosidase and 10 μL of different concentrations of sample solutions (dissolved in dimethyl sulfoxide solution, Triton-100 as cosolvent) were added to 160 μL of 67 mM phosphate buffer (pH 6.8), subsequently incubated at 37 °C for 20 minutes. Next, 20 μL of 10 mM PNPG was added to the reaction system, after 15 minutes of shaking at a constant temperature, the absorbance value was measured at 405 nm using a microplate reader. The α-glucosidase inhibition percentage is calculated as follows:

$$\alpha\text{-glucosidase inhibition (\%)} = \left(\frac{A_1 - A_2}{A_1}\right) \times 100$$

A1: 160 μL PB + 10 μL α-glucosidase + 10 μL dimethyl sulfoxide.

A2: 160 μL PB + 10 μL α-glucosidase + 10 μL sample solution.

IC_{50} was the concentration of an inhibitor that is required for 50% inhibition of enzyme.

4.5. α-Glucosidase inhibition type

In the light of the IC_{50} values of all the target compounds, enzymatic kinetic analysis of compound **12b** with superior inhibitory activity utilizing the Lineweaver-Burk plot. The experiment was carried out on the substrate concentrations of 0.1-0.7 mM in the absence and presence of the inhibitor. The data acquired were plotted as double reciprocal graph of 1/V (reciprocal of velocity) against 1/S (reciprocal of substrate concentration). The inhibitory mechanism of **12b** judged by double reciprocal plot.

4.6 Molecular docking

After the test of inhibitory activities, compounds with better inhibition effects were selected for molecular docking simulation to explore their interact with enzyme. The crystal structure of α-glucoamylase (PDB:2f6d) was used as the receptor of **MA** (or **CA**) derivatives ligands. The docking between **MA** (or **CA**) derivatives and enzyme was conducted with methods as described previously

[42], using Discovery studio version 2018.

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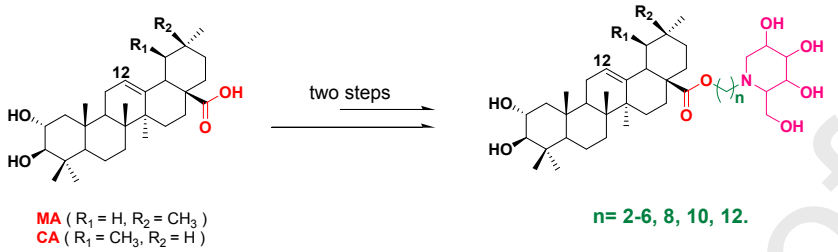
Highlight

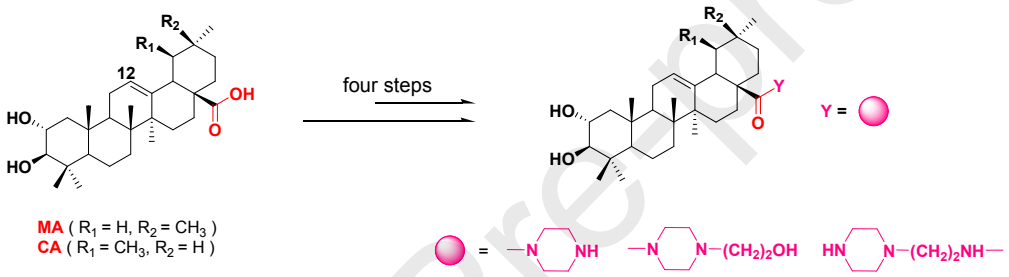
1. **MA /CA** coupled with 1-deoxynojirimycin (or piperazines) were synthesized.
2. α-Glucosidase inhibitory activities of the derivatives were evaluated *in vitro*.
3. Eight derivatives presented higher inhibitory activity than that of precursors.
4. Compound **12b** exhibited a better inhibitory than that of precursors and acarbose.

Graphical abstract

Two series of pentacyclic dihydroxyterpene carboxylic acid derivatives were synthesized via introduction of saturated nitrogen heterocycle segments (i.e. **1-DNJ** and piperazines) at C28 site in **MA** and **CA**. Some of the compounds exhibited a better α-glucosidase inhibitory activity than those of precursors and positive compound (acarbose) in the DMSO measurement system. Simultaneously, kinetics study and molecule docking were carried on the active compounds.



Scheme 1. Synthesis of **MA/CA-1-DNJ** derivatives



Scheme 2. Synthesis of **MA/CA**-piperazines derivatives

Conflict of interest statement

The authors declared that they have no conflicts of interest to this work.

We declare that we do not have any commercial or associative interest that represents a conflict of interest in connection with the work submitted