

Click chemistry-assisted synthesis of novel C-2 triazole-linked betulinic acid conjugates with azidothymidine as potential anti-HIV agents

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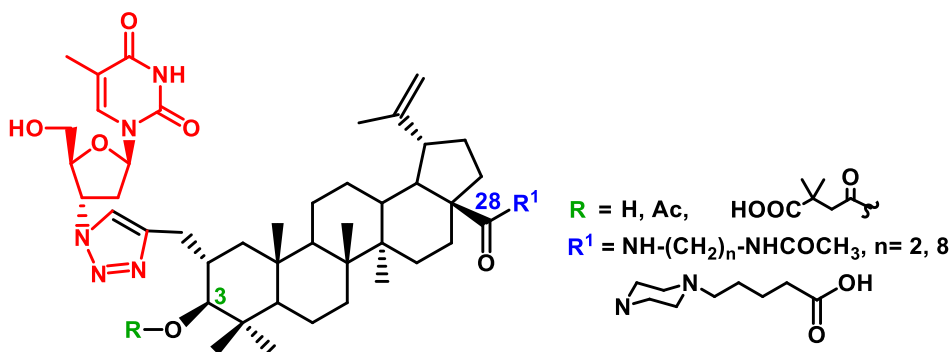
Received 05-21-2018

Accepted 07-30-2018

Published on line 08-18-2018

Abstract

A new synthetic approach to C-2 triazole-linked bioconjugates of lupane triterpenoids with 3'-azido-3'-deoxythymidine (AZT) based on Cu^I-catalyzed 1,3-cycloaddition between alkynes and azides is described. The proposed strategy towards AZT–betulinic acid hybrid molecules as potential anti-HIV agents makes it possible to vary the C-3 and C-28 pharmacophores in triterpene moieties. The C-2 propargyl-substituted betulinic acid and its mono- or bi-functional derivatives with side chain at C-3 and/or C-28 positions were successfully synthesized by employing the click reaction.



Keywords: Betulinic acid, Bevirimate, AZT, click chemistry, anti-HIV agents.

Introduction

The pentacyclic group of lupane triterpenoids (betulin and betulinic acid) represents one of the very important classes of plant natural products that are derived biosynthetically from squalene cyclization. These secondary metabolites possess a wide range of biological effects including antitumor, anti-inflammatory, antibacterial, antimalarial, and antiviral (anti-HIV) activities.¹⁻⁴ The broad spectrum of useful biological properties of lupane triterpenoids is successfully combined with their acceptable systemic toxicity towards animals. Owing to the presence of easily transformable functional groups (3-OH, 28-OH, 28-COOH, C-19 isoprenyl) in the triterpene skeleton, betulin and betulinic acid have a high synthetic potential and are actively used in transformations with the aim to design new drugs. Currently, numerous semisynthetic betulin and betulinic acid derivatives have been prepared; particular attention deserve new potential anti-HIV agents, which show antiviral activity when present in nanomolar concentrations.⁵⁻¹¹ (Figure 1)

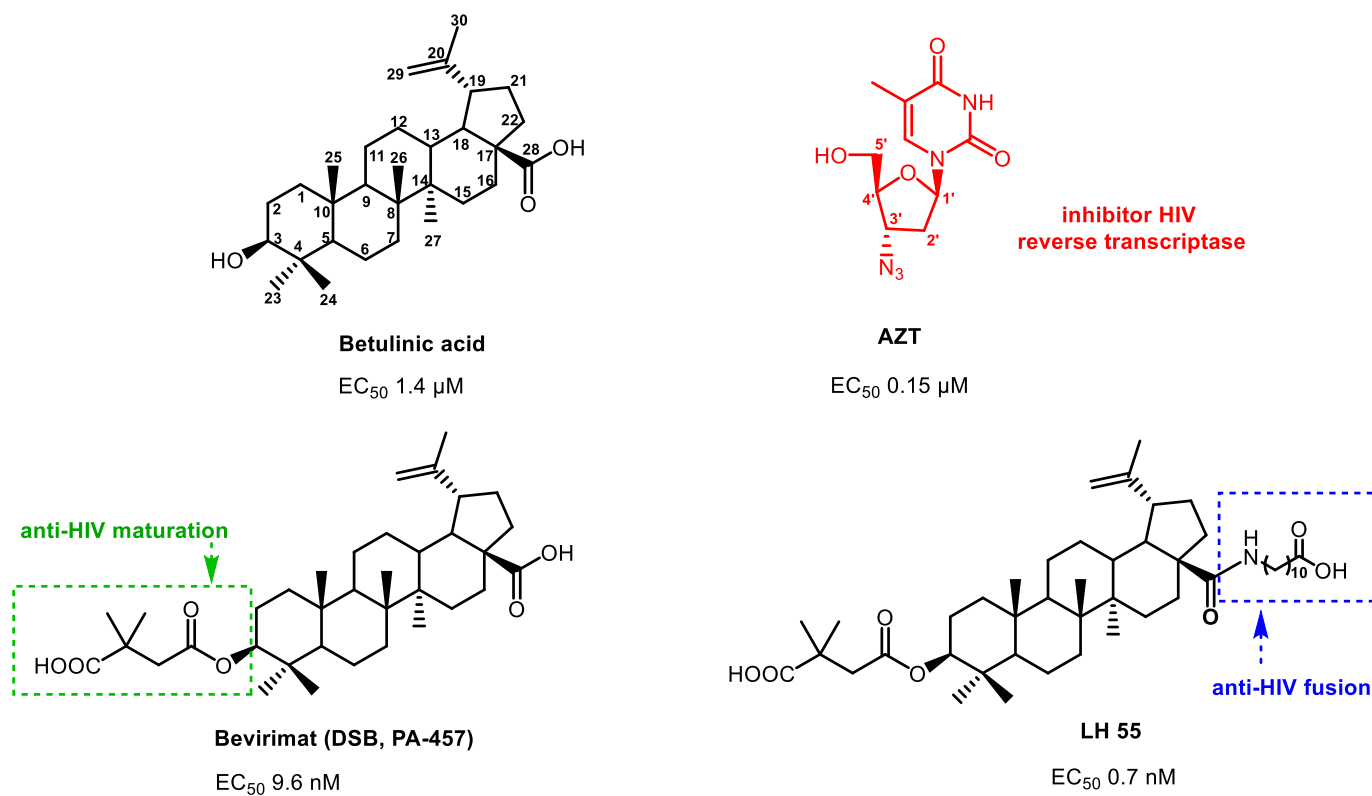


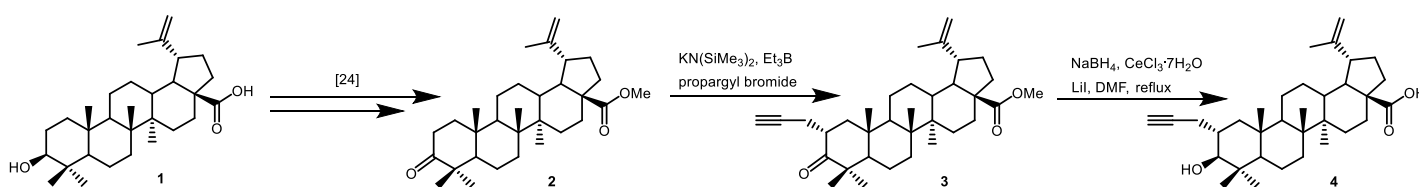
Figure 1. Chemical structures of betulinic acid and derivatives with potent HIV-1 antiviral activity.

The structure–activity relationship studies of anti-HIV-1 lupane triterpenes demonstrated that, in terms of the mechanism of antiviral action, betulinic acid derivatives are subdivided into two types, depending on the structures of C-3 and C-28 pharmacophores. The C-3 acyl derivatives of betulinic or dihydrobetulinic acid are antiretroviral compounds of a new class inhibiting virus protease, which plays a key role in HIV maturation at a late stage of virus replication.^{5,6,8} For example, 3-O-(3',3'-dimethylsuccinyl)betulinic acid (DSB, PA-457, MPC-4326, or Bevirimat), which is the most promising in this group of anti-HIV agents, prevents cleavage of the capsid protein p25 (CA-sp1) to mature capsid p24 (CA), which results in morphologically defective, non-infectious viral particles.⁸ Unlike Bevirimat and its 3-O-acyl analogues, C-28 amide betulinic acid derivatives act at the initial stage of HIV-1 entry into a human cell, thus preventing the virus fusion with the cell plasmatic membrane.¹²⁻¹⁴ The design of two parallel side chains at the C-3 and C-28 lupane skeleton atoms has resulted

in bifunctional multi-target antiretroviral agents. This type of lupane triterpenoids showed the best antiviral profile (enhanced viral suppression and control over drug-resistant HIV-1 strains) as compared with the corresponding mono-derivatives of betulin and betulinic acid.¹⁵⁻¹⁹ The Bevirimat analogues modified at the 28-COOH group acted simultaneously as both HIV-1 entry inhibitors and capsid maturation inhibitors. With the goal to prepare new multi-target antiretroviral drugs, pharmacophore hybridization of betulin and betulinic acid derivatives with AZT (3'-azido-3'-deoxythymidine), the first clinically available nucleoside HIV reverse transcriptase inhibitor, has been performed in several studies.²⁰⁻²³ In this case, the combination of two pharmacologically active molecules to hybrid compounds was performed via esterification or copper-catalyzed 1,3-dipolar cycloaddition, with betulin and betulinic acid C-3 and C-28 alkynyl esters or amides acting as the starting reactants. As a result, one or both (C-3 and C-28) pharmacophore groups considerably affecting the antiviral activity were replaced, in the desired products, by AZT residue. We have developed a new synthetic strategy towards triazole-linked AZT bioconjugates with lupane triterpenoids, using betulinic acid derivatives with a terminal acetylenic moiety at the C-2 atom of ring A. The new approach extends the synthetic opportunities for the variation of the C-3 and C-28 side chains in the triterpene moiety of the AZT-triterpenoid hybrids. An efficient method for the synthesis of C-2-propynyl 3-oxo-triterpene acid derivatives has been developed previously by our research team.²⁴ The C-2-acetylenic triterpenoid derivatives have been successfully used in the CuACC reactions with sugar azides.^{24,25} This communication reports the synthesis of a group of ten C-2 1,2,3-triazole-linked AZT conjugates with betulinic acid derivatives.

Results and Discussion

The basic substrate, C-2-propargyl-substituted betulinic acid **4**, was prepared from betulinic acid by the method developed by our research team,²⁴ with the key steps being α -alkylation of potassium enoxytriethylborate, generated from methyl betulonate **2** on treatment with $\text{KN}(\text{SiMe}_3)_2\text{-Et}_3\text{B}$ in DME, with propargyl bromide; stereoselective reduction of the 3-oxo group in triterpenoid **3** with $\text{NaBH}_4\text{-CeCl}_3$; and the subsequent demethylation of the sterically hindered 28-ester group on treatment with LiI in DMF (Scheme 1).

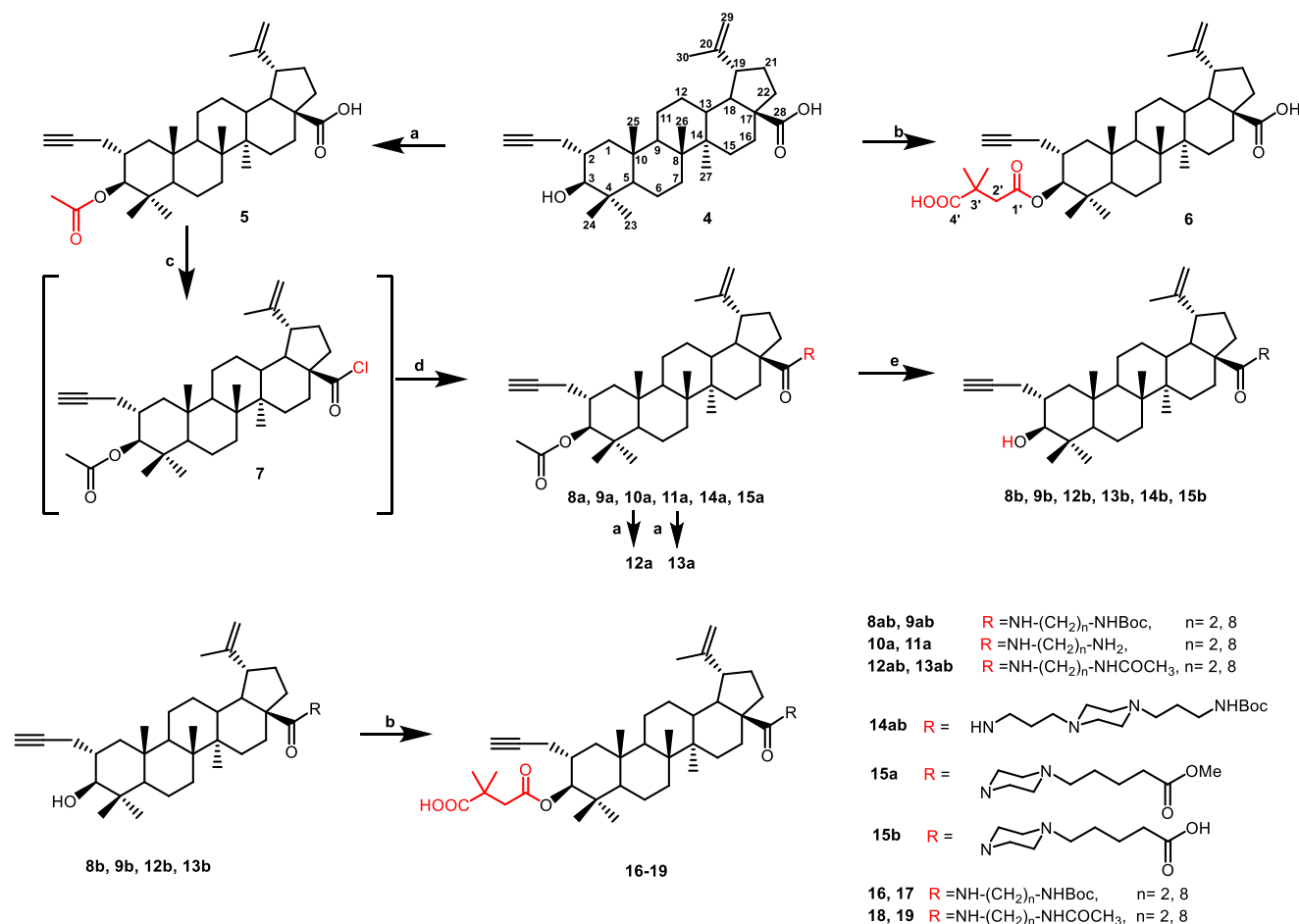


Scheme 1. Synthesis of betulinic acid C-2 propargyl derivatives.

The reaction of triterpenoid **4** with 2,2-dimethylsuccinic anhydride on refluxing in pyridine in the presence of DMAP resulted in the C-2-propynyl analogue of Bevirimat **6** in 40% yield (Scheme 2).

Acetate **5** obtained upon hydroxyl group protection in triterpenoid **4** was converted to C-28 amide derivatives **8a-11a**, **14**, and **15a** via the unstable acid chloride **7**. This reaction was carried out for *N*-Boc-protected or free alkylenediamines with short ($n=2$) or long ($n=8$) aminoalkane chains. Amide derivatives **10a** and **11a** with a primary terminal amino group were converted to *N*-acetyldiaminoalkane derivatives **12a** and **13a** by treatment with acetic anhydride in the presence of pyridine and DMAP. It is known from the literature that piperazine moiety is present in many biologically active compounds and pharmaceuticals and is widely used as a promising pharmacophore in the design and synthesis of new potential drugs.^{26,27} The incorporation

of the piperazine moiety into the C-28 side chain of Bevirimat analogues afforded compounds with high activity against HIV replication affecting Bevirimat-resistant viral strains.^{12,19} We synthesized C-28-piperazine-



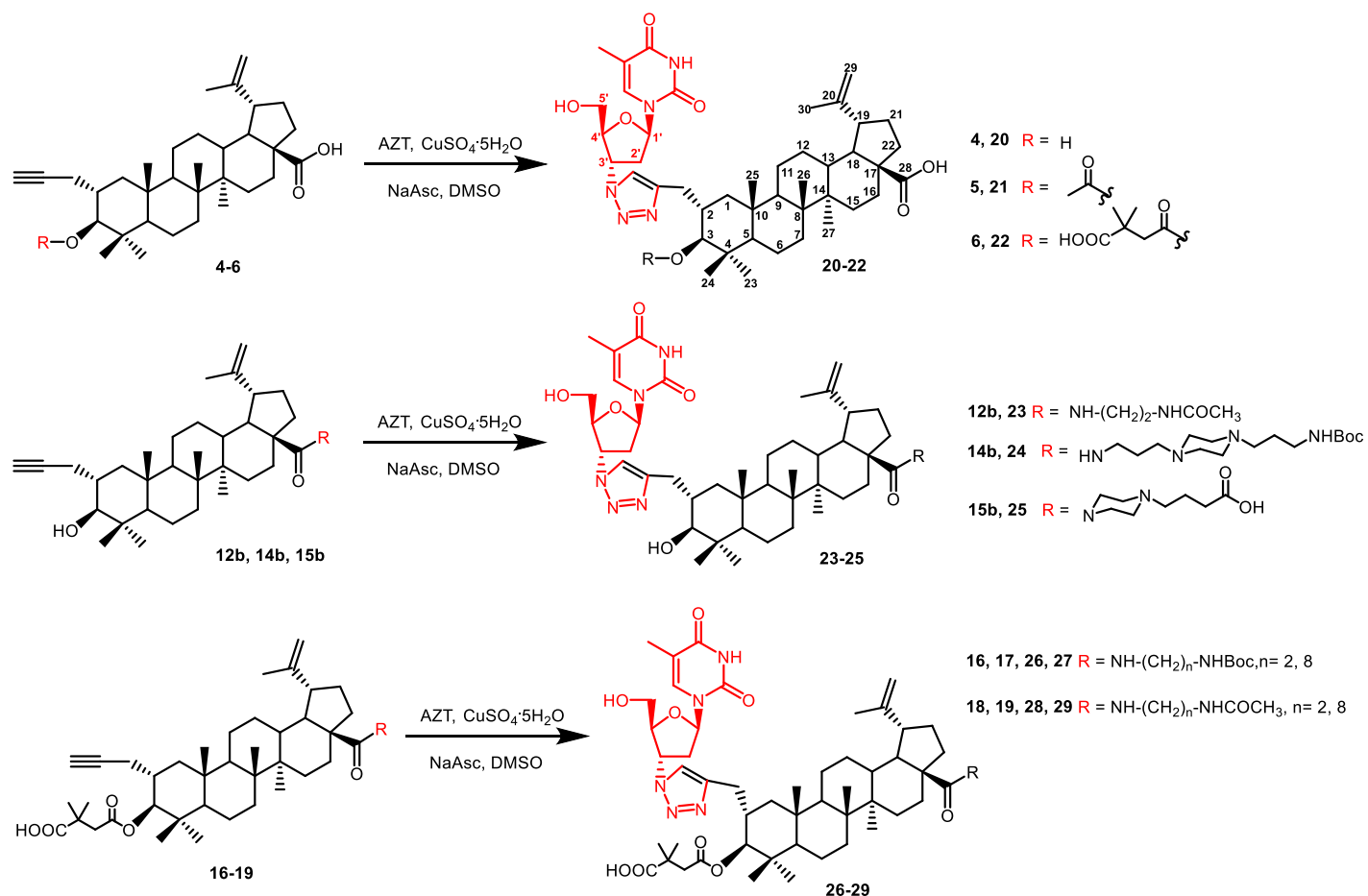
Reagents and conditions: a, Ac₂O, Py, DMAP, rt; b, 2,2-Dimethylsuccinic anhydride, Py, DMAP, reflux, Ar; c, (COCl)₂, CH₂Cl₂, 0°C-20°C; d, NH₂-(CH₂)_nNH₂ or BocNH-(CH₂)_nNH₂, n=2,8 or methyl 5-piperazine pentanoate or N-Boc-bisaminopropylpiperazine, Et₃N, CH₂Cl₂, rt; e, 4N NaOH, MeOH, THF, rt

Scheme 2. Synthesis of mono- and bi-functional betulinic acid derivatives with C-2 propargyl substituent.

linked lupane triterpenoids **14a**, **15a** by the reaction of chloride **7** with methyl 5-piperazinepentanoate and with N-Boc-protected 1,4-bis-(3-aminopropyl)piperazine. The piperazinepentanoic acid derivative was pre-synthesized by a reported procedure.¹² Hydrolysis of the acetate group in compounds **8a**, **9a**, and **12a-15a** with 4N NaOH in a MeOH-THF mixture furnished triterpenoids **8b**, **9b**, and **12b-15b**. Some of these compounds (**12b**, **14b** and **15b**) were involved in the CuACC reactions with AZT to afford the corresponding hybrid molecules **23-25** (Schemes 2 and 3). Triterpenoids **8b**, **9b**, **12b** and **13b** were converted into C-3 dimethylsuccinyl derivatives **16-19** in 42%-90% yields under the reaction conditions used for acylation of compound **4** into ester **6**. The reaction of C-2 propargyl betulinic acid derivatives **4** and **5** with AZT induced by CuI in Bu^tOH at 70 °C gave target compounds **20** and **21** in 70% and 55% yields, after column chromatography on SiO₂ (Scheme 3).

However, under these conditions, acetylenic derivatives **6** and **16-19** react with AZT over long periods of time, with the yields of final products being not higher than 32%. The reaction conditions and the yields of conjugates were substantially affected by replacement of the Bu^tOH solvent by DMSO. With the use of CuSO₄·5H₂O and sodium ascorbate in DMSO, substrates **6**, **12b**, **14b**, **15b**, and **16-19** react with AZT at room

temperature within 2-3 hours. The reactions are selective and the yields of triazole-linked conjugates **20-29**



Scheme 3. Synthesis of AZT-triterpenoid conjugates with side chains at C-3 or/and C-28 positions.

are 60%-73% after chromatography on SiO₂ for removing the solvent and copper and reactant traces. Our attempts to carry out the CuACC reactions for triterpenoids **10a** and **11a** with primary amino groups in the side chain were unsuccessful. The bioconjugates were formed in low yields, and isolation by column chromatography on SiO₂ was hampered by low chromatographic mobility of the polar compounds. Meanwhile, it follows from previous studies that the use of protected amines (N-Boc amino acids¹⁸ or N-acetylaminos¹⁶) in the design of bifunctional betulinic acid analogues does not have an adverse effect on the antiviral activities of the potential anti-HIV agents in comparison with the prototypes.

The structures of the obtained compounds were confirmed by 1D (¹H, ¹³C, APT) and 2D homo- (COSY, NOESY) and heteronuclear (HSQC, HMBC) experiments. It is known that esterification of betulinic acid with 2,2-dimethylsuccinic anhydride on refluxing in pyridine in the presence of DMAP affords a mixture of 3-O-(3,3'-dimethylsuccinyl)- and 3-O-(2,2'-dimethylsuccinyl)betulinic acids, with the 3,3'-dimethylsuccinyl isomer being formed predominantly (95:5 ratio of the regioisomers) [5, 6]. After purification by chromatography on SiO₂, the resulting dimethylsuccinyl derivatives **6**, **16-19** and their conjugates **22**, **26-29** were individual compounds, as shown by HPLC and NMR spectroscopy. The NMR spectra of compounds **6** and **16-19** showed similar chemical shifts; therefore, we discuss the spectral data for triterpenoid **6** as a typical representative of this series. The structure of the succinyl group of compound **6** was confirmed by the 2D (¹H-¹³C) HMBC spectra, which showed a correlation of the methylene proton signals at δ 2.67 and 2.73 ppm (two AB type doublets, J 15.0 Hz) with the C-1' carbon signal of the carbonyl group at δ 171.01 ppm. The proton signals for the geminal

methyl groups Me-3' were correlated with the signal at 183.39 ppm, which belonged to the C-4' atom of the carboxyl group. The assignment of the signal with δ 171.01 ppm to the C-1' the carbonyl carbon followed from correlation with the H-3 proton signal. The chemical shifts for the atoms of the terpene skeleton were also assigned considering published data.²⁴ The formation of triazole rings is evidenced by the characteristic $\underline{\text{CH}}=\text{C}-\text{N}$ signals at 7.45-7.90 ppm in the ^1H NMR spectra of compounds **20-29**. In the ^{13}C NMR spectra, the signals for the [1,5]-triazole carbon atoms $\underline{\text{CH}}=\text{C}-\text{N}$ and $\text{CH}=\underline{\text{C}}-\text{N}$ occur at 121.85-123.88 and 145.67-148.10 ppm, respectively.

Conclusions

Despite the advances made in antiretroviral therapy, there is a vital need for new anti-HIV agents. The challenges of control of the HIV infection are caused by fast appearance of drug-resistant HIV strains and high toxicity of pharmaceutical drugs, which generate numerous adverse effects on long-term administration. Currently, the development of new anti-HIV agents is focused on compounds that could act on two or more molecular targets and be active at different phases of the HIV replication cycle. New opportunities and prospects for the design of multi-target antiviral drugs were offered by the discovery of the Cu(I)-catalyzed azide-alkyne cycloaddition strategy (CuAAC reactions).²⁹ The CuAAC reactions or click-reactions are extensively employed in conjugate synthesis and pharmacophore hybridization of various organic compounds, owing to their versatility, high chemoselectivity, and mild conditions. In this study, we have prepared new trisubstituted betulinic acid derivatives containing 3-O-acyl and 28-amide side chains and a propynyl group at the C-2 position of ring A of the lupane core, including compounds **6**, **15b** and **19**, acetylenic analogues of known triterpenes,^{8,12,16} which are effective against HIV-1. Novel C-2 acetylenic triterpenoids were successfully conjugated with AZT using a click chemistry-based approach.

Experimental Section

General. IR spectra were obtained with use of a Bruker Vertex 70v spectrometer (thin films or solutions in CHCl_3). ^1H and ^{13}C NMR spectra were recorded on a Bruker AVANCE-500 instrument (500.13 (^1H) and 125.78 MHz (^{13}C)) or on Bruker AVANCE-400 (400.13 (^1H) and 100.62 MHz (^{13}C)) in CDCl_3 or in MeOD with Me_4Si as the internal standard. Mass spectra of new compounds were recorded on a Bruker-Autoflex III spectrometer (MALDI TOF, positive ion mode, sinapic acid as the matrices). Optical rotation was determined on a Perkin-Elmer-141 polarimeter. Specific rotation $[\alpha]_D$ is expressed in (deg mL)/(g dm); the concentration of the solution c is expressed in g/100 mL. Elemental analysis was carried out on a Carlo Erba 1106 analyzer. TLC was carried out on Sorbfil plates (Sorbpolimer, Krasnodar, Russia) in hexane-EtOAc and chloroform-methanol, spots were visualized with anisaldehyde. Silica gel L (KSKG grade, 50–160 μm) was employed for column chromatography. The starting compounds betulin, betulinic acid and reagents: BEt_3 (95%), $\text{KN}(\text{SiMe}_3)_2$ (1 M solution in THF), propargyl bromide, Lil, CuI, Bu^tOH , NaBH_4 , $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$, Et_3N , DMF, DME (dimethoxyethane), acetic anhydride, oxalylchloride, DMAP, 2,2-dimethylsuccinic anhydride, di-tert-butyl dicarbonate, dimethyl sulfoxide, L-ascorbic acid sodium salt, piperazine, methyl bromovalerate (97%), 3'-azido-3'-deoxythymidine, ethylenediamine, 1,8-diaminooctane 98%, 1,4-bis-(3-aminopropyl)piperazine $\geq 99\%$ (Acros Organics). The intermediates **1-5** were synthesized as we described in earlier paper.²⁴ Mono-Boc-protected bis-

aminopropylpiperazine, Boc-diaminoethane and Boc-diaminooctane and methyl 5-piperazine pentanoate were prepared according to known procedures.^{12,29}

General procedure for the preparation of conjugates 8a-11a, 14a and 15a. Oxalyl chloride (0.3 mL, 3 mmol) was added with stirring to a solution of triterpenoid 5 (1 mmol) in dry CH₂Cl₂ (5 mL) precooled to 0°C, and stirring of the reaction mixture was continued at room temperature for 2 h. Then the solvent and excess oxalyl chloride were removed under vacuum. The residue was treated with ethylenediamine (0.4 mL, 6 mmol), 1,8-diaminooctane (0.87 g, 6 mmol), *N*-Boc-bisaminopropylpiperazine (0.48 g, 1.6 mmol), *N*-Boc-ethylenediamine (0.26 g, 1.6 mmol), *N*-Boc-1,8-octanediamine (0.39 g, 1.6 mmol), or methyl 5-piperazinepentanoate (0.32 g, 1.6 mmol) and with triethylamine (0.2 mL, 1.6 mmol) in dry CH₂Cl₂ (15 mL), and the mixture was stirred at room temperature for 16–20 h until no starting material was observed by TLC. The solution was then diluted with CH₂Cl₂ (20 mL) and washed three times with brine and distilled water. The organic layer was dried over anhydrous MgSO₄ and concentrated under reduced pressure. The crude products were then chromatographed on silica gel [CHCl₃–MeOH (100:1→5:1)] to obtain pure compounds **8a-11a**, **14a** and **15a**.

***N*-[3β-Acetoxy-2α-propargyl-lup-20(29)-en-28-oyl]-*N'*-(tert-butoxycarbonyl)-2-ethylamine (8a).** White powder (0.60 g, 89%), mp 126–128 °C. [α]_D¹⁹ -24° (c 0.47, CHCl₃). IR (solution in CHCl₃, cm⁻¹): 3369, 3312 (NH), 1735, 1717, 1639 (C=O). ¹H NMR (500 MHz, CDCl₃): δ _H 6.35, 5.05 (both br s, 2H, NH), 4.73, 4.59 (both br s, 2H, H-29), 4.47 (d, 1H, *J* 10.0 Hz, H-3), 3.35–3.23 (m, 4H, –CH₂NH–, –CH₂NH–Boc), 3.16–3.10 (m, 1H, H-19), 2.49–0.80 (m, 26H, CH, CH₂ in pentacyclic skeleton and propargyl), 2.09 (s, 3H, COCH₃), 1.68 (s, 3H, H-30), 1.44 (s, 9H, C(CH₃)₃ in Boc), 0.96, 0.95, 0.89, 0.83, 0.81 (all s, 3H each, H-23–H-27). ¹³C NMR (125 MHz, CDCl₃): δ _C 177.2 (C-28), 171.1 (COCH₃), 156.9 (CONH–Boc), 150.9 (C-20), 109.4 (C-29), 83.1 (C-3), 82.6 (C in propargyl), 79.6 (C in Boc), 69.6 (CH in propargyl), 55.6 (C-17), 55.4 (C-5), 50.6 (C-9), 50.1 (C-18), 46.8 (C-19), 45.0 (C-1), 42.5 (C-14), 40.8 (CH₂ in ethylamine, C-8), 40.4 (CH₂ in ethylamine), 38.9 (C-4), 38.4 (C-13), 37.7 (C-22), 37.3 (C-10), 34.3 (C-7), 33.6 (C-16), 33.5 (C-2), 30.8 (C-21), 29.4 (C-15), 28.4 (CH₃ in Boc), 28.1 (C-24), 25.6 (C-12), 22.3 (CH₂ in propargyl), 21.0 (COCH₃, C-11), 19.4 (C-30), 18.3 (C-6), 17.1 (C-26), 16.2 (C-25, C-23), 14.6 (C-27). Anal. Calcd for C₄₂H₆₆N₂O₅: C, 74.29; H, 9.80. Found: C, 73.87, H, 9.76%. MS: *m/z* [M+Na]⁺, found 701.42 [C₄₂H₆₆N₂O₅]⁺ requires 701.49.

***N*-[3β-Acetoxy-2α-propargyl-lup-20(29)-en-28-oyl]-*N'*-(tert-butoxycarbonyl)-8-octylamine (9a).** White powder (0.61 g, 80%), mp 96–98 °C. [α]_D²² -23.3° (c 0.33, CHCl₃). IR (solution in CHCl₃, cm⁻¹): 3368, 3312 (NH), 1719, 1698, 1638 (C=O). ¹H NMR (500 MHz, CDCl₃): δ _H 5.67–5.65 (m, 1H, NH) 4.73 (br s, 1H, H-29), 4.57–5.55 (m, 2H, H-29, NH) 4.46 (d, 1H, *J* 10.0 Hz, H-3), 3.29–3.26 (m, 1H, H-19), 3.16–3.09 (m, 4H, –CH₂NH–, –CH₂NH–Boc), 2.50–0.80 (m, 26H, CH, CH₂ in pentacyclic skeleton, propargyl and 4H in octylamine) 2.08 (s, 3H, COCH₃), 1.67 (s, 3H, H-30), 1.43 (br s, 9H, CH₃ in Boc), 1.33–1.29 (m, 8H, CH₂ in octylamine), 0.96, 0.94, 0.88, 0.82, 0.80 (all s, 3H each, H-23–H-27). ¹³C NMR (125 MHz, CDCl₃): δ _C 176.0 (C-28), 171.1 (COCH₃), 156.0 (CONH–Boc), 151.0 (C-20), 109.4 (C-29), 83.1 (C-3), 82.6 (C in propargyl), 79.0 (C in Boc), 69.6 (CH in propargyl), 55.5 (C-17), 55.4 (C-5), 50.6 (C-9), 50.2 (C-18), 46.8 (C-19), 45.0 (C-1), 42.5 (C-14), 40.8 (C-8), 40.6 (CH₂ in octylamine), 39.1 (C-4), 38.9 (CH₂ in octylamine), 38.5 (C-13), 37.7 (C-22), 37.3 (C-10), 34.3 (C-7), 33.8 (C-2), 33.5 (C-16), 30.8 (C-21), 30.0 (CH₂ in octylamine), 29.8 (C-15), 29.4 (CH₂ in octylamine), 29.2 (CH₂ in octylamine), 28.4 (CH₃ in Boc), 28.1 (C-24), 26.9, 26.7 (CH₂ in octylamine), 25.6 (C-12), 22.3 (CH₂ in propargyl), 21.0 (COCH₃, C-11), 19.4 (C-30), 18.3 (C-6), 17.1 (C-26), 17.0 (C-23), 16.2 (C-25), 14.6 (C-27). Anal. Calcd for C₄₈H₇₈N₂O₅: C, 75.54; H, 10.30. Found: C, 75.48, H, 9.97%. MS: *m/z* [M+Na]⁺, found 785.36 [C₄₈H₇₈N₂O₅]⁺ requires 785.58.

2-Aminoethyl-3β-acetoxy-2α-propargyl-lup-20(29)-en-28-oate (10a). White powder (0.43 g, 74%), mp 152–154 °C. [α]_D¹⁸ -23° (c 0.53, CHCl₃). IR (solution in CHCl₃, cm⁻¹): 3309 (NH), 1733, 1638 (C=O). ¹H NMR (500 MHz, CDCl₃): δ _H 6.17 (t, 1H, *J* 5 Hz, NH), 4.73, 4.58 (both br s, 2H, H-29), 4.46 (d, 1H, *J* 10.0 Hz, H-3), 3.37–3.31, 3.27–3.22 (1H each, m, –CH₂NH–), 3.15–3.10 (m, 1H, H-19), 2.82 (t, 2H, *J* 10.0 Hz, –CH₂NH₂), 2.49–0.80 (m, 26H, CH,

CH₂ in pentacyclic skeleton and propargyl), 2.08 (s, 3H, COCH₃), 1.67 (s, 3H, H-30), 0.96, 0.94, 0.88, 0.81, 0.80 (all s, 3H each, H-23–H-27). ¹³C NMR (125 MHz, CDCl₃): δ_c 176.6 (C-28), 171.1 (COCH₃), 150.9 (C-20), 109.5 (C-29), 83.1 (C-3), 82.6 (C in propargyl), 69.7 (CH in propargyl), 55.7 (C-17), 55.4 (C-5), 50.6 (C-9), 50.1 (C-18), 46.8 (C-19), 45.0 (C-1), 42.5 (C-14), 41.7, 41.6 (CH₂ in ethylamine), 40.8 (C-4), 38.9 (C-8), 38.5 (C-13), 37.7 (C-22), 37.3 (C-10), 34.3 (C-7), 33.7 (C-2), 33.5 (C-16), 30.8 (C-21), 29.4 (C-15), 28.1 (C-24), 25.6 (C-12), 22.3 (CH₂ in propargyl), 21.03 (COCH₃, C-11), 19.4 (C-30), 18.3 (C-6), 17.1 (C-26), 16.3 (C-23), 16.2 (C-25), 14.6 (C-27). Anal. Calcd for C₃₇H₅₈N₂O₃: C, 76.77; H, 10.10. Found: C, 76.87, H, 9.96%. MS: *m/z* [M+Na]⁺, found 601.73 [C₃₇H₅₈N₂O₃]⁺ requires 601.43.

8-Amino-octyl-3β-acetoxy-2α-propargyl-lup-20(29)-en-28-oate (11a). White powder (0.53 g, 80%), mp 108–110 °C. [α]_D²² -21° (c 0.53, CHCl₃). IR (solution in CHCl₃, cm⁻¹): 3311 (NH), 1733, 1636 (C=O). ¹H NMR (500 MHz, CDCl₃): δ_H 5.63 (t, 1H, *J* 5 Hz, NH), 4.73, 4.58 (both br s, 2H, H-29), 4.47 (d, 1H, *J* 10.0 Hz, H-3), 3.31–3.26 (m, 1H, –CH₂NH–), 3.18–3.13 (m, 2H, –CH₂NH–, H-19), 2.68 (t, 2H, *J* 10.0 Hz, –CH₂NH₂), 2.50–0.80 (m, 26H, CH, CH₂ in pentacyclic skeleton and propargyl), 2.09 (s, 3H, COCH₃), 1.67 (s, 3H, H-30), 1.32–1.26 (m, 12H, CH₂ in octylamine), 0.95, 0.92, 0.86, 0.81, 0.78 (all s, 3H each, H-23–H-27). ¹³C NMR (125 MHz, CDCl₃): δ_c 175.9 (C-28), 171.1 (COCH₃), 151.0 (C-20), 109.4 (C-29), 83.1 (C-3), 82.6 (C in propargyl), 69.6 (CH in propargyl), 55.5 (C-17), 55.4 (C-5), 50.6 (C-9), 50.2 (C-18), 46.8 (C-19), 45.0 (C-1), 42.5 (C-14), 42.2 (CH₂ in octylamine), 40.8 (C-8), 39.2 (C-4), 38.9 (CH₂ in octylamine), 38.5 (C-13), 33.8 (CH₂ in octylamine), 37.7 (C-22), 37.3 (C-10), 34.3 (C-7), 33.9 (C-2), 33.5 (C-16), 30.8 (C-21), 29.9 (C-15), 29.4, 29.3 (CH₂ in octylamine), 28.1 (C-24), 27.0, 26.8 (CH₂ in octylamine), 25.6 (C-12), 22.3 (CH₂ in propargyl), 21.0 (COCH₃, C-11), 19.4 (C-30), 18.4 (C-6), 17.1 (C-26), 17.0 (C-23), 16.2 (C-25), 14.6 (C-27). Anal. Calcd for C₄₃H₇₀N₂O₃: C, 77.89; H, 10.64. Found: C, 78.04, H, 10.57%. MS: *m/z* [M+H]⁺, found 663.28 [C₄₃H₇₀N₂O₃]⁺ requires 663.55.

N-[3β-Acetoxy-2α-propargyl-lup-20(29)-en-28-oyl]-N'-(tert-butoxycarbonyl)-{3-[4-(3-aminopropyl)piperazinyl]propylamine (14a). White powder (0.68 g, 83%). mp 110–112 °C. [α]_D²² -21° (c 0.50, CHCl₃). IR (solution in CHCl₃, cm⁻¹): 3367, 3310 (NH), 1733, 1699, 1639 (C=O). ¹H NMR (500 MHz, CDCl₃): δ_H 6.94 (t, 1H, *J* 5 Hz, NH), 5.42 (br s, 1H, NH), 4.70, 4.55 (both br s, 2H, H-29), 4.44 (d, 1H, *J* 10.0 Hz, H-3), 3.32–3.26, 3.15–3.14 (both m, 5H, –CH₂NH–, –CH₂NH–Boc, H-19), 2.51–2.38 (m, 12H, CH₂ in piperazine and propylamine), 2.19–0.78 (m, 26H, CH, CH₂ in pentacyclic skeleton, propargyl and 4H in propylamine), 2.06 (s, 3H, COCH₃), 1.65 (s, 3H, H-30), 1.41 (br s, 9H, CH₃ in Boc), 0.94, 0.92, 0.86, 0.78, 0.75 (all s, 3H each, H-23–H-27). ¹³C NMR (125 MHz, CDCl₃): δ_c 176.2 (C-28), 171.1 (COCH₃), 156.0 (CONH–Boc), 151.0 (C-20), 109.3 (C-29), 83.1 (C-3), 82.5 (C in propargyl), 78.5 (C in Boc), 69.7 (CH in propargyl), 58.0, 56.8 (CH₂ in propylamine), 55.4 (C-17), 55.3 (C-5), 53.5, 53.1 (CH₂ in piperazine), 50.6 (C-9), 50.2 (C-18), 46.7 (C-19), 44.9 (C-1), 42.4 (C-14), 40.8 (C-8), 39.9 (CH₂ in propylamine), 39.5 (C-4), 38.9 (CH₂ in propylamine), 38.5 (C-13), 37.5 (C-22), 37.2 (C-10), 34.3 (C-7), 33.8 (C-2), 33.5 (C-16), 30.8 (C-21), 29.4 (C-15), 28.4 (CH₃ in Boc), 28.1 (C-24), 26.4 (CH₂ in propylamine), 25.5 (C-12), 25.1 (CH₂ in propylamine), 22.3 (CH₂ in propargyl), 21.0 (COCH₃, C-11), 19.4 (C-30), 18.3 (C-6), 17.1 (C-26), 17.0 (C-23), 16.2 (C-25), 14.5 (C-27). Anal. Calcd for C₅₀H₈₂N₄O₅: C, 73.31; H, 10.09. Found: C, 73.24, H, 9.87%. MS: *m/z* [M+H]⁺, found 819.52 [C₅₀H₈₂N₄O₅]⁺ requires 819.64.

Methyl N-[3β-acetoxy-2α-propargyl-lup-20(29)-en-28-oyl]-5-piperazinylpentanoate (15a). White powder (0.56 g, 78%), mp 116–118 °C. [α]_D¹⁸ -25.45° (c 0.64, CHCl₃). IR (solution in CHCl₃, cm⁻¹): 1736, 1632 (C=O). ¹H NMR (500 MHz, CDCl₃): δ_H 4.70, 4.54 (both br s, 2H, H-29), 4.45 (d, 1H, *J* 10.0 Hz, H-3), 3.65 (s, 3H, COOCH₃), 2.99–2.94 (m, 1H, H-19), 2.89–2.85 (m, 1H, H-13), 2.44–2.30 (m, 8H, piperazine) 2.19–0.78 (m, 25H, CH, CH₂ in pentacyclic skeleton, propargyl, 8H in pentanoate), 2.06 (s, 3H, COCH₃), 1.65 (s, 3H, H-30), 0.93, 0.92, 0.87, 0.80, 0.78 (all s, 3H each, H-23–H-27). ¹³C NMR (125 MHz, CDCl₃): δ_c 173.9 (COOCH₃), 173.4 (C-28), 171.0 (COCH₃), 151.3 (C-20), 109.2 (C-29), 86.8 (C in propargyl), 83.1 (C-3), 73.6 (CH in propargyl), 57.9, 55.4 (CH₂ in pentanoate), 54.5 (C-17), 53.4 (CH₂ in piperazine), 52.6 (C-18), 51.5 (COOCH₃), 50.8 (C-9), 45.7 (C-19), 45.0 (C-

1), 41.9 (C-14), 40.7 (C-4), 38.9 (C-8), 38.4 (C-2), 37.3 (C-10), 36.8 (C-13), 35.9 (C-22), 34.3 (C-7), 33.8 (CH₂ in piperazine), 32.5 (C-16), 31.2 (C-21), 29.7 (C-15), 28.1 (C-24), 26.1 (CH₂ in pentanoate), 25.3 (C-12), 22.3 (CH₂ in propargyl), 22.8 (CH₂ in pentanoate), 21.2 (C-11), 21.0 (COCH₃), 19.6 (C-30), 18.3 (C-6), 17.1 (C-26), 17.0 (C-23), 16.1 (C-25), 14.6 (C-27). Anal. Calcd for C₄₅H₇₀N₂O₅: C, 75.17; H, 9.81. Found: C, 75.21, H, 9.74%. MS: *m/z* [M-H]⁺, found 717.36 [C₄₅H₇₀N₂O₅]⁺ requires 717.52.

General procedure for the preparation of acetamides 12a and 13a. To a solution of the above amine intermediate **10a** or **11a** (1 mmol) in anhydrous pyridine (4 mL) were added acetic anhydride (0.2 mL, 2 mmol), DMAP (0.12 g, 1 mmol) and stirring of the reaction mixture was continued at room temperature for 2 h (monitoring by TLC). Then the mixture was diluted with H₂O (10 mL) and extracted with EtOAc (4×10 mL). The combined extracts were washed with brine, dried over anhydrous MgSO₄, and concentrated under reduced pressure. The crude products were then chromatographed on silica gel [CHCl₃-MeOH (100:1)] to obtain pure compounds **10a** and **13a**.

{[N-(3β-Acetoxy-2α-propargyl-lup-20(29)-en-28-oyl)-2-aminoethyl]carbamoyl}methane (12a). White powder (0.56 g, 90%), mp 148-150 °C. [α]_D¹⁸ -24° (c 0.44, CHCl₃). IR (solution in CHCl₃, cm⁻¹): 3310 (NH), 1734, 1718, 1637 (C=O). ¹H NMR (500 MHz, CDCl₃): δ_H 6.74, 6.49 (both br s, 2H, NH), 4.72, 4.59 (both br s, 2H, H-29), 4.46 (d, 1H, *J* 10.0 Hz, H-3), 3.39-3.32 (m, 4H, -CH₂NH-, CH₂NHCOCH₃), 3.12-3.07 (m, 1H, H-19), 2.47-0.80 (m, 26H, CH, CH₂ in pentacyclic skeleton and propargyl), 2.09 (s, 3H, COCH₃), 1.99 (s, 3H, -NHCOCH₃), 1.68 (s, 3H, H-30), 0.96, 0.93, 0.88, 0.82, 0.80 (all s, 3H each, H-23-H-27). ¹³C NMR (125 MHz, CDCl₃): δ_C 178.1 (C-28), 171.3 (NHCOCH₃), 171.1 (COCH₃), 150.7 (C-20), 109.6 (C-29), 83.0 (C-3), 82.5 (C in propargyl), 69.7 (CH in propargyl), 55.6 (C-17), 55.3 (C-5), 50.5 (C-9), 50.0 (C-18), 46.8 (C-19), 44.9 (C-1), 42.5 (C-14), 40.8 (CH₂ in ethylamine, C-4), 39.7 (CH₂ in ethylamine), 38.9 (C-8), 38.4 (C-13), 37.7 (C-22), 37.2 (C-10), 34.2 (C-7), 33.5 (C-2), 33.5 (C-16), 30.8 (C-21), 29.4 (C-15), 28.1 (C-24), 25.5 (C-12), 23.2 (NHCOCH₃), 22.3 (CH₂ in propargyl), 21.0 (COCH₃, C-11), 19.3 (C-30), 18.3 (C-6), 17.1 (C-26), 17.0 (C-23), 16.1 (C-25), 14.6 (C-27). Anal. Calcd for C₃₉H₆₀N₂O₄: C, 75.44; H, 9.74. Found: C, 74.38, H, 9.69%. MS: *m/z* [M+Na]⁺, found 643.37 [C₃₉H₆₀N₂O₄]⁺ requires 643.45.

{[N-(3β-Acetoxy-2α-propargyl-lup-20(29)-en-28-oyl)-8-aminoethyl]carbamoyl}methane (13a). White powder (0.56 g, 80%), mp 106-108 °C. [α]_D²² -23° (c 0.48, CHCl₃). IR (solution in CHCl₃, cm⁻¹): 3311 (NH), 1733 (C=O). ¹H NMR (500 MHz, CDCl₃): δ_H 5.77-5.71 (m, 2H, NH), 4.72, 4.57 (both br s, 2H, H-29), 4.46 (d, 1H, *J* 10.0 Hz, H-3), 3.22-3.14 (m, 5H, -CH₂NH-, CH₂NHCOCH₃, H-19), 2.47-0.80 (m, 26H, CH, CH₂ in pentacyclic skeleton and propargyl), 2.08 (s, 3H, COCH₃), 1.97 (s, 3H, -NHCOCH₃), 1.67 (s, 3H, H-30), 1.37-1.30 (m, 12H, CH₂ in octylamine), 0.96, 0.94, 0.88, 0.82, 0.80 (all s, 3H each, H-23-H-27). ¹³C NMR (125 MHz, CDCl₃): δ_C 176.0 (C-28), 171.1 (COCH₃), 170.0 (NHCOCH₃), 151.0 (C-20), 109.4 (C-29), 83.1 (C-3), 82.6 (C in propargyl), 69.7 (CH in propargyl), 55.5 (C-17), 55.4 (C-5), 50.6 (C-9), 50.1 (C-18), 46.8 (C-19), 45.0 (C-1), 42.5 (C-14), 40.8 (C-8), 39.6 (CH₂ in octylamine), 39.1 (C-4), 38.9 (CH₂ in octylamine), 38.5 (C-13), 37.7 (C-22), 37.3 (C-10), 34.3 (C-7), 33.8 (C-2), 33.5 (C-16), 30.8 (C-21), 29.8 (CH₂ in octylamine), 29.6 (C-15), 29.4 (CH₂ in octylamine), 29.1 (CH₂ in octylamine), 28.1 (C-24), 26.8 (CH₂ in octylamine), 25.6 (C-12), 23.3 (NHCOCH₃), 22.3 (CH₂ in propargyl), 21.0 (COCH₃, C-11), 19.4 (C-30), 18.3 (C-6), 17.0 (C-23, C-26), 16.2 (C-25), 14.6 (C-27). Anal. Calcd for C₄₅H₇₂N₂O₄: C, 76.66; H, 10.29. Found: C, 76.71, H, 10.32%. MS: *m/z* [M+H]⁺, found 705.26 [C₄₅H₇₂N₂O₄]⁺ requires 705.56.

General procedure for the preparation of compounds 8b, 9b, 12b-15b. To a solution of the appropriate ester intermediate **8a**, **9a**, **12a-15a** (1 mmol) in MeOH (8 mL) and THF (4 mL) was added 4 N NaOH (4 mL). The reaction mixture was stirred at room temperature for 15-20 h (monitoring by TLC) and then neutralized with 20% HCl. The solution was dried under vacuum and reconstituted with CH₂Cl₂. The organic layer was washed with brine and dried over anhydrous MgSO₄ and concentrated under reduced pressure to obtain pure compounds **8b**, **9b**, **12b-15b**.

***N*-[3 β -Hydroxy-2 α -propargyl-lup-20(29)-en-28-oyl]-*N'*-(tert-butoxycarbonyl)-2-ethylamine (8b).** White powder (0.58 g, 91%), mp 138-140 °C. $[\alpha]_D^{23}$ -14.6° (c 0.59, CH₂Cl₂). IR (solution in CH₂Cl₂, cm⁻¹): 3366, 3311 (NH), 1697, 1639 (C=O). ¹H NMR (500 MHz, CDCl₃): δ_H 6.49, 5.22 (both br s, 2H, NH), 4.69, 4.55 (both br s, 2H, H-29), 3.31-3.21 (m, 4H, -CH₂NH-, -CH₂NH-Boc), 3.11-3.06 (m, 1H, H-19), 2.95 (d, 1H, *J* 10.0 Hz, H-3), 2.49-0.80 (m, 26H, CH, CH₂ in pentacyclic skeleton and propargyl), 1.64 (s, 3H, H-30), 1.40 (s, 9H, CH₃ in Boc), 0.95, 0.94, 0.91, 0.83, 0.75 (all s, 3H each, H-23-H-27). ¹³C NMR (125 MHz, CDCl₃): δ_C 177.3 (C-28), 157.0 (CONH-Boc), 150.9 (C-20), 109.4 (C-29), 83.1 (C in propargyl), 81.3 (C-3), 79.5 (C in Boc), 69.9 (CH in propargyl), 55.6 (C-17), 55.5 (C-5), 50.6 (C-9), 50.1 (C-18), 46.7 (C-19), 44.8 (C-1), 42.5 (C-14), 40.7 (CH₂ in ethylamine, C-8), 40.3 (CH₂ in ethylamine), 39.1 (C-4), 38.4 (C-13), 37.7 (C-22), 37.3 (C-10), 34.8 (C-7), 34.3 (C-16), 33.5 (C-2), 30.8 (C-21), 29.4 (C-15), 28.4 (CH₃ in Boc, C-24), 25.6 (C-12), 22.4 (CH₂ in propargyl), 21.0 (C-11), 19.4 (C-30), 18.5 (C-6), 17.0 (C-26), 16.3 (C-25), 16.2 (C-23), 14.7 (C-27). Anal. Calcd for C₄₀H₆₄N₂O₄: C, 75.43; H, 10.13. Found: C, 75.37, H, 10.01%. MS: *m/z* [M+Na]⁺, found 659.45 [C₄₀H₆₄N₂O₄]⁺ requires 659.48.

***N*-[3 β -Hydroxy-2 α -propargyl-lup-20(29)-en-28-oyl]-*N'*-(tert-butoxycarbonyl)-8-octylamine (9b).** White powder (0.58 g, 80%), mp 110-112 °C. $[\alpha]_D^{24}$ -6.8° (c 0.24, CHCl₃). IR (solution in CHCl₃, cm⁻¹): 3366, 3311 (NH), 1697, 1636 (C=O). ¹H NMR (500 MHz, CDCl₃): δ_H 5.64-5.66 (m, 1H, NH) 4.74 (br s, 1H, H-29), 4.59-5.54 (m, 2H, H-29, NH), 3.32-3.27 (m, 1H, H-19), 3.19-3.10 (m, 4H, -CH₂NH-, -CH₂NH-Boc), 2.99 (d, 1H, *J* 10.0 Hz, H-3), 2.50-0.79 (m, 26H, CH, CH₂ in pentacyclic skeleton, propargyl and 4H in octylamine), 1.68 (s, 3H, H-30), 1.45 (br s, 9H, CH₃ in Boc), 1.36-1.31 (m, 8H, CH₂ in octylamine), 0.99, 0.98, 0.87, 0.80, 0.79 (all s, 3H each, H-23-H-27). ¹³C NMR (125 MHz, CDCl₃): δ_C 176.0 (C-28), 156.0 (CONH-Boc), 150.0 (C-20), 109.4 (C-29), 83.0 (C in propargyl), 81.5 (C-3), 79.1 (C in Boc), 69.9 (CH in propargyl), 55.6 (C-17), 55.5 (C-5), 50.6 (C-9), 50.2 (C-18), 46.8 (C-19), 44.9 (C-1), 44.6 (C-14), 40.8 (C-8), 40.6 (CH₂ in octylamine), 39.2 (CH₂ in octylamine), 39.1 (C-4), 38.5 (C-13), 37.8 (C-22), 37.4 (C-10), 34.8 (C-7), 34.4 (C-2), 33.9 (C-16), 30.9 (C-21), 30.0 (CH₂ in octylamine), 29.8 (C-15), 29.4 (CH₂ in octylamine), 29.2 (CH₂ in octylamine), 28.4 (CH₃ in Boc), 28.3 (C-24), 26.9 (CH₂ in octylamine), 26.7 (CH₂ in octylamine), 25.6 (C-12), 22.4 (CH₂ in propargyl), 21.0 (C-11), 19.5 (C-30), 18.5 (C-6), 17.0 (C-26), 16.2 (C-23, C-25), 14.7 (C-27). Anal. Calcd for C₄₆H₇₆N₂O₄: C, 76.62; H, 10.62. Found: C, 76.58, H, 10.57%. MS: *m/z* [M+K]⁺, found 759.46 [C₄₆H₇₆N₂O₄]⁺ requires 759.54.

{[*N*-(3 β -Hydroxy-2 α -propargyl-lup-20(29)-en-28-oyl)-2-aminoethyl]carbamoyl}methane (12b). White powder (0.46 g, 80%), mp 136-138 °C. $[\alpha]_D^{18}$ -32° (c 0.50, CHCl₃). IR (solution in CHCl₃, cm⁻¹): 3310 (NH), 1637 (C=O). ¹H NMR (500 MHz, CDCl₃): δ_H 6.76, 6.48 (both br s, 2H, NH), 4.72, 4.59 (both br s, 2H, H-29), 3.42-3.36 (m, 4H, -CH₂NH-, CH₂NHCOCH₃), 3.12-3.07 (m, 1H, H-19), 3.00 (d, 1H, *J* 10.0 Hz, H-3), 2.46-0.73 (m, 26H, CH, CH₂ in pentacyclic skeleton and propargyl), 1.99 (s, 3H, -NHCOCH₃), 1.68 (s, 3H, H-30), 0.99, 0.98, 0.93, 0.82, 0.78 (all s, 3H each, H-23-H-27). ¹³C NMR (125 MHz, CDCl₃): δ_C 178.1 (C-28), 171.4 (NHCOCH₃), 150.8 (C-20), 109.5 (C-29), 83.0 (C in propargyl), 81.4 (C-3), 70.0 (CH in propargyl), 55.7 (C-17), 50.5 (C-5, C-9), 50.1 (C-18), 46.8 (C-19), 44.8 (C-1), 42.5 (C-14), 40.7 (C-4, CH₂ in ethylamine), 39.7 (CH₂ in ethylamine), 39.1 (C-8), 38.4 (C-13), 37.8 (C-22), 37.3 (C-10), 34.8 (C-7), 34.3 (C-2), 33.5 (C-16), 30.8 (C-21), 29.4 (C-15), 28.3 (C-24), 25.6 (C-12), 23.2 (NHCOCH₃), 22.4 (CH₂ in propargyl), 21.0 (C-11), 19.4 (C-30), 18.5 (C-6), 17.0 (C-26), 16.2 (C-23, C-25), 14.7 (C-27). Anal. Calcd for C₃₇H₅₈N₂O₃: C, 76.77; H, 10.10. Found: C, 76.82, H, 10.04%. MS: *m/z* [M+Na]⁺, found 601.36 [C₃₇H₅₈N₂O₃]⁺ requires 601.43.

{[*N*-(3 β -Hydroxy-2 α -propargyl-lup-20(29)-en-28-oyl)-8-aminoethyl]carbamoyl}methane (13b). White powder (0.59 g, 89%), mp 112-114 °C. $[\alpha]_D^{22}$ -9.7° (c 0.29, CHCl₃). IR (solution in CHCl₃, cm⁻¹): 3309 (NH), 1637 (C=O). ¹H NMR (500 MHz, CDCl₃): δ_H 5.79-5.70 (m, 2H, NH), 4.71, 4.57 (both br s, 2H, H-29), 3.25-3.13 (m, 5H, -CH₂NH-, CH₂NHCOCH₃, H-19), 2.98 (d, 1H, *J* 10.0 Hz, H-3), 2.45-0.80 (m, 26H, CH, CH₂ in pentacyclic skeleton and propargyl), 1.97 (s, 3H, -NHCOCH₃), 1.67 (s, 3H, H-30), 1.37-1.29 (m, 12H, CH₂ in octylamine), 0.98, 0.97, 0.93, 0.85, 0.77 (all s, 3H each, H-23-H-27). ¹³C NMR (125 MHz, CDCl₃): δ_C 176.0 (C-28), 170.1 (NHCOCH₃), 151.0 (C-20), 109.4 (C-29), 83.1 (C in propargyl), 81.4 (C-3), 70.0 (CH in propargyl), 55.6 (C-17), 55.5 (C-5), 50.6 (C-9),

50.1 (C-18), 46.8 (C-19), 44.8 (C-1), 42.5 (C-14), 40.8 (C-8), 39.6 (CH₂ in octylamine), 39.1 (C-4, CH₂ in octylamine), 38.5 (C-13), 37.7 (C-22), 37.3 (C-10), 34.8 (C-7), 34.4 (C-2), 33.8 (C-16), 30.8 (C-21), 29.8 (CH₂ in octylamine), 29.5 (C-15), 29.4 (CH₂ in octylamine), 29.1 (CH₂ in octylamine), 29.1 (CH₂ in octylamine), 28.32 (C-24), 26.8 (CH₂ in octylamine), 25.6 (C-12), 23.3 (NHCOCH₃), 22.4 (CH₂ in propargyl), 21.0 (C-11), 19.4 (C-30), 18.5 (C-6), 17.0 (C-26), 16.2 (C-23, C-25), 14.7 (C-27). Anal. Calcd for C₄₃H₇₀N₂O₄: C, 77.89; H, 10.64. Found: C, 77.92, H, 10.57%. MS: *m/z* [M+H]⁺, found 663.39 [C₄₃H₇₀N₂O₄]⁺ requires 663.55.

***N*-[3β-Hydroxy-2α-propargyl-lup-20(29)-en-28-oyl]-*N'*-(tert-butoxycarbonyl)-{3-[4-(3-aminopropyl)piperazinyl]}propylamine (14b).** White powder (0.70 g, 90%), mp 122-124 °C. [α]_D²² -8° (c 0.52, CHCl₃). IR (solution in CHCl₃, cm⁻¹): 3351, 3309 (NH), 1697, 1638 (C=O). ¹H NMR (500 MHz, CDCl₃): δ_H 6.92 (br s, 1H, NH), 5.36 (br s, 1H, NH), 4.71, 4.55 (both br s, 2H, H-29), 3.37-3.27, 3.17-3.10 (both m, 5H, -CH₂NH-, -CH₂NH-Boc, H-19), 2.96 (d, 1H, *J* 10.0 Hz, H-3), 2.50-2.39 (m, 12H, CH₂ in piperazine and propylamine), 2.29-0.70 (m, 26H, CH, CH₂ in pentacyclic skeleton, propargyl and 4H in propylamine), 1.67 (s, 3H, H-30), 1.41 (br s, 9H, CH₃ in Boc), 0.96, 0.95, 0.92, 0.84, 0.76 (all s, 3H each, H-23-H-27). ¹³C NMR (125 MHz, CDCl₃): δ_C 176.3 (C-28), 156.1 (CONH-Boc), 151.1 (C-20), 109.3 (C-29), 83.1 (C in propargyl), 81.3 (C-3), 78.9 (C in Boc), 69.9 (CH in propargyl), 57.4 (CH₂ in propylamine), 56.8 (CH₂ in propylamine), 55.5 (CH₂ in piperazine), 55.4 (CH₂ in piperazine), 53.6 (C-17), 52.7 (C-5), 50.6 (C-9), 50.2 (C-18), 46.7 (C-19), 44.8 (C-1), 42.5 (C-14), 40.8 (C-8), 39.6 (CH₂ in propylamine), 39.1 (C-4), 39.0 (CH₂ in propylamine), 38.5 (C-13), 37.6 (C-22), 37.3 (C-10), 34.8 (C-7), 34.4 (C-2), 33.8 (C-16), 30.9 (C-21), 29.4 (C-15), 28.4 (CH₃ in Boc, C-24), 26.4 (CH₂ in propylamine), 25.6 (C-12), 25.0 (CH₂ in propylamine), 22.3 (CH₂ in propargyl), 21.0 (C-11), 19.4 (C-30), 18.5 (C-6), 17.0 (C-26), 16.3 (C-23, C-25), 14.7 (C-27). Anal. Calcd for C₄₈H₈₀N₄O₄: C, 74.18; H, 10.38. Found: C, 74.24, H, 9.84%. MS: *m/z* [M+H]⁺, found 777.56 [C₄₈H₈₀N₄O₄]⁺ requires 777.63.

***N*-[3β-Hydroxy-2α-propargyl-lup-20(29)-en-28-oyl]-5-piperazine-pentanoic acid (15b).** White powder (0.59 g, 89%), mp 234-236 °C. [α]_D²² -25.5° (c 0.5, CH₃OH). IR (solution in CH₃OH, cm⁻¹): 1633 (C=O). ¹H NMR (500 MHz, MeOD): δ_H 4.70, 4.59 (both br s, 2H, H-29), 3.19-3.15 (m, 2H, CH₂ in piperazine-pentanoic acid), 2.91-2.79 (m, 2H, H-19, H-13), 2.85 (d, 1H, *J* 10.0 Hz, H-3), 2.47-0.75 (m, 25H, CH, CH₂ in pentacyclic skeleton, propargyl, 12H in piperazine-pentanoic acid), 2.40-2.37 (m, 2H, -CH₂COOH), 1.65 (s, 3H, H-30), 1.00, 0.96, 0.95, 0.88, 0.75 (all s, 3H each, H-23-H-27). ¹³C NMR (125 MHz, MeOD): δ_C 179.6 (COOH), 178.3 (C-28), 154.7 (C-20), 113.3 (C-29), 86.8 (C in propargyl), 84.8 (C-3), 73.6 (CH in propargyl), 59.5 (C-5, CH₂ in pentanoic acid), 58.5 (C-17), 56.4 (C-18), 56.0 (CH₂ in piperazine), 54.7 (C-9), 49.6 (C-19), 48.7 (C-1), 45.8 (C-14), 44.6 (C-4), 43.0 (C-8), 41.2 (C-10), 40.9 (C-13), 39.7 (C-22), 38.6 (C-7), 38.2 (C-2), 37.2 (CH₂ in piperazine), 36.2 (C-16), 35.0 (C-21), 33.7 (C-15), 32.0 (C-24), 29.5 (C-12), 27.4 (CH₂ in pentanoic acid), 26.0 (CH₂ in propargyl), 25.9 (CH₂ in pentanoic acid), 25.0 (C-11), 23.1 (C-30), 22.4 (C-6), 20.8 (C-26), 20.0 (C-23), 19.8 (C-25), 18.4 (C-27). Anal. Calcd for C₄₂H₆₆N₂O₄: C, 76.09; H, 10.03. Found: C, 75.94, H, 9.97%. MS: *m/z* [M+H]⁺, found 663.27 [C₄₂H₆₆N₂O₄]⁺ requires 663.51.

General procedure for the preparation of compounds 6, 16-19. To a solution of the appropriate derivative of **4**, **8b**, **9b**, **12b** or **13b** (1 mmol) in anhydrous pyridine (16 mL) was added 2,2-dimethylsuccinic anhydride (0.5 mL, 4 mmol) and DMAP (0.24 g, 2 mmol). The reaction mixture was heated under reflux for 13 h (monitoring by TLC). Then the mixture was diluted with H₂O (30 mL) and extracted with EtOAc (4×30 mL). The combined extracts were washed with brine, dried over anhydrous MgSO₄, and concentrated under reduced pressure. The crude products were then chromatographed on silica gel [CHCl₃-MeOH (100:1)] to obtain pure compounds **6**, **16-19**.

3β-O-(3',3'-Dimethylsuccinyl)-2α-propargyl-lup-20(29)-en-28-oic acid (6). White powder (0.25 g, 40%), mp 148-150 °C. [α]_D¹⁹ -29.8° (c 0.59, CHCl₃). IR (solution in CHCl₃, cm⁻¹): 1733, 1700 (C=O). ¹H NMR (400 MHz, CDCl₃): δ_H 4.75, 4.62 (both br s, 2H, H-29), 4.52 (d, 1H, *J* 10.0 Hz, H-3), 3.04-2.97 (m, 1H, H-19), 2.73, 2.67 (1H each, d, *J* 15.5 Hz, -CH₂-CO-), 2.21-0.80 (m, 26H, CH, CH₂ in pentacyclic skeleton and propargyl), 1.70 (s, 3H, H-

30), 1.35 (br s, 6H, $-\text{C}(\text{CH}_3)_2-$), 0.99, 0.96, 0.90, 0.82, 0.81 (all s, 3H each, H-23–H-27). ^{13}C NMR (100 MHz, CDCl_3): δ_{C} 183.4 (COOH), 183.2 (C-28), 171.1 ($-\text{CH}_2-\text{CO}-$), 150.3 (C-20), 109.8 (C-29), 83.4 (C-3), 82.4 (C in propargyl), 69.9 (CH in propargyl), 56.4 (C-17), 55.3 (C-5, C-9), 49.2 (C-18), 46.9 (C-19), 44.8 (C-1), 44.3 ($-\text{CH}_2-\text{CO}-$), 42.4 (C-14), 40.7 (C-8), 40.4 ($-\text{C}(\text{CH}_3)_2-$), 38.9 (C-4), 38.3 (C-13), 37.2 (C-22), 37.1 (C-10), 34.2 (C-7), 33.4 (C-2), 32.1 (C-16), 30.5 (C-21), 29.6 (C-15), 28.2 (C-24), 25.5 ($-\text{C}(\text{CH}_3)_2-$), 25.4 (C-12), 22.2 (CH_2 in propargyl), 20.9 (C-11), 19.3 (C-30), 18.4 (C-6), 17.2 (C-26), 17.0 (C-23), 16.2 (C-25), 14.6 (C-27). Anal. Calcd for $\text{C}_{39}\text{H}_{58}\text{O}_6$: C, 75.20; H, 9.39. Found: C, 75.34, H, 9.43%. MS: m/z $[\text{M}+\text{Na}]^+$, found 645.30 $[\text{C}_{39}\text{H}_{58}\text{O}_6]^+$ requires 645.41.

***N*-[3 β -*O*-(3',3'-Dimethylsuccinyl)-2 α -propargyl-lup-20(29)-en-28-oyl]-*N'*-(tert-butoxycarbonyl)-2-ethylamine (16).** White powder (0.34 g, 45%), mp 110-112 °C. $[\alpha]_{\text{D}}^{23}$ -20.6° (c 0.47, CHCl_3). IR (solution in CHCl_3 , cm^{-1}): 3369, 3312 (NH), 1735, 1717, 1639 (C=O). ^1H NMR (500 MHz, CDCl_3): δ_{H} 6.41, 5.10 (both br s, 2H, NH), 4.74, 4.59 (both br s, 2H, H-29), 4.48 (d, 1H, J 10.0 Hz, H-3), 3.36-3.28 (m, 4H, $-\text{CH}_2\text{NH}-$, $-\text{CH}_2\text{NH}-\text{Boc}$), 3.15-3.11 (m, 1H, H-19), 2.70-2.66 (m, 2H, $-\text{CH}_2-\text{CO}-$), 2.47-0.80 (m, 26H, CH, CH_2 in pentacyclic skeleton and propargyl), 1.69 (s, 3H, H-30), 1.44 (s, 9H, CH_3 in Boc), 1.36 (br s, 6H, $-\text{C}(\text{CH}_3)_2-$), 0.97, 0.95, 0.88, 0.81, 0.80 (all s, 3H each, H-23–H-27). ^{13}C NMR (125 MHz, CDCl_3): δ_{C} 181.9 (COOH), 177.4 (C-28), 171.2 ($-\text{CH}_2-\text{CO}-$), 157.0 (CONH-Boc), 151.0 (C-20), 109.4 (C-29), 83.4 (C-3), 82.5 (C in propargyl), 79.7 (C in Boc), 69.8 (CH in propargyl), 55.6 (C-17), 55.5 (C-5), 50.6 (C-9), 50.1 (C-18), 46.7 (C-19), 45.0 (C-1), 44.2 ($-\text{CH}_2-\text{CO}-$), 42.5 (C-14), 40.8 (C-8), 40.6 (CH_2 in ethylamine), 40.3 (CH_2 in ethylamine, $-\text{C}(\text{CH}_3)_2-$), 38.9 (C-4), 38.4 (C-22), 37.7 (C-13), 37.2 (C-10), 34.3 (C-7), 33.5 (C-16), 33.4 (C-2), 30.8 (C-21), 29.4 (C-15), 28.4 (CH_3 in Boc), 28.1 (C-24), 25.6 ($-\text{C}(\text{CH}_3)_2-$), 25.3 (C-12), 22.2 (CH_2 in propargyl), 21.0 (C-11), 19.4 (C-30), 18.3 (C-6), 17.1 (C-26), 17.0 (C-23), 16.2 (C-25), 14.7 (C-27). Anal. Calcd for $\text{C}_{46}\text{H}_{72}\text{N}_2\text{O}_7$: C, 72.21; H, 9.49. Found: C, 72.26, H, 9.58%. MS: m/z $[\text{M}+\text{Na}]^+$, found 787.49 $[\text{C}_{46}\text{H}_{72}\text{N}_2\text{O}_7]^+$ requires 787.52.

***N*-[3 β -*O*-(3',3'-Dimethylsuccinyl)-2 α -propargyl-lup-20(29)-en-28-oyl]-*N'*-(tert-butoxycarbonyl)-8-octylamine (17).** White powder (0.76 g, 90%), mp 90-92 °C. $[\alpha]_{\text{D}}^{21}$ -18.3° (c 0.3, CHCl_3). IR (solution in CHCl_3 , cm^{-1}): 3311 (NH), 1711, 1639 (C=O). ^1H NMR (500 MHz, CDCl_3): δ_{H} 5.66 (m, 1H, NH) 4.73 (br s, 1H, H-29), 4.58-4.60 (m, 2H, H-29, NH), 4.48 (d, 1H, J 10.0 Hz, H-3), 3.28-3.10 (m, 5H, $-\text{CH}_2\text{NH}-$, $-\text{CH}_2\text{NH}-\text{Boc}$, H-19), 2.70-2.66 (m, 2H, $-\text{CH}_2-\text{CO}-$), 2.47-0.79 (m, 26H, CH, CH_2 in pentacyclic skeleton, propargyl and 4H in octylamine), 1.68 (s, 3H, H-30), 1.44 (br s, 9H, CH_3 in Boc), 1.32-1.30 (m, 8H, CH_2 in octylamine and 6H, $-\text{C}(\text{CH}_3)_2-$), 0.97, 0.94, 0.88, 0.80, 0.79 (all s, 3H each, H-23–H-27). ^{13}C NMR (125 MHz, CDCl_3): δ_{C} 182.6 (COOH), 176.3 (C-28), 171.3 ($-\text{CH}_2-\text{CO}-$), 156.0 (CONH-Boc), 151.0 (C-20), 109.4 (C-29), 83.4 (C-3), 82.4 (C in propargyl), 78.8 (C in Boc), 69.8 (CH in propargyl), 55.5 (C-17, C-5), 50.6 (C-9), 50.1 (C-18), 46.8 (C-19), 44.9 (C-1), 44.2 ($-\text{CH}_2-\text{CO}-$), 42.5 (C-14), 40.8 (C-8), 40.6 (CH_2 in octylamine), 40.3 ($-\text{C}(\text{CH}_3)_2-$), 39.2 (CH_2 in octylamine), 38.9 (C-4), 38.5 (C-13), 37.7 (C-22), 37.2 (C-10), 34.3 (C-7), 33.9 (C-2), 33.4 (C-16), 30.8 (C-21), 30.0 (C-15), 29.8 (CH_2 in octylamine), 29.4 (CH_2 in octylamine), 29.2 (CH_2 in octylamine), 28.4 (CH_3 in Boc), 28.1 (C-24), 26.9 (CH_2 in octylamine), 26.7 (CH_2 in octylamine), 25.6 ($-\text{C}(\text{CH}_3)_2-$), 25.5 ($-\text{C}(\text{CH}_3)_2-$), 25.3 (C-12), 22.2 (CH_2 in propargyl), 21.0 (C-11), 19.4 (C-30), 18.4 (C-6), 17.1 (C-26), 17.0 (C-23), 16.2 (C-25), 14.6 (C-27). Anal. Calcd for $\text{C}_{52}\text{H}_{84}\text{N}_2\text{O}_7$: C, 73.54; H, 9.97. Found: C, 73.48, H, 10.11%. MS: m/z $[\text{M}+\text{K}]^+$, found 887.59 $[\text{C}_{52}\text{H}_{84}\text{N}_2\text{O}_7]^+$ requires 887.59.

{[*N*-[3 β -*O*-(3',3'-Dimethylsuccinyl)-2 α -propargyl-lup-20(29)-en-28-oyl]-2-aminoethyl]-carbamoyl}methane (18). White powder (0.30 g, 42%), mp 154-156 °C. $[\alpha]_{\text{D}}^{23}$ -22.3° (c 0.44, CH_2Cl_2). IR (solution in CH_2Cl_2 , cm^{-1}): 3371, 3311 (NH), 1735, 1640 (C=O). ^1H NMR (500 MHz, CDCl_3): δ_{H} 7.11-7.08 (m, 1H, NH), 6.73 (br s, 1H, NH), 4.71, 4.58 (both br s, 2H, H-29), 4.45 (d, 1H, J 10.0 Hz, H-3), 3.36-3.06 (m, 4H, $-\text{CH}_2\text{NH}-$, $\text{CH}_2\text{NHCOCH}_3$), 3.10-3.09 (m, 1H, H-19), 2.71-2.61 (m, 2H, $-\text{CH}_2-\text{CO}-$), 2.46-0.80 (m, 26H, CH, CH_2 in pentacyclic skeleton and propargyl), 1.99 (s, 3H, $-\text{NHCOCH}_3$), 1.67 (s, 3H, H-30), 1.31 (br s, 6H, $-\text{C}(\text{CH}_3)_2-$), 0.97, 0.91, 0.87, 0.80, 0.78 (all s, 3H each, H-23–H-27). ^{13}C NMR (125 MHz, CDCl_3): δ_{C} 180.8 (COOH), 177.4 (C-28), 171.8 ($-\text{CH}_2-\text{CO}-$), 171.4 (NHCOCH_3), 151.0 (C-20), 109.4 (C-29), 83.2 (C-3), 82.4 (C in propargyl), 69.9 (CH in propargyl), 55.6 (C-17), 55.5 (C-5), 50.6 (C-9), 50.1 (C-18), 46.7 (C-19), 44.9 (C-1), 44.2 ($-\text{CH}_2-\text{CO}-$), 42.5 (C-14), 40.8 (C-8), 40.6 (CH_2 in

ethylamine), 40.2 (CH₂ in ethylamine, $-\underline{C}(\text{CH}_3)_2-$), 38.9 (C-4), 38.4 (C-10), 37.6 (C-13), 37.2 (C-22), 34.3 (C-7), 33.5 (C-16), 33.4 (C-2), 30.8 (C-21), 29.4 (C-15), 28.1 (C-24), 25.8 ($-\underline{C}(\text{CH}_3)_2-$), 25.5 ($-\underline{C}(\text{CH}_3)_2-$), 25.3 (C-12), 23.1 (NHCOCH₃), 22.2 (CH₂ in propargyl), 21.1 (C-11), 19.4 (C-30), 18.4 (C-6), 17.1 (C-23), 17.0 (C-26), 16.2 (C-25), 14.7 (C-27). Anal. Calcd for C₄₃H₆₆N₂O₆: C, 73.05; H, 9.41. Found: C, 73.10, H, 9.38%. MS: *m/z* [M+Na]⁺, found 729.49 [C₄₃H₆₆N₂O₆]⁺ requires 729.48.

{[N-(3β-O-(3',3'-Dimethylsuccinyl)-2α-propargyl-lup-20(29)-en-28-oyl)-8-aminoctyl]-carbamoyl}methane (19). White powder (0.39 g, 49%), mp 112-114 °C. $[\alpha]_{\text{D}}^{22}$ -22.2° (*c* 0.36, CHCl₃). IR (solution in CHCl₃, cm⁻¹): 3308 (NH), 1733 (C=O). ¹H NMR (500 MHz, CDCl₃): δ_H 5.87-5.72 (m, 2H, NH), 4.72, 4.58 (both br s, 2H, H-29), 4.47 (d, 1H, *J* 10.0 Hz, H-3), 3.22-3.14 (m, 5H, $-\text{CH}_2\text{NH}-$, $\text{CH}_2\text{NHCOCH}_3$, H-19), 2.70-2.59 (m, 2H, $-\text{CH}_2-\text{CO}-$), 2.49-0.80 (m, 26H, CH, CH₂ in pentacyclic skeleton and propargyl), 1.94 (s, 3H, $-\text{NHCOCH}_3$), 1.67 (s, 3H, H-30), 1.55-1.25 (m, 18H, CH₂ in octylamine and CH₃ in $-\underline{C}(\text{CH}_3)_2-$), 0.96, 0.93, 0.87, 0.80, 0.79 (all s, 3H each, H-23–H-27). ¹³C NMR (125 MHz, CDCl₃): δ_C 181.9 (COOH), 176.1 (C-28), 171.2 ($-\text{CH}_2-\underline{\text{C}}\text{O}-$), 170.7 (NHCOCH₃), 151.0 (C-20), 109.4 (C-29), 83.3 (C-3), 82.5 (C in propargyl), 69.8 (CH in propargyl), 55.5 (C-17, C-5), 50.6 (C-9), 50.1 (C-18), 46.8 (C-19), 44.9 (C-1), 44.2 ($-\text{CH}_2-\text{CO}-$), 42.5 (C-14), 40.8 (C-8), 40.3 ($-\underline{C}(\text{CH}_3)_2-$), 39.7 (CH₂ in octylamine), 39.2 (CH₂ in octylamine), 38.9 (C-4), 38.5 (C-13), 37.7 (C-10), 37.2 (C-22), 34.3 (C-7), 33.8 (C-2), 33.4 (C-16), 30.8 (C-21), 29.8 (C-15), 29.7 (CH₂ in octylamine), 29.4 (CH₂ in octylamine), 29.1 (CH₂ in octylamine), 28.1 (C-24), 26.8 (CH₂ in octylamine), 25.6 ($-\underline{C}(\text{CH}_3)_2-$), 25.5 ($-\underline{C}(\text{CH}_3)_2-$), 25.4 (C-12), 23.3 (NHCOCH₃), 22.2 (CH₂ in propargyl), 21.0 (C-11), 19.4 (C-30), 18.4 (C-6), 17.1 (C-26), 17.0 (C-23), 16.2 (C-25), 14.6 (C-27). Anal. Calcd for C₄₉H₇₈N₂O₆: C, 74.39; H, 9.94. Found: C, 74.43, H, 10.06%. MS: *m/z* [M+Na]⁺, found 813.36 [C₄₉H₇₈N₂O₆]⁺ requires 813.58.

General procedure for click reactions. A. To a solution of alkyne **4** or **5** (1 mmol) in Bu^tOH (15 mL) were added azidothymidine (0.21 g, 0.8 mmol), CuI (0.04 g, 0.2 mmol) and stirring of the reaction mixture at 70 °C for 12 h (monitoring by TLC). Then the mixture was chromatographed on silica gel [CHCl₃–MeOH (100:1→1:1)] to obtain pure compounds **20** and **21**.

B. To a solution of the alkyne **4-6**, **12b**, **14b**, **15b**, **16-19** (1 mmol) in DMSO (2 mL) were added azidothymidine (0.29 g, 1.1 mmol), sodium ascorbate (0.20 g, 1.01 mmol), CuSO₄·5H₂O (0.25 g, 1.01 mmol) and stirring of the reaction mixture was continued at room temperature for 2 h (monitoring by TLC). Then the mixture was chromatographed on silica gel [CHCl₃–MeOH (100:1→1:1)] to obtain pure compounds **20-29**.

[1-(3'-Deoxythymidine)-1H-1,2,3-triazol-4-yl]-2α-methyl-3β-hydroxy-lup-20(29)-en-28-oic acid (20). White powder (A, 0.53 g, 70%; B, 0.54 g, 71%), mp 206-208 °C. $[\alpha]_{\text{D}}^{18}$ -25.3° (*c* 0.55, CH₃OH). IR (solution in CH₃OH, cm⁻¹): 1682 (C=O). ¹H NMR (500 MHz, MeOD): δ_H 7.93 (s, 1H, H-Thy), 7.88 (s, 1H, H-triazol), 6.49 (t, 1H, *J* 5.0 Hz, H-1'-ribose), 5.44-5.41 (m, 1H, H-3'-ribose), 4.71, 4.59 (both br s, 2H, H-29), 4.37-4.36 (m, 1H, H-4'-ribose), 3.93 and 3.79 (1H each, dd, *J* 10.0, 5.0 Hz, H-5'-ribose), 3.19 (d, 1H, *J* 15.0 Hz, =C-CH₂-), 3.02-2.97 (m, 2H, H-19, H-2'-ribose), 2.83 (d, 1H, *J* 10 Hz, H-3), 2.77-2.74 (m, 1H, H-2'-ribose), 2.52 (dd, 1H, *J* 15.0, 10.0 Hz, =C-CH₂-), 2.29-0.60 (m, 23H, CH, CH₂ in pentacyclic skeleton), 1.92 (s, 3H, CH₃-Thy), 1.70 (s, 3H, H-30), 0.99, 0.98, 0.95, 0.81, 0.80 (all s, 3H each, H-23–H-27). ¹³C NMR (125 MHz, MeOD): δ_C 180.5 (C-28), 166.5, 152.4 (C=O-Thy), 152.1 (C-20), 148.1 (C-triazol), 138.4 (CH-Thy), 123.9 (CH-triazol), 111.8 (C-Thy), 110.4 (C-29), 86.8 (1'-ribose), 86.5 (4'-ribose), 83.1 (C-3), 62.2 (5'-ribose), 60.9 (3'-ribose), 57.6 (C-17), 57.1 (C-5), 52.0 (C-9), 50.0 (C-18), 49.0 (C-19), 46.4 (C-1), 43.7 (C-14), 42.1 (C-8), 40.6 (C-10), 39.7 (C-13), 39.1 (2'-ribose), 38.5 (C-4), 38.3 (C-22), 37.3 (C-2), 35.7 (C-7), 33.5 (C-16), 31.9 (C-21), 31.0 (C-15), 30.0 (=C-CH₂-), 29.2 (C-24), 27.0 (C-12), 22.2 (C-11), 19.8 (C-6, C-30), 17.9 (C-26), 17.7 (CH₃-Thy), 16.8 (C-23, C-25), 15.4 (C-27). Anal. Calcd for C₄₃H₆₃N₅O₇: C, 67.78; H, 8.33. Found: C, 68.32, H, 8.28%. MS: *m/z* [M+Na]⁺, found 784.33 [C₄₃H₆₃N₅O₇]⁺ requires 784.46.

[1-(3'-Deoxythymidine)-1H-1,2,3-triazol-4-yl]-2α-methyl-3β-acetoxylup-20(29)-en-28-oic acid (21). White powder (A, 0.44 g, 55%, B, 0.55g, 68%), mp 196-198 °C. $[\alpha]_{\text{D}}^{22}$ -14° (*c* 0.65, CH₃OH). IR (solution in CH₃OH, cm⁻¹): 1696 (C=O). ¹H NMR (500 MHz, MeOD): δ_H 7.93 (s, 1H, H-Thy), 7.90 (s, 1H, H-triazol), 6.48 (t, 1H, *J* 5.0 Hz, H-1'-

ribose), 5.44-5.40 (m, 1H, H-3'-ribose), 4.71, 4.60 (both br s, 2H, H-29), 2.52 (d, 1H, J 10.0 Hz, H-3), 4.38-4.36 (m, 1H, H-4'-ribose), 3.92 and 3.80 (1H each, dd, J 10.0, 5.0 Hz, H-5'-ribose), 3.04-2.99 (m, 1H, H-19), 2.95-2.90 (m, 1H, H-2'-ribose), 2.76-2.68 (m, 2H, H-2'-ribose, =C-CH₂-), 2.52 (dd, 1H, J 15.0, 10.0 Hz, =C-CH₂-), 2.27-0.60 (m, 23H, CH, CH₂ in pentacyclic skeleton), 2.07 (s, 3H, CH₃-Thy), 1.93 (s, 3H, COCH₃), 1.72 (s, 3H, H-30), 1.03, 0.96, 0.90, 0.86, 0.84 (all s, 3H each, H-23-H-27). ¹³C NMR (125 MHz, MeOD): δ_c 178.5 (C-28), 171.8 (COCH₃), 165.0 (C=O-Thy), 150.9 (C-20), 150.5 (C=O-Thy), 146.0 (C-triazol), 136.9 (CH-Thy), 122.4 (CH-triazol), 110.2 (C-Thy), 108.9 (C-29), 85.3 (1'-ribose), 85.0 (4'-ribose), 83.8 (C-3), 60.7 (5'-ribose), 59.4 (3'-ribose), 56.0 (C-17), 55.4 (C-5), 50.4 (C-9), 49.2 (C-18), 47.3 (C-19), 44.8 (C-1), 42.2 (C-14), 40.6 (C-4), 38.7 (C-8), 38.2 (C-13), 37.6 (2'-ribose), 37.0 (C-22), 36.7 (C-10), 34.0 (C-2), 31.9 (C-7), 30.3 (C-16), 29.4 (C-15, C-21), 28.4 (=C-CH₂-), 27.4 (C-24), 25.4 (C-12), 20.7 (C-11), 19.6 (COCH₃), 18.2 (C-30), 18.1 (C-6), 16.2 (C-26), 16.1 (C-23), 15.2 (C-25), 13.8 (C-27), 11.1 (CH₃-Thy). Anal. Calcd for C₄₅H₆₅N₅O₈: C, 67.22; H, 8.15. Found: C, 67.34, H, 8.24%. MS: m/z [M+Na]⁺, found 826.27 [C₄₅H₆₅N₅O₈]⁺ requires 826.47.

[1-(3'-Deoxythymidine)-1H-1,2,3-triazol-4-yl]-2 α -methyl-3 β -O-(3',3'-dimethylsuccinyl)lup-20(29)-en-28-oic acid (22). White powder (B, 0.56 g, 63%), mp 270-272 °C. $[\alpha]_D^{18}$ -1° (c 0.28, CH₃OH). IR (solution in CH₃OH, cm⁻¹): 1697 (C=O). ¹H NMR (500 MHz, MeOD): δ_H 7.66 (s, 1H, H-Thy), 7.45 (s, 1H, H-triazol), 6.25 (t, 1H, J 5.0 Hz, H-1'-ribose), 5.17-5.15 (m, 1H, H-3'-ribose), 4.47, 4.35 (both br s, 2H, H-29), 4.52 (d, 1H, J 10.0 Hz, H-3), 4.15-4.13 (m, 1H, H-4'-ribose), 3.74 and 3.60 (1H each, dd, J 10.0, 5.0 Hz, H-5'-ribose), 2.78-2.74 (m, 2H, H-19, H-2'-ribose), 2.35 and 2.52 (1H each, d, J 15.0 Hz, -CH₂-CO-), 2.53-2.30 (m, 3H, H-2'-ribose, =C-CH₂-), 2.03-0.50 (m, 23H, CH, CH₂ in pentacyclic skeleton), 1.71 (s, 3H, CH₃-Thy), 1.45 (s, 3H, H-30), 1.04 (br s, 6H, -C(CH₃)₂-), 0.75, 0.71, 0.63, 0.62, 0.58 (all s, 3H each, H-23-H-27). ¹³C NMR (125 MHz, MeOD): δ_c 182.8 (COOH), 179.7 (C-28), 172.7 (-CH₂-CO-), 164.5 (C=O-Thy), 150.6 (C-20), 150.3 (C=O-Thy), 145.7 (C-triazol), 136.5 (CH-Thy), 121.9 (CH-triazol), 110.7 (C-Thy), 108.9 (C-29), 85.3 (1'-ribose), 84.7 (4'-ribose), 83.6 (C-3), 60.4 (5'-ribose), 58.9 (3'-ribose), 55.9 (C-5), 55.0 (C-17), 50.0 (C-9, C-18), 46.6 (C-19), 44.7 (C-1), 44.3 (-CH₂-CO-), 42.0 (C-14), 40.3 (-C(CH₃)₂-), 38.6 (C-4), 37.8 (C-13), 37.6 (2'-ribose), 36.8 (C-8, C-22), 33.7 (C-10), 33.4 (C-2), 31.9 (C-7), 30.1 (C-16), 29.2 (C-15, C-21), 28.1 (=C-CH₂-), 27.7 (C-24), 25.7 (-C(CH₃)₂-), 25.0 (C-12), 25.0 (-C(CH₃)₂-), 20.5 (C-11), 18.6 (C-30), 17.9 (C-6), 16.6 (C-26), 16.3 (C-23), 15.4 (C-25), 14.1 (C-27), 11.6 (CH₃-Thy). Anal. Calcd for C₄₉H₇₁N₅O₁₀: C, 66.12; H, 8.04. Found: C, 66.23, H, 8.12%. MS: m/z [M+Na]⁺, found 912.49 [C₄₉H₇₁N₅O₁₀]⁺ requires 912.51.

[1-(3'-Deoxythymidine)-1H-1,2,3-triazol-4-yl]-[N-(2 α -methyl-3 β -hydroxy-lup-20(29)-en-28-oyl)-2-aminoethyl]carbamoyl]methane (23). White powder (B, 0.57 g, 67%), mp 192-194 °C. $[\alpha]_D^{22}$ -23.3° (c 0.54, CH₃OH). IR (solution in CH₃OH, cm⁻¹): 3311 (NH), 1636 (C=O). ¹H NMR (500 MHz, MeOD): δ_H 7.94 (s, 1H, H-Thy), 7.88 (s, 1H, H-triazol), 7.62 (br s, 1H, NH), 6.50 (t, 1H, J 5.0 Hz, H-1'-ribose), 5.44-5.42 (m, 1H, H-3'-ribose), 4.87, 4.70 (both br s, 2H, H-29), 4.37-4.36 (m, 1H, H-4'-ribose), 3.93 and 3.79 (1H each, dd, J 10.0, 5.0 Hz, H-5'-ribose), 3.88-3.28 (m, 4H, -CH₂NH-, CH₂NHCOCH₃), 3.19 (d, 1H, J 15.0 Hz, =C-CH₂-), 3.10-3.06 (m, 1H, H-19), 2.98-2.93 (m, 1H, H-2'-ribose), 2.82 (d, 1H, J 10.0 Hz, H-3), 2.79-2.74 (m, 1H, H-2'-ribose), 2.54-2.49 (m, 1H, =C-CH₂-), 2.12-0.59 (m, 23H, CH, CH₂ in pentacyclic skeleton and 1H, NH), 1.95 (s, 3H, -NHCOCH₃), 1.92 (s, 3H, CH₃-Thy), 1.69 (s, 3H, H-30), 0.99, 0.98, 0.94, 0.81, 0.80 (all s, 3H each, H-23-H-27). ¹³C NMR (125 MHz, MeOD): δ_c 179.7 (C-28), 173.8 (NHCOCH₃), 166.5 (C=O-Thy), 152.4 (C-20, C=O-Thy), 148.1 (C-triazol), 138.4 (CH-Thy), 123.8 (CH-triazol), 111.8 (C-Thy), 110.2 (C-29), 86.8 (1'-ribose), 86.5 (4'-ribose), 83.1 (C-3), 62.2 (5'-ribose), 60.9 (3'-ribose), 57.1 (C-5, C-17), 52.1 (C-9), 51.5 (C-18), 48.6 (C-19), 46.4 (C-1), 43.7 (C-14), 42.1 (C-8), 40.5 (C-4), 40.4 (CH₂ in ethylamine), 40.3 (CH₂ in ethylamine), 39.4 (C-13), 39.1 (2'-ribose), 39.0 (C-22), 38.5 (C-10), 37.3 (C-2), 35.7 (C-7), 34.2 (C-16), 32.0 (C-21), 30.7 (C-15), 29.9 (=C-CH₂-), 29.2 (C-24), 27.1 (C-12), 22.9 (NHCOCH₃), 22.2 (C-11), 19.8 (C-6, C-30), 17.6 (C-26), 17.1 (C-23), 16.9 (C-25), 15.3 (C-27), 12.7 (CH₃-Thy). Anal. Calcd for C₄₇H₇₁N₇O₇: C, 66.72; H, 8.46. Found: C, 66.65, H, 8.51%. MS: m/z [M+K]⁺, found 884.36 [C₄₇H₇₁N₇O₇]⁺ requires 884.51.

{[1-(3'-Deoxythymidine)-1H-1,2,3-triazol-4-yl]-N-[N'-(tert-butoxycarbonyl)-3-[4-(3-aminopropyl)piperazin-yl]propyl]}-2 α -methyl betulinic acid amide (24). White powder (B, 0.75 g, 72%), mp 142-144 °C. $[\alpha]_D^{22}$ -13° (c 0.63, CH₃OH). IR (solution in CH₃OH, cm⁻¹): 3310 (NH), 1637 (C=O). ¹H NMR (400 MHz, MeOD): δ_H 7.93 (s, 1H, H-Thy), 7.87 (s, 1H, H-triazole), 6.49 (t, 1H, *J* 5.0 Hz, H-1'-ribose), 5.44-5.41 (m, 1H, H-3'-ribose), 4.71, 4.59 (both br s, 2H, H-29), 4.39-4.34 (m, 1H, H-4'-ribose), 3.93 and 3.78 (1H each, dd, *J* 10.0, 5.0 Hz, H-5'-ribose), 3.29-2.93 (m, 7H, -CH₂NH-, -CH₂NH-Boc, H-19, H-2'-ribose, =C-CH₂-), 2.82 (d, 1H, *J* 12.0 Hz, H-3), 2.79-2.36 (m, 14H, CH₂ in piperazine and propylamine, H-2'-ribose, =C-CH₂-), 2.14-0.58 (m, 23H, CH, CH₂ in pentacyclic skeleton, 4H in propylamine and 2H, NH), 1.93 (s, 3H, CH₃-Thy), 1.70 (s, 3H, H-30), 1.45 (br s, 9H, CH₃ in Boc), 0.99, 0.98, 0.95, 0.83, 0.81 (all s, 3H each, H-23-H-27). ¹³C NMR (100 MHz, MeOD): δ_C 179.0 (C-28), 166.4 (C=O-Thy), 158.5 (CONH-Boc), 152.3 (C-20, C=O-Thy), 148.0 (C-triazole), 138.3 (CH-Thy), 123.8 (CH-triazole), 111.7 (C-Thy), 110.2 (C-29), 86.7 (1'-ribose), 86.5 (4'-ribose), 83.0 (C-3), 79.9 (C in Boc), 62.5 (5'-ribose), 60.9 (3'-ribose), 57.4 (CH₂ in propylamine), 57.0 (C-5, C-17), 56.8 (CH₂ in propylamine), 55.8, 53.7 (CH₂ in piperazine), 52.1 (C-9), 51.4 (C-18), 48.6 (C-19), 46.4 (C-1), 43.6 (C-14), 42.1 (C-8), 40.5 (C-10), 39.7 (C-13), 39.5 (CH₂ in propylamine), 39.1 (2'-ribose), 38.9 (CH₂ in propylamine), 38.6 (C-4), 38.4 (C-22), 37.3 (C-2), 35.7 (C-7), 34.3 (C-16), 32.0 (C-21), 30.6 (C-15), 29.9 (=C-CH₂-), 29.2 (C-24), 29.0 (CH₃ in Boc), 27.7 (CH₂ in propylamine), 27.4 (CH₂ in propylamine), 27.0 (C-12), 22.2 (C-11), 19.9 (C-6, C-30), 17.6 (C-26), 17.2 (C-23), 17.1 (C-25), 15.3 (C-27), 11.3 (CH₃-Thy). Anal. Calcd for C₅₈H₉₃N₉O₈: C, 66.70; H, 8.98. Found: C, 66.67, H, 8.87%. MS: *m/z* [M+H]⁺, found 1044.65 [C₅₈H₉₃N₉O₈]⁺ requires 1044.72.

{[1-(3'-Deoxythymidine)-1H-1,2,3-triazol-4-yl]-[N-2 α -methyl-3 β -hydroxy-lup-20(29)-en-28-oyl]}-5-piperazin-ylpentanoic acid (25). White powder (B, 0.56 g, 60%), mp 242-244 °C. $[\alpha]_D^{18}$ -12° (c 0.55, DMSO). IR (solution in CH₃OH, cm⁻¹): 1636 (C=O). ¹H NMR (500 MHz, MeOD): δ_H 7.93 (br s, 2H, H-Thy, H-triazol), 6.50 (t, 1H, *J* 5.0 Hz, H-1'-ribose), 5.55-5.52 (m, 1H, H-3'-ribose), 4.70, 4.60 (both br s, 2H, H-29), 4.39-4.34 (m, 1H, H-4'-ribose), 3.92 (1H, dd, *J* 10.0, 5.0 Hz, H-5'-ribose), 3.79-3.75 (m, 5H, H-5'-ribose and CH₂ in piperazine), 3.10-3.06 (m, 1H, H-19), 3.00-2.68 (m, 12H, H-3, H-13, H-2'-ribose, =C-CH₂-, CH₂ in piperazine and pentanoic acid), 2.19-0.78 (m, 22H, CH, CH₂ in pentacyclic skeleton and 6H in pentanoic acid), 1.94 (s, 3H, CH₃-Thy), 1.70 (s, 3H, H-30), 0.99, 0.98, 0.88, 0.87, 0.78 (all s, 3H each, H-23-H-27). ¹³C NMR (125 MHz, DMSO): δ_C 182.8 (COOH), 172.8 (C-28), 164.2 (C=O-Thy), 151.4 (C-20), 150.9 (C=O-Thy), 146.7 (C-triazol), 136.7 (CH-Thy), 122.3 (CH-triazol), 110.1 (C-Thy), 109.7 (C-29), 85.0 (1'-ribose), 84.3 (4'-ribose), 80.8 (C-3), 61.1 (5'-ribose), 59.3 (3'-ribose), 55.8 (C-5, CH₂ in pentanoic acid), 54.4 (C-17), 53.3 (CH₂ in piperazine), 52.7 (C-18), 50.8 (C-9), 46.0 (C-19), 45.4 (C-1), 41.9 (C-14), 40.8 (C-8), 39.6 (C-4), 38.0 (CH₂ in piperazine), 37.4 (C-10, 2'-ribose), 36.8 (C-13), 36.4 (C-2), 35.8 (C-7), 34.4 (C-22), 32.2 (C-16), 31.3 (C-21), 29.6 (C-15), 28.7 (C-24, =C-CH₂-), 26.2 (CH₂ in pentanoic acid), 25.7 (C-12), 23.4 (CH₂ in pentanoic acid), 21.1 (C-11), 19.3 (C-30), 18.7 (C-6), 16.9 (C-23), 16.8 (C-26), 16.1 (C-25), 14.5 (C-27), 12.7 (CH₃-Thy). Anal. Calcd for C₅₂H₇₉N₇O₈: C, 67.14; H, 8.56. Found: C, 67.21, H, 8.53%. MS: *m/z* [M+K]⁺, found 968.48 [C₅₂H₇₉N₇O₈]⁺ requires 968.56.

[1-(3'-Deoxythymidine)-1H-1,2,3-triazol-4-yl]-{[N-2 α -methyl-3 β -O-(3',3'-dimethylsuccinyl)-lup-20,29-en-28-oyl]-N'-(tert-butoxycarbonyl)}-2-ethylamine (26). White powder (B, 0.75 g, 73%), mp 278-280 °C. $[\alpha]_D^{23}$ -12.9° (c 1.08 C₂H₅OH). IR (solution in C₂H₅OH, cm⁻¹): 3434 (NH), 1697 (C=O). ¹H NMR (500 MHz, MeOD): δ_H 7.95 (s, 1H, H-Thy), 7.92 (s, 1H, H-triazol), 7.63 (br s, 1H, NH), 6.51 (t, 1H, *J* 5.0 Hz, H-1'-ribose), 5.43-5.40 (m, 1H, H-3'-ribose), 4.71, 4.59 (both br s, 2H, H-29), 4.51 (d, 1H, *J* 10.0 Hz, H-3), 4.38-4.34 (m, 1H, H-4'-ribose), 3.93 and 3.78 (1H each, dd, *J* 10.0, 5.0 Hz, H-5'-ribose), 3.30-3.16 (m, 4H, -CH₂NH-, -CH₂NH-Boc), 3.10-3.07 (m, 1H, H-19), 2.95-2.52 (m, 4H, CH₂, H-2'-ribose, =C-CH₂-), 2.67 and 2.59 (1H, each, d, *J* 15.5 Hz, -CH₂-CO-), 2.37-0.85 (m, 23H, CH, CH₂ in pentacyclic skeleton and 1H, NH), 1.93 (s, 3H, CH₃-Thy), 1.70 (s, 3H, H-30), 1.44 (s, 9H, CH₃ in Boc), 1.27 (br s, 6H, -C(CH₃)₂-), 1.01, 0.96, 0.89, 0.85, 0.84 (all s, 3H each, H-23-H-27). ¹³C NMR (125 MHz, MeOD): δ_C 182.8 (COOH), 179.8 (C-28), 174.5 (-CH₂-CO-), 166.5 (C=O-Thy), 158.9 (CONH-Boc), 152.5 (C-20, C=O-Thy), 147.7 (C-triazol), 138.4 (CH-Thy), 124.1 (CH-triazol), 111.9 (C-Thy), 110.1 (C-29), 86.8 (C-1'-ribose),

86.6 (4'-ribose), 85.2 (C-3), 80.3 (C in Boc), 62.3 (5'-ribose), 61.0 (3'-ribose), 57.1 (C-17), 57.0 (C-5), 52.1 (C-9), 51.5 (C-18), 48.6 (C-19), 46.5 (C-1), 45.7 ($-\underline{\text{CH}}_2\text{-CO-}$), 43.7 (C-14), 42.2 (C-8), 41.5 (C-4), 40.5 (CH_2 in ethylamine), 40.2 (CH_2 in ethylamine, $-\underline{\text{C}}(\text{CH}_3)_2-$), 39.5 (2'-ribose), 39.2 (C-13), 39.0 (C-22), 38.5 (C-10), 35.6 (C-2, C-7), 34.2 (C-16), 32.2 (C-21), 30.7 (C-15), 29.9 ($=\text{C-CH}_2-$), 29.1 (C-24), 29.0 ($-\text{C}(\underline{\text{CH}}_3)_2-$), 28.9 (CH_3 in Boc), 27.0 (C-12, $-\text{C}(\underline{\text{CH}}_3)_2-$), 22.3 (C-11), 19.8 (C-30), 19.6 (C-6), 17.9 (C-26), 17.6 (C-23), 17.0 (C-25), 15.3 (C-27), 12.7 (CH_3 -Thy). Anal. Calcd for $\text{C}_{56}\text{H}_{85}\text{N}_7\text{O}_{11}$: C, 65.15; H, 8.30. Found: C, 65.21, H, 8.27%. MS: m/z $[\text{M}+\text{Na}]^+$, found 1054.58 $[\text{C}_{56}\text{H}_{85}\text{N}_7\text{O}_{11}]^+$ requires 1054.62.

[1-(3'-Deoxythymidine)-1H-1,2,3-triazol-4-yl]-[*N*-2 α -methyl-3 β -O-(3',3'-dimethylsuccinyl)-lup-20,29-en-28-oyl]-*N'*-(tert-butoxycarbonyl)-8-octylamine (27). White powder (B, 1.07 g, 96%), mp 192-194 °C. $[\alpha]_{\text{D}}^{21}$ -8.45° (*c* 0.36, CH_3OH). IR (solution in CH_3OH , cm^{-1}): 3433 (NH), 1696 (C=O). ^1H NMR (500 MHz, MeOD): δ_{H} 7.94 (s, 1H, H-Thy), 7.91 (s, 1H, H-triazol), 7.57-7.56 (m, 1H, NH), 6.49 (t, 1H, *J* 5.0 Hz, H-1'-ribose), 5.43-5.40 (m, 1H, H-3'-ribose), 4.71 (br s, 1H, H-29), 4.60-4.59 (m, 2H, H-29, NH), 4.51 (d, 1H, *J* 10.0 Hz, H-3), 4.37-4.35 (m, 1H, H-4'-ribose), 3.80 and 3.66 (1H each, dd, *J* 10.0, 5.0 Hz, H-5'-ribose), 3.26-2.58 (m, 9H, $-\text{CH}_2\text{NH-}$, $-\text{CH}_2\text{NH-Boc}$, H-19, H-2'-ribose, $=\text{C-CH}_2-$), 2.61 and 2.58 (1H, each, d, *J* 15.5 Hz, $-\text{CH}_2\text{-CO-}$), 2.15-0.73 (m, 23H, CH, CH_2 in pentacyclic skeleton and 4H in octylamine), 1.93 (s, 3H, CH_3 -Thy), 1.70 (s, 3H, H-30), 1.45 (br s, 9H, CH_3 in Boc), 1.34-1.31 (m, 8H, CH_2 in octylamine and 6H, $-\text{C}(\text{CH}_3)_2-$), 1.02, 0.96, 0.90, 0.86, 0.84 (all s, 3H each, H-23-H-27). ^{13}C NMR (125 MHz, MeOD): δ_{C} 185.2 (COOH), 179.0 (C-28), 174.0 ($-\text{CH}_2\text{-CO-}$), 165.0 (C=O-Thy), 158.6 (CONH-Boc), 152.5 (C-20), 150.9 (C=O-Thy), 147.5 (C-triazol), 138.4 (CH-Thy), 124.1 (CH-triazol), 111.9 (C-Thy), 110.1 (C-29), 86.8 (1'-ribose), 86.5 (4'-ribose), 85.2 (C-3), 79.9 (C in Boc), 62.3 (5'-ribose), 61.0 (3'-ribose), 57.1 (C-17), 56.9 (C-5), 52.1 (C-9), 51.5 (C-18), 48.2 (C-19), 46.3 (C-1), 45.7 ($-\text{CH}_2\text{-CO-}$), 43.7 (C-14), 42.2 (C-8), 41.5 (C-4), 40.5 (CH_2 in octylamine), 40.2 ($-\underline{\text{C}}(\text{CH}_3)_2-$, CH_2 in octylamine), 39.6 (2'-ribose), 39.1 (C-13), 38.9 (C-22), 38.5 (C-10), 35.6 (C-7), 35.5 (C-2), 34.3 (C-16), 32.1 (C-21), 30.8 (C-15), 30.6 (CH_2 in octylamine), 30.1 (CH_2 in octylamine), 29.9 ($=\text{C-CH}_2-$), 29.1 (C-24), 29.0 ($-\text{C}(\underline{\text{CH}}_3)_2-$), 28.9 (CH_3 in Boc), 28.2 (CH_2 in octylamine), 28.0 (CH_2 in octylamine), 27.1 (C-12), 27.0 ($-\text{C}(\underline{\text{CH}}_3)_2-$), 22.3 (C-11), 19.9 (C-30), 19.6 (C-6), 17.9 (C-26), 17.7 (C-23), 17.0 (C-25), 15.3 (C-27), 12.69 (CH_3 -Thy). Anal. Calcd for $\text{C}_{62}\text{H}_{97}\text{N}_7\text{O}_{11}$: C, 66.70; H, 8.76. Found: C, 66.64, H, 8.69%. MS: m/z $[\text{M}+\text{K}]^+$, found 1154.50 $[\text{C}_{62}\text{H}_{97}\text{N}_7\text{O}_{11}]^+$ requires 1154.69.

[1-(3'-Deoxythymidine)-1H-1,2,3-triazol-4-yl]-[*N*-2 α -methyl-3 β -O-(3',3'-dimethylsuccinyl)lup-20,29-en-28-oyl]-2-aminoethyl]carbonyl]methane (28). White powder (B, 0.58 g, 60%), mp 248-250 °C. $[\alpha]_{\text{D}}^{22}$ -2.2° (*c* 0.36, $\text{C}_2\text{H}_5\text{OH}$). IR (solution in $\text{C}_2\text{H}_5\text{OH}$, cm^{-1}): 1714 (C=O). ^1H NMR (500 MHz, MeOD): δ_{H} 7.96 (s, 1H, H-Thy), 7.92 (s, 1H, H-triazol), 7.65 (m, 1H, NH), 6.50 (t, 1H, *J* 5.0 Hz, H-1'-ribose), 5.45-5.43 (m, 1H, H-3'-ribose), 4.70, 4.59 (both br s, 2H, H-29), 4.50 (d, 1H, *J* 10.0 Hz, H-3), 4.36-4.34 (m, 1H, H-4'-ribose), 3.93 and 3.80 (1H each, dd, *J* 10.0, 5.0 Hz, H-5'-ribose), 3.33-3.29 (m, 4H, $-\text{CH}_2\text{NH-}$, $\text{CH}_2\text{NHCOCH}_3$), 3.10-3.06 (m, 1H, H-19), 2.96-2.94 (m, 1H, H-2'-ribose), 2.84-2.53 (m, 3H, $=\text{C-CH}_2-$, H-2'-ribose), 2.67 and 2.58 (1H each, d, *J* 15.5 Hz, $-\text{CH}_2\text{-CO-}$), 2.39-0.72 (m, 23H, CH, CH_2 in pentacyclic skeleton and 1H, NH), 1.96 (s, 3H, $-\text{NHCOCH}_3$), 1.92 (s, 3H, CH_3 -Thy), 1.69 (s, 3H, H-30), 1.27 (br s, 6H, $-\text{C}(\text{CH}_3)_2-$), 1.01, 0.94, 0.89, 0.85, 0.83 (all s, 3H each, H-23-H-27). ^{13}C NMR (125 MHz, MeOD): δ_{C} 185.0 (COOH), 179.6 (C-28), 174.3 ($-\text{CH}_2\text{-CO-}$), 173.8 (NHCOCH_3), 166.5 (C=O-Thy), 152.5 (C-20), 152.4 (C=O-Thy), 147.4 (C-triazol), 138.4 (CH-Thy), 124.1 (CH-triazole), 111.8 (C-Thy), 110.2 (C-29), 86.8 (1'-ribose), 86.6 (4'-ribose), 85.1 (C-3), 62.3 (5'-ribose), 60.9 (3'-ribose), 57.1 (C-17), 57.0 (C-5), 52.0 (C-9), 51.5 (C-18), 48.6 (C-19), 46.4 (C-1), 45.8 ($-\text{CH}_2\text{-CO-}$), 43.7 (C-14), 42.2 (C-8), 40.5 (CH_2 in ethylamine), 40.5 (C-4), 40.2 (CH_2 in ethylamine, $-\underline{\text{C}}(\text{CH}_3)_2-$), 39.5 (2'-ribose), 39.2 (C-13), 39.0 (C-22), 38.5 (C-10), 35.5 (C-2, C-7), 34.2 (C-16), 32.0 (C-21), 30.7 (C-15), 29.9 ($=\text{C-CH}_2-$), 29.1 (C-24), 27.0 (C-12), 26.5 ($-\text{C}(\underline{\text{CH}}_3)_2-$), 22.9 (NHCOCH_3), 22.3 (C-11), 19.9 (C-30), 19.6 (C-6), 17.9 (C-23), 17.7 (C-26), 16.9 (C-25), 15.3 (C-27), 12.7 (CH_3 -Thy). Anal. Calcd for $\text{C}_{53}\text{H}_{79}\text{N}_7\text{O}_{10}$: C, 65.34; H, 8.17. Found: C, 65.29, H, 8.23%. MS: m/z $[\text{M}+\text{Na}]^+$, found 995.95 $[\text{C}_{53}\text{H}_{79}\text{N}_7\text{O}_{10}]^+$ requires 996.58.

[1-(3'-Deoxythymidine)-1H-1,2,3-triazole-4-yl]-{[N-2 α -methyl-3 β -O-(3',3'-dimethylsuccinyl)-lup-20,29-en-28-oyl]-8-aminoocetyl}carbamoyl}methane (29). White powder (B, 0.68 g, 64%), mp 194-196 °C. $[\alpha]_D^{21}$ -8.3° (c 0.36, CH₃OH). IR (solution in CH₃OH, cm⁻¹): 1732 (C=O). ¹H NMR (500 MHz, MeOD): δ_H 7.92 (s, 1H, H-Thy), 7.87 (s, 1H, H-triazol), 5.56 (m, 1H, NH), 6.46 (t, 1H, *J* 5.0 Hz, H-1'-ribose), 5.40-5.42 (m, 1H, H-3'-ribose), 4.69, 4.56 (both br s, 2H, H-29), 4.48 (d, 1H, *J* 10.0 Hz, H-3), 4.35-4.33 (m, 1H, H-4'-ribose), 3.90 and 3.77 (1H each, dd, *J* 10.0, 5.0 Hz, H-5'-ribose), 3.26-3.23 (m, 1H, H-19), 3.15-3.03 (m, 4H, -CH₂NH-, CH₂NHCOCH₃), 2.93-2.56 (m, 4H, =C-CH₂-, H-2'-ribose), 2.65 and 2.58 (1H each, d, *J* 15.0 Hz, -CH₂-CO-), 2.38-0.69 (m, 23H, CH, CH₂ in pentacyclic skeleton and 1H, NH), 1.90 (s, 3H, -NHCOCH₃), 1.91 (s, 3H, CH₃-Thy), 1.67 (s, 3H, H-30), 1.33-1.31 (m, 12H, CH₂ in octylamine), 1.26 (br s, 6H, -C(CH₃)₂-), 0.99, 0.93, 0.87, 0.83, 0.81 (all s, 3H each, H-23-H-27). ¹³C NMR (125 MHz, MeOD): δ_C 183.6 (C-28), 183.6 (COOH), 174.0 (-CH₂-CO-), 173.2 (NHCOCH₃), 166.5 (C=O-Thy), 152.5 (C-20, C=O-Thy), 147.4 (C-triazol), 138.4 (CH-Thy), 124.1 (CH-triazol), 111.8 (C-Thy), 110.1 (C-29), 86.8 (1'-ribose), 86.6 (4'-ribose), 85.1 (C-3), 62.3 (5'-ribose), 61.0 (3'-ribose), 57.0 (C-5, C-17), 52.1 (C-9), 51.6 (C-18), 48.2 (C-19), 46.3 (C-1), 45.6 (-CH₂-CO-), 43.7 (C-14), 42.2 (C-8), 40.7 (C-4), 40.7 (CH₂ in octylamine), 40.3 (-C(CH₃)₂-), 40.2 (2'-ribose), 39.6 (C-13), 39.1 (CH₂ in octylamine), 39.0 (C-22), 38.5 (C-10), 35.7 (C-2), 35.6 (C-7), 34.4 (C-16), 32.1 (C-21), 30.7 (C-15, CH₂ in octylamine), 30.5 (CH₂ in octylamine), 30.4 (CH₂ in octylamine), 29.8 (=C-CH₂-), 29.1 (C-24), 28.2 (CH₂ in octylamine), 28.1 (CH₂ in octylamine), 27.1 (C-12), 26.8 (-C(CH₃)₂-), 26.4 (-C(CH₃)₂-), 22.7 (NHCOCH₃), 22.3 (C-11), 19.8 (C-30), 19.6 (C-6), 17.9 (C-26), 17.6 (C-23), 17.0 (C-25), 15.3 (C-27), 12.7 (CH₃-Thy). Anal. Calcd for C₅₉H₉₁N₇O₁₀: C, 66.95; H, 8.67. Found: C, 66.88, H, 8.71%. MS: *m/z* [M+K]⁺, found 1096.53 [C₅₉H₉₁N₇O₁₀]⁺ requires 1096.65.

Acknowledgements

The authors are deeply thankful to the staff members of the analytical center "Agidel" at the Institute of Petrochemistry and Catalysis of RAS for spectral measurement. This work was performed with financial support from the Russian Science Foundation (Grant No. 16-13-10051).

Supplementary Material

Scans of the ¹H NMR and ¹³C NMR spectra of all new compounds.

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