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

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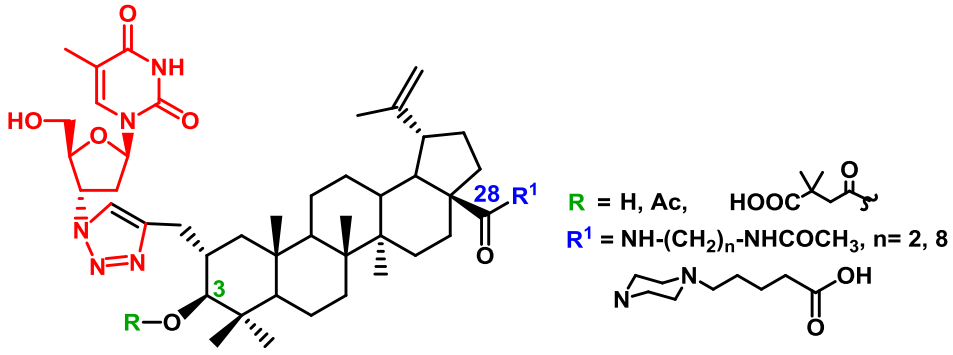
Abstract

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)

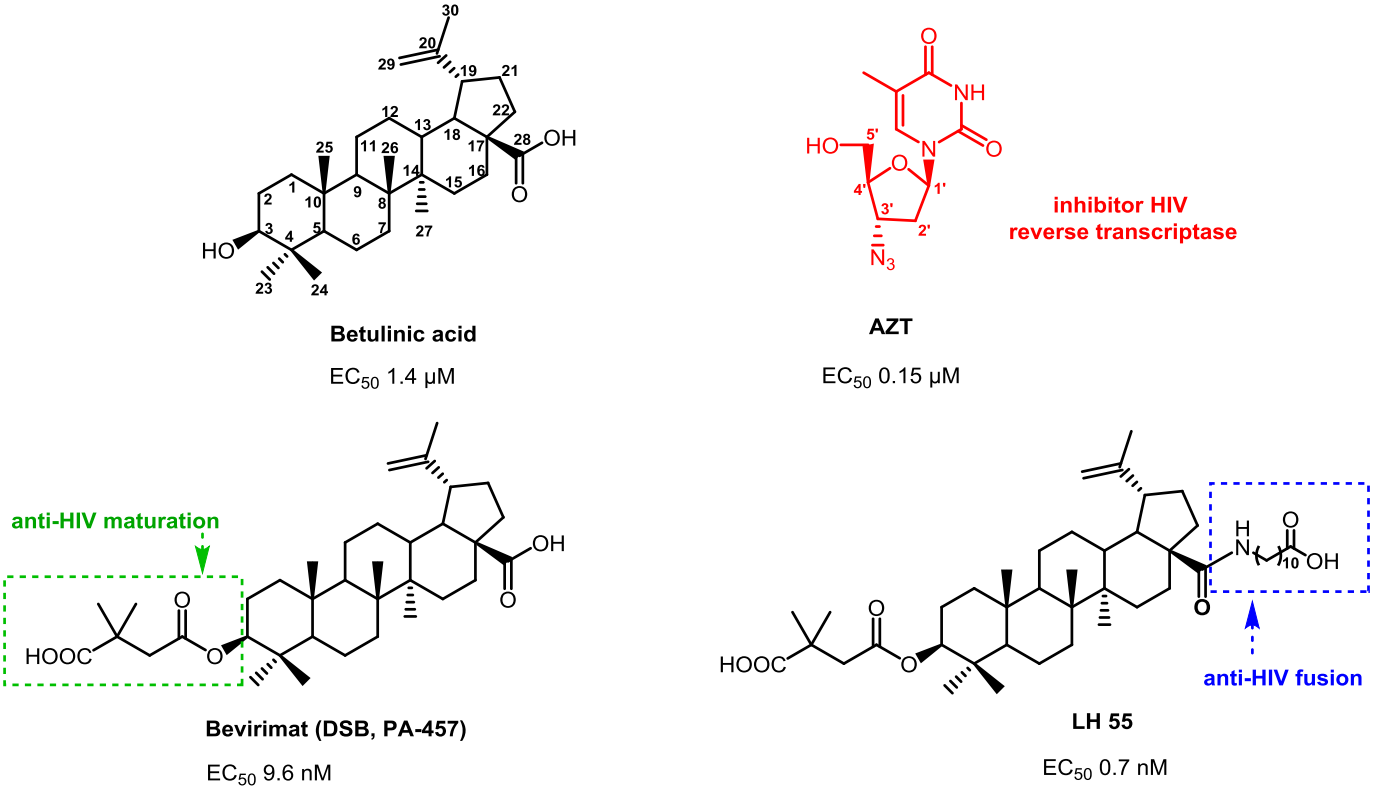


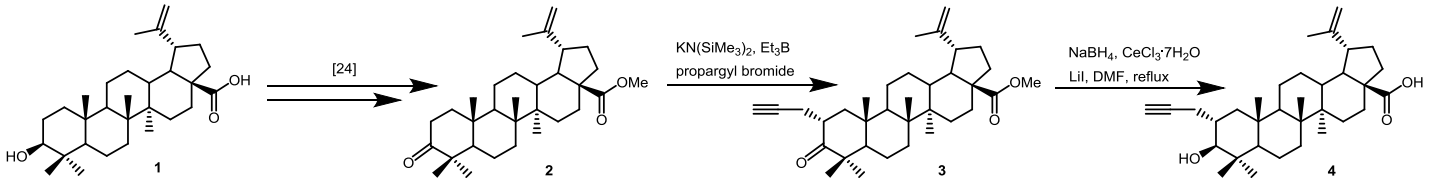
Figure 1. Chemical structures of betulinic acid and derivatives with potent HIV-1 antiviral activity.

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 $KN(SiMe_3)_2$–Et_3B in DME, with propargyl bromide; stereoselective reduction of the 3-oxo group in triterpenoid **3** with $NaBH_4$–$CeCl_3$; and the subsequent demethylation of the sterically hindered 28-ester group on treatment with LiI in DMF (Scheme 1).

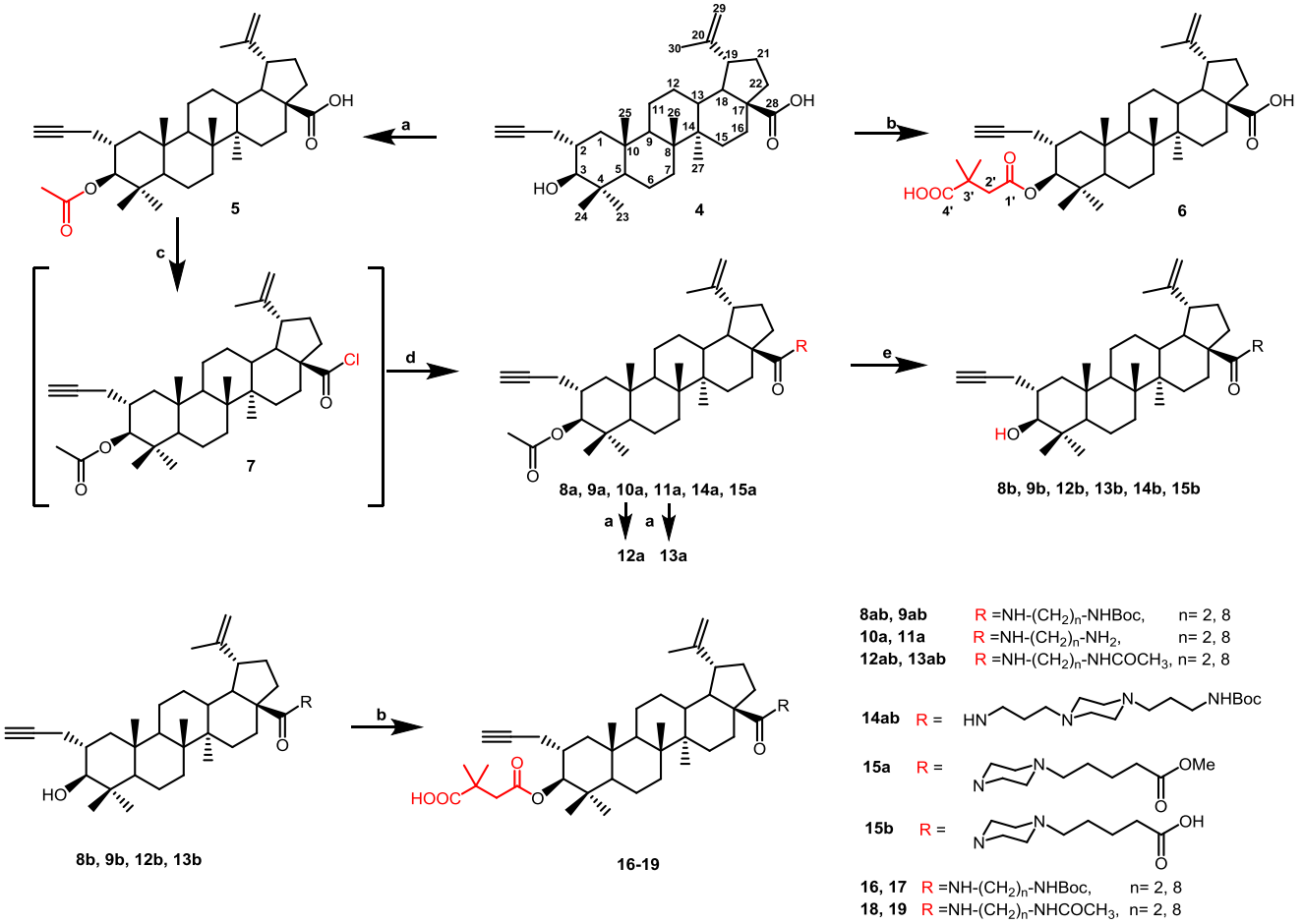


Scheme 1. Synthesis of betulinic acid C-2 propargyl derivatives.

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-



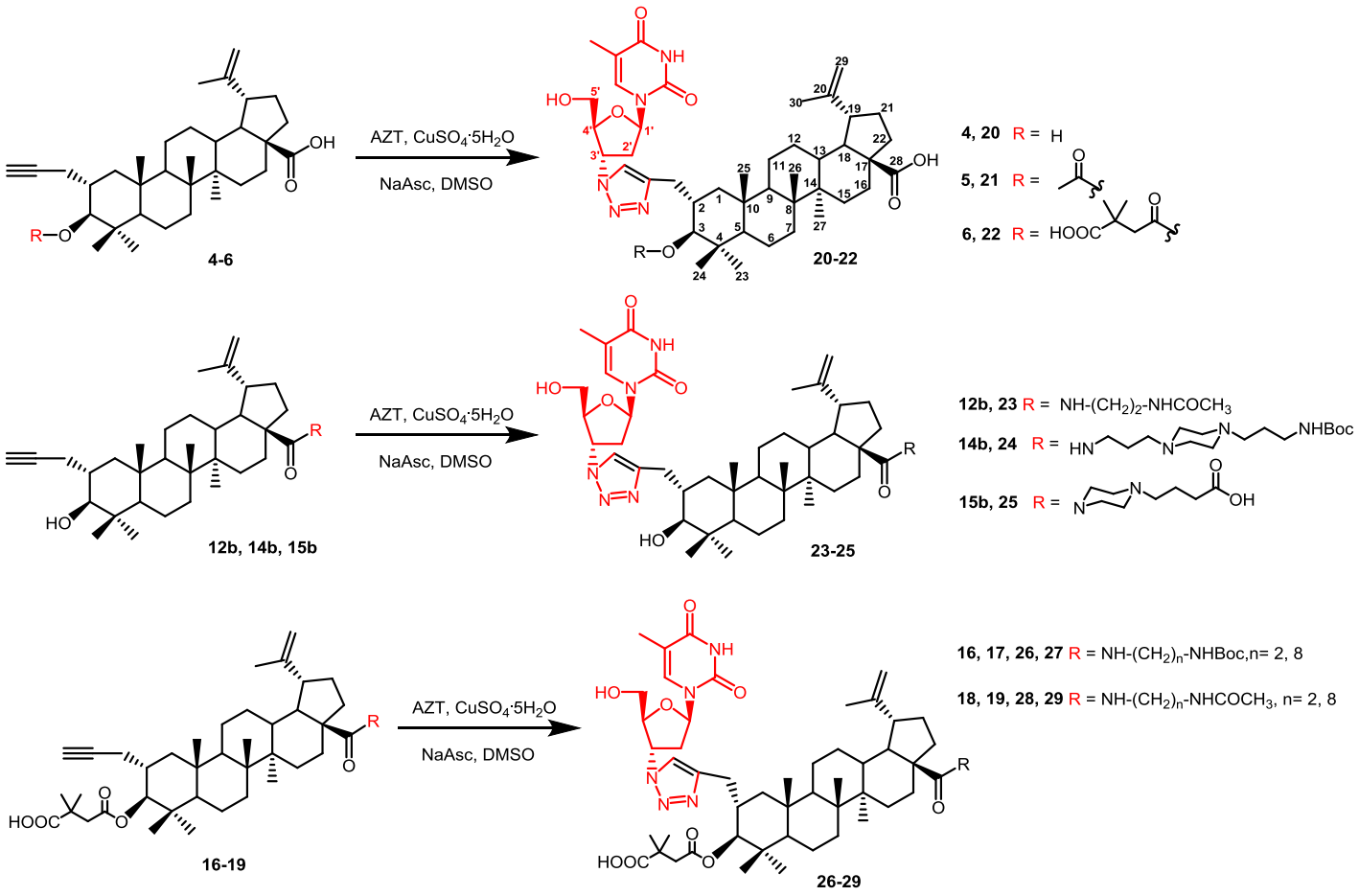
Reagents and conditions: a, Ac_2O, Py, DMAP, rt; *b,* 2,2-Dimethylsuccinic anhydride, Py, DMAP, reflux, Ar; *c,* $(COCl)_2$, CH_2Cl_2, 0°C-20°C; *d,* NH_2-(CH_2)nNH_2 or BocNH-(CH_2)nNH_2, n=2,8 or methyl 5-piperazine pentanoate or N-Boc-bisaminopropylpiperazine, Et_3N, CH_2Cl_2, rt; *e,* 4N NaOH, MeOH, 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 ^oC gave target compounds **20** and **21** in 70% and 55% yields, after column chromatography on SiO_2 (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 $CuSO_4 \cdot 5H_2O$ 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 SiO_2 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 SiO_2 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 acids[18] or N-acetylamines[16]) 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 (^{1}H, ^{13}C, 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 SiO_2, 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 (^{1}H-^{13}C) 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 CH=C-N signals at 7.45-7.90 ppm in the ^{1}H NMR spectra of compounds **20-29**. In the ^{13}C NMR spectra, the signals for the [1,5]-triazole carbon atoms CH=C-N and CH=C-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 $CHCl_3$). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AVANCE–500 instrument (500.13 (^{1}H) and 125.78 MHz (^{13}C)) or on Bruker AVANCE-400 (400.13 (^{1}H) 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%), $KN(SiMe_3)_2$ (1 M solution in THF), propargyl bromide, LiI, CuI, Bu^tOH, $NaBH_4$, $CeCl_3{\cdot}7H_2O$, Et_3N, DMF, DME (dimethoxyethane), acetic anhydride, oxalylcloride, 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 ≥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 CH_2Cl_2 (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 CH_2Cl_2 (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 CH_2Cl_2 (20 mL) and washed three times with brine and distilled water. The organic layer was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The crude products were then chromatographed on silica gel [$CHCl_3$–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. $[\alpha]_D^{19}$ -24° (*c* 0.47, $CHCl_3$). IR (solution in $CHCl_3$, cm^{-1}): 3369, 3312 (NH), 1735, 1717, 1639 (C=O). ^{1}H NMR (500 MHz, $CDCl_3$): 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, –*CH*$_2$NH–, –*CH*$_2$NH–Boc), 3.16-3.10 (m, 1H, H-19), 2.49-0.80 (m, 26H, CH, CH_2 in pentacyclic skeleton and propargyl), 2.09 (s, 3H, $COCH_3$), 1.68 (s, 3H, H-30), 1.44 (s, 9H, $C(CH_3)_3$ in Boc), 0.96, 0.95, 0.89, 0.83, 0.81 (all s, 3H each, H-23–H-27). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 177.2 (C-28), 171.1 ($\underline{C}OCH_3$), 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 (CH_2 in ethylamine, C-8), 40.4 (CH_2 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 (CH_3 in Boc), 28.1 (C-24), 25.6 (C-12), 22.3 (CH_2 in propargyl), 21.0 ($CO\underline{C}H_3$, 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 $C_{42}H_{66}N_2O_5$: C, 74.29; H, 9.80. Found: C, 73.87, H, 9.76%. MS: *m/z* $[M+Na]^+$, found 701.42 $[C_{42}H_{66}N_2O_5]^+$ 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. $[\alpha]_D^{22}$ -23.3° (*c* 0.33, $CHCl_3$). IR (solution in $CHCl_3$, cm^{-1}): 3368, 3312 (NH), 1719, 1698, 1638 (C=O). ^{1}H NMR (500 MHz, $CDCl_3$): 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, –*CH*$_2$NH–, –*CH*$_2$NH–Boc), 2.50-0.80 (m, 26H, CH, CH_2 in pentacyclic skeleton, propargyl and 4H in octylamine) 2.08 (s, 3H, $COCH_3$), 1.67 (s, 3H, H-30), 1.43 (br s, 9H, CH_3 in Boc), 1.33-1.29 (m, 8H, CH_2 in octylamine), 0.96, 0.94, 0.88, 0.82, 0.80 (all s, 3H each, H-23–H-27). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 176.0 (C-28), 171.1 ($\underline{C}OCH_3$), 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 (CH_2 in octylamine), 39.1 (C-4), 38.9 (CH_2 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 (CH_2 in octylamine), 29.8 (C-15), 29.4 (CH_2 in octylamine), 29.2 (CH_2 in octylamine), 28.4 (CH_3 in Boc), 28.1 (C-24), 26.9, 26.7 (CH_2 in octylamine), 25.6 (C-12), 22.3 (CH_2 in propargyl), 21.0 ($CO\underline{C}H_3$, 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 $C_{48}H_{78}N_2O_5$: C, 75.54; H, 10.30. Found: C, 75.48, H, 9.97%. MS: *m/z* $[M+Na]^+$, found 785.36 $[C_{48}H_{78}N_2O_5]^+$ 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. $[\alpha]_D^{18}$ -23° (*c* 0.53, $CHCl_3$). IR (solution in $CHCl_3$, cm^{-1}): 3309 (NH), 1733, 1638 (C=O). ^{1}H NMR (500 MHz, $CDCl_3$): 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, –*CH*$_2$NH–), 3.15-3.10 (m, 1H, H-19), 2.82 (t, 2H, *J* 10.0 Hz, –*CH*$_2$NH$_2$), 2.49-0.80 (m, 26H, CH,

CH_2 in pentacyclic skeleton and propargyl), 2.08 (s, 3H, $COCH_3$), 1.67 (s, 3H, H-30), 0.96, 0.94, 0.88, 0.81, 0.80 (all s, 3H each, H-23–H-27). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 176.6 (C-28), 171.1 ($\underline{C}OCH_3$), 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 (CH_2 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 (CH_2 in propargyl), 21.03 ($CO\underline{C}H_3$, 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 $C_{37}H_{58}N_2O_3$: C, 76.77; H, 10.10. Found: C, 76.87, H, 9.96%. MS: *m/z* $[M+Na]^+$, found 601.73 $[C_{37}H_{58}N_2O_3]^+$ requires 601.43.

8-Aminooctyl-3β-acetoxy-2α-propargyl-lup-20(29)-en-28-oate (**11a**)**.** White powder (0.53 g, 80%), mp 108-110 °C. $[\alpha]_D^{22}$ -21° (*c* 0.53, $CHCl_3$). IR (solution in $CHCl_3$, cm^{-1}): 3311 (NH), 1733, 1636 (C=O). ^{1}H NMR (500 MHz, $CDCl_3$): 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, –*CH*$_2$NH–), 3.18-3.13 (m, 2H, –*CH*$_2$NH–, H-19), 2.68 (t, 2H, *J* 10.0 Hz, –*CH*$_2$NH$_2$), 2.50-0.80 (m, 26H, CH, CH_2 in pentacyclic skeleton and propargyl), 2.09 (s, 3H, $COCH_3$), 1.67 (s, 3H, H-30), 1.32-1.26 (m, 12H, CH_2 in octylamine), 0.95, 0.92, 0.86, 0.81, 0.78 (all s, 3H each, H-23–H-27). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 175.9 (C-28), 171.1 ($\underline{C}OCH_3$), 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 (CH_2 in octylamine), 40.8 (C-8), 39.2 (C-4), 38.9 (CH_2 in octylamine), 38.5 (C-13), 33.8 (CH_2 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 (CH_2 in octylamine), 28.1 (C-24), 27.0, 26.8 (CH_2 in octylamine), 25.6 (C-12), 22.3 (CH_2 in propargyl), 21.0 ($CO\underline{C}H_3$, 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 $C_{43}H_{70}N_2O_3$: C, 77.89; H, 10.64. Found: C, 78.04, H, 10.57%. MS: m/z $[M+H]^+$, found 663.28 $[C_{43}H_{70}N_2O_3]^+$ 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. $[\alpha]_D^{22}$ -21° (*c* 0.50, $CHCl_3$). IR (solution in $CHCl_3$, cm^{-1}): 3367, 3310 (NH), 1733, 1699, 1639 (C=O). ^{1}H NMR (500 MHz, $CDCl_3$): 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, –*CH*$_2$NH–, –*CH*$_2$NH–Boc, H-19), 2.51-2.38 (m, 12H, CH_2 in piperazine and propylamine), 2.19-0.78 (m, 26H, CH, CH_2 in pentacyclic skeleton, propargyl and 4H in propylamine), 2.06 (s, 3H, $COCH_3$), 1.65 (s, 3H, H-30), 1.41 (br s, 9H, CH_3 in Boc), 0.94, 0.92, 0.86, 0.78, 0.75 (all s, 3H each, H-23–H-27). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 176.2 (C-28), 171.1 ($\underline{C}OCH_3$), 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 (CH_2 in propylamine), 55.4 (C-17), 55.3 (C-5), 53.5, 53.1 (CH_2 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 (CH_2 in propylamine), 39.5 (C-4), 38.9 (CH_2 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 ($\underline{C}H_3$ in Boc), 28.1 (C-24), 26.4 (CH_2 in propylamine), 25.5 (C-12), 25.1 (CH_2 in propylamine), 22.3 (CH_2 in propargyl), 21.0 ($CO\underline{C}H_3$, 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 $C_{50}H_{82}N_4O_5$: C, 73.31; H, 10.09. Found: C, 73.24, H, 9.87%. MS: *m/z* $[M+H]^+$, found 819.52 $[C_{50}H_{82}N_4O_5]^+$ 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. $[\alpha]_D^{18}$ -25.45° (*c* 0.64, $CHCl_3$). IR (solution in $CHCl_3$, cm^{-1}): 1736, 1632 (C=O). ^{1}H NMR (500 MHz, $CDCl_3$): 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, $COOCH_3$), 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, CH_2 in pentacyclic skeleton, propargyl, 8H in pentanoate), 2.06 (s, 3H, $COCH_3$), 1.65 (s, 3H, H-30), 0.93, 0.92, 0.87, 0.80, 0.78 (all s, 3H each, H-23–H-27). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 173.9 ($\underline{C}OOCH_3$), 173.4 (C-28), 171.0 ($\underline{C}OCH_3$), 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 (CH_2 in pentanoate), 54.5 (C-17), 53.4 (CH_2 in piperazine), 52.6 (C-18), 51.5 ($COO\underline{C}H_3$), 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 (CH_2 in piperazine), 32.5 (C-16), 31.2 (C-21), 29.7 (C-15), 28.1 (C-24), 26.1 (CH_2 in pentanoate), 25.3 (C-12), 22.3 (CH_2 in propargyl), 22.8 (CH_2 in pentanoate), 21.2 (C-11), 21.0 ($CO\underline{CH_3}$), 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 $C_{45}H_{70}N_2O_5$: C, 75.17; H, 9.81. Found: C, 75.21, H, 9.74%. MS: *m/z* $[M-H]^+$, found 717.36 $[C_{45}H_{70}N_2O_5]^+$ 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 H_2O (10 mL) and extracted with EtOAc (4×10 mL). The combined extracts were washed with brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The crude products were then chromatographed on silica gel [$CHCl_3$–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. $[\alpha]_D^{18}$ -24° (*c* 0.44, $CHCl_3$). IR (solution in $CHCl_3$, cm^{-1}): 3310 (NH), 1734, 1718, 1637 (C=O). ^{1}H NMR (500 MHz, $CDCl_3$): 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, –*CH*$_2$NH–, *CH*$_2$NHCOCH$_3$), 3.12-3.07 (m, 1H, H-19), 2.47-0.80 (m, 26H, CH, CH_2 in pentacyclic skeleton and propargyl), 2.09 (s, 3H, $COCH_3$), 1.99 (s, 3H, –NHCO*CH*$_3$), 1.68 (s, 3H, H-30), 0.96, 0.93, 0.88, 0.82, 0.80 (all s, 3H each, H-23–H-27). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 178.1 (C-28), 171.3 (NH$\underline{C}$OCH$_3$), 171.1 ($\underline{C}OCH_3$), 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 (CH_2 in ethylamine, C-4), 39.7 (CH_2 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 (NHCO$\underline{CH_3}$), 22.3 (CH_2 in propargyl), 21.0 ($CO\underline{CH_3}$, 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 $C_{39}H_{60}N_2O_4$: C, 75.44; H, 9.74. Found: C, 74.38, H, 9.69%. MS: *m/z* $[M+Na]^+$, found 643.37 $[C_{39}H_{60}N_2O_4]^+$ requires 643.45.

{[*N*-(3β-Acetoxy-2α-propargyl-lup-20(29)-en-28-oyl)-8-aminooctyl]carbamoyl}methane (**13a**)**.** White powder (0.56 g, 80%), mp 106-108 °C. $[\alpha]_D^{22}$ -23° (*c* 0.48, $CHCl_3$). IR (solution in $CHCl_3$, cm^{-1}): 3311 (NH), 1733 (C=O). ^{1}H NMR (500 MHz, $CDCl_3$): 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, –*CH*$_2$NH–, *CH*$_2$NHCOCH$_3$, H-19), 2.47-0.80 (m, 26H, CH, CH_2 in pentacyclic skeleton and propargyl), 2.08 (s, 3H, $COCH_3$), 1.97 (s, 3H, –NHCO*CH*$_3$), 1.67 (s, 3H, H-30), 1.37-1.30 (m, 12H, CH_2 in octylamine), 0.96, 0.94, 0.88, 0.82, 0.80 (all s, 3H each, H-23–H-27). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 176.0 (C-28), 171.1 ($\underline{C}OCH_3$), 170.0 (NH$\underline{C}$OCH$_3$), 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 (CH_2 in octylamine), 39.1 (C-4), 38.9 (CH_2 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 (CH_2 in octylamine), 29.6 (C-15), 29.4 (CH_2 in octylamine), 29.1 (CH_2 in octylamine), 28.1 (C-24), 26.8 (CH_2 in octylamine), 25.6 (C-12), 23.3 (NHCO$\underline{CH_3}$), 22.3 (CH_2 in propargyl), 21.0 ($CO\underline{CH_3}$, 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 $C_{45}H_{72}N_2O_4$: C, 76.66; H, 10.29. Found: C, 76.71, H, 10.32%. MS: *m/z* $[M+H]^+$, found 705.26 $[C_{45}H_{72}N_2O_4]^+$ 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 CH_2Cl_2. The organic layer was washed with brine and dried over anhydrous $MgSO_4$ and concentrated under reduced pressure to obtain pure compounds **8b, 9b, 12b-15b**.

***N*-[3β-Hydroxy-2α-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, CH_2Cl_2). IR (solution in CH_2Cl_2, cm^{-1}): 3366, 3311 (NH), 1697, 1639 (C=O). ^{1}H NMR (500 MHz, $CDCl_3$): 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, –*CH*$_2$NH–, –*CH*$_2$NH–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, CH_2 in pentacyclic skeleton and propargyl), 1.64 (s, 3H, H-30), 1.40 (s, 9H, CH_3 in Boc), 0.95, 0.94, 0.91, 0.83, 0.75 (all s, 3H each, H-23–H-27). ^{13}C NMR (125 MHz, $CDCl_3$): 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 (CH_2 in ethylamine, C-8), 40.3 (CH_2 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 (CH_3 in Boc, C-24), 25.6 (C-12), 22.4 (CH_2 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 $C_{40}H_{64}N_2O_4$: C, 75.43; H, 10.13. Found: C, 75.37, H, 10.01%. MS: *m/z* $[M+Na]^+$, found 659.45 $[C_{40}H_{64}N_2O_4]^+$ requires 659.48.

***N*-[3β-Hydroxy-2α-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, $CHCl_3$). IR (solution in $CHCl_3$, cm^{-1}): 3366, 3311 (NH), 1697, 1636 (C=O). ^{1}H NMR (500 MHz, $CDCl_3$): 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, –*CH*$_2$NH–, –*CH*$_2$NH–Boc), 2.99 (d, 1H, *J* 10.0 Hz, H-3), 2.50-0.79 (m, 26H, CH, CH_2 in pentacyclic skeleton, propargyl and 4H in octylamine), 1.68 (s, 3H, H-30), 1.45 (br s, 9H, CH_3 in Boc), 1.36-1.31 (m, 8H, CH_2 in octylamine), 0.99, 0.98, 0.87, 0.80, 0.79 (all s, 3H each, H-23–H-27). ^{13}C NMR (125 MHz, $CDCl_3$): 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 (CH_2 in octylamine), 39.2 (CH_2 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 (CH_2 in octylamine), 29.8 (C-15), 29.4 (CH_2 in octylamine), 29.2 (CH_2 in octylamine), 28.4 (CH_3 in Boc), 28.3 (C-24), 26.9 (CH_2 in octylamine), 26.7 (CH_2 in octylamine), 25.6 (C-12), 22.4 (CH_2 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 $C_{46}H_{76}N_2O_4$: C, 76.62; H, 10.62. Found: C, 76.58, H, 10.57%. MS: *m/z* $[M+K]^+$, found 759.46 $[C_{46}H_{76}N_2O_4]^+$ requires 759.54.

{[*N*-(3β-Hydroxy-2α-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, $CHCl_3$). IR (solution in $CHCl_3$, cm^{-1}): 3310 (NH), 1637 (C=O). ^{1}H NMR (500 MHz, $CDCl_3$): 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, –*CH*$_2$NH–, *CH*$_2$NHCOCH$_3$), 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, CH_2 in pentacyclic skeleton and propargyl), 1.99 (s, 3H, –NHCO*CH*$_3$), 1.68 (s, 3H, H-30), 0.99, 0.98, 0.93, 0.82, 0.78 (all s, 3H each, H-23–H-27). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 178.1 (C-28), 171.4 (NH<u>C</u>OCH$_3$), 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, CH_2 in ethylamine), 39.7 (CH_2 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 (NHCO<u>C</u>H$_3$), 22.4 (CH_2 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 $C_{37}H_{58}N_2O_3$: C, 76.77; H, 10.10. Found: C, 76.82, H, 10.04%. MS: *m/z* $[M+Na]^+$, found 601.36 $[C_{37}H_{58}N_2O_3]^+$ requires 601.43.

{[*N*-(3β-Hydroxy-2α-propargyl-lup-20(29)-en-28-oyl)-8-aminooctyl]carbamoyl}methane (**13b**)**.** White powder (0.59 g, 89%), mp 112-114 °C. $[\alpha]_D^{22}$ -9.7° (*c* 0.29, $CHCl_3$). IR (solution in $CHCl_3$, cm^{-1}): 3309 (NH), 1637 (C=O). ^{1}H NMR (500 MHz, $CDCl_3$): 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, –*CH*$_2$NH–, *CH*$_2$NHCOCH$_3$, H-19), 2.98 (d, 1H, *J* 10.0 Hz, H-3), 2.45-0.80 (m, 26H, CH, CH_2 in pentacyclic skeleton and propargyl), 1.97 (s, 3H, –NHCO*CH*$_3$), 1.67 (s, 3H, H-30), 1.37-1.29 (m, 12H, CH_2 in octylamine), 0.98, 0.97, 0.93, 0.85, 0.77 (all s, 3H each, H-23–H-27). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 176.0 (C-28), 170.1 (NH<u>C</u>OCH$_3$), 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 (CH_2 in octylamine), 39.1 (C-4, CH_2 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 (CH_2 in octylamine), 29.5 (C-15), 29.4 (CH_2 in octylamine), 29.1 (CH_2 in octylamine), 29.1 (CH_2 in octylamine), 28.32 (C-24), 26.8 (CH_2 in octylamine), 25.6 (C-12), 23.3 (NHCO$\underline{CH_3}$), 22.4 (CH_2 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 $C_{43}H_{70}N_2O_4$: C, 77.89; H, 10.64. Found: C, 77.92, H, 10.57%. MS: *m/z* $[M+H]^+$, found 663.39 $[C_{43}H_{70}N_2O_4]^+$ 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. $[\alpha]_D^{22}$ -8° (*c* 0.52, $CHCl_3$). IR (solution in $CHCl_3$, cm^{-1}): 3351, 3309 (NH), 1697, 1638 (C=O). ^{1}H NMR (500 MHz, $CDCl_3$): 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, –*CH*$_2$NH–, –*CH*$_2$NH–Boc, H-19), 2.96 (d, 1H, *J* 10.0 Hz, H-3), 2.50-2.39 (m, 12H, CH_2 in piperazine and propylamine), 2.29-0.70 (m, 26H, CH, CH_2 in pentacyclic skeleton, propargyl and 4H in propylamine), 1.67 (s, 3H, H-30), 1.41 (br s, 9H, CH_3 in Boc), 0.96, 0.95, 0.92, 0.84, 0.76 (all s, 3H each, H-23–H-27). ^{13}C NMR (125 MHz, $CDCl_3$): 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 (CH_2 in propylamine), 56.8 (CH_2 in propylamine), 55.5 (CH_2 in piperazine), 55.4 (CH_2 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 (CH_2 in propylamine), 39.1 (C-4), 39.0 (CH_2 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 (CH_3 in Boc, C-24), 26.4 (CH_2 in propylamine), 25.6 (C-12), 25.0 (CH_2 in propylamine), 22.3 (CH_2 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 $C_{48}H_{80}N_4O_4$: C, 74.18; H, 10.38. Found: C, 74.24, H, 9.84%. MS: *m/z* $[M+H]^+$, found 777.56 $[C_{48}H_{80}N_4O_4]^+$ 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. $[\alpha]_D^{22}$ -25.5° (*c* 0.5, CH_3OH). IR (solution in CH_3OH, cm^{-1}): 1633 (C=O). ^{1}H NMR (500 MHz, MeOD): δ_H 4.70, 4.59 (both br s, 2H, H-29), 3.19-3.15 (m, 2H, CH_2 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, CH_2 in pentacyclic skeleton, propargyl, 12H in piperazine-pentanoic acid), 2.40-2.37 (m, 2H, -C*H*$_2$COOH), 1.65 (s, 3H, H-30), 1.00, 0.96, 0.95, 0.88, 0.75 (all s, 3H each, H-23–H-27). ^{13}C 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, CH_2 in pentanoic acid), 58.5 (C-17), 56.4 (C-18), 56.0 (CH_2 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 (CH_2 in piperazine), 36.2 (C-16), 35.0 (C-21), 33.7 (C-15), 32.0 (C-24), 29.5 (C-12), 27.4 (CH_2 in pentanoic acid), 26.0 (CH_2 in propargyl), 25.9 (CH_2 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 $C_{42}H_{66}N_2O_4$: C, 76.09; H, 10.03. Found: C, 75.94, H, 9.97%. MS: *m/z* $[M+H]^+$, found 663.27 $[C_{42}H_{66}N_2O_4]^+$ 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 H_2O (30 mL) and extracted with EtOAc (4×30 mL). The combined extracts were washed with brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The crude products were then chromatographed on silica gel [$CHCl_3$–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. $[\alpha]_D^{19}$ -29.8° (*c* 0.59, $CHCl_3$). IR (solution in $CHCl_3$, cm^{-1}): 1733, 1700 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$): 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, –*CH*$_2$-CO–), 2.21-0.80 (m, 26H, CH, CH_2 in pentacyclic skeleton and propargyl), 1.70 (s, 3H, H-

30), 1.35 (br s, 6H, –C*(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 (–CH_2-<u>C</u>O–), 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 (–<u>C</u>H$_2$-CO–), 42.4 (C-14), 40.7 (C-8), 40.4 (–<u>C</u>(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 (–C(<u>C</u>H$_3$)$_2$–), 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 $C_{39}H_{58}O_6$: C, 75.20; H, 9.39. Found: C, 75.34, H, 9.43%. MS: *m/z* $[M+Na]^+$, found 645.30 $[C_{39}H_{58}O_6]^+$ requires 645.41.

***N*-[3β-*O*-(3',3'-Dimethylsuccinyl)-2α-propargyl-lup-20(29)-en-28-oyl]-N'-(tert-butoxycarbonyl)-2-ethylamine** (**16**)**.** White powder (0.34 g, 45%), mp 110-112 °C. $[\alpha]_D^{23}$ -20.6° (*c* 0.47, $CHCl_3$). IR (solution in $CHCl_3$, cm^{-1}): 3369, 3312 (NH), 1735, 1717, 1639 (C=O). ^{1}H 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, –*CH$_2$*NH–, –*CH$_2$*NH–Boc), 3.15-3.11 (m, 1H, H-19), 2.70-2.66 (m, 2H, –*CH$_2$*-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, –C*(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 (–CH_2-<u>C</u>O–), 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 (–<u>C</u>H$_2$-CO–), 42.5 (C-14), 40.8 (C-8), 40.6 (CH_2 in ethylamine), 40.3 (CH_2 in ethylamine, –<u>C</u>(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 (–C(<u>C</u>H$_3$)$_2$–), 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 $C_{46}H_{72}N_2O_7$: C, 72.21; H, 9.49. Found: C, 72.26, H, 9.58%. MS: *m/z* $[M+Na]^+$, found 787.49 $[C_{46}H_{72}N_2O_7]^+$ requires 787.52.

***N*-[3β-*O*-(3',3'-Dimethylsuccinyl)-2α-propargyl-lup-20(29)-en-28-oyl]-*N'*-(tert-butoxycarbonyl)-8-octylamine** (**17**)**.** White powder (0.76 g, 90%), mp 90-92 °C. $[\alpha]_D^{21}$ -18.3° (*c* 0.3, $CHCl_3$). IR (solution in $CHCl_3$, cm^{-1}): 3311 (NH), 1711, 1639 (C=O). ^{1}H 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, –*CH$_2$*NH–, –*CH$_2$*NH–Boc, H-19), 2.70-2.66 (m, 2H, –*CH$_2$*-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, –C*(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 (–CH_2-<u>C</u>O–), 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 (–<u>C</u>H$_2$-CO–), 42.5 (C-14), 40.8 (C-8), 40.6 (CH_2 in octylamine), 40.3 (–<u>C</u>(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 (–C(<u>C</u>H$_3$)$_2$–), 25.5 (–C(<u>C</u>H$_3$)$_2$–), 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 $C_{52}H_{84}N_2O_7$: C, 73.54; H, 9.97. Found: C, 73.48, H, 10.11%. MS: *m/z* $[M+K]^+$, found 887.59 $[C_{52}H_{84}N_2O_7]^+$ requires 887.59.

{[*N*-(3β-*O*-(3',3'-Dimethylsuccinyl)-2α-propargyl-lup-20(29)-en-28-oyl)-2-aminoethyl]-carbamoyl}methane (**18**)**.** White powder (0.30 g, 42%), mp 154-156 °C. $[\alpha]_D^{23}$ -22.3° (*c* 0.44, CH_2Cl_2). IR (solution in CH_2Cl_2, cm^{-1}): 3371, 3311 (NH), 1735, 1640 (C=O). ^{1}H 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, –*CH$_2$*NH–, *CH$_2$*NHCOCH$_3$), 3.10-3.09 (m, 1H, H-19), 2.71-2.61 (m, 2H, –*CH$_2$*-CO–), 2.46-0.80 (m, 26H, CH, CH_2 in pentacyclic skeleton and propargyl), 1.99 (s, 3H, –NHCO*CH$_3$*), 1.67 (s, 3H, H-30), 1.31 (br s, 6H, –C*(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 (–CH_2-<u>C</u>O–), 171.4 (NH<u>C</u>OCH$_3$), 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 (–<u>C</u>H$_2$-CO–), 42.5 (C-14), 40.8 (C-8), 40.6 (CH_2 in

ethylamine), 40.2 (CH_2 in ethylamine, –$\underline{C}(CH_3)_2$–), 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 (–C($\underline{CH_3}$)$_2$–), 25.5 (–C($\underline{CH_3}$)$_2$–), 25.3 (C-12), 23.1 (NHCO$\underline{CH_3}$), 22.2 (CH_2 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 $C_{43}H_{66}N_2O_6$: C, 73.05; H, 9.41. Found: C, 73.10, H, 9.38%. MS: *m/z* $[M+Na]^+$, found 729.49 $[C_{43}H_{66}N_2O_6]^+$ requires 729.48.

{[*N*-(3β-*O*-(3',3'-Dimethylsuccinyl)-2α-propargyl-lup-20(29)-en-28-oyl)-8-aminooctyl]-carbamoyl}methane (19). White powder (0.39 g, 49%), mp 112-114 °C. $[\alpha]_D^{22}$ -22.2° (*c* 0.36, $CHCl_3$). IR (solution in $CHCl_3$, cm^{-1}): 3308 (NH), 1733 (C=O). ^{1}H NMR (500 MHz, $CDCl_3$): 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, –*CH*$_2$NH–, *CH*$_2$NHCOCH$_3$, H-19), 2.70-2.59 (m, 2H, –*CH*$_2$-CO–), 2.49-0.80 (m, 26H, CH, CH_2 in pentacyclic skeleton and propargyl), 1.94 (s, 3H, –NHCO*CH*$_3$), 1.67 (s, 3H, H-30), 1.55-1.25 (m, 18H, CH_2 in octylamine and CH_3 in –C*(CH*$_3$*)*$_2$–), 0.96, 0.93, 0.87, 0.80, 0.79 (all s, 3H each, H-23–H-27). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 181.9 (COOH), 176.1 (C-28), 171.2 (–CH_2-$\underline{C}$O–), 170.7 (NH$\underline{C}$OCH$_3$), 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 (–$\underline{CH_2}$-CO–), 42.5 (C-14), 40.8 (C-8), 40.3 (–$\underline{C}(CH_3)_2$–), 39.7 (CH_2 in octylamine), 39.2 (CH_2 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 (CH_2 in octylamine), 29.4 (CH_2 in octylamine), 29.1(CH_2 in octylamine), 28.1 (C-24), 26.8 (CH_2 in octylamine), 25.6 (–C($\underline{CH_3}$)$_2$–), 25.5 (–C($\underline{CH_3}$)$_2$–), 25.4 (C-12), 23.3 (NHCO$\underline{CH_3}$), 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 $C_{49}H_{78}N_2O_6$: C, 74.39; H, 9.94. Found: C, 74.43, H, 10.06%. MS: *m/z* $[M+Na]^+$, found 813.36 $[C_{49}H_{78}N_2O_6]^+$ requires 813.58.

General procedure for click reactions. A. To a solution of alkyne **4** or **5** (1 mmol) in Bu^{t}OH (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 [$CHCl_3$–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), $CuSO_4 \cdot 5H_2O$ (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 [$CHCl_3$–MeOH (100:1→1:1)] to obtain pure compounds **20-29**.

[1-(3'-Deoxythymidine)-1*H*-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. $[\alpha]_D^{18}$ -25.3° (*c* 0.55, CH_3OH). IR (solution in CH_3OH, cm^{-1}): 1682 (C=O). ^{1}H 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-C*H*$_2$-), 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-C*H*$_2$-), 2.29-0.60 (m, 23H, CH, CH_2 in pentacyclic skeleton), 1.92 (s, 3H, CH_3-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). ^{13}C 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-$\underline{CH_2}$-), 29.2 (C-24), 27.0 (C-12), 22.2 (C-11), 19.8 (C-6, C-30), 17.9 (C-26), 17.7 (CH_3-Thy), 16.8 (C-23, C-25), 15.4 (C-27). Anal. Calcd for $C_{43}H_{63}N_5O_7$: C, 67.78; H, 8.33. Found: C, 68.32, H, 8.28%. MS: *m/z* $[M+Na]^+$, found 784.33 $[C_{43}H_{63}N_5O_7]^+$ requires 784.46.

[1-(3'-Deoxythymidine)-1*H*-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. $[\alpha]_D^{22}$ -14° (*c* 0.65, CH_3OH). IR (solution in CH_3OH, cm^{-1}): 1696 (C=O). ^{1}H 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-CH_2-), 2.52 (dd, 1H, *J* 15.0, 10.0 Hz, =C-CH_2-), 2.27-0.60 (m, 23H, CH, CH_2 in pentacyclic skeleton), 2.07 (s, 3H, CH_3-Thy), 1.93 (s, 3H, $COCH_3$), 1.72 (s, 3H, H-30), 1.03, 0.96, 0.90, 0.86, 0.84 (all s, 3H each, H-23–H-27). ^{13}C NMR (125 MHz, MeOD): δ_C 178.5 (C-28), 171.8 (COCH_3), 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-CH_2-), 27.4 (C-24), 25.4 (C-12), 20.7 (C-11), 19.6 ($COCH_3$), 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 (CH_3-Thy). Anal. Calcd for $C_{45}H_{65}N_5O_8$: C, 67.22; H, 8.15. Found: C, 67.34, H, 8.24%. MS: *m/z* $[M+Na]^+$, found 826.27 $[C_{45}H_{65}N_5O_8]^+$ requires 826.47.

[1-(3'-Deoxythymidine)-1*H*-1,2,3-triazol-4-yl]-2α-methyl-3β-*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, CH_3OH). IR (solution in CH_3OH, cm^{-1}): 1697 (C=O). ^{1}H 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, –*CH_2*-CO–), 2.53-2.30 (m, 3H, H-2'-ribose, =C-CH_2-), 2.03-0.50 (m, 23H, CH, CH_2 in pentacyclic skeleton), 1.71 (s, 3H, CH_3-Thy), 1.45 (s, 3H, H-30), 1.04 (br s, 6H, –*C$(CH_3)_2$*–), 0.75, 0.71, 0.63, 0.62, 0.58 (all s, 3H each, H-23–H-27). ^{13}C NMR (125 MHz, MeOD): δ_C 182.8 (COOH), 179.7 (C-28), 172.7 (–CH_2-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 (–CH_2-CO–), 42.0 (C-14), 40.3 (–C$(CH_3)_2$–), 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-CH_2-), 27.7 (C-24), 25.7 (–C$(CH_3)_2$–), 25.0 (C-12), 25.0 (–C$(CH_3)_2$–), 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 (CH_3-Thy). Anal. Calcd for $C_{49}H_{71}N_5O_{10}$: C, 66.12; H, 8.04. Found: C, 66.23, H, 8.12%. MS: *m/z* $[M+Na]^+$, found 912.49 $[C_{49}H_{71}N_5O_{10}]^+$ requires 912.51.

[1-(3'-Deoxythymidine)-1*H*-1,2,3-triazol-4-yl]-{[*N*-(2α-methyl-3β-hydroxy-lup-20(29)-en-28-oyl)-2-amino-ethyl]carbamoyl}methane (**23**). White powder (B, 0.57 g, 67%), mp 192-194 °C. $[\alpha]_D^{22}$ -23.3° (*c* 0.54, CH_3OH). IR (solution in CH_3OH, cm^{-1}): 3311 (NH), 1636 (C=O). ^{1}H 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, –*CH_2*NH–, *CH_2*NHCOCH_3), 3.19 (d, 1H, *J* 15.0 Hz, =C-CH_2-), 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-CH_2-), 2.12-0.59 (m, 23H, CH, CH_2 in pentacyclic skeleton and 1H, NH), 1.95 (s, 3H, –NHCO*CH_3*), 1.92 (s, 3H, CH_3-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). ^{13}C NMR (125 MHz, MeOD): δ_C 179.7 (C-28), 173.8 (NHCOCH_3), 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 (CH_2 in ethylamine), 40.3 (CH_2 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-CH_2-), 29.2 (C-24), 27.1 (C-12), 22.9 (NHCOCH_3), 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 (CH_3-Thy). Anal. Calcd for $C_{47}H_{71}N_7O_7$: C, 66.72; H, 8.46. Found: C, 66.65, H, 8.51%. MS: *m/z* $[M+K]^+$, found 884.36 $[C_{47}H_{71}N_7O_7]^+$ requires 884.51.

{[1-(3'-Deoxythymidine)-1*H*-1,2,3-triazol-4-yl]-N-[N'-(tert-butoxycarbonyl)-{3-[4-(3-aminopropyl)piperazin-yl]propyl}}-2α-methyl betulinic acid amide (**24**)**.** White powder (B, 0.75 g, 72%), mp 142-144 °C. $[\alpha]_D^{22}$ -13° (*c* 0.63, CH_3OH). IR (solution in CH_3OH, 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, –*CH*$_2$NH–, –*CH*$_2$NH–Boc, H-19, H-2'-ribose, =C-C*H*$_2$-), 2.82 (d, 1H, *J* 12.0 Hz, H-3), 2.79-2.36 (m, 14H, CH_2 in piperazine and propylamine, H-2'-ribose, =C-C*H*$_2$-), 2.14-0.58 (m, 23H, CH, CH_2 in pentacyclic skeleton, 4H in propylamine and 2H, NH), 1.93 (s, 3H, CH_3-Thy), 1.70 (s, 3H, H-30), 1.45 (br s, 9H, CH_3 in Boc), 0.99, 0.98, 0.95, 0.83, 0.81 (all s, 3H each, H-23–H-27). ^{13}C 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 (CH_2 in propylamine), 57.0 (C-5, C-17), 56.8 (CH_2 in propylamine), 55.8, 53.7 (CH_2 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 (CH_2 in propylamine), 39.1 (2'-ribose), 38.9 (CH_2 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-<u>CH</u>$_2$-), 29.2 (C-24), 29.0 (CH_3 in Boc), 27.7 (CH_2 in propylamine), 27.4 (CH_2 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 (CH_3-Thy). Anal. Calcd for $C_{58}H_{93}N_9O_8$: C, 66.70; H, 8.98. Found: C, 66.67, H, 8.87%. MS: *m/z* $[M+H]^+$, found 1044.65 $[C_{58}H_{93}N_9O_8]^+$ requires 1044.72.

{[1-(3'-Deoxythymidine)-1*H*-1,2,3-triazol-4-yl]-[*N*-2α-methyl-3β-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 CH_3OH, 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 CH_2 in piperazine), 3.10-3.06 (m, 1H, H-19), 3.00-2.68 (m, 12H, H-3, H-13, H-2'-ribose, =C-C*H*$_2$-, CH_2 in piperazine and pentanoic acid), 2.19-0.78 (m, 22H, CH, CH_2 in pentacyclic skeleton and 6H in pentanoic acid), 1.94 (s, 3H, CH_3-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). ^{13}C 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, CH_2 in pentanoic acid), 54.4 (C-17), 53.3 (CH_2 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 (CH_2 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-<u>CH</u>$_2$-), 26.2 (CH_2 in pentanoic acid), 25.7 (C-12), 23.4 (CH_2 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 (CH_3-Thy). Anal. Calcd for $C_{52}H_{79}N_7O_8$: C, 67.14; H, 8.56. Found: C, 67.21, H, 8.53%. MS: *m/z* $[M+K]^+$, found 968.48 $[C_{52}H_{79}N_7O_8]^+$ requires 968.56.

[1-(3'-Deoxythymidine)-1*H*-1,2,3-triazol-4-yl]-{[*N*-2α-methyl-3β-*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 C_2H_5OH). IR (solution in C_2H_5OH, 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, –*CH*$_2$NH–, –*CH*$_2$NH–Boc), 3.10-3.07 (m, 1H, H-19), 2.95-2.52 (m, 4H, CH_2, H-2'-ribose, =C-C*H*$_2$-), 2.67 and 2.59 (1H, each, d, *J* 15.5 Hz, –*CH*$_2$-CO–), 2.37-0.85 (m, 23H, CH, CH_2 in pentacyclic skeleton and 1H, NH), 1.93 (s, 3H, CH_3-Thy), 1.70 (s, 3H, H-30), 1.44 (s, 9H, CH_3 in Boc), 1.27 (br s, 6H, – C*(CH*$_3$*)*$_2$–), 1.01, 0.96, 0.89, 0.85, 0.84 (all s, 3H each, H-23–H-27). ^{13}C NMR (125 MHz, MeOD): δ_C 182.8 (COOH), 179.8 (C-28), 174.5 (–CH_2-<u>C</u>O–), 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 (–$\underline{C}H_2$-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, –$\underline{C}(CH_3)_2$–), 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 (=C-$\underline{C}H_2$-), 29.1 (C-24), 29.0 (–C($\underline{C}H_3)_2$–), 28.9 (CH_3 in Boc), 27.0 (C-12, –C($\underline{C}H_3)_2$–), 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 $C_{56}H_{85}N_7O_{11}$: C, 65.15; H, 8.30. Found: C, 65.21, H, 8.27%. MS: *m/z* $[M+Na]^+$, found 1054.58 $[C_{56}H_{85}N_7O_{11}]^+$ requires 1054.62.

[1-(3'-Deoxythymidine)-1*H*-1,2,3-triazol-4-yl]-{[*N*-2α-methyl-3β-*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. $[\alpha]_D^{21}$ -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, –*CH*$_2$NH–, –*CH*$_2$NH–Boc, H-19, H-2'-ribose, =C-C*H*$_2$-), 2.61 and 2.58 (1H, each, d, *J* 15.5 Hz, –*CH*$_2$-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, –C*(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 (–CH_2-$\underline{C}$O–), 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 (–$\underline{C}H_2$-CO–), 43.7 (C-14), 42.2 (C-8), 41.5 (C-4), 40.5 (CH_2 in octylamine), 40.2 (–$\underline{C}(CH_3)_2$–, 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 (=C-$\underline{C}H_2$-), 29.1 (C-24), 29.0 (–C($\underline{C}H_3)_2$–), 28.9 (CH_3 in Boc), 28.2 (CH_2 in octylamine), 28.0 (CH_2 in octylamine), 27.1 (C-12), 27.0 (–C($\underline{C}H_3)_2$–), 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 $C_{62}H_{97}N_7O_{11}$: C, 66.70; H, 8.76. Found: C, 66.64, H, 8.69%. MS: m/z $[M+K]^+$, found 1154.50 $[C_{62}H_{97}N_7O_{11}]^+$ requires 1154.69.

[1-(3'-Deoxythymidine)-1*H*-1,2,3-triazol-4-yl]-{[*N*-2α-methyl-3β-*O*-(3',3'-dimethylsuccinyl)lup-20,29-en-28-oyl)-2-aminoethyl]carbamoyl}methane (**28**). White powder (B, 0.58 g, 60%), mp 248-250 °C. $[\alpha]_D^{22}$ -2.2° (*c* 0.36, C_2H_5OH). IR (solution in C_2H_5OH, 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, –*CH*$_2$NH–, *CH*$_2$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, =C-C*H*$_2$-, H-2'-ribose), 2.67 and 2.58 (1H each, d, *J* 15.5 Hz, –*CH*$_2$-CO–), 2.39-0.72 (m, 23H, CH, CH_2 in pentacyclic skeleton and 1H, NH), 1.96 (s, 3H, –NHCO*CH*$_3$), 1.92 (s, 3H, CH_3-Thy), 1.69 (s, 3H, H-30), 1.27 (br s, 6H, –C*(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 (–CH_2-$\underline{C}$O–), 173.8 (NH$\underline{C}$OCH$_3$), 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 (–$\underline{C}H_2$-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, –$\underline{C}(CH_3)_2$–), 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 (=C-$\underline{C}H_2$-), 29.1 (C-24), 27.0 (C-12), 26.5 (–C($\underline{C}H_3)_2$–), 22.9 (NHCO$\underline{C}H_3$), 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 $C_{53}H_{79}N_7O_{10}$: C, 65.34; H, 8.17. Found: C, 65.29, H, 8.23%. MS: *m/z* $[M+Na]^+$, found 995.95 $[C_{53}H_{79}N_7O_{10}]^+$ requires 996.58.

[1-(3'-Deoxythymidine)-1*H*-1,2,3-triazole-4-yl]-{[*N*-2α-methyl-3β-*O*-(3',3'-dimethylsuccinyl)-lup-20,29-en-28-oyl)-8-aminooctyl]carbamoyl}methane (**29**). White powder (B, 0.68 g, 64%), mp 194-196 °C. $[\alpha]_D^{21}$ -8.3° (*c* 0.36, CH_3OH). IR (solution in CH_3OH, 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, –*CH*$_2$NH–, *CH*$_2$NHCOCH$_3$), 2.93-2.56 (m, 4H, =C-C*H*$_2$-, H-2'-ribose), 2.65 and 2.58 (1H each, d, *J* 15.0 Hz, –*CH*$_2$-CO–), 2.38-0.69 (m, 23H, CH, CH_2 in pentacyclic skeleton and 1H, NH), 1.90 (s, 3H, –NHCO*CH*$_3$), 1.91 (s, 3H, CH_3-Thy), 1.67 (s, 3H, H-30), 1.33-1.31 (m, 12H, CH_2 in octylamine), 1.26 (br s, 6H, –C*(CH*$_3$*)*$_2$–), 0.99, 0.93, 0.87, 0.83, 0.81 (all s, 3H each, H-23–H-27). ^{13}C NMR (125 MHz, MeOD): δ_C 183.6 (C-28), 183.6 (COOH), 174.0 (–CH_2-CO–), 173.2 (NHCOCH$_3$), 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 (–CH$_2$-CO–), 43.7 (C-14), 42.2 (C-8), 40.7 (C-4), 40.7 (CH_2 in octylamine), 40.3 (–C(CH$_3$)$_2$–), 40.2 (2'-ribose), 39.6 (C-13), 39.1 (CH_2 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, CH_2 in octylamine), 30.5 (CH_2 in octylamine), 30.4 (CH_2 in octylamine), 29.8 (=C-CH$_2$-), 29.1 (C-24), 28.2 (CH_2 in octylamine), 28.1 (CH_2 in octylamine), 27.1 (C-12), 26.8 (–C(CH$_3$)$_2$–), 26.4 (–C(CH$_3$)$_2$–), 22.7 (NHCOCH$_3$), 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 $C_{59}H_{91}N_7O_{10}$: C, 66.95; H, 8.67. Found: C, 66.88, H, 8.71%. MS: *m/z* $[M+K]^+$, found 1096.53 $[C_{59}H_{91}N_7O_{10}]^+$ requires 1096.65.

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Supplementary Material

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

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