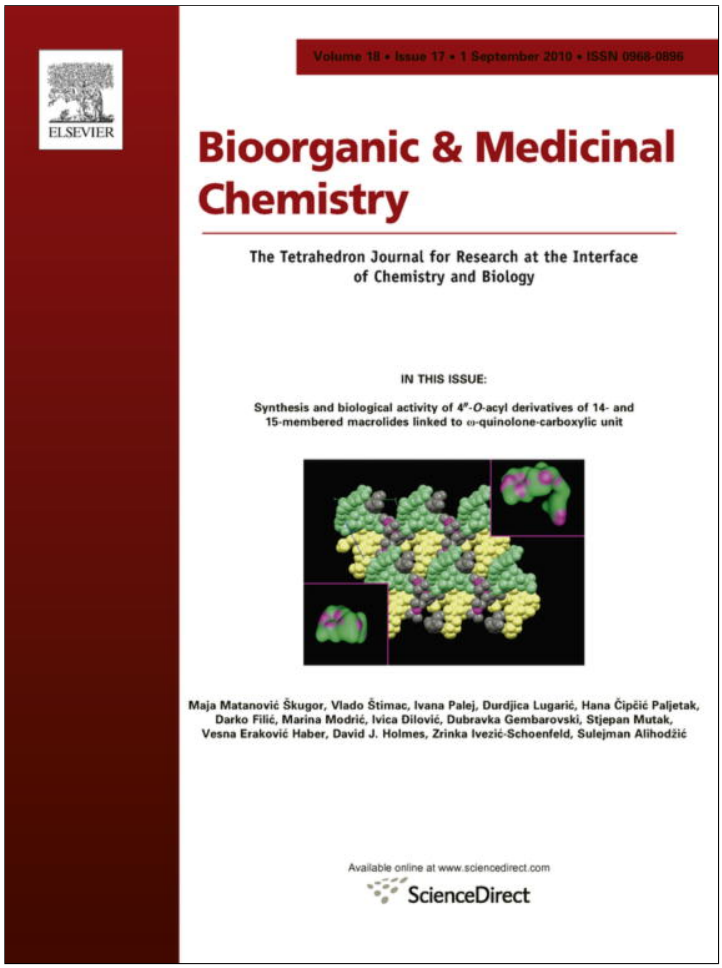

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Conjugates of betulin derivatives with AZT as potent anti-HIV agents

Juan Xiong [a], Yoshiki Kashiwada [a,*], Chin-Ho Chen [b], Keduo Qian [c], Susan L. Morris-Natschke [c], Kuo-Hsiung Lee [c,*], Yoshihisa Takaishi [a]

[a] Graduate School of Pharmaceutical Sciences, University of Tokushima, Tokushima 770-8505, Japan
[b] Medical Center, Duke University, Durham, NC 27710, USA
[c] Natural Products Research Laboratories, Eshelman School of Pharmacy, University of North Carolina, Chapel Hill, NC 27599-7568, USA

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ABSTRACT

Fourteen novel conjugates of 3,28-di-*O*-acylbetulins with AZT were prepared as anti-HIV agents, based on our previously reported potent anti-HIV triterpene leads, including 3-*O*-acyl and 3,28-di-*O*-acylbetulins. Nine of the conjugates (**49**–**53**, **55**, **56**, **59**, and **60**) exhibited potent anti-HIV activity at the submicromolar level, with EC_{50} values ranging from 0.040 to 0.098 μM in HIV-1_{NL4-3} infected MT-4 cells. These compounds were equipotent or more potent than 3-*O*-(3′,3′-dimethylsuccinyl)betulinic acid (**2**), which is currently in Phase IIb anti-AIDS clinical trial.

1. Introduction

Betulinic acid (**1**), a lupane-type triterpene, is widely distributed throughout the plant kingdom. Various biological activities[1–5] have been reported for **1**, including anti-HIV, anti-cancer, and anti-inflammatory properties. Our previous modification study on **1** led to the discovery of 3-*O*-(3′,3′-dimethylsuccinyl)betulinic acid (**2**, bevirimat, now also known as MPC-4326). Compound **2** exhibits potent anti-HIV activity and is currently in Phase IIb clinical trials in the US.[6–9] It is a first-in-class drug candidate as a viral maturation inhibitor, which disrupts the processing of capsid precursor p25 (CA-SP1) to mature capsid protein p24 (CA), resulting in generation of non-infectious HIV-1 virions.[10]

In subsequent research, various derivatives of betulin (**3a**) and dihydrobetulin (**3b**) were investigated based on the structural similarity of **1** and **3a**, **3b**.[11–14] Several analogs, including 3-*O*-glutaryldihydrobetulin (**4**),[14] 3,28-di-*O*-(3′,3′-dimethylglutaryl)betulin (**5**), and 3-*O*-(3′,3′-dimethylsuccinyl)-28-*O*-(2′′,2′′-dimethylsuccinyl)betulin (**6**)[12,13] exhibited comparable or greater anti-HIV activity compared with the structurally related **2**[15] (Fig. 1).

In a continuing study of potent anti-HIV agents based on the betulin scaffold, we wanted to explore the conjugation of our unique HIV-1 maturation inhibitors with other classes of anti-HIV agents, because the strategy of multi-target therapeutics could be more efficacious and less prone to resistance than monotherapies.[16,17] Although it is more challenging to create multi-target therapeutics by building multi-target actions into one single chemical entity rather than mixing monotherapies,[16,18] the multi-targeted single agent could greatly simplify treatment regimens and reduce the risk of drug–drug interactions.[16] Herein, we report our preliminary research on conjugation of 3′-azido-3′-deoxythymidine (AZT),[19] the first clinically approved nucleoside reverse transcriptase inhibitor (NRTI), with betulin derivatives. The hybrid conjugates were formed through a linker with ester bonds, which are easy to hydrolyze and subsequently release the parent compounds, betulin derivative and AZT, to exert their functions.

2. Design

Initially, we considered where to link AZT to the triterpene skeleton. 3,28-Di-*O*-acylbetulin derivatives contain two free carboxylic acid groups, which appear to be ideal fragments for constructing conjugates. Previous studies suggested that the free terminal carboxylic acid in the 3-*O*-acyl group is essential for anti-maturation activity; thus, the other –COOH group in the 28-*O*-acyl moiety was considered to be the appropriate conjugating site (Fig. 2).

Secondly, we considered the identity of the 3-*O*-acyl group (R_1). Our prior modification studies on **1**, **3a**, and **3b** showed that the esterification of the 3-OH with 3′,3′-dimethylglutaryl or 3′,3′-dimethylsuccinyl fragments produced significantly active derivatives (e.g., **5** and **6**).[6,12,14,20–22] However, the **3a**-derivatives bearing a 3-*O*-glutaryl group exhibited only weak or moderate anti-HIV activity.[14] In contrast, introduction of a glutaryl group onto the

* Corresponding authors. Tel./fax: +81 88 633 7276 (Y.K.); tel.: +1 919 962 0066; fax: +1 919 966 3893 (K.-H.L.).
E-mail addresses: kasiwada@ph.tokushima-u.ac.jp (Y. Kashiwada), khlee@unc.edu (K.-H. Lee).

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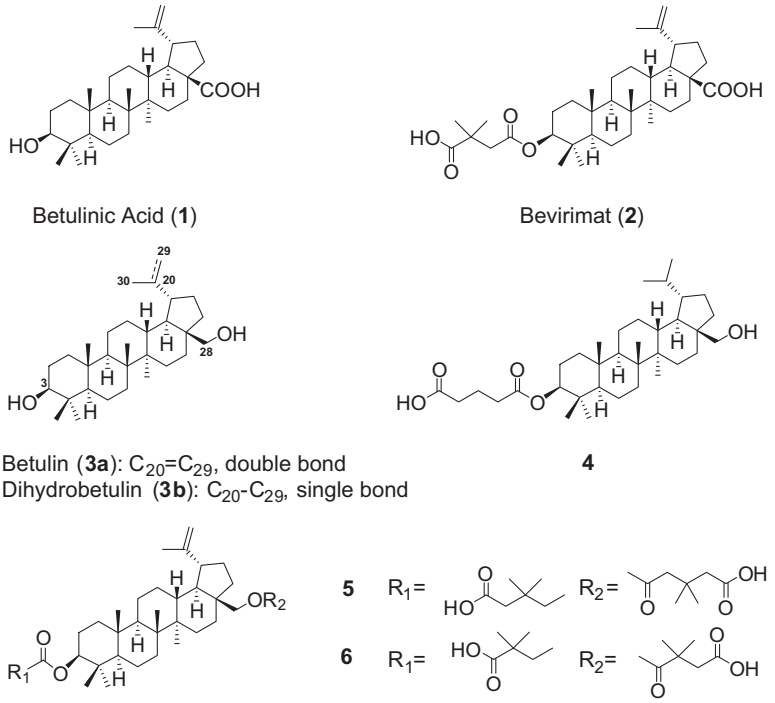


Figure 1. Betulinic acid, betulin and their derivatives which demonstrated potent anti-HIV activities.

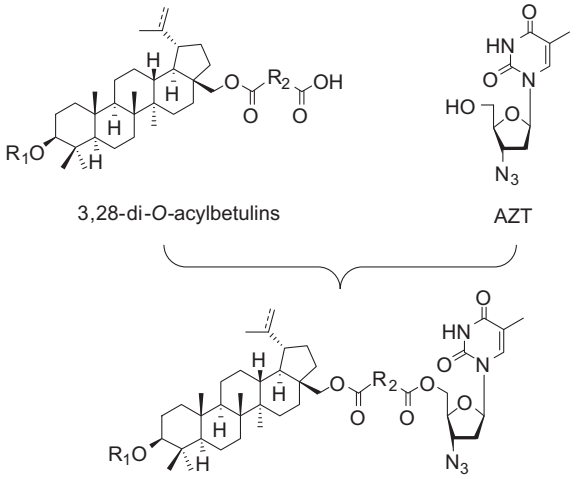


Figure 2. General structure of hybrid-type anti-HIV agents.

3-OH of **3b** led to a dramatic increase of anti-HIV potency as seen in compound **4**. Therefore, in this study, triterpenes with the lup-20(29)-ene scaffold of **3a** were acylated with 3,3-dimethylglutaryl (**54**) and 3,3-dimethylsuccinyl (**49**–**53**) moieties, while those with the lupane scaffold of **3b** were also acylated with a glutaryl group (**58**–**61**), as well as the two preceding moieties (**55**–**57** and **62**).

Thirdly, we considered the identity of the 28-*O*-acyl group (R_2). Although previous biological data for betulin derivatives suggested that the group at this position might be not essential for the anti-HIV activity of this compound type, it could still have some influence on potency.[12] In addition, here the 28-*O*-acyl group is also being used as a linker in the conjugates. Therefore, the identity of the linking ester group might play a vital part in the anti-HIV activity of hybrid conjugates. Among the 3,28-di-*O*-acylbetulin derivatives previously studied, compounds **5** and **6** exhibited the greatest potency, and thus the 3,3-dimethylglutaryl and 2,2-dimethylsuccinyl groups found in these two compounds were used for constructing the triterpene-AZT conjugates. Succinyl, glutaryl, and 3,3-dimethylsuccinyl esters were also investigated as the 28-*O*-acyl moiety in the conjugate compounds.

The preparation of 14 new conjugates of 3,28-di-*O*-acylbetulins with AZT and evaluation of anti-HIV activity are described in this paper. Table 1 lists the structural identities of the 3- and 28-*O*-acyl side chains, and the degree of saturation of the C_{20}–C_{29} bond for all intermediates (**21**–**48**) and final conjugates (**49**–**62**).

3. Chemistry

The synthetic route to conjugated products (**49**–**62**) is outlined in Schemes 1 and 2. The key intermediate 3-*O*-acylbetulins (**11**–**13**) were successfully prepared by the methods described previously[14] as shown in Scheme 1. Protection of the 28-OH group with triphenylmethyl (or trityl) chloride yielded betulin 28-*O*-trityl ether (**7**), which was further treated with an appropriate dicarboxylic acid or anhydride in anhydrous pyridine in the presence of 4-dimethylaminopyridine (DMAP) to furnish the corresponding 3-*O*-acyl-28-*O*-tritylbetulins (**8**–**10**). As was found in previous studies, the reaction of **7** with 2,2-dimethylsuccinic acid gave a mixture of 3-*O*-2′,2′-dimethylsuccinyl- and -3′,3′-dimethylsuccinylbetulin derivatives, in which the latter isomer (**8**) was the major product. The isomers were separated by silica gel chromatography, and their structures were assigned by 2D NMR analysis (HMBC). For **8** and **9**, the protecting trityl group was subsequently cleaved with pyridium *p*-toluenesulfonate (PPTS) in CH_2Cl_2–EtOH to yield 3-*O*-acylbetulins (**11** and **12**, respectively). An ethyl ester side-product was obtained predominately by removing the 28-*O*-trityl group from 3-*O*-glutaryl-28-*O*-tritylbetulin (**10**) with PPTS; however, the desired product (**13**) was obtained exclusively by refluxing **10** with Lewis acid $FeCl_3$ in 95% THF.

Hydrogenation of 3-*O*-acylbetulins (**11**–**13**) with H_2/Pd–C in EtOAc–EtOH afforded the 3-*O*-acyldihydrobetulins (**14**, **15**, and **4**, respectively) almost quantitatively. Before a second acyl moiety was introduced at the C-28 position, the free terminal carboxylic acid in the 3-*O*-acyl group was first protected as the

diphenyldiazomethyl ester. Treatment of 3-*O*-acylbetulins (**11**, **12**) and -dihydrobetulins (**14**, **15**, **4**) with freshly prepared diphenyldiazomethane in MeOH produced the protected derivatives (**16**–**20**) in quantitative yield.

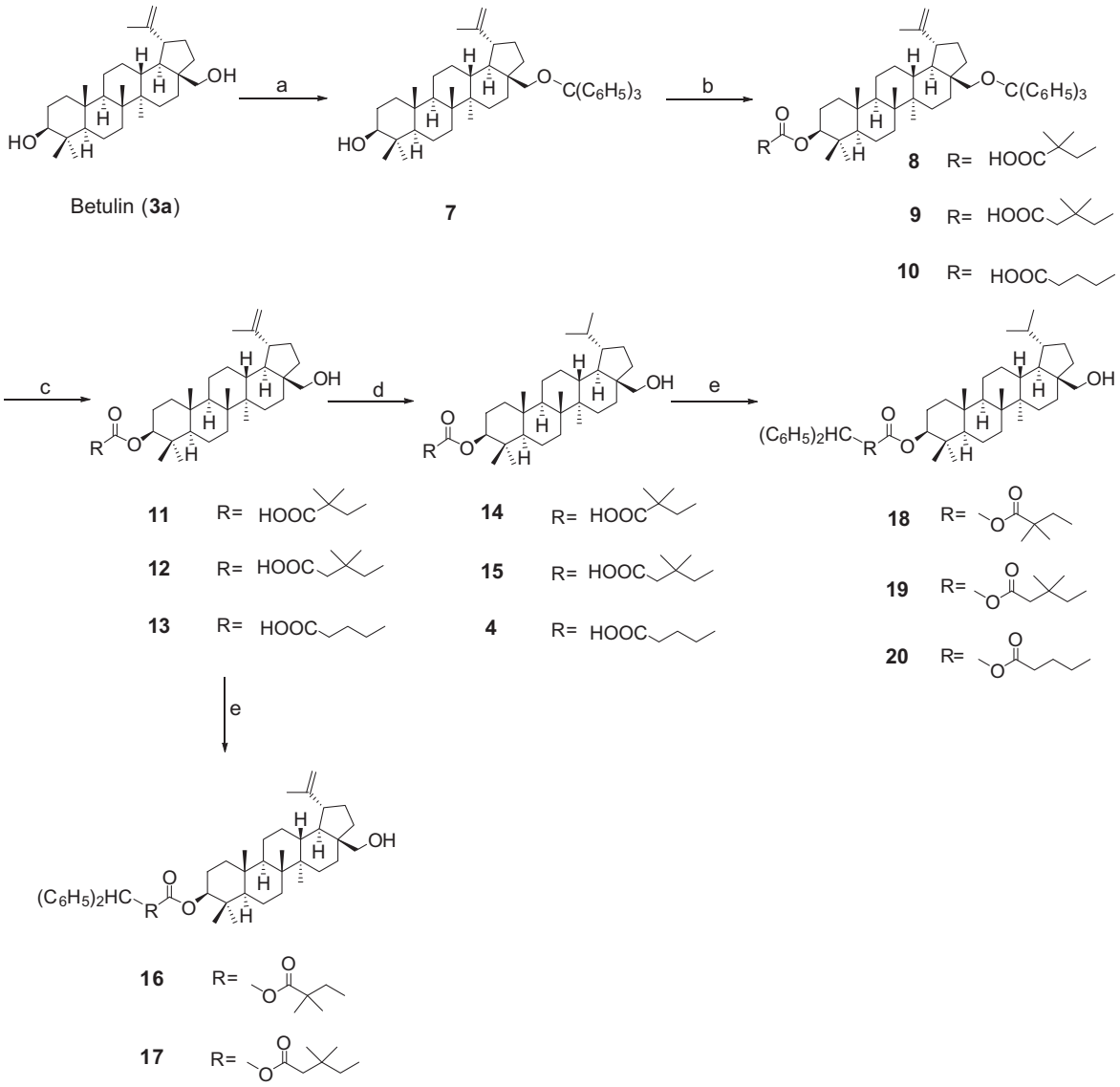
The 3,28-di-*O*-acylbetulins (**21**–**34**) were readily prepared by heating the protected 3-*O*-acylbetulin derivatives with an appropriate dicarboxylic acid or anhydride overnight in the presence of DMAP and dry pyridine (Scheme 2). The two isomeric products obtained when a dimethylsuccinyl group was introduced at C-28 of **16**, **18**, and **20** were successfully separated by preparative HPLC, yielding corresponding pure derivatives. The orientation of the dimethylsuccinyl group attached to the C-28 hydroxy group of **22**/**23**, **27**/**28**, and **30**/**31** was established by 2D NMR analyses (HSQC and HMBC). The 28-*O*-(3″,3″-dimethylsuccinyl)betulin derivative was the major product in each case. The electron-donating effect of the dimethyl groups on the adjacent carboxyl group would cause decreased electrophilicity, resulting in different yields of the two isomers in acylation reactions either at C-3 or C-28.

Conjugation of the 3,28-di-*O*-acylbetulin (**21**–**26**) and -dihydrobetulin derivatives (**27**–**34**) with AZT in the presence of dicyclohexylcarbodiimide (DCC) and DMAP in CH_2Cl_2 gave the corresponding conjugates (**35**–**48**). However, the corresponding anhydride was also obtained in each case, resulting in only a moderate yield of the desired conjugate. Finally, the terminal protecting group on the 3-*O*-acyl moiety was removed with 80% acetic acid to afford the target conjugates (**49**–**62**).

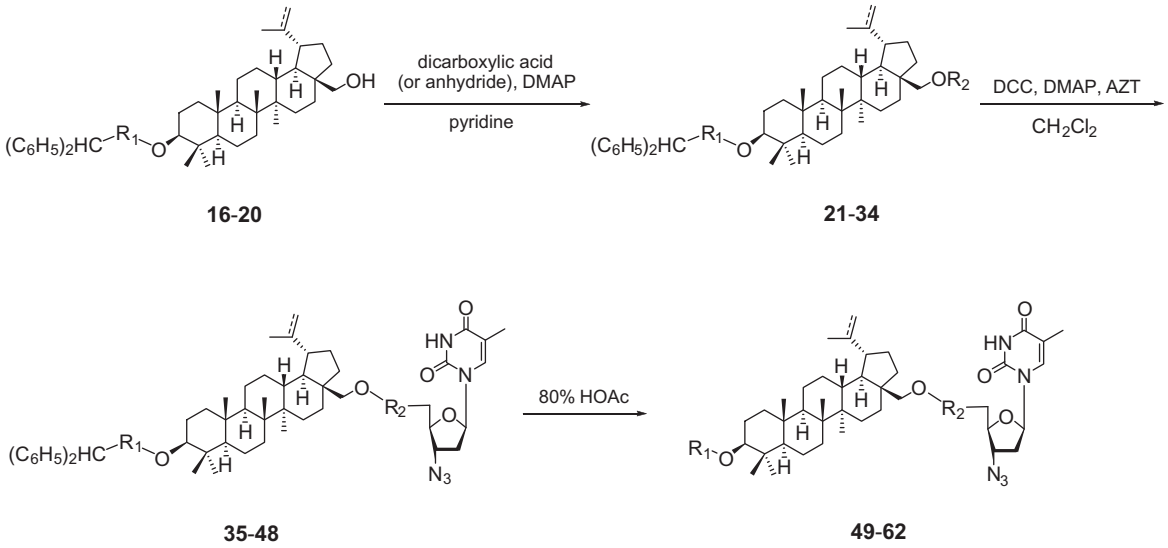
4. Results and discussion

The anti-HIV-1 replication activities of the newly synthesized conjugates (**49**–**62**) were evaluated in HIV-1_{NL4-3} infected MT-4 cells in parallel with AZT. The bioassay results are summarized in Table 2.

In the MT-4 screening system, nine conjugates (**49**–**53**, **55**, **56**, **59**, and **60**) exhibited potent anti-HIV activity at a submicromolar level (EC_{50} values ranging from 0.040 to 0.098 μM), and thus, were equipotent or more potent than **2**. Compounds **51** and **49**, which have a 3-*O*-(3′,3′-dimethylsuccinyl) moiety together with a 28-*O*-(2″,2″-dimethylsuccinyl) or 28-*O*-succinyl group, respectively, linked to AZT, exhibited the highest potency, with EC_{50} values of 0.040 and 0.045 μM, respectively. Interestingly, all three conjugates (**51**, **56**, and **59**) with a 2,2-dimethylsuccinyl linking group



Scheme 1. Reagents and conditions: (a) trityl chloride, DAMP, DMF, reflux; (b) dicarboxylic acid (or anhydride), DMAP, pyridine, reflux; (c) PPTS, CH_2Cl_2–EtOH or $FeCl_3$, 95% THF, reflux; (d) H_2, 10% Pd/C, EtOAc–EtOH, rt; (e) diphenyldiazomethane, MeOH, rt.

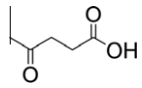


Scheme 2. General synthetic route to conjugates of betulin derivatives with AZT.

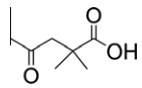
Table 1
Ester side chains of **21**–**62**.

Compound	C_{20}–C_{29}	R_1	R_2
21, **35**, **49**	C═C	B[b]	A[a]
22, **36**, **50**		B	B
23, **37**, **51**		B	B_2[c]
24, **38**, **52**		B	C[d]
25, **39**, **53**		B	D[e]
26, **40**, **54**		D	D
27, **41**, **55**	C—C	B	B
28, **42**, **56**		B	B_2
29, **43**, **57**		B	D
30, **44**, **58**		C	B
31, **45**, **59**		C	B_2
32, **46**, **60**		C	C
33, **47**, **61**		C	D
34, **48**, **62**		D	D

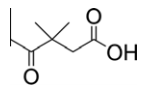
[a] A, succinyl



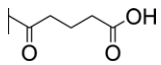
[b] B, 3,3-dimethylsuccinyl



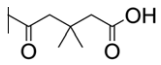
[c] B_2, 2,2-dimethylsuccinyl



[d] C, glutaryl



[e] D, 3,3-dimethylglutaryl



at C-28 generally showed higher potency than their corresponding congeners with the same 3-*O*-acyl group, but a different 28-*O*-acyl group (**51** compared with **50**, **52**, and **53**; **56** compared with **55** and **57**; **59** compared with **58**, **60**, and **61**). Of particular note, the conjugates (**50**, **55**, and **58**) with a 3,3-dimethylsuccinyl moiety as the linking unit at C-28 showed decreased activity in HIV-1 infected MT-4 cells relative to those with a 2,2-dimethylsuccinyl group (**51**, **56**, and **59**). These results confirmed our previous finding that a 2,2-dimethylsuccinyl is superior to a 3,3-dimethylsuccinyl side chain at the C-28 position of anti-HIV triterpene analogs. For example, compound **6** was reported to be 230-fold more potent against HIV replication in H9 lymphocytes assay than its isomer with a 3,3-dimethylsuccinyl side chain at C-28.[13]

Table 2
Anti-HIV-1 data of **49**–**62** against HIV-1_{NL4-3} infected MT-4 cells[a]

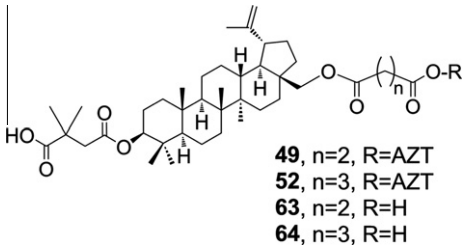
Compound	EC_{50}[b] (μM)	IC_{50}[c] (μM)	TI[d]
49	0.045	7.1	158
50	0.098	7.0	71
51	0.040	5.4	135
52	0.060	8.7	145
53	0.063	8.1	129
54	0.18	7.7	43
55	0.087	9.0	103
56	0.056	7.7	138
57	0.29	9.0	31
58	0.26	7.2	28
59	0.073	8.0	110
60	0.093	9.0	97
61	1.21	8.5	7
62	0.36	9.8	27
2	0.096[e]	>5[e]	>52[e]
AZT	0.027	>37.4	>1385

[a] Data presented are averages of at least two separate experiments.
[b] Concentration that inhibits HIV-1_{NL4-3} replication by 50%.
[c] Concentration that inhibits mock-infected MT-4 cell growth by 50%.
[d] $TI = IC_{50}/EC_{50}$.
[e] Data are taken from Ref. 23.

Among conjugates containing glutaryl or dimethyglutaryl esters, **59** and **60** [3-*O*-glutaryl, 28-*O*-(2″,2″-dimethylsuccinyl), EC_{50} 0.073 μM and 3,28-di-*O*-glutaryl, EC_{50} 0.093 μM] were equipotent with **2**. However, **54** and **62** [3,28-di-*O*-(3′,3′-dimethylglutaryl)] showed only moderate activity, and **61** [3-*O*-glutaryl, 28-*O*-(3″,3″-glutaryl)] was the weakest compound.

Comparison of the anti-HIV potency of dihydrobetulin conjugates **55**–**57** with that of betulin conjugates **50**, **51**, and **53** suggested that hydrogenation of the isopropylidene group at C-19 did not help to increase the anti-HIV potency. Finally, comparison of data for **49**/**63** and **52**/**64** in Table 3 showed that hybrid conju-

Table 3
Anti-HIV-1 data of conjugates **49**, **52** and analogous carboxylic acids **63**, **64** against HIV-1_{NL4-3} infected MT-4 cells[a]



Compound	EC_{50}[b] (μM)	IC_{50}[c] (μM)	TI[d]
49	0.045	7.1	158
63	0.18	11.3	63
52	0.060	8.7	145
64	0.310	>14.6	>47
2	0.096[e]	>5[e]	>52[e]
AZT	0.027	>37.4	>1385

[a] Data presented are averages of at least two separate experiments.
[b] Concentration that inhibits HIV-1_{NL4-3} replication by 50%.
[c] Concentration that inhibits mock-infected MT-4 cell growth by 50%.
[d] TI = IC_{50}/EC_{50}.
[e] Data are taken from Ref. 23.

gate compounds were four- and fivefold more active, respectively, than the corresponding compounds not linked to AZT.

In conclusion, 14 novel conjugates of 3,28-di-*O*-acyl-betulins with AZT were prepared as anti-HIV-1 agents. In MT-4 cells, nine of the conjugates demonstrated potent anti-HIV activity at a submicromolar level with EC_{50} values ranging from 0.040 to 0.098 μM, and thus, were equipotent or more potent than **2**. A 2,2-dimethylsuccinyl group at the C-28 position served as the best linker between the triterpene scaffold and AZT in this study.

5. Experimental

5.1. General Experimental Procedures

Optical rotations were measured with a JASCO P-2200 digital polarimeter. NMR spectra (400 MHz for ^1H, 100 MHz for ^{13}C, using TMS as internal standard) were recorded on a Bruker AVANCE 400 spectrometer. HRESIMS was obtained on a Waters LCT Premier. Column chromatography was performed with silica gel 60 N (63–210 nm, Merck); Preparative HPLC was carried out on Mightysil RP-18 GP column (250 × 20 mm i.d., Kanto Chemical Co., Inc.) or Cosmosil column (Cholester, 250 × 20 mm i.d.; πNAP, 250 × 20 mm i.d.; Nacalai Tesque). Unless otherwise indicated, all reagents were purchased from commercial suppliers and used without further purification.

5.2. Chemical preparation

5.2.1. 28-*O*-Tritylbetulin (7)

To a solution of **3a** (1.02 g, 2.30 mmol) in DMF (15 mL) were added dimethylaminopyridine (DMAP, 0.33 g, 2.70 mmol) and triphenylmethyl chloride (1.26 g, 4.52 mmol). After refluxing for 6 h, the reaction mixture was poured into ice-water, and extracted with $CHCl_3$. The organic layer was washed with 2 N HCl solution and brine, dried over Na_2SO_4 and concentrated. The obtained residue was chromatographed over silica gel column (hexane/EtOAc = 10:1) to afford **7** as a white solid (1.16 g, 73.5% yield). $[\alpha]_D^{25}$ −2.1° (*c* 1.49, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.54 (3H, s, CH_3-26), 0.77 (3H, s, CH_3-24), 0.78 (3H, s, CH_3-25), 0.91 (3H, s, CH_3-27), 0.97 (3H, s, CH_3-23), 1.65 (3H, s, CH_3-30), 2.15–2.24 (3H, m, H-22, H-16 and H-19), 2.92 (1H, d, *J* = 8.8 Hz, H-28), 3.15–3.19 (2H, m, H-28 and H-3), 4.53, 4.59 (each 1H, br s, H_2-29), 7.23 (3H, t, *J* = 7.2 Hz, trityl H-4′), 7.31 (6H, t, *J* = 7.6, 7.2 Hz, trityl H-3′, 5′), 7.49 (6H, d, *J* = 7.6 Hz, trityl H-2′, 6′); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.7 (C-27), 15.3 (C-24), 15.9 (C-26), 16.1 (C-25), 18.3 (C-6), 19.1 (C-30), 20.7 (C-11), 25.2 (C-12), 26.9 (C-15), 27.4 (C-2), 28.0 (C-23), 29.9 (C-21), 30.2 (C-16), 34.2 (C-7), 35.2 (C-22), 37.1 (C-10), 37.3 (C-13), 38.7 (C-1), 38.8 (C-4), 40.6 (C-8), 42.5 (C-14), 47.6 (C-17), 47.7 (C-19), 48.9 (C-18), 50.3 (C-9), 55.3 (C-5), 59.6 (C-28), 79.0 (C-3), 85.9 (trityl C(Ph_3), 109.3 (C-29), 126.8 (trityl C-4′), 127.7 (trityl C-2′, 6′), 128.8 (trityl C-3′, 5′), 144.5 (trityl C-1′), 150.8 (C-20). HRESIMS (positive) *m*/*z* 707.4781 $[M+Na]^+$ (calcd for $C_{49}H_{64}O_2Na$, 707.4804).

5.2.2. General procedure for preparation of 3-*O*-acyl-28-*O*-tritylbetulins (8–10)

3-*O*-Acyl-28-*O*-tritylbetulins were prepared by refluxing a solution of **7** (1 equiv), appropriate dicarboxylic acid (4 equiv) or anhydride (4–5 equiv) and DMAP (1–2 equiv) in anhydrous pyridine (10–20 mL) overnight. After cooling to room temperature, the reaction mixture was diluted with ice-water, and extracted with $CHCl_3$. The organic layer was washed with water, 2 N HCl solution and brine, dried over Na_2SO_4, and concentrated. The crude product was purified by silica gel column chromatography (hexane/EtOAc = 10:1).

5.2.2.1. 3-*O*-(3′,3′-Dimethylsuccinyl)-28-*O*-tritylbetulin (8). Yield 38.9% (starting from 4.48 g of **7** and 2,2-dimethylsuccinic acid); white solid; 3-*O*-(2′,2′-dimethylsuccinyl)-28-*O*-tritylbetulin was also separated as by-product (11.1% yield). $[\alpha]_D^{25}$ +2.1° (*c* 1.25, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.53 (3H, s, CH_3-26), 0.79 (3H, s, CH_3-25), 0.81 (3H, s, CH_3-24), 0.84 (3H, s, CH_3-23), 0.90 (3H, s, CH_3-27), 1.30, 1.31 (each 3H, s, dimethylsuccinyl CH_3), 1.65 (3H, s, CH_3-30), 2.15–2.24 (3H, m, H-22, H-16 and H-19), 2.57, 2.68 (each 1H, d, *J* = 15.6 Hz, dimethylsuccinyl H_2-2′), 2.92, 3.15 (each 1H, d, *J* = 8.8 Hz, H_2-28), 4.48 (1H, dd, *J* = 5.2, 11.2 Hz, H-3), 4.53, 4.59 (each 1H, br s, H_2-29), 7.23 (3H, t, *J* = 7.2 Hz, trityl H-4′), 7.31 (6H, t, *J* = 8.0, 7.2 Hz, trityl H-3′, 5′), 7.50 (6H, d, *J* = 8.0 Hz, trityl H-2′, 6′); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.7 (C-27), 15.9 (C-26), 16.1 (C-25), 16.5 (C-24), 18.2 (C-6), 19.1 (C-30), 20.7 (C-11), 23.6 (C-2), 25.1 (C-12), 25.0, 25.6 (dimethylsuccinyl CH_3), 26.9 (C-15), 27.9 (C-23), 29.9 (C-21), 30.1 (C-16), 34.1 (C-7), 35.2 (C-22), 37.0 (C-10), 37.2 (C-13), 37.7 (C-4), 38.3 (C-1), 40.5 (dimethylsuccinyl C-3′), 40.6 (C-8), 42.5 (C-14), 44.7 (dimethylsuccinyl C-2′), 47.6 (C-17), 47.8 (C-19), 48.9 (C-18), 50.2 (C-9), 55.3 (C-5), 59.5 (C-28), 81.6 (C-3), 85.8 (trityl C(Ph_3), 109.4 (C-29), 126.8 (trityl C-4′), 127.7 (trityl C-2′, 6′), 128.8 (trityl C-3′, 5′), 144.5 (trityl C-1′), 150.8 (C-20), 170.9 (dimethylsuccinyl COO−), 182.8 (dimethylsuccinyl COOH). HRESIMS (positive) *m*/*z* 835.5286 $[M+Na]^+$ (calcd for $C_{55}H_{72}O_5Na$, 835.5277).

5.2.2.2. 3-*O*-(3′,3′-Dimethylglutaryl)-28-*O*-tritylbetulin (9). Yield 86.6% (starting from 956 mg of **7** and 3,3-dimethylglutaric anhydride); white solid. $[\alpha]_D^{24}$ +7.5° (*c* 0.52, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.55 (3H, s, CH_3-26), 0.81 (3H, s, CH_3-25), 0.85 (3H, s, CH_3-24), 0.86 (3H, s, CH_3-23), 0.91 (3H, s, CH_3-27), 1.16 (6H, s, dimethylglutaryl CH_3), 1.65 (3H, s, CH_3-30), 2.15–2.24 (3H, m, H-22, H-16 and H-19), 2.40, 2.47 (each 1H, d, *J* = 14.0 Hz, dimethylglutaryl H_2-2′), 2.48 (2H, s, dimethylglutaryl H_2-4′), 2.92, 3.15 (each 1H, d, *J* = 8.8 Hz, H_2-28), 4.49 (1H, dd, *J* = 4.8, 10.8 Hz, H-3), 4.54, 4.60 (each 1H, br s, H_2-29), 7.23 (3H, t, *J* = 7.6 Hz, trityl H-4′), 7.31 (6H, t, *J* = 7.6 Hz, trityl H-3′, 5′), 7.50 (6H, d, *J* = 7.6 Hz, trityl H-2′, 6′); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.7 (C-27), 15.9 (C-26), 16.1 (C-25), 16.5 (C-24), 18.2 (C-6), 19.1 (C-30), 20.8 (C-11), 23.8 (C-2), 25.2 (C-12), 27.0 (C-15), 27.9, 28.0 (dimethylglutaryl CH_3), 28.0 (C-23), 30.0 (C-21), 30.2 (C-16), 32.7 (dimethylglutaryl C-3′),

34.2 (C-7), 35.2 (C-22), 37.1 (C-10), 37.3 (C-13), 37.7 (C-4), 38.4 (C-1), 40.7 (C-8), 42.5 (C-14), 45.2 (dimethylglutaryl C-4′), 45.7 (dimethylglutaryl C-2′), 47.6 (C-17), 47.8 (C-19), 49.0 (C-18), 50.3 (C-9), 55.4 (C-5), 59.7 (C-28), 81.5 (C-3), 85.9 (trityl C(Ph)$_3$), 109.4 (C-29), 126.8 (trityl C-4′), 127.7 (trityl C-2′, 6′), 128.8 (trityl C-3′, 5′), 144.5 (trityl C-1′), 150.8 (C-20), 172.3 (dimethylglutaryl COO−), 175.9 (dimethylglutaryl COOH). HRESIMS (positive) *m*/*z* 849.5403 [M+Na]$^+$ (calcd for $C_{56}H_{74}O_5Na$, 849.5434).

5.2.2.3. 3-*O*-Glutaryl-28-*O*-tritylbetulin (10). Yield 84.1% (starting from 1.07 g of **7** and glutaric anhydride); white solid. $[\alpha]_D^{25}$ +5.1° (*c* 1.96, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.53 (3H, s, CH_3-26), 0.79 (3H, s, CH_3-25), 0.83 (3H, s, CH_3-24), 0.83 (3H, s, CH_3-23), 0.90 (3H, s, CH_3-27), 1.65 (3H, s, CH_3-30), 1.97 (2H, quint, *J* = 7.2 Hz, glutary H_2-3′), 2.15–2.24 (3H, m, H-22, H-16 and H-19), 2.39 (2H, t, *J* = 7.2 Hz, glutary H_2-2′), 2.43 (2H, s, glutaryl H_2-4′), 2.92, 3.15 (each 1H, d, *J* = 8.8 Hz, H_2-28), 4.48 (1H, dd, *J* = 5.6, 10.8 Hz, H-3), 4.53, 4.59 (each 1H, br s, H_2-29), 7.23 (3H, t, *J* = 7.2 Hz, trityl H-4′), 7.31 (6H, t, *J* = 8.0, 7.2 Hz, trityl H-3′, 5′), 7.50 (6H, d, *J* = 8.0 Hz, trityl H-2′, 6′); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.7 (C-27), 15.8 (C-26), 16.1 (C-25), 16.5 (C-24), 18.2 (C-6), 19.1 (C-30), 20.0 (glutaryl C-3′), 20.8 (C-11), 23.7 (C-2), 25.1 (C-12), 27.0 (C-15), 28.0 (C-23), 29.9 (C-21), 30.1 (C-16), 32.9 (glutaryl C-4′), 33.6 (glutaryl C-2′), 34.1 (C-7), 35.2 (C-22), 37.0 (C-10), 37.2 (C-13), 37.8 (C-4), 38.3 (C-1), 40.6 (C-8), 42.5 (C-14), 47.6 (C-17), 47.8 (C-19), 48.9 (C-18), 50.2 (C-9), 55.3 (C-5), 59.5 (C-28), 81.1 (C-3), 85.8 (trityl C(Ph)$_3$), 109.4 (C-29), 126.8 (trityl C-4′), 127.7 (trityl C-2′, 6′), 128.8 (trityl C-3′, 5′), 144.5 (trityl C-1′), 150.8 (C-20), 172.6 (glutaryl COO−), 178.1 (glutaryl COOH). HRESIMS (positive) *m*/*z* 821.5139 [M+Na]$^+$ (calcd for $C_{54}H_{70}O_5Na$, 821.5121).

5.2.3. General procedure for preparation of 3-*O*-acylbetulins (11 and 12)

3-*O*-Acyl-28-*O*-tritylbetulin (1 equiv) was dissolved in EtOH–CH_2Cl_2 and then pyridium *p*-toluenesulfonate (PPTS) (3–5 equiv) was added. The reaction mixture was refluxed at 70 °C overnight. After evaporation under reduced pressure, ice-water was added to the residue, and extraction was performed with $CHCl_3$. The organic layer was washed with water and brine, dried over Na_2SO_4, and concentrated. The residue was subjected over silica gel column (hexane/EtOAc = 1:1) to give pure product.

5.2.3.1. 3-*O*-(3′,3′-Dimethylsuccinyl)betulin (11). Yield 58.9% (starting from 1.51 g of **8**); white solid. $[\alpha]_D^{25}$ +24.1° (*c* 1.95, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.81 (3H, s, CH_3-24), 0.84 (6H, s, CH_3-23, 25), 0.97 (3H, s, CH_3-27), 1.02 (3H, s, CH_3-26), 1.28, 1.30 (each 3H, s, dimethylsuccinyl CH_3), 1.73 (3H, s, CH_3-30), 2.38 (1H, dt, *J* = 5.6, 10.4 Hz, H-19), 2.56, 2.67 (each 1H, d, *J* = 15.6 Hz, dimethylsuccinyl H_2-2′), 3.34, 3.80 (each 1H, d, *J* = 10.8 Hz, H_2-28), 4.49 (1H, dd, *J* = 5.2, 10.4 Hz, H-3), 4.58, 4.68 (each 1H, br s, H_2-29); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.7 (C-27), 16.0 (C-26), 16.1 (C-25), 16.5 (C-24), 18.2 (C-6), 19.0 (C-30), 20.8 (C-11), 23.6 (C-2), 25.1 (C-12), 25.0, 25.6 (dimethylsuccinyl CH_3), 27.0 (C-15), 27.9 (C-23), 29.1 (C-16), 29.7 (C-21), 33.9 (C-22), 34.1 (C-7), 37.0 (C-10), 37.3 (C-13), 37.7 (C-4), 38.4 (C-1), 40.5 (dimethylsuccinyl C-3′), 40.9 (C-8), 42.7 (C-14), 44.7 (dimethylsuccinyl C-2′), 47.7 (C-17), 47.8 (C-19), 48.7 (C-18), 50.3 (C-9), 55.4 (C-5), 60.5 (C-28), 81.5 (C-3), 109.7 (C-29), 150.4 (C-20), 170.9 (dimethylsuccinyl COO−), 182.6 (dimethylsuccinyl COOH). HRESIMS (positive) *m*/*z* 593.4171 [M+Na]$^+$ (calcd for $C_{36}H_{58}O_5Na$, 593.4182).

5.2.3.2. 3-*O*-(3′,3′-Dimethylglutaryl)betulin (12). Yield 67.2% (starting from 1.0 g of **9**); white solid. $[\alpha]_D^{25}$ +24.0° (*c* 1.88, $CHCl_3$). ^{1}H NMR (C_5D_5N, 400 MHz) δ 0.79 (3H, s, CH_3-25), 0.92 (3H, s, CH_3-24), 0.94 (3H, s, CH_3-23), 0.96 (3H, s, CH_3-26), 1.03 (3H, s, CH_3-27), 1.36, 1.37 (each 3H, s, dimethylglutaryl CH_3), 1.76 (3H, s, CH_3-30), 2.11–2.17 (1H, m, H-21), 2.37–2.45 (2H, m, H-16 and H-22), 2.61 (1H, dt, *J* = 5.6, 10.8 Hz, H-19), 2.74, 2.79 (each 1H, d, *J* = 16.0 Hz, dimethylglutaryl H_2-2′), 2.76 (2H, s, dimethylglutaryl H_2-4′), 3.65, 4.06 (each 1H, d, *J* = 10.8 Hz, H_2-28), 4.71–4.74 (1H, m, H-3), 4.74, 4.88 (each 1H, br s, H_2-29); ^{13}C NMR (C_5D_5N, 100 MHz) δ 14.9 (C-27), 16.1 (C-26), 16.2 (C-25), 16.9 (C-24), 18.4 (C-6), 19.3 (C-30), 21.0 (C-11), 24.2 (C-2), 25.6 (C-12), 27.5 (C-15), 28.0 (dimethylglutaryl CH_3), 28.1 (C-23), 30.0 (C-16), 30.4 (C-21), 32.7 (dimethylglutaryl C-3′), 34.4 (C-7), 34.9 (C-22), 37.2 (C-10), 37.5 (C-13), 37.9 (C-4), 38.5 (C-1), 41.2 (C-8), 43.0 (C-14), 45.9 (dimethylglutaryl C-4′, 2′), 48.3 (C-19), 48.5 (C-17), 49.1 (C-18), 50.5 (C-9), 55.5 (C-5), 59.4 (C-28), 80.6 (C-3), 109.9 (C-29), 151.2 (C-20), 171.9 (dimethylglutaryl COO−), 174.4 (dimethylglutaryl COOH). HRESIMS (positive) *m*/*z* 607.4351 [M+Na]$^+$ (calcd for $C_{37}H_{60}O_5Na$, 607.4338).

5.2.3.3. 3-*O*-Glutarylbetulin (13). To a solution of **10** (1.50 g, 1.88 mmol) in 95% THF (50 mL) was added anhydrous $FeCl_3$ (1.22 g, 7.52 mmol). The solution was refluxed overnight. After cooling to room temperature, the solvent was evaporated in vacuo and the residue was dissolved in $CHCl_3$. The $CHCl_3$ solution was washed with water and brine, dried over Na_2SO_4, filtrated and concentrated. The crude product was purified by silica column chromatography (hexane/EtOAc = 2:1) to give **13** as a white solid (600 mg, yield 57.4%). $[\alpha]_D^{25}$ +25.1° (*c* 3.45, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.84 (3H, s, CH_3-24), 0.85 (3H, s, CH_3-23), 0.86 (3H, s, CH_3-25), 0.99 (3H, s, CH_3-27), 1.03 (3H, s, CH_3-26), 1.69 (3H, s, CH_3-30), 1.98 (2H, quint, *J* = 7.2 Hz, glutary H_2-3′), 2.35–2.44 (1H, m, H-19), 2.39 (2H, t, *J* = 7.2 Hz, glutary H_2-2′), 2.43 (2H, s, glutaryl H_2-4′), 3.35, 3.81 (each 1H, d, *J* = 10.8 Hz, H_2-28), 4.49 (1H, dd, *J* = 5.6, 10.4 Hz, H-3), 4.59, 4.69 (each 1H, br s, H_2-29); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.7 (C-27), 16.0 (C-26), 16.1 (C-25), 16.5 (C-24), 18.2 (C-6), 19.1 (C-30), 20.1 (glutaryl C-3′), 20.9 (C-11), 23.7 (C-2), 25.2 (C-12), 27.1 (C-15), 28.0 (C-23), 29.2 (C-16), 29.8 (C-21), 32.9 (glutaryl C-4′), 33.7 (glutaryl C-2′), 34.0 (C-22), 34.2 (C-7), 37.1 (C-10), 37.3 (C-13), 37.8 (C-4), 38.4 (C-1), 41.0 (C-8), 42.7 (C-14), 47.8 (C-17), 47.8 (C-19), 48.8 (C-18), 50.3 (C-9), 55.4 (C-5), 60.6 (C-28), 81.1 (C-3), 109.7 (C-29), 150.4 (C-20), 172.6 (glutaryl COO−), 177.6 (glutaryl COOH). HRESIMS (positive) *m*/*z* 579.4027 [M+Na]$^+$ (calcd for $C_{35}H_{56}O_5Na$, 579.4025).

5.2.4. General procedure of hydrogenation

3-*O*-Acyl-dihydrobetulin derivatives (**4**, **14**, and **15**) were prepared by treating a solution of 3-*O*-acylbetulin derivative (250–400 mg) in EtOAc–EtOH with 10% palladium catalyst (Pd–C, 240–800 mg) under hydrogen atmosphere overnight with stirring. The reaction mixture was filtered, and the filtrate was concentrated under reduced pressure to give a white solid. The purity of the product was confirmed by NMR analyses and used in the next reaction without further purification.

5.2.4.1. 3-*O*-(3′,3′-Dimethylsuccinyl)dihydrobetulin (14). Yield 100% (starting from 395 mg of **11** and 240 mg of 10% Pd–C); white solid. $[\alpha]_D^{24}$ −9.3° (*c* 1.5, $CHCl_3$). ^{1}H NMR (C_5D_5N, 400 MHz) δ 0.79 (6H, s, CH_3-25), 0.82, 0.89 (each 2H, d, *J* = 8.0 Hz, CH_3-29, 30), 0.94 (3H, s, CH_3-24), 0.96 (3H, s, CH_3-23, 26), 0.98 (3H, s, CH_3-27), 1.53 (6H, s, dimethylsuccinyl CH_3), 2.38–2.41 (2H, m, H-16 and H-22), 2.88, 2.94 (each 1H, d, *J* = 15.6 Hz, dimethylsuccinyl H_2-2′), 3.58, 4.04 (each 1H, d, *J* = 10.4 Hz, H_2-28), 4.76 (1H, dd, *J* = 4.4, 11.6 Hz, H-3); ^{13}C NMR (C_5D_5N, 100 MHz) δ 14.8 (C-27), 15.2 (C-29), 16.1 (C-26), 16.2 (C-25), 16.9 (C-24), 18.4 (C-6), 21.1 (C-11), 22.3 (C-21), 23.2 (C-30), 24.1 (C-2), 25.9, 26.2 (dimethylsuccinyl CH_3), 27.2 (C-12), 27.4 (C-15), 28.1 (C-23), 29.8 (C-20), 30.1 (C-16), 34.5 (C-7), 34.9 (C-22), 37.0 (C-13), 37.2 (C-10), 38.0 (C-4), 38.5 (C-1), 40.9 (dimethylsuccinyl C-3′), 41.2 (C-8), 43.1 (C-14), 45.0 (C-19), 45.2 (dimethylsuccinyl C-2′), 48.6 (C-17),

48.4 (C-18), 50.1 (C-9), 55.5 (C-5), 59.4 (C-28), 80.9 (C-3), 171.6 (dimethylsuccinyl COO−), 179.3 (dimethylsuccinyl COOH). HRESIMS (positive) *m*/*z* 595.4327 $[M+Na]^+$ (calcd for $C_{36}H_{60}O_5Na$, 595.4338).

5.2.4.2. 3-*O*-(3′,3′-Dimethylglutaryl)dihydrobetulin (15). Yield 97.4% (starting from 250 mg of **12** and 250 mg of 10% Pd–C); white solid. $[\alpha]_D^{25}$ −8.9° (*c* 1.54, $CHCl_3$). ^1H NMR (C_5D_5N, 400 MHz) δ 0.82 (3H, s, CH_3-25), 0.83, 0.90 (each 2H, d, *J* = 8.0 Hz, CH_3-29, 30), 0.93 (3H, s, CH_3-24), 0.95 (3H, s, CH_3-23), 0.97 (3H, s, CH_3-26), 1.00 (3H, s, CH_3-27), 1.37, 1.37 (each 3H, s, dimethylglutaryl CH_3), 2.37–2.41 (2H, m, H-16 and H-22), 2.75, 2.79 (each 1H, d, *J* = 14.4 Hz, dimethylglutaryl H_2-2′), 2.77 (2H, s, dimethylglutaryl H_2-4′), 3.59, 4.05 (each 1H, d, *J* = 10.8 Hz, H_2-28), 4.74 (1H, dd, *J* = 4.4, 11.6 Hz, H-3); ^{13}C NMR (C_5D_5N, 100 MHz) δ 14.8 (C-27), 15.2 (C-29), 16.1 (C-26), 16.2 (C-25), 16.9 (C-24), 18.4 (C-6), 21.1 (C-11), 22.3 (C-21), 23.2 (C-30), 24.2 (C-2), 27.2 (C-12), 27.4 (C-15), 28.0 (dimethylglutaryl CH_3), 28.1 (C-23), 29.8 (C-20), 30.1 (C-16), 32.7 (dimethylglutaryl C-3′), 34.5 (C-7), 34.9 (C-22), 37.0 (C-13), 37.2 (C-10), 37.9 (C-4), 38.5 (C-1), 41.2 (C-8), 43.1 (C-14), 45.0 (C-19), 45.9 (dimethylglutaryl C-4′, 2′), 48.4 (C-18), 48.6 (C-17), 50.2 (C-9), 55.5 (C-5), 59.4 (C-28), 80.7 (C-3), 172.0 (dimethylglutaryl COO−), 174.4 (dimethylglutaryl COOH). HRESIMS (positive) *m*/*z* 609.4493 $[M+Na]^+$ (calcd for $C_{37}H_{62}O_5Na$, 609.4495).

5.2.4.3. 3-*O*-Glutaryl-dihydrobetulin (4). Yield 91.1% (starting from 387 mg of **13** and 800 mg of 10% Pd–C); white solid. $[\alpha]_D^{25}$ −5.4° (*c* 2.40, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.78, 0.85 (each 2H, d, *J* = 8.0 Hz, CH_3-29, 30), 0.85 (3H, s, CH_3-24), 0.85 (3H, s, CH_3-23), 0.87 (3H, s, CH_3-25), 0.96 (3H, s, CH_3-27), 1.04 (3H, s, CH_3-26), 1.99 (2H, quint, *J* = 7.2 Hz, glutary H_2-3′), 2.40 (2H, t, *J* = 7.2 Hz, glutary H_2-2′), 2.43 (2H, s, glutaryl H_2-4′), 3.32, 3.79 (each 1H, d, *J* = 10.8 Hz, H_2-28), 4.50 (1H, dd, *J* = 6.4, 10.0 Hz, H-3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.6 (C-27), 14.9 (C-29), 16.0 (C-26), 16.1 (C-25), 16.6 (C-24), 18.2 (C-6), 20.1 (glutaryl C-3′), 20.9 (C-11), 21.7 (C-21), 22.9 (C-30), 23.7 (C-2), 26.9 (C-12), 26.9 (C-15), 28.0 (C-23), 29.3 (C-16), 29.5 (C-20), 33.0 (glutaryl C-4′), 33.7 (glutaryl C-2′), 34.0 (C-22), 34.3 (C-7), 36.9 (C-13), 37.1 (C-10), 37.8 (C-4), 38.4 (C-1), 41.0 (C-8), 42.9 (C-14), 44.6 (C-19), 47.9 (C-17), 48.1 (C-18), 50.0 (C-9), 55.4 (C-5), 60.6 (C-28), 81.1 (C-3), 172.7 (glutaryl COO−), 177.9 (glutaryl COOH). HRESIMS (positive) *m*/*z* 581.4180 $[M+Na]^+$ (calcd for $C_{35}H_{58}O_5Na$, 581.4182).

5.2.5. General procedure for syntheses of 3-*O*-acylbetulin benzhydryl ester derivatives (16–20)

To a solution of 3-*O*-acylbetulin derivatives (1 equiv) in CH_2Cl_2–CH_3OH, freshly prepared diphenyldiazomethane was added until the reaction solution turned pink. The resulting mixture was kept stirring at room temperature overnight. After evaporated solvent in vacuo, the residue was subjected over silica gel column (hexane/EtOAc = 10:1) to give the desired product.

5.2.5.1. 3-*O*-(3′,3′-Dimethylsuccinyl)betulin benzhydryl ester (16). Yield 100% (starting from 265 mg of **11**); white solid. $[\alpha]_D^{17}$ +16.9° (*c* 1.74, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.75 (3H, s, CH_3-24), 0.79 (3H, s, CH_3-23), 0.80 (3H, s, CH_3-25), 0.99 (3H, s, CH_3-27), 1.03 (3H, s, CH_3-26), 1.32, 1.32 (each 3H, s, dimethylsuccinyl CH_3), 1.70 (3H, s, CH_3-30), 2.40 (1H, dt, *J* = 5.6, 10.4 Hz, H-19), 2.66, 2.70 (each 1H, d, *J* = 16.0 Hz, dimethylsuccinyl H_2-2′), 3.34, 3.80 (each 1H, d, *J* = 10.8 Hz, H_2-28), 4.45 (1H, dd, *J* = 5.2, 10.8 Hz, H-3), 4.60, 4.70 (each 1H, br s, H_2-29), 6.87 (1H, s, $CH(Ph)_2$), 7.25–7.34 (10H, m, aromatic-H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.7 (C-27), 15.9 (C-26), 16.0 (C-25), 16.4 (C-24), 18.1 (C-6), 19.0 (C-30), 20.8 (C-11), 23.5 (C-2), 25.1 (C-12), 25.1, 25.4 (dimethylsuccinyl CH_3), 27.0 (C-15), 27.8 (C-23), 29.1 (C-16), 29.7 (C-21), 33.9 (C-22), 34.1 (C-7), 37.0 (C-10), 37.2 (C-13), 37.6 (C-4), 38.3 (C-1), 40.6 (dimethylsuccinyl C-3′), 40.9 (C-8), 42.6 (C-14), 44.5 (dimethylsuccinyl C-2′), 47.7 (C-17), 47.8 (C-19), 48.7 (C-18), 50.2 (C-9), 55.3 (C-5), 60.4 (C-28), 76.9 ($CH(Ph)_2$), 81.2 (C-3), 109.7 (C-29), 127.0 (benzhydryl C-2′, 6′), 127.7 (benzyhydryl C-4′), 128.3 (benzhydryl C-3′, 5′), 140.3 (benzhydryl C-1′), 150.4 (C-20), 170.8 (dimethylsuccinyl 1′-COO−), 175.3 (dimethylsuccinyl 4′-COO−). HRESIMS (positive) *m*/*z* 759.4958 $[M+Na]^+$ (calcd for $C_{49}H_{68}O_5Na$, 759.4964).

5.2.5.2. 3-*O*-(3′,3′-Dimethyglutaryl)betulin benzhydryl ester (17). Yield 100% (starting from 207 mg of **12**); white solid. $[\alpha]_D^{27}$ +18.6° (*c* 1.29, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.81 (3H, s, CH_3-24), 0.84 (6H, s, CH_3-23, 25), 0.99 (3H, s, CH_3-27), 1.03 (3H, s, CH_3-26), 1.09 (6H, s, dimethylglutaryl CH_3), 1.70 (3H, s, CH_3-30), 2.34–2.45 (1H, m, H-19), 2.36, 2.43 (each 1H, d, *J* = 14.4 Hz, dimethylglutaryl H_2-2′), 2.55, 2.58 (each 1H, d, *J* = 14.4 Hz, dimethylglutaryl H_2-4′), 3.34, 3.81 (each 1H, d, *J* = 10.8 Hz, H_2-28), 4.47 (1H, dd, *J* = 4.8, 11.2 Hz, H-3), 4.60, 4.70 (each 1H, br s, H_2-29), 6.89 (1H, s, $CH(Ph)_2$), 7.25–7.39 (10H, m, aromatic-H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.7 (C-27), 16.0 (C-26), 16.1 (C-25), 16.6 (C-24), 18.2 (C-6), 19.0 (C-30), 20.8 (C-11), 23.8 (C-2), 25.2 (C-12), 27.0 (C-15), 27.6, 27.7 (dimethylglutaryl CH_3), 28.0 (C-23), 29.2 (C-16), 29.7 (C-21), 32.8 (dimethylglutaryl C-3′), 33.9 (C-22), 34.1 (C-7), 37.0 (C-10), 37.3 (C-13), 37.7 (C-4), 38.4 (C-1), 40.9 (C-8), 42.7 (C-14), 45.5 (dimethylsuccinyl C-4′), 45.8 (dimethylsuccinyl C-2′), 47.8 (C-17), 47.8 (C-19), 48.7 (C-18), 50.3 (C-9), 55.4 (C-5), 60.5 (C-28), 76.7 ($CH(Ph)_2$), 80.9 (C-3), 109.7 (C-29), 127.1 (benzhydryl C-2′, 6′), 127.8 (benzyhydryl C-4′), 128.4 (benzhydryl C-3′, 5′), 140.2, 140.3 (benzhydryl C-1′), 150.4 (C-20), 170.8 (dimethylglutaryl 5′-COO−), 171.6 (dimethylglutaryl 1′-COO−). HRESIMS (positive) *m*/*z* 773.5124 $[M+Na]^+$ (calcd for $C_{50}H_{70}O_5Na$, 773.5121).

5.2.5.3. 3-*O*-(3′,3′-Dimethylsuccinyl)dihydrobetulin benzhydryl ester (18). Yield 100% (starting from 400 mg of **14**); white solid. $[\alpha]_D^{27}$ −7.9° (*c* 5.27, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.75 (3H, s, CH_3-24), 0.79 (3H, s, CH_3-23), 0.78, 0.85 (each 2H, d, *J* = 8.0 Hz, CH_3-29, 30), 0.81 (3H, s, CH_3-25), 0.96 (3H, s, CH_3-27), 1.03 (3H, s, CH_3-26), 1.31, 1.32 (each 3H, s, dimethylsuccinyl CH_3), 2.66, 2.70 (each 1H, d, *J* = 15.6 Hz, dimethylsuccinyl H_2-2′), 3.31, 3.78 (each 1H, d, *J* = 10.8 Hz, H_2-28), 4.45 (1H, dd, *J* = 5.0, 10.8 Hz, H-3), 6.87 (1H, s, $CH(Ph)_2$), 7.27–7.33 (10H, m, aromatic-H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.6 (C-27), 14.9 (C-29), 15.9 (C-26), 16.0 (C-25), 16.5 (C-24), 18.1 (C-6), 20.8 (C-11), 21.7 (C-21), 22.9 (C-30), 23.5 (C-2), 25.2, 25.4 (dimethylsuccinyl CH_3), 26.8 (C-12), 26.9 (C-15), 27.9 (C-23), 29.3 (C-16), 29.5 (C-20), 34.0 (C-22), 34.2 (C-7), 36.8 (C-13), 37.0 (C-10), 37.6 (C-4), 38.3 (C-1), 40.7 (dimethylsuccinyl C-3′), 40.9 (C-8), 42.8 (C-14), 44.5 (C-19 and dimethylsuccinyl C-2′), 47.9 (C-17), 48.0 (C-18), 49.9 (C-9), 55.3 (C-5), 60.6 (C-28), 77.0 ($CH(Ph)_2$), 81.3 (C-3), 127.0 (benzhydryl C-2′, 6′), 127.7 (benzyhydryl C-4′), 128.4 (benzhydryl C-3′, 5′), 140.3 (benzhydryl C-1′), 170.8 (dimethylsuccinyl 1′-COO−), 175.4 (dimethylsuccinyl 4′-COO−). HRESIMS (positive) *m*/*z* 761.5118 $[M+Na]^+$ (calcd for $C_{49}H_{70}O_5Na$, 761.5121).

5.2.5.4. 3-*O*-(3′,3′-Dimethylglutaryl)dihydrobetulin benzhydryl ester (19). Yield 85.3% (starting from 228 mg of **15**); white solid. $[\alpha]_D^{24}$ −7.7° (*c* 1.26, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.79 (3H, s, CH_3-24), 0.82 (3H, s, CH_3-23, 25), 0.76, 0.83 (each 2H, d, *J* = 8.0 Hz, CH_3-29, 30), 0.94 (3H, s, CH_3-27), 1.00 (3H, s, CH_3-26), 1.07 (6H, s, dimethylglutaryl CH_3), 2.34, 2.41 (each 1H, d, *J* = 14.4 Hz, dimethylglutaryl H_2-2′), 2.53, 2.56 (each 1H, d, *J* = 14.4 Hz, dimethylglutaryl H_2-4′), 3.30, 3.76 (each 1H, d, *J* = 10.8 Hz, H_2-28), 4.46 (1H, dd, *J* = 4.8, 10.8 Hz, H-3), 6.87 (1H, s, $CH(Ph)_2$), 7.23–7.34 (10H, m, aromatic-H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.5 (C-27), 14.8 (C-29), 15.9 (C-26), 16.0 (C-25), 16.5 (C-24), 18.1 (C-6), 20.7 (C-11), 21.6 (C-21), 22.9 (C-30), 23.7

(C-2), 26.8 (C-12), 26.8 (C-15), 27.5, 27.6 (dimethylglutaryl CH_3), 27.9 (C-23), 29.3 (C-16), 29.4 (C-20), 32.7 (dimethylglutaryl C-3′), 34.0 (C-22), 34.1 (C-7), 36.7 (C-13), 36.9 (C-10), 37.6 (C-4), 38.3 (C-1), 40.9 (C-8), 42.8 (C-14), 44.5 (C-19), 45.3 (dimethylglutaryl C-4′), 45.7 (dimethylglutaryl C-2′), 47.8 (C-17), 48.0 (C-18), 49.9 (C-9), 55.2 (C-5), 60.1 (C-28), 76.6 ($CH(Ph)_2$), 80.8 (C-3), 127.0 (benzhydryl C-2′, 6′), 127.7 (benzyhydryl C-4′), 128.3 (benzhydryl C-3′, 5′), 140.2 (benzhydryl C-1′), 170.7 (dimethylglutaryl 5′-COO−), 171.5 (dimethylglutaryl 1′-COO−). HRESIMS (positive) *m*/*z* 775.5303 $[M+Na]^+$ (calcd for $C_{50}H_{72}O_5Na$, 775.5277).

5.2.5.5. 3-*O*-Glutaryl-dihydrobetulin benzhydryl ester (20). Yield 96.4% (starting from 332 mg of **4**); white solid. $[\alpha]_D^{27}$ −4.2° (*c* 3.84, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.84 (3H, s, CH_3-24), 0.85 (3H, s, CH_3-23), 0.79, 0.85 (each 2H, d, *J* = 8.0 Hz, CH_3-29, 30), 0.87 (3H, s, CH_3-25), 0.97 (3H, s, CH_3-27), 1.03 (3H, s, CH_3-26), 2.00 (2H, t, *J* = 7.2 Hz, glutaryl H_2-3′), 2.36 (2H, t, *J* = 7.2 Hz, glutaryl H_2-2′), 2.51 (2H, t, *J* = 7.2 Hz, glutaryl H_2-4′), 3.32, 3.78 (each 1H, d, *J* = 10.8 Hz, H_2-28), 4.50 (1H, dd, *J* = 5.6, 10.4 Hz, H-3), 6.90 (1H, s, $CH(Ph)_2$), 7.26–7.34 (10H, m, aromatic-H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.6 (C-27), 14.9 (C-29), 16.0 (C-26), 16.1 (C-25), 16.5 (C-24), 18.2 (C-6), 20.4 (glutaryl C-3′), 20.9 (C-11), 21.7 (C-21), 22.9 (C-30), 23.7 (C-2), 26.9 (C-12), 26.9 (C-15), 28.0 (C-23), 29.3 (C-16), 29.5 (C-20), 33.6 (glutaryl C-4′), 33.7 (glutaryl C-2′), 34.0 (C-22), 34.3 (C-7), 36.8 (C-13), 37.1 (C-10), 37.8 (C-4), 38.4 (C-1), 41.0 (C-8), 42.9 (C-14), 44.6 (C-19), 47.9 (C-17), 48.1 (C-18), 50.0 (C-9), 55.3 (C-5), 60.6 (C-28), 76.9 ($CH(Ph)_2$), 81.0 (C-3), 127.1 (benzhydryl C-2′, 6′), 127.9 (benzyhydryl C-4′), 128.5 (benzhydryl C-3′, 5′), 140.2 (benzhydryl C-1′), 171.9 (glutaryl 5′-COO−), 172.6 (glutaryl 1′-COO−). HRESIMS (positive) *m*/*z* 747.4962 $[M+Na]^+$ (calcd for $C_{48}H_{68}O_5Na$, 747.4964).

5.2.6. General procedure for syntheses of 3,28-di-*O*-acylbetulin derivatives (21–34)

3,28-Di-*O*-acylbetulin derivatives were prepared by refluxing a solution of 3-*O*-acylbetulin benzhydryl ester derivatives (1 equiv), DMAP (1.5–4.5 equiv) and appropriate dicarboxylic acid (6–9 equiv) or anhydride (3–6 equiv) in anhydrous pyridine (5–8 mL) overnight. After cooling to room temperature, the reaction mixture was poured into ice-water, and extracted with $CHCl_3$. The organic layer was washed with water, 2 N HCl solution and brine in turn, dried over Na_2SO_4, and concentrated. The residue was chromatographed over silica gel column ($CHCl_3$ or hexane/EtOAc = 5:1) or purified by preparative HPLC.

5.2.6.1. 3-*O*-(4′-Benzhydryloxy-3′,3′-dimethylsuccinyl)-28-*O*-succinylbetulin (21). Yield 76.8% (starting from 504.6 mg of **16** and succinic anhydride); white solid. $[\alpha]_D^{18}$ +5.6° (*c* 0.5, $CHCl_3$). ^1H NMR ($CDCl_3$, 500 MHz) δ 0.73 (3H, s, CH_3-24), 0.77 (6H, s, CH_3-23 and CH_3-25), 0.96 (3H, s, CH_3-27), 1.01 (3H, s, CH_3-26), 1.30, 1.31 (each 3H, s, dimethylsuccinyl CH_3), 1.68 (3H, s, CH_3-30), 2.43 (1H, dt, *J* = 5.5, 10.9 Hz, H-19), 2.64, 2.69 (each 1H, d, *J* = 15.8 Hz, 3-*O*-dimethylsuccinyl H_2-2′), 2.68 (4H, t, *J* = 7.3 Hz, 28-*O*-succinyl H_2-2″, H_2-3″), 3.88, 4.30 (each 1H, d, *J* = 10.8 Hz, H_2-28), 4.43 (1H, dd, *J* = 5.2, 11.2 Hz, H-3), 4.59, 4.68 (each 1H, br s, H_2-29), 6.85 (1H, s, $CH(Ph)_2$), 7.24–7.32 (10H, m, aromatic-H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.7 (C-27), 16.0 (C-26), 16.1 (C-25), 16.5 (C-24), 18.1 (C-6), 19.1 (C-30), 20.7 (C-11), 23.5 (C-2), 25.1 (C-12), 25.2, 25.4 (3-*O*-dimethylsuccinyl CH_3), 27.0 (C-15), 27.9 (C-23), 28.8 (28-*O*-succinyl C-3″), 29.0 (28-*O*-succinyl C-2″), 29.5 (C-21), 29.7 (C-16), 34.0 (C-7), 34.5 (C-22), 37.0 (C-10), 37.5 (C-13), 37.6 (C-4), 38.3 (C-1), 40.7 (dimethylsuccinyl C-3′), 40.8 (C-8), 42.6 (C-14), 44.5 (3-*O*-dimethylsuccinyl C-2′), 46.4 (C-17), 47.7 (C-19), 48.7 (C-18), 50.2 (C-9), 55.3 (C-5), 63.2 (C-28), 77.0 ($CH(Ph)_2$), 81.3 (C-3), 109.9 (C-29), 127.0 (benzhydryl C-2′, 6′), 127.7 (benzyhydryl C-4′), 128.4 (benzhydryl C-3′, 5′), 140.3 (benzhydryl C-1′), 150.1 (C-20), 170.9 (3-*O*-dimethylsuccinyl 1′-COO−), 172.5 (28-*O*-succinyl 1″-COO−), 175.4 (3-*O*-dimethylsuccinyl 4′-COO−), 176.8 (28-*O*-succinyl COOH). HRESIMS (positive) *m*/*z* 859.5112 $[M+Na]^+$ (calcd for $C_{53}H_{72}O_8Na$, 859.5125).

5.2.6.2. 3-*O*-(4′-Benzhydryloxy-3′,3′-dimethylsuccinyl)-28-*O*-(3″,3″-dimethylsuccinyl)betulin (22) and 3-*O*-(4′-benzhydryloxy-3′,3′-dimethylsuccinyl)-28-*O*-(2″,2″-dimethylsuccinyl)betulin (23). Yield 68.4% and 31.6%, respectively (starting from 114 mg of **16** and 2,2-dimethylsuccinic acid); separated by preparative HPLC (πNAP, MeOH/2% HOAc = 97:3) for spectroscopic analysis. For synthesis, mixture was used for next reaction without purification.

*Compound **22**:* $[\alpha]_D^{26}$ +6.0° (*c* 6.81, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.75 (3H, s, CH_3-24), 0.79 (3H, s, CH_3-23), 0.80 (3H, s, CH_3-25), 0.97 (3H, s, CH_3-27), 1.03 (3H, s, CH_3-26), 1.32 (12H, s, dimethylsuccinyl CH_3), 1.70 (3H, s, CH_3-30), 2.43 (1H, dt, *J* = 5.6, 10.8 Hz, H-19), 2.64, 2.70 (each 1H, d, *J* = 16.0 Hz, 3-*O*-dimethylsuccinyl H_2-2′), 2.66 (2H, s, 28-*O*-dimethylsuccinyl H_2-2″), 3.88, 4.29 (each 1H, d, *J* = 10.8 Hz, H_2-28), 4.45 (1H, dd, *J* = 5.2, 10.8 Hz, H-3), 4.61, 4.70 (each 1H, br s, H_2-29), 6.87 (1H, s, $CH(Ph)_2$), 7.25–7.33 (10H, m, aromatic-H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.8 (C-27), 16.1 (C-26), 16.1 (C-25), 16.5 (C-24), 18.2 (C-6), 19.2 (C-30), 20.9 (C-11), 23.6 (C-2), 25.2 (C-12), 25.2, 25.4 (3-*O*-dimethylsuccinyl CH_3), 25.3, 25.4 (28-*O*-dimethylsuccinyl CH_3), 27.0 (C-15), 27.9 (C-23), 29.6 (C-21), 29.8 (C-16), 34.2 (C-7), 34.6 (C-22), 37.1 (C-10), 37.7 (C-4, C-13), 38.4 (C-1), 40.7 (dimethylsuccinyl C-3′, C-3″), 40.9 (C-8), 42.7 (C-14), 44.4 (28-*O*-dimethylsuccinyl C-2″), 44.6 (3-*O*-dimethylsuccinyl C-2′), 46.3 (C-17), 47.7 (C-19), 48.9 (C-18), 50.3 (C-9), 55.4 (C-5), 63.1 (C-28), 77.0 ($CH(Ph)_2$), 81.3 (C-3), 109.8 (C-29), 127.0, 127.1 (benzhydryl C-2′, 6′), 127.7 (benzyhydryl C-4′), 128.4 (benzhydryl C-3′, 5′), 140.4 (benzhydryl C-1′), 150.1 (C-20), 170.8 (3-*O*-dimethylsuccinyl 1′-COO−), 171.5 (28-*O*-dimethylsuccinyl 1″-COO−), 175.4 (3-*O*-dimethylsuccinyl 4′-COO−), 182.4 (28-*O*-dimethylsuccinyl COOH). HRESIMS (positive) *m*/*z* 887.5421 $[M+Na]^+$ (calcd for $C_{55}H_{76}O_8Na$, 887.5438).

*Compound **23**:* $[\alpha]_D^{27}$ +6.3° (*c* 3.15, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.75 (3H, s, CH_3-24), 0.79 (3H, s, CH_3-23), 0.80 (3H, s, CH_3-25), 0.98 (3H, s, CH_3-27), 1.03 (3H, s, CH_3-26), 1.31, 1.32 (each 3H, s, 3-*O*-dimethylsuccinyl CH_3), 1.32 (6H, s, 28-*O*-dimethylsuccinyl CH_3), 1.70 (3H, s, CH_3-30), 2.44 (1H, dt, *J* = 5.6, 10.8 Hz, H-19), 2.64, 2.70 (each 1H, d, *J* = 15.6 Hz, 3-*O*-dimethylsuccinyl H_2-2′), 2.66 (2H, s, 28-*O*-dimethylsuccinyl H_2-3″), 3.85, 4.32 (each 1H, d, *J* = 10.8 Hz, H_2-28), 4.45 (1H, dd, *J* = 5.2, 10.8 Hz, H-3), 4.61, 4.70 (each 1H, br s, H_2-29), 6.87 (1H, s, $CH(Ph)_2$), 7.24–7.32 (10H, m, aromatic-H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.8 (C-27), 16.0 (C-26), 16.1 (C-25), 16.5 (C-24), 18.2 (C-6), 19.2 (C-30), 20.8 (C-11), 23.6 (C-2), 25.2 (C-12), 25.2, 25.4 (3-*O*-dimethylsuccinyl CH_3), 25.3, 25.5 (28-*O*-dimethylsuccinyl CH_3), 27.0 (C-15), 27.9 (C-23), 29.6 (C-21), 29.9 (C-16), 34.1 (C-7), 34.5 (C-22), 37.1 (C-10), 37.7 (C-4, 13), 38.4 (C-1), 40.7 (dimethylsuccinyl C-3′, C-2″), 40.9 (C-8), 42.7 (C-14), 44.0 (28-*O*-dimethylsuccinyl C-3″), 44.6 (3-*O*-dimethylsuccinyl C-2′), 46.6 (C-17), 47.8 (C-19), 48.9 (C-18), 50.3 (C-9), 55.4 (C-5), 63.3 (C-28), 77.0 ($CH(Ph)_2$), 81.3 (C-3), 109.8 (C-29), 127.0, 127.1 (benzhydryl C-2′, 6′), 127.7 (benzyhydryl C-4′), 128.4 (benzhydryl C-3′, 5′), 140.4 (benzhydryl C-1′), 150.1 (C-20), 170.8 (3-*O*-dimethylsuccinyl 1′-COO−), 175.4 (3-*O*-dimethylsuccinyl 4′-COO−, 28-*O*-dimethylsuccinyl COOH), 177.0 (28-*O*-dimethylsuccinyl 1″-COO–. HRESIMS (positive) *m*/*z* 887.5440 $[M+Na]^+$ (calcd for $C_{55}H_{76}O_8Na$, 887.5438).

5.2.6.3. 3-*O*-(4′-Benzhydryloxy-3′,3′-dimethylsuccinyl)-28-*O*-glutarylbetulin (24). Yield 59.5% (starting from 406 mg of **16** and glutaric anhydride); white solid. $[\alpha]_D^{15}$ +10.8° (*c* 0.5, $CHCl_3$). ^1H NMR ($CDCl_3$, 500 MHz) δ 0.73 (3H, s, CH_3-24), 0.77 (6H, s, CH_3-23 and CH_3-25), 0.96 (3H, s, CH_3-27), 1.01 (3H, s, CH_3-26),

1.30, 1.31 (each 3H, s, dimethylsuccinyl CH_3), 1.68 (3H, s, CH_3-30), 1.97 (2H, quint, J = 7.2 Hz, 28-*O*-glutaryl H_2-3″), 2.41–2.46 (1H, m, J = 5.5, 10.9 Hz, H-19), 2.43 (2H, t, J = 7.2 Hz, 28-*O*-glutaryl H_2-2″), 2.44 (2H, t, J = 7.2 Hz, 28-*O*-glutaryl H_2-4″), 2.64, 2.69 (each 1H, d, J = 15.8 Hz, 3-*O*-dimethylsuccinyl H_2-2′), 3.85, 4.28 (each 1H, d, J = 10.8 Hz, H_2-28), 4.43 (1H, dd, J = 5.2, 11.4 Hz, H-3), 4.59, 4.68 (each 1H, br s, H_2-29), 6.85 (1H, s, $CH(Ph)_2$), 7.24–7.32 (10H, m, aromatic-H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.7 (C-27), 16.0 (C-26), 16.1 (C-25), 16.5 (C-24), 18.1 (C-6), 19.1 (C-30), 20.0 (28-*O*-glutaryl C-3″), 20.8 (C-11), 23.5 (C-2), 25.1 (C-12), 25.2, 25.4 (3-*O*-dimethylsuccinyl CH_3), 27.0 (C-15), 27.9 (C-23), 29.5 (C-21), 29.7 (C-16), 32.8 (28-*O*-glutaryl C-4″), 33.3 (28-*O*-glutaryl C-2″), 34.1 (C-7), 34.5 (C-22), 37.0 (C-10), 37.6 (2C, C-13 and C-4), 38.4 (C-1), 40.7 (3-*O*-dimethylsuccinyl C-3′), 40.9 (C-8), 42.7 (C-14), 44.5 (3-*O*-dimethylsuccinyl C-2′), 46.4 (C-17), 47.7 (C-19), 48.8 (C-18), 50.2 (C-9), 55.3 (C-5), 62.8 (C-28), 77.0 ($CH(Ph)_2$), 81.3 (C-3), 109.9 (C-29), 127.0 (benzhydryl C-2′, 6′), 127.7 (benzyhydryl C-4′), 128.4 (benzhydryl C-3′, 5′), 140.3 (benzhydryl C-1′), 150.1 (C-20), 170.9 (3-*O*-dimethylsuccinyl 1′-COO−), 173.3 (28-*O*-glutaryl 1″-COO−), 175.4 (3-*O*-dimethylsuccinyl 4′-COO−), 177.7 (28-*O*-glutaryl COOH). HRESIMS (positive) m/z 873.5286 $[M+Na]^+$ (calcd for $C_{54}H_{74}O_8Na$, 873.5281).

5.2.6.4. 3-*O*-(4′-Benzhydryloxy-3′,3′-dimethylsuccinyl)-28-*O*-(3″,3″-dimethylglutaryl)betulin (25). Yield 87.0% (starting from 222 mg of **16** and 3,3-dimethylglutaric acid); white solid. $[\alpha]_D^{25}$ +6.8° (c 3.59, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.74 (3H, s, CH_3-24), 0.79 (3H, s, CH_3-23), 0.79 (3H, s, CH_3-25), 0.98 (3H, s, CH_3-27), 1.03 (3H, s, CH_3-26), 1.16 (6H, s, dimethylglutaryl CH_3), 1.31, 1.32 (each 3H, s, dimethylsuccinyl CH_3), 1.70 (3H, s, CH_3-30), 2.40–2.50 (1H, m, H-19), 2.47, 2.48 (each 2H, s, dimethylglutaryl H_2-2″, 4″), 2.65, 2.70 (each 1H, d, J = 16.0 Hz, 3-*O*-dimethylsuccinyl H_2-2′), 3.86, 4.29 (each 1H, d, J = 10.8 Hz, H_2-28), 4.44 (1H, dd, J = 5.2, 10.8 Hz, H-3), 4.60, 4.70 (each 1H, br s, H_2-29), 6.87 (1H, s, $CH(Ph)_2$), 7.24–7.33 (10H, m, aromatic-H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.7 (C-27), 16.0 (C-26), 16.1 (C-25), 16.5 (C-24), 18.1 (C-6), 19.1 (C-30), 20.8 (C-11), 23.5 (C-2), 25.2 (C-12), 25.2, 25.4 (3-*O*-dimethylsuccinyl CH_3), 26.9 (C-15), 27.8 (28-*O*-dimethylsuccinyl CH_3), 27.9 (C-23), 29.5 (C-21), 29.8 (C-16), 32.6 (dimethylglutaryl C-3″), 34.0 (C-7), 34.6 (C-22), 37.0 (C-10), 37.6 (C-4, 13), 38.3 (C-1), 40.7 (dimethylsuccinyl C-3′), 40.8 (C-8), 42.6 (C-14), 44.5 (3-*O*-dimethylsuccinyl C-2′), 45.1 (dimethylglutaryl C-4″), 45.3 (dimethylglutaryl C-2″), 46.2 (C-17), 47.7 (C-19), 48.8 (C-18), 50.2 (C-9), 55.3 (C-5), 62.8 (C-28), 77.0 ($CH(Ph)_2$), 81.3 (C-3), 109.9 (C-29), 127.0 (benzhydryl C-2′, 6′), 127.7 (benzyhydryl C-4′), 128.4 (benzhydryl C-3′, 5′), 140.3 (benzhydryl C-1′), 150.0 (C-20), 170.9 (3-*O*-dimethylsuccinyl 1′-COO−), 172.7 (28-*O*-dimethylglutaryl 1″-COO−), 175.4 (3-*O*-dimethylsuccinyl 4′-COO−), 176.9 (28-*O*-dimethylglutaryl COOH). HRESIMS (positive) m/z 901.5583 $[M+Na]^+$ (calcd for $C_{56}H_{78}O_8Na$, 901.5594).

5.2.6.5. 3-*O*-(5′-Benzhydryloxy-3′,3′-dimethylglutaryl)-28-*O*-(3″,3″-dimethylglutaryl)betulin (26). Yield 100% (starting from 150 mg of **17** and 3,3-dimethylglutaric anhydride); white solid. $[\alpha]_D^{16}$ +7.3° (c 3.36, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.81 (3H, s, CH_3-24), 0.84 (3H, s, CH_3-23, 25), 0.98 (3H, s, CH_3-27), 1.04 (3H, s, CH_3-26), 1.09 (6H, s, 3-*O*-dimethylglutaryl CH_3), 1.16 (6H, s, 28-*O*-dimethylglutaryl CH_3), 1.70 (3H, s, CH_3-30), 2.43–2.45 (1H, m, H-19), 2.36, 2.43 (each 1H, d, J = 14.4 Hz, 3-*O*-dimethylglutaryl H_2-2′), 2.47, 2.48 (each 2H, s, 28-*O*-dimethylglutaryl H_2-2″, 4″), 2.55, 2.58 (each 1H, d, J = 14.4 Hz, 3-*O*-dimethylglutaryl H_2-4′), 3.86, 4.29 (each 1H, d, J = 11.2 Hz, H_2-28), 4.47 (1H, dd, J = 4.8, 11.2 Hz, H-3), 4.60, 4.70 (each 1H, br s, H_2-29), 6.89 (1H, s, $CH(Ph)_2$), 7.25–7.33 (10H, m, aromatic-H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.7 (C-27), 16.0 (C-26), 16.1 (C-25), 16.6 (C-24), 18.1 (C-6), 19.1 (C-30), 20.8 (C-11), 23.8 (C-2), 25.2 (C-12), 27.0 (C-15), 27.6, 27.7 (3-*O*-dimethylglutaryl CH_3), 27.8 (28-*O*-dimethylglutaryl CH_3), 28.0 (C-23), 29.5 (C-21), 29.8 (C-16), 32.6 (28-*O*-dimethylglutaryl C-3″), 32.8 (28-*O*-dimethylglutaryl C-3′), 34.1 (C-7), 34.6 (C-22), 37.0 (C-10), 37.6 (C-4, 13), 38.4 (C-1), 40.9 (C-8), 42.7 (C-14), 45.1 (28-*O*-dimethylglutaryl C-4″), 45.3 (28-*O*-dimethylglutaryl C-2″), 45.4 (3-*O*-dimethylglutaryl C-4′), 45.8 (3-*O*-dimethylglutaryl C-2′), 46.2 (C-17), 47.7 (C-19), 48.8 (C-18), 50.2 (C-9), 55.4 (C-5), 62.9 (C-28), 76.7 ($CH(Ph)_2$), 80.9 (C-3), 109.9 (C-29), 127.1 (benzhydryl C-2′, 6′), 127.8 (benzyhydryl C-4′), 128.4 (benzhydryl C-3′, 5′), 140.2, 140.3 (benzhydryl C-1′), 150.0 (C-20), 170.8 (3-*O*-dimethylglutaryl 5′-COO−), 171.7 (3-*O*-dimethylglutaryl 1′-COO−), 172.8 (28-*O*-dimethylglutaryl 1″-COO−), 176.5 (28-*O*-dimethylglutaryl COOH). HRESIMS (positive) m/z 915.5771 $[M+Na]^+$ (calcd for $C_{57}H_{80}O_8Na$, 915.5751).

5.2.6.6. 3-*O*-(4′-Benzhydryloxy-3′,3′-dimethylsuccinyl)-28-*O*-(3″,3″-dimethylsuccinyl)dihydrobetulin (27) and 3-*O*-(4′-benzhydryloxy-3′,3′-dimethylsuccinyl)-28-*O*-(2″,2″-dimethylsuccinyl)-dihydrobetulin (28). Total yield 96.3% (starting from 330 mg of **18** and 2,2-dimethylsuccinic acid); used in next reaction without purification. For spectroscopic analysis, a small amount of sample was further purified by preparative HPLC (πNAP, MeOH/2% HOAc = 97:3); white solid.

Compound ***27****:* $[\alpha]_D^{26}$ −12.3° (c 3.50, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.75 (3H, s, CH_3-24), 0.77, 0.85 (each 3H, d, J = 8.0 Hz, CH_3-29, 30), 0.79 (3H, s, CH_3-23), 0.80 (3H, s, CH_3-25), 0.94 (3H, s, CH_3-27), 1.03 (3H, s, CH_3-26), 1.31, 1.32 (each 3H, s, 3-*O*-dimethylsuccinyl CH_3), 1.31 (6H, s, 28-*O*-dimethylsuccinyl CH_3), 2.65 (2H, s, 28-*O*-dimethylsuccinyl H_2-2″), 2.66, 2.70 (each 1H, d, J = 15.6 Hz, 3-*O*-dimethylsuccinyl H_2-2′), 3.85, 4.26 (each 1H, d, J = 11.2 Hz, H_2-28), 4.45 (1H, dd, J = 5.2, 10.8 Hz, H-3), 6.87 (1H, s, $CH(Ph)_2$), 7.25–7.33 (10H, m, aromatic-H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.6 (C-27), 14.9 (C-29), 16.0 (C-25, C-26), 16.5 (C-24), 18.1 (C-6), 20.8 (C-11), 21.5 (C-21), 22.9 (C-30), 23.5 (C-2), 25.2, 25.4 (3-*O*-dimethylsuccinyl CH_3), 25.3, 25.4 (28-*O*-dimethylsuccinyl CH_3), 26.8 (C-12, C-15), 27.9 (C-23), 29.4 (C-20), 29.8 (C-16), 34.1 (C-7), 34.6 (C-22), 36.9 (C-10), 37.1 (C-13), 37.6 (C-4), 38.3 (C-1), 40.5 (28-*O*-dimethylsuccinyl C-3″), 40.7 (3-*O*-dimethylsuccinyl C-3′), 40.9 (C-8), 42.8 (C-14), 44.4 (28-*O*-dimethylsuccinyl C-2″), 44.5 (C-19, 3-*O*-dimethylsuccinyl C-2′), 46.4 (C-17), 48.1 (C-18), 49.9 (C-9), 55.3 (C-5), 63.1 (C-28), 77.0 ($CH(Ph)_2$), 81.3 (C-3), 127.0, 127.1 (benzhydryl C-2′, 6′), 127.7 (benzyhydryl C-4′), 128.4 (benzhydryl C-3′, 5′), 140.3 (benzhydryl C-1′), 170.9 (3-*O*-dimethylsuccinyl 1′-COO−), 171.6 (28-*O*-dimethylsuccinyl 1″-COO−), 175.4 (3-*O*-dimethylsuccinyl 4′-COO−), 182.9 (28-*O*-dimethylsuccinyl COOH). HRESIMS (positive) m/z 889.5585 $[M+Na]^+$ (calcd for $C_{55}H_{78}O_8Na$, 889.5594).

Compound ***28****:* $[\alpha]_D^{27}$ −11.4° (c 2.30, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.75 (3H, s, CH_3-24), 0.78, 0.85 (each 3H, d, J = 8.0 Hz, CH_3-29, 30), 0.79 (3H, s, CH_3-23), 0.80 (3H, s, CH_3-25), 0.95 (3H, s, CH_3-27), 1.03 (3H, s, CH_3-26), 1.32, 1.31 (each 3H, s, 3-*O*-dimethylsuccinyl CH_3), 1.31 (each 3H, s, 28-*O*-dimethylsuccinyl CH_3), 2.66, 2.70 (each 1H, d, J = 15.6 Hz, 3-*O*-dimethylsuccinyl H_2-2′), 2.65 (2H, s, 28-*O*-dimethylsuccinyl H_2-3″), 3.79, 4.31 (each 1H, d, J = 10.8 Hz, H_2-28), 4.45 (1H, dd, J = 5.2, 11.2 Hz, H-3), 6.87 (1H, s, $CH(Ph)_2$), 7.25–7.33 (10H, m, aromatic-H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.6 (C-27), 14.9 (C-29), 16.0 (C-25, C-26), 16.5 (C-24), 18.1 (C-6), 20.8 (C-11), 21.5 (C-21), 22.9 (C-30), 23.5 (C-2), 25.2, 25.4 (3-*O*-dimethylsuccinyl CH_3), 25.4, 25.5 (28-*O*-dimethylsuccinyl CH_3), 26.8 (C-12, C-15), 27.9 (C-23), 29.4 (C-20), 29.9 (C-16), 34.1 (C-7), 34.7 (C-22), 37.0 (C-10), 37.1 (C-13), 37.7 (C-4), 38.4 (C-1), 40.7 (3-*O*-dimethylsuccinyl C-3′, 28-*O*-dimethylsuccinyl 2″), 40.9 (C-8), 42.8 (C-14), 43.9 (28-*O*-dimethylsuccinyl C-3″), 44.5 (C-19, 3-*O*-dimethylsuccinyl C-2′), 46.6 (C-17), 48.2 (C-18), 49.9 (C-9), 55.3 (C-5), 63.3 (C-28), 77.0 ($CH(Ph)_2$), 81.3 (C-3), 127.0, 127.1 (benzhydryl C-2′, 6′), 127.7

(benzyhydryl C-4′), 128.4 (benzhydryl C-3′, 5′), 140.3 (benzhydryl C-1′), 170.9 (3-*O*-dimethylsuccinyl 1′-COO−), 175.4 (3-*O*-dimethylsuccinyl 4′-COO−, 28-*O*-dimethylsuccinyl 1″-COOH), 177.0 (28-*O*-dimethylsuccinyl 1″-COO−). HRESIMS (positive) *m*/*z* 889.5590 $[M+Na]^+$ (calcd for $C_{55}H_{78}O_8Na$, 889.5594).

5.2.6.7. 3-*O*-(4′-Benzhydryloxy-3′,3′-dimethylsuccinyl)-28-*O*-(3″,3″-dimethylglutaryl)dihydrobetulin (29). Yield 100% (starting from 110 mg of **18** and 3,3-dimethylglutaric anhydride); white solid. $[\alpha]_D^{26}$ −10.2° (*c* 2.04, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.74 (3H, s, CH_3-24), 0.78 (3H, s, CH_3-23), 0.78, 0.85 (each 3H, d, *J* = 8.0 Hz, CH_3-29, 30), 0.80 (3H, s, CH_3-25), 0.95 (3H, s, CH_3-27), 1.04 (3H, s, CH_3-26), 1.15 (6H, s, dimethylglutaryl CH_3), 1.31, 1.32 (each 3H, s, dimethylsuccinyl CH_3), 2.46, 2.48 (each 2H, s, dimethylglutaryl H_2-2″, 4″), 2.65, 2.71 (each 1H, d, *J* = 16.0 Hz, 3-*O*-dimethylsuccinyl H_2-2′), 3.83, 4.28 (each 1H, d, *J* = 10.8 Hz, H_2-28), 4.45 (1H, dd, *J* = 5.2, 11.2 Hz, H-3), 6.86 (1H, s, $CH(Ph)_2$), 7.25–7.33 (10H, m, aromatic-H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.6 (C-27), 14.9 (C-29), 16.0 (C-25, C-26), 16.5 (C-24), 18.1 (C-6), 20.7 (C-11), 21.6 (C-21), 22.9 (C-30), 23.5 (C-2), 25.2, 25.4 (3-*O*-dimethylsuccinyl CH_3), 26.8 (C-12), 26.9 (C-15), 27.9 (C-23, 28-*O*-dimethylsuccinyl CH_3), 29.4 (C-20), 29.9 (C-16), 32.7 (dimethylglutaryl C-3″), 34.1 (C-7), 34.7 (C-22), 37.0 (C-10), 37.2 (C-13), 37.6 (C-4), 38.4 (C-1), 40.7 (dimethylsuccinyl C-3′), 40.9 (C-8), 42.8 (C-14), 44.5 (C-19, 3-*O*-dimethylsuccinyl C-2′), 45.1 (dimethylglutaryl C-4″), 45.4 (dimethylglutaryl C-2″), 46.4 (C-17), 48.1 (C-18), 49.9 (C-9), 55.3 (C-5), 63.0 (C-28), 77.0 ($CH(Ph)_2$), 81.3 (C-3), 127.0 (benzhydryl C-2′, 6′), 127.7 (benzyhydryl C-4′), 128.4 (benzhydryl C-3′, 5′), 140.3 (benzhydryl C-1′), 170.9 (3-*O*-dimethylsuccinyl 1′-COO−), 173.0 (28-*O*-dimethylglutaryl 1″-COO−), 175.4 (3-*O*-dimethylsuccinyl 4′-COO−), 176.0 (28-*O*-dimethylglutaryl COOH). HRESIMS (positive) *m*/*z* 903.5748 $[M+Na]^+$ (calcd for $C_{56}H_{80}O_8Na$, 903.5751).

5.2.6.8. 3-*O*-(5′-Benzhydryloxyglutaryl)-28-*O*-(3″,3″-dimethylsuccinyl)dihydrobetulin (30) and 3-*O*-(5′-benzhydryloxyglutaryl)-28-O-(2″,2″-dimethylsuccinyl)dihydrobetulin (31). Total yield 98.9% (starting from 225 mg of **20** and 2,2-dimethylsuccinic acid); used for next reaction without purification. For spectroscopic analysis, a small amount of sample was further purified by preparative HPLC (πNAP, $CH_3OH/H_2O/CH_3COOH$ = 95:4:1); colorless oil.

Compound ***30****:* $[\alpha]_D^{27}$ −7.1° (*c* 3.50, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.78, 0.85 (each 3H, d, *J* = 8.0 Hz, CH_3-29, 30), 0.84 (each 3H, s, CH_3-23, 24), 0.87 (3H, s, CH_3-25), 0.96 (3H, s, CH_3-27), 1.05 (3H, s, CH_3-26), 1.32 (6H, s, 28-*O*-dimethylsuccinyl CH_3), 2.00 (2H, quint, *J* = 7.2 Hz, 3-*O*-glutaryl H_2-3′), 2.36 (2H, t, *J* = 7.2 Hz, 3-*O*-glutaryl H_2-2′), 2.51 (2H, t, *J* = 7.2 Hz, 3-*O*-glutaryl H_2-4′), 2.65 (2H, s, 28-*O*-dimethylsuccinyl H_2-2″), 3.85, 4.28 (each 1H, d, *J* = 10.8 Hz, H_2-28), 4.49 (1H, dd, *J* = 6.0, 10.0 Hz, H-3), 6.90 (1H, s, $CH(Ph)_2$), 7.26–7.34 (10H, m, aromatic-H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.6 (C-27), 14.9 (C-29), 16.1 (C-25, C-26), 16.5 (C-24), 18.2 (C-6), 20.3 (glutaryl C-3′), 20.8 (C-11), 21.6 (C-21), 22.9 (C-30), 23.7 (C-2), 25.3 (28-*O*-dimethylsuccinyl CH_3), 26.8 (C-12), 26.9 (C-15), 28.0 (C-23), 29.4 (C-20), 29.8 (C-16), 33.6 (glutaryl C-4′), 33.7 (glutaryl C-2′), 34.2 (C-7), 34.7 (C-22), 37.0 (C-10), 37.2 (C-13), 37.8 (C-4), 38.4 (C-1), 40.5 (28-*O*-dimethylsuccinyl C-3″), 40.9 (C-8), 42.9 (C-14), 44.4 (28-*O*-dimethylsuccinyl C-2″), 44.5 (C-19), 46.4 (C-17), 48.2 (C-18), 50.0 (C-9), 55.3 (C-5), 63.1 (C-28), 76.9 ($CH(Ph)_2$), 81.0 (C-3), 127.0 (benzhydryl C-2′, 6′), 127.9 (benzyhydryl C-4′), 128.5 (benzhydryl C-3′, 5′), 140.2 (benzhydryl C-1′), 171.5 (28-*O*-dimethylsuccinyl 1″-COO−), 171.9 (3-*O*-glutaryl 5′-COO−), 172.6 (3-*O*-glutaryl 1′-COO−), 182.6 (28-*O*-dimethylsuccinyl COOH). HRESIMS (positive) *m*/*z* 875.5408 $[M+Na]^+$ (calcd for $C_{54}H_{76}O_8Na$, 875.5438).

Compound ***31****:* $[\alpha]_D^{27}$ −7.4° (*c* 1.26, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.79, 0.85 (each 3H, d, *J* = 8.0 Hz, CH_3-29, 30), 0.84 (each 3H, s, CH_3-23, 24), 0.87 (3H, s, CH_3-25), 0.96 (3H, s, CH_3-27), 1.05 (3H, s, CH_3-26), 1.31 (6H, s, 28-*O*-dimethylsuccinyl CH_3), 2.00 (2H, quint, *J* = 7.2 Hz, 3-*O*-glutaryl H_2-3′), 2.36 (2H, t, *J* = 7.2 Hz, 3-*O*-glutaryl H_2-2′), 2.50 (2H, t, *J* = 7.2 Hz, 3-*O*-glutaryl H_2-4′), 2.65 (2H, s, 28-*O*-dimethylsuccinyl H_2-3″), 3.81, 4.32 (each 1H, d, *J* = 10.8 Hz, H_2-28), 4.49 (1H, dd, *J* = 6.0, 10.0 Hz, H-3), 6.90 (1H, s, $CH(Ph)_2$), 7.26–7.34 (10H, m, aromatic-H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.7 (C-27), 14.9 (C-29), 16.1 (C-25, C-26), 16.6 (C-24), 18.2 (C-6), 20.4 (glutaryl C-3′), 20.8 (C-11), 21.6 (C-21), 22.9 (C-30), 23.7 (C-2), 25.4, 25.5 (28-*O*-dimethylsuccinyl CH_3), 26.8 (C-12), 26.9 (C-15), 28.0 (C-23), 29.4 (C-20), 29.9 (C-16), 33.6 (glutaryl C-4′), 33.7 (glutaryl C-2′), 34.2 (C-7), 34.7 (C-22), 37.0 (C-10), 37.2 (C-13), 37.8 (C-4), 38.4 (C-1), 40.8 (28-*O*-dimethylsuccinyl C-2″), 40.9 (C-8), 42.9 (C-14), 43.9 (28-*O*-dimethylsuccinyl C-3″), 44.6 (C-19), 46.7 (C-17), 48.2 (C-18), 50.0 (C-9), 55.4 (C-5), 63.4 (C-28), 77.0 ($CH(Ph)_2$), 81.0 (C-3), 127.0 (benzhydryl C-2′, 6′), 127.9 (benzyhydryl C-4′), 128.5 (benzhydryl C-3′, 5′), 140.2 (benzhydryl C-1′), 171.9 (3-*O*-glutaryl 5′-COO−), 172.6 (3-*O*-glutaryl 1′-COO−), 175.8 (28-*O*-dimethylsuccinyl 1″-COOH), 177.1 (28-*O*-dimethylsuccinyl COO−). HRESIMS (positive) *m*/*z* 875.5450 $[M+Na]^+$ (calcd for $C_{54}H_{76}O_8Na$, 875.5438).

5.2.6.9. 3-*O*-(5′-Benzhydryloxyglutaryl)-28-*O*-glutaryldihydrobetulin (32). Yield 94.9% (starting from 89 mg of **20** and glutaric anhydride); colorless oil. $[\alpha]_D^{27}$ −1.2° (*c* 1.04, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.78, 0.84 (each 3H, d, *J* = 8.0 Hz, CH_3-29, 30), 0.83 (3H, s, CH_3-24), 0.84 (3H, s, CH_3-24), 0.87 (3H, s, CH_3-25), 0.96 (3H, s, CH_3-27), 1.06 (3H, s, CH_3-26), 1.98 (2H, quint, *J* = 7.2 Hz, 28-*O*-glutaryl H_2-3″), 2.00 (2H, quint, *J* = 7.2 Hz, 3-*O*-glutaryl H_2-3′), 2.36 (2H, t, *J* = 7.2 Hz, 3-*O*-glutaryl H_2-2′), 2.43 (2H, t, *J* = 7.2 Hz, 28-*O*-glutaryl H_2-2″), 2.44 (2H, t, *J* = 7.2 Hz, 28-*O*-glutaryl H_2-4″), 2.50 (2H, t, *J* = 7.2 Hz, 3-*O*-glutaryl H_2-4′), 3.84, 4.30 (each 1H, d, *J* = 10.8 Hz, H_2-28), 4.49 (1H, dd, *J* = 6.0, 10.4 Hz, H-3), 6.90 (1H, s, $CH(Ph)_2$), 7.26–7.33 (10H, m, aromatic-H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.6 (C-27), 14.9 (C-29), 16.1 (C-25, C-26), 16.6 (C-24), 18.2 (C-6), 20.0 (28-*O*-glutaryl C-3″), 20.4 (3-*O*-glutaryl C-3′), 20.8 (C-11), 21.6 (C-21), 22.9 (C-30), 23.7 (C-2), 26.8 (C-12), 27.0 (C-15), 28.0 (C-23), 29.4 (C-20), 29.9 (C-16), 32.8 (28-*O*-glutaryl C-4″), 33.3 (28-*O*-glutaryl C-2″), 33.6 (3-*O*-glutaryl C-4′), 33.7 (3-*O*-glutaryl C-2′), 34.2 (C-7), 34.7 (C-22), 37.1 (C-10), 37.2 (C-13), 37.8 (C-4), 38.4 (C-1), 41.0 (C-8), 42.9 (C-14), 44.6 (C-19), 46.6 (C-17), 48.2 (C-18), 50.0 (C-9), 55.4 (C-5), 62.9 (C-28), 77.0 ($CH(Ph)_2$), 81.0 (C-3), 127.1 (benzhydryl C-2′, 6′), 127.9 (benzyhydryl C-4′), 128.5 (benzhydryl C-3′, 5′), 140.2 (benzhydryl C-1′), 171.9 (3-*O*-glutaryl 5′-COO−), 172.6 (3-*O*-glutaryl 1′-COO−), 173.3 (28-*O*-glutaryl 1″-COO−), 177.3 (28-*O*-glutaryl COOH). HRESIMS (positive) *m*/*z* 861.5292 $[M+Na]^+$ (calcd for $C_{53}H_{74}O_8Na$, 861.5281).

5.2.6.10. 3-*O*-(5′-Benzhydryloxyglutaryl)-28-*O*-(3″,3″-dimethylglutaryl)dihydrobetulin (33). Yield 91.6% (starting from 82 mg of **20** and 3,3-dimethylglutaric anhydride); colorless oil. $[\alpha]_D^{27}$ −5.4° (*c* 1.43, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.78, 0.84 (each 3H, d, *J* = 8.0 Hz, CH_3-29, 30), 0.83 (3H, s, CH_3-24), 0.84 (3H, s, CH_3-24), 0.87 (3H, s, CH_3-25), 0.97 (3H, s, CH_3-27), 1.06 (3H, s, CH_3-26), 1.16 (6H, s, 28-*O*-dimethylglutaryl CH_3), 2.00 (2H, quint, *J* = 7.2 Hz, 3-*O*-glutaryl H_2-3′), 2.36 (2H, t, *J* = 7.2 Hz, 3-*O*-glutaryl H_2-2′), 2.46 (2H, s, 28-*O*-dimthylglutaryl H_2-2″), 2.49 (2H, s, 28-*O*-glutaryl H_2-4″), 2.50 (2H, t, *J* = 7.2 Hz, 3-*O*-glutaryl H_2-4′), 3.84, 4.30 (each 1H, d, *J* = 10.8 Hz, H_2-28), 4.49 (1H, dd, *J* = 5.6, 10.8 Hz, H-3), 6.90 (1H, s, $CH(Ph)_2$), 7.26–7.33 (10H, m, aromatic-H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.7 (C-27), 14.9 (C-29), 16.1 (C-25, C-26), 16.6 (C-24), 18.2 (C-6), 20.4 (3-*O*-glutaryl C-3′), 20.8 (C-11), 21.6 (C-21), 22.9 (C-30), 23.7 (C-2), 26.8 (C-12), 26.9 (C-15), 27.9 (28-*O*-dimethylglutaryl CH_3), 28.0 (C-23), 29.4 (C-20), 29.9 (C-16), 32.7 (28-*O*-dimethylglutaryl C-3″), 33.6 (3-*O*-glutaryl C-4′), 33.7 (3-*O*-glutaryl C-2′), 34.2 (C-7), 34.7 (C-22), 37.1 (C-10), 37.2 (C-13),

37.8 (C-4), 38.4 (C-1), 41.0 (C-8), 42.9 (C-14), 44.6 (C-19), 45.1 (28-*O*-dimethylglutaryl C-4″), 45.4 (28-*O*-dimethylglutaryl C-2″), 46.4 (C-17), 48.2 (C-18), 50.0 (C-9), 55.4 (C-5), 63.1 (C-28), 77.0 ($CH(Ph)_2$), 81.0 (C-3), 127.1 (benzhydryl C-2′, 6′), 127.9 (benzyhydryl C-4′), 128.5 (benzhydryl C-3′, 5′), 140.2 (benzhydryl C-1′), 171.9 (3-*O*-glutaryl 5′-COO−), 172.6 (3-*O*-glutaryl 1′-COO−), 173.0 (28-*O*-dimethylglutaryl 1″-COO−), 175.6 (28-*O*-dimethylglutaryl COOH). HRESIMS (positive) *m*/*z* 889.5605 $[M+Na]^+$ (calcd for $C_{55}H_{78}O_8Na$, 889.5594).

5.2.6.11. 3-*O*-(5′-Benzhydryloxy-3′,3′-dimethylglutaryl)-28-*O*-(3″,3″-dimethylglutaryl)dihydrobetulin (34). Yield 97% (starting from 137 mg of **19** and 3,3-dimethylglutaric anhydride); white solid. $[\alpha]_D^{28}$ −9.3° (*c* 2.94, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.78, 0.83 (each 3H, d, *J* = 8.0 Hz, CH_3-29, 30), 0.81 (3H, s, CH_3-24), 0.84 (3H, s, CH_3-24), 0.85 (3H, s, CH_3-25), 0.96 (3H, s, CH_3-27), 1.05 (3H, s, CH_3-26), 1.09 (6H, s, 3-*O*-dimethylglutaryl CH_3), 1.15 (6H, s, 28-*O*-dimethylglutaryl CH_3), 2.36, 2.43 (each 1H, d, *J* = 14.4 Hz, 3-*O*-dimethylglutaryl H_2-2′), 2.46 (2H, s, 28-*O*-dimthylglutaryl H_2-2″), 2.48 (2H, s, 28-*O*-dimethylglutaryl H_2-4″), 2.55, 2.58 (each 1H, d, *J* = 14.4 Hz, 3-*O*-dimethylglutaryl H_2-4′), 3.83, 4.29 (each 1H, d, *J* = 11.2 Hz, H_2-28), 4.47 (1H, dd, *J* = 4.8, 10.8 Hz, H-3), 6.89 (1H, s, $CH(Ph)_2$), 7.25–7.34 (10H, m, aromatic-H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.6 (C-27), 14.9 (C-29), 16.0 (C-25, C-26), 16.6 (C-24), 18.1 (C-6), 20.8 (C-11), 21.6 (C-21), 22.9 (C-30), 23.7 (C-2), 26.8 (C-12, C-15), 27.6, 27.7 (3-*O*-dimethylglutaryl CH_3), 27.9 (28-*O*-dimethylglutaryl CH_3), 28.0 (C-23), 29.4 (C-20), 29.9 (C-16), 32.6 (28-*O*-dimethylglutaryl C-3″), 32.8 (3-*O*-dimethylglutaryl C-3′), 34.2 (C-7), 34.7 (C-22), 37.0 (C-10), 37.2 (C-13), 37.6 (C-4), 38.4 (C-1), 41.0 (C-8), 42.8 (C-14), 44.5 (C-19), 45.1 (28-*O*-dimethylglutaryl C-4″), 45.3 (28-*O*-dimethylglutaryl C-2″), 45.4 (3-*O*-dimethylglutaryl C-4′), 45.8 (3-*O*-dimethylglutaryl C-2′), 46.4 (C-17), 48.1 (C-18), 49.9 (C-9), 55.3 (C-5), 63.0 (C-28), 76.7 ($CH(Ph)_2$), 80.9 (C-3), 127.1 (benzhydryl C-2′, 6′), 127.8 (benzyhydryl C-4′), 128.4 (benzhydryl C-3′, 5′), 140.2, 140.3 (benzhydryl C-1′), 170.8 (3-*O*-dimethylglutaryl 5′-COO−), 171.7 (3-*O*-dimethylglutaryl 1′-COO−), 172.9 (28-*O*-dimethylglutaryl 1″-COO−), 176.4 (28-*O*-dimethylglutaryl COOH). HRESIMS (positive) *m*/*z* 917.5843 $[M+Na]^+$ (calcd for $C_{57}H_{82}O_8Na$, 917.5907).

5.2.7. General procedure for coupling of 3,28-di-*O*-acylbetulin derivatives with AZT (35–48)

To a solution of 3,28-di-*O*-acylbetulin derivatives (1 equiv) in CH_2Cl_2 (4–10 mL) was added DMAP (2 equiv), DCC (2 equiv) and 3′-azido-3′-dexoythymidine (AZT, 2 equiv). The reaction mixture was kept stirring at room temperature for overnight. After filtration, the filtrate was concentrated and the residue was chromatographed over silica gel column (hexane/EtOAc = 2:1) or purified by HPLC.

5.2.7.1. 3′-Azido-3′-deoxythymidine 5′-yl 3-*O*-(4′-benzhydryloxy-3′,3′-dimethylsuccinyl)-lup-20(29)en-28-yl succinate (35). Yield 41.7% (starting from 80 mg of **21**); white solid. $[\alpha]_D^{18}$ +6.2° (*c* 0.53, $CHCl_3$). ^1H NMR ($CDCl_3$, 500 MHz) δ 0.72 (3H, s, CH_3-24), 0.76 (3H, s, CH_3-23), 0.77 (3H, s, CH_3-25), 0.95 (3H, s, CH_3-27), 1.01 (3H, s, CH_3-26), 1.29, 1.30 (each 3H, s, 3-*O*-dimethylsuccinyl CH_3), 1.68 (3H, s, CH_3-30), 1.95 (3H, br s, AZT-CH_3), 2.33–2.50 (3H, m, AZT-H_2-2′ and H-19), 2.62–2.79 (4H, m, 28-*O*-succinyl H_2-2″, 3″), 2.64, 2.68 (each 1H, d, *J* = 16.0 Hz, 3-*O*-dimethylsuccinyl H_2-2′), 3.86, 4.30 (each 1H, d, *J* = 11.2 Hz, H_2-28), 4.05 (1H, q-like, AZT-H-4′), 4.21–4.24 (1H, m, AZT-H-3′), 4.30 (1H, dd, *J* = 3.4, 12.0 Hz, AZT-H_2-5a′), 4.52 (1H, dd, *J* = 4.0, 12.0 Hz, AZT-H_2-5b′), 4.42 (1H, dd, *J* = 5.2, 11.2 Hz, H-3), 4.59, 4.68 (each 1H, br s, H_2-29), 6.15 (1H, t-like, *J* = 6.3 Hz, AZT-H-1′), 6.84 (1H, s, $CH(Ph)_2$), 7.24–7.32 (11H, m, aromatic-H and AZT-H-6), 8.13 (1H, br s, AZT-NH); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 12.6 AZT-CH_3, 14.7 (C-27), 16.0 (C-26), 16.1 (C-25), 16.5 (C-24), 18.1 (C-6), 19.1 (C-30), 20.7 (C-11), 23.5 (C-2), 25.1 (C-12), 25.2, 25.4 (3-*O*-dimethylsuccinyl CH_3), 27.0 (C-15), 27.9 (C-23), 29.0 (28-*O*-succinyl C-2″, 3″), 29.5 (C-21), 29.7 (C-16), 34.1 (C-7), 34.5 (C-22), 37.0 (C-10), 37.6 (AZT-C-2′), 37.6 (C-13), 37.7 (C-4), 38.3 (C-1), 40.7 (dimethylsuccinyl C-3′), 40.8 (C-8), 42.7 (C-14), 44.5 (3-*O*-dimethylsuccinyl C-2′), 46.4 (C-17), 47.7 (C-19), 48.7 (C-18), 50.2 (C-9), 55.3 (C-5), 60.1 (AZT-C-3′), 63.1 (AZT-C-5′), 63.3 (C-28), 77.0 ($CH(Ph)_2$), 81.3 (C-3), 81.9 (AZT-C-4′), 85.1 (AZT-C-1′), 110.0 (C-29), 111.3 (AZT-C-5), 127.0, 127.1 (benzhydryl C-2′, 6′), 127.7 (benzyhydryl C-4′), 128.4 (benzhydryl C-3′, 5′), 135.3 (AZT-C-6), 140.3 (benzhydryl C-1′), 149.8 (AZT-C-2), 150.0 (C-20), 163.1 (AZT-C-4), 170.9 (3-*O*-dimethylsuccinyl 1′-COO−), 172.0 (28-*O*-succinyl 4″-COO-AZT), 172.6 (28-*O*-succinyl 1″-COO−), 175.4 (3-*O*-dimethylsuccinyl 4′-COO−). HRESIMS (positive) *m*/*z* 1108.6014 $[M+Na]^+$ (calcd for $C_{63}H_{83}N_5O_{11}Na$, 1108.5987).

5.2.7.2. 1-(3′-Azido-3′-deoxythymidine-5′-yl)-4-[3-*O*-(4′-benzhydryloxy-3′,3′-dimethylsuccinyl)-lup-20(29)en-28-yl] 2,2-dimethylsuccinate (36) and 4-(3′-Azido-3′-deoxythymidine-5′-yl)-1-[3-*O*-(4′-benzhydryloxy-3′,3′-dimethylsuccinyl)-lup-20(29)en-28-yl] 2,2-dimethylsuccinate (37). Total yield 49.3% (starting from 296 mg of mixture of **22** and **23**); used for next reaction without separation. A small amount of sample mixture was separated by HPLC (cholester, CH_3OH/H_2O = 97:3) for spectroscopic analyses.

Compound ***36****:* $[\alpha]_D^{27}$ +7.2° (*c* 1.77, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.74 (3H, s, CH_3-24), 0.78 (each 3H, s, CH_3-23, 25), 0.96 (3H, s, CH_3-27), 1.02 (3H, s, CH_3-26), 1.30, 1.31 (each 3H, s, 28-*O*-dimethylsuccinyl CH_3), 1.31, 1.32 (each 3H, s, 3-*O*-dimethylsuccinyl CH_3), 1.68 (3H, s, CH_3-30), 1.94 (3H, br s, AZT-CH_3), 2.26–2.33, 2.44–2.50 (each 1H, m, AZT-H_2-2′), 2.37–2.44 (1H, m, H-19), 2.65, 2.69 (each 1H, d, *J* = 16.0 Hz, 3-*O*-dimethylsuccinyl H_2-2′), 2.61, 2.75 (each 1H, d, *J* = 16.4 Hz, 28-*O*-dimethylsuccinyl H_2-2″), 3.84, 4.29 (each 1H, d, *J* = 10.8 Hz, H_2-28), 4.09 (1H, q-like, AZT-H-4′), 4.26–4.30 (1H, m, AZT-H-3′), 4.30, 4.52 (each 1H, dd, *J* = 4.0, 12.0 Hz, AZT-H_2-5′), 4.43 (1H, dd, *J* = 5.2, 10.8 Hz, H-3), 4.60, 4.69 (each 1H, br s, H_2-29), 6.18 (1H, t-like, *J* = 6.4 Hz, AZT-H-1′), 6.86 (1H, s, $CH(Ph)_2$), 7.24–7.33 (11H, m, aromatic-H and AZT-H-6), 8.56 (1H, br s, AZT-NH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.5 AZT-CH_3, 14.7 (C-27), 15.9 (C-26), 16.1 (C-25), 16.5 (C-24), 18.1 (C-6), 19.1 (C-30), 20.7 (C-11), 23.5 (C-2), 25.2 (C-12), 25.2, 25.4 (3-*O*-dimethylsuccinyl CH_3), 25.1, 25.9 (28-*O*-dimethylsuccinyl CH_3), 27.0 (C-15), 27.9 (C-23), 29.5 (C-21), 29.7 (C-16), 34.1 (C-7), 34.5 (C-22), 37.0 (C-10), 37.4 (AZT-C-2′), 37.6 (C-4, 13), 38.3 (C-1), 40.7 (dimethylsuccinyl C-3′, C-3″), 40.8 (C-8), 42.7 (C-14), 44.5 (3-*O*-dimethylsuccinyl C-2′), 44.6 (28-*O*-dimethylsuccinyl C-2″), 46.3 (C-17), 47.7 (C-19), 48.7 (C-18), 50.2 (C-9), 55.3 (C-5), 60.4 (AZT-C-3′), 63.1 (C-28), 63.0 (AZT-C-5′), 77.0 ($CH(Ph)_2$), 81.2 (C-3), 81.9 (AZT-C-4′), 84.8 (AZT-C-1′), 110.0 (C-29), 111.4 (AZT-C-5), 127.0, 127.1 (benzhydryl C-2′, 6′), 127.7 (benzyhydryl C-4′), 128.4 (benzhydryl C-3′, 5′), 135.0 (AZT-C-6), 140.4 (benzhydryl C-1′), 149.9 (C-20 and AZT-C-2), 163.3 (AZT-C-4), 170.8 (3-*O*-dimethylsuccinyl 1′-COO−), 171.7 (28-*O*-dimethylsuccinyl 1″-COO−), 175.4 (3-*O*-dimethylsuccinyl 4′-COO−), 176.4 (28-*O*-dimethylsuccinyl 4″-COO-AZT). HRESIMS (positive) *m*/*z* 1136.6310 $[M+Na]^+$ (calcd for $C_{65}H_{87}N_5O_{11}Na$, 1136.6300).

Compound ***37****:* $[\alpha]_D^{27}$ +11.6° (*c* 3.64, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.73 (3H, s, CH_3-24), 0.77 (3H, s, CH_3-23), 0.78 (3H, s, C-25), 0.96 (3H, s, CH_3-27), 1.02 (3H, s, CH_3-26), 1.30, 1.32 (each 3H, s, 3-*O*-dimethylsuccinyl CH_3), 1.31, 1.34 (each 3H, s, 28-*O*-dimethylsuccinyl CH_3), 1.69 (3H, s, CH_3-30), 1.95 (3H, br s, AZT-CH_3), 2.33–2.50 (3H, m, AZT-H_2-2′ and H-19), 2.62, 2.66 (each 1H, d, *J* = 16.4 Hz, 28-*O*-dimethylsuccinyl H_2-3″), 2.64, 2.69 (each 1H, d, *J* = 16.0 Hz, 3-*O*-dimethylsuccinyl H_2-2′), 3.85, 4.29 (each 1H, d, *J* = 10.8 Hz, H_2-28), 4.04 (1H, q-like, AZT-H-4′), 4.18–4.22 (1H, m, AZT-H-3′), 4.26 (1H, dd, *J* = 4.0, 12.0 Hz, AZT-H-5a′), 4.42 (1H, dd,

J = 4.4, 12.0 Hz, AZT-H-5b′), 4.43 (1H, dd, *J* = 4.8, 10.4 Hz, H-3), 4.60, 4.69 (each 1H, br s, H_2-29), 6.15 (1H, t-like, *J* = 6.4 Hz, AZT-H-1′), 6.85 (1H, s, $CH(Ph)_2$), 7.24–7.32 (11H, m, aromatic-H and AZT-H-6), 8.94 (1H, br s, AZT-NH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.6 AZT-CH_3, 14.7 (C-27), 15.9 (C-26), 16.0 (C-25), 16.5 (C-24), 18.1 (C-6), 19.1 (C-30), 20.7 (C-11), 23.5 (C-2), 25.2 (C-12), 25.2, 25.5 (3-*O*-dimethylsuccinyl CH_3), 25.4, 25.8 (28-*O*-dimethylsuccinyl CH_3), 27.0 (C-15), 27.9 (C-23), 29.5 (C-21), 29.8 (C-16), 34.1 (C-7), 34.5 (C-22), 37.0 (C-10), 37.5 (AZT-C-2′), 37.6 (C-4, 13), 38.3 (C-1), 40.7 (3-*O*-dimethylsuccinyl C-3′), 40.8 (C-8), 41.0 (28-*O*-dimethylsuccinyl C-2″), 42.7 (C-14), 43.8 (28-*O*-dimethylsuccinyl C-3″), 44.5 (3-*O*-dimethylsuccinyl C-2′), 46.5 (C-17), 47.7 (C-19), 48.8 (C-18), 50.2 (C-9), 55.3 (C-5), 60.3 (AZT-C-3′), 62.9 (AZT-C-5′), 63.2 (C-28), 77.0 ($CH(Ph)_2$), 81.2 (C-3), 81.7 (AZT-C-4′), 85.2 (AZT-C-1′), 109.9 (C-29), 111.3 (AZT-C-5), 127.0, 127.1 (benzhydryl C-2′, 6′), 127.7 (benzyhydryl C-4′), 128.4 (benzhydryl C-3′, 5′), 135.3 (AZT-C-6), 140.3 (benzhydryl C-1′), 150.0 (C-20 and AZT-C-2), 163.5 (AZT-C-4), 170.7 (28-*O*-dimethylsuccinyl 4″-COO-AZT), 170.8 (3-*O*-dimethylsuccinyl 1′-COO−), 175.4 (3-*O*-dimethylsuccinyl 4′-COO−), 176.9 (28-*O*-dimethylsuccinyl 1″-COO−). HRESIMS (positive) *m*/*z* 1136.6299 $[M+Na]^+$ (calcd for $C_{65}H_{87}N_5O_{11}Na$, 1136.6300).

5.2.7.3. 3′-Azido-3′-deoxythymidine-5′-yl 3-*O*-(4′-benzhydryloxy-3′,3′-dimethylsuccinyl)-lup-20(29)en-28-yl glutarate (38). Yield 47.4% (starting from 180 mg of **24**); white solid. $[\alpha]_D^{15}$ +24.2° (*c* 0.5, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.73 (3H, s, CH_3-24), 0.77 (3H, s, CH_3-23), 0.78 (3H, s, CH_3-25), 0.96 (3H, s, CH_3-27), 1.01 (3H, s, CH_3-26), 1.30, 1.31 (each 3H, s, 3-*O*-dimethylsuccinyl CH_3), 1.68 (3H, s, CH_3-30), 1.94 (3H, s, AZT-CH_3), 1.99 (2H, quint, *J* = 7.0 Hz, 28-*O*-glutaryl H_2-3″), 2.42 (2H, t, *J* = 7.0 Hz, 28-*O*-glutaryl H_2-2″), 2.47 (2H, t, *J* = 7.2 Hz, 28-*O*-glutaryl H_2-4″), 2.33–2.50 (3H, m, AZT-H_2-2′ and H-19), 2.64, 2.69 (each 1H, d, *J* = 16.0 Hz, 3-*O*-dimethylsuccinyl H_2-2′), 3.85, 4.28 (1H, d, *J* = 11.2 Hz, H_2-28a), 4.06 (1H, m, AZT-H-4′), 4.23 (1H, m, AZT-H-3′), 4.32 (1H, dd, *J* = 3.5, 12.2 Hz, AZT-H-5a′), 4.39 (1H, dd, *J* = 4.8, 12.2 Hz, AZT-H-5b′), 4.43 (1H, dd, *J* = 4.8, 11.2 Hz, H-3), 4.59, 4.69 (each 1H, br s, H_2-29), 6.10 (1H, t-like, *J* = 5.5 Hz, AZT-H-1′), 6.85 (1H, s, $CH(Ph)_2$), 7.21–7.32 (11H, m, aromatic-H and AZT-H-6), 9.37 (1H, br s, AZT-NH); ^{13}C NMR ($CDCl_3$, 125 MHz) ^{13}C NMR ($CDCl_3$, 125 MHz) δ 12.6 AZT-CH_3, 14.7 (C-27), 15.9 (C-26), 16.0 (C-25), 16.4 (C-24), 18.0 (C-6), 19.0 (C-30), 19.9 (28-*O*-glutaryl C-3″), 20.7 (C-11), 23.5 (C-2), 25.0 (C-12), 25.1, 25.3 (3-*O*-dimethylsuccinyl CH_3), 26.9 (C-15), 27.8 (C-23), 29.4 (C-21), 29.7 (C-16), 33.0 (28-*O*-glutaryl C-4″), 33.1 (28-*O*-glutaryl C-2″), 34.0 (C-7), 34.4 (C-22), 36.9 (C-10), 37.4 (AZT-C-2′), 37.5 (C-13), 37.6 (C-4), 38.3 (C-1), 40.6 (dimethylsuccinyl C-3′), 40.8 (C-8), 42.6 (C-14), 44.4 (3-*O*-dimethylsuccinyl C-2′), 46.3 (C-17), 47.6 (C-19), 48.7 (C-18), 50.1 (C-9), 55.2 (C-5), 60.5 (AZT-C-3′), 62.8 (C-28), 63.3 (AZT-C-5′), 76.9 ($CH(Ph)_2$), 81.2 (C-3), 81.6 (AZT-C-4′), 85.6 (AZT-C-1′), 109.9 (C-29), 111.2 (AZT-C-5), 126.9, 127.0 (benzhydryl C-2′, 6′), 127.7 (benzyhydryl C-4′), 128.3 (benzhydryl C-3′, 5′), 135.4 (AZT-C-6), 140.2, 140.3 (benzhydryl C-1′), 149.9 (C-20), 150.0 (AZT-C-2), 163.4 (AZT-C-4), 170.8 (3-*O*-dimethylsuccinyl 1′-COO−), 172.3 (28-*O*-glutaryl 5″-COO-AZT), 173.1 (28-*O*-glutaryl 1″-COO−), 175.3 (3-*O*-dimethylsuccinyl 4′-COO−). HRESIMS (positive) *m*/*z* 1122.6141 $[M+Na]^+$ (calcd for $C_{64}H_{85}N_5O_{11}Na$, 1122.6143).

5.2.7.4. 3′-Azido-3′-deoxythymidine-5′-yl 3-*O*-(4′-benzhydryloxy-3′,3′-dimethylsuccinyl)-lup-20(29)en-28-yl 3,3-dimethylglutarate (39). Yield 74.2% (starting from 120 mg of **25**); white solid. $[\alpha]_D^{26}$ +14.1° (*c* 2.55, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.74 (3H, s, CH_3-24), 0.78 (each 3H, s, CH_3-23, 25), 0.96 (3H, s, CH_3-27), 1.01 (3H, s, CH_3-26), 1.13, 1.16 (each 3H, s, 28-*O*-dimethylglutaryl CH_3), 1.30, 1.31 (each 3H, s, 3-*O*-dimethylsuccinyl CH_3), 1.69 (3H, s, CH_3-30), 1.95 (3H, br s, AZT-CH_3), 2.30–2.35, 2.40–2.51 (2H, m, AZT-H_2-2′), 2.35–2.42 (1H, m, H-19), 2.43, 2.50 (each 1H, d, *J* = 16.0 Hz, 28-*O*-dimethylglutaryl H_2-2″), 2.49, 2.56 (each 1H, d, *J* = 16.0 Hz, 28-*O*-dimethylglutaryl H_2-4″), 2.65, 2.69 (each 1H, d, *J* = 16.0 Hz, 3-*O*-dimethylsuccinyl H_2-2′), 3.82, 4.26 (each 1H, d, *J* = 10.8 Hz, H_2-28), 4.07 (1H, q-like, AZT-H-4′), 4.20–4.25 (1H, m, AZT-H-3′), 4.27 (1H, dd, *J* = 3.6, 12.0 Hz, AZT-H-5a′), 4.44 (1H, dd, *J* = 4.4, 12.0 Hz, AZT-H-5b′), 4.44 (1H, dd, *J* = 4.4, 12.0 Hz, H-3), 4.60, 4.69 (each 1H, br s, H_2-29), 6.15 (1H, t-like, *J* = 6.4 Hz, AZT-H-1′), 6.86 (1H, s, $CH(Ph)_2$), 7.24–7.33 (11H, m, aromatic-H and AZT-H-6), 8.78 (1H, br s, AZT-NH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.6 AZT-CH_3, 14.7 (C-27), 16.0 (C-26), 16.1 (C-25), 16.5 (C-24), 18.1 (C-6), 19.1 (C-30), 20.8 (C-11), 23.5 (C-2), 25.2 (C-12), 25.2, 25.4 (3-*O*-dimethylsuccinyl CH_3), 27.0 (C-15), 27.9 (28-*O*-dimethylglutaryl CH_3), 28.0 (C-23), 29.5 (C-21), 29.8 (C-16), 32.6 (28-*O*-dimethylglutaryl C-3″), 34.1 (C-7), 34.6 (C-22), 37.0 (C-10), 37.5 (AZT-C-2′), 37.6 (C-4, 13), 38.3 (C-1), 40.7 (3-*O*-dimethylsuccinyl C-3′), 40.8 (C-8), 42.6 (C-14), 44.5 (3-*O*-dimethylsuccinyl C-2′, 28-*O*-dimethylglutaryl C-4″), 45.0 (28-*O*-dimethylglutaryl C-2″), 46.2 (C-17), 47.7 (C-19), 48.7 (C-18), 50.2 (C-9), 55.3 (C-5), 60.4 (AZT-C-3′), 62.6 (C-28), 62.7 (AZT-C-5′), 77.0 ($CH(Ph)_2$), 81.2 (C-3), 81.8 (AZT-C-4′), 85.2 (AZT-C-1′), 109.9 (C-29), 111.3 (AZT-C-5), 127.0, 127.1 (benzhydryl C-2′, 6′), 127.7 (benzyhydryl C-4′), 128.4 (benzhydryl C-3′, 5′), 135.2 (AZT-C-6), 140.3 (benzhydryl C-1′), 150.0 (C-20 and AZT-C-2), 163.4 (AZT-C-4), 170.8 (3-*O*-dimethylsuccinyl 1′-COO−), 171.1 (28-*O*-dimethylglutaryl 5″-COO-AZT), 172.3 (28-*O*-dimethylglutaryl 1″-COO−), 175.4 (3-*O*-dimethylsuccinyl 4′-COO−). HRESIMS (positive) *m*/*z* 1150.6467 $[M+Na]^+$ (calcd for $C_{66}H_{89}N_5O_{11}Na$, 1150.6456).

5.2.7.5. 3″-Azido-3′-deoxythymidine-5′-yl 3-*O*-(4′-benzhydryloxy-3′,3′-dimethylglutaryl)-lup-20(29)en-28-yl 3,3-dimethylglutarate (40). Yield 58.8% (starting from 143 mg of **26**); white solid. $[\alpha]_D^{26}$ +13.5° (*c* 4.13, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.80 (3H, s, CH_3-24), 0.82 (6H, s, CH_3-23, 25), 0.97 (3H, s, CH_3-27), 1.02 (3H, s, CH_3-26), 1.08 (6H, s, 3-*O*-dimethylglutaryl CH_3), 1.12, 1.15 (each 3H, s, 28-*O*-dimethylglutaryl CH_3), 1.68 (3H, s, CH_3-30), 1.95 3H, br s, AZT-CH_3), 2.32–2.50 (3H, m, AZT-H_2-2′ and H-19), 2.34, 2.41 (each 1H, d, *J* = 14.4 Hz, 3-*O*-dimethylglutaryl H_2-2′), 2.44, 2.50 (each 1H, d, *J* = 14.4 Hz, 28-*O*-dimethylglutaryl H_2-2″), 2.49, 2.56 (each 1H, d, *J* = 14.4 Hz, 28-*O*-dimethylglutaryl H_2-3″), 2.54, 2.57 (each 1H, d, *J* = 14.4 Hz, 3-*O*-dimethylglutaryl H_2-4′), 3.82, 4.26 (each 1H, d, *J* = 11.2 Hz, H_2-28), 4.06 (1H, q-like, AZT-H-4′), 4.21–4.28 (1H, m, AZT-H-3′), 4.26 (1H, dd, *J* = 3.6, 12.0 Hz, AZT-H-5a′), 4.43 (1H, dd, *J* = 4.4, 12.0 Hz, AZT-H-5b′), 4.46 (1H, dd, *J* = 4.8, 11.2 Hz, H-3), 4.59, 4.69 (each 1H, br s, H_2-29), 6.15 (1H, t-like, *J* = 6.4 Hz, AZT-H-1′), 6.88 (1H, s, $CH(Ph)_2$), 7.24–7.33 (11H, m, aromatic-H and AZT-H-6), 9.07 (1H, br s, AZT-NH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.5 AZT-CH_3, 14.7 (C-27), 15.9 (C-26), 16.1 (C-25), 16.6 (C-24), 18.1 (C-6), 19.1 (C-30), 20.7 (C-11), 23.7 (C-2), 25.1 (C-12), 26.9 (C-15), 27.6, (3-*O*-dimethylglutaryl CH_3), 27.8, 27.9 (28-*O*-dimethylglutaryl CH_3), 27.9 (C-23), 29.5 (C-21), 29.8 (C-16), 32.5 (28-*O*-dimethylglutaryl C-3″), 32.8 (3-*O*-dimethylglutaryl C-3′), 34.1 (C-7), 34.6 (C-22), 37.0 (C-10), 37.5 (AZT-C-2′, C-13), 37.6 (C-4), 38.3 (C-1), 40.8 (C-8), 42.6 (C-14), 44.5 (28-*O*-dimethylglutaryl C-4″), 45.0 (28-*O*-dimethylsuccinyl C-2″), 45.4 (3-*O*-dimethylglutaryl C-4′), 45.7 (3-*O*-dimethylglurayl C-2′), 46.2 (C-17), 47.6 (C-19), 48.7 (C-18), 50.2 (C-9), 55.3 (C-5), 60.4 (AZT-C-3′), 62.6 (C-28), 62.7 (AZT-C-5′), 76.6 ($CH(Ph)_2$), 80.8 (C-3), 81.7 (AZT-C-4′), 85.2 (AZT-C-1′), 109.9 (C-29), 111.3 (AZT-C-5), 127.1 (benzhydryl C-2′, 6′), 127.7 (benzyhydryl C-4′), 128.4 (benzhydryl C-3′, 5′), 135.2 (AZT-C-6), 140.2 (benzhydryl C-1′), 149.9 (C-20), 150.0 (AZT-C-2), 163.5 (AZT-C-4), 170.8 (3-*O*-dimethylglutaryl 5′-COO−), 171.1 (28-*O*-dimethylglutaryl 5″-COO-AZT), 171.6 (3-*O*-dimethylglutaryl 1′-COO−), 172.2 (28-*O*-dimethylglutaryl 1″-COO−). HRESIMS

(positive) *m*/*z* 1164.6608 $[M+Na]^+$ (calcd for $C_{67}H_{91}N_5O_{11}Na$, 1164.6613).

5.2.7.6. 1-(3′-Azido-3′-deoxythymidine-5′-yl)-4-[3-*O*-(4′-benzhydryl-3′,3′-dimethylsuccinyl)-lup-28-yl] 2,2-dimethylsuccinate (41) and 4-(3′-Azido-3′-deoxythymidine-5′-yl)-1-[3-*O*-(4′-benzhydryl-3′,3′-dimethylsuccinyl)-lup-28-yl] 2,2-dimethylsuccinate (42). Total yield 36.0% (starting from 285 mg of mixture of **27** and **28**); used for next reaction without purification. For spectroscopic analysis, a small amount of sample was further purified by preparative HPLC (cholester, CH_3OH/H_2O = 97:3); white solid.

Compound ***41****:* $[\alpha]_D^{30}$ −6.7° (*c* 1.69, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.77, 0.84 (each 3H, d, *J* = 8.0 Hz, CH_3-29, 30), 0.74 (3H, s, CH_3-24), 0.78 (3H, s, CH_3-23), 0.79 (3H, s, CH_3-25), 0.94 (3H, s, CH_3-27), 1.01 (3H, s, CH_3-26), 1.31 (12H, s, 3-*O*, 28-*O*-dimethylsuccinyl CH_3), 1.94 (3H, br s, AZT-CH_3), 2.25–2.32, 2.44–2.50 (each 1H, m, AZT-H_2-2′), 2.65, 2.70 (each 1H, d, *J* = 16.0 Hz, 3-*O*-dimethylsuccinyl H_2-2′), 2.59, 2.75 (each 1H, d, *J* = 16.4 Hz, 28-*O*-dimethylsuccinyl H_2-2″), 3.81, 4.28 (each 1H, d, *J* = 11.2 Hz, H_2-28), 4.09 (1H, q-like, AZT-H-4′), 4.25–4.29 (1H, m, AZT-H-3′), 4.29 (1H, dd, *J* = 4.4, 12.0 Hz, AZT-H-5a′), 4.52 (1H, dd, *J* = 4.0, 12.0 Hz, AZT-H-5b′), 4.44 (1H, dd, *J* = 5.2, 10.8 Hz, H-3), 6.18 (1H, t-like, *J* = 6.4 Hz, AZT-H-1′), 6.86 (1H, s, $CH(Ph)_2$), 7.24–7.33 (11H, m, aromatic-H and AZT-H-6), 8.59 (1H, br s, AZT-NH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.4 AZT-CH_3, 14.6 (C-27), 14.8 (C-29), 15.9 (C-26), 16.0 (C-25), 16.5 (C-24), 18.1 (C-6), 20.7 (C-11), 21.5 (C-21), 22.9 (C-30), 23.5 (C-2), 25.2, 25.4 (3-*O*-dimethylsuccinyl CH_3), 25.0, 25.9 (28-*O*-dimethylsuccinyl CH_3), 26.8 (C-12), 26.8 (C-15), 27.9 (C-23), 29.4 (C-20), 29.8 (C-16), 34.1 (C-7), 34.6 (C-22), 36.9 (C-10), 37.1 (C-13), 37.4 (AZT-C-2′), 37.6 (C-4), 38.3 (C-1), 40.7 (dimethylsuccinyl C-3′, C-3″), 40.9 (C-8), 42.8 (C-14), 44.5 (3-*O*-dimethylsuccinyl C-2′, C-19), 44.6 (28-*O*-dimethylsuccinyl C-2″), 46.5 (C-17), 48.1 (C-18), 49.9 (C-9), 55.3 (C-5), 60.4 (AZT-C-3′), 63.1 (C-28), 63.3 (AZT-C-5′), 77.0 ($CH(Ph)_2$), 81.3 (C-3), 81.9 (AZT-C-4′), 84.8 (AZT-C-1′), 111.4 (AZT-C-5), 127.0, 127.1 (benzhydryl C-2′, 6′), 127.7 (benzyhydryl C-4′), 128.4 (benzhydryl C-3′, 5′), 135.0 (AZT-C-6), 140.3 (benzhydryl C-1′), 150.0 (AZT-C-2), 163.3 (AZT-C-4), 170.9 (3-*O*-dimethylsuccinyl 1′-COO−), 171.7 (28-*O*-dimethylsuccinyl 1″-COO−), 175.4 (3-*O*-dimethylsuccinyl 4′-COO−), 176.5 (28-*O*-dimethylsuccinyl 4″-COO-AZT). HRESIMS (positive) *m*/*z* 1116.6604 $[M+H]^+$ (calcd for $C_{65}H_{90}N_5O_{11}$, 1116.6637).

Compound ***42****:* $[\alpha]_D^{30}$ −1.8° (*c* 2.69, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.77, 0.84 (each 3H, d, *J* = 8.0 Hz, CH_3-29, 30), 0.74 (3H, s, CH_3-24), 0.78 (3H, s, CH_3-23), 0.80 (3H, s, CH_3-25), 0.94 (3H, s, CH_3-27), 1.02 (3H, s, CH_3-26), 1.31 (6H, s, 3-*O*-dimethylsuccinyl CH_3), 1.31, 1.34 (each 3H, s, 28-*O*-dimethylsuccinyl CH_3), 1.96 (3H, br s, AZT-CH_3), 2.32–2.39, 2.44–2.50 (each 1H, m, AZT-H_2-2′), 2.65, 2.70 (each 1H, d, *J* = 16.0 Hz, 3-*O*-dimethylsuccinyl H_2-2′), 2.61, 2.66 (each 1H, d, *J* = 16.0 Hz, 28-*O*-dimethylsuccinyl H_2-3″), 3.81, 4.29 (each 1H, d, *J* = 10.8 Hz, H_2-28), 4.04 (1H, q-like, AZT-H-4′), 4.18–4.22 (1H, m, AZT-H-3′), 4.26 (1H, dd, *J* = 3.6, 12.4 Hz, AZT-H-5a′), 4.42 (1H, dd, *J* = 4.4, 12.4 Hz, AZT-H-5b′), 4.44 (1H, dd, *J* = 5.2, 10.8 Hz, H-3), 6.15 (1H, t-like, *J* = 6.4 Hz, AZT-H-1′), 6.86 (1H, s, $CH(Ph)_2$), 7.24–7.33 (11H, m, aromatic-H and AZT-H-6), 8.93 (1H, br s, AZT-NH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.5 AZT-CH_3, 14.6 (C-27), 14.9 (C-29), 16.0 (C-26, 25), 16.5 (C-24), 18.1 (C-6), 20.7 (C-11), 21.5 (C-21), 22.9 (C-30), 23.5 (C-2), 25.2, 25.4 (3-*O*-dimethylsuccinyl CH_3), 25.4, 25.8 (28-*O*-dimethylsuccinyl CH_3), 26.8 (C-12), 26.9 (C-15), 27.9 (C-23), 29.4 (C-20), 29.9 (C-16), 34.1 (C-7), 34.6 (C-22), 36.9 (C-10), 37.1 (C-13), 37.5 (AZT-C-2′, 37.6 (C-4), 38.3 (C-1), 40.7 (3-*O*-dimethylsuccinyl C-3′), 40.9 (C-8), 41.0 (28-*O*-dimethylsuccinyl C-2″), 42.8 (C-14), 43.8 (28-*O*-dimethylsuccinyl C-3″), 44.5 (3-*O*-dimethylsuccinyl C-2′, C-19), 46.7 (C-17), 48.1 (C-18), 49.9 (C-9), 55.3 (C-5), 60.2 (AZT-C-3′), 62.8 (AZT-C-5′), 63.3 (C-28), 77.0 ($CH(Ph)_2$), 81.3 (C-3), 81.7 (AZT-C-4′), 85.1 (AZT-C-1′), 111.3 (AZT-C-5), 127.0, 127.1 (benzhydryl C-2′, 6′), 127.7 (benzyhydryl C-4′), 128.4 (benzhydryl C-3′, 5′), 135.3 (AZT-C-6), 140.3 (benzhydryl C-1′), 150.0 (AZT-C-2), 163.5 (AZT-C-4), 170.7 (28-*O*-dimethylsuccinyl 4″-COO−AZT), 170.8 (3-*O*-dimethylsuccinyl 1′-COO−), 175.4 (3-*O*-dimethylsuccinyl 4′-COO−), 176.9 (28-*O*-dimethylsuccinyl 1″-COO−). HRESIMS (positive) *m*/*z* 1138.6445 $[M+Na]^+$ (calcd for $C_{65}H_{89}N_5O_{11}Na$, 1138.6456).

5.2.7.7. 3′-Azido-3′-deoxythymidine-5′-yl 3-*O*-(4′-benzhydryloxy-3′,3′-dimethylsuccinyl)-lup-28-yl 3,3-dimethylglutarate (43). Yield 66.1% (starting from 118 mg of **29**); white solid. $[\alpha]_D^{26}$ −0.32° (*c* 1.53, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.76, 0.83 (each 3H, d, *J* = 8.0 Hz, CH_3-29, 30), 0.73 (3H, s, CH_3-24), 0.77 (3H, s, CH_3-23), 0.78 (3H, s, CH_3-25), 0.93 (3H, s, CH_3-27), 1.00 (3H, s, CH_3-26), 1.11, 1.14 (each 3H, s, 28-*O*-dimethylglutaryl CH_3), 1.29, 1.30 (each 3H, s, 3-*O*-dimethylsuccinyl CH_3), 1.94 (3H, br s, AZT-CH_3), 2.31–2.38, 2.43–2.50 (2H, m, AZT-H_2-2′), 2.41, 2.48 (each 1H, d, *J* = 14.4 Hz, 28-*O*-dimethylglutaryl H_2-2″), 2.47, 2.55 (each 1H, d, *J* = 15.2 Hz, 28-*O*-dimethylglutaryl H_2-4″), 2.63, 2.68 (each 1H, d, *J* = 16.0 Hz, 3-*O*-dimethylsuccinyl H_2-2′), 3.77, 4.24 (each 1H, d, *J* = 10.8 Hz, H_2-28), 4.05 (1H, q-like, AZT-H-4′), 4.19–4.23 (1H, m, AZT-H-3′), 4.25 (1H, dd, *J* = 4.4, 12.0 Hz, AZT-H-5a′), 4.43 (1H, dd, *J* = 4.4, 12.0 Hz, AZT-H-5b′), 4.43 (1H, dd, *J* = 4.4, 12.0 Hz, H-3), 6.14 (1H, t-like, *J* = 6.4 Hz, AZT-H-1′), 6.85 (1H, s, $CH(Ph)_2$), 7.23–7.31 (11H, m, aromatic-H and AZT-H-6), 8.48 (1H, br s, AZT-NH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.6 AZT-CH_3, 14.6 (C-27), 14.9 (C-29), 16.0 (C-26, 25), 16.5 (C-24), 18.1 (C-6), 20.8 (C-11), 21.6 (C-21), 22.9 (C-30), 23.5 (C-2), 25.2, 25.4 (3-*O*-dimethylsuccinyl CH_3), 26.8 (C-12), 26.9 (C-15), 27.9 (28-*O*-dimethylglutaryl CH_3), 28.0 (C-23), 29.4 (C-20), 29.9 (C-16), 32.6 (28-*O*-dimethylglutaryl C-3″), 34.2 (C-7), 34.7 (C-22), 37.0 (C-10), 37.1 (C-13), 37.5 (AZT-C-2′), 37.7 (C-4), 38.3 (C-1), 40.7 (3-*O*-dimethylsuccinyl C-3′), 40.9 (C-8), 42.8 (C-14), 44.5 (3-*O*-dimethylsuccinyl C-2′, 28-*O*-dimethylglutaryl C-4″, C-19), 45.0 (28-*O*-dimethylsuccinyl C-2″), 46.4 (C-17), 48.1 (C-18), 49.9 (C-9), 55.3 (C-5), 60.4 (AZT-C-3′), 62.7 (C-28, AZT-C-5′), 77.0 ($CH(Ph)_2$), 81.3 (C-3), 81.8 (AZT-C-4′), 85.2 (AZT-C-1′), 111.3 (AZT-C-5), 127.0, 127.1 (benzhydryl C-2′, 6′), 127.7 (benzyhydryl C-4′), 128.4 (benzhydryl C-3′, 5′), 135.2 (AZT-C-6), 140.3 (benzhydryl C-1′), 149.9 (AZT-C-2), 163.2 (AZT-C-4), 170.8 (3-*O*-dimethylsuccinyl 1′-COO−), 171.2 (28-*O*-dimethylglutaryl 5″-COO-AZT), 172.3 (28-*O*-dimethylglutaryl 1″-COO−), 175.4 (3-*O*-dimethylsuccinyl 4′-COO−). HRESIMS (positive) *m*/*z* 1130.6781 $[M+H]^+$ (calcd for $C_{66}H_{92}N_5O_{11}$, 1130.6793).

5.2.7.8. 1-(3′-Azido-3′-deoxythymidine-5′-yl)-4-[3-*O*-(4′-benzhydryloxyglutaryl)-lup-28-yl] 2,2-dimethylsuccinate (44) and 4-(3′-Azido-3′-deoxythymidine-5′-yl)-1-[3-*O*-(4′-benzhydryloxyglutaryl)-lup-28-yl] 2,2-dimethylsuccinate (45). Yield 15.8% and 10.5%, respectively (starting from 208 mg of mixture of **30** and **31**); separated by preparative HPLC (cholester, MeOH/H_2O = 97:3); colorless oil.

Compound ***44****:* $[\alpha]_D^{27}$ −1.96° (*c* 0.72, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.77, 0.85 (each 3H, d, *J* = 8.0 Hz, CH_3-29, 30), 0.83 (3H, s, CH_3-24), 0.84 (3H, s, CH_3-23), 0.86 (3H, s, CH_3-25), 0.96 (3H, s, CH_3-27), 1.03 (3H, s, CH_3-26), 1.31, 1.32 (each 3H, s, 28-*O*-dimethylsuccinyl CH_3), 1.94 (3H, br s, AZT-CH_3), 2.00 (2H, quint, *J* = 7.2 Hz, 3-*O*-glutaryl H_2-3′), 2.26–2.35, 2.44–2.50 (each 1H, m, AZT-H_2-2′), 2.35 (2H, t, *J* = 7.2 Hz, 3-*O*-glutaryl H_2-2′), 2.50 (2H, t, *J* = 7.2 Hz, 3-*O*-glutaryl H_2-4′), 2.60, 2.74 (each 1H, d, *J* = 16.0 Hz, 28-*O*-dimethylsuccinyl H_2-2″), 3.82, 4.28 (each 1H, d, *J* = 10.8 Hz, H_2-28), 4.09 (1H, q-like, AZT-H-4′), 4.25–4.30 (1H, m, AZT-H-3′), 4.28 (1H, dd, *J* = 4.0, 12.0 Hz, AZT-H-5a′), 4.51 (1H, dd, *J* = 4.0, 12.0 Hz, AZT-H-5b′), 4.49 (1H, dd, *J* = 6.0, 10.0 Hz, H-3), 6.17 (1H, t-like, *J* = 6.4 Hz, AZT-H-1′), 6.89 (1H, s, $CH(Ph)_2$), 7.25–7.34 (11H, m, aromatic-H and AZT-H-6), 8.71 (1H, br s, AZT-NH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.4 AZT-CH_3, 14.6 (C-27), 14.9 (C-29), 16.0

(C-26), 16.1 (C-25), 16.5 (C-24), 18.2 (C-6), 20.4 (3-*O*-glutaryl C-3′), 20.8 (C-11), 21.6 (C-21), 22.9 (C-30), 23.7 (C-2), 25.1, 25.8 (28-*O*-dimethylsuccinyl CH_3), 26.8 (C-12), 26.9 (C-15), 28.0 (C-23), 29.4 (C-20), 29.9 (C-16), 33.6 (3-*O*-glutaryl C-4′), 33.7 (3-*O*-glutaryl C-2′), 34.2 (C-7), 34.6 (C-22), 37.0 (C-10), 37.2 (C-13), 37.5 (AZT-C-2′), 37.8 (C-4), 38.4 (C-1), 40.7 (28-*O*-dimethylsuccinyl C-3″), 40.9 (C-8), 42.9 (C-14), 44.5 (C-19), 44.6 (28-*O*-dimethylsuccinyl C-2″), 46.5 (C-17), 48.1 (C-18), 49.9 (C-9), 55.3 (C-5), 60.4 (AZT-C-3′), 63.1 (C-28), 63.3 (AZT-C-5′), 76.9 ($CH(Ph)_2$), 81.0 (C-3), 82.0 (AZT-C-4′), 84.9 (AZT-C-1′), 111.4 (AZT-C-5), 127.0 (benzhydryl C-2′, 6′), 127.9 (benzyhydryl C-4′), 128.5 (benzhydryl C-3′, 5′), 135.0 (AZT-C-6), 140.2 (benzhydryl C-1′), 150.0 (AZT-C-2), 163.4 (AZT-C-4), 171.7 (28-*O*-dimethylsuccinyl 1″-COO−), 171.9 (3-*O*-glutaryl 5′-COO−), 172.6 (3-*O*-glutaryl 1′-COO−), 176.5 (28-*O*-dimethylsuccinyl 4″-COO-AZT). HRESIMS (positive) *m*/*z* 1102.6483 $[M+H]^+$ (calcd for $C_{64}H_{88}N_5O_{11}$, 1102.6480).

Compound ***45****:* $[\alpha]_D^{27}$ +1.4° (*c* 0.99, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.77, 0.85 (each 3H, d, *J* = 8.0 Hz, CH_3-29, 30), 0.83 (3H, s, CH_3-24), 0.84 (3H, s, CH_3-23), 0.86 (3H, s, CH_3-25), 0.96 (3H, s, CH_3-27), 1.05 (3H, s, CH_3-26), 1.31, 1.34 (each 3H, s, 28-*O*-dimethylsuccinyl CH_3), 1.96 (3H, br s, AZT-CH_3), 2.00 (2H, quint, *J* = 7.2 Hz, 3-*O*-glutaryl H_2-3′), 2.33–2.52 (2H, m, AZT-H_2-2′), 2.35 (2H, t, *J* = 7.2 Hz, 3-*O*-glutaryl H_2-2′), 2.50 (2H, t, *J* = 7.2 Hz, 3-*O*-glutaryl H_2-4′), 2.62, 2.66 (each 1H, d, *J* = 16.0 Hz, 28-*O*-dimethylsuccinyl H_2-2″), 3.82, 4.30 (each 1H, d, *J* = 10.8 Hz, H_2-28), 4.05 (1H, q-like, AZT-H-4′), 4.17–4.22 (1H, m, AZT-H-3′), 4.26 (1H, dd, *J* = 3.6, 12.0 Hz, AZT-H-5a′), 4.42 (1H, dd, *J* = 4.0, 12.0 Hz, AZT-H-5b′), 4.49 (1H, dd, *J* = 6.0, 10.0 Hz, H-3), 6.15 (1H, t-like, *J* = 6.4 Hz, AZT-H-1′), 6.89 (1H, s, $CH(Ph)_2$), 7.25–7.34 (11H, m, aromatic-H and AZT-H-6), 8.74 (1H, br s, AZT-NH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.5 AZT-CH_3, 14.6 (C-27), 14.9 (C-29), 16.0 (C-26), 16.1 (C-25), 16.5 (C-24), 18.1 (C-6), 20.4 (3-*O*-glutaryl C-3′), 20.8 (C-11), 21.6 (C-21), 22.9 (C-30), 23.7 (C-2), 25.5, 25.8 (28-*O*-dimethylsuccinyl CH_3), 26.8 (C-12), 26.9 (C-15), 28.0 (C-23), 29.4 (C-20), 29.9 (C-16), 33.6 (3-*O*-glutaryl C-4′), 33.7 (3-*O*-glutaryl C-2′), 34.2 (C-7), 34.7 (C-22), 37.0 (C-10), 37.2 (C-13), 37.5 (AZT-C-2′), 37.8 (C-4), 38.4 (C-1), 40.9 (C-8), 41.0 (28-*O*-dimethylsuccinyl C-2″), 42.9 (C-14), 43.8 (28-*O*-dimethylsuccinyl C-3″), 44.6 (C-19), 46.7 (C-17), 48.2 (C-18), 50.0 (C-9), 55.3 (C-5), 60.3 (AZT-C-3′), 62.9 (AZT-C-5′), 63.3 (C-28), 76.9 ($CH(Ph)_2$), 81.0 (C-3), 81.8 (AZT-C-4′), 85.2 (AZT-C-1′), 111.3 (AZT-C-5), 127.0 (benzhydryl C-2′, 6′), 127.9 (benzyhydryl C-4′), 128.5 (benzhydryl C-3′, 5′), 135.3 (AZT-C-6), 140.2 (benzhydryl C-1′), 150.0 (AZT-C-2), 163.4 (AZT-C-4), 170.7 (28-*O*-dimethylsuccinyl 4″-COO-AZT), 171.9 (3-*O*-glutaryl 5′-COO−), 172.6 (3-*O*-glutaryl 1′-COO−), 176.8 (28-*O*-dimethylsuccinyl 1″-COO−). HRESIMS (positive) *m*/*z* 1102.6475 $[M+H]^+$ (calcd for $C_{64}H_{88}N_5O_{11}$, 1102.6480).

5.2.7.9. 3′-Azido-3′-deoxythymidine-5′-yl 3-*O*-(4′-benzhydryloxyglutaryl)-lup-28-yl glutarate (46). Yield 49.8% (starting from 79 mg of **32**); colorless oil. $[\alpha]_D^{27}$ +4.4° (*c* 0.93, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.78, 0.84 (each 3H, d, *J* = 8.0 Hz, CH_3-29, 30), 0.83 (each 3H, s, CH_3-24, CH_3-23), 0.86 (3H, s, CH_3-25), 0.96 (3H, s, CH_3-27), 1.05 (3H, s, CH_3-26), 1.94 (3H, d, *J* = 1.2 Hz, AZT-CH_3), 1.99 (4H, quint, *J* = 7.2 Hz, 3-*O*, 28-*O*-glutaryl H_2-3′), 2.32–2.52 (2H, m, AZT-H_2-2′), 2.35 (2H, t, *J* = 7.2 Hz, 3-*O*-glutaryl H_2-2′), 2.41 (2H, t, *J* = 7.2 Hz, 28-*O*-glutaryl H_2-2″), 2.46 (2H, t, *J* = 7.2 Hz, 28-*O*-glutaryl H_2-4″), 2.50 (2H, t, *J* = 7.2 Hz, 3-*O*-glutaryl H_2-4′), 3.83, 4.30 (each 1H, d, *J* = 11.2 Hz, H_2-28), 4.07 (1H, q-like, AZT-H-4′), 4.20–4.24 (1H, m, AZT-H-3′), 4.32 (1H, dd, *J* = 4.0, 12.0 Hz, AZT-H-5a′), 4.40 (1H, dd, *J* = 4.4, 12.0 Hz, AZT-H-5b′), 4.49 (1H, dd, *J* = 6.0, 10.4 Hz, H-3), 6.10 (1H, t-like, *J* = 6.4 Hz, AZT-H-1′), 6.89 (1H, s, $CH(Ph)_2$), 7.25–7.33 (11H, m, aromatic-H and AZT-H-6), 9.04 (1H, br s, AZT-NH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.5 AZT-CH_3, 14.6 (C-27), 14.8 (C-29), 16.0 (C-26, C-25), 16.5 (C-24), 18.1 (C-6), 20.0 (28-*O*-glutaryl C-3″), 20.3 (3-*O*-glutaryl C-3′), 20.8 (C-11), 21.6 (C-21), 22.8 (C-30), 23.7 (C-2), 26.8 (C-12), 26.9 (C-15), 28.0 (C-23), 29.4 (C-20), 29.9 (C-16), 33.1 (28-*O*-glutaryl C-4″), 33.2 (28-*O*-glutaryl C-2″), 33.6 (3-*O*-glutaryl C-4′), 33.7 (3-*O*-glutaryl C-2′), 34.2 (C-7), 34.6 (C-22), 37.0 (C-10), 37.2 (C-13), 37.4 (AZT-C-2′), 37.8 (C-4), 38.3 (C-1), 40.9 (C-8), 42.8 (C-14), 44.5 (C-19), 46.5 (C-17), 48.1 (C-18), 49.9 (C-9), 55.3 (C-5), 60.6 (AZT-C-3′), 62.9 (C-28), 63.3 (AZT-C-5′), 76.8 ($CH(Ph)_2$), 81.0 (C-3), 81.7 (AZT-C-4′), 85.6 (AZT-C-1′), 111.3 (AZT-C-5), 127.0 (benzhydryl C-2′, 6′), 127.8 (benzyhydryl C-4′), 128.4 (benzhydryl C-3′, 5′), 135.3 (AZT-C-6), 140.2 (benzhydryl C-1′), 150.0 (AZT-C-2), 163.5 (AZT-C-4), 171.8 (3-*O*-glutaryl 5′-COO−), 172.3 (28-*O*-glutaryl 5″-COO-AZT), 172.6 (3-*O*-glutaryl 1′-COO−), 173.1 (28-*O*-glutaryl 1″-COO−). HRESIMS (positive) *m*/*z* 1112.6271 $[M+Na]^+$ (calcd for $C_{63}H_{87}N_5O_{11}Na$, 1112.6300).

5.2.7.10. 3′-Azido-3′-deoxythymidine-5′-yl 3-*O*-(4′-benzhydryloxyglutaryl)-lup-28-yl 3,3-dimethylglutarate (47). Yield 48.7% (starting from 76 mg of **33**); colorless oil. $[\alpha]_D^{27}$ +4.1° (*c* 0.54, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.78, 0.84 (each 3H, d, *J* = 8.0 Hz, CH_3-29, 30), 0.83 (3H, s, CH_3-24), 0.84 (3H, s, CH_3-23), 0.86 (3H, s, CH_3-25), 0.96 (3H, s, CH_3-27), 1.04 (3H, s, CH_3-26), 1.12, 1.15 (each 3H, s, 28-*O*-dimethylglutaryl CH_3), 1.95 (3H, d, *J* = 1.2 Hz, AZT-CH_3), 2.00 (2H, quint, *J* = 7.2 Hz, 3-*O*-glutaryl H_2-3′), 2.32–2.52 (2H, m, AZT-H_2-2′), 2.35 (2H, t, *J* = 7.2 Hz, 3-*O*-glutaryl H_2-2′), 2.43, 2.49 (each 1H, d, *J* = 14.4 Hz, 28-*O*-dimethylglutaryl H_2-2″), 2.48, 2.56 (each 1H, d, *J* = 14.4 Hz, 28-*O*-dimethylglutaryl H_2-4″), 2.50 (2H, t, *J* = 7.2 Hz, 3-*O*-glutaryl H_2-4′), 3.79, 4.27 (each 1H, d, *J* = 11.2 Hz, H_2-28), 4.07 (1H, q-like, AZT-H-4′), 4.20–4.28 (1H, m, AZT-H-3′), 4.26 (1H, dd, *J* = 3.6, 12.0 Hz, AZT-H-5a′), 4.43 (1H, dd, *J* = 4.4, 12.0 Hz, AZT-H-5b′), 4.49 (1H, dd, *J* = 6.0, 10.4 Hz, H-3), 6.15 (1H, t-like, *J* = 6.4 Hz, AZT-H-1′), 6.89 (1H, s, $CH(Ph)_2$), 7.25–7.33 (11H, m, aromatic-H and AZT-H-6), 8.91 (1H, br s, AZT-NH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.5 AZT-CH_3, 14.6 (C-27), 14.8 (C-29), 16.0 (C-26, C-25), 16.5 (C-24), 18.1 (C-6), 20.3 (3-*O*-glutaryl C-3′), 20.8 (C-11), 21.6 (C-21), 22.8 (C-30), 23.7 (C-2), 26.8 (C-12), 26.9 (C-15), 27.8, 27.9 (28-*O*-dimethylglutaryl CH_3), 28.0 (C-23), 29.4 (C-20), 29.9 (C-16), 32.5 (28-*O*-dimethylglutaryl C-3″), 33.6 (3-*O*-glutaryl C-4′), 33.7 (3-*O*-glutaryl C-2′), 34.2 (C-7), 34.7 (C-22), 37.0 (C-10), 37.2 (C-13), 37.5 (AZT-C-2′), 37.8 (C-4), 38.3 (C-1), 40.9 (C-8), 42.8 (C-14), 44.5 (28-*O*-dimethylglutaryl C-4″ and C-19), 45.1 (28-*O*-dimethylglutaryl C-2″), 46.4 (C-17), 48.1 (C-18), 49.9 (C-9), 55.3 (C-5), 60.5 (AZT-C-3′), 62.7 (C-28, and AZT-C-5′), 76.9 ($CH(Ph)_2$), 81.0 (C-3), 81.8 (AZT-C-4′), 85.2 (AZT-C-1′), 111.3 (AZT-C-5), 127.0 (benzhydryl C-2′, 6′), 127.9 (benzyhydryl C-4′), 128.5 (benzhydryl C-3′, 5′), 135.2 (AZT-C-6), 140.2 (benzhydryl C-1′), 150.1 (AZT-C-2), 163.5 (AZT-C-4), 171.1 (28-*O*-dimethylglutaryl 5″-COO-AZT), 171.8 (3-*O*-glutaryl 5′-COO−), 172.2 (28-*O*-dimethylglutaryl 1″-COO−), 172.6 (3-*O*-glutaryl 1′-COO−). HRESIMS (positive) *m*/*z* 1138.6449 $[M+Na]^+$ (calcd for $C_{65}H_{89}N_5O_{11}Na$, 1138.6456).

5.2.7.11. 3′-Azido-3′-deoxythymidine-5′-yl 3-*O*-(4′-benzhydryloxy-3′,3′-dimethylglutaryl)-lup-28-yl 3,3-dimethylglutarate (48). Yield 68.3% (starting from 126 mg of **34**); colorless oil. $[\alpha]_D^{26}$ +0.97° (*c* 2.37, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.78, 0.84 (each 3H, d, *J* = 8.0 Hz, CH_3-29, 30), 0.81 (3H, s, CH_3-24), 0.83 (6H, s, CH_3-23, CH_3-25), 0.95 (3H, s, CH_3-27), 1.03 (3H, s, CH_3-26), 1.09 (6H, s, 3-*O*-dimethylglutaryl CH_3), 1.12, 1.15 (each 3H, s, 28-*O*-dimethylglutaryl CH_3), 1.95 (3H, br s, AZT-CH_3), 2.32–2.52 (2H, m, AZT-H_2-2′), 2.35, 2.42 (each 1H, d, *J* = 14.4 Hz, 3-*O*-dimethylglutaryl H_2-2′), 2.43, 2.49 (each 1H, d, *J* = 14.4 Hz, 28-*O*-dimethylglutaryl H_2-2″), 2.48, 2.56 (each 1H, d, *J* = 14.4 Hz, 28-*O*-dimethylglutaryl H_2-4″), 2.55, 2.58 (each 1H, d, *J* = 14.4 Hz, 3-*O*-dimethylglutaryl H_2-4′), 3.79, 4.26 (each 1H, d, *J* = 11.2 Hz, H_2-28), 4.07 (1H, q-like, AZT-H-4′), 4.21–4.28 (1H, m, AZT-H-3′), 4.26 (1H, dd, *J* = 3.6, 12.4 Hz, AZT-H-5a′), 4.44 (1H, dd, *J* = 4.4, 12.4 Hz, AZT-H-5b′), 4.47 (1H, dd,

J = 4.8, 10.8 Hz, H-3), 6.15 (1H, t-like, J = 6.4 Hz, AZT-H-1′), 6.89 (1H, s, CH(Ph)$_2$), 7.22–7.34 (11H, m, aromatic-H and AZT-H-6), 8.97 (1H, br s, AZT-NH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.6 AZT-CH_3, 14.6 (C-27), 14.9 (C-29), 16.0 (C-26, C-25), 16.6 (C-24), 18.1 (C-6), 20.7 (C-11), 21.6 (C-21), 22.9 (C-30), 23.7 (C-2), 26.8 (C-12), 26.9 (C-15), 27.6 (3-*O*-dimethylglutaryl CH_3), 27.9, 28.0 (28-*O*-dimethylglutaryl CH_3), 28.0 (C-23), 29.4 (C-20), 29.9 (C-16), 32.6 (28-*O*-dimethylglutaryl C-3″), 32.8 (3-*O*-dimethylglutaryl C-3′), 34.2 (C-7), 34.7 (C-22), 37.0 (C-10), 37.1 (C-13), 37.5 (AZT-C-2′), 37.6 (C-4), 38.3 (C-1), 40.9 (C-8), 42.8 (C-14), 44.5 (28-*O*-dimethylglutaryl C-4″ and C-19), 45.0 (28-*O*-dimethylglutaryl C-2″), 45.5 (3-*O*-glutaryl C-4′), 45.8 (3-*O*-glutaryl C-2′), 46.4 (C-17), 48.1 (C-18), 49.9 (C-9), 55.3 (C-5), 60.4 (AZT-C-3′), 62.7 (C-28, and AZT-C-5′), 76.7 (CH(Ph)$_2$), 80.9 (C-3), 81.8 (AZT-C-4′), 85.2 (AZT-C-1′), 111.3 (AZT-C-5), 127.1 (benzhydryl C-2′, 6′), 127.8 (benzyhydryl C-4′), 128.4 (benzhydryl C-3′, 5′), 135.3 (AZT-C-6), 140.2 (benzhydryl C-1′), 150.0 (AZT-C-2), 163.6 (AZT-C-4), 170.8 (3-*O*-dimethylglutaryl 5′-COO−), 171.2 (28-*O*-dimethylglutaryl 5″-COO-AZT), 171.6 (3-*O*-dimethylglutaryl 1′-COO−), 172.3 (28-*O*-dimethylglutaryl 1″-COO−). HRESIMS (positive) m/z 1144.6917 $[M+H]^+$ (calcd for $C_{67}H_{94}N_5O_{11}$, 1144.6950).

5.2.8. General procedure for removing benzhydryl group (49–62)

The final products were prepared by refluxing of a solution of benzdryl ester derivative in 80% HOAc (2–6 mL) overnight. After cooling to room temperature, the reaction mixture was extracted with $CHCl_3$, and the organic layer was washed with water and brine, dried over Na_2SO_4 and concentrated. The residue was purified by preparative HPLC (cholester, MeOH/H_2O/HOAc = 93:6:1).

5.2.8.1. 3′-Azido-3′-deoxythymidine-5′-yl 3-*O*-(3′,3′-dimethylsuccinyl)-lup-20(29)en-28-yl succinate (49). Yield 46.5% (starting from 62 mg of **35**); white solid. $[\alpha]_D^{18}$ +7.2° (c 0.57, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.80 (3H, s, CH_3-24), 0.82 (3H, s, CH_3-23), 0.83 (3H, s, CH_3-25), 0.96 (3H, s, CH_3-27), 1.00 (3H, s, CH_3-26), 1.29, 1.31 (each 3H, s, 3-*O*-dimethylsuccinyl CH_3), 1.68 (3H, s, CH_3-30), 1.94 (3H, d, J = 0.9 Hz, AZT-CH_3), 2.33–2.49 (3H, m, AZT-H_2-2′ and H-19), 2.57, 2.68 (each 1H, d, J = 15.6 Hz, 3-*O*-dimethylsuccinyl H_2-2′), 2.67–2.77 (4H, m, 28-*O*-succinyl H_2-2″, 3″), 3.86, 4.30 (each 1H, d, J = 11.2 Hz, H_2-28), 4.05 (1H, q-like, AZT-H-4′), 4.21–4.25 (1H, m, AZT-H-3′), 4.30 (1H, dd, J = 3.4, 12.3 Hz, AZT-H_2-5a′), 4.49 (1H, dd, J = 5.2, 11.2 Hz, H-3), 4.52 (1H, dd, J = 4.3, 12.3 Hz, AZT-H_2-5b′), 4.58, 4.68 (each 1H, br s, H_2-29), 6.14 (1H, t-like, J = 6.3 Hz, AZT-H-1′), 7.30 (1H, d, J = 1.2 Hz, AZT-H-6), 8.68 (1H, br s, AZT-NH); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 12.6 AZT-CH_3, 14.7 (C-27), 16.0 (C-26), 16.1 (C-25), 16.5 (C-24), 18.1 (C-6), 19.1 (C-30), 20.8 (C-11), 23.6 (C-2), 25.1 (C-12), 25.1, 25.6 (3-*O*-dimethylsuccinyl CH_3), 27.0 (C-15), 27.9 (C-23), 29.0 (28-*O*-succinyl C-2″, 3″), 29.5 (C-21), 29.7 (C-16), 34.1 (C-7), 34.6 (C-22), 37.0 (C-10), 37.6 (AZT-C-2′ and C-13), 37.7 (C-4), 38.3 (C-1), 40.4 (dimethylsuccinyl C-3′), 40.9 (C-8), 42.7 (C-14), 44.7 (3-*O*-dimethylsuccinyl C-2′), 46.4 (C-17), 47.7 (C-19), 48.7 (C-18), 50.2 (C-9), 55.4 (C-5), 60.1 (AZT-C-3′), 63.1 (AZT-C-5′), 63.4 (C-28), 81.5 (C-3), 81.9 (AZT-C-4′), 85.2 (AZT-C-1′), 110.0 (C-29), 111.3 (AZT-C-5), 135.4 (AZT-C-6), 149.9 (AZT-C-2), 150.0 (C-20), 163.5 (AZT-C-4), 171.1 (3-*O*-dimethylsuccinyl 1′-COO−), 172.0 (28-*O*-succinyl 4″-COO-AZT), 172.6 (28-*O*-succinyl 1″-COO−), 180.8 (3-*O*-dimethylsuccinyl 4′-COOH). HRESIMS (positive) m/z 942.5218 $[M+Na]^+$ (calcd for $C_{50}H_{73}N_5O_{11}Na$, 942.5204).

5.2.8.2. 1-(3′-Azido-3′-deoxythymidine-5′-yl)-4-[3-*O*-(3′,3′-dimethylsuccinyl)-lup-20(29)en-28-yl] 2,2-dimethylsuccinate (50) and 4-(3′-Azido-3′-deoxythymidine-5′-yl)-1-[3-*O*-(3′,3′-dimethylsuccinyl)-lup-20(29)en-28-yl] 2,2-dimethylsuccinate (51). Total yield 78.9% (starting from 105 mg of mixture of **36** and **37**); in a ratio of 2:1; white solid.

*Compound **50**:* $[\alpha]_D^{29}$ +8.2° (c 2.38, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.81 (3H, s, CH_3-24), 0.83 (each 3H, s, CH_3-23, 25), 0.96 (3H, s, CH_3-27), 1.00 (3H, s, CH_3-26), 1.29, 1.30 (each 3H, s, 3-*O*-dimethylsuccinyl CH_3), 1.30, 1.31 (each 3H, s, 28-*O*-dimethylsuccinyl CH_3), 1.68 (3H, s, CH_3-30), 1.93 (3H, br s, AZT-CH_3), 2.26–2.33, 2.44–2.50 (each 1H, m, AZT-H_2-2′), 2.37–2.44 (1H, m, H-19), 2.56, 2.68 (each 1H, d, J = 16.0 Hz, 3-*O*-dimethylsuccinyl H_2-2′), 2.60, 2.74 (each 1H, d, J = 16.4 Hz, 28-*O*-dimethylsuccinyl H_2-2″), 3.84, 4.27 (each 1H, d, J = 11.2 Hz, H_2-28), 4.09 (1H, q-like, AZT-H-4′), 4.25–4.31 (2H, m, AZT-H-3′ and AZT-H-5a′), 4.51 (1H, dd, J = 4.0, 12.0 Hz, AZT-H-5b′), 4.48 (1H, dd, J = 5.6, 11.2 Hz, H-3), 4.59, 4.68 (each 1H, br s, H_2-29), 6.16 (1H, t-like, J = 6.4 Hz, AZT-H-1′), 7.28 (1H, d, J = 0.8 Hz, AZT-H-6), 9.38 (1H, br s, AZT-NH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.4 AZT-CH_3, 14.7 (C-27), 15.9 (C-26), 16.1 (C-25), 16.5 (C-24), 18.1 (C-6), 19.1 (C-30), 20.7 (C-11), 23.6 (C-2), 25.1 (C-12), 25.1, 25.6 (3-*O*-dimethylsuccinyl CH_3), 25.1, 25.9 (28-*O*-dimethylsuccinyl CH_3), 27.0 (C-15), 27.9 (C-23), 29.5 (C-21), 29.7 (C-16), 34.1 (C-7), 34.5 (C-22), 37.0 (C-10), 37.5 (AZT-C-2′), 37.6 (C-13), 37.7 (C-4), 38.4 (C-1), 40.5 (3-*O*-dimethylsuccinyl C-3′), 40.7 (28-*O*-dimethylsuccinyl C-3″), 40.8 (C-8), 42.7 (C-14), 44.6 (28-*O*-dimethylsuccinyl C-2″), 44.7 (3-*O*-dimethylsuccinyl C-2′), 46.3 (C-17), 47.7 (C-19), 48.7 (C-18), 50.2 (C-9), 55.4 (C-5), 60.4 (AZT-C-3′), 63.1 (C-28), 63.0 (AZT-C-5′), 81.5 (C-3), 82.0 (AZT-C-4′), 84.9 (AZT-C-1′), 110.0 (C-29), 111.3 (AZT-C-5), 135.2 (AZT-C-6), 149.9 (C-20), 150.1 (AZT-C-2), 164.0 (AZT-C-4), 171.1 (3-*O*-dimethylsuccinyl 1′-COO−), 171.7 (28-*O*-dimethylsuccinyl 1″-COO−), 176.5 (28-*O*-dimethylsuccinyl 4″-COO-AZT), 182.2 (3-*O*-dimethylsuccinyl 4′-COOH). HRESIMS (positive) m/z 970.5511 $[M+Na]^+$ (calcd for $C_{52}H_{77}N_5O_{11}Na$, 970.5517).

*Compound **51**:* $[\alpha]_D^{27}$ +15.6° (c 4.68, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.80 (3H, s, CH_3-24), 0.82 (6H, s, CH_3-23, C-25), 0.96 (3H, s, CH_3-27), 1.01 (3H, s, CH_3-26), 1.28, 1.29 (each 3H, s, 3-*O*-dimethylsuccinyl CH_3), 1.30, 1.33 (each 3H, s, 28-*O*-dimethylsuccinyl CH_3), 1.67 (3H, s, CH_3-30), 1.94 (3H, br s, AZT-CH_3), 2.33–2.50 (3H, m, AZT-H_2-2′ and H-19), 2.61, 2.65 (each 1H, d, J = 16.4 Hz, 28-*O*-dimethylsuccinyl H_2-3″), 2.56, 2.67 (each 1H, d, J = 15.6 Hz, 3-*O*-dimethylsuccinyl H_2-2′), 3.83, 4.27 (each 1H, d, J = 10.8 Hz, H_2-28), 4.03 (1H, q-like, AZT-H-4′), 4.18–4.22 (1H, m, AZT-H-3′), 4.25 (1H, dd, J = 4.0, 12.4 Hz, AZT-H-5a′), 4.41 (1H, dd, J = 4.4, 12.4 Hz, AZT-H-5b′), 4.48 (1H, dd, J = 5.2, 10.8 Hz, H-3), 4.58, 4.67 (each 1H, br s, H_2-29), 6.12 (1H, t-like, J = 6.4 Hz, AZT-H-1′), 7.31 (1H, d, J = 0.8 Hz, AZT-H-6), 9.95 (1H, br s, AZT-NH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.5 AZT-CH_3, 14.7 (C-27), 15.9 (C-26), 16.0 (C-25), 16.4 (C-24), 18.1 (C-6), 19.1 (C-30), 20.7 (C-11), 23.5 (C-2), 25.1 (C-12), 24.9, 25.6 (3-*O*-dimethylsuccinyl CH_3), 25.4, 25.7 (28-*O*-dimethylsuccinyl CH_3), 26.9 (C-15), 27.8 (C-23), 29.5 (C-21), 29.8 (C-16), 34.0 (C-7), 34.5 (C-22), 37.0 (C-10), 37.5 (AZT-C-2′ and C-13), 37.6 (C-4), 38.3 (C-1), 40.4 (3-*O*-dimethylsuccinyl C-3′), 40.8 (C-8), 41.0 (28-*O*-dimethylsuccinyl C-2″), 42.6 (C-14), 43.8 (28-*O*-dimethylsuccinyl C-3″), 44.7 (3-*O*-dimethylsuccinyl C-2′), 46.5 (C-17), 47.7 (C-19), 48.8 (C-18), 50.2 (C-9), 55.3 (C-5), 60.2 (AZT-C-3′), 62.9 (AZT-C-5′), 63.2 (C-28), 81.5 (C-3), 81.8 (AZT-C-4′), 85.3 (AZT-C-1′), 109.9 (C-29), 111.2 (AZT-C-5), 135.6 (AZT-C-6), 149.9 (C-20), 150.2 (AZT-C-2), 164.4 (AZT-C-4), 170.7 (28-*O*-dimethylsuccinyl 4″-COO-AZT), 171.0 (3-*O*-dimethylsuccinyl 1′-COO−), 176.9 (28-*O*-dimethylsuccinyl 1″-COO−), 182.7 (3-*O*-dimethylsuccinyl 4′-COOH). HRESIMS (positive) m/z 970.5490 $[M+Na]^+$ (calcd for $C_{52}H_{77}N_5O_{11}Na$, 970.5517).

5.2.8.3. 3′-Azido-3′-deoxythymidine-5′-yl 3-*O*-(3′,3′-dimethylsuccinyl)-lup-20(29)en-28-yl glutarate (52). Yield 42.7% (starting from 90 mg of **38**); white solid. $[\alpha]_D^{15}$ +18.8° (c 0.6, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.81 (3H, s, CH_3-24), 0.83 (3H, s, CH_3-23), 0.83 (3H, s, CH_3-25), 0.96 (3H, s, CH_3-27), 1.02 (3H, s, CH_3-26), 1.29, 1.31 (each 3H, s, 3-*O*-dimethylsuccinyl CH_3), 1.68 (3H, s, CH_3-30), 1.94 (3H, d, J = 1.2 Hz, AZT-CH_3), 1.99 (2H, quint, J = 7.2 Hz,

28-*O*-glutaryl H_2-3″), 2.33–2.49 (3H, m, AZT-H_2-2′ and H-19), 2.42 (2H, t, *J* = 7.2 Hz, 28-*O*-glutaryl H_2-2″), 2.46 (2H, t, *J* = 7.2 Hz, 28-*O*-glutaryl H_2-4″), 2.57, 2.67 (each 1H, d, *J* = 15.8 Hz, 3-*O*-dimethylsuccinyl H_2-2′), 3.85, 4.28 (each 1H, d, *J* = 10.8 Hz, H_2-28), 4.07 (1H, q-like, AZT-H-4′), 4.20–4.24 (1H, m, AZT-H-3′), 4.32 (1H, dd, *J* = 3.9, 12.3 Hz, AZT-H_2-5a′), 4.40 (1H, dd, *J* = 4.7, 12.3 Hz, AZT-H_2-5b′), 4.49 (1H, dd, *J* = 5.2, 11.2 Hz, H-3), 4.59, 4.68 (each 1H, br s, H_2-29), 6.09 (1H, t-like, *J* = 6.3 Hz, AZT-H-1′), 7.21 (1H, d, *J* = 1.1 Hz, AZT-H-6); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 12.6 AZT-CH_3, 14.7 (C-27), 16.0 (C-26), 16.1 (C-25), 16.5 (C-24), 18.1 (C-6), 19.1 (C-30), 20.0 (28-*O*-glutaryl C-3″), 20.8 (C-11), 23.6 (C-2), 25.1 (C-12), 25.1, 25.6 (3-*O*-dimethylsuccinyl CH_3), 27.0 (C-15), 27.9 (C-23), 29.5 (C-21), 29.8 (C-16), 33.1 (28-*O*-glutaryl C-4″), 33.2 (28-*O*-glutaryl C-2″), 34.1 (C-7), 34.6 (C-22), 37.0 (C-10), 37.5 (AZT-C-2′), 37.6 (C-13), 37.7 (C-4), 38.4 (C-1), 40.4 (dimethylsuccinyl C-3′), 40.9 (C-8), 42.7 (C-14), 44.8 (3-*O*-dimethylsuccinyl C-2′), 46.4 (C-17), 47.7 (C-19), 48.7 (C-18), 50.2 (C-9), 55.4 (C-5), 60.6 (AZT-C-3′), 63.0 (C-28), 63.3 (AZT-C-5′), 81.6 (C-3), 81.7 (AZT-C-4′), 85.7 (AZT-C-1′), 110.0 (C-29), 111.3 (AZT-C-5), 135.5 (AZT-C-6), 149.8 (C-20), 149.9 (AZT-C-2), 163.5 (AZT-C-4), 171.2 (3-*O*-dimethylsuccinyl 1′-COO−), 172.3 (28-*O*-glutaryl 5″-COO-AZT), 173.1 (28-*O*-glutaryl 1″-COO−), 180.8 (3-*O*-dimethylsuccinyl 4′-COOH). HRESIMS (positive) *m*/*z* 956.5361 $[M+Na]^+$ (calcd for $C_{51}H_{75}N_5O_{11}Na$, 956.5361).

5.2.8.4. 3′-Azido-3′-deoxythymidine-5′-yl 3-*O*-(3′,3′-dimethylsuccinyl)-lup-20(29)en-28-yl 3,3-dimethylglutarate (53). Yield 87.3% (starting from 114 mg of **39**); white solid. $[\alpha]_D^{27}$ +15.3° (*c* 2.84, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.80 (3H, s, CH_3-24), 0.83 (each 3H, s, CH_3-23, 25), 0.96 (3H, s, CH_3-27), 1.01 (3H, s, CH_3-26), 1.12, 1.15 (each 3H, s, 28-*O*-dimethylglutaryl CH_3), 1.29, 1.30 (each 3H, s, 3-*O*-dimethylsuccinyl CH_3), 1.68 (3H, s, CH_3-30), 1.94 (3H, br s, AZT-CH_3), 2.30–2.35, 2.40–2.51 (2H, m, AZT-H_2-2′), 2.35–2.42 (1H, m, H-19), 2.44, 2.49 (each 1H, d, *J* = 16.0 Hz, 28-*O*-dimethylglutaryl H_2-2″), 2.49, 2.55 (each 1H, d, *J* = 16.0 Hz, 28-*O*-dimethylglutaryl H_2-4″), 2.56, 2.68 (each 1H, d, *J* = 16.0 Hz, 3-*O*-dimethylsuccinyl H_2-2′), 3.82, 4.26 (each 1H, d, *J* = 11.2 Hz, H_2-28), 4.07 (1H, q-like, AZT-H-4′), 4.20–4.25 (1H, m, AZT-H-3′), 4.26 (1H, dd, *J* = 4.0, 12.0 Hz, AZT-H-5a′), 4.43 (1H, dd, *J* = 4.4, 12.0 Hz, AZT-H-5b′), 4.48 (1H, dd, *J* = 5.2, 10.8 Hz, H-3), 4.60, 4.69 (each 1H, br s, H_2-29), 6.14 (1H, t-like, *J* = 6.4 Hz, AZT-H-1′), 7.29 (1H, d, *J* = 1.2 Hz, AZT-H-6), 9.43 (1H, br s, AZT-NH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.5 AZT-CH_3, 14.7 (C-27), 16.0 (C-26), 16.1 (C-25), 16.5 (C-24), 18.1 (C-6), 19.1 (C-30), 20.8 (C-11), 23.6 (C-2), 25.1 (C-12), 25.0, 25.6 (3-*O*-dimethylsuccinyl CH_3), 27.0 (C-15), 27.9 (28-*O*-dimethylglutaryl CH_3), 28.0 (C-23), 29.5 (C-21), 29.8 (C-16), 32.6 (28-*O*-dimethylglutaryl C-3″), 34.1 (C-7), 34.6 (C-22), 37.0 (C-10), 37.5 (AZT-C-2′, C-13), 37.7 (C-4), 38.4 (C-1), 40.4 (3-*O*-dimethylsuccinyl C-3′), 40.8 (C-8), 42.7 (C-14), 44.5 (28-*O*-dimethylglutaryl C-4″), 44.7 (3-*O*-dimethylsuccinyl C-2′), 45.0 (28-*O*-dimethylglutaryl C-2″), 46.2 (C-17), 47.7 (C-19), 48.7 (C-18), 50.2 (C-9), 55.4 (C-5), 60.4 (AZT-C-3′), 62.7 (C-28), 62.8 (AZT-C-5′), 81.5 (C-3), 81.8 (AZT-C-4′), 85.3 (AZT-C-1′), 109.9 (C-29), 111.2 (AZT-C-5), 135.4 (AZT-C-6), 150.0 (C-20), 150.1 (AZT-C-2), 163.9 (AZT-C-4), 171.0 (3-*O*-dimethylsuccinyl 1′-COO−), 171.2 (28-*O*-dimethylglutaryl 5″-COO-AZT), 172.3 (28-*O*-dimethylglutaryl 1″-COO−), 182.1 (3-*O*-dimethylsuccinyl 4′-COOH). HRESIMS (positive) *m*/*z* 962.5881 $[M+H]^+$ (calcd for $C_{53}H_{80}N_5O_{11}$, 962.5854).

5.2.8.5. 3′-Azido-3′-deoxythymidine-5′-yl 3-*O*-(3′,3′-dimethylglutaryl)-lup-20(29)en-28-yl 3,3-dimethylglutarate (54). Yield 84.2% (starting from 107 mg of **40**); white solid. $[\alpha]_D^{26}$ +15.6° (*c* 3.09, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.84 (each 3H, s, CH_3-24, 25), 0.85 (6H, s, CH_3-23), 0.97 (3H, s, CH_3-27), 1.02 (3H, s, CH_3-26), 1.12, 1.15 (each 3H, s, 28-*O*-dimethylglutaryl CH_3), 1.15 (6H, s, 3-*O*-dimethylglutaryl CH_3), 1.68 (3H, s, CH_3-30), 1.94 (3H, br s, AZT-CH_3), 2.32–2.51 (3H, m, AZT-H_2-2′ and H-19), 2.40, 2.47 (each 1H, d, *J* = 14.4 Hz, 3-*O*-dimethylglutaryl H_2-2′), 2.46 (2H, s, 3-*O*-dimethylglutaryl H_2-4′), 2.44, 2.49 (each 1H, d, *J* = 14.4 Hz, 28-*O*-dimethylglutaryl H_2-2″), 2.48, 2.56 (each 1H, d, *J* = 14.4 Hz, 28-*O*-dimethylglutaryl H_2-3″), 3.81, 4.26 (each 1H, d, *J* = 11.2 Hz, H_2-28), 4.07 (1H, q-like, AZT-H-4′), 4.20–4.28 (1H, m, AZT-H-3′), 4.26 (1H, dd, *J* = 4.0, 12.4 Hz, AZT-H-5a′), 4.43 (1H, dd, *J* = 4.0, 12.4 Hz, AZT-H-5b′), 4.49 (1H, dd, *J* = 5.2, 11.6 Hz, H-3), 4.60, 4.69 (each 1H, br s, H_2-29), 6.14 (1H, t-like, *J* = 6.4 Hz, AZT-H-1′), 7.29 (1H, br s, AZT-H-6), 9.41 (1H, br s, AZT-NH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.5 AZT-CH_3, 14.7 (C-27), 16.0 (C-26), 16.1 (C-25), 16.6 (C-24), 18.1 (C-6), 19.1 (C-30), 20.8 (C-11), 23.7 (C-2), 25.1 (C-12), 27.0 (C-15), 27.9 (3-*O*-dimethylglutaryl CH_3), 27.9, 28.0 (28-*O*-dimethylglutaryl CH_3), 28.0 (C-23), 29.5 (C-21), 29.8 (C-16), 32.6 (28-*O*-dimethylglutaryl C-3″, 3-*O*-dimethylglutaryl C-3′), 34.1 (C-7), 34.6 (C-22), 37.0 (C-10), 37.5 (AZT-C-2′, C-13), 37.6 (C-4), 38.3 (C-1), 40.8 (C-8), 42.7 (C-14), 44.5 (28-*O*-dimethylglutaryl C-4″), 45.0 (28-*O*-dimethylsuccinyl C-2″), 45.2 (3-*O*-dimethylglutaryl C-4′), 45.6 (3-*O*-dimethylglurayl C-2′), 46.2 (C-17), 47.7 (C-19), 48.7 (C-18), 50.2 (C-9), 55.4 (C-5), 60.4 (AZT-C-3′), 62.6 (C-28), 62.7 (AZT-C-5′), 81.3 (C-3), 81.8 (AZT-C-4′), 85.3 (AZT-C-1′), 109.9 (C-29), 111.2 (AZT-C-5), 135.4 (AZT-C-6), 150.0 (C-20), 150.1 (AZT-C-2), 164.0 (AZT-C-4), 171.2 (28-*O*-dimethylglutaryl 5″-COO-AZT), 172.3 (3-*O*-dimethylglutaryl 1′-COO−, 28-*O*-dimethylglutaryl 1″-COO−), 176.0 (3-*O*-dimethylglutaryl 5′-COOH). HRESIMS (positive) *m*/*z* 998.5824 $[M+Na]^+$ (calcd for $C_{54}H_{81}N_5O_{11}Na$, 998.5830).

5.2.8.6. 1-(3′-Azido-3′-deoxythymidine-5′-yl)-4-[3-*O*-(3′,3′-dimethylsuccinyl)-lup-28-yl] 2,2-dimethylsuccinate (55) and 4-(3′-Azido-3′-deoxythymidine-5′-yl)-1-[3-*O*-(3′,3′-dimethylsuccinyl)-lup-28-yl] 2,2-dimethylsuccinate (56). Total yield 56.7% (starting from 148 mg of mixture of **41** and **42**); in a ratio of 1.1:1; white solid.

*Compound **55**:* $[\alpha]_D^{30}$ −4.2° (*c* 2.99, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.76, 0.83 (each 3H, d, *J* = 8.0 Hz, CH_3-29, 30), 0.82 (3H, s, CH_3-24), 0.84 (6H, s, CH_3-23, CH_3-25), 0.94 (3H, s, CH_3-27), 1.01 (3H, s, CH_3-26), 1.31 (6H, s, 3-*O*-dimethylsuccinyl CH_3), 1.30, 1.31 (each 1H, s, 28-*O*-dimethylsuccinyl CH_3), 1.93 (3H, br s, AZT-CH_3), 2.25–2.32, 2.44–2.50 (each 1H, m, AZT-H_2-2′), 2.57, 2.68 (each 1H, d, *J* = 15.6 Hz, 3-*O*-dimethylsuccinyl H_2-2′), 2.59, 2.73 (each 1H, d, *J* = 16.4 Hz, 28-*O*-dimethylsuccinyl H_2-2″), 3.81, 4.27 (each 1H, d, *J* = 10.8 Hz, H_2-28), 4.09 (1H, q-like, AZT-H-4′), 4.25–4.29 (1H, m, AZT-H-3′), 4.28 (1H, dd, *J* = 4.4, 12.0 Hz, AZT-H-5a′), 4.52 (1H, dd, *J* = 3.6, 12.0 Hz, AZT-H-5b′), 4.49 (1H, dd, *J* = 5.2, 10.8 Hz, H-3), 6.16 (1H, t-like, *J* = 6.4 Hz, AZT-H-1′), 7.27 (1H, br s, AZT-H-6), 9.31 (1H, br s, AZT-NH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.4 AZT-CH_3, 14.6 (C-27), 14.8 (C-29), 16.0 (C-26, C-25), 16.5 (C-24), 18.1 (C-6), 20.8 (C-11), 21.6 (C-21), 22.8 (C-30), 23.6 (C-2), 25.1, 25.6 (3-*O*-dimethylsuccinyl CH_3), 25.0, 25.8 (28-*O*-dimethylsuccinyl CH_3), 26.8 (C-12), 26.9 (C-15), 27.9 (C-23), 29.4 (C-20), 29.8 (C-16), 34.2 (C-7), 34.6 (C-22), 37.0 (C-10), 37.2 (C-13), 37.5 (AZT-C-2′), 37.7 (C-4), 38.4 (C-1), 40.4 (3-*O*-dimethylsuccinyl C-3′), 40.7 (28-*O*-dimethylsuccinyl C-3″), 40.9 (C-8), 42.8 (C-14), 44.5 (C-19), 44.6 (28-*O*-dimethylsuccinyl C-2″), 44.7 (3-*O*-dimethylsuccinyl C-2′), 46.5 (C-17), 48.1 (C-18), 49.9 (C-9), 55.4 (C-5), 60.4 (AZT-C-3′), 63.1 (C-28), 63.3 (AZT-C-5′), 81.5 (C-3), 82.0 (AZT-C-4′), 84.9 (AZT-C-1′), 111.3 (AZT-C-5), 135.2 (AZT-C-6), 150.2 (AZT-C-2), 164.0 (AZT-C-4), 171.0 (3-*O*-dimethylsuccinyl 1′-COO−), 171.7 (28-*O*-dimethylsuccinyl 1″-COO−), 176.5 (28-*O*-dimethylsuccinyl 4″-COO-AZT), 182.0 (3-*O*-dimethylsuccinyl 4′-COOH). HRESIMS (positive) *m*/*z* 950.5848 $[M+H]^+$ (calcd for $C_{52}H_{80}N_5O_{11}$, 950.5854).

*Compound **56**:* $[\alpha]_D^{27}$ −2.5° (*c* 1.74, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.77, 0.84 (each 3H, d, *J* = 8.0 Hz, CH_3-29, 30), 0.82 (3H, s, CH_3-24), 0.85 (6H, s, CH_3-23, CH_3-25), 0.95 (3H, s, CH_3-27), 1.00 (3H, s, CH_3-26), 1.31 (each 3H, s, 3-*O*-dimethylsuccinyl

CH_3), 1.30, 1.33 (each 3H, s, 28-*O*-dimethylsuccinyl CH_3), 1.95 (3H, br s, AZT-CH_3), 2.32–2.39, 2.44–2.50 (each 1H, m, AZT-H_2-2′), 2.57, 2.68 (each 1H, d, *J* = 15.6 Hz, 3-*O*-dimethylsuccinyl H_2-2′), 2.61, 2.66 (each 1H, d, *J* = 16.0 Hz, 28-*O*-dimethylsuccinyl H_2-3″), 3.81, 4.29 (each 1H, d, *J* = 10.8 Hz, H_2-28), 4.04 (1H, q-like, AZT-H-4′), 4.17–4.22 (1H, m, AZT-H-3′), 4.26 (1H, dd, *J* = 3.6, 12.0 Hz, AZT-H-5a′), 4.42 (1H, dd, *J* = 4.4, 12.0 Hz, AZT-H-5b′), 4.50 (1H, dd, *J* = 5.2, 10.8 Hz, H-3), 6.13 (1H, t-like, *J* = 6.4 Hz, AZT-H-1′), 7.30 (1H, d, br s, AZT-H-6), 9.16 (1H, br s, AZT-NH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.5 AZT-CH_3, 14.7 (C-27), 14.9 (C-29), 16.0 (C-26, 25), 16.5 (C-24), 18.2 (C-6), 20.8 (C-11), 21.6 (C-21), 22.9 (C-30), 23.6 (C-2), 25.1, 25.6 (3-*O*-dimethylsuccinyl CH_3), 25.5, 25.8 (28-*O*-dimethylsuccinyl CH_3), 26.8 (C-12), 26.9 (C-15), 27.9 (C-23), 29.4 (C-20), 30.0 (C-16), 34.2 (C-7), 34.7 (C-22), 37.0 (C-10), 37.2 (C-13), 37.5 (AZT-C-2′), 37.7 (C-4), 38.4 (C-1), 40.4 (3-*O*-dimethylsuccinyl C-3′), 40.9 (C-8), 41.1 (28-*O*-dimethylsuccinyl C-2″), 42.9 (C-14), 43.9 (28-*O*-dimethylsuccinyl C-3″), 44.6 (C-19), 44.7 (3-*O*-dimethylsuccinyl C-2′), 46.7 (C-17), 48.2 (C-18), 50.0 (C-9), 55.4 (C-5), 60.3 (AZT-C-3′), 63.0 (AZT-C-5′), 63.4 (C-28), 81.5 (C-3), 81.8 (AZT-C-4′), 85.3 (AZT-C-1′), 111.3 (AZT-C-5), 135.4 (AZT-C-6), 150.0 (AZT-C-2), 163.8 (AZT-C-4), 170.8 (28-*O*-dimethylsuccinyl 4″-COO−AZT), 171.0 (3-*O*-dimethylsuccinyl 1′-COO−), 176.9 (28-*O*-dimethylsuccinyl 1″-COO−), 181.7 (3-*O*-dimethylsuccinyl 4′-COOH). HRESIMS (positive) *m*/*z* 950.5873 $[M+H]^+$ (calcd for $C_{52}H_{80}N_5O_{11}$, 950.5854).

5.2.8.7. 3′-Azido-3′-deoxythymidine-5′-yl 3-*O*-(3′,3′-dimethylsuccinyl)-lup-28-yl 3,3-dimethylglutarate (57). Yield 45.6% (starting from 84 mg of **43**); white solid. $[\alpha]_D^{27}$ −0.02° (*c* 2.12, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.77, 0.84 (each 3H, d, *J* = 8.0 Hz, CH_3-29, 30), 0.82 (3H, s, CH_3-24), 0.85 (6H, s, CH_3-23, CH_3-25), 0.95 (3H, s, CH_3-27), 1.03 (3H, s, CH_3-26), 1.12, 1.15 (each 3H, s, 28-*O*-dimethylglutaryl CH_3), 1.30, 1.31 (each 3H, s, 3-*O*-dimethylsuccinyl CH_3), 1.95 (3H, br s, AZT-CH_3), 2.33–2.40, 2.43–2.50 (2H, m, AZT-H_2-2′), 2.42, 2.48 (each 1H, d, *J* = 14.4 Hz, 28-*O*-dimethylglutaryl H_2-2″), 2.49, 2.56 (each 1H, d, *J* = 15.2 Hz, 28-*O*-dimethylglutaryl H_2-4″), 2.57, 2.68 (each 1H, d, *J* = 15.6 Hz, 3-*O*-dimethylsuccinyl H_2-2′), 3.79, 4.26 (each 1H, d, *J* = 10.8 Hz, H_2-28), 4.07 (1H, q-like, AZT-H-4′), 4.20–4.23 (1H, m, AZT-H-3′), 4.26 (1H, dd, *J* = 3.6, 12.0 Hz, AZT-H-5a′), 4.44 (1H, dd, *J* = 4.4, 12.0 Hz, AZT-H-5b′), 4.50 (1H, dd, *J* = 5.2, 10.4 Hz, H-3), 6.14 (1H, t-like, *J* = 6.4 Hz, AZT-H-1′), 7.29 (1H, br s, AZT-H-6), 9.15 (1H, br s, AZT-NH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.5 AZT-CH_3, 14.6 (C-27), 14.9 (C-29), 16.0 (C-26, 25), 16.5 (C-24), 18.2 (C-6), 20.8 (C-11), 21.6 (C-21), 22.9 (C-30), 23.6 (C-2), 25.1, 25.6 (3-*O*-dimethylsuccinyl CH_3), 26.8 (C-12), 26.9 (C-15), 27.9 (28-*O*-dimethylglutaryl CH_3), 28.0 (C-23), 29.4 (C-20), 29.9 (C-16), 32.6 (28-*O*-dimethylglutaryl C-3″), 34.2 (C-7), 34.8 (C-22), 37.0 (C-10), 37.2 (C-13), 37.6 (AZT-C-2′), 37.7 (C-4), 38.4 (C-1), 40.4 (3-*O*-dimethylsuccinyl C-3′), 40.9 (C-8), 42.9 (C-14), 44.5 (28-*O*-dimethylglutaryl C-4″, C-19), 44.7 (3-*O*-dimethylsuccinyl C-2′), 45.1 (28-*O*-dimethylsuccinyl C-2″), 46.4 (C-17), 48.1 (C-18), 50.0 (C-9), 55.4 (C-5), 60.5 (AZT-C-3′), 62.8 (C-28, AZT-C-5′), 81.5 (C-3), 81.9 (AZT-C-4′), 85.3 (AZT-C-1′), 111.3 (AZT-C-5), 135.4 (AZT-C-6), 150.1 (AZT-C-2), 163.8 (AZT-C-4), 171.0 (3-*O*-dimethylsuccinyl 1′-COO−), 171.2 (28-*O*-dimethylglutaryl 5″-COO-AZT), 172.3 (28-*O*-dimethylglutaryl 1″-COO−), 181.8 (3-*O*-dimethylsuccinyl 4′-COOH). HRESIMS (positive) *m*/*z* 964.6037 $[M+H]^+$ (calcd for $C_{53}H_{82}N_5O_{11}$, 964.6011).

5.2.8.8. 1-(3′-Azido-3′-deoxythymidine-5′-yl)-4-(3-*O*-glutaryl-lup-28-yl) 2,2-dimethylsuccinate (58). Yield 82.5% (starting from 20.4 mg of **44**); white solid. $[\alpha]_D^{27}$ −1.9° (*c* 1.11, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.77, 0.84 (each 3H, d, *J* = 8.0 Hz, CH_3-29, 30), 0.85 (6H, s, CH_3-24, CH_3-23), 0.87 (3H, s, CH_3-25), 0.95 (3H, s, CH_3-27), 1.02 (3H, s, CH_3-26), 1.30, 1.31 (each 3H, s, 28-*O*-dimethylsuccinyl CH_3), 1.94 (3H, br s, AZT-CH_3), 1.98 (2H, quint, *J* = 7.2 Hz, 3-*O*-glutaryl H_2-3′), 2.26–2.35, 2.44–2.51 (each 1H, m, AZT-H_2-2′), 2.40 (2H, t, *J* = 7.2 Hz, 3-*O*-glutaryl H_2-2′), 2.44 (2H, t, *J* = 7.2 Hz, 3-*O*-glutaryl H_2-4′), 2.60, 2.74 (each 1H, d, *J* = 16.0 Hz, 28-*O*-dimethylsuccinyl H_2-2″), 3.82, 4.28 (each 1H, d, *J* = 10.8 Hz, H_2-28), 4.09 (1H, q-like, AZT-H-4′), 4.25–4.30 (1H, m, AZT-H-3′), 4.28 (1H, dd, *J* = 4.0, 12.0 Hz, AZT-H-5a′), 4.51 (1H, dd, *J* = 4.0, 12.0 Hz, AZT-H_2-5b′), 4.49 (1H, dd, *J* = 5.2, 10.0 Hz, H-3), 6.16 (1H, t-like, *J* = 6.4 Hz, AZT-H-1′), 7.28 (1H, d, *J* = 1.2 Hz, AZT-H-6), 8.96 (1H, br s, AZT-NH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.4 AZT-CH_3, 14.6 (C-27), 14.9 (C-29), 16.0 (C-26), 16.1 (C-25), 16.6 (C-24), 18.2 (C-6), 20.1 (3-*O*-glutaryl C-3′), 20.8 (C-11), 21.6 (C-21), 22.9 (C-30), 23.7 (C-2), 25.1, 25.9 (28-*O*-dimethylsuccinyl CH_3), 26.8 (C-12), 26.9 (C-15), 28.0 (C-23), 29.4 (C-20), 29.9 (C-16), 32.9 (3-*O*-glutaryl C-4′), 33.7 (3-*O*-glutaryl C-2′), 34.2 (C-7), 34.7 (C-22), 37.1 (C-10), 37.2 (C-13), 37.5 (AZT-C-2′), 37.8 (C-4), 38.4 (C-1), 40.7 (28-*O*-dimethylsuccinyl C-3″), 40.9 (C-8), 42.9 (C-14), 44.6 (C-19, 28-*O*-dimethylsuccinyl C-2″), 46.5 (C-17), 48.2 (C-18), 50.0 (C-9), 55.4 (C-5), 60.4 (AZT-C-3′), 63.2 (C-28), 63.3 (AZT-C-5′), 81.1 (C-3), 82.0 (AZT-C-4′), 84.9 (AZT-C-1′), 111.3 (AZT-C-5), 135.2 (AZT-C-6), 150.0 (AZT-C-2), 163.7 (AZT-C-4), 171.7 (28-*O*-dimethylsuccinyl 1″-COO−), 172.7 (3-*O*-glutaryl 1′-COO−), 176.5 (28-*O*-dimethylsuccinyl 4″-COO-AZT), 177.1 (3-*O*-glutaryl 5′-COOH). HRESIMS (positive) *m*/*z* 936.5716 $[M+H]^+$ (calcd for $C_{51}H_{78}N_5O_{11}$, 936.5698).

5.2.8.9. 4-(3′-Azido-3′-deoxythymidine-5′-yl)-1-(3-*O*-glutaryl-lup-28-yl) 2,2-dimethylsuccinate (59). Yield 66.1% (starting from 32.6 mg of **45**); white solid. $[\alpha]_D^{27}$ +2.3° (*c* 1.66, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.77, 0.84 (each 3H, d, *J* = 8.0 Hz, CH_3-29, 30), 0.85 (6H, s, CH_3-24, CH_3-23), 0.87 (3H, s, CH_3-25), 0.96 (3H, s, CH_3-27), 1.04 (3H, s, CH_3-26), 1.31, 1.34 (each 3H, s, 28-*O*-dimethylsuccinyl CH_3), 1.96 (3H, br s, AZT-CH_3), 1.98 (2H, quint, *J* = 7.2 Hz, 3-*O*-glutaryl H_2-3′), 2.32–2.51 (2H, m, AZT-H_2-2′), 2.40 (2H, t, *J* = 7.2 Hz, 3-*O*-glutaryl H_2-2′), 2.43 (2H, t, *J* = 7.2 Hz, 3-*O*-glutaryl H_2-4′), 2.61, 2.66 (each 1H, d, *J* = 16.4 Hz, 28-*O*-dimethylsuccinyl H_2-2″), 3.81, 4.30 (each 1H, d, *J* = 10.8 Hz, H_2-28), 4.05 (1H, q-like, AZT-H-4′), 4.17–4.23 (1H, m, AZT-H-3′), 4.26 (1H, dd, *J* = 3.6, 12.4 Hz, AZT-H-5a′), 4.42 (1H, dd, *J* = 4.4, 12.4 Hz, AZT-H-5b′), 4.49 (1H, dd, *J* = 5.2, 10.8 Hz, H-3), 6.14 (1H, t-like, *J* = 6.4 Hz, AZT-H-1′), 7.31 (1H, d, *J* = 0.8 Hz, AZT-H-6), 9.14 (1H, br s, AZT-NH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.5 AZT-CH_3, 14.7 (C-27), 14.9 (C-29), 16.0 (C-26), 16.1 (C-25), 16.6 (C-24), 18.2 (C-6), 20.1 (3-*O*-glutaryl C-3′), 20.8 (C-11), 21.6 (C-21), 22.9 (C-30), 23.7 (C-2), 25.5, 25.8 (28-*O*-dimethylsuccinyl CH_3), 26.8 (C-12), 26.9 (C-15), 28.0 (C-23), 29.4 (C-20), 29.9 (C-16), 32.9 (3-*O*-glutaryl C-4′), 33.7 (3-*O*-glutaryl C-2′), 34.2 (C-7), 34.7 (C-22), 37.0 (C-10), 37.2 (C-13), 37.5 (AZT-C-2′), 37.8 (C-4), 38.4 (C-1), 40.9 (C-8), 41.1 (28-*O*-dimethylsuccinyl C-2″), 42.9 (C-14), 43.9 (28-*O*-dimethylsuccinyl C-3″), 44.6 (C-19), 46.7 (C-17), 48.2 (C-18), 50.0 (C-9), 55.4 (C-5), 60.3 (AZT-C-3′), 62.9 (AZT-C-5′), 63.3 (C-28), 81.1 (C-3), 81.8 (AZT-C-4′), 85.2 (AZT-C-1′), 111.3 (AZT-C-5), 135.5 (AZT-C-6), 150.1 (AZT-C-2), 163.8 (AZT-C-4), 170.8 (28-*O*-dimethylsuccinyl 4″-COO-AZT), 172.7 (3-*O*-glutaryl 1′-COO−), 176.9 (28-*O*-dimethylsuccinyl 1″-COO−), 177.3 (3-*O*-glutaryl 5′-COOH). HRESIMS (positive) *m*/*z* 936.5694 $[M+H]^+$ (calcd for $C_{51}H_{78}N_5O_{11}$, 936.5698).

5.2.8.10. 3′-Azido-3′-deoxythymidine-5′-yl 3-*O*-glutaryl-lup-28-yl glutarate (60). Yield 58.7% (starting from 41.2 mg of **46**); white solid. $[\alpha]_D^{27}$ +7.0° (*c* 1.40, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.78, 0.84 (each 3H, d, *J* = 8.0 Hz, CH_3-29, 30), 0.84 (6H, s, CH_3-24, CH_3-23), 0.87 (3H, s, CH_3-25), 0.96 (3H, s, CH_3-27), 1.05 (3H, s, CH_3-26), 1.94 (3H, d, *J* = 1.2 Hz, AZT-CH_3), 1.97 (2H, quint, *J* = 7.2 Hz, 3-*O*-glutaryl H_2-3′), 1.99 (2H, quint, *J* = 7.2 Hz, 28-*O*-glutaryl H_2-3″), 2.34–2.51 (2H, m, AZT-H_2-2′), 2.40 (2H, t, *J* = 7.2 Hz, 3-*O*-glutaryl H_2-2′), 2.41 (2H, t, *J* = 7.2 Hz, 28-*O*-glutaryl H_2-2″), 2.43 (2H,

t, J = 7.2 Hz, 3-*O*-glutaryl H_2-4′), 2.46 (2H, t, J = 7.2 Hz, 28-*O*-glutaryl H_2-4″), 3.83, 4.29 (each 1H, d, J = 11.2 Hz, H_2-28), 4.07 (1H, q-like, AZT-H-4′), 4.20–4.24 (1H, m, AZT-H-3′), 4.32 (1H, dd, J = 4.0, 12.0 Hz, AZT-H-5a′), 4.40 (1H, dd, J = 4.4, 12.0 Hz, AZT-H-5b′), 4.49 (1H, dd, J = 6.0, 10.4 Hz, H-3), 6.09 (1H, t-like, J = 6.4 Hz, AZT-H-1′), 7.23 (1H, br s, AZT-H-6), 9.10 (1H, br s, AZT-NH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.5 AZT-CH_3, 14.6 (C-27), 14.9 (C-29), 16.0 (C-26, C-25), 16.6 (C-24), 18.2 (C-6), 20.1 (28-*O*-glutaryl C-3″, 3-*O*-glutaryl C-3′), 20.8 (C-11), 21.6 (C-21), 22.9 (C-30), 23.7 (C-2), 26.8 (C-12), 26.9 (C-15), 28.0 (C-23), 29.4 (C-20), 29.9 (C-16), 32.9 (3-*O*-glutaryl C-4′), 33.1 (28-*O*-glutaryl C-4″), 33.2 (28-*O*-glutaryl C-2″), 33.7 (3-*O*-glutaryl C-2′), 34.2 (C-7), 34.7 (C-22), 37.0 (C-10), 37.2 (C-13), 37.5 (AZT-C-2′), 37.8 (C-4), 38.4 (C-1), 41.0 (C-8), 42.9 (C-14), 44.6 (C-19), 46.6 (C-17), 48.2 (C-18), 50.0 (C-9), 55.4 (C-5), 60.6 (AZT-C-3′), 63.0 (C-28), 63.3 (AZT-C-5′), 81.1 (C-3), 81.8 (AZT-C-4′), 85.7 (AZT-C-1′), 111.3 (AZT-C-5), 135.5 (AZT-C-6), 150.0 (AZT-C-2), 163.7 (AZT-C-4), 172.3 (28-*O*-glutaryl 5″-COO-AZT), 172.7 (3-*O*-glutaryl 1′-COO−), 173.1 (28-*O*-glutaryl 1″-COO−), 177.2 (3-*O*-glutaryl 5′-COOH). HRESIMS (positive) m/z 922.5557 $[M+H]^+$ (calcd for $C_{60}H_{76}N_5O_{11}$, 922.5541).

5.2.8.11. 3′-Azido-3′-deoxythymidine-5′-yl 3-*O*-glutaryl-lup-28-yl 3,3-dimethylglutarate (61). Yield 75.6% (starting from 39 mg of **47**); white solid. $[\alpha]_D^{27}$ +3.5° (c 2.13, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.77, 0.84 (each 3H, d, J = 8.0 Hz, CH_3-29, 30), 0.85 (6H, s, CH_3-24, CH_3-23), 0.86 (3H, s, CH_3-25), 0.95 (3H, s, CH_3-27), 1.03 (3H, s, CH_3-26), 1.12, 1.15 (each 3H, s, 28-*O*-dimethylglutaryl CH_3), 1.95 (3H, d, J = 1.2 Hz, AZT-CH_3), 1.97 (2H, quint, J = 7.2 Hz, 3-*O*-glutaryl H_2-3′), 2.32–2.51 (2H, m, AZT-H_2-2′), 2.40 (2H, t, J = 7.2 Hz, 3-*O*-glutaryl H_2-2′), 2.42, 2.49 (each 1H, d, J = 14.4 Hz, 28-*O*-dimethylglutaryl H_2-2″), 2.43 (2H, t, J = 7.2 Hz, 3-*O*-glutaryl H_2-4′), 2.48, 2.56 (each 1H, d, J = 15.2 Hz, 28-*O*-dimethylglutaryl H_2-4″), 3.79, 4.27 (each 1H, d, J = 10.8 Hz, H_2-28), 4.07 (1H, q-like, AZT-H-4′), 4.20–4.28 (1H, m, AZT-H-3′), 4.26 (1H, dd, J = 3.6, 12.4 Hz, AZT-H-5a′), 4.44 (1H, dd, J = 4.4, 12.4 Hz, AZT-H-5b′), 4.49 (1H, dd, J = 5.2, 10.8 Hz, H-3), 6.14 (1H, t-like, J = 6.4 Hz, AZT-H-1′), 7.30 (1H, d, J = 0.8 Hz, AZT-H-6), 9.18 (1H, br s, AZT-NH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.5 AZT-CH_3, 14.6 (C-27), 14.9 (C-29), 16.0 (C-26, C-25), 16.6 (C-24), 18.2 (C-6), 20.1 (3-*O*-glutaryl C-3′), 20.8 (C-11), 21.6 (C-21), 22.9 (C-30), 23.7 (C-2), 26.8 (C-12), 26.9 (C-15), 27.9, 28.0 (28-*O*-dimethylglutaryl CH_3), 28.0 (C-23), 29.4 (C-20), 29.9 (C-16), 32.6 (28-*O*-dimethylglutaryl C-3″), 32.9 (3-*O*-glutaryl C-4′), 33.7 (3-*O*-glutaryl C-2′), 34.2 (C-7), 34.7 (C-22), 37.0 (C-10), 37.2 (C-13), 37.6 (AZT-C-2′), 37.8 (C-4), 38.4 (C-1), 40.9 (C-8), 42.9 (C-14), 44.5 (28-*O*-dimethylglutaryl C-4″ and C-19), 45.1 (28-*O*-dimethylglutaryl C-2″), 46.4 (C-17), 48.1 (C-18), 50.0 (C-9), 55.4 (C-5), 60.4 (AZT-C-3′), 62.7 (C-28 and AZT-C-5′), 81.1 (C-3), 81.9 (AZT-C-4′), 85.3 (AZT-C-1′), 111.3 (AZT-C-5), 135.4 (AZT-C-6), 150.1 (AZT-C-2), 163.8 (AZT-C-4), 171.2 (28-*O*-dimethylglutaryl 5″-COO-AZT), 172.3 (28-*O*-dimethylglutaryl 1″-COO−), 172.7 (3-*O*-glutaryl 1′-COO−), 177.3 (3-*O*-glutaryl 5′-COOH). HRESIMS (positive) m/z 950.5876 $[M+H]^+$ (calcd for $C_{52}H_{80}N_5O_{11}$, 950.5854).

5.2.8.12. 3′-Azido-3′-deoxythymidine-5′-yl 3-*O*-(3′,3′-dimethylglutaryl)-lup-28-yl 3,3-dimethylglutarate (62). Yield 76.4% (starting from 87.7 mg of **48**); white solid. $[\alpha]_D^{29}$ +0.64° (c 2.78, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.77, 0.84 (each 3H, d, J = 8.0 Hz, CH_3-29, 30), 0.83 (3H, s, CH_3-24), 0.85 (6H, s, CH_3-23, CH_3-25), 0.95 (3H, s, CH_3-27), 1.03 (3H, s, CH_3-26), 1.15 (6H, s, 3-*O*-dimethylglutaryl CH_3), 1.12, 1.15 (each 3H, s, 28-*O*-dimethylglutaryl CH_3), 1.95 (3H, br s, AZT-CH_3), 2.32–2.51 (2H, m, AZT-H_2-2′), 2.41, 2.47 (each 1H, d, J = 14.4 Hz, 3-*O*-dimethylglutaryl H_2-2′), 2.42, 2.48 (each 1H, d, J = 14.4 Hz, 28-*O*-dimethylglutaryl H_2-2″), 2.47 (2H, s, 3-*O*-dimethylglutaryl H_2-4′), 2.48, 2.56 (each 1H, d, J = 15.2 Hz, 28-*O*-dimethylglutaryl H_2-4″), 3.79, 4.27 (each 1H, d, J = 10.8 Hz, H_2-28), 4.07 (1H, q-like, AZT-H-4′), 4.20–4.28 (1H, m, AZT-H-3′), 4.26 (1H, dd, J = 3.6, 12.0 Hz, AZT-H-5a′), 4.44 (1H, dd, J = 4.4, 12.0 Hz, AZT-H-5b′), 4.50 (1H, dd, J = 5.2, 10.8 Hz, H-3), 6.14 (1H, t-like, J = 6.4 Hz, AZT-H-1′), 7.29 (1H, d, J = 1.2 Hz, AZT-H-6), 9.19 (1H, br s, AZT-NH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.5 AZT-CH_3, 14.6 (C-27), 14.9 (C-29), 16.0 (C-26, C-25), 16.6 (C-24), 18.2 (C-6), 20.8 (C-11), 21.6 (C-21), 22.9 (C-30), 23.8 (C-2), 26.8 (C-12), 26.9 (C-15), 27.9 (28-*O*-dimethylglutaryl CH_3), 27.9, 28.0 (3-*O*-dimethylglutaryl CH_3), 28.0 (C-23), 29.4 (C-20), 29.9 (C-16), 32.6 (28-*O*-dimethylglutaryl C-3″), 32.7 (3-*O*-dimethylglutaryl C-3′), 34.2 (C-7), 34.7 (C-22), 37.0 (C-10), 37.2 (C-13), 37.6 (AZT-C-2′), 37.7 (C-4), 38.4 (C-1), 40.9 (C-8), 42.9 (C-14), 44.6 (28-*O*-dimethylglutaryl C-4″ and C-19), 45.1 (28-*O*-dimethylglutaryl C-2″), 45.2 (3-*O*-glutaryl C-4′), 45.7 (3-*O*-glutaryl C-2′), 46.4 (C-17), 48.1 (C-18), 50.0 (C-9), 55.4 (C-5), 60.4 (AZT-C-3′), 62.7 (C-28, and AZT-C-5′), 81.4 (C-3), 81.8 (AZT-C-4′), 85.3 (AZT-C-1′), 111.3 (AZT-C-5), 135.4 (AZT-C-6), 150.1 (AZT-C-2), 163.8 (AZT-C-4), 171.2 (28-*O*-dimethylglutaryl 5″-COO-AZT), 172.3 (28-*O*-dimethylglutaryl 1″-COO−, 3-*O*-dimethylglutaryl 1′-COO−), 175.6 (3-*O*-dimethylglutaryl 5′-COOH). HRESIMS (positive) m/z 1000.5991 $[M+Na]^+$ (calcd for $C_{54}H_{83}N_5O_{11}Na$, 1000.5987).

5.3. HIV-1_{NL4-3} inhibition assay in MT-4 lymphocytes

A previously described procedure was used in the experiments.[21,23]

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.bmc.2010.06.092. These data include MOL files and InChiKeys of the most important compounds described in this article.

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