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Influence of intramolecular hydrogen bonds on regioselectivity of glycosylation. Synthesis of lupane-type saponins bearing the OSW-1 saponin disaccharide unit and its isomers

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ABSTRACT

A series of lupane-type saponins bearing OSW-1 disaccharide unit as well as its regio- and stereoisomers were prepared and used for the structure–activity relationships (SAR) study. Unexpected preference for 1→4-linked regioisomers and an unusual inversion of the conformation of the sugar rings were noted. Cytotoxic activity of new lupane compounds was evaluated *in vitro* and revealed that some saponins exhibited an interesting bioactivity profile against human cancer cell lines. Influence of the protecting groups on the cytotoxicity was investigated. These results open the way to the synthesis of various lupane-type triterpene and saponin derivatives as potential anticancer compounds.

1. Introduction

Saponins are a large family of steroid or triterpenoid glycosides, widely distributed in plants and in some marine organisms,[1] in which hydrophilic mono- or oligosaccharides are attached to a hydrophobic sapogenin backbone. They possess interesting biological properties including antitumor, antiviral, antifungal, and anti-inflammatory activity, which are extensively studied and reviewed in the last years.[2] Natural saponins based on betulin scaffold occur less frequently[3] than those having other triterpene-type aglycones, although growing interest in their synthesis is noticeable.[4]

Saponin OSW-1 (**1**) was isolated by Sashida et al in 1992 from the bulbs of *Ornithogalum saudersiae* together with a number of other cholestane glycosides (Fig. 1).[5] It was found that OSW-1 exhibited extremely potent cytotoxicity against a wide range of malignant tumor cells in nanomolar concentration (IC_{50} = 0.1–0.7 nM), about 10–100 times more potent than that of the clinically applied anticancer agents.[6] Structure, biological activity, chemical synthesis, and modifications of saponin OSW-1 and its congeners have been recently exhaustively reviewed.[7]

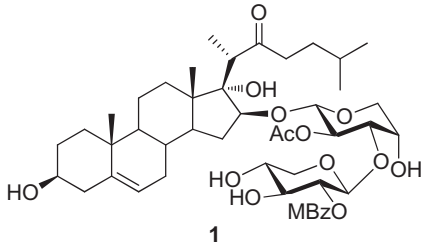

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Fig. 1. OSW-1 saponin.

The disaccharide part is crucial to the antitumor activities of the molecule. SAR studies revealed that removal of the acetyl (Ac) and/or the 4-methoxybenzoyl (MBz) groups located at the disaccharide moiety diminished the cytotoxicity by three orders of magnitude.[6,8] On the other hand, steroidal part of OSW-1 can tolerate some modifications without significant loss of activity.[9] Therefore, we speculated

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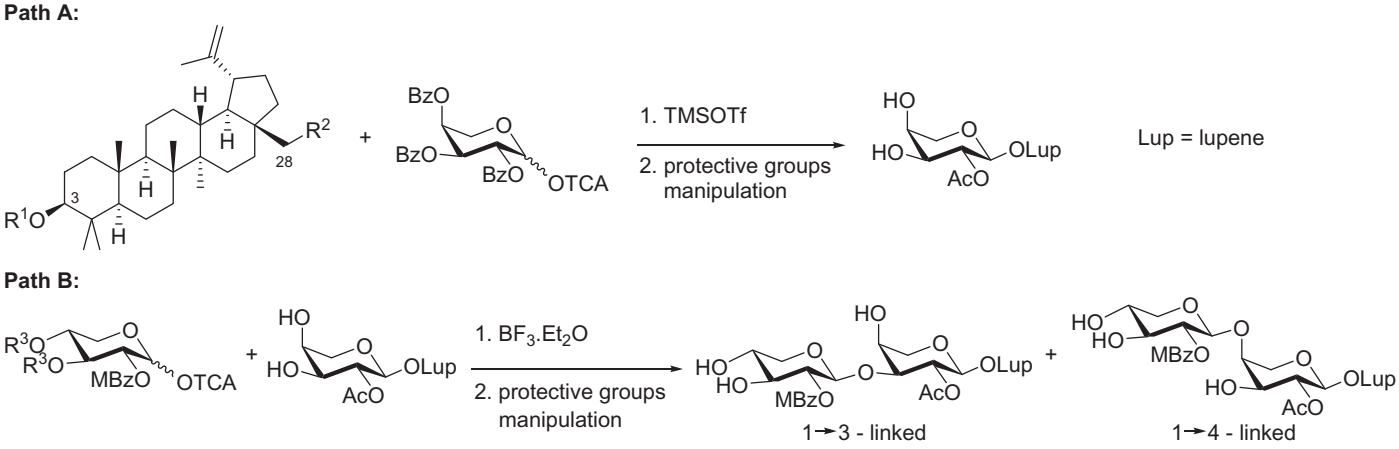


Scheme 1. General methodology for the synthesis of lupane-type saponins bearing regio- and stereoisomers of OSW-1 disaccharide moiety.

that betulin analogues of OSW-1 might also show interesting bioactivity.[4a,f,g,10,11] As a part of our study directed to the search of new anticancer drugs based on lupanes isolated from white birch bark, we decided to prepare lupane saponins bearing OSW-1 disaccharide fragment.

In this paper we report on the synthesis of lupane saponins bearing regio- and stereoisomers of OSW-1 disaccharide unit. The synthetic strategy is directed toward glycosylation of lupeol and betulin derivatives with L- and D-arabinopyranose donors. Subsequent protective groups manipulation and glycosylation with D- or L-xylose derivatives followed by saponification afforded free saponins which cytotoxicity was tested against series of normal and cancer cell lines. Strong influence of intramolecular hydrogen bond on the regioselectivity of glycosylation was observed.

2. Results and discussion

Coupling of the aglycon with the OSW-1 disaccharide donor is considered as one of the key steps in all known approaches to OSW-1 saponin and its congeners.[7] In the first attempt to lupane-type analogues of OSW-1 saponin we tried to couple appropriately protected OSW-1 disaccharide with lupanes. However, glycosylation of lupanes with OSW-1 disaccharide unit donor[12,13] failed due to the presence of acetyl group at the 2-O position of the sugar. It is well known that during glycosylation of lupane triterpenes with acetylated glycosyl donors, acetyl migration occurs as a main process instead of the formation of a glycoside. Recently we developed a modified methodology allowing us to use acetylated donors for glycosylation of betulin; however, it was ineffective in this case.[14] Therefore, we proposed an approach shown in Scheme 1 in which the disaccharide moiety was built onto the lupane framework stepwise. For the synthesis of lupenyl arabinopyranoside diols (Path A) perbenzoylated Schmidt donors, for which acyl migration was not observed, were used. Further coupling with xylopyranoside donors (Path B) gave the required disaccharides in which the 1→3 and 1→4 connections within sugars are present. Usually slight preference for the 1→4 connected disaccharide was observed. No optimization was performed because both regioisomers were indispensable for further biological tests.

Betulin derivatives **2**–**5**, lupeol (**6**), and glycosyl donors **7**–**11** were used as starting materials (Fig. 2). Regardless of the method used for their preparation, donors **7** (L-arabino) and **8** (D-arabino) were contaminated by variable amounts of inseparable corresponding furanosyl trichloroacetimidates. Therefore, minute amounts of furanosides were isolated as side products after some glycosylation reaction.

2.1. Synthesis of lupenyl L-arabinopyranosides

In the first step we focused on the synthesis of betulin derivatives. Reaction of 3-O-acetylbetulin (**2**)[15] with trichloroacetimidate **7**[16] afforded glycoside **12** (92%). Small amounts of furanoside **13** (7%) was also isolated. Deesterification of **12** with K_2CO_3 in methanol gave a mixture of products; due to known resistance of betulin acetate to basic hydrolysis, 3-O-acetyl group was only partially removed.[4f,g] The above crude mixture was treated with dimethoxypropane; subsequent reacetylation under the standard conditions (Ac_2O, pyridine) afforded diacetate **14** in 88% total yield after three steps. Final hydrolysis of the 3,4-O-acetonide yielded the desired acceptor **15** (92%, Scheme 2).

Recently, we found that allylation of the 3-OH group of selected betulin derivatives significantly increases cytotoxicity.[17] Thus,

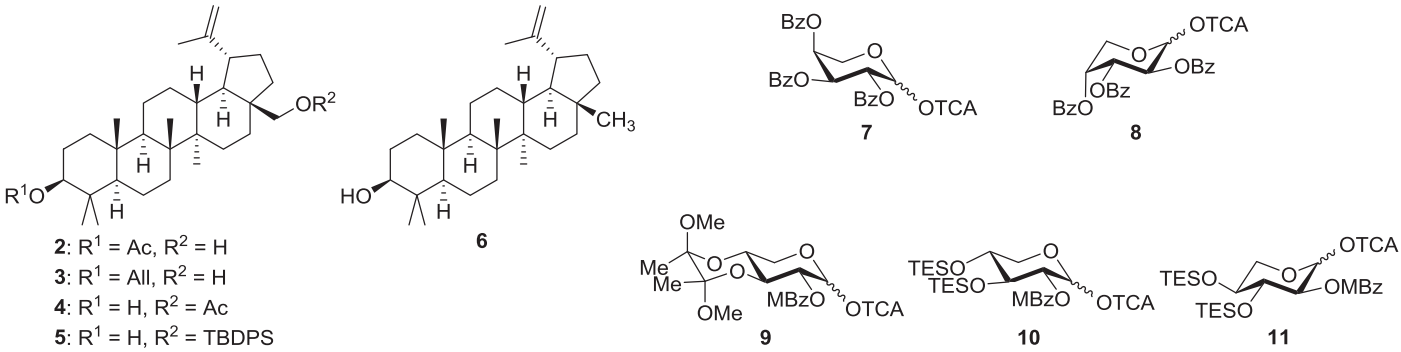
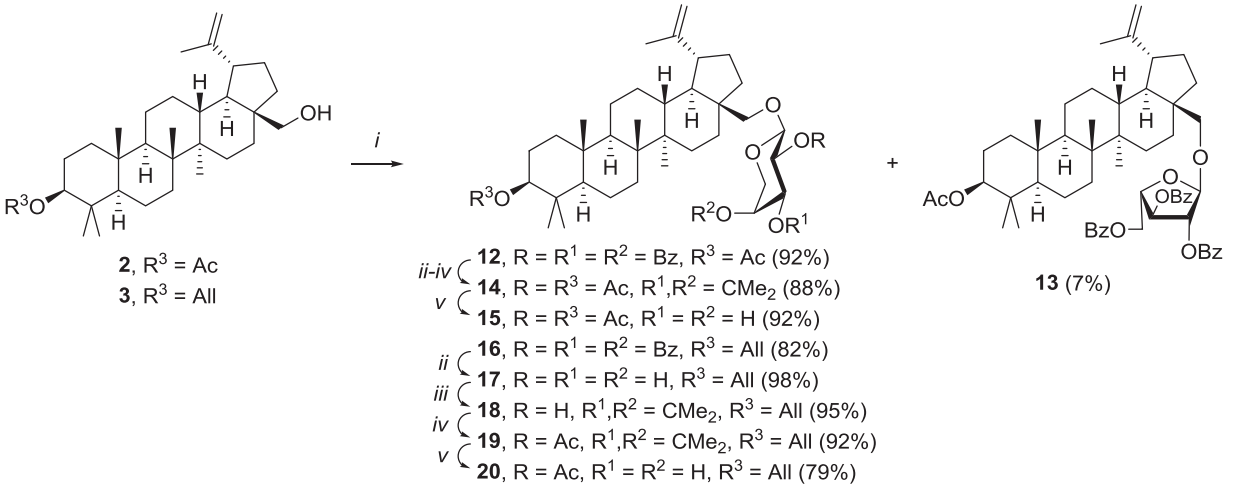


Fig. 2. Structures of lupane triterpenes and glycosyl donors.



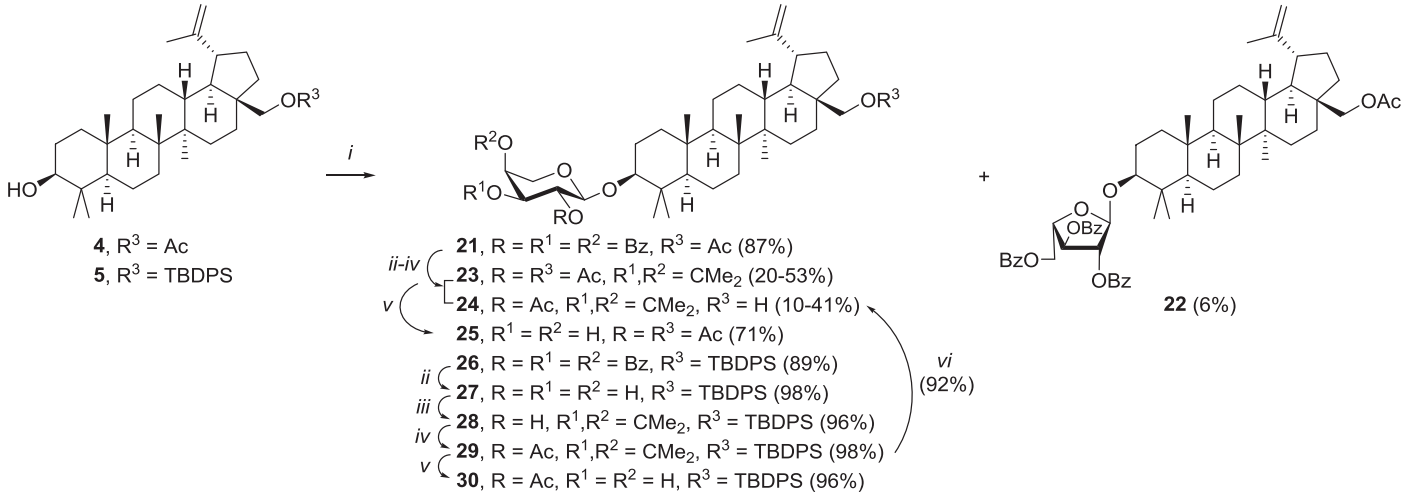
Scheme 2. Reagents and conditions: (*i*) **7**, CH_2Cl_2, molecular sieves, TMSOTf; (*ii*) K_2CO_3, methanol; (*iii*) DMF, dimethoxypropane, *p*-TsOH; (*iv*) Ac_2O, Py; (*v*) *p*-TsOH, methanol, ethyl acetate.

we also prepared 3-O-allyl betulin derivative **20** for comparison of its cytotoxic activity with the corresponding lupane 3-O-acetyl and 3-OH derivatives. Starting from 3-O-allyl betulin (**3**)[4a] and using the same methodology as described for **15**, glycoside **20** was obtained in 55% total yield (Scheme 2).

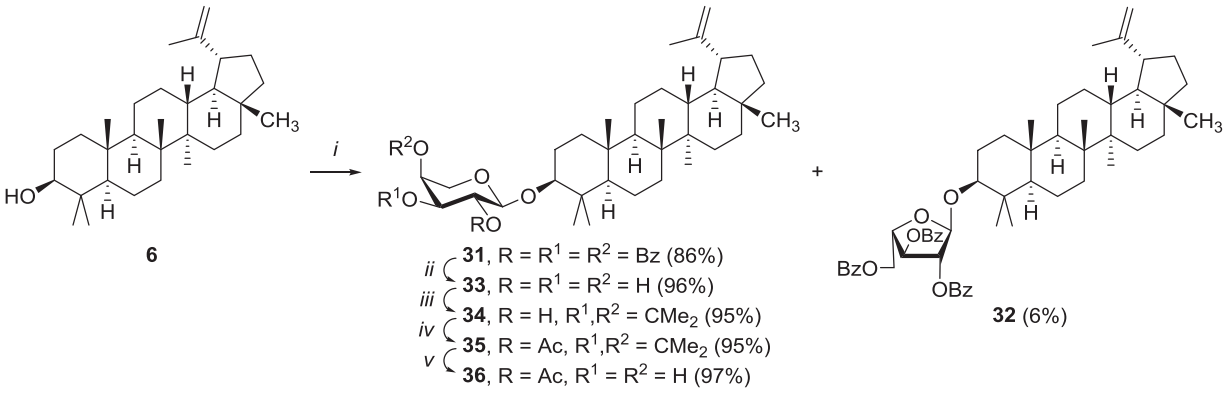
The first attempt to betulin derivatives bearing sugar moiety at the lupane O-3 position started from 28-O-acetyl-betulin (**4**).[18] Its glycosylation with **7** gave L-arabinopyranoside **21** and the corresponding L-furanoside **22** in 87% and 6% yield, respectively. Debenzoylation of **21** with potassium carbonate followed by acetonide formation and reacetylation afforded, however, a complex mixture of products. It is likely that unidentified side-products were formed by the rearrangement of the lupane core under acidic conditions.[19] Essential for further synthesis derivative **23** was isolated in moderate yield (20–53%). Significant amount of monoacetate **24** (10–41%) was also obtained. This reaction was capricious and difficult to control, and provided the desired product in low yield together with large amounts of unidentified contaminants. Compound **24** was also obtained independently by desilylation of **29**. Attempts to reacetylation of **24** failed; starting material was recovered and partial decomposition was also observed. It is likely that such phenomenon was caused by rarely observed influence of a substituent distant to the reacting center of lupane-type triterpenes.[4a,c] Its origin is unclear, but it must be considered as an explanation for some unsuccessful trials. Treatment of **23** with *p*-TsOH gave required diacetate **25** in good yield (71%). However, due to low yield of **23** and unpredictability of the above reactions, further tests have been suspended.

A new approach to the synthesis was initiated from silylated betulin **5**.[20] According to the procedure described for **15**, compound **5** was easily converted into **30** by glycosylation with **7** followed by standard deprotection/protection steps in 79% total yield (Scheme 3).

Saponin **31** was prepared in 86% yield by glycosylation of lupeol (**6**)[4f] with L-arabinopyranosyl trichloroacetimidate **7**. Small amount of furanosyl derivative **32** (6%) was also isolated. Deesterification of **31** with potassium carbonate in methanol led to free saponin **33** in 96% yield. Reaction with dimethoxypropane in the presence of



Scheme 3. Reagents and conditions: (*i*) **7**, CH_2Cl_2, molecular sieves, TMSOTf; (*ii*) K_2CO_3, methanol; (*iii*) DMF, dimethoxypropane, *p*-TsOH; (*iv*) Ac_2O, Py; (*v*) *p*-TsOH, methanol, ethyl acetate; (*vi*) Bu_4NF, AcOH, THF.



Scheme 4. Reagents and conditions: (*i*) **7**, CH_2Cl_2, molecular sieves, TMSOTf; (*ii*) K_2CO_3, methanol; (*iii*) DMF, dimethoxypropane, *p*-TsOH; (*iv*) Ac_2O, Py; (*v*) *p*-TsOH, methanol, ethyl acetate.

p-TsOH (**34**, 95%) followed by acetylation (**35**, 95%), and acetal hydrolysis gave required acetate **36** (72% total yield after five steps; Scheme 4).

2.2. Synthesis of saponins bearing the OSW-1 disaccharide unit

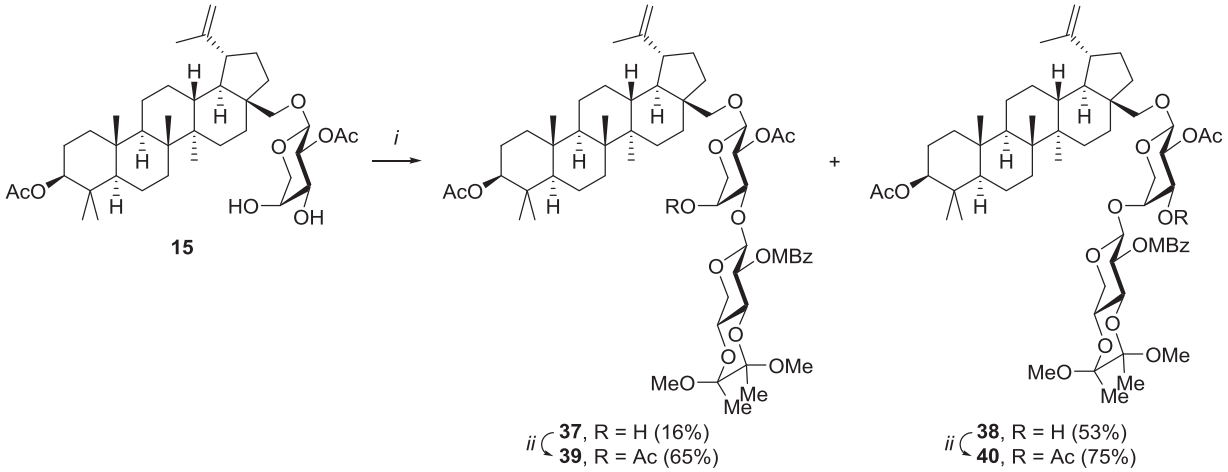
Our first synthesis of the desired disaccharides in this series began with a TMSOTf catalyzed coupling of **15** with glycosyl donor **9**[12,21] protected with butane-2,3-diacetal (BDA-acetal) which afforded a mixture of **37** (16%) and **38** (53%) easily separated by chromatography. Structure of these products was assigned by the NMR spectra of their di-acetates **39** and **40** (Scheme 5). The ^1H–^{13}C HMBC spectral data showed that glycosylation preferentially took place at the 4-OH to give 1→4-linked disaccharide **38** as the main product, whereas 1→3-linked disaccharide **37** was observed as minor component. Origin of this unusual regioselectivity will be discussed later in the text. Surprisingly, all attempts to deprotect the BDA-acetal caused decomposition of the starting materials. This issue has forced us to use donor **10**.[13]

Coupling of arabinoside **15** with **10** afforded a mixture of **41** and **42** (total yield 65%), which was only partially separable. Desilylation of this mixture with CSA allowed us to isolate pure disaccharides **43** (39%) and **44** (51%). Type of connection was confirmed independently by acetylation and desilylation of analytical samples of **41** and **42**; corresponding diacetates (**45**, 58% and **46**, 90% after two steps, respectively) were obtained and used for NMR analysis (Scheme 6).

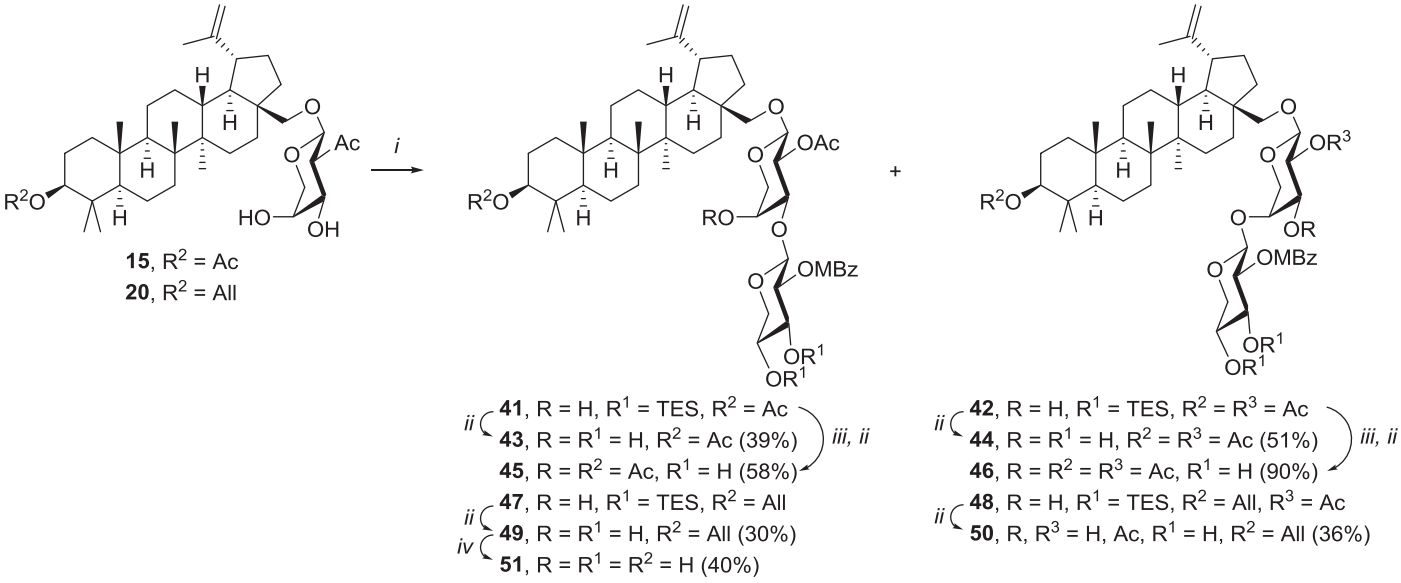
Similarly, reaction of allylated arabinoside **20** with donor **10** gave the mixture of **47** and **48** in 71% yield. Desilylation and chromatographic separation afforded two fractions. The first one (**50**, 36%) comprised a mixture of 1→4 linked disaccharides acetylated at the O-2 or O-3 positions; the latter was formed by a migration of an acetyl group, in which the process was already observed in our earlier studies.[12] The second fraction was identified as 1→3 connected disaccharide **49** (30%). It must be noted that in most cases studied here, acetyl migration was observed and at least traces of 3-O-acetates were detected in the NMR spectra of 1→4 connected disaccharides. Deallylation of **49** afforded free disaccharide **51**, although in moderate yield only (40%; Scheme 6).

Glycosylation of **30** with **10** afforded disaccharides **52** and **53** in 78% total yield; further deprotection as described above gave saponins **54** (25%, slightly contaminated by unknown compound) and **55** (62%). Deprotection of **54** yielded pure disaccharide **56** in 57%. Similar desilylation of **55** afforded 1→4 linked disaccharides as inseparable mixture (80%) comprising unexpected 3-OAc derivative **57**, formed by acetyl migration, as main component and **58** present in smaller amounts (Scheme 7).

Finally, coupling of **36** with D-xylopyranosyl trichloroacetimidate **10**, carried out in the presence of $BF_3 \times OEt_2$ at –40 °C, afforded a mixture of products (**59**/**60**) in 76% total yield. Desilylation of crude **59**/**60** mixture by acidic hydrolysis gave desired disaccharides **61** (17%) and **62** (67%). The position of the connection was additionally confirmed by acetylation of **59**/**60** mixture (to give **63**/**64**; 74%



Scheme 5. Reagents and conditions: (*i*) **9**, CH_2Cl_2, molecular sieves, TMSOTf; (*ii*) Ac_2O, Py.

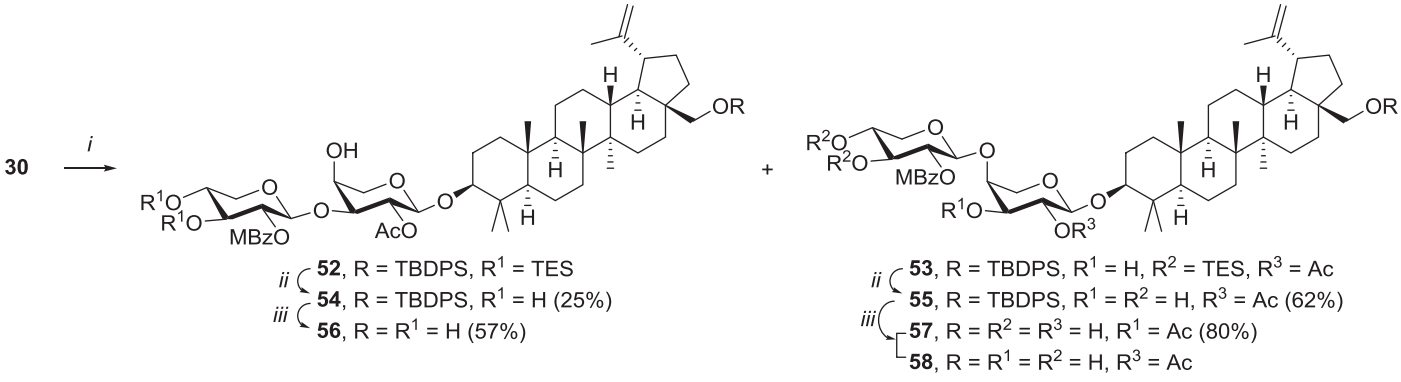


Scheme 6. Reagents and conditions: (*i*) **10**, CH_2Cl_2, molecular sieves, $BF_3.OEt_2$; (*ii*) CSA, MeOH, CH_2Cl_2; (*iii*) Ac_2O, Py; (*iv*) (a) [Ir]; (b) *p*-TsOH.

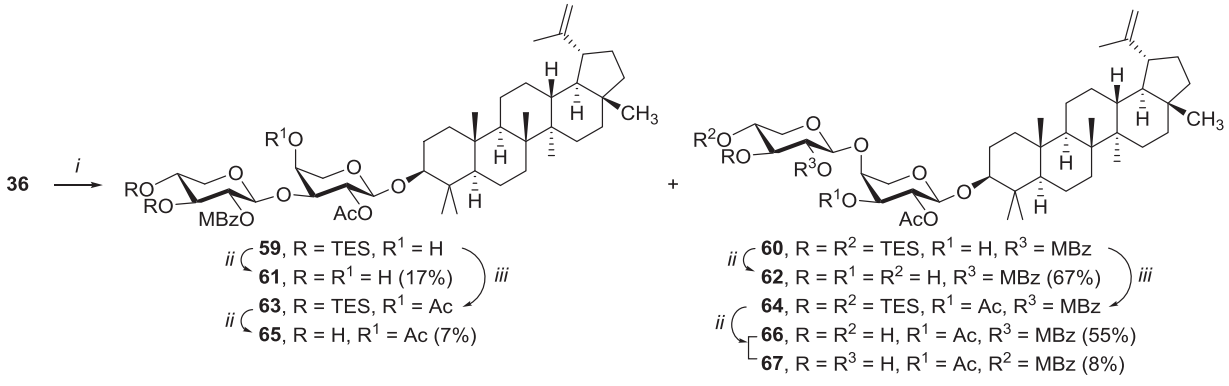
yield) followed by hydrolysis to afford **66** as the main product (55%). Compounds **67** (8%), in which *p*-methoxybenzoyl group migrated to position 4-OH of xylopyranoside ring, and **65** (7%) were isolated as minor components (Scheme 8). It is likely that significant decomposition of **63** in acidic media took place causing lowering of the yield of 1→3-linked disaccharide **65**. The above results show that compounds in which disaccharide is connected to the lupane O-3 position are unstable and easily rearrange or decompose during deprotection even under very mild conditions.

2.3. Saponins bearing stereoisomers of OSW-1 disaccharide unit

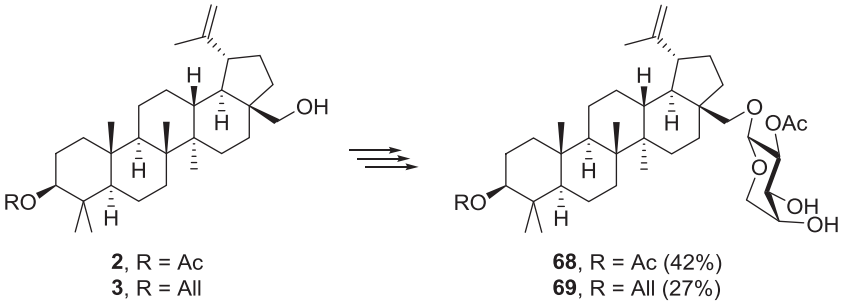
The same methodology was used for preparation of saponins bearing stereoisomers of OSW-1 disaccharide unit. The details of



Scheme 7. Reagents and conditions: (*i*) **10**, CH_2Cl_2, molecular sieves, $BF_3.OEt_2$; (*ii*) CSA, MeOH, CH_2Cl_2; (*iii*) Bu_4NF, AcOH, THF.



Scheme 8. Reagents and conditions: (*i*) **10**, CH_2Cl_2, molecular sieves, $BF_3.OEt_2$; (*ii*) CSA, CH_2Cl_2, methanol; (*iii*) Ac_2O, Py.



Scheme 9. Synthesis of 28-O-(2-O-acetyl-α-D-arabinopyranosyl) betulins.

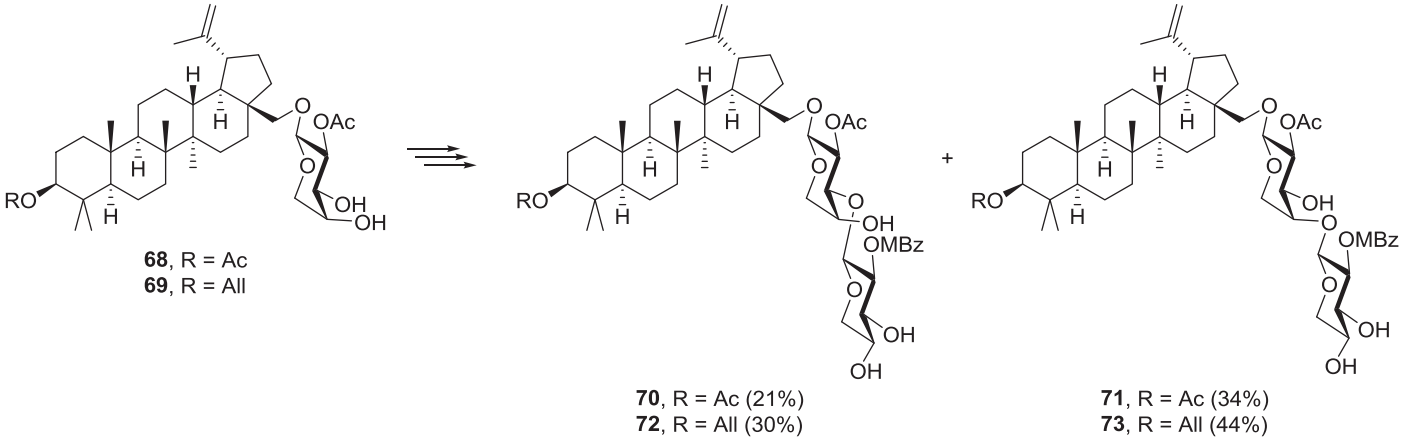
these preparations including analytical data are presented in the *Supplementary material*. Thus, acceptor **68** was prepared from betulin **2** and D-arabinopyranosyl trichloroacetimidate **8**[16] in 42% total yield. Arabinoside **69** was prepared in 27% total yield after 5 steps, from acceptor **3** (Scheme 9).

Corresponding disaccharides consisted of L-xylose and D-arabinose (**70**–**73**) were obtained by glycosylation of **68** or **69** with L-xylose glycosyl donor **11**[12] (Scheme 10). Glycosylation of **68** or **69** with **10** afforded the corresponding disaccharides bearing D-xylose and D-arabinose with slight preference for the 1→3 linked products (**74** and **76**); 1→4 linked disaccharides **75** and **77** were isolated as minor products (Scheme 11). Those having L-xylose and L-arabinose in sugar part (**78** and **79**) were prepared by glycosylation of **20** with donor **11** (Scheme 12).

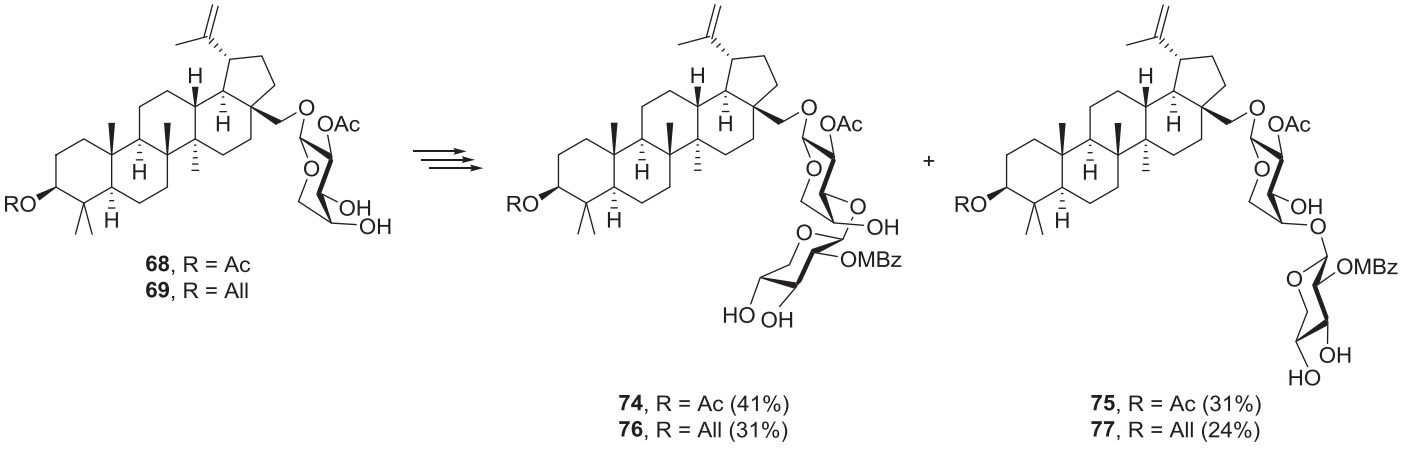
Derivatives **80**–**84** bearing D-arabinopyranoside moiety were prepared by glycosylation of lupeol (**6**) with donor **8** and subsequent manipulation of protecting groups; they were used for NMR studies (Scheme 13).

2.4. Configurational assignments

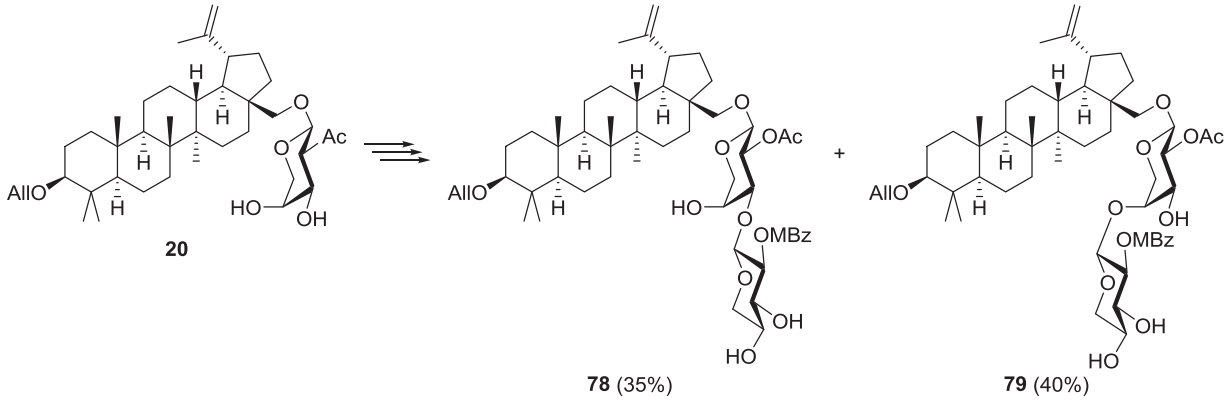
The structures of all new compounds were confirmed by extended 1D and 2D NMR experiments, as well as elemental analysis and HRMS. Structures of **26**–**28** were confirmed by comparison with



Scheme 10. Synthesis of OSW-1 analogues bearing L-xylose and D-arabinose in disaccharide part.



Scheme 11. Synthesis of OSW-1 analogues bearing D-xylose and D-arabinose in disaccharide part.



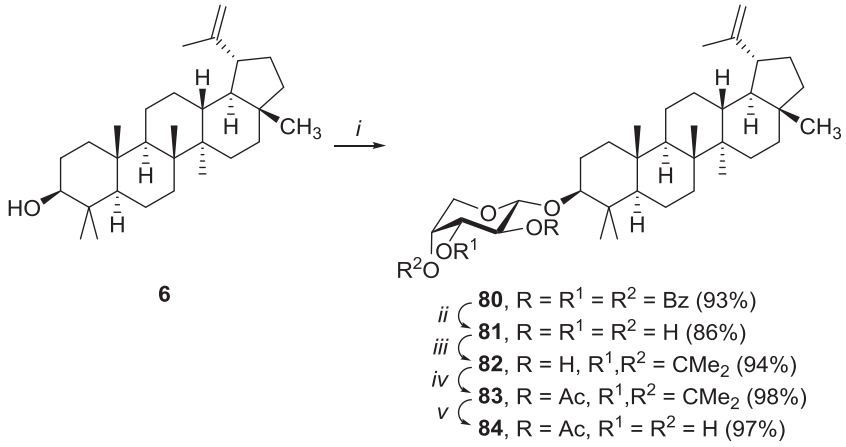
Scheme 12. Synthesis of OSW-1 analogues bearing L-xylose and L-arabinose in disaccharide part.

the literature data. As expected, in all cases studied in this report 1,2-*trans*-glycosides were formed exclusively due to the presence of benzoyl and *p*-methoxybenzoyl protecting groups in the donor molecules, which directed the anomeric selectivity of the glycosidation reaction.[22] These observations were strongly supported by the $^{1}J_{C1\text{-}H1}$ coupling constants.[23] The classification of the glycosylation position within disaccharide moiety was readily confirmed by HMBC analyses that showed the correlation between the ^{1}H signals of H-3 (or H-4) and ^{13}C signals of C-1′. Additionally, the ^{13}C NMR spectra of disaccharides indicated characteristic deshielding effects of the C-3 (or C-4) signals. In some cases, free hydroxyl groups were acetylated and the ^{1}H NMR spectra of acetates **45**, **46**, **65** and **66** showed characteristic "acylation shift"; the H-3 or H-4 resonances (depending on the glycosylation position) of the arabinose residue were deshielded with comparison to the free hydroxyl derivatives. These observations clearly proved the position of the glycosidic linkages.

2.5. Influence of the hydrogen bond on the regioselectivity of glycosylation

It is commonly believed that hydroxyl groups in equatorial positions are more reactive than axially oriented ones in six-membered rings. However, in almost all cases presented above, glycosylation took place preferentially at the axially oriented 4-OH group of arabinopyranoside ring, leading to unexpected 1→4 connected disaccharides. These results are in line with our previous observations that clearly showed that the regioselectivity of the glycosylation of arabinopyranoside 3,4-diols depends on the configuration at the anomeric center of acceptor. Acceptors bearing the axially oriented substituent at the anomeric position provided the expected 1→3 linked regioisomers, whereas in case of equatorially oriented aglycon part, the 1→4 linked regioisomers were obtained as slightly preferred products.[12] Reversed selectivity of some L-arabinopyranoside derivatives was reported in literature[24] and was explained by an influence of a bulky substituent at the O-2 position[25] or inversion of the pyranoside ring, which adopts unusual $^{1}C_4$ conformation.[20,26] Inversion process was confirmed by the NMR data in which low values of $J_{1,2}$ coupling constant were observed. As a result of conformational mobility, the 4-OH group occupies more reactive equatorial position. Ring inversion and its consequences were discussed in the literature; however, the origin of this phenomenon was not defined yet.[20,26a] Such ring-mobility was observed only for the corresponding 3,4-diols; the pyranoside ring returns to the normal $^{4}C_1$ chair conformation after protection or glycosylation.

We suppose that in case of α-L-arabinoside **A** ($^{4}C_1$ conformation) ring inversion to conformer **A′** ($^{1}C_4$ conformation) is strongly supported by the formation of the hydrogen bond between the 3-OH and the anomeric oxygen atom and is additionally strengthened by the anomeric effect. Corresponding coupling constants measured in $CDCl_3$ solution for diols **15**, **30** and **36**—$J_{1,2}$ = 2.0–3.9 Hz and $^{1}J_{C1,H1}$ = 165.5–166.9 Hz—prove the equatorial position of the anomeric hydrogen atom and the preference for conformer **A′**. Similar effect was observed for α-D-arabinopyranoside **B** ($^{1}C_4$), which was



Scheme 13. Reagents and conditions: (*i*) **8**, CH_2Cl_2, molecular sieves, TMSOTf; (*ii*) K_2CO_3, methanol; *(iii)* DMF, dimethoxypropane, *p*-TsOH; (*iv*) Ac_2O, Py; (*v*) *p*-TsOH, methanol, ethyl acetate.

Table 1
Selected $J_{1,2}$ and $^{1}J_{C1,H1}$ coupling constants values for anomeric atoms

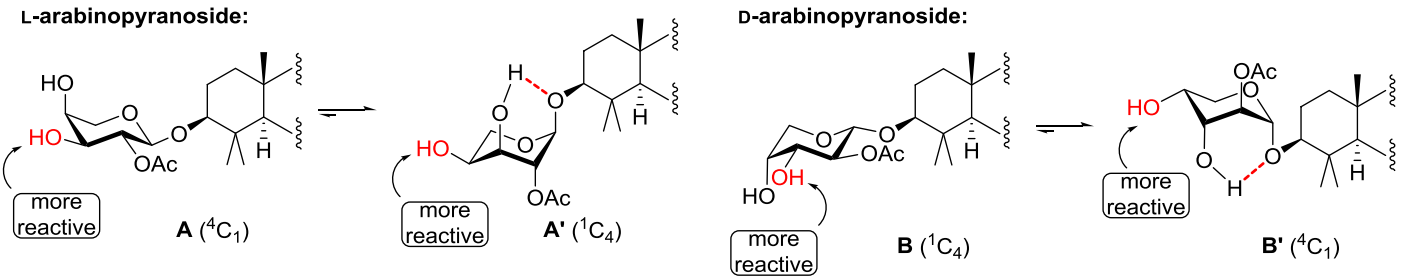
Compound	Solvent	Atom	^{1}H [ppm]	$J_{1,2}$ [Hz]	Atom	^{13}C [ppm]	$^{1}J_{C1-H1}$ [Hz]
Arabinosides:							
12	$CDCl_3$	H-1	4.70	6.2	C-1	101.6	159.9
15	$CDCl_3$	H-1	4.55	3.7	C-1	99.0	166.9
15	CD_3OD	H-1	4.32	7.5	C-1	102.1	160.5
26	$CDCl_3$	H-1	4.77	6.4	C-1	103.0	159.0
30	$CDCl_3$	H-1	4.59	2.0	C-1	100.7	165.5
36	$CDCl_3$	H-1	4.63	3.9	C-1	100.7	166.6
36	CD_3OD:$CDCl_3$ [a]	H-1	4.37	7.5	C-1	103.4	160.7
68	$CDCl_3$	H-1	4.55	3.5	C-1	99.0	166.9
80	$CDCl_3$	H-1	4.84	5.7	C-1	97.6	162.3
84	$CDCl_3$	H-1	4.69	2.1	C-1	94.9	166.9
84	CD_3OD:$CDCl_3$ [a]	H-1	4.40	7.2	C-1	98.4	157.8
(1→3) Connected disaccharides:							
43	$CDCl_3$	H-1	4.23	6.1	C-1	101.1	159.7
		H-1′	4.68	6.7	C-1′	101.8	162.0
45	$CDCl_3$	H-1	4.32	6.4	C-1	101.6	162.2
		H-1′	4.94	4.1	C-1′	99.6	169.4
45	CD_3OD:$CDCl_3$ [b]	H-1	4.26	7.8	C-1	102.3	157.6
		H-1′	4.65	~6.3	C-1′	102.5	161.0
61	$CDCl_3$	H-1	4.26	7.4	C-1	103.3	156.3
		H-1′	4.66	6.7	C-1′	101.8	161.4
65	$CDCl_3$	H-1	4.38	7.1	C-1	103.3	159.0
		H-1′	4.95	3.4	C-1′	99.6	168.0
65	CD_3OD:$CDCl_3$ [b]	H-1	4.34	7.9	C-1	103.5	159.4
		H-1′	4.65	7.5	C-1′	102.4	161.4
(1→4) Connected disaccharides:							
38	$CDCl_3$	H-1	4.34	5.2	C-1	100.6	162.0
		H-1′	4.72	6.8	C-1′	103.2	163.6
40	$CDCl_3$	H-1	4.45	2.4	C-1	98.4	166.2
		H-1′	4.59	7.3	C-1′	101.9	162.1
40	CD_3OD:$CDCl_3$ [b]	H-1	4.37	5.5	C-1	100.3	160.8
		H-1′	4.61	7.4	C-1′	102.9	162.4

[a] 85:15 v/v solution.
[b] 3:1 v/v solution.

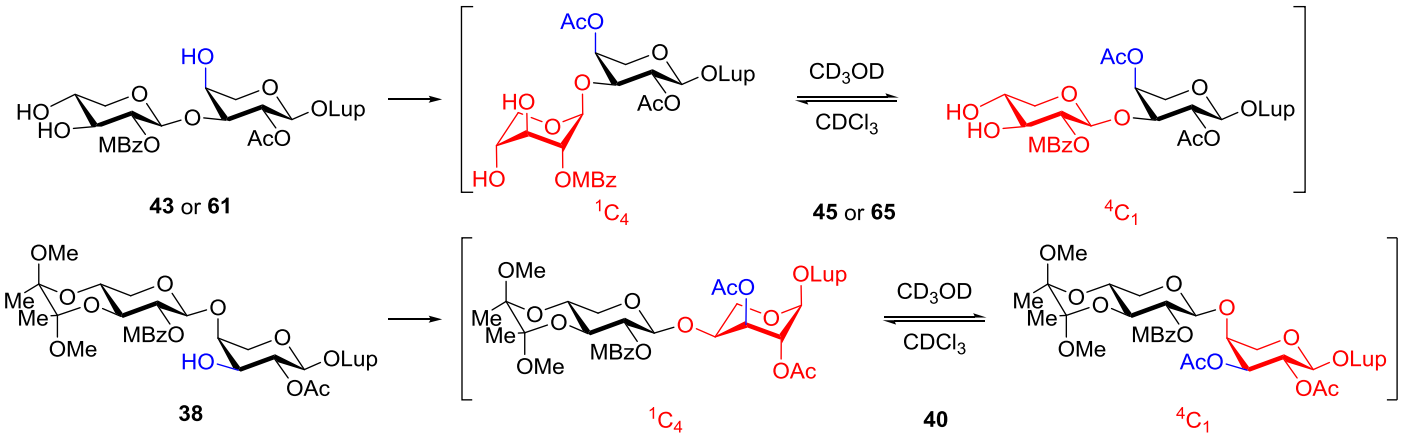
flipping into conformer **B'** ($^{4}C_1$). Ring inversion was confirmed by coupling constants measured in $CDCl_3$ solution for compounds **68** and **84**—$J_{1,2}$ = 2.1–3.5 Hz and $^{1}J_{C1,H1}$ = 166.9 Hz. Ring-flipping was observed only for the corresponding 3,4-diols; for protected derivatives **12**, **26** and **80**, the measured coupling constant values ($J_{1,2}$ = 5.7–6.4 Hz and $^{1}J_{C1,H1}$ = 159.0–162.3 Hz) remain in the expected range for **A** (or **B**) conformer. Addition of methanol, which breaks intramolecular hydrogen bonds, to the solution of **15**, **36** and **84** significantly changed the coupling constant values giving $J_{1,2}$ = 7.2–7.5 Hz and $^{1}J_{C1,H1}$ = 157.8–160.7 Hz. Such values are characteristic for the axially oriented anomeric hydrogen atom and correspond to conformers **A** and **B**. These data clearly confirm the participation of the hydrogen bond in stabilization of preferred conformers **A'** and **B'** in aprotic solvents and return to conformers **A** (or **B**) by breaking the hydrogen bond in the presence of methanol (Table 1, Scheme 14). Recently, we observed the same phenomenon in the case of allyl arabinopyranosides.[12]

It is known that intramolecular hydrogen bonds increase reactivity of hydroxyl group in glycosylation reaction.[27] The above results show that relative position of the hydroxyl group has a much greater impact on reactivity than intramolecular hydrogen bond in which the hydroxyl is involved. As observed, hydroxyl group in equatorial position is still more reactive than hydroxyl group involved in the hydrogen bond as hydrogen donor. Question about the possible role of ring inversion in regioselective glycosylation of the sugar diols remains unanswered. Earlier observations of reversed regioselectivity during glycosylation of some galactopyranoside diols[28] may suggest, however, that the hydrogen bond supported ring inversion plays an important role. This is only the plausible assumption and proposed mechanism should be carefully investigated before its final approval.

An another type of interactions was observed for some 1→3 linked disaccharides. For compounds **43** and **61** having free 4-OH hydroxyl group at the L-arabinopyranoside part, both sugars



Scheme 14. Proposed formation of the hydrogen bond under aprotic conditions.



Scheme 15. Observed ring inversion in disaccharide derivatives (Lup = lupene).

occurred in the expected $^4C_1$ conformation, which was confirmed by the corresponding coupling constants: $J_{1,2}$ = 6.1–7.4 Hz and $^1J_{C1,H1}$ = 156.3–162.0 Hz. Acetylation of the 4-OH hydroxyl group in the L-arabinopyranoside ring caused substantial changes in xyloside ring. Observed coupling constants for D-xylopyranoside part of **45** and **65** reached $J_{1,2}$ = 3.4–4.1 Hz and $^1J_{C1,H1}$ = 168.0–169.4 Hz, which correspond to the theorethically unfavorable $^1C_4$ conformation. Values of the considered coupling constants for L-arabinopyranoside part remained in the same range: $J_{1,2}$ = 6.4–7.1 Hz and $^1J_{C1,H1}$ = 159.0–162.2 Hz. Addition of methanol to the solution of **45** and **65** promoted recovery of the xylopyranoside ring to the expected $^4C_1$ conformation of the xyloside ring. Observed coupling constant values $J_{1,2}$ = 6.3–7.5 Hz and $^1J_{C1,H1}$ = 161.0–161.4 Hz are in accordance with the values expected for sugar ring in the $^4C_1$ conformation. It is likely that the above process is also supported by a formation of any kind of hydrogen bonds (Table 1, Scheme 15).

An interesting ring flipping of the L-arabinose fragment was observed for 1→4 linked BDA protected derivatives **38** and **40**. Whereas both sugar parts in **38** (bearing free OH group at the C-3 position of arabinoside) were in $^4C_1$ conformations, acetylation of the 3-OH position caused flipping of the arabinose ring to $^1C_4$ conformation in **40**. Also in this case, inversion process was reversible and the addition of methanol restored the $^4C_1$ conformation. The origin of the above phenomenon is unknown, but steric factors may play significant role (Table 1, Scheme 15).

2.6. *Results of* in vitro *anticancer activity assays*

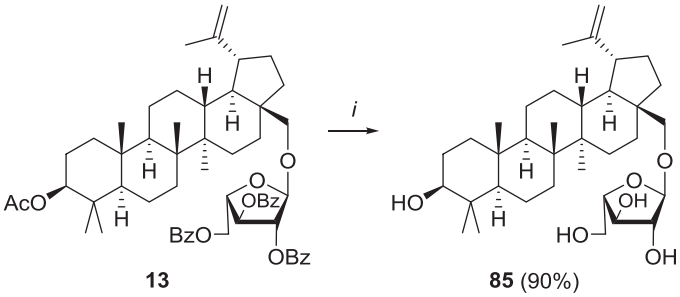
Anticancer activities of the studied lupane saponins with a modified sugar part were tested *in vitro* against normal human BJ fibroblasts and cancer cell lines of various histopathological origins, including T-lymphoblastic leukemia CEM, breast adenocarcinoma MCF7, cervical carcinoma HeLa and malignant melanoma G361 lines. Detailed procedure for the cytotoxicity assay was described previously.[11]

All tested arabinosides were active except fully deprotected furanoside **85** (obtained by treatment of furanoside **13** with KOH in ethanol; Scheme 16). Derivatives of lupeol were moderately cytotoxic, although acetal **34** was highly selective against HeLa and G-361 cell lines (IC_{50} 7.9 and 16.0 μM, respectively). Betulin derivatives were usually highly active. The most cytotoxic was acetal **24** (IC_{50} 1.5–5.5 μM). No significant differences between saponins bearing α-L-Arap (**15**) and α-D-Arap (**68**) were observed. Disaccharides with lupeol as aglycon were inactive. This observation was in accordance with our previously reported suggestions that oxygen atom in the triterpene C-28 position is necessary for cytotoxicity. Betulin derivatives connected to 1→3-linked disaccharides and having triterpene 3-OH group free or protected as acetate were highly active (IC_{50} up to 6.0 μM). Compounds protected as allyl ether were only moderately active (IC_{50} approx. 26.0–45.3 μM), except **78**, which was slightly selective against CEM and HeLa cell lines (IC_{50} 13.6–16.5 μM). No significant differences between 1→3- and 1→4-linked disaccharides were observed. The complete results obtained from Calcein AM assays are presented in the *Supplementary material*.

A striking observation from these data was that on the human BJ fibroblasts, in most cases, new derivatives have similar or higher cytotoxicity in comparison with cancer cell lines. These results suggest that cancer and normal cells respond similarly to certain structure of the lupane saponins. Lupane saponins bearing OSW-1 disaccharide moiety are also less cytotoxic than the natural OSW-1 saponin. As we mentioned in Section 1, disaccharide moiety is necessary for activity of OSW-1 saponin, whereas steroidal part can tolerate some modifications without loss of activity. Our results clearly show, however, that it is also necessary for efficient and strong bonding to the receptors. It is obvious that lupane (pentacyclic triterpene) core is structurally too far from original steroid and does not fit to the receptor harbor.

3. Conclusion

In conclusion, a series of lupane-type saponins bearing regio- and stereoisomers of OSW-1 disaccharide were synthesized and evaluated for their cytotoxic activities toward normal and cancer cell lines. Selected saponins showed interesting cytotoxic activity profiles against human cancer cell lines. Required derivatives were obtained by a glycosylation of suitably protected arabinopyranosides having the 3,4-diol function. Both regioisomers, usually easily



Scheme 16. Reagents and conditions: (*i*) KOH, ethanol.

separated, were prepared, thus opening an easy access to all possible derivatives in which sugar components were 1→3-linked or 1→4-linked. To our best knowledge, migration of acetyl and *p*-methoxybenzoyl groups within OSW-1 disaccharide part was observed for the first time. Unexpected preference for 1→4-linked regioisomers was noted. Plausible mechanism, based on the NMR studies explaining such regioselectivity, was presented. Unusual ring mobility and inversion of the conformation of the sugar rings were detected for some arabinopyranosides and xylopyranosides. We suppose that observed ring inversion may affect the relative reactivity of the hydroxyl groups and, as a result, influence regioselectivity of the glycosylation reaction.

4. Experimental section

4.1. General

Silica gel HF_{254} and Silica gel 230–400 mesh (E. Merck) were used for TLC and column chromatography, respectively. The following mixtures of solvents were used as eluents: **eluent A**: hexane–ethyl acetate, 40:1 → 9:1; **eluent B**: hexane–ethyl acetate, 40:1 → 5:1; **eluent C**: hexane–ethyl acetate, 5:1 then hexane–ethyl acetate–methanol, 5:3:1; **eluent D**: hexane–ethyl acetate, 40:1 → 7:3; **eluent E**: hexane–ethyl acetate, 20:1 → 5:1 then hexane–ethyl acetate–methanol, 5:3:0.5; **eluent F**: hexane–ethyl acetate, 5:1 → 7:3; **eluent G**: hexane–ethyl acetate, 10:1 → 1:1; **eluent H**: hexane–ethyl acetate–methanol, 5:3:1. ^{1}H and ^{13}C NMR spectra were recorded at 298 K with a Varian NMR-vnmrs600 or vnmrs500 spectrometer using standard experimental conditions and Varian software (ChemPack 4.1). Configurational assignments were based on the NMR measurements, generated using two-dimensional techniques like COSY and ^{1}H–^{13}C gradient selected HSQC (*g*-HSQC), as well as ^{1}H–^{13}C gradient selected HMBC (*g*-HMBC) in several cases. Internal TMS was used as the ^{1}H and ^{13}C NMR chemical shift standard. *J* values are given in hertz (Hz). High-resolution mass spectra (HRMS ESI) were acquired with MARINER and MaldiSYNAPT G2-S HDMS (Waters) mass spectrometers. Optical rotations were measured with a JASCO P-2000 automatic polarimeter.

4.2. General method for glycosylation—synthesis of arabinopyranosides

A solution of glycosyl donor (2.10 mmol) and the corresponding triterpene (2.00 mmol) in CH_2Cl_2 (25 mL) was stirred for 20 min at rt over molecular sieves (4 Å, 500 mg, finely ground), then cooled to –40 °C and TMSOTf (100 μL, 0.55 mmol) was added. After 30 min the reaction was quenched with Et_3N (1 mL), and the solvents were evaporated under diminished pressure. Column chromatography of the residue gave the protected arabinopyranoside.

4.2.1. 3β-*O*-Acetyl-28-*O*-(2,3,4-tri-*O*-benzoyl-α-L-arabinopyranosyl) betulin (**12**) *and* 3β-*O*-acetyl-28-*O*-(2,3,5-tri-*O*-benzoyl-α-L-arabinofuranosyl) betulin (**13**)

Eluent B. Arabinofuranoside **13** (7%) was eluted as the first product; the second fraction contained arabinopyranoside **12** (92%).

*Data for **12***. White foam. $[\alpha]_D^{20}$ 103.4 (*c* 0.8, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.31–8.07 (m, 15 H, Ar), 5.73 (dd, 1 H, $J_{2,1}$ 6.2, $J_{2,3}$ 8.6 Hz, H-2), 5.68–5.69 (m, 1 H, H-4), 5.63 (dd, 1 H, $J_{3,2}$ 8.6, $J_{3,4}$ 3.5 Hz, H-3), 4.70 (d, 1 H, $J_{1,2}$ 6.2 Hz, H-1), 4.66–4.67 (m, 2 H, lupane H-29), 4.56 (br s, 1 H, lupane H-29), 4.46 (dd, 1 H, *J* 5.3, 10.8 Hz, lupane H-3), 4.32 (dd, 1 H, $J_{5,4}$ 4.2, $J_{5,5'}$ 12.8 Hz, H-5), 3.91 (dd, 1 H, $J_{5,4}$ 2.1, $J_{5,5'}$ 12.8 Hz, H-5), 3.67 (d, 1 H, *J* 9.0 Hz, lupane H-28), 3.58 (m, 1 H, *J* 9.0 Hz, lupane H-28), 2.33–2.38 (m, 1 H, lupane H-19), 2.04 (s, 3 H, CH_3), 1.95–2.01 (m, 1 H), 1.81–1.83 (m, 1 H), 1.65 (s, 3 H, lupane C-30), 0.91 (s, 3 H, CH_3), 0.86 (s, 3 H, CH_3), 0.84 (s, 6 H, 2 × CH_3), 0.83 (s, 3 H, CH_3), 0.74–1.62 (m, 21 H, lupane protons), 0.62–0.64 (m, 1 H, lupane H-5). ^{13}C NMR (600 MHz, $CDCl_3$) δ: 171.0, 165.7, 165.6, 165.1, 150.4 (lupane C-20), 128.3–133.3 (Ar), 109.6 (lupane C-29), 101.6 (C-1), 80.9 (lupane C-3), 70.5 (C-3), 70.0 (C-2), 68.6 (lupane C-28), 68.4 (C-4), 62.5 (C-5), 55.3, 50.2, 48.7, 47.9, 47.0 (C), 42.5 (C), 40.7 (C), 38.3 (CH_2), 37.8 (C), 37.6, 37.0 (C), 34.8 (CH_2), 33.8 (CH_2), 29.7 (CH_2), 29.2 (CH_2), 27.9, 27.0 (CH_2), 25.0 (CH_2), 23.7 (CH_2), 21.3, 20.8 (CH_2), 19.0, 18.1 (CH_2), 16.5, 16.1, 15.9, 14.7. Anal. Calcd for $C_{58}H_{72}O_{10}$ (929.21): C, 74.97; H, 7.81. Found: C, 74.73; H, 7.83.

*Data for **13***. White foam. $[\alpha]_D^{20}$ 23.1 (*c* 0.3, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.29–8.08 (m, 15 H, Ar), 5.56 (d, 1 H, *J* 4.6 Hz, H-3), 5.54 (s, 1 H, H-2), 5.27 (s, 1 H, H-1), 4.84 (dd, 1 H, $J_{5,4}$ 3.6, $J_{5,5'}$ 11.9 Hz, H-5), 4.66–4.70 (m, 2 H, H-5, lupane 29), 4.58 (br s, 1 H, lupane 29), 4.53–4.55 (m, 1 H, H-4), 4.47 (dd, 1 H, *J* 5.4, 11.0 Hz, lupane H-3), 3.60 (d, 1 H, *J* 9.2 Hz, lupane 28), 3.56 (d, 1 H, *J* 9.2 Hz, lupane 28), 2.43–2.48 (m, 1 H, lupane H-19), 2.06–2.08 (m, 1 H), 2.04 (s, 3 H, CH_3), 1.95–2.01 (m, 1 H), 1.68 (s, 3 H, lupane C-30), 1.01 (s, 3 H, CH_3), 0.97 (s, 3 H, CH_3), 0.84 (s, 3 H, CH_3), 0.84 (s, 3 H, CH_3), 0.83 (s, 3 H, CH_3), 0.77–0.79 (m, 1 H, lupane H-5), 0.86–1.75 (m, 21 H, lupane protons). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 171.0, 166.2, 165.7, 165.4, 150.4 (lupane C-20), 128.3–133.5 (Ar), 109.6 (lupane C-29), 105.9 (C-1), 81.6 (C-2), 81.4 (C-4), 80.9 (lupane C-3), 77.9 (C-3), 65.3 (lupane 28), 63.9 (C-5), 55.3 (lupane C-5), 50.3, 48.7, 47.8, 47.0 (C), 42.7 (C), 40.9 (C), 38.4 (CH_2), 37.8 (C), 37.5, 37.0 (C), 34.8 (CH_2), 34.1 (CH_2), 29.8 (CH_2), 29.7 (CH_2), 27.9, 27.2 (CH_2), 25.2 (CH_2), 23.7 (CH_2), 21.3, 20.8 (CH_2), 19.2, 18.1 (CH_2), 16.5, 16.1, 16.0, 14.7. Anal. Calcd for $C_{58}H_{72}O_{10} \times ½H_2O$ (938.22): C, 74.25; H, 7.84. Found: C, 74.26; H, 7.94.

4.2.2. 3β-*O*-Allyl-28-*O*-(2,3,4-tri-O-benzoyl-α-L-arabinopyranosyl) betulin (**16**)

Eluent A. White foam. Yield 82%. $[\alpha]_D^{20}$ 96.2 (c 0.4, chloroform). ν_{max} (film): 2942, 2869, 1730, 1452, 1281, 1262, 1093, 1069, 1027, 710 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.31–8.07 (m, 15 H, Ar), 5.89–5.96 (m, 1 H, allyl =C*H*), 5.73 (dd, 1 H, $J_{2,1}$ 6.3, $J_{2,3}$ 8.6 Hz, H-2), 5.68–5.69 (m, 1 H, H-4), 5.62 (dd, 1 H, $J_{3,2}$ 8.6, $J_{3,4}$ 3.6 Hz, H-3), 5.24–5.28 (m, 1 H, allyl =CH_2), 5.11–5.13 (m, 1 H, allyl =CH_2), 4.69 (d, 1 H, $J_{1,2}$ 6.3 Hz, H-1), 4.65–4.66 (m, 1 H, lupane H-29), 4.56 (br s, 1 H, lupane H-29), 4.32 (dd, 1 H, $J_{5,4}$ 4.1, $J_{5,5'}$ 12.9 Hz, H-5), 4.10–4.13 (m, 1 H, allyl OCH_2), 3.86–3.92 (m, 2 H, H-5, allyl OCH_2), 3.67 (d, 1 H, *J* 9.0 Hz, lupane H-28), 3.58 (d, 1 H, *J* 9.0 Hz, lupane H-28), 2.78 (dd, 1 H, *J* 4.3, 11.7 Hz, lupane H-3), 2.33–2.38 (m, 1 H, lupane H-19), 1.95–2.01 (m, 2 H), 1.81–1.83 (m, 1 H), 1.68–1.72 (m, 1 H), 1.65 (s, 3 H, CH_3), 0.95 (s, 3 H, CH_3), 0.90 (s, 3 H, CH_3), 0.81 (s, 3 H, CH_3), 0.79 (s, 3 H, CH_3), 0.78–1.67 (m, 22 H, lupane protons), 0.62–0.64 (m, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 165.7, 165.6, 165.1, 150.4 (lupane C-20), 135.9, 128.3–133.4 (Ar), 115.9 (allyl CH_2), 109.6 (lupane C-29), 101.7 (C-1), 86.3 (lupane C-3), 70.6 (CH_2), 70.6, 70.0, 68.7 (CH_2), 68.5, 62.6 (C-5), 55.8, 50.3, 48.7, 47.9, 47.0 (C), 42.5 (C), 40.8 (C), 38.8 (C), 38.6 (CH_2), 37.6, 37.1 (C), 34.8 (CH_2), 33.9 (CH_2), 29.8 (CH_2), 29.2 (CH_2), 28.1, 27.0 (CH_2), 25.1 (CH_2), 23.1 (CH_2), 20.8 (CH_2), 19.0, 18.1 (CH_2), 16.3, 16.1, 15.9, 14.7. Anal. Calcd for $C_{59}H_{74}O_9$ (927.24): C, 76.43; H, 8.04. Found: C, 76.33; H, 8.23.

4.2.3. 28-*O*-Acetyl-3β-*O*-(2,3,4-tri-*O*-benzoyl-α-L-arabinopyranosyl) betulin (**21**) *and* 28-*O*-acetyl-3-β-*O*-(2,3,5-tri-*O*-benzoyl-α-L-arabinofuranosyl) betulin (**22**)

Eluent B. Arabinofuranoside **22** (6%) was eluted as the first product; the second fraction contained arabinopyranoside **21** (87%).

*Data for **21***. Yield 87%. $[\alpha]_D^{20}$ 99.1 (*c* 0.5 chloroform). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.30–8.07 (m, 15 H, Ar), 5.75 (dd, 1H, $J_{2,1}$ 6.3, $J_{2,3}$ 8.7 Hz, H-2), 5.66–5.68 (m, 1 H, H-4), 5.59 (dd, 1 H, $J_{3,2}$ 8.7, $J_{3,4}$ 3.6 Hz, H-3), 4.78 (d, 1 H, $J_{1,2}$ 6.3 Hz, H-1), 4.68–4.69 (m, 1 H, lupane H-29), 4.59 (br s, 1 H, lupane H-29), 4.33 (dd, 1 H, $J_{5,4}$ 4.0, $J_{5,5'}$ 12.9 Hz, H-5), 4.24 (d, 1 H, *J* 11.0 Hz, lupane H-28), 3.84–3.88 (m, 2 H, H-5, lupane H-28), 3.13 (dd, 1 H, *J* 4.7, 11.7 Hz, lupane H-3), 2.41–2.46 (m, 1 H, lupane H-19), 2.06 (s, 3 H, CH_3), 1.92–1.99 (m, 1 H), 1.80–1.86 (m, 2 H), 1.74–1.78 (m, 2 H), 1.68 (s, 3 H, lupane C-30), 1.00 (s,

3 H, CH_3), 0.95 (s, 3 H, CH_3), 0.81 (s, 3 H, CH_3), 0.77 (s, 3 H, CH_3), 0.64 (s, 3 H, CH_3), 0.74–1.67 (m, 18 H, lupane protons), 0.63 (br s, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 171.6, 165.8, 165.6, 165.2, 150.1 (lupane C-20), 128.3–133.3 (Ar), 109.8 (lupane C-29), 103.0 (C-1), 90.1 (lupane C-3), 70.7, 70.2, 68.6, 62.8 (lupane C-28), 62.4 (C-5), 55.5 (lupane C-5), 50.3, 48.8, 47.7, 46.3 (C), 42.6 (C), 40.8 (C), 39.0 (C), 38.7 (CH_2), 37.5, 36.8 (C), 34.5 (CH_2), 34.1 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 27.7, 27.0 (CH_2), 26.1 (CH_2), 25.2 (CH_2), 21.0, 20.8 (CH_2), 19.1, 18.1 (CH_2), 16.0, 16.0, 14.7. Anal. Calcd for $C_{58}H_{72}O_{10}$ (929.21): C, 74.97; H, 7.81. Found: C, 74.96; H, 7.82.

Data for ***22***. Yield 6%; mainly α-anomer. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.30–8.08 (m, 15 H, Ar), 5.57 (d, 1 H, *J* 4.8 Hz, H-3), 5.50 (br s, 1 H, H-2), 5.34 (s, 1 H, H-1), 4.79 (dd, 1 H, $J_{5,4}$ 3.6, $J_{5,5'}$ 11.8 Hz, H-5), 4.68–4.69 (m, 1 H, lupane 29), 4.67 (dd, 1 H, $J_{5,4}$ 5.1, $J_{5,5'}$ 11.8 Hz, H-5), 4.60–4.63 (m, 1 H, H-4), 4.59 (br s, 1 H, lupane 29), 4.25 (d, 1 H, *J* 10.9 Hz, lupane 28), 3.86 (d, 1 H, *J* 10.9 Hz, lupane 28), 3.19 (dd, 1 H, *J* 4.6, 11.7 Hz, lupane H-3), 2.42–2.47 (m, 1 H, lupane H-19), 2.07 (s, 3 H, CH_3), 1.92–2.00 (m, 1 H), 1.83–1.88 (m, 2 H), 1.75–1.79 (m, 1 H), 1.68 (s, 3 H, lupane C-30), 1.03 (s, 3 H, CH_3), 1.02 (s, 3 H, CH_3), 0.97 (s, 3 H, CH_3), 0.86 (s, 3 H, CH_3), 0.85 (s, 3 H, CH_3), 0.77–1.73 (m, 19 H, lupane protons), 0.71–0.73 (m, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 171.6, 166.2, 165.7, 165.5, 150.1 (lupane C-20), 128.3–133.4 (Ar), 109.8 (lupane C-29), 107.5 (C-1), 87.8, 82.2, 80.7, 77.7, 63.9 (CH_2), 62.9 (CH_2), 55.5 (lupane C-5), 50.3, 48.8, 47.7, 46.3 (C), 42.7 (C), 40.9 (C), 39.0 (C), 38.6 (CH_2), 37.6, 36.9 (C), 34.5 (CH_2), 34.2 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 28.0, 27.0 (CH_2), 25.6 (CH_2), 25.2 (CH_2), 21.0, 20.8 (CH_2), 19.1, 18.2 (CH_2), 16.2, 16.1, 16.0, 14.7. Anal. Calcd for $C_{58}H_{72}O_{10}$ (929.21): C, 74.97; H, 7.81. Found: C, 74.95; H, 7.81.

4.2.4. 28-*O*-*tert*-Butyldiphenylsilyl-3β-*O*-(2,3,4-tri-*O*-benzoyl-α-L-arabinopyranosyl) betulin (**26**)

Eluent B. Yield 89%. $[\alpha]_D^{20}$ 77.4 (*c* 0.5 chloroform); lit.:[29] $[\alpha]_D^{20}$ 71.0 (*c* 1.0, chloroform). NMR data of compound **26** match the literature.[29] Anal. Calcd for $C_{72}H_{88}O_9Si$ (1125.58): C, 76.83; H, 7.88. Found: C, 76.66; H, 7.84.

4.2.5. 3β-*O*-(2,3,4-Tri-*O*-benzoyl-α-L-arabinopyranosyl) lupeol (**31**) *and* 3β-*O*-(2,3,5-tri-*O*-benzoyl-α-L-arabinofuranosyl) lupeol (**32**)

Eluent A. Arabinofuranoside **32** (6%) was eluted as the first product; the second fraction contained arabinopyranoside **31** (86%).

Data for ***31***. White foam. $[\alpha]_D^{20}$ 109.7 (*c* 0.5, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.26–8.07 (m, 15 H, Ar), 5.76 (dd, 1 H, $J_{2,1}$ 6.4, $J_{2,3}$ 8.9 Hz, H-2), 5.66–5.68 (m, 1 H, H-4), 5.59 (dd, 1 H, $J_{3,2}$ 8.9, $J_{3,4}$ 3.6 Hz, H-3), 4.78 (d, 1 H, $J_{1,2}$ 6.4 Hz, H-1), 4.68–4.69 (m, 1 H, lupane H-29), 4.56–4.57 (m, 1 H, lupane H-29), 4.33 (dd, 1 H, $J_{5,4}$ 4.0, $J_{5,5'}$ 13.0 Hz, H-5), 3.87 (dd, 1 H, $J_{5,4}$ 2.0, $J_{5,5'}$ 13.0 Hz, H-5), 3.13 (dd, 1 H, *J* 4.8, 11.6 Hz, lupane H-3), 2.34–2.40 (m, 1 H, lupane H-19), 1.88–1.95 (m, 1 H), 1.83–1.86 (m, 1 H), 1.74–1.81 (m, 1 H), 1.68 (s, 3 H, lupane C-30), 1.00 (s, 3 H, CH_3), 0.92 (s, 3 H, CH_3), 0.81 (s, 3 H, CH_3), 0.78 (s, 3 H, CH_3), 0.77 (s, 3 H, CH_3), 0.64 (s, 4 H, lupane H-5, CH_3), 0.79–1.67 (m, 21 H, lupane protons). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 165.8, 165.6, 165.2, 151.0 (lupane C-20), 133.3–128.3 (Ar), 109.3 (lupane C-29), 103.0 (C-1), 90.1 (lupane C-3), 70.7 (C-3), 70.3 (C-2), 68.7 (C-4), 62.6 (C-5), 55.6 (lupane C-5), 50.4, 48.3, 48.0, 43.0 (C), 42.8 (C), 40.8 (C), 40.0 (CH_2), 39.0 (C), 38.7 (CH_2), 38.0, 36.9 (C), 35.6 (CH_2), 34.2 (CH_2), 29.8 (CH_2), 27.7, 27.4 (CH_2), 26.1 (CH_2), 25.1 (CH_2), 20.9 (CH_2), 19.3, 18.1 (CH_2), 18.0, 16.1, 15.9, 14.5. Anal. Calcd for $C_{56}H_{70}O_8$ (871.18): C, 77.21; H, 8.10. Found: C, 77.11; H, 8.28.

Data for ***32***. White foam. $[\alpha]_D^{20}$ 23.4 (*c* 0.3, chloroform). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.31–8.09 (m, 15 H, Ar), 5.58 (d, 1 H, $J_{1,2}$ 4.8 Hz, H-1), 5.51–5.52 (m, 1 H, lupane H-29), 5.36 (br s, 1 H, lupane H-29), 4.81 (dd, 1 H, $J_{5,4}$ 3.6, $J_{5,5'}$ 11.7 Hz, H-5), 4.67–4.70 (m, 2 H, H-5), 4.62–4.64 (m, 1 H), 4.58–4.59 (m, 1 H), 3.21 (dd, 1 H, *J* 4.5, 11.5 Hz, lupane H-3), 2.36–2.42 (m, 1 H, lupane H-19), 1.86–1.97 (m, 2 H), 1.70 (s, 3 H, lupane C-30), 1.05 (s, 3 H, CH_3), 1.03 (s, 3 H, CH_3), 0.96 (s, 3 H, CH_3), 0.87 (s, 6 H, 2 × CH_3), 0.80 (s, 3 H, CH_3), 0.73–0.75 (m, 1 H, lupane H-5), 0.89–1.78 (m, 21 H, lupane protons). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 166.2, 165.7, 165.5, 151.0 (lupane C-20), 128.3–133.4 (Ar), 109.3 (lupane C-29), 107.5 (C-1), 87.8 (lupane C-3), 82.2, 80.7, 77.7, 64.0 (C-5), 55.5 (lupane C-5), 50.4, 48.3, 48.0, 43.0 (C), 42.8 (C), 40.9 (C), 40.0 (CH_2), 39.0 (C), 38.6 (CH_2), 38.0, 36.9 (C), 35.6 (CH_2), 34.3 (CH_2), 29.8 (CH_2), 28.1, 27.4 (CH_2), 25.6 (CH_2), 25.1 (CH_2), 20.9 (CH_2), 19.3, 18.3 (CH_2), 18.0, 16.2, 16.2, 16.0, 14.5. Anal. Calcd for $C_{56}H_{70}O_8 \times H_2O$ (889.18): C, 75.64; H, 8.16. Found: C, 75.28; H, 7.97. HR-MS (ESI) calc. for $C_{56}H_{70}NaO_8$ $[M + Na]^+$: 893.4968. Found: 893.4960.

4.2.6. 3β-*O*-(2,3,4-Tri-*O*-benzoyl-α-D-arabinopyranosyl) lupeol (**80**)

Eluent A. White foam. Yield 93%. $[\alpha]_D^{20}$ –60.6 (*c* 0.3, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.32–8.06 (m, 15 H, Ar), 5.67–5.69 (m, 1 H, H-4), 5.65 (dd 1 H, $J_{2,1}$ 5.7, $J_{2,3}$ 8.2 Hz, H-2), 5.59 (dd, 1 H, $J_{3,2}$ 8.2, $J_{3,4}$ 3.6 Hz, H-3), 4.84 (d, 1 H, $J_{1,2}$ 5.7 Hz, H-1), 4.68–4.69 (m, 1 H, lupane H-29), 4.56 (br s, 1 H, lupane H-29), 4.34 (dd, 1 H, $J_{5,4}$ 4.6, $J_{5,5'}$ 12.7 Hz, H-5), 3.86 (dd, 1 H, $J_{5,4}$ 2.4, $J_{5,5'}$ 12.7 Hz, H-5), 3.28 (dd, 1 H, *J* 4.4, 11.9 Hz, lupane H-3), 2.34–2.39 (m, 1H, lupane H-19), 1.88–1.95 (m, 1 H), 1.68 (s, 3 H, CH_3), 1.04 (s, 3 H, CH_3), 1.00 (s, 3 H, CH_3), 0.92 (s, 3 H, CH_3), 0.77 (s, 3 H, CH_3), 0.72 (s, 3 H, CH_3), 0.67 (s, 3 H, CH_3), 0.67–1.67 (m, 23 H, lupane protons). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 165.8, 165.6, 165.2, 151.0 (lupane C-20), 128.3–133.3 (Ar), 109.3 (lupane C-29), 97.6 (C-1), 84.7 (lupane C-3), 70.6, 70.4, 68.4, 62.0 (C-5), 55.8, 50.4, 48.3, 48.0, 43.0 (C), 42.8 (C), 40.9 (C), 40.0 (CH_2), 38.4 (CH_2), 38.3, 38.0, 37.0 (C), 35.6 (CH_2), 34.3 (CH_2), 29.8 (CH_2), 28.1, 27.4 (CH_2), 26.1 (CH_2), 22.6 (CH_2), 20.9 (CH_2), 19.3, 18.3 (CH_2), 18.0, 16.0, 15.9, 14.5. Anal. Calcd for $C_{56}H_{70}O_8 \times 1½\ H_2O$ (898.18): C, 74.88; H, 8.19. Found: C, 74.68; H, 8.29.

4.3. General procedure for debenzoylation of lupenyl arabinosides

A suspension of protected saponin (1.50 mmol) and K_2CO_3 (50 mg) in MeOH (40 mL) was stirred for 1 h, then neutralized with Amberlyst 15 resin (H^+ form), filtered through a PTFE syringe filter, and concentrated. The residue was purified by column chromatography to afford the title compound.

4.3.1. 3β-*O*-Allyl-28-*O*-α-L-arabinopyranosyl betulin (**17**)

Eluent E. Yield 98%, amorphous powder. $[\alpha]_D^{20}$ 7.7 (c 0.4, chloroform). ν_{max} (film): 3414, 2942, 2869, 1454, 1137, 1087, 1070, 999, 757 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.88–5.97 (m, 1 H, allyl =*CH*), 5.24–5.28 (m, 1 H, allyl =*CH*$_2$), 5.11–5.13 (m, 1 H, allyl =*CH*$_2$), 4.67 (br s, 1 H, lupane H-29), 4.58 (s, 1 H, lupane H-29), 4.27 (d, 1 H, $J_{1,2}$ 5.5 Hz, H-1), 4.10–4.14 (m, 1 H, allyl O*CH*$_2$), 3.93–3.95 (m, 1 H, H-4), 3.86–3.92 (m, 2 H), 3.72–3.77 (m, 2 H), 3.64 (d, 1 H, *J* 9.4 Hz, lupane H-28), 3.59 (dd, 1 H, $J_{5,4}$ 2.2, $J_{5,5'}$ 12.4 Hz, H-5), 3.53 (d, 1 H, *J* 9.4 Hz, lupane H-28), 2.80 (dd, 1 H, *J* 4.1, 11.7 Hz, lupane H-3), 2.36–2.44 (m, 1 H, lupane H-19), 1.86–2.00 (m, 3 H), 1.68 (s, 3 H, CH_3), 1.02 (s, 3 H, CH_3), 0.97 (s, 3 H, CH_3), 0.96 (s, 3 H, CH_3), 0.83 (s, 3 H, CH_3), 0.78 (s, 3 H, CH_3), 0.79–1.73 (m, 23 H, lupane protons), 0.67–0.69 (m, 1 H, lupane H-5). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 150.3 (lupane C-20), 135.9, 115.9 (CH_2), 109.7 (lupane C-29), 102.9 (C-1), 86.2 (lupane C-3), 72.3, 71.4, 70.6 (CH_2), 68.0 (CH_2), 67.0, 64.3 (C-5), 55.8 (lupane C-5), 50.3, 48.8, 47.7, 47.0 (C), 42.7 (C), 40.9 (C), 38.8 (C), 38.6 (CH_2), 37.6, 37.1 (C), 34.8 (CH_2), 34.2 (CH_2), 29.7 (CH_2), 29.7 (CH_2), 28.1, 27.1 (CH_2), 25.2 (CH_2), 23.1 (CH_2), 20.8 (CH_2), 19.1, 18.2 (CH_2), 16.3, 16.1, 16.1, 14.7. Anal. Calcd for $C_{38}H_{62}O_6 \times ½\ H_2O$ (623.92): C, 73.15; H, 10.18. Found: C, 72.94; H, 10.22.

4.3.2. 28-*O*-*tert*-Butyldiphenylsilyl-3β-*O*-α-L-arabinopyranosyl betulin (**27**)

Eluent C. Yield 98%, amorphous powder. $[\alpha]_D^{20}$ –12.9 (*c* 0.3, chloroform); lit.:[20] $[\alpha]_D^{20}$ –10.2 (*c* 0.5, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.34–7.70 (m, 10 H, Ar), 4.59–4.60 (m, 1 H, lupane H-29),

4.53 (br s, 1 H, lupane H-29), 4.39 (d, 1 H, $J_{1,2}$ 5.6 Hz, H-1), 3.88–3.91 (m, 2 H), 3.75–3.78 (m, 1 H), 3.71–3.72 (m, 1 H), 3.68 (d, 1 H, *J* 9.9 Hz, lupane H-28), 3.56 (dd, 1 H, $J_{5,4}$ 1.9, $J_{5,5'}$ 11.9 Hz, H-5), 3.32 (d, 1 H, *J* 9.9 Hz, lupane H-28), 3.11 (dd, 1 H, *J* 4.5, 11.7 Hz, lupane H-3), 2.24–2.28 (m, 1 H, lupane H-19), 2.11–2.14 (m, 2 H), 1.80–1.85 (m, 2 H), 1.65 (s, 3 H, CH_3), 1.06 (s, 9 H, *t*Bu), 0.96 (s, 3 H, CH_3), 0.92 (s, 3 H, CH_3), 0.79 (s, 3 H, CH_3), 0.77 (s, 3 H, CH_3), 0.70 (s, 3 H, CH_3), 0.82–1.70 (m, 22 H, lupane protons), 0.66–0.67 (m, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 150.8 (lupane C-20), 127.6–135.7 (Ar), 109.4 (lupane C-29), 104.2 (C-1), 89.9 (lupane C-3), 72.2, 71.6, 66.8, 63.8 (CH_2), 61.0 (CH_2), 55.5, 50.3, 48.4, 48.4 (C), 47.8, 42.6 (C), 40.8 (C), 39.1 (C), 38.6 (CH_2), 37.2, 36.8 (C), 34.5 (CH_2), 34.1 (CH_2), 29.8 (CH_2), 29.5 (CH_2), 28.1, 27.0 (CH_2), 26.9 (*t*Bu), 25.9 (CH_2), 25.1 (CH_2), 20.7 (CH_2), 19.4, 19.1 (C), 18.2 (CH_2), 16.4, 16.0, 15.7, 14.6, 14.2 (C). Anal. Calcd for $C_{51}H_{76}O_6Si \times ½H_2O$ (822.26): C, 74.50; H, 9.44. Found: C, 74.35; H, 9.44.

4.3.3. 3β-*O*-(α-L-Arabinopyranosyl) lupeol (**33**)

Eluent C. Yield 96%, amorphous powder. $[\alpha]_D^{20}$ 9.3 (*c* 0.5, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 4.67–4.68 (m, 1 H, lupane H-29), 4.55–4.56 (m, 1 H, lupane H-29), 4.37 (d, 1 H, $J_{1,2}$ 5.9 Hz, H-1), 3.87–3.92 (m, 2 H, H-4, lupane H-3), 3.75 (dd, 1 H, $J_{2,1}$ 5.9, $J_{2,3}$ 7.5 Hz, H-2), 3.69 (dd, 1 H, $J_{3,2}$ 7.5, $J_{3,4}$ 3.0 Hz, H-3), 3.53 (dd, 1 H, $J_{5,4}$ 1.8, $J_{5,5'}$ 11.7 Hz, H-5), 3.11 (dd, 1 H, $J_{5,4}$ 4.5, $J_{5,5'}$ 11.7 Hz, H-5), 2.33–2.39 (m, 1 H, lupane H-19), 1.87–1.94 (m, 1 H), 1.79–1.84 (m, 1 H), 1.67 (s, 3 H, CH_3), 1.01 (s, 3 H, CH_3), 0.95 (s, 3 H, CH_3), 0.92 (s, 3 H, CH_3), 0.82 (s, 3 H, CH_3), 0.78 (s, 3 H, CH_3), 0.77 (s, 3 H, CH_3), 0.76–1.71 (m, 24 H, lupane protons), 0.67–0.69 (m, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 150.9 (lupane C-20), 109.3 (lupane C-29), 104.3 (C-1), 89.9 (lupane C-3), 72.3, 71.6, 66.9, 64.0 (C-5), 55.5, 50.4, 48.3, 47.9, 43.0 (C), 42.8 (C), 40.8 (C), 40.0 (CH_2), 39.1 (C), 38.7 (CH_2), 38.0, 36.9 (C), 35.6 (CH_2), 34.2 (CH_2), 29.8 (CH_2), 28.1, 27.4 (CH_2), 25.9 (CH_2), 25.1 (CH_2), 20.9 (CH_2), 19.3, 18.2 (CH_2), 18.0, 16.4, 16.1, 16.0, 14.5. Anal. Calcd for $C_{35}H_{58}O_5$ (558.85): C, 75.22; H, 10.46. Found: C, 75.12; H, 10.35.

4.3.4. 3β-*O*-(α-D-Arabinopyranosyl) lupeol (**81**)

Eluent C. Yield 86%, amorphous powder. $[\alpha]_D^{20}$ 47.5 (*c* 0.3, chloroform); lit.:[16] $[\alpha]_D^{20}$ 26.8 (*c* 1.25, chloroform). NMR spectral data of **81** were in agreement with those published in the literature.[16]

4.4. Synthesis of isopropylidene derivatives—general method

To a solution of deprotected arabinopyranoside (1.00 mmol) in DMF (15 mL), 2,2-dimethoxypropane (5 mL) and *p*-TsOH (80 mg) were added. A solution was stirred for 3 h, then neutralized with triethylamine (1 mL) and concentrated. The residue was purified by column chromatography to afford the title compound.

4.4.1. 3β-*O*-Allyl-28-*O*-(3,4-*O*-isopropylidene-α-L-arabinopyranosyl) betulin (**18**)

Eluent A. Yield 95%, amorphous powder. $[\alpha]_D^{20}$ 23.7 (c 0.4, chloroform). ν_{max} (film): 3466, 2942, 2870, 1455, 1374, 1218, 1123, 1086, 1070, 1042, 757 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$):δ: 5.89–5.97 (m, 1 H, allyl =C*H*), 5.24–5.28 (m, 1 H, allyl =CH_2), 5.11–5.13 (m, 1 H, allyl =CH_2), 4.66–4.67 (m, 1 H, lupane H-29), 4.57 (br s, 1 H, lupane H-29), 4.18–4.24 (m, 2 H), 4.07–4.14 (m, 3 H), 3.86–3.90 (m, 1 H, allyl OCH_2), 3.79 (dd, 1 H, $J_{5,4}$ 3.2, $J_{5,5'}$ 13.2 Hz, H-5), 3.61–3.64 (m, 2 H), 3.51 (d, 1 H, *J* 9.2 Hz, lupane H-28), 2.80 (dd, 1 H, *J* 4.1, 11.7 Hz, lupane H-3), 2.37–2.43 (m, 1 H, lupane H-19), 1.92–2.00 (m, 3 H), 1.67 (s, 3 H, CH_3), 1.55 (s, 3 H, CH_3), 1.37 (s, 3 H, CH_3), 1.01 (s, 3 H, CH_3), 0.97 (s, 3 H, CH_3), 0.96 (s, 3 H, CH_3), 0.83 (s, 3 H, CH_3), 0.78 (s, 3 H, CH_3), 0.79–1.73 (m, 21 H, lupane protons), 0.67–0.68 (m, 1 H, lupane C-5). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 150.5 (lupane C-20), 135.9, 115.9 (CH_2), 110.1 (C), 109.6 (lupane C-29), 102.7 (C-1), 86.3 (lupane C-3), 78.0, 73.8, 73.1, 70.6 (CH_2), 67.6 (CH_2), 63.1 (CH_2), 55.8, 50.4, 48.8, 47.8, 47.1 (C), 42.7 (C), 40.9 (C), 38.8 (C), 38.6 (CH_2), 37.6, 37.1, 34.7 (CH_2), 34.2 (CH_2), 29.7 (CH_2), 28.1, 28.0, 27.1 (CH_2), 26.0, 25.2 (CH_2), 23.1 (CH_2), 20.8 (CH_2), 19.1, 18.2 (CH_2), 16.3, 16.1, 16.1, 14.8. Anal. Calcd for $C_{41}H_{66}O_6 \times ½ H_2O$ (663.99): C, 74.17; H, 10.17. Found: C, 74.08; H, 10.11.

4.4.2. 28-*O*-*tert*-Butyldiphenylsilyl-3β-*O*-(3,4-*O*-isopropylidene-α-L-arabinopyranosyl) betulin (**28**)

Eluent D. Yield 96%, amorphous powder. $[\alpha]_D^{20}$ 3.1 (*c* 0.3, chloroform); lit.:[20] $[\alpha]_D^{20}$ 1.7 (*c* 1.0, chloroform). NMR data of compound **28** match the literature.[20] Anal. Calcd for $C_{54}H_{80}O_6Si$ (853.32): C, 76.01; H, 9.45. Found: C, 75.77; H, 9.45.

4.4.3. 3β-*O*-(3,4-*O*-Isopropylidene-α-L-arabinopyranosyl) lupeol (**34**)

Eluent D. Yield 95%, amorphous powder. $[\alpha]_D^{20}$ 31.0 (*c* 0.5, chloroform). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 4.68–4.69 (m, 1 H, lupane H-29), 4.56–4.57 (m, 1 H, lupane H-29), 4.17–4.22 (m, 3 H), 4.06 (dd, 1 H, *J* 5.7, 7.6 Hz), 3.74–3.77 (m, 1 H), 3.63 (t, 1 H, *J* 7.7 Hz), 3.10 (dd, 1 H, *J* 4.7, 11.5 Hz), 2.35–2.40 (m, 1 H, lupane H-19), 1.88–1.96 (m, 1 H), 1.77–1.83 (m, 1 H), 1.68 (s, 3 H, CH_3), 1.54 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3), 1.02 (s, 3 H, CH_3), 0.97 (s, 3 H, CH_3), 0.93 (s, 3 H, CH_3), 0.84 (s, 3 H, CH_3), 0.81 (s, 3 H, CH_3), 0.79 (s, 3 H, CH_3), 0.85–1.67 (m, 22 H, lupane protons), 0.68–0.70 (m, 1 H, lupane H-5). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 150.9 (lupane C-20), 110.0, 109.3 (lupane C-29), 104.3 (C-1), 89.0 (lupane C-3), 78.1, 74.3, 73.2, 63.1 (C-5), 55.6, 50.4, 48.3, 48.0, 43.0 (C), 42.8 (C), 40.8 (C), 40.0 (CH_2), 39.1 (C), 38.7 (CH_2), 38.0, 36.9 (C), 35.6 (CH_2), 34.3 (CH_2), 29.8 (CH_2), 28.2, 28.0, 27.4 (CH_2), 26.1 (CH_2), 26.1, 25.1 (CH_2), 20.9 (CH_2), 19.3, 18.2 (CH_2), 18.0, 16.5, 16.1, 16.0, 14.5. Anal. Calcd for $C_{38}H_{62}O_5$ (598.91): C, 76.21; H, 10.43. Found: C, 76.54; H, 10.68.

4.4.4. 3β-*O*-(3,4-*O*-Isopropylidene-α-D-arabinopyranosyl) lupeol (**82**)

Eluent D. Yield 94%, amorphous powder. $[\alpha]_D^{20}$ 24.3 (*c* 0.2, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 4.68–4.69 (m, 1 H, lupane H-29), 4.56–4.57 (m, 1 H, lupane H-29), 4.21–4.23 (m, 2 H, H-1, H-4), 4.17 (dd, 1 H, $J_{5,4}$ 2.7, $J_{5,5'}$ 13.3 Hz, H-5), 4.07 (dd, 1 H, $J_{3,4}$ 6.0, $J_{3,2}$ 7.7 Hz, H-3), 3.75 (dd, 1 H, $J_{5,4}$ 3.4, $J_{5,5'}$ 13.3 Hz, H-5), 3.57 (t, 1 H, *J* 7.7 Hz, H-2), 3.23 (dd, 1 H, *J* 4.3, 11.9 Hz, lupane H-3), 2.35–2.40 (m, 1 H, lupane H-19), 1.88–1.95 (m, 2 H), 1.68 (s, 3 H, CH_3), 1.55 (s, 3 H, CH_3), 1.37 (s, 3 H, CH_3), 1.03 (s, 3 H, CH_3), 0.99 (s, 3 H, CH_3), 0.92 (s, 3 H, CH_3), 0.84 (s, 3 H, CH_3), 0.79 (s, 3 H, CH_3), 0.77 (s, 3 H, CH_3), 0.81–1.70 (m, 22 H, lupane protons), 0.69–0.70 (m, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 151.0 (lupane C-20), 110.1 (C), 109.3 (lupane C-29), 99.1 (C-1), 83.9 (lupane C-3), 78.1, 73.7, 73.2, 63.2 (C-5), 55.9, 50.4, 48.3, 47.9, 43.0 (C), 42.8 (C), 40.9 (C), 40.0 (CH_2), 38.4 (CH_2), 38.2 (C), 38.0, 37.0 (C), 35.6 (CH_2), 34.3 (CH_2), 29.8 (CH_2), 28.0, 27.4 (CH_2), 26.0, 25.1 (CH_2), 23.1 (CH_2), 20.9 (CH_2), 19.3, 18.3 (CH_2), 18.0, 16.3, 16.1, 16.0, 14.4. HRMS (ESI) calc. for $C_{38}H_{62}NaO_5$ $[M + Na]^+$: 621.4495. Found: 621.4501. Anal. Calcd for $C_{38}H_{62}O_5 \times ½ H_2O$ (607.92): C, 75.08; H, 10.45. Found: C, 75.45; H, 10.03.

4.5. Acetylation—general method

A solution of saponin (0.80 mmol) in pyridine (5 mL) and acetic anhydride (2 mL) was stirred for 3 h. Solvents were coevaporated with toluene twice and the residue was purified by column chromatography to afford the title compound.

4.5.1. 3β-*O*-Acetyl-28-*O*-(2-*O*-acetyl-3,4-*O*-isopropylidene-α-L-arabinopyranosyl) betulin (**14**)

Arabinoside **12** was debenzoylated using the procedure **4.3**. Crude product (a mixture of 3β-O-acetyl-28-O-α-L-arabinopyranosyl betulin and 3β-28-O-α-L-arabinopyranosyl betulin) was protected as 3,4-O-isopropylidene derivative using the procedure **4.4** and then

acetylated as described above. Column chromatography (eluent B) gave the title compound as amorphous powder. Yield 88% after 3 steps. $[\alpha]_D^{20}$ 18.8 (*c* 0.5, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 5.03 (t, 1 H, $J_{2,1} = J_{2,3} = 6.6$ Hz, H-2), 4.65–4.66 (m, 1 H, lupane H-29), 4.56 (br s, 1 H, lupane H-29), 4.47 (dd, 1 H, *J* 5.2, 11.1 Hz, lupane H-3), 4.32 (d, 1 H, $J_{1,2}$ 6.6 Hz, H-1), 4.25–4.27 (m, 1 H, H-4), 4.16 (dd, 1 H, $J_{3,2}$ 6.6, $J_{3,4}$ 5.8 Hz, H-3), 4.11 (dd, 1 H, $J_{5,4}$ 4.1, $J_{5,5'}$ 13.0 Hz, H-5), 3.77 (dd, 1 H, $J_{5,4}$ 4.0, $J_{5,5'}$ 13.0 Hz, H-5), 3.57 (d, 1 H, *J* 9.1 Hz, lupane H-28), 3.42 (m, 1 H, *J* 9.1 Hz, lupane H-28), 2.36–2.40 (m, 1 H, lupane H-19), 2.08 (s, 3 H, CH_3), 2.04 (s, 3 H, CH_3), 1.87–1.98 (m, 3 H), 1.67 (s, 3 H, CH_3), 1.56 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3), 1.02 (s, 3 H, CH_3), 0.96 (s, 3 H, CH_3), 0.85 (s, 6 H, 2 × CH_3), 0.84 (s, 3 H, CH_3), 0.86–1.64 (m, 20 H, lupane protons), 0.78–0.80 (m, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 170.9, 169.4, 150.5 (lupane C-20), 110.3, 109.6 (lupane C-29), 100.6 (C-1), 80.9 (lupane C-3), 75.9, 72.5, 72.3, 67.7 (CH_2), 62.0 (CH_2), 55.3, 50.2, 48.6, 47.9, 47.0 (C), 42.7 (C), 40.9 (C), 38.3 (CH_2), 37.8 (C), 37.6, 37.0 (C), 34.7 (CH_2), 34.1 (CH_2), 29.7 (CH_2), 29.5 (CH_2), 27.9, 27.7, 27.1 (CH_2), 26.1, 25.1 (CH_2), 23.7 (CH_2), 21.3, 20.9, 20.8 (CH_2), 19.0, 18.1 (CH_2), 16.5, 16.1, 16.0, 14.8. Anal. Calcd for $C_{42}H_{66}O_8$ (698.99): C, 72.17; H, 9.52. Found: C, 72.29; H, 9.52.

4.5.2. 3β-*O*-Allyl-28-*O*-(2-*O*-acetyl-3,4-*O*-isopropylidene-α-L-arabinopyranosyl) betulin (**19**)

Eluent A. Yield 92%, amorphous powder. $[\alpha]_D^{20}$ 19.2 (c 0.3, chloroform). ν_{max} (film): 2942, 2870, 1755, 1372, 1221, 1124, 1090, 1055, 758 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.88–5.98 (m, 1 H, allyl =C*H*), 5.24–5.28 (m, 1 H, allyl =CH_2), 5.11–5.13 (m, 1 H, allyl =CH_2), 5.03 (t, 1 H, $J_{2,1} = J_{2,3} = 6.6$ Hz, H-2), 4.66 (br s, 1 H, lupane H-29), 4.56 (br s, 1 H, lupane H-29), 4.31 (d, 1 H, $J_{1,2}$ 6.6 Hz, H-1), 4.24–4.27 (m, 1 H), 4.15–4.17 (m, 1 H), 4.10–4.14 (m, 2 H), 3.86–3.90 (m, 1 H, OCH_2), 3.77 (dd, 1 H, $J_{5,4}$ 3.9, $J_{5,5'}$ 13.0 Hz, H-5), 3.57 (d, 1 H, *J* 9.2 Hz, lupane H-28), 3.42 (d, 1 H, *J* 9.2 Hz, lupane H-28), 2.80 (dd, 1 H, *J* 4.1, 11.7 Hz, lupane H-3), 2.35–4.40 (m, 1 H, lupane H-19), 2.07 (s, 3 H, CH_3), 1.86–1.98 (m, 3 H), 1.66 (s, 3 H, CH_3), 1.56 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3), 1.02 (s, 3 H, CH_3), 0.96 (s, 3 H, CH_3), 0.96 (s, 3 H, CH_3), 0.83 (s, 3 H, CH_3), 0.78 (s, 3 H, CH_3), 0.79–1.73 (m, 20 H, lupane protons), 0.67–0.69 (m, 1 H, lupane C-5). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 169.4, 150.6 (lupane C-20), 135.9, 115.9 (CH_2), 110.3 (C), 109.5 (lupane C-29), 100.6 (C-1), 86.3 (lupane C-3), 75.9, 72.5, 72.4, 70.6 (CH_2), 67.8 (CH_2), 62.1 (CH_2), 55.8 (lupane C-5), 50.4, 48.7, 47.9, 47.0 (C), 42.7 (C), 40.9 (C), 38.8 (C), 38.6 (CH_2), 37.6, 37.1 (C), 34.7 (CH_2), 34.2 (CH_2), 29.7 (CH_2), 29.5 (CH_2), 28.1, 27.8, 27.1 (CH_2), 26.2, 25.2 (CH_2), 23.1 (CH_2), 20.9, 20.8 (CH_2), 19.1, 18.2 (CH_2), 16.3, 16.1, 16.1, 14.8. Anal. Calcd for $C_{43}H_{68}O_7$ (697.02): C, 74.10; H, 9.83.Found: C, 74.17; H, 9.71.

4.5.3. 28-*O*-Acetyl-3β-*O*-(2-*O*-acetyl-3,4-*O*-isopropylidene-α-L-arabinopyranosyl) betulin (**23**) *and* 3β-*O*-(2-*O*-acetyl-3,4-*O*-isopropylidene-α-L-arabinopyranosyl) betulin (**24**)

Arabinoside **21** was transformed into the title compounds using procedure described for **14** (*Method A*). Column chromatography (eluent B) gave **23** (20–53%) and **24** (10–41%) as amorphous powders in variable proportion depending on batch.

Synthesis of **24**—*Method B*. To a solution of **29** (100 mg, 0.11 mmol) in THF (3 mL), tetrabutylammonium fluoride (1 M in THF, 1.00 mL, 1.00 mmol) was added followed by acetic acid (57 μL, 1.00 mmol) and the mixture was stirred in a sealed tube at 60 °C for 24 h. The mixture was then concentrated and the residue was purified by column chromatography (eluent F) to give the title compound (67 mg, 92%) as a foam.

*Data for **23***. $[\alpha]_D^{20}$ 24.8 (*c* 0.2, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 5.05 (t, 1 H, $J_{2,1} = J_{2,3} = 7.3$ Hz, H-2), 4.68–4.69 (m, 1 H, lupane H-29), 4.59 (br s, 1 H, lupane H-29), 4.36 (d, 1 H, $J_{1,2}$ 7.3 Hz, H-1), 4.23–4.25 (m, 2 H, H-4, lupane H-28), 4.11–4.17 (m, 2 H, H-3, H-5), 3.86 (d, 1 H, *J* 11.0 Hz, lupane H-28), 3.75 (dd, 1 H, $J_{5,4}$ 3.7, $J_{5,5'}$ 13.2 Hz, H-5), 2.99 (dd, 1 H, *J* 4.7, 11.5 Hz, lupane H-3), 2.42–2.46 (m, 1 H, lupane H-19), 2.09 (s, 3 H, CH_3), 2.07 (s, 3 H, CH_3), 1.92–2.00 (m, 1 H), 1.83–1.85 (m, 1 H), 1.75–1.78 (m, 2 H), 1.68 (s, 3 H, lupane C-30), 1.56 (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3), 1.02 (s, 3 H, CH_3), 0.96 (s, 3 H, CH_3), 0.89 (s, 3 H, CH_3), 0.81 (s, 3 H, CH_3), 0.73 (s, 3 H, CH_3), 0.84–1.70 (m, 19 H, lupane protons), 0.64–0.66 (m, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 171.5, 169.4, 150.1 (lupane C-20), 110.5 (C), 109.8 (lupane C-29), 102.3 (C-1), 89.3 (lupane C-3), 76.4, 73.3, 72.9, 62.7 (CH_2), 62.3 (CH_2), 55.6, 50.4, 48.8, 47.6, 46.3 (C), 42.6 (C), 40.9 (C), 39.0 (C), 38.7 (CH_2), 37.5, 36.9 (C), 34.5 (CH_2), 34.2 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 27.7, 27.6, 27.0 (CH_2), 26.2, 26.0 (CH_2), 25.2 (CH_2), 21.1, 21.0, 20.8 (CH_2), 19.1, 18.1 (CH_2), 16.1, 16.0, 16.0, 14.7. Anal. Calcd for $C_{42}H_{66}O_8$ (698.99): C, 72.17; H, 9.52. Found: C, 72.19; H, 9.68.

*Data for **24***. Yield 92%. $[\alpha]_D^{20}$ 32.7 (*c* 0.3, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 5.05 (t, 1 H, $J_{2,1} = J_{2,3} = 7.4$ Hz, H-2), 4.68–4.69 (m, 1 H, lupane H-29), 4.58 (br s, 1 H, lupane H-29), 4.36 (d, 1 H, $J_{1,2}$ 7.4 Hz, H-1), 4.23–4.25 (m, 1 H, H-4), 4.16 (dd, 1 H, $J_{5,4}$ 3.3, $J_{5,5'}$ 13.2 Hz, H-5), 4.13 (dd, 1 H, $J_{3,2}$ 7.4, $J_{3,4}$ 5.8 Hz, H-3), 3.79 (d, 1 H, *J* 10.8 Hz, lupane H-28), 3.75 (dd, 1 H, $J_{5,4}$ 3.7, $J_{5,5'}$ 13.2 Hz, H-5), 3.33 (d, 1 H, *J* 10.8 Hz, lupane H-28), 3.00 (dd, 1 H, *J* 4.7, 11.6 Hz, lupane H-3), 2.35–2.41 (m, 1 H, lupane H-19), 2.09 (s, 3 H, CH_3), 1.84–1.93 (m, 3 H), 1.71–1.78 (m, 1 H), 1.68 (s, 3 H, lupane C-30), 1.56 (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3), 1.01 (s, 3 H, CH_3), 0.96 (s, 3 H, CH_3), 0.89 (s, 3 H, CH_3), 0.81 (s, 3 H, CH_3), 0.73 (s, 3 H, CH_3), 0.84–1.65 (m, 20 H, lupane protons), 0.65–0.67 (m, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 169.5, 150.4 (lupane C-20), 110.5 (C), 109.7 (lupane C-29), 102.3 (C-1), 89.3 (lupane C-3), 76.4 (C-3), 73.3 (C-2), 73.0 (C-4), 62.4 (C-5), 60.5 (lupane C-28), 55.6, 50.4, 48.8, 47.8, 42.7 (C), 40.9 (C), 39.0 (C), 38.7 (CH_2), 37.3, 36.9 (C), 34.2 (CH_2), 34.0 (CH_2), 29.7 (CH_2), 29.2 (CH_2), 27.7, 27.6, 27.0 (CH_2), 26.2, 26.0 (CH_2), 25.2 (CH_2), 21.1, 20.8 (CH_2), 19.1, 18.2 (CH_2), 16.1, 16.1, 16.0, 14.7. Anal. Calcd for $C_{40}H_{64}O_7$ (656.95): C, 73.13; H, 9.82. Found: C, 73.29; H, 9.67.

4.5.4. 28-*O*-*tert*-Butyldiphenylsilyl-3β-*O*-(2-*O*-acetyl-3,4-*O*-isopropylidene-α-L-arabinopyranosyl) betulin (**29**)

Eluent B. Yield 98%, amorphous powder. $[\alpha]_D^{20}$ 7.8 (*c* 0.3, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.36–7.70 (m, 10 H, Ar), 5.05 (t, 1 H, $J_{2,1} = J_{2,3} = 7.4$ Hz, H-2), 4.59–4.60 (m, 1 H, lupane H-29), 4.52–4.53 (m, 1 H, lupane H-29), 4.35 (d, 1 H, $J_{1,2}$ 7.4 Hz, H-1), 4.23–4.25 (m, 1 H, H-4), 4.15 (dd, 1 H, $J_{5,4}$ 2.8, $J_{5,5'}$ 13.2 Hz, H-5), 4.12 (dd, 1 H, $J_{3,2}$ 7.4, $J_{3,4}$ 1.7 Hz, H-3), 3.75 (dd, 1 H, $J_{5,4}$ 3.7, $J_{5,5'}$ 13.2 Hz, H-5), 3.68 (d, 1 H, *J* 9.9 Hz, lupane H-28), 3.32 (d, 1 H, *J* 9.9 Hz, lupane H-28), 2.98 (dd, 1 H, *J* 4.7, 11.6 Hz, lupane H-3), 2.23–2.28 (m, 1 H), 2.11–2.14 (m, 2 H), 2.09 (s, 3 H, CH_3), 1.80–1.87 (m, 1 H), 1.73–1.76 (m, 1 H), 1.67–1.69 (m, 1 H), 1.64 (s, 3 H, lupane C-30), 1.56 (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3), 1.06 (s, 9 H, *t*Bu), 0.91 (s, 3 H, CH_3), 0.88 (s, 3 H, CH_3), 0.75 (s, 3 H, CH_3), 0.72 (s, 3 H, CH_3), 0.69 (s, 3 H, CH_3), 0.73–1.64 (m, 18 H, lupane protons), 0.61–0.63 (m, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 169.4, 150.8 (lupane C-20), 127.6–135.7 (Ar), 110.5 (C), 109.4 (lupane C-29), 102.3 (C-1), 89.3 (lupane C-3), 76.4, 73.3, 73.0, 62.4 (CH_2), 61.1 (CH_2), 55.5, 50.3, 48.5, 48.4 (C), 47.8, 42.6 (C), 40.8 (C), 39.0 (C), 38.6 (CH_2), 37.2, 36.8 (C), 34.5 (CH_2), 34.1 (CH_2), 29.8 (CH_2), 29.5 (CH_2), 27.7, 27.6, 27.0 (CH_2), 26.9 (*t*Bu), 26.2, 26.0 (CH_2), 25.2 (CH_2), 21.1, 20.7 (CH_2), 19.1, 18.2 (CH_2), 16.1, 16.0, 15.7, 14.7. Anal. Calcd for $C_{56}H_{82}O_7Si$ (895.36): C, 75.12; H, 9.23. Found: C, 75.09; H, 9.38.

4.5.5. 3β-*O*-(2-*O*-Acetyl-3,4-*O*-isopropylidene-α-L-arabinopyranosyl) lupeol (**35**)

Eluent B. Yield 95%. M.p. 177–178 °C. $[\alpha]_D^{20}$ 38.5 (*c* 0.6, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 5.03 (t, 1 H, $J_{2,1} = J_{2,3} = 7.4$ Hz, H-2), 4.67–4.68 (m, 1 H, lupane H-29), 4.55–4.56 (m, 1 H, lupane H-29), 4.35 (d, 1 H, $J_{1,2}$ 7.4 Hz, H-1), 4.22–4.24 (m, 1 H, H-4), 4.10–4.16 (m, 2 H, H-3, H-5), 3.74 (dd, 1 H, $J_{5,4}$ 3.7, $J_{5,5'}$ 13.2 Hz, H-5), 2.98 (dd, 1 H, *J* 4.7, 11.7 Hz, lupane H-3), 2.34–2.38 (m, 1 H, lupane H-19), 2.08 (s, 3 H, CH_3), 1.87–1.94 (m, 1 H), 1.73–1.77 (m, 1 H), 1.67 (s, 3 H, CH_3),

1.54 (s, 3 H, CH_3), 1.34 (s, 3 H, CH_3), 1.00 (s, 3 H, CH_3), 0.91 (s, 3 H, CH_3), 0.87 (s, 3 H, CH_3), 0.80 (s, 3 H, CH_3), 0.77 (s, 3 H, CH_3), 0.71 (s, 3 H, CH_3), 0.83–1.71 (m, 21 H, lupane protons), 0.64–0.65 (m, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 169.4, 150.9 (lupane C-20), 110.4, 109.3 (lupane C-29), 102.3 (C-1), 89.3 (lupane C-3), 76.4, 73.3, 73.0, 62.4 (C-5), 55.6, 50.4, 48.3, 47.9, 43.0 (C), 42.8 (C), 40.8 (C), 40.0 (CH_2), 39.0 (C), 38.7 (CH_2), 38.0, 36.9 (C), 35.6 (CH_2), 34.3 (CH_2), 29.8 (CH_2), 27.7, 27.4 (CH_2), 26.2 (CH_2), 26.0, 25.1 (CH_2), 21.1, 20.9 (CH_2), 19.3, 18.2 (CH_2), 18.0, 16.1, 16.1, 15.9, 14.5. Anal. Calcd for $C_{40}H_{64}O_6$ (640.95): C, 74.96; H, 10.07. Found: C, 74.84; H, 10.27.

4.5.6. 3β-*O*-(2-*O*-Acetyl-3,4-*O*-isopropylidene-α-D-arabinopyranosyl) lupeol (**83**)

Eluent B. Yield 98%, amorphous powder. $[\alpha]_D^{20}$ 23.1 (*c* 0.3, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 4.99 (t, 1 H, *J* 7.0 Hz, H-2), 4.68–4.69 (m, 1 H, lupane H-29), 4.56–4.57 (m, 1 H, lupane H-29), 4.44 (d, 1 H, $J_{1,2}$ 6.8 Hz, H-1), 4.25–4.27 (m, 1 H, H-4), 4.11–4.16 (m, 2 H, H-3, H-5), 3.74 (dd, 1 H, $J_{5,4}$ 4.1, $J_{5,5'}$ 13.0 Hz, H-5), 3.16 (dd, 1 H, *J* 4.4, 11.8 Hz, lupane H-3), 2.35–2.40 (m, 1 H, lupane H-19), 2.07 (s, 3 H, CH_3), 1.88–1.95 (m, 1 H), 1.68 (s, 3 H, CH_3), 1.57 (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3), 1.02 (s, 3 H, CH_3), 0.97 (s, 3 H, CH_3), 0.92 (s, 3 H, CH_3), 0.82 (s, 3 H, CH_3), 0.78 (s, 3 H, CH_3), 0.72 (s, 3 H, CH_3), 0.73–1.67 (m, 22 H, lupane protons), 0.66–0.68 (m, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 169.4, 151.0 (lupane C-20), 110.4 (C), 109.2 (lupane C-29), 96.8 (C-1), 83.7 (lupane C-3), 76.1, 72.9, 72.6, 62.2 (C-5), 55.8, 50.4, 48.3, 48.0, 43.0 (C), 42.8 (C), 40.9 (C), 40.0 (CH_2), 38.4 (CH_2), 38.2 (C), 38.0, 37.0 (C), 35.5 (CH_2), 34.3 (CH_2), 29.8 (CH_2), 28.0, 27.7, 27.4 (CH_2), 26.1, 25.1 (CH_2), 22.6 (CH_2), 21.0, 20.9 (CH_2), 19.3, 18.3 (CH_2), 18.0, 16.1, 16.1, 16.0, 14.5. Anal. Calcd for $C_{40}H_{64}O_6$ (640.95): C, 74.96; H, 10.07. Found: C, 74.81; H, 10.17.

4.6. Hydrolysis of isopropylidene protection—general method

To a solution of isopropylidene derivative (0.75 mmol) in ethyl acetate (10 mL) and methanol (10 mL), a solution of *p*-TsOH (80 mg) in ethyl acetate (1 mL) and methanol (1 mL) was added. A solution was stirred for 3–4 h until no more starting material was detected on TLC, then neutralized with triethylamine (1 mL) and concentrated. The residue was purified by column chromatography to afford the title compound.

4.6.1. 3β-*O*-Acetyl-28-*O*-(2-*O*-acetyl-α-L-arabinopyranosyl) betulin (**15**)

Eluent E. Yield 92%, amorphous powder. $[\alpha]_D^{20}$ 5.2 (*c* 0.4, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 4.99 (t, 1 H, $J_{2,1}$ 3.6, $J_{2,3}$ 5.5 Hz, H-2), 4.67–4.68 (m, 1 H, lupane H-29), 4.59 (br s, 1 H, lupane H-29), 4.57 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 4.47 (dd, 1 H, *J* 5.1, 11.1 Hz, lupane H-3), 3.90–3.93 (m, 1 H, H-4), 3.84 (dd, 1 H, $J_{3,2}$ 5.5, $J_{3,4}$ 3.6 Hz, H-3), 3.71 (dd, 1 H, $J_{5,4}$ 7.9, $J_{5,5'}$ 11.9 Hz, H-5), 3.65 (dd, 1 H, $J_{5,4}$ 4.4, $J_{5,5'}$ 11.9 Hz, H-5), 3.59 (d, 1 H, *J* 9.4 Hz, lupane H-28), 3.49 (m, 1 H, *J* 9.4 Hz, lupane H-28), 2.37–2.42 (m, 1 H, lupane H-19), 2.12 (s, 3 H, CH_3), 2.04 (s, 3 H, CH_3), 1.89–1.98 (m, 2 H), 1.75–1.79 (m, 1 H), 1.68 (s, 3 H, CH_3), 1.01 (s, 3 H, CH_3), 0.97 (s, 3 H, CH_3), 0.85 (s, 6 H, 2 × CH_3), 0.84 (s, 3 H, CH_3), 0.95–1.67 (m, 22 H, lupane protons), 0.78–0.80 (m, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 171.0, 170.1, 150.1 (lupane C-20), 109.9 (lupane C-29), 99.0 (C-1), 80.9 (lupane C-3), 70.9, 69.5, 67.8 (CH_2), 65.2, 61.0 (CH_2), 55.3, 50.2, 48.7, 47.7, 46.9 (C), 42.7 (C), 40.9 (C), 38.3 (CH_2), 37.8 (C), 37.6, 37.0 (C), 34.9 (CH_2), 34.1 (CH_2), 29.7 (CH_2), 29.5 (CH_2), 27.9, 27.0 (CH_2), 25.1 (CH_2), 23.6 (CH_2), 21.3, 20.9, 20.8 (CH_2), 19.1, 18.1 (CH_2), 16.5, 16.1, 16.0, 14.8. Anal. Calcd for $C_{39}H_{62}O_8$ (658.93): C, 71.09; H, 9.48. Found: C, 70.97; H, 9.29.

4.6.2. 3β-*O*-Allyl-28-*O*-(2-*O*-acetyl-α-L-arabinopyranosyl) betulin (**20**)

Eluent F. Yield 79%, amorphous powder. $[\alpha]_D^{20}$ 9.5 (c 0.3, chloroform). ν_{max} (film): 3410, 2943, 2869, 1739, 1455, 1371, 1238, 1137, 1068, 1014, 758 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.89–5.97 (m, 1 H, allyl =C*H*), 5.24–5.28 (m, 1 H, allyl =CH_2), 5.11–5.13 (m, 1 H, allyl =CH_2), 4.98 (dd, 1 H, $J_{2,1}$ 3.7, $J_{2,3}$ 5.6 Hz, H-2), 4.68–4.69 (m, 1 H, lupane H-29), 4.58 (br s, 1 H, lupane H-29), 4.55 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 4.10–4.14 (m, 1 H, allyl O = CH_2), 3.84–3.91 (m, 3 H), 3.72 (dd, 1 H, $J_{5,4}$ 7.7, $J_{5,5'}$ 11.9 Hz, H-5), 3.65 (dd, 1 H, $J_{5,4}$ 4.3, $J_{5,5'}$ 11.9 Hz, H-5), 3.59 (d, 1 H, *J* 9.4 Hz, lupane H-28), 3.49 (d, 1 H, *J* 9.4 Hz, lupane H-28), 2.80 (dd, 1 H, *J* 4.1, 11.7 Hz, lupane H-3), 2.35–2.42 (m, 1 H, lupane H-19), 2.11 (s, 3 H, CH_3), 1.89–1.98 (m, 2 H), 1.75–1.79 (m, 1 H), 1.68 (s, 3 H, CH_3), 1.01 (s, 3 H, CH_3), 0.97 (s, 3 H, CH_3), 0.96 (s, 3 H, CH_3), 0.83 (s, 3 H, CH_3), 0.78 (s, 3 H, CH_3), 0.79–1.73 (m, 20 H, lupane protons), 0.67–0.69 (m, 1 H, lupane C-5). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 170.2, 150.1 (lupane C-20), 135.9, 115.9 (CH_2), 109.8 (lupane C-29), 99.0 (C-1), 86.3 (lupane C-3), 71.0, 70.6 (CH_2), 69.6, 67.8 (CH_2), 65.3, 61.2 (CH_2), 55.8 (lupane C-5), 50.3, 48.7, 47.7, 46.9 (C), 42.7 (C), 40.9 (C), 38.8 (C), 38.6 (CH_2), 37.6, 37.1 (C), 34.9 (CH_2), 34.2 (CH_2), 29.7 (CH_2), 29.5 (CH_2), 28.1, 27.0 (CH_2), 25.2 (CH_2), 23.1 (CH_2), 20.9, 20.8 (CH_2), 19.1, 18.2 (CH_2), 16.2, 16.1, 16.1, 14.8. Anal. Calcd for $C_{40}H_{64}O_7 \times ½\ H_2O$ (665.96): C, 72.14; H, 9.84. Found: C, 72.37; H, 9.79.

4.6.3. 28-*O*-Acetyl-3β-*O*-(2-*O*-acetyl-α-L-arabinopyranosyl) betulin (**25**)

Eluent E. Yield 71%, amorphous powder. $[\alpha]_D^{20}$ 2.1 (*c* 0.5, chloroform). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 4.97 (dd, 1 H, $J_{2,1}$ 3.8, $J_{2,3}$ 5.8 Hz, H-2), 4.68–4.69 (m, 1 H, lupane H-29), 4.64 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1), 4.59 (br s, 1 H, lupane H-29), 4.24 (d, 1 H, *J* 11.0 Hz, lupane H-28), 3.88–3.91 (m, 1 H, H-4), 3.80–3.86 (m, 3 H, H-3, H-5, lupane H-28), 3.60 (dd, 1 H, $J_{5,4}$ 3.9, $J_{5,5'}$ 11.9 Hz, H-5), 3.10 (dd, 1 H, *J* 4.6, 11.6 Hz, lupane H-3), 2.41–2.47 (m, 1 H, lupane H-19), 2.11 (s, 3 H, CH_3), 2.07 (s, 3 H, CH_3), 1.92–2.01 (m, 1 H), 1.75–1.86 (m, 2 H), 1.68 (s, 3 H, lupane C-30), 1.03 (s, 3 H, CH_3), 0.96 (s, 3 H, CH_3), 0.95 (s, 3 H, CH_3), 0.83 (s, 3 H, CH_3), 0.77 (s, 3 H, CH_3), 0.86–1.70 (m, 22 H, lupane protons), 0.67–0.69 (m, 1 H, lupane H-5). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 171.6, 170.3, 150.1 (lupane C-20), 109.8 (lupane C-29), 100.7 (C-1), 90.4 (lupane C-3), 71.4, 69.9, 65.6, 62.8 (CH_2), 61.4 (CH_2), 55.5, 50.3, 48.8, 47.7, 46.3 (C), 42.7 (C), 40.9 (C), 39.0 (C), 38.6 (CH_2), 37.5, 36.8 (C), 34.5 (CH_2), 34.1 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 27.9, 27.0 (CH_2), 25.8 (CH_2), 25.2 (CH_2), 21.0, 20.9, 20.8 (CH_2), 19.1, 18.2 (CH_2), 16.2, 16.0, 16.0, 14.7. Anal. Calcd for $C_{39}H_{62}O_8$ (658.92): C, 71.09; H, 9.48. Found: C, 70.88; H, 9.61.

4.6.4. 28-*O*-*tert*-Butyldiphenylsilyl-3β-*O*-(2-*O*-acetyl-α-L-arabinopyranosyl) betulin (**30**)

Eluent E. Yield 96%, amorphous powder. $[\alpha]_D^{20}$ –11.8 (*c* 0.4, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.36–7.70 (m, 10 H, Ar), 4.97 (dd, 1 H, $J_{2,1}$ 3.9, $J_{2,3}$ 5.8 Hz, H-2), 4.63 (d, 1 H, $J_{1,2}$ 3.9 Hz, H-1), 4.59–4.60 (m, 1 H, lupane H-29), 4.52 (br d, 1 H, lupane H-29), 3.87–3.91 (m, 1 H, H-4), 3.79–3.82 (m, 2 H), 3.68 (d, 1 H, *J* 9.9 Hz, lupane H-28), 3.59 (dd, 1 H, $J_{5,4}$ 3.9, $J_{5,5'}$ 11.9 Hz, H-5), 3.29–3.33 (m, 2 H), 3.08 (dd, 1 H, *J* 4.6, 11.7 Hz, lupane H-3), 2.24–2.28 (m, 1 H), 2.11–2.14 (m, 1 H), 2.11 (s, 3 H, CH_3), 1.77–1.87 (m, 2 H), 1.65 (s, 3 H, lupane C-30), 1.06 (s, 9 H, *t*Bu), 0.95 (s, 3 H, CH_3), 0.91 (s, 3 H, CH_3), 0.77 (s, 3 H, CH_3), 0.76 (s, 3 H, CH_3), 0.70 (s, 3 H, CH_3), 0.79–1.70 (m, 21 H, lupane protons), 0.64–0.66 (m, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 170.3, 150.8 (lupane C-20), 127.6–135.7 (Ar), 109.4 (lupane C-29), 100.7 (C-1), 90.4 (lupane C-3), 71.4, 69.9, 65.6, 61.5 (CH_2), 61.0 (CH_2), 55.4, 50.3, 48.5, 48.4 (C), 47.8, 42.6 (C), 40.8 (C), 39.0 (C), 38.6 (CH_2), 37.2, 36.8 (C), 34.5 (CH_2), 34.1 (CH_2), 29.8 (CH_2), 29.5 (CH_2), 27.9, 27.0 (CH_2), 26.9 (*t*Bu), 25.8 (CH_2), 25.1 (CH_2), 21.1, 20.8 (CH_2), 19.4 (C), 19.1, 18.2 (CH_2), 16.2, 16.0, 15.7, 14.7, 14.2 (C). Anal. Calcd for $C_{53}H_{78}O_7Si \times H_2O$ (873.31): C, 72.89; H, 9.23. Found: C, 73.16; H, 9.43.

4.6.5. 3β-*O*-(2-*O*-Acetyl-α-L-arabinopyranosyl) lupeol (**36**)

Eluent E. Yield 97%, amorphous powder. $[\alpha]_D^{20}$ 9.1 (*c* 0.4, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 4.96 (dd, 1 H, $J_{2,1}$ 3.8, $J_{2,3}$ 5.7 Hz,

H-2), 4.67–4.68 (m, 1 H, lupane H-29), 4.63 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1), 4.55–4.56 (m, 1 H, lupane H-29), 3.87–3.90 (m, 1 H, H-4), 3.78–3.82 (m, 2 H, H-3, H-5), 3.59 (dd, 1 H, $J_{5,4}$ 4.0, $J_{5,5'}$ 11.9 Hz, H-5), 3.09 (dd, 1 H, *J* 4.6, 11.5 Hz, lupane H-3), 2.34–2.38 (m, 1 H, lupane H-19), 2.10 (s, 3 H, CH_3), 1.87–1.94 (m, 1 H), 1.78–1.81 (m, 1 H), 1.67 (s, 3 H, CH_3), 1.01 (s, 3 H, CH_3), 0.94 (s, 3 H, CH_3), 0.92 (s, 3 H, CH_3), 0.82 (s, 3 H, CH_3), 0.77 (s, 3 H, CH_3), 0.75 (s, 3 H, CH_3), 0.78–1.71 (m, 23 H, lupane protons), 0.66–0.68 (m, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 170.3, 150.9 (lupane C-20), 109.3 (lupane C-29), 100.7 (C-1), 90.4 (lupane C-3), 71.3, 69.9, 65.6, 61.4 (C-5), 55.5, 50.4, 48.3, 47.9, 43.0 (C), 42.8 (C), 40.8 (C), 40.0 (CH_2), 39.0 (C), 38.6 (CH_2), 38.0, 36.8 (C), 35.5 (CH_2), 34.2 (CH_2), 29.8 (CH_2), 27.9, 27.4 (CH_2), 25.8 (CH_2), 25.1 (CH_2), 20.9 (CH_2), 19.3, 18.2 (CH_2), 18.0, 16.2, 16.0, 15.9, 14.5. Anal. Calcd for $C_{37}H_{60}O_6$ (600.89): C, 73.96; H, 10.07. Found: C, 73.76; H, 10.09.

4.6.6. 3β-*O*-Acetyl-28-*O*-(2-*O*-acetyl-α-D-arabinopyranosyl) betulin (**68**)

Hydrolysis of **89** (see *Supplementary material*) afforded the title compound. Eluent E. Yield 94%, amorphous powder. $[\alpha]_D^{20}$ 25.6 (*c* 0.2, chloroform). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 4.99 (dd, 1 H, $J_{2,1}$ 3.5, $J_{2,3}$ 5.5 Hz, H-2), 4.67–4.68 (m, 1 H, lupane H-29), 4.59 (br s, 1 H, lupane H-29), 4.56 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 4.47 (dd, 1 H, *J* 5.4, 10.8 Hz, lupane H-3), 4.03 (d, 1 H, *J* 9.5 Hz, lupane H-28), 3.91–3.93 (m, 1 H, H-4), 3.84 (dd, 1 H, $J_{3,2}$ 5.3, $J_{3,4}$ 3.5 Hz, H-3), 3.74 (dd, 1 H, $J_{5,4}$ 8.0, $J_{5,5'}$ 11.8 Hz, H-5), 3.65 (dd, 1 H, $J_{5,4}$ 4.3, $J_{5,5'}$ 11.8 Hz, H-5), 3.07 (m, 1 H, *J* 9.5 Hz, lupane H-28), 2.32–2.39 (m, 1 H, lupane H-19), 2.11 (s, 3 H, CH_3), 2.04 (s, 3 H, CH_3), 1.80–1.95 (m, 3 H), 1.68 (s, 3 H, CH_3), 1.03 (s, 3 H, CH_3), 0.97 (s, 3 H, CH_3), 0.85 (s, 6 H, 2 × CH_3), 0.84 (s, 3 H, CH_3), 0.86–1.72 (m, 22 H, lupane protons), 0.76–0.80 (m, 1 H, lupane H-5). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 171.0, 170.2, 150.1 (lupane C-20), 109.9 (lupane C-29), 99.0 (C-1), 80.9 (lupane C-3), 71.0, 69.6, 67.8 (CH_2), 65.3, 61.0 (CH_2), 55.4, 50.3, 48.8, 47.9, 46.9 (C), 42.7 (C), 40.9 (C), 38.4 (CH_2), 37.8 (C), 37.6, 37.1 (C), 34.3 (CH_2), 34.1 (CH_2), 30.0 (CH_2), 29.6 (CH_2), 27.9, 27.1 (CH_2), 25.1 (CH_2), 23.7 (CH_2), 21.3, 20.9, 20.8 (CH_2), 19.0, 18.1 (CH_2), 16.5, 16.1, 16.0, 14.7. Anal. Calcd for $C_{39}H_{62}O_8$ (658.93): C, 71.09; H, 9.48. Found: C, 71.15; H, 9.51.

4.6.7. 3β-*O*-Allyl-28-*O*-(2-*O*-acetyl-α-D-arabinopyranosyl) betulin (**69**)

Glycosylation of **3** with **8** was performed according to the procedure **4.2.** to yield crude 3β-O-allyl-28-O-(2,3,4-tri-*O*-benzoyl-α-D-arabinopyranosyl) betulin. Debenzoylation using the procedure **4.3.** afforded 3β-O-allyl-28-O-(α-D-arabinopyranosyl) betulin which, without further purification, was transformed into 3β-O-allyl-28-O-(3,4-O-isopropylidene-α-D-arabinopyranosyl) betulin as described in procedure **4.4.** It was further acetylated (general method **4.5.**) to afford crude 3β-O-allyl-28-O-(2-O-acetyl-3,4-O-isopropylidene-α-D-arabinopyranosyl) betulin. Hydrolysis of isopropylidene group gave the title compound as amorphous powder in 27% total yield (after five steps). Eluent B. $[\alpha]_D^{20}$ 29.4 (c 0.3, chloroform). ν_{max} (film): 3360, 2943, 2869, 1738, 1725, 1374, 1258, 1106, 1085, 1066, 1017, 756 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ: 5.88–5.96 (m, 1 H, allyl =C*H*), 5.23–5.27 (m, 1 H, allyl =CH_2), 5.10–5.12 (m, 1 H, allyl =CH_2), 4.97 (dd, 1 H, $J_{2,1}$ 3.6, $J_{2,3}$ 5.6 Hz, H-2), 4.66 (br s, 1 H, lupane H-29), 4.58 (br s, 1 H, lupane H-29), 4.54 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 4.09–4.13 (m, 1 H, allyl OCH_2), 4.02 (d, 1 H, *J* 9.3 Hz, lupane H-28), 3.82–3.91 (m, 3 H, H-3, H-4, allyl OCH_2), 3.74 (dd, 1 H, $J_{5,4}$ 7.9, $J_{5,5'}$ 11.8 Hz, H-5), 3.64 (dd, 1 H, $J_{5,4}$ 4.2, $J_{5,5'}$ 11.8 Hz, H-5), 3.06 (d, 1 H, *J* 9.3 Hz, lupane H-28), 2.79 (dd, 1 H, *J* 4.1, 11.7 Hz, lupane H-3), 2.33–2.39 (m, 1 H, lupane H-19), 2.11 (s, 3 H, CH_3), 1.67 (s, 3 H, CH_3), 1.02 (s, 3 H, CH_3), 0.96 (s, 3 H, CH_3), 0.95 (s, 3 H, CH_3), 0.82 (s, 3 H, CH_3), 0.78 (s, 3 H, CH_3), 0.84–1.72 (m, 25 H, lupane protons), 0.66–0.68 (m, 1 H, lupane C-5). ^{13}C NMR (125 MHz, $CDCl_3$): δ: 170.2, 150.1 (lupane C-20), 135.9, 115.9, 109.8 (lupane C-29), 99.0 (C-1), 86.3 (lupane C-3), 71.0, 70.6, 69.7, 67.8, 65.3, 61.1, 55.8, 50.4, 48.8, 47.9, 46.9, 42.7, 40.9, 38.8, 38.6, 37.5, 37.1, 34.3, 34.2, 30.1, 29.7, 28.1, 27.1, 25.2, 23.1, 20.9, 20.8, 19.1, 18.2, 16.3, 16.1, 16.0, 14.8. Anal. Calcd for $C_{40}H_{64}O_7 \times 2\ H_2O$ (692.92): C, 69.33; H, 9.89. Found: C, 69.50; H, 9.31.

4.6.8. 3β-*O*-(2-*O*-Acetyl-α-D-arabinopyranosyl) lupeol (**84**)

Eluent E. Yield 97%, amorphous powder. $[\alpha]_D^{20}$ 48.6 (*c* 0.3, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 4.90 (dd, 1 H, $J_{2,1}$ 3.4, $J_{2,3}$ 5.4 Hz, H-2), 4.74 (d, 1 H, $J_{1,2}$ 3.4 Hz, H-1), 4.68–4.69 (m, 1 H, lupane H-29), 4.56–4.57 (m, 1 H, lupane H-29), 3.89–3.91 (m, 1 H, H-4), 3.85 (br s, 1 H, H-3), 3.81 (dd, 1 H, $J_{5,4}$ 8.3, $J_{5,5'}$ 11.8 Hz, H-5), 3.62 (dd, 1 H, $J_{5,4}$ 4.3, $J_{5,5'}$ 11.8 Hz, H-5), 3.26 (dd, 1 H, *J* 4.1, 11.8 Hz, lupane H-3), 2.35–2.40 (m, 1 H, lupane H-19), 2.10 (s, 3 H, CH_3), 1.88–1.95 (m, 1 H), 1.68 (s, 3 H, CH_3), 1.03 (s, 3 H, CH_3), 1.01 (s, 3 H, CH_3), 0.93 (s, 3 H, CH_3), 0.84 (s, 3 H, CH_3), 0.79 (s, 3 H, CH_3), 0.76 (s, 3 H, CH_3), 0.77–1.71 (m, 24 H, lupane protons), 0.70–0.71 (m, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 170.2, 150.9 (lupane C-20), 109.3 (lupane C-29), 94.9 (C-1), 84.9 (lupane C-3), 71.3, 69.5, 65.2, 61.2 (C-5), 55.6, 50.4, 48.3, 47.9, 43.0 (C), 42.8 (C), 40.8 (C), 40.0 (CH_2), 38.2 (CH_2), 38.2 (C), 38.0, 37.0 (C), 35.5 (CH_2), 34.2 (CH_2), 29.8 (CH_2), 28.5, 27.4 (CH_2), 25.1 (CH_2), 22.4 (CH_2), 20.9 (CH_2), 20.9, 19.3, 18.2 (CH_2), 18.0, 16.4, 16.0, 16.0, 14.5. Anal. Calcd for $C_{37}H_{60}O_6$ (600.89): C, 73.96; H, 10.07. Found: C, 73.99; H, 10.07.

4.7. Synthesis of disaccharides—general methods

Method A. A solution of 2-O-acetyl-arabinoside (1.00 equiv) and the corresponding glycosyl donor (1.20 equiv) in CH_2Cl_2 (15 mL) was stirred for 20 min at rt over molecular sieves (4 Å, 500 mg, finely ground), then cooled to –40 °C and $BF_3 \times OEt_2$ (0.50 equiv) in CH_2Cl_2 (4 mL) was added over 10 min *via* syringe pump. The mixture was stirred for 30 min, reaction was quenched with Et_3N (1 mL), and the solvents were evaporated under diminished pressure. Column chromatography of the residue gave the protected disaccharides.

Method B. A solution of 2-O-acetyl-arabinoside (1.00 equiv) and the corresponding glycosyl donor (1.10 equiv) in CH_2Cl_2 (10 mL) was stirred for 20 min at rt over molecular sieves (4 Å, 300 mg, finely ground), then cooled to –40 °C and TMSOTf (0.50 equiv) was added. The mixture was stirred for 30 min, reaction was quenched with Et_3N (1 mL), and the solvents were evaporated under diminished pressure. Column chromatography of the residue gave the protected disaccharides.

4.7.1. 3β-*O*-Acetyl-28-*O*-[3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-2-*O*-(4-methoxybenzoyl)-β-D-xylopyranosyl-(1→3)-2-*O*-acetyl-β-L-arabinopyranosyl] betulin (**37**) *and* 3β-*O*-acetyl-28-*O*-[3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-2-*O*-(4-methoxybenzoyl)-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-β-L-arabinopyranosyl] betulin (**38**)

Method B. Eluent G. (1→4)-Linked disaccharide **38** was eluted as the first product; the second fraction contained (1→3)-linked disaccharide **37**.

*Data for **37***. Amorphous powder. Yield 16% (50 mg). $[\alpha]_D^{20}$ 79.0 (*c* 0.2, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.98–7.99 (m, 2 H, Ar), 6.91–6.93 (m, 2 H, Ar), 5.15 (dd, 1 H, $J_{2,1}$ 7.6, $J_{2,3}$ 9.8 Hz, H-2′), 5.00 (dd, 1 H, $J_{2,1}$ 6.1, $J_{2,3}$ 7.8 Hz, H-2), 4.65 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1′), 4.62–4.63 (m, 1 H, lupane H-29), 4.54 (br s, 1 H, lupane H-29), 4.46 (dd, 1 H, *J* 5.2, 11.0 Hz, lupane H-3), 4.24 (d, 1 H, $J_{1,2}$ 6.1 Hz, H-1), 3.98–4.00 (m, 1 H, H-4), 3.94–3.97 (m, 2 H, H-5, H-5′), 3.84–3.91 (m, 5 H, H-3′, H-4′, OCH_3), 3.45–3.50 (m, 3 H, H-5, H-5′, lupane H-28), 3.31 (d, 1 H, *J* 9.5 Hz, lupane H-28), 3.26 (s, 3 H, OCH_3), 3.17 (s, 3 H, OCH_3), 2.30–2.35 (m, 1 H, lupane H-19), 2.04 (s, 3 H, CH_3), 1.82–1.93 (m, 3 H), 1.65 (s, 3 H, CH_3), 1.64 (s, 3 H, CH_3), 1.27 (s, 3 H, CH_3), 1.22 (s, 3 H, CH_3), 0.96 (s, 3 H, CH_3), 0.91 (s, 3 H, CH_3), 0.84 (s, 3 H, CH_3), 0.83 (m, 6 H, 2 × CH_3), 0.88–1.68 (m, 17 H, lupane protons), 0.76–0.78 (m, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 170.9, 168.9, 164.2, 163.4 (*Ar*-OMe), 150.6 (lupane C-20), 131.8 (Ar), 122.3

(Ar), 113.6 (Ar), 109.5 (lupane C-29), 103.4 (C-1′, $^1J_{C1,H1}$ 161.8 Hz), 101.0 (C-1, $^1J_{C1,H1}$ 160.0 Hz), 99.8 (C), 99.6 (C), 80.9 (lupane C-3), 80.2 (C-3), 70.9 (C-2″), 70.7 (C-3″), 70.6 (C-2), 67.3 (lupane C-28), 67.0 (C-4), 65.6 (C-4″), 64.2 (C-5″), 63.5 (C-5), 55.4 (OCH_3), 55.3 (lupane C-5), 50.3, 48.6, 48.0, 47.9, 47.7, 46.8, 42.6, 40.8, 38.3, 37.8, 37.6, 37.0, 34.6, 34.1, 29.7, 29.4, 27.9, 27.0, 25.1, 23.7, 21.3, 20.8, 20.4, 19.0, 18.2, 17.6, 17.5, 16.5, 16.1, 16.0, 14.7. Anal. Calcd for $C_{58}H_{86}O_{16} \times {}^3/_2\ H_2O$ (1066.35): C, 65.33; H, 8.41. Found: C, 65.42; H, 8.18.

Data for ***38***. Amorphous powder. Yield 53% (165 mg). $[\alpha]_D^{20}$ 72.3 (*c* 0.3, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.98–8.00 (m, 2 H, Ar), 6.90–6.92 (m, 2 H, Ar), 5.18 (dd, 1 H, $J_{2,1}$ 6.8, $J_{2,3}$ 9.5 Hz, H-2″), 4.91 (dd, 1 H, $J_{2,1}$ 5.2, $J_{2,3}$ 7.4 Hz, H-2), 4.72 (d, 1 H, $J_{1,2}$ 6.8 Hz, H-1″), 4.65 (br s, 1 H, lupane H-29), 4.56 (br s, 1 H, lupane H-29), 4.46 (dd, 1 H, *J* 5.1, 11.1 Hz, lupane H-3), 4.34 (d, 1 H, $J_{1,2}$ 5.2 Hz, H-1), 3.91–4.01 (m, 4 H, H-3′, H-4′, H-5, H-5″), 3.86–3.90 (m, 1 H, H-4), 3.85 (s, 3 H, OCH_3), 3.66–3.70 (m, 1 H, H-3), 3.50–3.56 (m, 3 H, H-5, H-5′, lupane H-28), 3.41 (d, 1 H, *J* 9.3 Hz, lupane H-28), 3.26 (s, 3 H, OCH_3), 3.23 (s, 3 H, OCH_3), 2.33–2.37 (m, 1 H, lupane H-19), 2.04 (s, 3 H, CH_3), 2.04 (s, 3 H, CH_3), 1.82–1.93 (m, 3 H), 1.66 (s, 3 H, CH_3), 1.27 (s, 3 H, CH_3), 1.25 (s, 3 H, CH_3), 1.00 (s, 3 H, CH_3), 0.95 (s, 3 H, CH_3), 0.84 (s, 3 H, CH_3), 0.84 (s, 3 H, CH_3), 0.83 (s, 3 H, CH_3), 0.89–1.64 (m, 21 H, lupane protons), 0.77–0.79 (m, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 171.0, 169.7, 165.2, 163.6 (*Ar*-OMe), 150.5 (lupane C-20), 132.8 (Ar), 122.0 (Ar), 113.7 (Ar), 109.6 (lupane C-29), 103.2 (C-1″), 100.6 (C-1), 99.8 (C), 99.5 (C), 80.9 (lupane C-3), 75.6 (C-4), 72.0 (C-2), 71.7 (C-2″), 70.2 (C-3″), 69.6 (C-3), 67.8 (lupane C-28), 65.3 (C-4″), 64.1 (C-5″), 62.1 (C-5), 55.4 (OCH_3), 55.3 (lupane C-5), 50.3, 48.7, 48.0, 47.8, 47.7, 47.0, 42.7, 40.9, 38.3, 37.8, 37.6, 37.1, 34.7, 34.1, 29.8, 29.5, 27.9, 27.1, 25.1, 23.7, 21.3, 21.0, 20.8, 19.1, 18.2, 17.6, 17.5, 16.5, 16.2, 16.0, 14.8. Anal. Calcd for $C_{58}H_{86}O_{16} \times {}^3/_2\ H_2O$ (1066.35): C, 65.33; H, 8.41. Found: C, 65.07; H, 8.23.

4.7.2. 3β-*O*-Acetyl-28-*O*-[2-*O*-(4-methoxybenzoyl)-3,4-di-*O*-triethylsilyl-β-D-xylopyranosyl-(1→3)-2-*O*-acetyl-α-L-arabinopyranosyl] betulin (**41**) *and* 3β-*O*-Acetyl-28-*O*-[2-*O*-(4-methoxybenzoyl)-3,4-di-*O*-triethylsilyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-α-L-arabinopyranosyl] betulin (**42**)

Method A. Eluent D. Isolated as a mixture of regioisomers (450 mg, 65%) as amorphous powder.

4.7.3. 3β-*O*-Allyl-28-*O*-[2-*O*-(4-methoxybenzoyl)-3,4-di-*O*-triethylsilyl-β-D-xylopyranosyl-(1→3)-2-*O*-acetyl-α-L-arabinopyranosyl] betulin (**47**) *and* 3β-*O*-allyl-28-*O*-[2-*O*-(4-methoxybenzoyl)-3,4-di-*O*-triethylsilyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-α-L-arabinopyranosyl] betulin (**48**)

Method A. Eluent A. Isolated as a mixture of regioisomers (265 mg, 71%) as amorphous powder.

4.7.4. 28-*O*-*tert*-Butyldiphenylsilyl-3β-*O*-[2-*O*-(4-methoxybenzoyl)-3,4-di-*O*-triethylsilyl-β-D-xylopyranosyl-(1→3)-2-*O*-acetyl-α-L-arabinopyranosyl] betulin (**52**) *and* 28-*O*-*tert*-butyldiphenylsilyl-3β-*O*-[2-*O*-(4-methoxybenzoyl)-3,4-di-*O*-triethylsilyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-α-L-arabinopyranosyl] betulin (**53**)

Method A. Eluent D. Isolated as a mixture of regioisomers (633 mg, 78%) as amorphous powder.

4.7.5. 3β-*O*-[2-*O*-(4-methoxybenzoyl)-3,4-di-*O*-triethylsilyl-β-D-xylopyranosyl-(1→3)-2-*O*-acetyl-α-L-arabinopyranosyl] lupeol (**59**) *and* 3β-*O*-[2-*O*-(4-methoxybenzoyl)-3,4-di-*O*-triethylsilyl-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-α-L-arabinopyranosyl] lupeol (**60**)

Method A. Eluent D. Isolated as a mixture of regioisomers in approximate ratio 3.9:1.0 (496 mg, 76%) as amorphous powder.

4.8. 3β-*O*-Acetyl-28-*O*-[3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-2-*O*-(4-methoxybenzoyl)-β-D-xylopyranosyl-(1→3)-2,4-di-*O*-acetyl-β-L-arabinopyranosyl] betulin (**39**)

Disaccharide **37** (0.05 mmol) was acetylated according to general method **4.5.** Preparative TLC of the residue (eluent F) gave the title saponin (32 mg, 65%). $[\alpha]_D^{20}$ 82.1 (*c* 0.20, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.95–7.97 (m, 2 H, Ar), 6.91–6.92 (m, 2 H, Ar), 5.22 (br s, 1 H, H-4), 5.01–5.11 (m, 2 H, H-2, H-2″), 4.62–4.63 (m, 2 H, H-1′, lupane H-29), 4.46 (dd, 1 H, *J* 5.2, 11.1 Hz, lupane H-3), 4.19 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 4.01 (m, 1 H, $J_{5,4}$ 2.5, $J_{5,5'}$ 13.2 Hz, H-5), 3.84–3.92 (m, 3 H, H-3′, H-4′, H-5″), 3.85 (s, 3 H, OCH_3), 3.79 (dd, 1 H, $J_{3,2}$ 9.6, $J_{3,4}$ 3.7 Hz, H-3), 3.51–3.55 (m, 2 H, H-5, lupane H-28), 3.39–3.42 (m, 2 H, H-5′, lupane H-28), 3.25 (s, 3 H, OCH_3), 3.18 (s, 3 H, OCH_3), 2.29–2.33 (m, 1 H, lupane H-19), 2.15 (s, 3 H, CH_3), 2.04 (s, 3 H, CH_3), 1.89–1.93 (m, 1 H), 1.82–1.85 (m, 1 H), 1.71–1.75 (m, 1 H), 1.64 (s, 3 H, CH_3), 1.63 (s, 3 H, CH_3), 1.27 (s, 3 H, CH_3), 1.21 (s, 3 H, CH_3), 0.98 (s, 3 H, CH_3), 0.92 (s, 3 H, CH_3), 0.84 (s, 3 H, CH_3), 0.84 (m, 6 H, 2 × CH_3), 0.90–1.65 (m, 21 H, lupane protons), 0.77–0.79 (m, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 170.9, 170.8, 168.6, 164.2, 163.3, 150.4 (lupane C-20), 131.7 (Ar), 126.0 (Ar), 122.4 (Ar), 113.5 (Ar), 109.5 (lupane C-29), 103.4 (C-1′, $^1J_{C1,H1}$ 161.8 Hz), 102.5 (C-1, $^1J_{C1,H1}$ 160.0 Hz), 99.7 (C), 99.5 (C), 80.8 (lupane C-3), 76.9 (C-3), 71.4 (C-2″), 70.6 (C-2), 70.5 (C-3′ or C-4″), 70.2 (C-4), 68.1 (lupane C-28), 65.3 (C-3′ or C-4″), 63.9 (C-5″), 63.7 (C-5), 55.4 (OCH_3), 55.3 (lupane C-5), 50.2, 48.6, 47.9, 47.8, 47.6, 46.9, 42.6, 40.8, 38.3, 37.8, 37.6, 37.0, 34.5, 34.1, 29.6, 29.3, 27.9, 27.0, 25.0, 23.7, 21.3, 21.1, 20.8, 20.3, 19.0, 18.1, 17.6, 17.5, 16.5, 16.1, 16.0, 14.8. Anal. Calcd for $C_{60}H_{88}O_{17}$ (1081.36): C, 66.64; H, 8.20. Found: C, 66.42; H, 8.04.

4.9. 3β-*O*-Acetyl-28-*O*-[3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-2-*O*-(4-methoxybenzoyl)-β-D-xylopyranosyl-(1→4)-2,3-di-*O*-acetyl-β-L-arabinopyranosyl] betulin (**40**)

Disaccharide **38** (0.05 mmol) was acetylated according to general method **4.5.** Preparative TLC of the residue (eluent F) gave the title saponin (40 mg, 75%). $[\alpha]_D^{20}$ 37.4 (*c* 0.2, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.97–7.98 (m, 2 H, Ar), 6.90–6.92 (m, 2 H, Ar), 5.14 (dd, 1 H, $J_{2,1}$ 7.3, $J_{2,3}$ 9.8 Hz, H-2″), 4.93–4.97 (m, 2 H, H-2, H-3), 4.66–4.67 (m, 1 H, lupane H-29), 4.59 (d, 1 H, $J_{1,2}$ 7.3 Hz, H-1″), 4.57 (br s, 1 H, lupane H-29), 4.44–4.47 (m, 2 H, $J_{1,2}$ 2.4 Hz, H-1, lupane H-3), 4.04–4.08 (m, 1 H, H-4), 3.85–4.00 (m, 4 H, H-3′, H-4′, H-5, H-5″), 3.85 (s, 3 H, OCH_3), 3.58 (dd, 1 H, $J_{5,4}$ 3.7, $J_{5,5'}$ 11.2 Hz, H-5), 3.45–3.48 (m, 2 H, H-5′, lupane H-28), 3.36 (d, 1 H, *J* 8.9 Hz, lupane H-28), 3.26 (s, 3 H, OCH_3), 3.18 (s, 3 H, OCH_3), 2.36–2.40 (m, 1 H, lupane H-19), 2.06 (s, 3 H, CH_3), 2.03 (s, 3 H, CH_3), 1.91–1.95 (m, 2 H), 1.83–1.86 (m, 1 H), 1.67 (s, 3 H, CH_3), 1.28 (s, 3 H, CH_3), 1.22 (s, 3 H, CH_3), 0.98 (s, 3 H, CH_3), 0.94 (s, 3 H, CH_3), 0.84 (s, 3 H, CH_3), 0.83 (s, 3 H, CH_3), 0.83 (s, 3 H, CH_3), 0.92–1.69 (m, 23 H, lupane protons), 0.77–0.78 (m, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 171.0, 170.2, 169.0, 164.5, 163.4, 150.5 (lupane C-20), 131.7 (Ar), 122.3 (Ar), 113.6 (Ar), 109.6 (lupane C-29), 101.9 (C-1″), 99.7 (C), 99.5 (C), 98.5 (C-1), 80.9 (lupane C-3), 70.9 (C-2″), 70.8 (C-4), 70.6 (C-3″), 69.1 and 68.0 (C-2, C-3), 66.7 (lupane C-28), 65.7 (C-4″), 64.1 (C-5″), 60.0 (C-5), 55.4 (OCH_3), 55.3 (lupane C-5), 50.2, 48.7, 47.9, 47.8, 47.6, 46.9, 42.6, 40.8, 38.3, 37.8, 37.5, 37.0, 34.6, 34.1, 29.8, 29.4, 27.9, 27.0, 25.1, 23.7, 21.3, 21.3, 20.9, 20.8, 19.1, 18.1, 17.6, 17.5, 16.5, 16.1, 16.0, 14.7. Anal. Calcd for $C_{60}H_{88}O_{17}$ (1081.36): C, 66.64; H, 8.20. Found: C, 66.54; H, 8.16.

4.10. Hydrolysis of triethylsilyl group—general methods

Method A. To a solution of silylated disaccharide (0.10 mmol) in methanol (4 mL) and dichloromethane (2 mL) camphorsulfonic acid (CSA, 10 mg) was added and the mixture was stirred at rt for 30–60 min. Reaction was quenched with Et_3N (0.5 mL), and the solvents

were evaporated under diminished pressure. Preparative TLC of the residue (hexane–ethyl acetate–methanol, 5:3:0.5) gave the title saponin.

Method B. Product of glycosylation (disaccharide, 0.05 mmol) was acetylated under standard conditions (pyridine, Ac_2O), then coevaporated with toluene (3–4 times), filtered through short silica column (hexane–ethyl acetate, 5:1 containing 0.5% of Et_3N) and evaporated to dryness. The residue was dissolved in methanol (4 mL)–dichloromethane (2 mL) mixture and camphorsulfonic acid (CSA, 10 mg) was added. The stirring was continued for 30–60 min. Reaction was quenched with Et_3N (0.5 mL), and the solvents were evaporated under diminished pressure. Preparative TLC of the residue (hexane–ethyl acetate–methanol, 5:3:0.5) gave the title saponin.

4.10.1. 3β-*O*-Acetyl-28-*O*-[2-*O*-(4-methoxybenzoyl)-β-D-xylopyranosyl-(1→3)-2-*O*-acetyl-α-L-arabinopyranosyl] betulin (**43**) *and* 3β-*O*-acetyl-28-*O*-[2-*O*-(4-methoxybenzoyl)-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-α-L-arabinopyranosyl] betulin (**44**)

Method A. Starting from mixture of **41**/**42** saponins **44** (51%) and **43** (39%) were obtained.

*Data for **43***. $[\alpha]_D^{20}$ 0.6 (*c* 0.2, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.93–7.95 (m, 2 H, Ar), 6.86–6.88 (m, 2 H, Ar), 5.06 (dd, 1 H, $J_{2,1}$ 6.6, $J_{2,3}$ 8.4 Hz, H-2), 4.98 (dd, 1 H, $J_{2,1}$ 6.8, $J_{2,3}$ 8.3 Hz, H-2′), 4.67 (d, 1 H, $J_{1,2}$ 6.8 Hz, H-1′), 4.63 (br s, 1 H, lupane H-29), 4.54 (br s, 1 H, lupane H-29), 4.46 (dd, 1 H, *J* 5.2, 10.9 Hz, lupane H-3), 4.22 (d, 1 H, $J_{1,2}$ 6.6 Hz, H-1), 4.09 (dd, 1H, $J_{5,4}$ 4.6, $J_{5,5'}$ 11.6 Hz, H-5′), 4.05 (br s, 1 H, H-4), 3.99 (dd, 1 H, $J_{5,4}$ 3.4, $J_{5,5'}$ 12.4 Hz, H-5), 3.81–3.81 (s, 4 H, H-4′, OCH_3), 3.71–3.74 (m, 2 H, H-3, H-3′), 3.54 (d, 1 H, *J* 9.2 Hz, lupane H-28), 3.48 (d, 1 H, $J_{5,5'}$ 12.4 Hz, H-5), 3.34–3.37 (m, 2 H, H-5′, lupane H-28), 2.29–2.36 (m, 1 H, lupane H-19), 2.04 (s, 3 H, CH_3), 1.87–1.94 (m, 1 H), 1.80–1.84 (m, 1 H), 1.64 (s, 3 H, CH_3), 1.62 (s, 3 H, CH_3), 0.97 (s, 3 H, CH_3), 0.91 (s, 3 H, CH_3), 0.84 (s, 3 H, CH_3), 0.83 (s, 6 H, 2 × CH_3), 0.88–1.66 (m, 24 H, lupane protons), 0.76–0.78 (m, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 171.0, 169.5, 165.9, 163.7 (*Ar*-OMe), 150.5 (lupane C-20), 132.1 (Ar), 121.6 (Ar), 113.6 (Ar), 109.5 (lupane C-29), 102.0 (C-1′), 101.4 (C-1), 80.9 (lupane C-3), 80.1 (C-3), 74.5 (C-3′), 73.7 (C-2′), 70.5 (C-2), 69.6 (C-4′), 67.7 (lupane C-28), 67.3 (C-4), 64.9 (C-5′), 64.3 (C-5), 55.4 (OCH_3), 55.3 (lupane C-5), 50.2, 48.6, 47.8, 46.9, 42.6, 40.8, 38.3, 37.7, 37.5, 37.0, 34.6, 34.1, 29.6, 29.3, 27.9, 26.9, 25.0, 23.6, 21.3, 20.8, 20.3, 19.0, 18.1, 16.5, 16.1, 16.0, 14.8. Anal. Calcd for $C_{52}H_{76}O_{14}$ (925.18): C, 67.51; H, 8.28. Found: C, 67.33; H, 8.43. HR-MS (ESI) calc. for $C_{52}H_{76}NaO_{14}$ $[M + Na]^+$: 947.5133. Found: 947.5121.

*Data for **44***. $[\alpha]_D^{20}$ –13.5 (*c* 0.3, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.96–7.98 (m, 2 H, Ar), 6.89–6.91 (m, 2 H, Ar), 5.00 (dd, 1 H, $J_{2,1}$ 6.2, $J_{2,3}$ 7.8 Hz, H-2′), 4.89 (dd, 1 H, $J_{2,1}$ 5.2, $J_{2,3}$ 7.3 Hz, H-2), 4.82 (d, 1 H, $J_{1,2}$ 6.2 Hz, H-1′), 4.64–4.65 (m, 1 H, lupane H-29), 4.56 (br s, 1 H, lupane H-29), 4.46 (dd, 1 H, *J* 5.3, 11.0 Hz, lupane H-3), 4.36 (d, 1 H, $J_{1,2}$ 5.2 Hz, H-1), 4.13 (dd, 1H, $J_{5,4}$ 4.5, $J_{5,5'}$ 11.7 Hz, H-5′), 4.02 (dd, 1 H, $J_{5,4}$ 5.3, $J_{5,5'}$ 12.2 Hz, H-5), 3.93–3.95 (m, 1 H, H-4), 3.85 (s, 3 H, OCH_3), 3.78–3.83 (m, 1 H, H-4′), 3.74–3.77 (m, 2 H, H-3, H-3′), 3.55–3.57 (m, 2 H, H-5, lupane H-28), 3.39–3.43 (m, 2 H, H-5′, lupane H-28), 2.31–2.37 (m, 1 H, lupane H-19), 2.04 (s, 3 H, CH_3), 2.04 (s, 3 H, CH_3), 1.79–1.93 (m, 2 H), 1.66 (s, 3 H, CH_3), 1.00 (s, 3 H, CH_3), 0.95 (s, 3 H, CH_3), 0.84 (s, 6 H, 2 × CH_3), 0.83 (s, 3 H, CH_3), 0.97–1.63 (m, 25 H, lupane protons), 0.77–0.79 (m, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 170.1, 170.0, 166.4, 163.8 (*Ar*-OMe), 150.3 (lupane C-20), 132.0 (Ar), 121.4 (Ar), 113.8 (Ar), 109.7 (lupane C-29), 101.3 (C-1′, $^1J_{C1,H1}$ 162.5 Hz), 100.5 (C-1, $^1J_{C1,H1}$ 163.0 Hz), 80.9 (lupane C-3), 75.3 (C-4), 74.1 (C-3), 73.8 (C-2′), 72.0 (C-2), 69.7 (C-4′), 69.6 (C-3′), 68.0 (lupane C-28), 64.4 (C-5′), 62.0 (C-5), 55.4 (OCH_3), 55.3 (lupane C-5), 50.2, 48.6, 47.8, 46.9 (C), 42.6 (C), 40.8 (C), 38.3 (CH_2), 37.8 (C), 37.5, 37.0 (C), 34.7 (CH_2), 34.1 (CH_2), 29.7 (CH_2), 29.4 (CH_2), 27.9, 27.0 (CH_2), 25.1 (CH_2), 23.6 (CH_2), 21.3, 20.9, 20.8 (CH_2), 19.0, 18.1 (CH_2), 16.5, 16.1, 16.0, 14.7. Anal. Calcd for $C_{52}H_{76}O_{14} \times 1½\ H_2O$ (952.20): C, 65.59; H, 8.36. Found: C, 65.42; H, 8.54. HR-MS (ESI) calc. for $C_{52}H_{76}NaO_{14}$ $[M + Na]^+$: 947.5133. Found: 947.5146.

4.10.2. 3β-*O*-Acetyl-28-*O*-[2-*O*-(4-methoxybenzoyl)-β-D-xylopyranosyl-(1→3)-2,4-di-*O*-acetyl-α-L-arabinopyranosyl] betulin (**45**) *and* 3β-*O*-acetyl-28-*O*-[2-*O*-(4-methoxybenzoyl)-β-D-xylopyranosyl-(1→4)-2,3-di-*O*-acetyl-α-L-arabinopyranosyl] betulin (**46**)

An analytical sample of **41**/**42** mixture was separated by preparative TLC (hexane–ethyl acetate, 5:1 containing 0.5% Et_3N) to afford pure disaccharides **41** and **42**. They were transformed into acetates **45** and **46** according to Method B.

*Data for **45***. Yield 58%. $[\alpha]_D^{20}$ –0.4 (*c* 0.3, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.94–7.96 (m, 2 H, Ar), 6.92–6.93 (m, 2 H, Ar), 5.21–5.23 (m, 1 H, H-4), 5.18 (dd, 1 H, $J_{2,1}$ 6.4, $J_{2,3}$ 8.5 Hz, H-2), 4.94 (d, 1 H, $J_{1,2}$ 4.1 Hz, H-1′), 4.89 (dd, 1 H, $J_{2,1}$ 4.1, $J_{2,3}$ 5.3 Hz, H-2′), 4.64–4.65 (m, 1 H, lupane H-29), 4.56 (br s, 1 H, lupane H-29), 4.46 (dd, 1 H, *J* 5.1, 11.1 Hz, lupane H-3), 4.32 (d, 1 H, $J_{1,2}$ 6.4 Hz, H-1), 4.16–4.18 (m, 1 H, H-5′), 4.03 (dd, 1 H, $J_{5,4}$ 4.0, $J_{5,5'}$ 12.8 Hz, H-5), 3.95 (dd, 1 H, $J_{3,2}$ 8.5, $J_{3,4}$ 3.3 Hz, H-3), 3.87 (s, 3 H, OCH_3), 3.81–3.83 (m, 1 H, H-3′), 3.74–3.76 (m, 1 H, H-4′), 3.56–3.59 (m, 2 H, H-5, lupane H-28), 3.52 (dd, 1 H, $J_{5,4}$ 5.2, $J_{5,5'}$ 12.2 Hz, H-5′), 3.44 (d, 1 H, *J* 9.3 Hz, lupane H-28), 2.32–2.36 (m, 1 H, lupane H-19), 2.14 (s, 3 H, CH_3), 2.04 (s, 3 H, CH_3), 2.01 (s, 3 H, CH_3), 1.78–1.98 (m, 3 H), 1.66 (s, 3 H, CH_3), 1.00 (s, 3 H, CH_3), 0.94 (s, 3 H, CH_3), 0.84 (s, 3 H, CH_3), 0.84 (s, 3 H, CH_3), 0.84 (s, 3 H, CH_3), 0.95–1.64 (m, 22 H, lupane protons), 0.78–0.79 (m, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 171.0, 170.8, 169.4, 163.9 (*Ar*-OMe), 150.4 (lupane C-20), 131.9 (Ar), 121.3 (Ar), 113.8 (Ar), 109.6 (lupane C-29), 101.6 (C-1), 99.6 (C-1′), 80.8 (lupane C-3), 75.3 (C-3), 74.4 (C-2′), 71.0 (C-3′), 70.3 (C-2), 69.3 (C-4), 69.0 (C-4′), 68.2 (lupane C-28), 62.3 (C-5, C-5′), 55.5 (OCH_3), 55.3 (lupane C-5), 50.2, 48.6, 47.9, 46.9, 42.6, 40.8, 38.3, 37.8, 37.6, 37.0, 34.6, 34.1, 29.7, 29.3, 27.9, 27.0, 25.0, 23.621.3, 21.1, 20.8, 20.7, 19.0, 18.1, 16.5, 16.1, 16.0, 14.8. Anal. Calcd for $C_{54}H_{78}O_{15} \times 1½\ H_2O$ (994.24): C, 65.24; H, 8.21. Found: C, 65.30; H, 8.18. HR-MS (ESI) calc. for $C_{54}H_{78}NaO_{15}$ $[M + Na]^+$: 989.5238. Found: 989.5236.

*Data for **46***. Yield 90%. $[\alpha]_D^{20}$ –24.0 (*c* 0.3, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.97–7.99 (m, 2 H, Ar), 6.91–6.93 (m, 2 H, Ar), 5.00–5.04 (m, 2 H, H-2, H-3), 4.93 (dd, 1 H, $J_{2,1}$ 6.3, $J_{2,3}$ 7.9 Hz, H-2′), 4.72 (d, 1 H, $J_{1,2}$ 6.3 Hz, H-1′), 4.65–4.66 (m, 1 H, lupane H-29), 4.57 (br s, 1 H, lupane H-29), 4.46 (dd, 1 H, *J* 5.4, 10.9 Hz, lupane H-3), 4.43 (d, 1 H, $J_{1,2}$ 3.9 Hz, H-1), 4.09–4.12 (m, 2 H, H-4, H-5′), 4.02 (dd, 1 H, $J_{5,4}$ 6.9, $J_{5,5'}$ 11.7 Hz, H-5), 3.86 (s, 3 H, OCH_3), 3.78–3.82 (m, 1 H, H-4′), 3.73 (t, 1 H, $J_{3,2} = J_{3,4} = 7.9$ Hz, H-3′), 3.61 (dd, 1 H, $J_{5,4}$ 3.2, $J_{5,5'}$ 11.7 Hz, H-5), 3.52 (d, 1 H, *J* 9.2 Hz, lupane H-28), 3.38–3.41 (m, 2 H, H-5′, lupane H-28), 2.34–2.39 (m, 1 H, lupane H-19), 2.06 (s, 3 H, CH_3), 2.04 (s, 3 H, CH_3), 1.83–1.98 (m, 3 H), 1.78 (s, 3 H, CH_3), 1.67 (s, 3 H, CH_3), 1.00 (s, 3 H, CH_3), 0.94 (s, 3 H, CH_3), 0.84 (s, 6 H, 2 × CH_3), 0.83 (s, 3 H, CH_3), 0.97–1.63 (m, 22 H, lupane protons), 0.77–0.79 (m, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 171.0, 170.3, 169.1, 166.2, 163.8 (*Ar*-OMe), 150.4 (lupane C-20), 132.0 (Ar), 121.6 (Ar), 113.8 (Ar), 109.6 (lupane C-29), 100.5 (C-1′, $^1J_{C1,H1}$ 164.0 Hz), 99.5 (C-1, $^1J_{C1,H1}$ 164.2 Hz), 80.9 (lupane C-3), 74.2 (C-3′), 73.5 (C-2′), 71.6 (C-4), 69.9 (C-4′), 69.2 (C-2, C-3), 67.3 (lupane C-28), 64.3 (C-5′), 61.3 (C-5), 55.4 (OCH_3), 55.3 (C-5), 50.2, 48.6, 47.8, 46.9 (C), 42.6 (C), 40.8 (C), 38.3 (CH_2), 37.8 (C), 37.5, 37.0 (C), 34.6 (CH_2), 34.1 (CH_2), 29.7 (CH_2), 29.4 (CH_2), 27.9, 27.0 (CH_2), 25.1 (CH_2), 23.7 (CH_2), 21.3, 20.8, 20.8 (CH_2), 20.4, 19.1, 18.1 (CH_2), 16.5, 16.1, 16.0, 14.7. Anal. Calcd for $C_{54}H_{78}O_{15} \times H_2O$ (985.23): C, 65.83; H, 8.18. Found: C, 65.94; H, 8.07. HR-MS (ESI) calc. for $C_{54}H_{78}NaO_{15}$ $[M + Na]^+$: 989.5238. Found: 989.5255.

4.10.3. 3β-*O*-Allyl-28-*O*-[2-*O*-(4-methoxybenzoyl)-β-D-xylopyranosyl-(1→3)-2-*O*-acetyl-α-L-arabinopyranosyl] betulin (**49**)

Method A. Starting from mixture of **47**/**48**, saponins **50** (in approx. ratio 1:1, 36%) and **49** (30%) were obtained. It is likely that **50** comprised a mixture of (1→4)-linked disaccharides acetylated at O-2 or O-3 positions of the arabinopyranoside ring.

*Data for **49***. $[\alpha]_D^{20}$ 0.1 (c 0.3, chloroform). ν_{max} (film): 3445, 2941, 2869, 1721, 1605, 1257, 1171, 1131, 1087, 1071, 1034, 757 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ:7.96–7.97 (m, 2 H, Ar), 6.89–6.91 (m, 2 H, Ar), 5.89–5.96 (m, 1 H, allyl =C*H*), 5.24–5.27 (m, 1 H, allyl =CH_2), 5.11–5.13 (m, 1 H, allyl =CH_2), 5.06 (dd, 1 H, $J_{2,1}$ 6.0, $J_{2,3}$ 7.8 Hz, H-2), 4.97 (dd, 1 H, $J_{2,1}$ 6.6, $J_{2,3}$ 8.2 Hz, H-2′), 4.71 (d, 1 H, $J_{1,2}$ 6.6 Hz, H-1′), 4.63 (br s, 1 H, lupane H-29), 4.54 (br s, 1 H, lupane H-29), 4.26 (d, 1 H, $J_{1,2}$ 6.0 Hz, H-1), 4.10–4.14 (m, 2 H), 4.00 (br s, 1 H), 3.96 (dd, 1 H, *J* 4.4, 12.2 Hz), 3.86–3.89 (m, 1 H, allyl CH_2O), 3.82–3.85 (m, 4 H), 3.78 (dd, 1 H, *J* 3.2, 8.0 Hz), 3.73 (t, 1 H, *J* 8.2 Hz), 3.49–3.53 (m, 2 H), 3.38 (dd, 1 H, *J* 9.1, 11.6 Hz), 3.33 (d, 1 H, *J* 9.2 Hz), 2.79 (dd, 1 H, *J* 4.2, 11.7 Hz, lupane H-3), 2.30–2.35 (m, 1 H, lupane H-19), 1.87–1.94 (m, 1 H), 1.81–1.84 (m, 1 H), 1.71 (m, 3 H, CH_3), 1.64 (s, 3 H, CH_3), 0.96 (s, 3 H, CH_3), 0.95 (s, 3 H, CH_3), 0.90 (m, 3 H, CH_3), 0.81 (m, 3 H, CH_3), 0.78 (s, 3 H, CH_3), 0.82–1.67 (m, 24 H, lupane protons), 0.65–0.67 (m, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$):169.5, 166.1, 163.9, 150.6 (lupane C-20), 135.9, 132.2, 121.5, 115.9 (CH_2), 113.7, 109.5 (lupane C-29), 101.8, 101.0 (C-1), 86.3 (lupane C-3), 80.0, 74.6, 73.9, 70.6 (CH_2), 70.5, 69.8, 67.5 (CH_2), 66.9, 64.7 (CH_2), 63.7 (CH_2), 55.8, 55.5, 50.4, 48.6, 47.9, 46.9 (C), 42.6 (C), 40.9 (C), 38.8 (C), 38.6 (CH_2), 37.6, 37.1 (C), 34.6 (CH_2), 34.2 (CH_2), 29.7 (CH_2), 29.3 (CH_2), 28.1, 27.0 (CH_2), 25.2 (CH_2), 23.1 (CH_2), 20.8 (CH_2), 20.5, 19.1, 18.2 (CH_2), 16.3, 16.1, 16.0, 14.8. Anal. Calcd for $C_{53}H_{78}O_{13}$ (923.21): C, 68.25; H, 8.50. Found: C, 68.13; H, 8.44.

4.10.4. 28-*O*-*tert*-Butyldiphenylsilyl-3β-*O*-[2-*O*-(4-methoxybenzoyl)-β-D-xylopyranosyl-(1→3)-2-*O*-acetyl-α-L-arabinopyranosyl] betulin (**54**) *and* 28-*O*-*tert*-butyldiphenylsilyl-3β-*O*-[2-*O*-(4-methoxybenzoyl)-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-α-L-arabinopyranosyl] betulin (**55**)

Method A. Starting from mixture of **52**/**53**, saponins **55** (62%) and **54** (25%, slightly contaminated by unknown component) were obtained.

*Data for **54***. $[\alpha]_D^{20}$ –0.5 (*c* 0.2, chloroform). ^1H NMR (600 MHz, $CDCl_3$) δ: 7.92–7.94 (m, 2 H, Ar), 7.36–7.69 (m, 10 H), 6.86–6.87 (m, 2 H, Ar), 5.08 (dd, 1 H, $J_{2,1}$ 7.2, $J_{2,3}$ 8.9 Hz, H-2), 4.98 (dd, 1 H, $J_{2,1}$ 6.4, $J_{2,3}$ 7.5 Hz, H-2′), 4.66 (d, 1 H, $J_{1,2}$ 6.4 Hz, H-1′), 4.59 (br s, 1 H, lupane H-29), 4.52 (br s, 1 H, lupane H-29), 4.26 (d, 1 H, $J_{1,2}$ 7.2 Hz, H-1), 4.08 (dd, 1H, $J_{5,4}$ 4.1, $J_{5,5'}$ 11.4 Hz, H-5'), 4.03 (br s, 1 H, H-4), 3.97 (d, 1 H, *J* 12.1 Hz, lupane H-28), 3.81–3.83 (m, 4 H, H-4′, OCH_3), 3.71–3.74 (m, 1 H, H-3′), 3.65–3.68 (m, 2 H, H-3, H-5), 3.43 (d, 1 H, *J* 12.1 Hz, lupane H-28), 3.30–3.36 (m, 2 H, H-5, H-5′), 2.93 (dd, 1 H, *J* 4.3, 11.7 Hz, lupane H-3), 2.22–2.27 (m, 1 H, lupane H-19), 2.10–2.13 (m, 2 H), 1.70–1.86 (m, 2 H), 1.64 (s, 3 H, CH_3), 1.59 (s, 3 H, CH_3), 1.05 (m, 9 H, *t*Bu), 0.89 (s, 3 H, CH_3), 0.77 (s, 3 H, CH_3), 0.69 (s, 3 H, CH_3), 0.67 (s, 3 H, CH_3), 0.60 (s, 3 H, CH_3), 0.73–1.53 (m, 22 H, lupane protons), 0.56–0.57 (m, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 169.6, 165.8, 163.7 (*Ar*-OMe), 150.8 (lupane C-20), 113.7–135.7 (Ar), 109.4 (lupane C-29), 103.2 (C-1, $^1J_{C1,H1}$ 161.1 Hz), 101.8 (C-1′, $^1J_{C1,H1}$ 162.0 Hz), 89.5 (lupane C-3), 80.5 (C-3), 74.2 (C-3′), 73.6 (C-2′), 70.7 (C-2), 69.5 (C-4′), 67.9 (C-4), 64.8 (C-5′, lupane C-28), 61.1 (C-5), 55.5 (lupane C-5), 55.4 (OCH_3), 50.3, 48.5, 48.4, 47.8, 42.6, 40.8, 38.9, 38.6, 37.2, 36.8, 34.5, 34.2, 29.9, 29.5, 27.6, 27.0, 26.9 (*t*Bu), 25.9, 25.2, 20.7, 20.4, 19.4, 19.1, 18.1, 16.1, 16.0, 15.7, 14.7. Anal. Calcd for $C_{66}H_{92}O_{13}Si \times 2\ H_2O$ (1157.58): C, 68.48; H, 8.36. Found: C, 68.41; H, 8.18. HR-MS (ESI) calc. for $C_{66}H_{92}NaO_{13}Si$ $[M + Na]^+$: 1143.6205. Found: 1143.6204.

*Data for **55***. $[\alpha]_D^{20}$ –26.7 (*c* 0.2, chloroform). ^1H NMR (600 MHz, $CDCl_3$) δ: 7.97–7.98 (m, 2 H, Ar), 7.36–7.70 (m, 10 H), 6.90–6.91 (m, 2 H, Ar), 4.99 (dd, 1 H, $J_{2,1}$ 5.9, $J_{2,3}$ 7.5 Hz, H-2′), 4.90 (dd, 1 H, $J_{2,1}$ 5.2, $J_{2,3}$ 7.4 Hz, H-2), 4.84 (d, 1 H, $J_{1,2}$ 5.9 Hz, H-1′), 4.59–4.60 (m, 1 H, lupane H-29), 4.52 (br s, 1 H, lupane H-29), 4.46 (d, 1 H, $J_{1,2}$ 5.2 Hz, H-1), 4.14 (dd, 1H, $J_{5,4}$ 4.3, $J_{5,5'}$ 11.8 Hz, H-5′), 4.04 (dd, 1 H, $J_{5,4}$ 5.6, $J_{5,5'}$ 12.3 Hz, H-5), 3.92–3.94 (m, 1 H, H-4), 3.85 (s, 3 H, OCH_3), 3.79–3.83 (m, 1 H, H-4′), 3.74–3.77 (m, 2 H, H-3, H-3′), 3.68 (d, 1 H, *J* 10.0 Hz, lupane H-28), 3.53 (dd, 1 H, $J_{5,4}$ 2.7, $J_{5,5'}$ 12.3 Hz, H-5), 3.42 (dd, 1H, $J_{5,4}$ 7.9, $J_{5,5'}$ 11.8 Hz, H-5′), 3.32 (d, 1 H, *J* 10.0 Hz, lupane H-28), 3.01 (dd, 1 H, *J* 4.6, 11.7 Hz, lupane H-3), 2.23–2.28 (m, 1 H, lupane H-19), 2.11–2.14 (m, 2 H), 2.05 (s, 3 H, CH_3), 1.72–1.87 (m, 2 H), 1.64 (s, 3 H, CH_3), 1.06 (m, 9 H, *t*Bu), 0.90 (s, 3 H, CH_3), 0.90 (s, 3 H, CH_3), 0.73 (s, 3 H, CH_3), 0.70 (s, 3 H, CH_3), 0.68 (s, 3 H, CH_3), 0.75–1.67 (m, 22 H, lupane protons), 0.60–0.62 (m, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 170.1, 166.4, 163.9 (*Ar*-OMe), 150.8 (lupane C-20), 113.8–135.7 (Ar), 109.4 (lupane C-29), 101.8 (C-1, $^1J_{C1,H1}$ 165.0 Hz), 101.2 (C-1′, $^1J_{C1,H1}$ 165.6 Hz), 90.2 (lupane C-3), 75.4 (C-4), 73.9 (C-3′), 73.7 (C-2′), 72.2 (C-2), 69.8 (C-3), 69.7 (C-4′), 64.1 (C-5′), 62.0 (C-5), 61.1 (lupane C-28), 55.5 (lupane C-5), 55.4 (OCH_3), 50.3, 48.5, 48.4, 47.8, 42.6, 40.8, 39.0, 38.6, 37.2, 36.8, 34.5, 34.1, 29.9, 29.5, 27.8, 27.0, 26.9 (*t*Bu), 25.8, 25.2, 21.0, 20.7, 19.4, 19.1, 18.2, 16.2, 16.0, 15.7, 14.7. Anal. Calcd for $C_{66}H_{92}O_{13}Si \times 1½\ H_2O$ (1148.57): C, 69.02; H, 8.34. Found: C, 69.05; H, 8.35. HR-MS (ESI) calc. for $C_{66}H_{96}NO_{13}Si$ $[M + NH_4]^+$: 1138.6651. Found: 1138.6658.

4.10.5. 3β-*O*-[2-*O*-(4-Methoxybenzoyl)-β-D-xylopyranosyl-(1→3)-2-*O*-acetyl-α-L-arabinopyranosyl] lupeol (**61**) *and* 3β-*O*-[2-*O*-(4-methoxybenzoyl)-β-D-xylopyranosyl-(1→4)-2-*O*-acetyl-α-L-arabinopyranosyl] lupeol (**62**)

Method A. Starting from mixture of **59**/**60**, saponins **62** (237 mg, 67%) and **61** (60 mg, 17%) were obtained.

*Data for **61***: $[\alpha]_D^{20}$ 11.6 (*c* 0.1, chloroform). ^1H NMR (600 MHz, $CDCl_3$) δ: 7.94–7.96 (m, 2 H, Ar), 6.86–6.88 (m, 2 H, Ar), 5.08 (dd, 1 H, $J_{2,1}$ 7.4, $J_{2,3}$ 9.2 Hz, H-2), 4.99 (dd, 1 H, $J_{2,1}$ 6.7, $J_{2,3}$ 8.1 Hz, H-2′), 4.68–4.69 (m, 1 H, lupane H-29), 4.66 (d, 1 H, $J_{1,2}$ 6.7 Hz, H-1′), 4.56 (br s, 1 H, lupane H-29), 4.26 (d, 1 H, $J_{1,2}$ 7.4 Hz, H-1), 4.05–4.08 (m, 2 H, H-4, H-5′), 3.99 (dd, 1 H, $J_{5,4}$ 1.9, $J_{5,5'}$ 12.0 Hz, H-5), 3.80–3.83 (m, 4 H, H-4′, OCH_3), 3.76 (t, 1 H, $J_{3,2} = J_{3,4} = 8.1$ Hz, H-3′), 3.68 (dd, 1 H, $J_{3,2}$ 9.2, $J_{3,4}$ 3.1 Hz, H-3), 3.44 (d, 1 H, $J_{5,5'}$ 12.0 Hz, H-5), 3.35 (dd, 1 H, $J_{5,4}$ 9.2, *J* 11.5 Hz, H-5′), 2.95 (dd, 1 H, *J* 4.5, 11.4 Hz, lupane H-3), 2.34–2.39 (m, 1 H, lupane H-19), 1.73–1.95 (m, 2 H), 1.68 (s, 3 H, CH_3), 1.57 (s, 3 H, CH_3), 1.01 (s, 3 H, CH_3), 0.99 (s, 3 H, CH_3), 0.91 (s, 3 H, CH_3), 0.78 (s, 3 H, CH_3), 0.78 (s, 3 H, CH_3), 0.77 (s, 3 H, CH_3), 0.80–1.66 (m, 24 H, lupane protons), 0.60–0.61 (m, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 169.5, 165.8, 163.7 (*Ar*-OMe), 150.9 (lupane C-20), 132.2 (Ar), 121.8 (Ar), 113.6 (Ar), 109.3 (lupane C-29), 103.3 (C-1), 101.8 (C-1′), 89.5 (lupane C-3), 80.4 (C-3), 74.1 (C-3′), 73.5 (C-2′), 70.7 (C-2), 69.4 (C-4′), 67.8 (C-4), 64.9 (C-5), 64.9 (C-5′), 55.6, 55.4, 50.4, 48.3, 47.9, 43.0, 42.7, 40.8, 40.0, 38.9, 38.6, 38.0, 36.8, 35.6, 34.2, 29.8, 27.6, 27.4, 26.0, 25.1, 20.9, 20.4, 19.7, 19.3, 18.1, 18.0, 16.1, 16.1, 15.9, 14.5. Anal. Calcd for $C_{50}H_{74}O_{12} \times 1½\ H_2O$ (894.17): C, 67.16; H, 8.68. Found: C, 67.01; H, 8.35.

*Data for **62***: $[\alpha]_D^{20}$ –5.2 (*c* 0.2, chloroform). ^1H NMR (600 MHz, $CDCl_3$) δ: 7.96–7.98 (m, 2 H, Ar), 6.88–6.90 (m, 2 H, Ar), 5.00 (dd, 1 H, $J_{2,1}$ 6.1, $J_{2,3}$ 7.5 Hz, H-2′), 4.89 (dd, 1 H, $J_{2,1}$ 5.4, $J_{2,3}$ 7.6 Hz, H-2), 4.81 (d, 1 H, $J_{1,2}$ 6.1 Hz, H-1′), 4.68–4.69 (m, 1 H, lupane H-29), 4.57 (br s, 1 H, lupane H-29), 4.44 (d, 1 H, $J_{1,2}$ 5.4 Hz, H-1), 4.12 (dd, 1 H, $J_{5,4}$ 4.4, *J* 11.7 Hz, H-5′), 4.06 (dd, 1 H, $J_{5,4}$ 5.4, $J_{5,5'}$ 12.4 Hz, H-5), 3.80–3.84 (m, 4 H, H-4′, OCH_3), 3.73–3.77 (m, 2 H, H-3, H-3′), 3.52 (dd, 1 H, $J_{5,4}$ 2.6, $J_{5,5'}$ 12.4 Hz, H-5), 3.40 (dd, 1 H, $J_{5,4}$ 8.1, $J_{5,5'}$ 11.7 Hz, H-5′), 3.02 (dd, 1 H, *J* 4.6, 11.7 Hz, lupane H-3), 2.35–2.40 (m, 1 H, lupane H-19), 2.04 (s, 3 H, CH_3), 1.88–1.95 (m, 1 H), 1.73–1.77 (m, 1 H), 1.68 (s, 3 H, CH_3), 1.01 (s, 3 H, CH_3), 0.92 (s, 3 H, CH_3), 0.89 (s, 3 H, CH_3), 0.80 (s, 3 H, CH_3), 0.78 (s, 3 H, CH_3), 0.70 (s, 3 H, CH_3), 0.83–1.67 (m, 25H, lupane protons), 0.63–0.65 (m, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 170.1, 166.3, 163.8 (*Ar*-OMe), 150.9 (lupane C-20), 132.2 (Ar), 121.5 (Ar), 113.8 (Ar), 109.3 (lupane C-29), 101.9

(C-1, $^1J_{C1,H1}$ 157.1 Hz), 101.4 (C-1′, $^1J_{C1,H1}$ 163.1 Hz), 90.2 (lupane C-3), 75.7 (C-4), 73.9 (C-3′), 73.7 (C-2′), 72.3 (C-2), 69.9 (C-3), 69.6 (C-4′), 64.3 (C-5′), 62.2 (C-5), 55.5, 55.4, 50.4, 48.3, 47.9, 43.0, 42.8, 40.8, 40.0, 39.0, 38.6, 38.0, 36.8, 35.6, 34.2, 29.8, 27.7, 27.4, 25.8, 25.1, 21.0, 20.9, 19.3, 18.2, 18.0, 16.2, 16.0, 15.9, 14.5. Anal. Calcd for $C_{50}H_{74}O_{12} \times H_2O$ (885.16): C, 67.85; H, 8.65. Found: C, 67.82; H, 8.73.

4.10.6. 3β-*O*-[2-*O*-(4-Methoxybenzoyl)-β-D-xylopyranosyl-(1→3)-2,4-di-*O*-acetyl-α-L-arabinopyranosyl] lupeol (**65**), 3β-*O*-[2-*O*-(4-methoxybenzoyl)-β-D-xylopyranosyl-(1→4)-2,3-di-*O*-acetyl-α-L-arabinopyranosyl] lupeol (**66**) *and* 3β-*O*-[4-*O*-(4-methoxybenzoyl)-β-D-xylopyranosyl-(1→4)-2,3-di-*O*-acetyl-α-L-arabinopyranosyl] lupeol (**67**)

Method B. Acetylation of **59**/**60** mixture gave inseparable **63**/**64** mixture. Its desilylation afforded saponins **67** (8 mg, 8%), **66** (53 mg, 55%) and **65** (7 mg, 7%).

*Data for **65***. $[\alpha]_D^{20}$ 16.1 (*c* 0.2, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.93–7.95 (m, 2 H, Ar), 6.92–6.94 (m, 2 H, Ar), 5.21–5.24 (m, 2 H, H-2, H-4), 4.95 (d, 1 H, $J_{1,2}$ 3.4 Hz, H-1′), 4.88 (dd, 1 H, $J_{2,1}$ 3.4, $J_{2,3}$ 4.5 Hz, H-2′), 4.68–4.69 (m, 1 H, lupane H-29), 4.56 (br s, 1 H, lupane H-29), 4.38 (d, 1 H, $J_{1,2}$ 7.1 Hz, H-1), 4.20 (dd, 1 H, $J_{5,4}$ 3.0, *J* 12.3 Hz, H-5′), 4.02 (dd, 1 H, $J_{5,4}$ 3.1, $J_{5,5'}$ 13.1 Hz, H-5), 3.90 (dd, 1 H, $J_{3,2}$ 9.3, $J_{3,4}$ 3.6 Hz, H-3), 3.87 (s, 3 H, OCH_3), 3.83 (br s, 1 H, H-3′), 3.75 (br s, 1 H, H-4′), 3.52–3.55 (m, 2 H, H-5, H-5′), 3.02 (dd, 1 H, *J* 5.1, 11.3 Hz, lupane H-3), 2.35–2.39 (m, 1 H, lupane H-19), 2.13 (s, 3 H, CH_3), 2.03 (s, 3 H, CH_3), 1.88–1.94 (m, 1 H), 1.69–1.76 (m, 1 H), 1.68 (s, 3 H, CH_3), 1.01 (s, 3 H, CH_3), 0.92 (s, 3 H, CH_3), 0.88 (s, 3 H, CH_3), 0.81 (s, 3 H, CH_3), 0.78 (s, 3 H, CH_3), 0.72 (s, 3 H, CH_3), 0.73–1.65 (m, 23 H, lupane protons), 0.64–0.66 (m, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 170.9, 169.4, 165.1, 163.9 (*Ar*-OMe), 150.9 (lupane C-20), 131.9 (Ar), 121.3 (Ar), 113.8 (Ar), 109.3 (lupane C-29), 103.3 (C-1), 99.6 (C-1′), 90.1 (lupane C-3), 76.1 (C-3), 71.1 (C-2′), 70.8 (C-2), 70.5 (C-3′), 69.7 (C-4), 68.9 (C-4′), 63.0 (C-5), 62.1 (C-5′), 55.6, 55.5, 50.4, 48.3, 47.9, 43.0, 42.8, 40.8, 40.0, 39.0, 38.7, 38.0, 36.9, 35.6, 34.3, 29.8, 27.7, 27.4, 26.0, 25.1, 21.1, 20.9, 20.9, 19.3, 18.2, 18.0, 16.1, 16.0, 15.9, 14.7. HR-MS (ESI) calc. for $C_{52}H_{76}NaO_{13}$ $[M+Na]^+$: 931.5184. Found: 931.5167.

*Data for **66***. $[\alpha]_D^{20}$ −13.9 (*c* 0.2, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.97–7.99 (m, 2 H, Ar), 6.91–6.93 (m, 2 H, Ar), 5.08 (dd, 1 H, $J_{2,1}$ 5.3, $J_{2,3}$ 7.6 Hz, H-2), 4.96 (dd, 1 H, $J_{3,2}$ 7.6, $J_{3,4}$ 3.0 Hz, H-3), 4.93 (dd, 1 H, $J_{2,1}$ 5.9, $J_{2,3}$ 7.4 Hz, H-2′), 4.73 (d, 1 H, $J_{1,2}$ 5.9 Hz, H-1′), 4.68–4.69 (m, 1 H, lupane H-29), 4.57 (br s, 1 H, lupane H-29), 4.46 (d, 1 H, $J_{1,2}$ 5.3 Hz, H-1), 4.07–4.12 (m, 3 H, H-4, H-5, H-5′), 3.86 (s, 3 H, OCH_3), 3.76–3.80 (br s, 1 H, H-4′), 3.73–3.75 (br s, 1 H, H-3′), 3.55 (dd, 1 H, $J_{5,4}$ 4.6, $J_{5,5'}$ 14.0 Hz, H-5), 3.39 (dd, 1 H, $J_{5,4}$ 7.9, *J* 11.9 Hz, H-5′), 2.99 (dd, 1 H, *J* 4.6, 11.4 Hz, lupane H-3), 2.35–2.40 (m, 1 H, lupane H-19), 2.04 (s, 3 H, CH_3), 1.88–1.93 (m, 1 H), 1.83 (s, 3 H, CH_3), 1.73–1.75 (m, 1 H), 1.68 (s, 3 H, CH_3), 1.01 (s, 3 H, CH_3), 0.92 (s, 3 H, CH_3), 0.87 (s, 3 H, CH_3), 0.80 (s, 3 H, CH_3), 0.78 (s, 3 H, CH_3), 0.69 (s, 3 H, CH_3), 0.82–1.67 (m, 23 H, lupane protons), 0.63–0.65 (m, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 170.4, 169.1, 166.2 (C = O), 163.8 (*Ar*-OMe), 150.9 (lupane C-20), 132.1 (Ar), 121.6 (Ar), 113.8 (Ar), 109.3 (lupane C-29), 101.8 (C-1, $^1J_{C1,H1}$ 162.6 Hz), 100.7 (C-1′, $^1J_{C1,H1}$ 164.5 Hz), 89.7 (lupane C-3), 73.8 (C-3′), 73.4 (C-2′), 72.5 (C-4), 70.3 (C-3), 69.9 (C-4′), 69.7 (C-2), 64.0 (C-5′), 62.6 (C-5), 55.5, 55.4, 50.4, 48.3, 47.9, 43.0, 42.8, 40.8, 40.0, 39.0, 38.6, 38.0, 36.8, 35.6, 34.2, 29.8, 27.7, 27.4, 25.8, 25.1, 20.9, 20.9, 20.5, 19.3, 18.2, 18.0, 16.1, 16.0, 15.9, 14.5. Anal. Calcd for $C_{52}H_{76}O_{13}$ (909.18): C, 68.70; H, 8.43. Found: C, 68.59; H, 8.38.

*Data for **67***. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.97–7.99 (m, 2 H, Ar), 6.91–6.92 (m, 2 H, Ar), 5.14 (dd, 1 H, $J_{2,1}$ 5.5, $J_{2,3}$ 7.8 Hz, H-2), 5.01–5.05 (m, 2 H, H-3, H-4′), 4.68–4.69 (m, 1 H, lupane H-29), 4.56–4.57 (m, 1 H, lupane H-29), 4.49 (d, 1 H, $J_{1,2}$ 5.5 Hz, H-1), 4.38 (d, 1 H, $J_{1,2}$ 6.9 Hz, H-1′), 4.18 (dd, 1 H, $J_{5,4}$ 5.0, *J* 11.7 Hz, H-5′), 4.11 (dd, 1 H, $J_{5,4}$ 5.3, $J_{5,5'}$ 11.8 Hz, H-5), 4.08–4.09 (m, 1 H, H-4), 3.83–3.87 (m, 4 H, H-3′, OCH_3), 3.55–3.59 (m, 2 H, H-2′, H-5), 3.38 (dd, 1 H, $J_{5,4}$ 9.0, $J_{5,5'}$ 11.7 Hz, H-5′), 3.04 (dd, 1 H, *J* 4.7, 11.6 Hz, lupane H-3), 2.35–2.40 (m, 1 H, lupane H-19), 2.10 (s, 3 H, CH_3), 2.08 (s, 3 H, CH_3), 1.88–1.95 (m, 1 H), 1.79–1.82 (m, 1 H), 1.68 (s, 3 H, CH_3), 1.02 (s, 3 H, CH_3), 0.93 (s, 3 H, CH_3), 0.91 (s, 3 H, CH_3), 0.83 (s, 3 H, CH_3), 0.79 (s, 3 H, CH_3), 0.75 (s, 3 H, CH_3), 0.74–1.73 (m, 23 H, lupane protons), 0.66–0.68 (m, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 170.9, 169.4, 165.7, 163.7, 150.9 (lupane C-20), 131.8 (Ar), 121.7 (Ar), 113.7 (Ar), 109.3 (lupane C-29), 104.5 (C-1′), 101.6 (C-1), 89.8 (lupane C-3), 74.2 (C-4), 73.1 (C-2, C-3′), 71.4 (C-4′), 70.8 (C-3), 69.9 (C-2), 62.8 (C-5), 62.6 (C-5′), 55.6, 55.4, 50.4, 48.3, 47.9, 43.0, 42.8, 40.8, 40.0, 39.0, 38.6, 38.0, 36.9, 35.6, 34.3, 29.8, 27.8, 27.4, 25.8, 25.1, 20.9, 20.9, 19.3, 18.2, 18.0, 16.2, 16.1, 15.9, 14.5. HR-MS (ESI) calc. for $C_{52}H_{76}NaO_{13}$ $[M+Na]^+$: 931.5184. Found: 931.5175.

4.11. Deallylation—general method

A solution of hydrogen activated iridium complex $[Ir(COD)(MePPh_2)_2]PF_6$ (5 mg)[10] was transferred into solution of the corresponding allyl ether (0.10 mmol) in THF (3 mL) and stirred at rt for 4 h. Then, methanol (2 mL) and *p*-TsOH (30 mg) were added; the mixture was stirred at rt for an additional 6 h, and concentrated under reduced pressure. The residue was purified by preparative TLC (eluent H) to afford the title compound.

4.11.1. 3β-28-*O*-[2-*O*-(4-Methoxybenzoyl)-β-D-xylopyranosyl-(1→3)-2-*O*-acetyl-α-L-arabinopyranosyl] betulin (**51**)

Starting from **49** the title compound (40%) was obtained. $[\alpha]_D^{20}$ 16.6 (*c* 0.3, chloroform). ν_{max} (film): 3418, 2941, 2869, 1734, 1719, 1605, 1371, 1256, 1171, 1100, 1073, 1046, 757 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3/CD_3OD$): δ: 8.01–8.03 (m, 2 H, Ar), 6.97–6.98 (m, 2 H, Ar), 5.05–5.08 (m, 1 H), 4.94 (t, 1 H, *J* 8.1 Hz), 4.54 (br s, 1 H), 4.20 (d, 1 H, *J* 7.6 Hz), 4.08 (br s, 1 H), 4.00 (dd, 1 H, *J* 4.2, 11.5 Hz), 3.97 (br s, 1 H), 3.89 (s, 3 H, OCH_3), 3.75 (dd, 1 H, *J* 3.0, 9.5 Hz), 3.63–3.71 (m, 2 H), 3.59 (d, 1 H, *J* 9.2 Hz), 3.55 (d, 1 H, *J* 12.7 Hz), 3.31 (d, 1 H, *J* 11.5 Hz), 3.15 (dd, 1 H, *J* 5.8, 10.3 Hz, lupane C-3), 2.31–2.33 (m, 1 H, lupane C-19), 1.68–1.92 (m, 4 H), 1.65 (s, 3 H, CH_3), 1.53 (s, 3 H, CH_3), 1.01 (s, 3 H, CH_3), 0.96 (s, 3 H, CH_3), 0.95 (s, 3 H, CH_3), 0.84 (s, 3 H, CH_3), 0.76 (s, 3 H, CH_3), 0.85–1.63 (m, 26 H, lupane protons), 0.68–0.70 (m, 1 H, lupane C-5). HRMS (ESI): m/z calcd for $C_{50}H_{74}NaO_{13}$ $[M+Na]^+$: 905.5027. Found: 905.5021.

4.12. 3β-*O*-[2-*O*-(4-methoxybenzoyl)-β-D-xylopyranosyl-(1→3)-2-*O*-acetyl-α-L-arabinopyranosyl] betulin (**56**)

To a solution of **54** (78 mg, 0.069 mmol) in THF (2 mL), tetrabutylammonium fluoride (1 M in THF, 0.59 mL, 0.59 mmol) was added followed by acetic acid (34 μL, 0.59 mmol) and the mixture was stirred in a screw tap tube at 60 °C for 24 h. The mixture was then concentrated and the residue was purified by preparative TLC (hexane–ethyl acetate–methanol, 5:3:1) to afford the title compound (35 mg, 57%) as a foam. $[\alpha]_D^{20}$ 2.5 (*c* 0.2, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.93–7.95 (m, 2 H, Ar), 6.86–6.87 (m, 2 H, Ar), 5.08 (m, 1 H, H-2), 4.98 (m, 1 H, H-2′), 4.68 (br s, 1 H, lupane H-29), 4.65 (d, 1 H, $J_{1,2}$ 6.5 Hz, H-1′), 4.58 (br s, 1 H, lupane H-29), 4.26 (d, 1 H, $J_{1,2}$ 7.3 Hz, H-1), 4.04–4.08 (m, 2 H, H-4, H-5′), 3.98 (br d, 1 H, $J_{5,5'}$ 12.0 Hz, H-5), 3.78–3.84 (m, 5 H, H-4′, lupane H-28, OCH_3), 3.72–3.74 (m, 1 H, H-3′), 3.67 (br d, 1 H, *J* 9.4 Hz, H-3), 3.44 (br d, 1 H, $J_{5,5'}$ 12.0 Hz, H-5), 3.31–3.35 (m, 2 H, H-5′, lupane H-28), 2.95 (dd, 1 H, *J* 4.1, 11.3 Hz, lupane H-3), 2.35–2.39 (m, 1 H, lupane H-19), 1.83–1.97 (m, 3 H), 1.67 (s, 3 H, CH_3), 1.56 (s, 3 H, CH_3), 0.98 (s, 3 H, CH_3), 0.94 (s, 3 H, CH_3), 0.78 (s, 3 H, CH_3), 0.76 (s, 3 H, CH_3), 0.61 (m, 4 H, lupane H-5, CH_3), 0.87–1.74 (m, 24 H, lupane protons). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 169.6, 165.8, 163.7 (*Ar*-OMe), 150.4 (lupane C-20), 132.1 (Ar), 121.7 (Ar), 113.7 (Ar), 109.7 (lupane C-29), 103.3 (C-1, $^1J_{C1,H1}$ 159.5 Hz), 101.9 (C-1′, $^1J_{C1,H1}$ 163.0 Hz), 89.5 (lupane C-3),

80.5 (C-3), 74.2 (C-3′), 73.6 (C-2′), 70.7 (C-2), 69.5 (C-4′), 67.9 (C-4), 64.9 (C-5, C-5′), 60.5 (lupane C-28), 55.6 (lupane C-5), 55.5 (OCH_3), 50.4, 48.8, 47.8, 42.6, 40.9, 38.9, 38.7, 37.3, 36.8, 34.2, 34.0, 29.8, 29.2, 27.6, 27.0, 26.0, 25.2, 20.8, 20.4, 19.1, 18.1, 16.1, 16.1, 16.0, 15.0.HR-MS (ESI) calc. for $C_{50}H_{74}NaO_{13}$ $[M+Na]^+$: 905.5027. Found: 905.5015.

4.13. 3β-*O*-[2-*O*-(4-methoxybenzoyl)-β-D-xylopyranosyl-(1→4)-3-*O*-acetyl-α-L-arabinopyranosyl] betulin (**57**)

Starting from **55** (245 mg, 0.218 mmol) and using procedure described for **56**, the title compound was obtained (155 mg, 80%). Product contained minute amounts of 2-OAc isomer **58**. *Data for **57**.* ^{1}H NMR (600 MHz, $CDCl_3$) δ: selected signals—4.99–5.01 (m, 1 H, H-2′), 4.77 (dd, 1 H, *J* 3.4, 9.3 Hz, H-3), 4.68 (br s, 1 H, lupane H-29), 4.58–4.59 (m, 2 H, H-1′, lupane H-29), 4.26 (d, 1 H, $J_{1,2}$ 6.7 Hz, H-1), 4.05–4.10 (m, 1 H, H-5), 4.03 (dd, 1 H, $J_{5,4}$ 4.8, $J_{5,5'}$ 11.9 Hz, H-5′), 4.00 (br s, 1 H, H-4), 3.73–3.79 (m, 3 H, H-2, H-3′, H-4′), 3.50 (d, 1 H, $J_{5,5'}$ 11.5 Hz, H-5), 3.19–3.22 (m, 2 H, lupane H-28), 3.07 (dd, 1 H, *J* 4.5, 11.7 Hz, lupane H-3), 1.72 (s, 3 H, CH_3), 1.68 (s, 3 H, CH_3). ^{13}C NMR (150 MHz, $CDCl_3$) δ: selected signals—109.6 (lupane C-29), 105.1 (C-1, $^1J_{C1,H1}$ 160.0 Hz), 102.3 (C-1′, $^1J_{C1,H1}$ 163.2 Hz), 89.7 (lupane C-3), 74.6 (C-3′), 74.5 (C-4), 73.7 (C-2′), 73.2 (C-3), 70.1 (C-4′), 69.5 (C-2), 64.9 (C-5′), 64.8 (C-5), 60.4 (lupane C-28). HR-MS (ESI) calc. for $C_{50}H_{74}NaO_{13}$ $[M+Na]^+$: 905.5027. Found: 905.5005.

4.14. 28-*O*-α-L-Arabinofuranosyl betulin (**85**)

A mixture of **13** (67 mg, 0.072 mmol), EtOH (5 mL) and KOH (20 mg) was refluxed for 2 h, diluted with water (10 mL) and extracted with ethyl acetate (3 × 10 mL). Organic extracts were dried (Na_2SO_4) and evaporated. Column chromatography (eluent G) of the residue gave 38 mg (90%) of the title compound. M.p. 169–174 °C (dec). $[\alpha]_D^{20}$ –37.0 (*c* 0.3, chloroform). ^{1}H NMR (600 MHz, $CDCl_3$/CD_3OD) δ: 4.96 (s, 1 H, H-1), 4.68 (br s, 1 H, lupane H-29), 4.58 (br s, 1 H, lupane H-29), 4.10–4.11 (m, 1 H), 4.00 (s, 1 H), 3.97 (br s, 1 H), 3.82 (dd, 1 H, $J_{5,4}$ 2.5, $J_{5,5'}$ 11.8 Hz, H-5), 3.75 (dd, 1 H, $J_{5,4}$ 2.3, $J_{5,5'}$ 11.8 Hz, H-5), 3.51 (br s, 2 H, lupane H-28), 3.17 (dd, 1 H, *J* 5.8, 10.4 Hz, lupane H-3), 2.38–2.44 (m, 1 H, lupane H-19), 1.88–1.97 (m, 2 H), 1.70–1.74 (m, 1 H), 1.68 (s, 3 H, CH_3), 1.02 (s, 3 H, CH_3), 0.97 (s, 3 H, CH_3), 0.96 (s, 3 H, CH_3), 0.83 (s, 3 H, CH_3), 0.76 (s, 3 H, CH_3), 0.78–1.65 (m, 24 H, lupane protons), 0.67–0.69 (m, 1 H, lupane H-5). ^{13}C NMR (150 MHz, $CDCl_3$/CD_3OD) δ: 150.3 (lupane C-20), 109.6 (lupane C-29), 108.5 (C-1), 86.7, 79.0, 78.8, 77.6, 65.8 (CH_2), 61.4 (CH_2), 55.2, 50.3, 48.6, 47.7, 46.7 (C), 42.6 (C), 40.8 (C), 38.7 (CH_2), 38.6 (C), 37.5, 37.0 (C), 34.8 (CH_2), 34.1 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 27.8, 27.0 (CH_2), 25.1 (CH_2), 20.8 (CH_2), 19.0, 18.2 (CH_2), 16.0, 15.9, 15.3, 14.7. Anal. Calcd for $C_{35}H_{58}O_6 \times ½H_2O$ (583.86): C, 72.00; H, 10.19. Found: C, 72.01; H, 10.10. HR-MS (ESI) calc. for $C_{35}H_{58}NaO_6$ $[M+Na]^+$: 597.4131. Found: 597.4128.

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Appendix: Supplementary material

Supplementary data to this article can be found online at doi:10.1016/j.carres.2016.01.010.

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