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Selective killing of cancer cells with triterpenoic acid amides – the substantial role of an aromatic moiety alignment

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Graphical Abstract:

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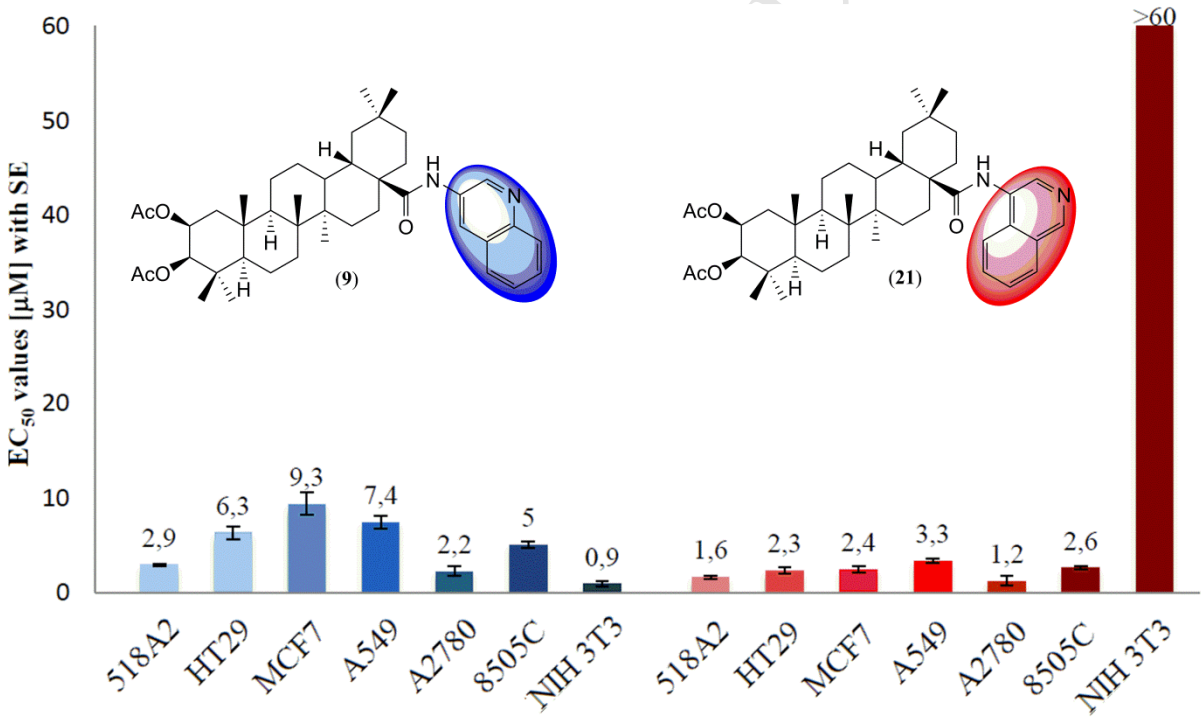


A small structural difference (3-quinolinyl / 4-isoquinolinyl) has a strong impact on cytotoxicity and malignant/non-malignant cell selectivity.

Abstract

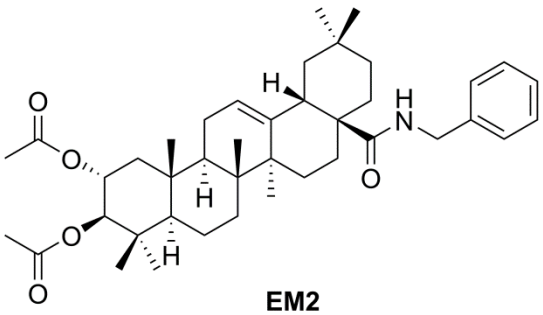
2,3-Di-*O*-acetyl-triterpenoic acid derived amides possessing a (2β, 3β) configuration in ring A and two acetyl groups were previously shown to possess high cytotoxicity for human tumor cell lines but to exhibit low cytotoxicity for non-malignant mouse fibroblasts. In this study, augustic acid (**1**) and 2-*epi*-corosolic acid (**2**) were chosen as starting points for the synthesis of analogs. While augustic acid derived 3-quinolinyl amide **9** gave low EC_{50} values in SRB assays but was cytotoxic for all lines, the isomeric 4-isoquinolinyl amide **21** was very cytotoxic for the tumor cell lines but significantly less cytotoxic for the mouse fibroblasts NIH 3T3. In addition, a triacetylated 4-isoquinolinyl derivative of asiatic acid (**28**) gave EC_{50} = 80 nM (for A2780 ovarian cancer cells). As shown by additional experiments (acridine orange/propidium iodide staining, fluorescence spectroscopy and cell cycle investigations) these compounds act mainly by apoptosis.

Keywords: maslinic acid, oleanolic acid, asiatic acid, tumor cells, SRB assay, apoptosis

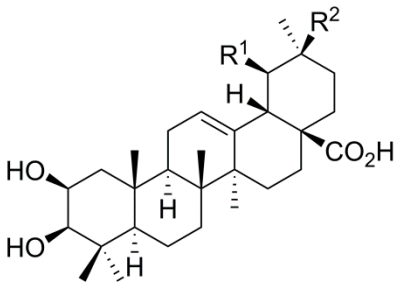
1. Introduction

Despite of improved technology and medical progress for the last decades, cancer remains one of the world's leading causes of death finally resulting in approximately 8 million deaths globally per year.[1] Options to treat this family of diseases include surgery, radiotherapy, chemotherapy or a combination thereof. Many of the chemotherapeutics commonly applied for the treatment of cancer are characterized altogether by a high degree of non-selective toxicity for the cells. For example, *cis*-platinum (one of the most common used chemotherapeutics accounting to annually sales of approximately 3 billion Euro) is highly active for many types of human tumors [2] (e.g. ovarian cancer as well as cancer of the head, neck, testes but also for treating small cell lung cancer), but this drug also exhibits strong nephro- and neurotoxic effects.[3] Thus, a main goal of an effective treatment of cancer pursues to kill cancer cells selectively without any (or negligible) damage to non-malignant cells. Modern therapeutic schemes to achieve these goals include, for example, prodrug targeting,[4] advanced drug delivery systems [5, 6] or by applying light [7, 8] or heat [9, 10] or by a selective drug targeting using magnetic triggering.[11, 12]

In the course of investigating a small library of maslinic acid derivative compounds, we discovered an interesting molecule named **EM2** (Fig. 1), and this di-*O*-acetylated benzylamide of maslinic acid exhibited rather low EC_{50} values (sulforhodamine B assays [13] (SRB), EC_{50} = 0.5 μM for human ovarian cancer cells) while being significantly less toxic for non-malignant mouse fibroblasts (NIH 3T3, EC_{50} = 33.8 μM).[14] We considered **EM2** as an ideal basis to start additional investigations concerning the biological activity of pentacyclic triterpenoid analogs carrying an additional nitrogen containing heterocycle attached to ring E by a suitable spacer. In addition, we became also interested in possible effects of the presence/absence of acetyl groups in ring A onto cytotoxicity and/or selectivity of the compounds. Hence, a panel of analogs was synthesized, and their cytotoxicity measured using SRB assays. For selected compounds (showing low EC_{50} values for the cancer cells and high EC_{50} values for the mouse fibroblasts), cell cycle investigations, annexin V/propidium iodide staining experiments as well as visual inspections of the cells by fluorescence microscopy were carried out.



EM2



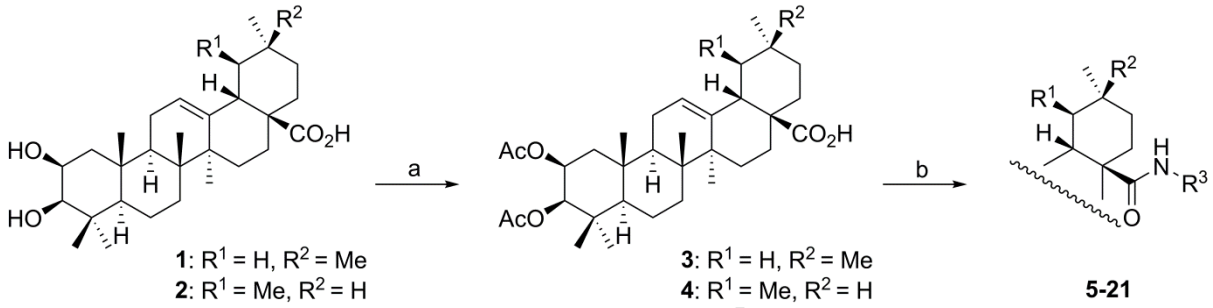
augustic acid (1): R^1 = H, R^2 = Me
2-epi-corosolic acid (2): R^1 = Me, R^2 = H

Fig. 1. Structures of **EM2**, augustic acid (**1**) and 2-epi-corosolic acid (**2**).

2. Results and discussion

Augustic acid (**1**, Fig. 1) and 2-epi-corosolic acid (**2**) were chosen as starting points for the synthesis of analogs. Both of these compounds carry two hydroxyl functions in ring A showing a (2β, 3β)-configuration, and they are easily accessed by synthesis.[15-18] Acetylation of **1** or **2** gave diacetates **3** and **4** (Scheme 1) whose reactions under Schotten-Baumann conditions with oxalyl chloride followed by the addition of an amine furnished amides **5**–**21** in moderate to excellent isolated yields between 38 and 90%. Amides **5**–**21** were

characterized by NMR, IR, UV-vis spectroscopy and ESI-MS. Thus, in the IR spectra of these amides a strong absorption band at v = 1506–1534 cm^{-1} was detected being characteristic for the presence of a NHCO moiety. In their UV-vis spectra the aromatic chromophore gave characteristic absorption maxima between λ = 244–279 nm for the pyridinyl substituted compounds while for the quinolinyl amides absorption maxima λ = 241-335 nm were detected. As far as their ^{1}H NMR spectra are concerned, the signal for the NH moiety was detected between δ = 10.30–10.37 ppm for the 8-quinolinyl amides while all of the other compounds this signal was found between δ = 7.77–8.10 ppm, respectively.[19, 20]



Scheme 1. Synthesis of compounds **3**–**21**: (a) Ac_2O, TEA, DMAP, DCM, 25°C, 20h, 65–79%; (b) oxalyl choride, TEA, DMF, DCM, 25°C, 2h; then: R^3-NH_2, TEA, DMAP, DCM, 25°C, 2d, 38–90%.

The compounds were subjected to SRB assays,[13] the results of which are summarized in Table 1.

Table 1. Cytotoxicity of selected compounds (EC_{50} values in μM from SRB assays after 96 hours of treatment; the values are averaged from three independent experiments performed each in triplicate; confidence interval CI = 95 %; n.d. not detected). Human cancer cell lines: 518A2 (melanoma), HT29 (colorectal adenocarcinoma), MCF7 (breast adenocarcinoma), A549 (lung adenocarcinoma), A2780 (ovarian carcinoma), 8505C (thyroid carcinoma); NIH 3T3: nonmalignant mouse fibroblasts.

EC_{50}	R^1	R^2	R^3	518A2	HT29	MCF7	A549	A2780	8505C	NIH 3T3
1	H	Me	-	25.7±0.7	>30	25.1±2.2	n.d.	n.d.	n.d.	>30
2	Me	H	-	>30	>30	29.1±0.7	>30	24.9±2.7	>30	>30
3	H	Me	-	13.8±1.0	23.1± 0.6	16.1± 3.8	n.d.	n.d.	n.d.	>30

4	Me	H	-	17.9±0.6	16.2±1.2	10.4±2.9	15.6±0.4	17.9±0.6	15.6±0.5	12.7± 0.7
5	H	Me	3-pyridinyl	1.7±0.5	2.2±0.2	2.0±0.2	2.8±0.4	0.9±0.1	2.3±0.4	2.4±0.2
6	Me	H	3-pyridinyl	2.0±0.1	3.2±0.1	3.5±0.3	3.5±0.2	2.0±0.1	2.7±0.3	4.2±0.3
7	H	Me	4-pyridinyl	4.2±0.5	2.7±0.2	3.1±0.7	4.0±0.3	1.6±0.7	4.1±0.3	1.8±0.2
8	Me	H	4-pyridinyl	8.3±0.2	9.4±0.6	9.0±1.3	10.1±0.9	8.3±0.2	8.5±0.1	5.7±0.9
9	H	Me	3-quinolinyl	2.9±0.1	6.3±0.7	9.3±1.3	7.4±0.7	2.2±0.6	5.0±0.4	0.9±0.3
10	Me	H	3-quinolinyl	2.5±0.2	6.5±1.4	3.2±0.4	3.4±0.4	2.8±0.4	3.1±0.2	2.2±0.2
11	H	Me	4-quinolinyl	2.4±0.2	4.1±0.3	4.3±0.4	4.2±0.3	2.0±0.9	3.4±0.2	2.9±0.8
12	Me	H	4-quinolinyl	6.4±0.3	5.5±0.6	4.0±1.0	8.2±0.7	3.5±0.1	6.6±0.8	5.2±0.9
13	H	Me	5-quinolinyl	1.2±0.2	2.4±0.2	2.5±0.1	3.0±0.4	0.7±0.1	2.3±0.2	8.6±1.8
14	Me	H	5-quinolinyl	2.0±0.8	3.6±0.5	5.5±1.0	3.7±0.5	2.7±0.5	3.2±0.3	>60
15	H	Me	6-quinolinyl	2.9±0.1	4.4±0.4	5.8±0.8	4.9±0.5	2.0±0.5	3.8±0.2	0.6±0.1
16	Me	H	6-quinolinyl	4.2±0.2	9.2±1.0	6.5±1.3	5.3±0.4	4.2±0.1	4.3±0.1	0.9±0.1
17	H	Me	7-quinolinyl	1.6±0.2	1.3±0.1	1.4±0.2	2.6±0.1	1.0±0.1	1.6±0.1	0.7±0.1
18	Me	H	7-quinolinyl	2.4±0.2	2.0±0.2	1.6±0.4	3.1±0.0	1.8±0.0	2.5±0.5	1.8±0.1
19	H	Me	8-quinolinyl	6.2±1.0	>30	24.6±9.7	>30	5.1±0.9	16.1±3.5	>30
20	Me	H	8-quinolinyl	13.3±1.4	>30	>30	>30	6.7±0.9	>30	>30
21	H	Me	4-isoquinolinyl	1.6±0.2	2.3±0.4	2.4±0.4	3.3±0.3	1.2±0.6	2.6±0.2	>60

Compounds **5**–**8** carrying a pyridine substituent showed an improved cytotoxicity as compared to acetylated acids **3** and **4**. Thus, compound **5** gave an EC_{50} = 0.9 μM for the human carcinoma cell line A2780 but selectivity between the human tumor cell lines and non-malignant mouse fibroblasts NIH 3T3 remained low for these compounds. A different performance, however, was observed during the biological evaluation of quinolinyl substituted compounds – depending on their substitution pattern. While the cytotoxicity of compounds **9**–**12** and **15**–**18** was similar to that of the pyridinyl substituted amides, 8-quinolinyl derivatives (**19** and **20**) showed selective cytotoxicity towards different human tumor cell lines. However, their overall cytotoxicity was low, and their solubility in water was quite poor. As a consequence, we discarded these compounds from additional investigations. 5-Quinolinyl substituted compounds **13** and **14**, however, performed better because they gave rather low EC_{50} values, they were cytotoxic to the human tumor cell lines but of significantly lowered cytotoxicity for the non-malignant mouse fibroblasts. From these findings we presumed a potentially existing connection between cytotoxicity and the orientation of the

aromatic system, and – as a consequence – we synthesized 4-isoquinolinyl compound **21**. Compounds **9** (a 3-quinolinyl derivative) and **21** are formally distinct from each other by a re-orientation of the aromatic substituent. (Fig. 2)

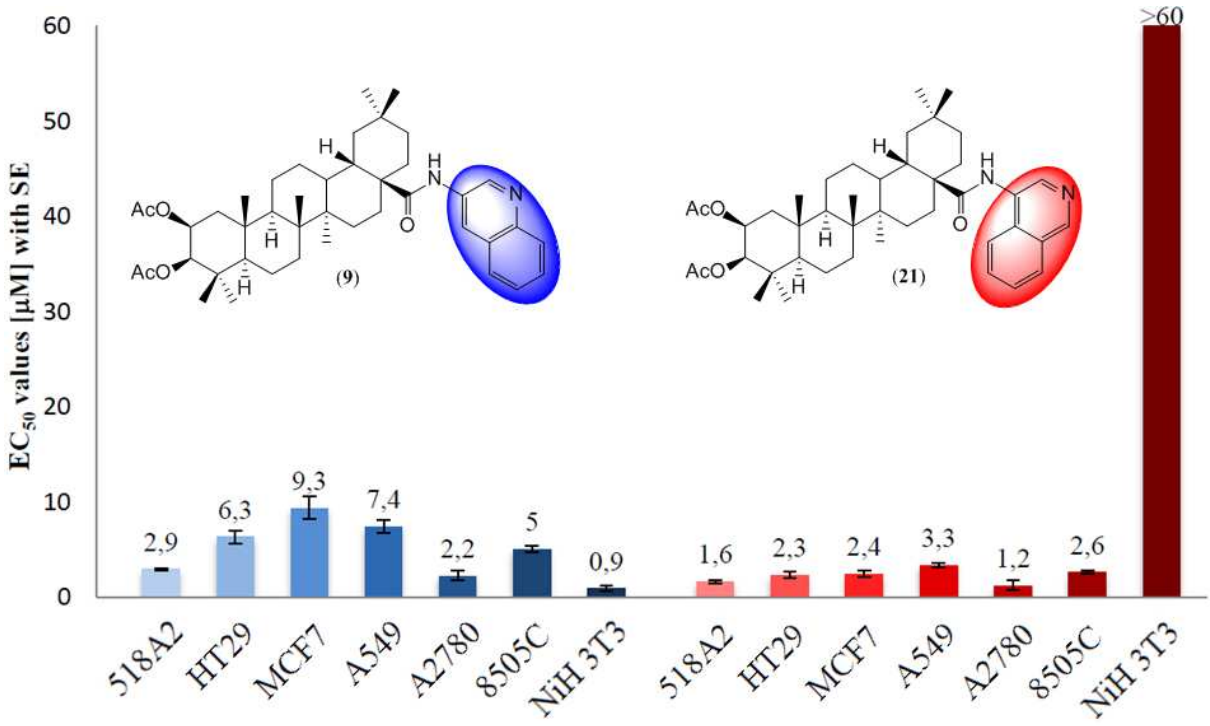
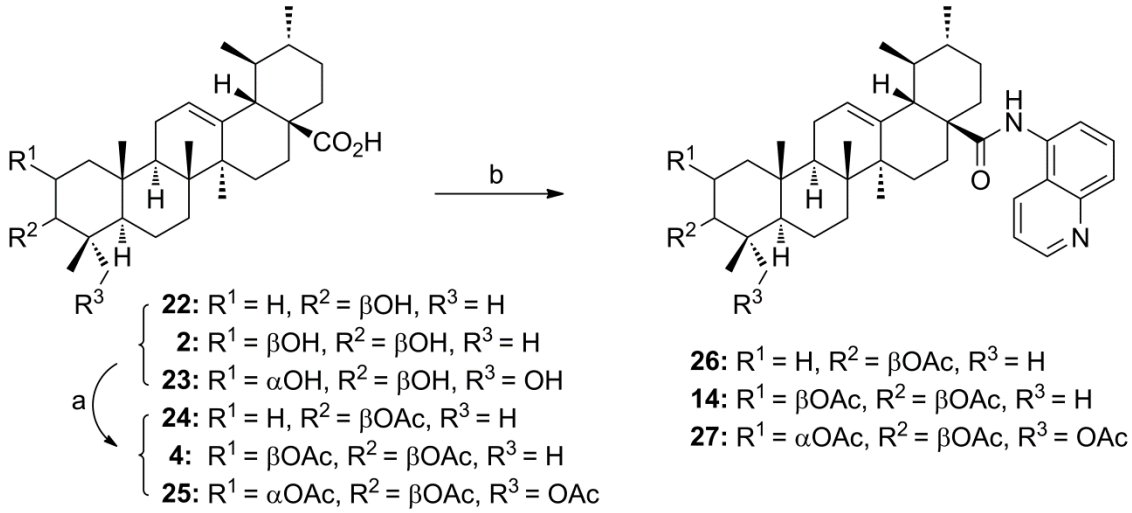


Fig. 2. Comparison of cytotoxicity of 3-quinolinyl amide **9** and 4-isoquinolinyl amide **21** (EC_{50} values from SRB assays in µM) for different human tumor cell lines and nonmalignant mouse fibroblasts (NIH 3T3).

While this re-orientation had only a slight but significant effect in gaining high cytotoxicity, its impact on the selectivity for tumor cells was dramatically enhanced, and selectivity factors greater/equal 50 were observed.

To get a first impression of the impact of the presence of the hydroxyl groups of ring A, some derivatives of ursolic and asiatic acid were synthesized (Scheme 2).



Scheme 2. Synthesis of compounds **4, 14, 24**–**27**: (a) Ac_2O, TEA, DMAP, DCM, 25 °C, 20 h, 65–89%; (b) oxalyl choride, TEA, DMF, DCM, 25°C, 2h; then 5-aminoquinoline, TEA, DMAP, DCM, 25 °C, 2 d, 52–87%.

The cytotoxic activities of acetylated amides of ursolic acid [21-26] has already been investigated by several groups in detail while for asiatic acid mainly amides without additional acetyl groups in ring A have been investigated so far. [27, 28] Screening of our analogs for their cytotoxic activity showed (cf. Table 2) gave for compound **26** (an ursolic acid derived 5-quinolinyl derivative) an almost complete loss of selectivity between cancer cells and nonmalignant mouse fibroblasts. For analog **27** (derived from asiatic acid), however, selectivity was maintained, and an increased cytotoxicity was gained.

Table 2. Cytotoxicity of selected compounds (EC_{50} values in μM from SRB assays after 96 hours of treatment; the values are averaged from three independent experiments performed each in triplicate; confidence interval CI = 95 %). Human cancer cell lines: 518A2 (melanoma), HT29 (colorectal adenocarcinoma), MCF7 (breast adenocarcinoma), A549 (lung adenocarcinoma), A2780 (ovarian carcinoma), 8505C (thyroid carcinoma); NIH 3T3: nonmalignant mouse fibroblasts.

EC_{50}	518A2	HT29	MCF7	A549	A2780	8505C	NIH 3T3
14	2.0±0.8	3.6±0.5	5.5±1.0	3.7±0.5	2.7±0.5	3.2±0.3	> 60
26	3.5±0.9	5.1±0.4	3.9±0.1	5.1±0.6	4.4±0.6	3.5±0.0	3.5±0.2

27	0.5±0.1	0.8±0.1	1.4±0.1	1.1±0.1	0.4±0.2	0.9±0.0	10.2±4.0

Within the panel of compounds investigated so far, two factors appear particularly critical for obtaining cytotoxic as well as tumor-selective compounds, viz. the presence of an isoquinolinyl moiety at position 28 as well as a minimum of three *O*-acetyl groups attached to ring A. Combining these factors led to the synthesis of compound **28**, an 4-isoquinolinyl derivative of asiatic acid whose EC_{50} values are depicted in Figure 3.

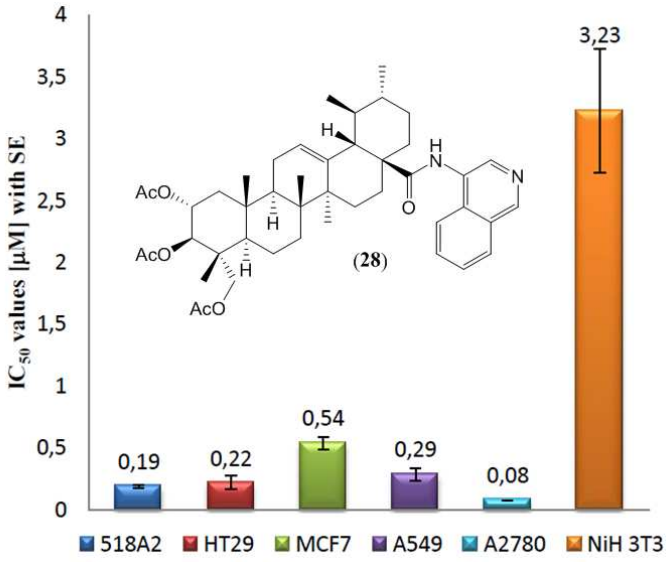


Fig. 3. Cytotoxicity of compound **28** [EC_{50} values (in µM from SRB assays)] for different human tumor cell lines and non-malignant mouse fibroblasts (NIH 3T3).

Hence, we managed the synthesis of a triterpenoid derivative showing both low EC_{50} values (for example, EC_{50} = 80 nM for A2780 human ovarian cancer) but also high tumor/nonmalignant cell selectivity (EC_{50} = 3.23 µM for NIH 3T3, thus a selectivity index of 40).

To have a better understanding of the cytotoxicity of these compounds (and their mode of action) some additional experiments were carried out (Fig. 4). A2780 Ovarian cancer cells were incubated with compounds **9**, **11**, **13**, **15**, **21**, **27** and **28**, and annexin V/propidiuum iodide staining experiments as well as quantitative FACS experiments were performed.

Incubation of the cells with each of the compounds for two days showed a significant increase in the number of cells having died by apoptosis; even more cells had died by secondary necrosis. (Fig. 4 B)

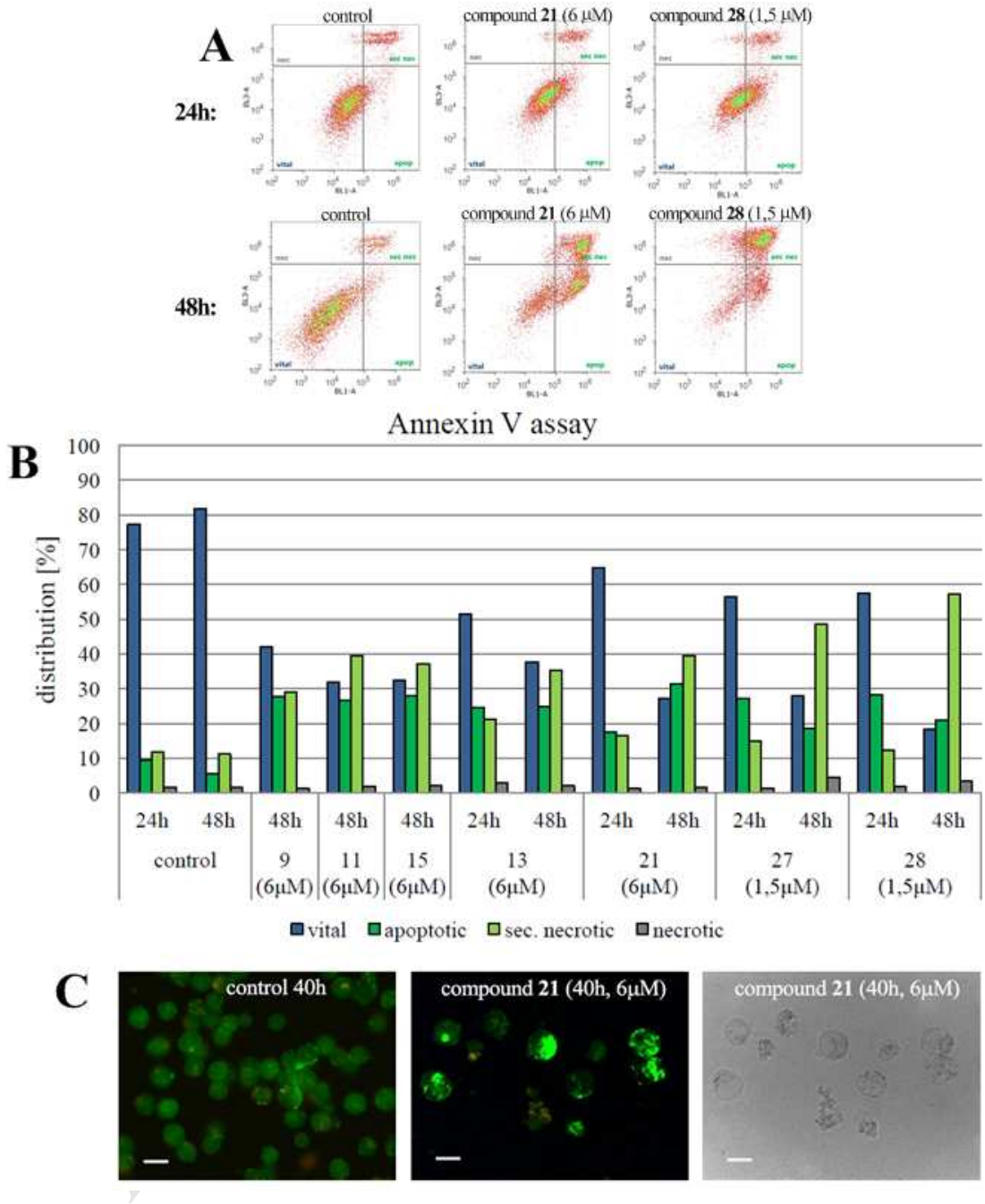


Fig. 4. (A) Representative samples of FACS based annexin V/PI assay of A2780 cells after 24h and 48h treatment with **21** and **28**. (**B**) Evaluation of annexin V/PI assay: treatment of A2780 cells with derivatives **9**, **11**, **13, 15**, **21**, **27** and **28** after 24h and 48h. Diagram with arithmetic population distribution [%], determined by Attune® Cytometric Software vl 1.2.5. (**C**) Fluorescence microscopic and bright-field microscopic images (scale bar = 20 µm): control (A2780, 40h); treatment of A2780 cells with **21**.

Treatment of the cells with compound **28** for 24 h, however, showed the number of apoptotic cells significantly higher than that of cells having died of secondary necrosis. For example, treatment of A2780 cells with compound **28** (concentration as low as 1.5 μM, treatment for 24 h) gave an increase in the number of apoptotic cells (as compared to control) of 20% while the number of cells having died of necrosis or secondary necrosis remained unchanged. Prolongation of the time of incubation (up to 48 hours) led to a decrease of apoptotic cells by 10% while the number of secondary necrotic cells increased by 45% (compared to control).

Furthermore, inspection of dead A2780 cells (after having been incubated with **21**, 6 μM, 40 h) by fluorescence microscopy and application of an acridine orange/propidium iodide staining (AO/PI, Fig. 4C) allowed the identification of apoptose induced modifications of the cell membrane. Comparison of cells (treated either with **21** or untreated) showed for the untreated cells the complete absence of apoptosis while the cells that were treated with **21** showed an unsymmetrical distribution of AO (typically crescent and granular) [27] and membrane blebbing – both findings are characteristic hallmarks for the presence of apoptosis. Some of the cells were shining in orange – these cells were at a secondary necrotic stage.

For the investigation of the cell cycle, A2780 cells were incubated with compounds **9**, **11**, **13**, **15**, **21**, **27** and **28** for 24h and 48h, respectively. Inspection of the results showed after an incubation for 24 h a decrease of the G1 peak together with a simultaneous increase of cells in the S phase and a complete loss of the G2 peak (Fig. 5). After incubation of the cells for 48 h, a decrease of the S phase was observed, and a subG1 peak appeared. This hypodiploidic peak can be explained by a cleavage of DNA; the presence of this peak is usually regarded as one of the typical hallmarks of apoptotic cells. The results from some additional investigations of the cell cycle as well as quantitative FACS measurements have been compiled in the supplementary material.

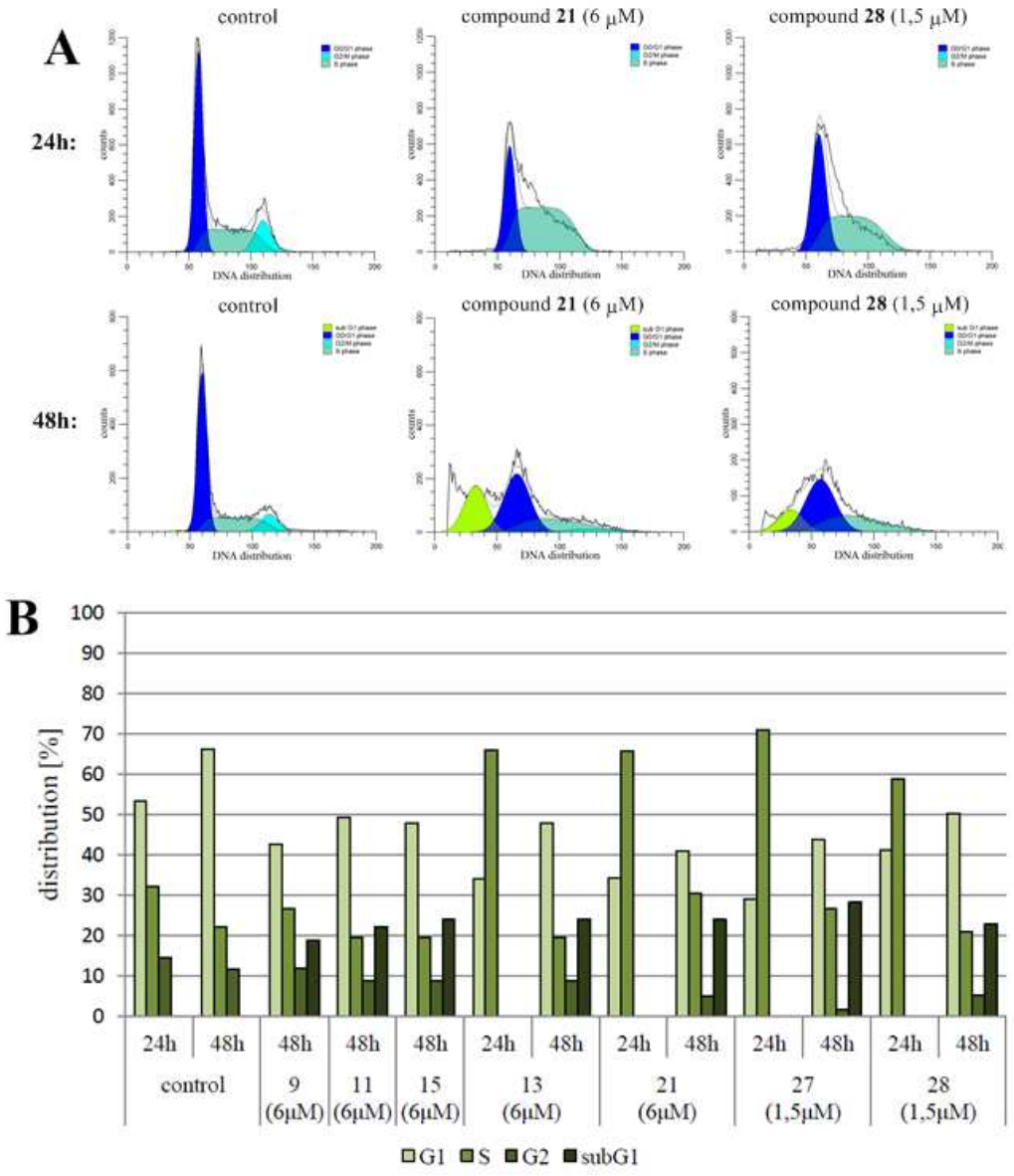


Fig. 5. (**A**): Representative examples for cell cycle evaluation of A2780 cells after 24h and 48h treatment with derivatives **21** and **28** via ModFit V 4.0.5. (**B**): Diagram with arithmetic means of the population distribution [%] of A2780 cells treated with **9**, **11**, **13**, **15**, **21**, **27** and **28** for 24h and 48h.

3. Conclusion

In this study amides of 2,3-O-acetyl-augustic acid and -2-epi-corosolic acid were synthesized, and their cytotoxicity was determined photometric SRB assays. While augustic acid derived 3-quinolinyl amide **9** gave low EC_{50} values in SRB assays (EC_{50} = 2.2 to 9.3 µM) but was cytotoxic for all lines including non-malignant mouse fibroblasts (EC_{50} = 0.9 µM), the

isomeric 4-isoquinolinyl amide **21** was even higher cytotoxic for the tumor cell lines (EC_{50} = 1.2 to 2.6 μM) but significantly less cytotoxic for the mouse fibroblasts NIH 3T3 (EC_{50} > 60 mM). In addition, a triacetylated 4-isoquinolinyl derivative of asiatic acid (**28**) gave rather low EC_{50} = 80 nM (for A2780 ovarian cancer cells) values. As shown by additional experiments (acridine orange/propidium iodide staining, fluorescence spectroscopy and cell cycle investigations) these compounds act mainly by apoptosis. These derivatives can function as ideal starting points for further screening and testing.

4. Experimental Part

4.1.General

Information about equipment and general techniques has been compiled in the supplementary materials section.

4.2.Syntheses

*4.2.1. 2β, 3β-Diacetyloxy-olean-12-en-28-oic acid (**3**)*

To a solution of **1** (950 mg, 2.01 mmol) in dry DCM (100 mL), acetic anhydride (820 mg, 8.04 mmol), triethylamine (915 mg, 9.05 mmol) and DMAP (25 mg, 0.20 mmol) were added, and the mixture was stirred at room temperature for 20 hours. Et_2O (500 mL) was added, and the organic layer was washed with diluted HCl (0.1 M, 1 × 500 mL), water (2 × 500 mL) and brine (1 × 250 mL), dried ($MgSO_4$), filtrated and concentrated in vacuum. The residue was subjected to column chromatography (silica gel, hexane/ethyl acetate, 8:2) to provide **3** (884 mg, 79%) as a white solid; m.p. 322 °C (decomp.) (lit.[28]: 148–150 °C); R_F = 0.24 (silica gel, hexane/ethyl acetate, 8:2); $[\alpha]_D$ = +83.81° (*c* = 0.32, $CHCl_3$); IR (KBr): ν = 2944*s*, 1744*vs*, 1698*s*, 1464*w*, 1436*w*, 1366*m*, 1252*s*, 1196*m*, 1160*w*, 1058*m*, 1030*m* cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 5.33–5.30 (*m*, 1 H, H–2), 5.27 (*dd*, *J* = 3.6, 3.6 Hz, 1 H, H–12), 4.62 (*d*, *J* = 3.9 Hz, 1 H, H–3), 2.82 (*dd*, *J* = 13.9, 4.5 Hz, 1 H, H–18), 2.08 (*s*, 3 H, H–32), 2.02 (*s*, 3 H, H–34), 2.01–1.91 (*m*, 3 H, H–1a + H–16a + H–11a), 1.89–1.69 (*m*, 3 H, H–11b + H–22a + H–15a), 1.64–1.41 (*m*, 7 H, H–6a + H–6b + H–16b + H–19a + H–22b + H–9 + H–7a), 1.38–1.28 (*m*, 3 H, H–7b + H–21a + H–1b), 1.24–1.11 (*m*, 2 H, H–21b + H–19b), 1.20 (*s*, 3 H, H–25), 1.12 (*s*, 3 H, H–27), 1.09–1.03 (*m*, 1 H, H–15b), 1.04 (*s*, 3 H, H–23), 1.00–0.96 (*m*, 1 H, H–5), 0.92 (*s*, 3 H, H–29), 0.90 (*s*, 3 H, H–30), 0.90 (*s*, 3 H, H–24), 0.76 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 184.3 (C–28), 170.9 (C–33), 170.4 (C–31), 143.9 (C–13), 122.6 (C–12), 78.1 (C–3), 69.8 (C–2), 55.4 (C–5), 48.2 (C–9), 46.7 (C–17), 45.9 (C–19),

42.0 (C–1), 41.8 (C–14), 41.1 (C–18), 39.5 (C–8), 37.5 (C–4), 37.0 (C–10), 33.9 (C–21), 33.2 (C–30), 32.6 (C–22), 32.6 (C–7), 30.8 (C–20), 29.3 (C–24), 27.7 (C–15), 26.2 (C–27), 23.7 (C–29), 23.6 (C–11), 22.9 (C–16), 21.4 (C–32), 21.0 (C–34), 18.1 (C–6), 17.8 (C–23), 17.5 (C–26), 16.1 (C–25) ppm; MS (ESI): *m*/*z* (%) = 557.2 ($[M+H]^+$, 13), 574.3 ($[M+NH_4]^+$, 100), 579.4 ($[M+Na]^+$, 21), 1249.1 ($[2M+Na]^+$, 87); analysis calculated for $C_{34}H_{52}O_6$ (556.77): C 73.34, H 9.41; found: C 73.18, H 9.57.

*4.2.2. 2β, 3β-Diacetyloxy-urs-12-en-28-oic acid (**4**)*

Following the procedure given for **1**, from **2** compound **4** (728 mg, 65%) was obtained as a white solid; m.p. 247–252 °C; R_F = 0.48 (silica gel, hexane/ethyl acetate, 7:3); $[\alpha]_D$ = +75.00° (*c* = 0.39, $CHCl_3$); IR (KBr): ν = 3410*m*, 2950*s*, 2872*m*, 1746*vs*, 1698*s*, 1458*m*, 1398*m*, 1370*s*, 1254*vs*, 1234*s*, 1194*m*, 1160*m*, 1056*m*, 1030*s*, 972*m* cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 5.32 (*ddd*, *J* = 3.8, 3.8, 3.5 Hz, 1 H, H–2), 5.24 (*dd*, *J* = 3.6, 3.6 Hz, 1 H, H–12), 4.63 (*d*, *J* = 3.9 Hz, 1 H, H–3), 2.18 (*d*, *J* = 11.2 Hz, 1 H, H–18), 2.08–1.84 (*m*, 4 H, H–11a + H–11b + H–15a + H–16a), 2.04 (*s*, 3 H, H–32), 2.02 (*s*, 3 H, H–34), 1.97 (*dd*, *J* = 6.8, 3.9 Hz, 1 H, H–1a), 1.75–1.63 (*m*, 3 H, H–16b + H–22a + H–22b), 1.61–1.43 (*m*, 5 H, H–6a + H–6b + H–7a + H–9 + H–21a), 1.39–1.24 (*m*, 4 H, H–1b + H–7b + H–19 + H–21b), 1.22 (*s*, 3 H, H–25), 1.14–1.03 (*m*, 1 H, H–15b), 1.07 (*s*, 3 H, H–27), 1.04 (*s*, 3 H, H–23), 1.03–0.96 (*m*, 2 H, H–5 + H–20), 0.95 (*d*, *J* = 6.3 Hz, 3 H, H–30), 0.90 (*s*, 3 H, H–24), 0.86 (*d*, *J* = 6.4 Hz, 3 H, H–29), 0.79 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 183.7 (C–28), 170.9 (C–33), 170.4 (C–31), 138.3 (C–13), 125.7 (C–12), 78.1 (C–3), 69.8 (C–2), 55.3 (C–5), 52.6 (C–18), 48.1 (C–17), 48.1 (C–9), 42.2 (C–14), 42.1 (C–1), 39.8 (C–8), 39.1 (C–19), 39.0 (C–20), 37.5 (C–4), 36.9 (C–22), 36.9 (C–10), 32.9 (C–7), 30.7 (C–21), 29.3 (C–24), 28.0 (C–15), 24.1 (C–16), 23.8 (C–27), 23.5 (C–11), 21.4 (C–32), 21.3 (C–30), 21.0 (C–34), 18.1 (C–6), 17.8 (C–23), 17.3 (C–26), 17.2 (C–29), 16.3 (C–25) ppm; MS (ESI): *m*/*z* (%) = 555.5 ($[M-H]^-$, 63), 1111.2 ($[2M-H]^-$, 100), 1133.5 ($[2M-2H+Na]^-$, 28); analysis calculated for $C_{34}H_{52}O_6$ (556.77): C 73.34, H 9.41; found: C 73.09, H 9.61.

*4.2.3. 2β, 3β-Diacetyloxy-olean-12-en-28-oic acid 3-pyridinyl amide (**5**)*

To a solution of **3** (100 mg, 0.18 mmol) in dry DCM (10 mL), oxalyl chloride (70 mg, 0.55 mmol), triethylamine (3 mg, 0.03 mmol) and DMF (2 mg, 0.03 mmol) were added, and the mixture was stirred at room temperature for 2 hours. The solvent was removed under reduced pressure, the residue was dissolved in dry THF (1 × 10 mL), the solvent was removed, and the residue was immediately dissolved in dry DCM (10 mL). The solution was

cooled to 0 °C and triethylamine (24 mg, 0.24 mmol), DMAP (2 mg, 0.02 mmol) as well as 3-aminopyridine (52 mg, 0.55 mmol) were added. After 2 days of stirring, Et_2O (100 mL) was added, the organic was washed with diluted HCl (0.1 M, 1 × 100 mL), water (2 × 100 mL) and brine (1 × 50 mL), dried ($MgSO_4$), filtrated and evaporated to dryness. Column chromatography (silica gel, hexane/ethyl acetate, 7:3) afforded **5** (85 mg, 75%) as a white solid; m.p. 156–160 °C; R_F = 0.60 (silica gel, chloroform/ethyl acetate, 1:1); $[\alpha]_D$ = +70.84° (*c* = 0.34, $CHCl_3$); UV-vis ($CHCl_3$): λ_{max} (log ε) = 244 nm (3.81), 279 nm (3.30) ; IR (KBr): ν = 3388*m*, 2950*s*, 2878*m*, 1746*vs*, 1684*m*, 1586*m*, 1524*s*, 1480*s*, 1418*m*, 1366*s*, 1252*vs*, 1234*s*, 1192*m*, 1158*m*, 1056*m*, 1030*m*, 708*m* cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.40 (*d*, *J* = 2.5 Hz, 1 H, H–36), 8.31 (*dd*, *J* = 4.7, 1.4 Hz, 1 H, H–37), 8.22 (*ddd*, *J* = 8.4, 2.5, 1.5 Hz, 1 H, H–39), 7.77 (*s*, 1 H, NH), 7.24 (*dd*, *J* = 8.3, 4.7 Hz, 1 H, H–38), 5.57 (*dd*, *J* = 3.4, 3.4 Hz, 1 H, H–12), 5.31 (*ddd*, *J* = 3.7, 3.7, 3.7 Hz, 1 H, H–2), 4.60 (*d*, *J* = 3.9 Hz, 1 H, H–3), 2.67 (*dd*, *J* = 12.7, 3.2 Hz, 1 H, H–18), 2.12–1.90 (*m*, 4 H, H–16a + H–11a + H–11b + H–1a), 2.04 (*s*, 3 H, H–32), 2.02 (*s*, 3 H, H–34), 1.87–1.65 (*m*, 4 H, H–19a + H–22a + H–22b + H–16b), 1.64–1.52 (*m*, 3 H, H–15a + H–6a + H–9), 1.52–1.22 (*m*, 7 H, H–7a + H–7b + H–6b + H–21a + H–21b + H–1b + H–19b), 1.19 (*s*, 3 H, H–27), 1.14 (*s*, 3 H, H–25), 1.09 (*ddd*, *J* = 14.1, 2.8, 2.8 Hz, 1 H, H–15b), 1.02 (*s*, 3 H, H–23), 0.98–0.92 (*m*, 1 H, H–5), 0.93 (*s*, 6 H, H–29 + H–30), 0.88 (*s*, 3 H, H–24), 0.71 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.3 (C–28), 170.8 (C–33), 170.4 (C–31), 145.3 (C–37), 145.2 (C–13), 141.1 (C–36), 134.9 (C–35), 127.2 (C–39), 123.8 (C–38), 123.5 (C–12), 78.0 (C–3), 69.6 (C–2), 55.2 (C–5), 48.1 (C–9), 47.5 (C–17), 46.7 (C–19), 42.7 (C–18), 42.5 (C–14), 42.1 (C–1), 39.7 (C–8), 37.4 (C–4), 36.8 (C–10), 34.2 (C–21), 33.0 (C–30), 32.5 (C–22), 32.4 (C–7), 30.9 (C–20), 29.2 (C–24), 27.4 (C–15), 25.9 (C–27), 24.2 (C–16), 23.9 (C–11), 23.7 (C–29), 21.4 (C–32), 21.0 (C–34), 18.0 (C–6), 17.8 (C–23), 17.2 (C–26), 16.1 (C–25) ppm; MS (ESI): *m*/*z* (%) = 633.5 ($[M+H]^+$, 100), 1265.1 ($[2M+H]^+$, 16); analysis calculated for $C_{39}H_{56}N_2O_5$ (632.87): C 74.01, H 8.92, N 4.43; found: C 73.82, H 9.03, N 4.19.

*4.2.4. 2β, 3β-Diacetyloxy-ursan-12-en-28-oic acid 3-pyridinyl amide (**6**)*

As described for **5**, compound **6** (120 mg, 56%) was obtained from **4** and 3-aminopyridine as a white solid; m.p. 146–149 °C; R_F = 0.42 (silica gel, hexane/ethyl acetate, 4:6); $[\alpha]_D$ = +51.20° (*c* = 0.35, $CHCl_3$); UV-vis ($CHCl_3$): λ_{max} (log ε) = 244 nm (4.02), 279 nm (3.57); IR (KBr): ν = 3394*m*, 2928*s*, 2872*m*, 1746*vs*, 1684*m*, 1618*w*, 1586*m*, 1526*s*, 1480*s*, 1485*m*, 1418*s*, 1398*m*, 1370*s*, 1326*m*, 1252*vs*, 1234*vs*, 1192*m*, 1156*m*, 1106*w*, 1078*m*, 1056*m*, 1030*s*, 972*m*, 944*m*, 754*m*, 706*m* cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.39 (*d*, *J* = 2.2 Hz, 1 H,

H–36), 8.31 (*dd*, *J* = 4.7, 1.1 Hz, 1 H, H–37), 8.19 (*ddd*, *J* = 8.4, 2.4, 1.4 Hz, 1 H, H–39), 7.76 (*s*, 1 H, NH), 7.24 (*dd*, *J* = 8.3, 4.7 Hz, 1 H, H–38), 5.51 (*dd*, *J* = 3.5, 3.5 Hz, 1 H, H–12), 5.32 (*ddd*, *J* = 3.8, 3.8, 3.5 Hz, 1 H, H–2), 4.61 (*d*, *J* = 3.9 Hz, 1 H, H–3), 2.12–1.93 (*m*, 6 H, H–1a + H–11a + H–11b + H–16a + H–18 + H–22a), 2.04 (*s*, 3 H, H–32), 2.02 (*s*, 3 H, H–34), 1.87–1.81 (*m*, 1 H, H–16b), 1.75–1.67 (*m*, 1 H, H–15a), 1.62–1.45 (*m*, 6 H, H–6a + H–7a + H–9 + H–19 + H–21a + H–22b), 1.42 (*d*, *J* = 11.8, 2.9 Hz, 1 H, H–6b), 1.39–1.26 (*m*, 3 H, H–1b + H–7b + H–21b), 1.15 (*s*, 3 H, H–25), 1.13 (*s*, 3 H, H–27), 1.11–1.08 (*m*, 1 H, H–15b), 1.04–0.90 (*m*, 2 H, H–5 + H–20), 1.02 (*s*, 3 H, H–23), 0.98 (*d*, *J* = 6.0 Hz, 3 H, H–30), 0.92 (*d*, *J* = 6.5 Hz, 3 H, H–29), 0.89 (*s*, 3 H, H–24), 0.70 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.1 (C–28), 170.8 (C–33), 170.4 (C–31), 145.2 (C–37), 141.0 (C–36), 140.5 (C–13), 135.0 (C–35), 127.2 (C–39), 126.3 (C–12), 123.8 (C–38), 78.0 (C–3), 69.6 (C–2), 55.2 (C–5), 54.4 (C–18), 49.0 (C–17), 48.1 (C–9), 43.0 (C–14), 42.2 (C–1), 40.0 (C–19), 39.8 (C–8), 39.2 (C–20), 37.4 (C–4), 37.2 (C–22), 36.8 (C–10), 32.7 (C–7), 31.0 (C–21), 29.3 (C–24), 27.9 (C–15), 25.2 (C–16), 23.8 (C–11), 23.5 (C–27), 21.4 (C–32), 21.3 (C–30), 21.0 (C–34), 18.0 (C–6), 17.8 (C–23), 17.4 (C–29), 17.1 (C–26), 16.3 (C–25) ppm; MS (ESI): *m*/*z* (%) = 633.7 ($[M+H]^+$, 100), 1265.5 ($[2M+H]^+$, 46); analysis calculated for $C_{39}H_{56}N_2O_5$ (632.87): C 74.01, H 8.92, N 4.43; found: C 73.84, H 9.09, N 4.35.

4.2.5. 2β, 3β-Diacetyloxy-olean-12-en-28-oic acid 4-pyridinyl amide (7)

As described for **5**, compound **7** (62 mg, 55%) was obtained from **3** and 4-aminopyridine as a white solid; m.p. 171–174 °C; R_F = 0.31 (silica gel, chloroform/ethyl acetate, 1:1); $[\alpha]_D$ = +32.92° (*c* = 0.31, MeOH); UV-vis (MeOH): λ_{max} (log ε) = 248 nm (4.21); IR (KBr): ν = 3386*m*, 2950*s*, 2878*m*, 1746*vs*, 1696*m*, 1588*s*, 1506*s*, 1474*m*, 1412*m*, 1366*s*, 1326*m*, 1252*vs*, 1236*s*, 1200*m*, 1158*m*, 1056*m*, 1030*m*, 1012*m*, 992*m*, 822*m* cm^{-1}; ^{1}H NMR (500 MHz, CD_3OD): δ = 8.39–8.36 (*m*, 2 H, H–37), 7.70–7.67 (*m*, 2 H, H–36), 5.42 (*dd*, *J* = 3.5, 3.5 Hz, 1 H, H–12), 5.32 (*ddd*, *J* = 3.7, 3.7, 3.7 Hz, 1 H, H–2), 4.58 (*d*, *J* = 3.9 Hz, 1 H, H–3), 2.99 (*dd*, *J* = 13.2, 3.4 Hz, 1 H, H–18), 2.20 (*ddd*, *J* = 14.0, 14.0, 3.8 Hz, 1 H, H–16a), 2.07–1.90 (*m*, 3 H, H–11a + H–11b + H–1a), 2.02 (*s*, 3 H, H–32), 1.99 (*s*, 3 H, H–34), 1.86–1.75 (*m*, 2 H, H–19a + H–16b), 1.73–1.61 (*m*, 4 H, H–22a + H–22b + H–15a + H–9), 1.61–1.42 (*m*, 4 H, H–6a + H–6b + H–7a + H–21a), 1.38 (*dd*, *J* = 15.0, 3.7 Hz, 1 H, H–1b), 1.32–1.18 (*m*, 3 H, H–7b + H–21b + H–19b), 1.21 (*s*, 3 H, H–27), 1.21 (*s*, 3 H, H–25), 1.12 (*ddd*, *J* = 13.9, 3.0, 3.0 Hz, 1 H, H–15b), 1.06 (*s*, 3 H, H–23), 1.05–1.01 (*m*, 1 H, H–5), 0.98 (*s*, 3 H, H–29), 0.94 (*s*, 3 H, H–30), 0.90 (*s*, 3 H, H–24), 0.72 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, CD_3OD): δ = 179.4 (C–28), 172.5 (C–33), 172.1 (C–31), 150.5 (C–37), 148.4 (C–35), 145.3 (C–13),

124.0 (C–12), 115.8 (C–36), 79.6 (C–3), 70.8 (C–2), 56.4 (C–5), 49.3 (C–9), 48.9 (C–17), 47.4 (C–19), 43.1 (C–14), 42.8 (C–1), 42.3 (C–18), 40.7 (C–8), 38.3 (C–4), 37.9 (C–10), 35.0 (C–21), 33.6 (C–7), 33.5 (C–30), 33.4 (C–22), 31.6 (C–20), 29.5 (C–24), 28.5 (C–15), 26.6 (C–27), 24.6 (C–11), 24.1 (C–29), 23.8 (C–16), 21.2 (C–32), 20.8 (C–34), 19.0 (C–6), 18.2 (C–23), 17.7 (C–26), 16.6 (C–25) ppm; MS (ESI): *m*/*z* (%) = 633.4 ($[M+H]^+$, 100); analysis calculated for $C_{39}H_{56}N_2O_5$ (632.87): C 74.01, H 8.92, N 4.43; found: C 73.79, H 9.13, N 4.22.

*4.2.6. 2β, 3β-Diacetyloxy-ursan-12-en-28-oic acid 4-pyridinyl amide (**8**)*

As described for **5**, compound **8** (41 mg, 56%) was obtained from **4** and 4-aminopyridine as a white solid; m.p. 160–163 °C; R_F = 0.23 (silica gel, hexane/ethyl acetate, 3:7); $[\alpha]_D$ = +41.60° (*c* = 0.86, $CHCl_3$); UV-vis ($CHCl_3$): λ_{max} (log ε) = 248 nm (3.90); IR (KBr): ν = 3422*s*, 2950*m*, 2872*w*, 1744*m*, 1690*m*, 1636*m*, 1588*m*, 1506*m*, 1432*s*, 1414*s*, 1384*vs*, 1328*s*, 1252*m*, 1234*m*, 1196*w*, 1156*w*, 1052*w*, 1032*w*, 1010*w* cm^{-1}; ^1H NMR (500 MHz, CD_3OD): δ = 8.36 (*dd*, *J* = 5.0, 1.5 Hz, 2 H, H–37), 7.67 (*dd*, *J* = 4.9, 1.6 Hz, 2 H, H–36), 5.42 (*dd*, *J* = 3.6, 3.6 Hz, 1 H, H–12), 5.32 (*ddd*, *J* = 3.9, 3.9, 3.2 Hz, 1 H, H–2), 4.59 (*d*, *J* = 4.0 Hz, 1 H, H–3), 2.37 (*d*, *J* = 10.4 Hz, 1 H, H–18), 2.23–2.15 (*m*, 1 H, H–16a), 2.03–1.95 (*m*, 3 H, H–1a + H–11a + H–11b), 2.01 (*s*, 3 H, H–32), 1.99 (*s*, 3 H, H–34), 1.91–1.82 (*m*, 2 H, H–15a + H–16b), 1.82–1.76 (*m*, 1 H, H–22a), 1.70–1.46 (*m*, 7 H, H–6a + H–6b + H–7a + H–9 + H–19 + H–21a + H–22b), 1.44–1.36 (*m*, 2 H, H–1b + H–21b), 1.35–1.30 (*m*, 1 H, H–7b), 1.19 (*s*, 3 H, H–25), 1.17 (*s*, 3 H, H–27), 1.14–1.08 (*m*, 2 H, H–15b + H–20), 1.07–1.01 (*m*, 1 H, H–5), 1.06 (*s*, 3 H, H–23), 1.00 (*d*, *J* = 6.4 Hz, 3 H, H–30), 0.95 (*d*, *J* = 6.5 Hz, 3 H, H–29), 0.90 (*s*, 3 H, H–24), 0.70 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, CD_3OD): δ = 179.4 (C–28), 172.5 (C–33), 172.1 (C–31), 150.5 (C–37), 148.4 (C–35), 140.1 (C–13), 127.1 (C–12), 115.7 (C–36), 79.6 (C–3), 70.7 (C–2), 56.3 (C–5), 53.8 (C–18), 50.2 (C–17), 49.1 (C–9), 43.4 (C–14), 43.0 (C–1), 40.9 (C–8), 40.7 (C–19), 40.1 (C–20), 38.3 (C–4), 37.8 (C–10), 37.8 (C–22), 33.8 (C–7), 31.7 (C–21), 29.5 (C–24), 28.9 (C–15), 25.0 (C–16), 24.5 (C–11), 24.3 (C–27), 21.5 (C–30), 21.1 (C–32), 20.8 (C–34), 19.0 (C–6), 18.2 (C–23), 17.7 (C–29), 17.6 (C–26), 16.6 (C–25) ppm; MS (ESI): *m*/*z* (%) = 633.5 ($[M+H]^+$, 100), 1287.5 ($[2M+Na]^+$, 1); analysis calculated for $C_{39}H_{56}N_2O_5$ (632.87): C 74.01, H 8.92, N 4.43; found: C 73.75, H 8.83, N 4.31.

*4.2.7. 2β, 3β-Diacetyloxy-olean-12-en-28-oic acid 3-quinolinyl amide (**9**)*

As described for **5**, compound **9** (88 mg, 72%) was obtained from **3** and 3-aminoquinoline as a white solid; m.p. 174–177 °C; R_F = 0.69 (silica gel, chloroform/ethyl acetate, 1:1); $[\alpha]_D$ = +110.93° (*c* = 0.32, $CHCl_3$); UV-vis ($CHCl_3$): λ_{max} (log ε) = 254 nm (4.60), 322 nm (3.69),

335 nm (3.70); IR (KBr): ν = 3388*w*, 2948*s*, 2876*m*, 1746*vs*, 1684*m*, 1608*w*, 1534*s*, 1486*s*, 1468*m*, 1420*m*, 1364*s*, 1252*vs*, 1196*m*, 1158*m*, 1056*m*, 1030*m* cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.91 (*d*, *J* = 2.4 Hz, 1 H, H–43), 8.55 (*d*, *J* = 2.6 Hz, 1 H, H–36), 8.03–8.00 (*m*, 2 H, H–38 + NH), 7.78 (*d*, *J* = 8.0 Hz, 1 H, H–39), 7.61 (*ddd*, *J* = 8.4, 6.9, 1.4 Hz, 1 H, H–40), 7.52 (*ddd*, *J* = 8.1, 6.9, 1.2 Hz, 1 H, H–41), 5.65 (*dd*, *J* = 3.5, 3.5 Hz, 1 H, H–12), 5.32 (*ddd*, *J* = 3.8, 3.8, 3.8 Hz, 1 H, H–2), 4.61 (*d*, *J* = 3.9 Hz, 1 H, H–3), 2.75 (*dd*, *J* = 12.9, 3.6 Hz, 1 H, H–18), 2.18–1.95 (*m*, 4 H, H–16a + H–11a + H–11b + H–1a), 2.04 (*s*, 3 H, H–32), 2.02 (*s*, 3 H, H–34), 1.90–1.71 (*m*, 4 H, H–19a + H–22a + H–22b + H–16b), 1.68–1.52 (*m*, 3 H, H–15a + H–6a + H–9), 1.52–1.23 (*m*, 7 H, H–7a + H–7b + H–6b + H–21a + H–21b + H–1b + H–19b), 1.22 (*s*, 3 H, H–27), 1.15–1.09 (*m*, 1 H, H–15b), 1.12 (*s*, 3 H, H–25), 1.01 (*s*, 3 H, H–23), 0.98–0.94 (*m*, 1 H, H–5), 0.97 (*s*, 3 H, H–29), 0.96 (*s*, 3 H, H–30), 0.88 (*s*, 3 H, H–24), 0.70 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.6 (C–28), 170.9 (C–33), 170.4 (C–31), 145.4 (C–37), 145.3 (C–13), 143.8 (C–36), 131.6 (C–35), 129.1 (C–38), 128.5 (C–42), 128.3 (C–40), 128.0 (C–39), 127.4 (C–41), 123.8 (C–43), 123.7 (C–12), 78.0 (C–3), 69.6 (C–2), 55.2 (C–5), 48.1 (C–9), 47.7 (C–17), 46.8 (C–19), 42.8 (C–18), 42.6 (C–14), 42.1 (C–1), 39.7 (C–8), 37.4 (C–4), 36.8 (C–10), 34.3 (C–21), 33.1 (C–30), 32.5 (C–22), 32.4 (C–7), 30.9 (C–20), 29.2 (C–24), 27.4 (C–15), 26.0 (C–27), 24.4 (C–16), 23.9 (C–11), 23.7 (C–29), 21.4 (C–32), 21.0 (C–34), 18.0 (C–6), 17.8 (C–23), 17.2 (C–26), 16.1 (C–25) ppm; MS (ESI): *m*/*z* (%) = 683.5 ($[M+H]^+$, 100); analysis calculated for $C_{43}H_{58}N_2O_5$ (682.93): C 75.62, H 8.56, N 4.10; found: C 75.47, H 8.77, N 3.98.

*4.2.8. 2β, 3β-Diacetyloxy-ursan-12-en-28-oic acid 3-quinolinyl amide (**10**)*

As described for **5**, compound **10** (60 mg, 65%) was obtained from **4** and 3-aminoquinoline as a white solid; m.p. 141–143 °C; R_F = 0.38 (silica gel, hexane/ethyl acetate, 6:4); $[\alpha]_D$ = +84.40° (*c* = 0.31, $CHCl_3$); UV-vis ($CHCl_3$): λ_{max} (log ε) = 254 nm (4.60), 322 nm (3.66), 336 nm (3.66); IR (KBr): ν = 3396*m*, 2924*s*, 2870*m*, 2852*m*, 1744*vs*, 1684*m*, 1608*w*, 1576*w*, 1534*s*, 1486*m*, 1468*m*, 1458*m*, 1420*m*, 1396*m*, 1364*s*, 1252*vs*, 1234*s*, 1196*m*, 1158*w*, 1144*w*, 1116*w*, 1102*w*, 1078*w*, 1056*m*, 1030*m* cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.86 (*d*, *J* = 2.5 Hz, 1 H, H–43), 8.55 (*d*, *J* = 2.6 Hz, 1 H, H–36), 8.02 (*d*, *J* = 9.1 Hz, 1 H, H–38), 7.79–7.77 (*m*, 1 H, H–41), 7.63–7.59 (*m*, 1 H, H–39), 7.54–7.50 (*m*, 1 H, H–40), 5.59 (*dd*, *J* = 3.6, 3.6 Hz, 1 H, H–12), 5.32 (*ddd*, *J* = 3.8, 3.8, 3.5 Hz, 1 H, H–2), 4.61 (*d*, *J* = 3.9 Hz, 1 H, H–3), 2.17–1.97 (*m*, 6 H, H–1a + H–11a + H–11b + H–16a + H–18 + H–22a), 2.04 (*s*, 3 H, H–32), 2.02 (*s*, 3 H, H–34), 1.92–1.86 (*m*, 1 H, H–16b), 1.79–1.70 (*m*, 1 H, H–15a), 1.68–1.46 (*m*, 6 H, H–6a + H–7a + H–9 + H–19 + H–21a + H–22b), 1.44–1.34 (*m*, 3 H, H–1b + H–

6b + H–21b), 1.32–1.26 (*m*, 1 H, H–7b), 1.17–1.10 (*m*, 1 H, H–15b), 1.15 (*s*, 3 H, H–27), 1.12 (*s*, 3 H, H–25), 1.08–0.98 (*m*, 4 H, H–20 + H–30), 1.00 (*s*, 3 H, H–23), 0.97–0.93 (*m*, 1 H, H–5), 0.95 (*d*, *J* = 6.5 Hz, 3 H, H–29), 0.88 (*s*, 3 H, H–24), 0.68 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.4 (C–28), 170.9 (C–33), 170.4 (C–31); 145.3 (C–42), 143.8 (C–43), 140.7 (C–13), 131.7 (C–35), 129.1 (C–41), 128.5 (C–37), 128.2 (C–39), 128.0 (C–40), 127.3 (C–38), 126.4 (C–12), 123.7 (C–36), 78.0 (C–3), 69.6 (C–2), 55.2 (C–5), 54.4 (C–18), 49.1 (C–17), 48.1 (C–9), 43.0 (C–14), 42.2 (C–1), 40.0 (C–19), 39.8 (C–8), 39.2 (C–20), 37.4 (C–22), 37.2 (C–4), 36.8 (C–10), 32.7 (C–7), 31.0 (C–21), 29.3 (C–24), 28.0 (C–15), 25.4 (C–16), 23.8 (C–11), 23.5 (C–27), 21.4 (C–32), 21.3 (C–30), 21.0 (C–34), 18.0 (C–6), 17.8 (C–23), 17.4 (C–29), 17.2 (C–26), 16.3 (C–25) ppm; MS (ESI): *m*/*z* (%) = 683.5 ($[M+H]^+$, 100), 1365.3 ($[2M+H]^+$, 38); analysis calculated for $C_{43}H_{58}N_2O_5$ (682.93): C 75.62, H 8.56, N 4.10; found: C 75.51, H 8.89, N 3.99.

*4.2.9. 2β, 3β-Diacetyloxy-olean-12-en-28-oic acid 4-quinolinyl amide (**11**)*

As described for **5**, compound **11** (49 mg, 40%) was obtained from **3** and 4-aminoquinoline as a white solid; m.p. 226–227 °C; R_F = 0.72 (silica gel, chloroform/ethyl acetate, 1:1); $[\alpha]_D$ = +17.60° (*c* = 0.29, $CHCl_3$); UV-vis ($CHCl_3$): λ_{max} (log ε) = 299 nm (4.03), 315 nm (3.88); IR (KBr): ν = 2946*s*, 2870*m*, 1744*vs*, 1692*m*, 1624*m*, 1570*m*, 1522*s*, 1494*s*, 1458*s*, 1432*s*, 1396*m*, 1366*m*, 1314*m*, 1252*vs*, 1236*s*, 1162*m*, 1056*m*, 1030*m*, 1012*m* cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.83 (*d*, *J* = 5.1 Hz, 1 H, H–37), 8.58 (*s*, 1 H, NH), 8.49 (*d*, *J* = 5.1 Hz, 1 H, H–36), 8.13 (*d*, *J* = 8.3 Hz, 1 H, H–39), 7.76–7.71 (*m*, 2 H, H–41 + H–42), 7.59 (*ddd*, *J* = 8.3, 7.0, 1.2 Hz, 1 H, H–40), 5.76 (*dd*, *J* = 3.5, 3.5 Hz, 1 H, H–12), 5.30 (*ddd*, *J* = 3.8, 3.8, 3.8 Hz, 1 H, H–2), 4.60 (*d*, *J* = 3.9 Hz, 1 H, H–3), 2.85 (*dd*, *J* = 12.9, 3.8 Hz, 1 H, H–18), 2.16 (*ddd*, *J* = 14.0, 14.0, 3.8 Hz, 1 H, H–16a), 2.03–1.82 (*m*, 6 H, H–11a + H–11b + H–1a + H–19a + H–22a + H–16b), 2.02 (*s*, 3 H, H–32), 2.02 (*s*, 3 H, H–34), 1.78 (*ddd*, *J* = 14.0, 14.0, 4.3 Hz, 1 H, H–22b), 1.66 (*ddd*, *J* = 13.9, 13.9, 4.3 Hz, 1 H, H–15a), 1.61–1.41 (*m*, 4 H, H–9 + H–6a + H–21a + H–7a), 1.41–1.21 (*m*, 5 H, H–6b + H–19b + H–1b + H–21b + H–7b), 1.23 (*s*, 3 H, H–27), 1.14 (*ddd*, *J* = 13.7, 3.1, 3.1 Hz, 1 H, H–15b), 0.99 (*s*, 3 H, H–25), 0.98 (*s*, 3 H, H–29), 0.98 (*s*, 6 H, H–30 + H–23), 0.96–0.91 (*m*, 1 H, H–5), 0.87 (*s*, 3 H, H–24), 0.51 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.5 (C–28), 170.9 (C–33), 170.4 (C–31), 151.6 (C–37), 149.0 (C–35), 145.3 (C–13), 140.7 (C–38), 130.9 (C–39), 129.4 (C–41), 126.3 (C–40), 124.1 (C–12), 120.2 (C–43), 118.9 (C–42), 110.3 (C–36), 78.0 (C–3), 69.6 (C–2), 55.3 (C–5), 48.8 (C–17), 48.1 (C–9), 46.9 (C–19), 43.1 (C–18), 42.5 (C–14), 42.0 (C–1), 39.6 (C–8), 37.4 (C–4), 36.7 (C–10), 34.2 (C–21), 33.1 (C–30), 32.8 (C–22), 32.4 (C–7), 30.9

(C–20), 29.2 (C–24), 27.4 (C–15), 26.2 (C–27), 24.5 (C–16), 23.8 (C–29), 23.7 (C–11), 21.4 (C–32), 21.0 (C–34), 17.9 (C–6), 17.7 (C–23), 16.8 (C–26), 16.0 (C–25) ppm; MS (ESI): *m*/*z* (%) = 683.4 ($[M+H]^+$, 100); analysis calculated for $C_{43}H_{58}N_2O_5$ (682.93): C 75.62, H 8.56, N 4.10; found: C 75.41, H 8.81, N 4.00.

*4.2.10. 2β, 3β-Diacetyloxy-ursan-12-en-28-oic acid 4-quinolinyl amide (**12**)*

As described for **5**, compound **12** (47 mg, 38%) was obtained from **4** and 4-aminoquinoline as a white solid; m.p. 162–164 °C; R_F = 0.56 (silica gel, chloroform/ethyl acetate, 1:1); $[\alpha]_D$ = -9.12° (*c* = 0.27, $CHCl_3$); UV-vis ($CHCl_3$): λ_{max} (log ε) = 300 nm (4.03), 315 nm (3.90); IR (KBr): ν = 2928*s*, 2872*m*, 1744*vs*, 1692*m*, 1570*m*, 1518*s*, 1494*s*, 1458*s*, 1394*m*, 1370*m*, 1310*m*, 1252*vs*, 1234*s*, 1196*m*, 1158*w*, 1056*m*, 1030*m* cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.82 (*d*, *J* = 5.2 Hz, 1 H, H–37), 8.56 (*s*, 1 H, NH), 8.46 (*d*, *J* = 5.2 Hz, 1 H, H–36), 8.18 (*d*, *J* = 8.5 Hz, 1 H, H–39), 7.77–7.73 (*m*, 2 H, H–41 + H–42), 7.63–7.58 (*m*, 1 H, H–40), 5.69–5.66 (*m*, 1 H, H–12), 5.32–5.28 (*m*, 1 H, H–2), 4.59 (*d*, *J* = 3.6 Hz, 1 H, H–3), 2.22–1.91 (*m*, 7 H, H–18 + H–16a + H–16b + H–11a + H–11b + H–22a + H–1a), 2.01 (*s*, 6 H, H–32 + H–34), 1.81–1.31 (*m*, 10 H, H–15a + H–22b + H–21a + H–21b + H–19 + H–9 + H–7a + H–6a + H–6b + H–1b), 1.31–1.24 (*m*, 1 H, H–7b), 1.18–1.12 (*m*, 1 H, H–15b), 1.16 (*s*, 3 H, H–27), 1.11–0.91 (*m*, 2 H, H–20 + H–5), 1.03–0.98 (*m*, 12 H, H–23 + H–25 + H–29 + H–30), 0.87 (*s*, 3 H, H–24), 0.54 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.4 (C–28), 170.9 (C–33), 170.4 (C–31), 151.1 (C–37), 148.4 (C–35), 141.3 (C–38), 140.5 (C–13), 130.4 (C–39), 129.6 (C–41), 126.7 (C–12), 126.5 (C–40), 120.2 (C–43), 118.9 (C–42), 110.3 (C–36), 78.0 (C–3), 69.6 (C–2), 55.3 (C–5), 54.6 (C–18), 50.3 (C–17), 48.1 (C–9), 42.9 (C–14), 42.1 (C–1), 40.1 (C–19), 39.8 (C–8), 39.2 (C–20), 37.4 (C–22), 37.4 (C–4), 36.7 (C–10), 32.6 (C–7), 31.0 (C–21), 29.2 (C–24), 27.9 (C–15), 25.5 (C–16), 23.8 (C–11), 23.5 (C–27), 21.4 (C–32), 21.3 (C–30), 21.0 (C–34), 18.0 (C–6), 17.7 (C–23), 17.5 (C–29), 16.9 (C–26), 16.1 (C–25) ppm; MS (ESI): *m*/*z* (%) = 683.5 ($[M+H]^+$, 100); analysis calculated for $C_{43}H_{58}N_2O_5$ (682.93): C 75.62, H 8.56, N 4.10; found: C 75.33, H 8.69, N 3.85.

*4.2.11. 2β, 3β-Diacetyloxy-olean-12-en-28-oic acid 5-quinolinyl amide (**13**)*

As described for **5**, compound **13** (82 mg, 67%) was obtained from **3** and 5-aminoquinoline as a white solid; m.p. 167–168 °C; R_F = 0.60 (silica gel, chloroform/ethyl acetate, 1:1); $[\alpha]_D$ = +38.91° (*c* = 0.34, $CHCl_3$); UV-vis ($CHCl_3$): λ_{max} (log ε) = 242 nm (4.49), 307 nm (3.77), 317 nm (3.77); IR (KBr): ν = 3386*w*, 2948*s*, 2866*m*, 1746*vs*, 1684*m*, 1594*w*, 1572*w*, 1522*m*, 1488*s*, 1396*m*, 1364*s*, 1252*vs*, 1196*m*, 1156*m*, 1056*m*, 1030*m*, 798*m* cm^{-1}; ^1H NMR (500

MHz, $CDCl_3$): δ = 8.93 (*dd*, *J* = 4.2, 1.5 Hz, 1 H, H–40), 8.14–8.12 (*m*, 2 H, H–42 + H–36), 8.10 (*s*, 1 H, NH), 7.92 (*ddd*, *J* = 8.5, 0.9, 0.9 Hz, 1 H, H–38), 7.69 (*dd*, *J* = 8.4, 7.7 Hz, 1 H, H–37), 7.43 (*dd*, *J* = 8.6, 4.2 Hz, 1 H, H–41), 5.63 (*dd*, *J* = 3.5, 3.5 Hz, 1 H, H–12), 5.30 (*ddd*, *J* = 3.9, 3.9, 3.9 Hz, 1 H, H–2), 4.60 (*d*, *J* = 3.9 Hz, 1 H, H–3), 2.86 (*dd*, *J* = 12.8, 4.1 Hz, 1 H, H–18), 2.14 (*ddd*, *J* = 14.0, 14.0, 3.9 Hz, 1H, H–16a), 2.02 (*s*, 6 H, H–32 + H–34), 1.99–1.94 (*m*, 3 H, H–11a + H–11b + H–1a), 1.92–1.79 (*m*, 4 H, H–19a + H–22a + H–22b + H–16b), 1.74 (*ddd*, *J* = 14.1, 14.1, 4.4 Hz, 1H, H–15a), 1.61–1.36 (*m*, 5 H, H–9 + H–6a + H–6b + H–7a + H–21a), 1.36–1.24 (*m*, 4 H, H–19b + H–1b + H–21b + H–7b), 1.23 (*s*, 3 H, H–27), 1.15 (*ddd*, *J* = 13.8, 3.1, 3.1 Hz, 1H, H–15b), 1.06 (*s*, 3 H, H–25), 1.00 (*s*, 3 H, H–23), 1.00 (*s*, 3 H, H–29), 0.98–0.94 (*m*, 1 H, H–5), 0.97 (*s*, 3 H, H–30), 0.88 (*s*, 3 H, H–24), 0.67 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.0 (C–28), 170.8 (C–33), 170.4 (C–31), 150.3 (C–40), 148.8 (C–39), 145.4 (C–13), 132.9 (C–35), 129.7 (C–37), 129.3 (C–42), 126.7 (C–38), 123.5 (C–12), 122.2 (C–43), 120.8 (C–41), 120.2 (C–36), 78.0 (C–3), 69.6 (C–2), 55.3 (C–5), 48.1 (C–9), 48.1 (C–17), 46.9 (C–19), 43.0 (C–18), 42.6 (C–14), 42.0 (C–1), 39.7 (C–8), 37.4 (C–4), 36.8 (C–10), 34.3 (C–21), 33.1 (C–30), 33.1 (C–22), 32.5 (C–7), 30.9 (C–20), 29.2 (C–24), 27.4 (C–15), 26.1 (C–27), 24.2 (C–16), 23.8 (C–29), 23.7 (C–11), 21.4 (C–32), 21.0 (C–34), 18.0 (C–6), 17.7 (C–23), 17.4 (C–26), 16.1 (C–25) ppm; MS (ESI): *m*/*z* (%) = 683.6 ($[M+H]^+$, 100); analysis calculated for $C_{43}H_{58}N_2O_5$ (682.93): C 75.62, H 8.56, N 4.10; found: C 75.53, H 8.71, N 3.76.

*4.2.12. 2β, 3β-Diacetyloxy-ursan-12-en-28-oic acid 5-quinolinyl amide (**14**)*

As described for **5**, compound **14** (43 mg, 58%) was obtained from **4** and 5-aminoquinoline as a white solid; m.p. 144–146 °C; R_F = 0.35 (silica gel, hexane/ethyl acetate, 4:6); $[\alpha]_D$ = +18.90° (*c* = 1.02, $CHCl_3$); UV-vis ($CHCl_3$): λ_{max} (log ε) = 241 nm (4.42), 308 nm (3.71), 317 nm (3.71); IR (KBr): ν = 3346*m*, 2948*s*, 2872*m*, 1744*vs*, 1658*s*, 1620*m*, 1596*m*, 1572*m*, 1518*s*, 1488*s*, 1458*s*, 1398*s*, 1366*s*, 1320*m*, 1252*vs*, 1234*vs*, 1194*s*, 1156*m*, 1114*m*, 1078*m*, 1056*s*, 1030*s*, 996*m*, 972*m*, 944*m*, 798*s*, 754*s* cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.92 (*dd*, *J* = 4.2, 1.5 Hz, 1 H, H–40), 8.13 (*d*, *J* = 8.6 Hz, 1 H, H–42), 8.03 (*s*, 1 H, NH), 8.02 (*d*, *J* = 6.8 Hz, 1 H, H–36), 7.92 (*d*, *J* = 8.5 Hz, 1 H, H–38), 7.68 (*dd*, *J* = 8.1, 8.1 Hz, 1 H, H–37), 7.41 (*dd*, *J* = 8.6, 4.2 Hz, 1 H, H–41), 5.55 (*dd*, *J* = 3.3, 3.3 Hz, 1 H, H–12), 5.30 (*ddd*, *J* = 3.7, 3.7, 3.5 Hz, 1 H, H–2), 4.60 (*d*, *J* = 3.9 Hz, 1 H, H–3), 2.19 (*d*, *J* = 10.5 Hz, 1 H, H–18), 2.17–2.10 (*m*, 1 H, H–16a), 2.06–1.95 (*m*, 4 H, H–1a + H–11a + H–11b + H–22a), 2.02 (*s*, 3 H, H–32), 2.01 (*s*, 3 H, H–34), 1.95–1.80 (*m*, 2 H, H–15a + H–16b), 1.77–1.69 (*m*, 1 H, H–22b), 1.63–1.47 (*m*, 5 H, H–6a + H–7a + H–9 + H–19 + H–21a), 1.46–1.29 (*m*, 4 H, H–1b

+ H–6b + H–7b + H–21b), 1.18–1.12 (*m*, 1 H, H–15b), 1.16 (*s*, 3 H, H–27), 1.11–1.03 (*m*, 1 H, H–20), 1.08 (*s*, 3 H, H–25), 1.01 (*d*, *J* = 3.9 Hz, 3 H, H–30), 1.01 (*s*, 3 H, H–23), 0.99–0.93 (*m*, 1 H, H–5), 0.97 (*d*, *J* = 6.4 Hz, 3 H, H–29), 0.88 (*s*, 3 H, H–24), 0.71 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.8 (C–28), 170.8 (C–33), 170.4 (C–31), 150.3 (C–40), 148.8 (C–39), 140.4 (C–13), 133.0 (C–35), 129.6 (C–37), 129.5 (C–42), 126.7 (C–38), 126.2 (C–12), 122.3 (C–43), 120.7 (C–41), 120.5 (C–36), 78.0 (C–3), 69.6 (C–2), 55.3 (C–5), 54.6 (C–18), 49.5 (C–17), 48.1 (C–9), 43.0 (C–14), 42.1 (C–1), 40.1 (C–19), 39.9 (C–8), 39.3 (C–20), 37.8 (C–22), 37.4 (C–4), 36.8 (C–10), 32.9 (C–7), 31.0 (C–21), 29.2 (C–24), 27.9 (C–15), 25.2 (C–16), 23.7 (C–27), 23.6 (C–11), 21.4 (C–32), 21.3 (C–30), 21.0 (C–34), 18.0 (C–6), 17.8 (C–23), 17.5 (C–26), 17.5 (C–29), 16.2 (C–25) ppm; MS (ESI): *m*/*z* (%) = 683.5 ($[M+H]^+$, 100), 705.3 ($[M+Na]^+$, 3), 1365.3 ($[2M+H]^+$, 15), 1387.6 ($[2M+Na]^+$, 10), 1403.1 ($[2M+K]^+$, 3); analysis calculated for $C_{43}H_{58}N_2O_5$ (682.93): C 75.62, H 8.56, N 4.10; found: C 75.39, H 8.82, N 4.03.

*4.2.13. 2β, 3β-Diacetyloxy-olean-12-en-28-oic acid 6-quinolinyl amide (**15**)*

As described for **5**, compound **15** (109 mg, 89%) was obtained from **3** and 6-aminoquinoline as a white solid; m.p. 167–169 °C; R_F = 0.63 (silica gel, chloroform/ethyl acetate, 1:1); $[\alpha]_D$ = +101.63° (*c* = 0.37, $CHCl_3$); UV-vis ($CHCl_3$): λ_{max} (log ε) = 247 nm (4.70), 274 nm (3.86), 282 nm (3.84), 322 nm (3.70), 335 nm (3.68); IR (KBr): ν = 3396*w*, 2948*s*, 2878*m*, 1744*vs*, 1684*m*, 1626*w*, 1600*w*, 1532*s*, 1496*m*, 1464*m*, 1430*m*, 1364*s*, 1252*vs*, 1194*m*, 1156*w*, 1118*w*, 1056*m*, 1030*m*, 1012*m* cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.81 (*dd*, *J* = 4.2, 1.7 Hz, 1 H, H–39), 8.49 (*d*, *J* = 2.4 Hz, 1 H, H–43), 8.09 (*dd*, *J* = 8.1, 1.6 Hz, 1 H, H–41), 8.01 (*d*, *J* = 9.0 Hz, 1 H, H–37), 7.94 (*s*, 1 H, NH), 7.39–7.34 (*m*, 2 H, H–40 + H–36), 5.62 (*dd*, *J* = 3.6, 3.6 Hz, 1 H, H–12), 5.31 (*ddd*, *J* = 3.8, 3.8, 3.8 Hz, 1 H, H–2), 4.61 (*d*, *J* = 3.9 Hz, 1 H, H–3), 2.73 (*dd*, *J* = 12.7, 3.5 Hz, 1 H, H–18), 2.17–1.94 (*m*, 4 H, H–16a + H–11a + H–11b + H–1a), 2.03 (*s*, 3 H, H–32), 2.02 (*s*, 3 H, H–34), 1.90–1.70 (*m*, 4 H, H–19a + H–22a + H–22b + H–16b), 1.70–1.52 (*m*, 3 H, H–15a + H–9 + H–6a), 1.52–1.23 (*m*, 7 H, H–7a + H–7b + H–21a + H–21b + H–6b + H–1b + H–19b), 1.21 (*s*, 3 H, H–27), 1.15–1.08 (*m*, 1 H, H–15b), 1.14 (*s*, 3 H, H–25), 1.01 (*s*, 3 H, H–23), 0.98–0.94 (*m*, 1 H, H–5), 0.96 (*s*, 3 H, H–29), 0.95 (*s*, 3 H, H–30), 0.88 (*s*, 3 H, H–24), 0.70 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.1 (C–28), 170.9 (C–33), 170.4 (C–31), 149.4 (C–40), 145.7 (C–41), 145.4 (C–13), 136.0 (C–35), 136.0 (C–38), 130.2 (C–42), 129.1 (C–37), 123.4 (C–12), 123.1 (C–43), 121.7 (C–39), 116.0 (C–36), 78.0 (C–3), 69.7 (C–2), 55.3 (C–5), 48.1 (C–9), 47.5 (C–17), 46.8 (C–19), 42.8 (C–18), 42.5 (C–14), 42.1 (C–1), 39.7 (C–8), 37.5 (C–4), 36.8 (C–10), 34.3 (C–21), 33.1

(C–30), 32.6 (C–22), 32.4 (C–7), 30.9 (C–20), 29.2 (C–24), 27.4 (C–15), 26.0 (C–27), 24.4 (C–16), 23.9 (C–11), 23.7 (C–29), 21.4 (C–32), 21.0 (C–34), 18.0 (C–6), 17.7 (C–23), 17.1 (C–26), 16.2 (C–25) ppm; MS (ESI): *m*/*z* (%) = 683.5 ($[M+H]^+$, 100); analysis calculated for $C_{43}H_{58}N_2O_5$ (682.93): C 75.62, H 8.56, N 4.10; found: C 75.59, H 8.80, N 3.85.

*4.2.14. 2β, 3β-Diacetyloxy-ursan-12-en-28-oic acid 6-quinolinyl amide (**16**)*

As described for **5**, compound **16** (200 mg, 87%) was obtained from **4** and 6-aminoquinoline as a white solid; m.p. 156–159 °C; R_F = 0.39 (silica gel, hexane/ethyl acetate, 4:6); $[\alpha]_D$ = +76.70° (*c* = 0.31, $CHCl_3$); UV-vis ($CHCl_3$): λ_{max} (log ε) = 248 nm (4.62), 284 nm (3.77), 322 nm (3.60), 335 nm (3.60); IR (KBr): ν = 3394*m*, 2928*s*, 2872*m*, 1744*vs*, 1682*s*, 1626*m*, 1600*m*, 1576*m*, 1534*s*, 1496*s*, 1458*s*, 1430*s*, 1398*m*, 1378*s*, 1364*s*, 1252*vs*, 1234*vs*, 1194*s*, 1156*m*, 1138*m*, 1118*m*, 1078*m*, 1056*m*, 1030*s*, 966*m*, 944*m*, 934*m*, 828*m*, 752*m* cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.81 (*dd*, *J* = 4.2, 1.7 Hz, 1 H, H–39), 8.46 (*d*, *J* = 2.4 Hz, 1 H, H–43), 8.09 (*d*, *J* = 6.8 Hz, 1 H, H–41), 8.01 (*d*, *J* = 9.0 Hz, 1 H, H–37), 7.95 (*s*, 1 H, NH), 7.37–7.34 (*m*, 2 H, H–40 + H–36), 5.57 (*dd*, *J* = 3.5, 3.5 Hz, 1 H, H–12), 5.31 (*ddd*, *J* = 3.8, 3.8, 3.8 Hz, 1 H, H–2), 4.61 (*d*, *J* = 3.9 Hz, 1 H, H–3), 2.16–2.03 (*m*, 4 H, H–11a + H–11b + H–16a + H–18), 2.03 (*s*, 3 H, H–32), 2.02 (*s*, 3 H, H–34), 2.03–1.97 (*m*, 2 H, H–1a + H–22a), 1.88 (*dd*, *J* = 8.3, 6.3 Hz, 1 H, H–16b), 1.80–1.72 (*m*, 1 H, H–15a), 1.67–1.46 (*m*, 6 H, H–6a + H–7a + H–9 + H–19 + H–21a + H–22b), 1.44–1.34 (*m*, 3 H, H–1b + H–6b + H–21b), 1.32–1.26 (*m*, 1 H, H–7b), 1.16–1.10 (*m*, 1 H, H–15b), 1.15 (*s*, 3 H, H–27), 1.13 (*s*, 3 H, H–25), 1.06–0.98 (*m*, 1 H, H–20), 1.00 (*d*, *J* = 2.3 Hz, 3 H, H–30), 0.99 (*s*, 3 H, H–23), 0.97–0.93 (*m*, 1 H, H–5), 0.95 (*d*, *J* = 6.4 Hz, 3 H, H–29), 0.88 (*s*, 3 H, H–24), 0.68 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.9 (C–28), 170.8 (C–33), 170.4 (C–31), 149.4 (C–39), 145.6 (C–38), 140.6 (C–13), 136.1 (C–35), 136.1 (C–41), 130.2 (C–37), 129.1 (C–42), 126.2 (C–12), 123.0 (C–36), 121.7 (C–40), 115.9 (C–43), 78.0 (C–3), 69.6 (C–2), 55.2 (C–5), 54.4 (C–18), 48.9 (C–17), 48.1 (C–9), 43.0 (C–14), 42.2 (C–1), 40.0 (C–19), 39.8 (C–8), 39.3 (C–20), 37.4 (C–4), 37.2 (C–22), 36.8 (C–10), 32.7 (C–7), 31.0 (C–21), 29.2 (C–24), 28.0 (C–15), 25.3 (C–16), 23.8 (C–11), 23.5 (C–27), 21.4 (C–32), 21.3 (C–30), 21.0 (C–34), 18.0 (C–6), 17.8 (C–23), 17.5 (C–29), 17.1 (C–26), 16.3 (C–25) ppm; MS (ESI): *m*/*z* (%) = 683.7 ($[M+H]^+$, 100), 1365.3 ($[2M+H]^+$, 34), 1388.3 ($[2M+Na]^+$, 4); analysis calculated for $C_{43}H_{58}N_2O_5$ (682.93): C 75.62, H 8.56, N 4.10; found: C 75.41, H 8.74, N 3.91.

*4.2.15. 2β, 3β-Diacetyloxy-olean-12-en-28-oic acid 7-quinolinyl amide (**17**)*

As described for **5**, compound **17** (104 mg, 85%) was obtained from **3** and 7-aminoquinoline as a white solid; m.p. 167–170 °C; R_F = 0.67 (silica gel, chloroform/ethyl acetate, 1:1); $[\alpha]_D$ = +48.44° (*c* = 0.27, $CHCl_3$); UV-vis ($CHCl_3$): λ_{max} (log ε) = 247 nm (4.85), 275 nm (4.14), 324 nm (3.99), 335 nm (3.95); IR (KBr): ν = 2948*s*, 2866*m*, 1744*vs*, 1684*m*, 1624*m*, 1526*m*, 1496*s*, 1458*s*, 1430*s*, 1364*m*, 1252*vs*, 1192*w*, 1156*m*, 1056*m*, 1030*m* cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.86 (*dd*, *J* = 4.3, 1.7 Hz, 1 H, H–38), 8.10 (*dd*, *J* = 8.3, 1.1 Hz, 1 H, H–42), 8.07 (*dd*, *J* = 8.9, 2.1 Hz, 1 H, H–43), 7.98 (*s*, 1 H, NH), 7.90 (*d*, *J* = 2.0 Hz, 1 H, H–36), 7.77 (*d*, *J* = 8.9 Hz, 1 H, H–40), 7.32 (*dd*, *J* = 8.2, 4.3 Hz, 1 H, H–39), 5.61 (*dd*, *J* = 3.4, 3.4 Hz, 1 H, H–12), 5.32 (*ddd*, *J* = 3.7, 3.7, 3.7 Hz, 1 H, H–2), 4.62 (*d*, *J* = 3.9 Hz, 1 H, H–3), 2.73 (*dd*, *J* = 12.3, 3.4 Hz, 1 H, H–18), 2.16–1.92 (*m*, 4 H, H–16a + H–11a + H–11b + H–1a), 2.04 (*s*, 3 H, H–32), 2.02 (*s*, 3 H, H–34), 1.90–1.63 (*m*, 5 H, H–19a + H–22a + H–22b + H–16b + H–15a), 1.62–1.36 (*m*, 5 H, H–9 + H–21a + H–7a + H–6a + H–6b), 1.36–1.24 (*m*, 4 H, H–1b + H–19b + H–21b + H–7b), 1.21 (*s*, 3 H, H–27), 1.15–1.08 (*m*, 1 H, H–15b), 1.14 (*s*, 3 H, H–25), 1.01 (*s*, 3 H, H–23), 0.99–0.94 (*m*, 1 H, H–5), 0.96 (*s*, 3 H, H–29), 0.95 (*s*, 3 H, H–30), 0.88 (*s*, 3 H, H–24), 0.75 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.0 (C–28), 170.9 (C–33), 170.4 (C–31), 150.9 (C–38), 148.8 (C–37), 145.2 (C–13), 139.6 (C–35), 135.9 (C–42), 128.7 (C–40), 125.5 (C–41), 123.6 (C–12), 121.1 (C–43), 120.1 (C–39), 117.1 (C–36), 78.0 (C–3), 69.7 (C–2), 55.3 (C–5), 48.2 (C–9), 47.6 (C–17), 46.8 (C–19), 42.8 (C–18), 42.5 (C–14), 42.1 (C–1), 39.7 (C–8), 37.5 (C–4), 36.8 (C–10), 34.3 (C–21), 33.1 (C–30), 32.6 (C–22), 32.4 (C–7), 30.9 (C–20), 29.2 (C–24), 27.4 (C–15), 26.0 (C–27), 24.3 (C–16), 23.9 (C–11), 23.8 (C–29), 21.4 (C–32), 21.0 (C–34), 18.0 (C–6), 17.8 (C–23), 17.2 (C–26), 16.2 (C–25) ppm; MS (ESI): *m*/*z* (%) = 683.6 ($[M+H]^+$, 100), 1365.4 ($[2M+H]^+$, 15); analysis calculated for $C_{43}H_{58}N_2O_5$ (682.93): C 75.62, H 8.56, N 4.10; found: C 75.43, H 8.69, N 3.86.

*4.2.16. 2β, 3β-Diacetyloxy-ursan-12-en-28-oic acid 7-quinolinyl amide (**18**)*

As described for **5**, compound **18** (83 mg, 68%) was obtained from **4** and 7-aminoquinoline as a white solid; m.p. 157–162 °C; R_F = 0.51 (silica gel, chloroform/ethyl acetate, 1:1); $[\alpha]_D$ = +24.50° (*c* = 0.28, $CHCl_3$); UV-vis ($CHCl_3$): λ_{max} (log ε) = 248 nm (4.90), 275 nm (4.24), 325 nm (4.06), 335 nm (4.02); IR (KBr): ν = 2948*s*, 2872*m*, 1744*vs*, 1684*m*, 1624*m*, 1582*w*, 1528*m*, 1496*s*, 1456*s*, 1430*s*, 1364*m*, 1252*vs*, 1236*s*, 1194*m*, 1156*w*, 1056*m*, 1032*m* cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.86 (*d*, *J* = 3.9 Hz, 1 H, H–38), 8.09 (*d*, *J* = 8.2 Hz, 1 H, H–42), 8.04 (*d*, *J* = 9.2 Hz, 1 H, H–43), 7.99 (*s*, 1 H, NH), 7.87 (*s*, 1 H, H–36), 7.76 (*d*,

J = 8.9 Hz, 1 H, H–40), 7.31 (*dd*, *J* = 8.2, 4.2 Hz, 1 H, H–39), 5.57–5.54 (*m*, 1 H, H–12), 5.33–5.30 (*m*, 1 H, H–2), 4.61 (*d*, *J* = 3.8 Hz, 1 H, H–3), 2.16–1.96 (*m*, 6 H, H–11a + H–11b + H–16a + H–22a + H–1a + H–18), 2.03 (*s*, 3 H, H–32), 2.02 (*s*, 3 H, H–34), 1.92–1.85 (*m*, 1 H, H–16b), 1.78 (*ddd*, *J* = 13.6, 13.6, 3.7 Hz, 1 H, H–15a), 1.69–1.46 (*m*, 6 H, H–6a + H–7a + H–9 + H–19 + H–21a + H–22b), 1.44–1.25 (*m*, 4 H, H–6b + H–21b + H–7b + H–1b), 1.16–1.09 (*m*, 1 H, H–15b), 1.15 (*s*, 3 H, H–27), 1.13 (*s*, 3 H, H–25), 1.06–0.98 (*m*, 7 H, H–20 + H–30 + H–23), 0.98–0.92 (*m*, 1 H, H–5), 0.95 (*d*, *J* = 6.3 Hz, 3 H, H–29), 0.88 (*s*, 3 H, H–24), 0.73 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.8 (C–28), 170.9 (C–33), 170.4 (C–31), 150.9 (C–38), 148.8 (C–37), 140.4 (C–13), 139.7 (C–35), 135.9 (C–42), 128.6 (C–40), 126.3 (C–12), 125.5 (C–41), 121.1 (C–43), 120.1 (C–39), 116.9 (C–36), 78.0 (C–3), 69.6 (C–2), 55.2 (C–5), 54.5 (C–18), 49.0 (C–17), 48.2 (C–9), 43.0 (C–14), 42.2 (C–1), 40.0 (C–19), 39.9 (C–8), 39.3 (C–20), 37.4 (C–4), 37.2 (C–22), 36.8 (C–10), 32.8 (C–7), 31.0 (C–21), 29.3 (C–24), 28.0 (C–15), 25.3 (C–16), 23.8 (C–11), 23.5 (C–27), 21.4 (C–32), 21.3 (C–30), 21.0 (C–34), 18.0 (C–6), 17.8 (C–23), 17.5 (C–29), 17.1 (C–26), 16.4 (C–25) ppm; MS (ESI): *m*/*z* (%) = 683.6 ($[M+H]^+$, 100), 1365.5 ($[2M+H]^+$, 20); analysis calculated for $C_{43}H_{58}N_2O_5$ (682.93): C 75.62, H 8.56, N 4.10; found: C 75.47, H 8.73, N 3.92.

*4.2.17. 2β, 3β-Diacetyloxy-olean-12-en-28-oic acid 8-quinolinyl amide (**19**)*

As described for **5**, compound **19** (136 mg, 90%) was obtained from **3** and 8-aminoquinoline as a white solid; m.p. 140–145 °C; R_F = 0.86 (silica gel, chloroform/ethyl acetate, 1:1); $[\alpha]_D$ = +24.59° (*c* = 0.36, $CHCl_3$); UV-vis ($CHCl_3$): λ_{max} (log ε) = 247 nm (4.52), 324 nm (3.70); IR (KBr): ν = 3332*m*, 2950*vs*, 2866*s*, 1744*vs*, 1672*s*, 1528*vs*, 1486*vs*, 1464*s*, 1424*s*, 1364*s*, 1326*s*, 1250*vs*, 1192*s*, 1162*s*, 1056*s*, 1030*s*, 1010*s*, 944*m*, 826*s*, 792*s*, 756*m*, 684*m*, 602*m* cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 10.37 (*s*, 1 H, NH), 8.85 (*dd*, *J* = 7.5, 1.4 Hz, 1 H, H–43), 8.80 (*dd*, *J* = 4.2, 1.6 Hz, 1 H, H–37), 8.14 (*dd*, *J* = 8.3, 1.6 Hz, 1 H, H–39), 7.53–7.43 (*m*, 3 H, H–42 + H–41 + H–38), 5.71 (*dd*, *J* = 3.5, 3.5 Hz, 1 H, H–12), 5.30 (*ddd*, *J* = 3.7, 3.7, 3.7 Hz, 1 H, H–2), 4.60 (*d*, *J* = 3.9 Hz, 1 H, H–3), 2.99 (*dd*, *J* = 13.0, 3.7 Hz, 1 H, H–18), 2.16 (*ddd*, *J* = 13.8, 13.8, 3.9 Hz, 1 H, H–16a), 2.01 (*s*, 6 H, H–32 + H–34), 2.00–1.68 (*m*, 8 H, H–1a + H–11a + H–11b + H–16b + H–19a + H–22a + H–22b + H–15a), 1.59–1.39 (*m*, 4 H, H–9 + H–6a + H–7a + H–21a), 1.38–1.19 (*m*, 5 H, H–6b + H–19b + H–1b + H–21b + H–7b), 1.20 (*s*, 3 H, H–27), 1.10 (*ddd*, *J* = 13.6, 3.3, 3.3 Hz, 1H, H–15b), 0.98 (*s*, 6 H, H–25 + H–29), 0.97 (*s*, 3 H, H–23), 0.96 (*s*, 3 H, H–30), 0.95–0.91 (*m*, 1 H, H–5), 0.86 (*s*, 3 H, H–24), 0.51 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.1 (C–28), 170.8 (C–33), 170.4 (C–31), 148.0 (C–37), 143.4 (C–13), 139.2 (C–36), 136.3 (C–39), 135.1 (C–35), 128.1 (C–

40), 127.7 (C–42), 124.0 (C–12), 121.6 (C–38), 121.2 (C–41), 116.6 (C–43), 78.1 (C–3), 69.8 (C–2), 55.3 (C–5), 48.2 (C–17), 48.2 (C–9), 46.8 (C–19), 42.3 (C–18), 42.2 (C–14), 42.1 (C–1), 39.7 (C–8), 37.4 (C–4), 36.7 (C–10), 34.5 (C–21), 33.2 (C–30), 33.1 (C–22), 32.5 (C–7), 30.9 (C–20), 29.2 (C–24), 27.6 (C–15), 26.1 (C–27), 24.3 (C–16), 23.8 (C–29), 23.7 (C–11), 21.4 (C–32), 21.0 (C–34), 18.0 (C–6), 17.7 (C–23), 16.6 (C–26), 16.0 (C–25) ppm; MS (ESI): *m*/*z* (%) = 683.3 ($[M+H]^+$, 100); analysis calculated for $C_{43}H_{58}N_2O_5$ (682.93): C 75.62, H 8.56, N 4.10; found: C 75.52, H 8.68, N 3.94.

*4.2.18. 2β, 3β-Diacetyloxy-ursan-12-en-28-oic acid 8-quinolinyl amide (**20**)*

As described for **5**, compound **20** (83 mg, 90%) was obtained from **4** and 8-aminoquinoline as a white solid; m.p. 145–147 °C; R_F = 0.58 (silica gel, hexane/ethyl acetate, 7:3); $[\alpha]_D$ = -5.00° (*c* = 0.29, $CHCl_3$); UV-vis ($CHCl_3$): λ_{max} (log ε) = 247 nm (4.51), 324 nm (3.71); IR (KBr): ν = 3440*m*, 3364*m*, 2948*s*, 2870*m*, 1744*vs*, 1672*m*, 1596*w*, 1578*w*, 1526*vs*, 1486*s*, 1456*m*, 1424*m*, 1378*m*, 1324*m*, 1252*vs*, 1234*s*, 1194*m*, 1156*m*, 1132*w*, 1116*w*, 1102*w*, 1084*w*, 1058*m*, 1030*m*, 826*m*, 792*m*, 756*m* cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 10.30 (*s*, 1 H, NH), 8.84–8.82 (*m*, 1 H, H–43), 8.81–8.79 (*m*, 1 H, H–37), 8.15 (*dd*, *J* = 8.3, 1.6 Hz, 1 H, H–39), 7.53–7.49 (*m*, 1 H, H–42), 7.48–7.44 (*m*, 2 H, H–41 + H–38), 5.69 (*dd*, *J* = 3.6, 3.6 Hz, 1 H, H–12), 5.29 (*ddd*, *J* = 3.8, 3.8, 3.5 Hz, 1 H, H–2), 4.59 (*d*, *J* = 3.9 Hz, 1 H, H–3), 2.33 (*d*, *J* = 10.8 Hz, 1 H, H–18), 2.20–2.12 (*m*, 1 H, H–16a), 2.04–1.80 (*m*, 6 H, H–1a + H–11a + H–11b + H–15a + H–16b + H–22a), 2.01 (*s*, 3 H, H–32), 2.00 (*s*, 3 H, H–36), 1.73–1.65 (*m*, 1 H, H–22b), 1.62–1.38 (*m*, 6 H, H–6a + H–7a + H–9 + H–19 + H–21a + H–21b), 1.38–1.28 (*m*, 2 H, H–1b + H–6b), 1.28–1.22 (*m*, 1 H, H–7b), 1.15–1.03 (*m*, 2 H, H–15b + H–20), 1.14 (*s*, 3 H, H–27), 1.01–0.98 (*m*, 6 H, H–29 + H–30), 0.96 (*s*, 6 H, H–23) + H–25), 0.95–0.90 (*m*, 1 H, H–5), 0.86 (*s*, 3 H, H–24), 0.51 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.0 (C–28), 170.8 (C–33), 170.4 (C–31), 147.9 (C–37), 139.2 (C–36), 138.0 (C–13), 136.4 (C–39), 135.2 (C–35), 128.1 (C–40), 127.7 (C–42), 127.2 (C–12), 121.5 (C–38), 121.2 (C–41), 116.6 (C–43), 78.1 (C–3), 69.8 (C–2), 55.3 (C–5), 53.9 (C–18), 49.6 (C–17), 48.2 (C–9), 42.5 (C–14), 42.2 (C–1), 40.0 (C–19), 39.9 (C–8), 39.2 (C–20), 37.6 (C–22), 37.4 (C–4), 36.7 (C–10), 32.7 (C–7), 31.2 (C–21), 29.2 (C–24), 28.0 (C–15), 25.3 (C–16), 23.8 (C–27), 23.5 (C–11), 21.4 (C–30 + C–32), 21.0 (C–34), 18.0 (C–6), 17.8 (C–23), 17.5 (C–29), 16.6 (C–26), 16.2 (C–25) ppm; MS (ESI): *m*/*z* (%) = 683.7 ($[M+H]^+$, 100); analysis calculated for $C_{43}H_{58}N_2O_5$ (682.93): C 75.62, H 8.56, N 4.10; found: C 75.46, H 8.65, N 3.81.

*4.2.19. 2β, 3β-Diacetyloxy-olean-12-en-28-oic acid 4-isoquinolinyl amide (**21**)*

As described for **5**, compound **21** (71 mg, 58%) was obtained from **3** and 4-aminoisoquinoline as a white solid; m.p. 176–180 °C; R_F = 0.69 (silica gel, chloroform/ethyl acetate, 1:1); $[\alpha]_D$ = +39.41° (*c* = 0.35, $CHCl_3$); UV-vis ($CHCl_3$): λ_{max} (log ε) = 290 nm (3.75), 302 nm (3.75), 324 nm (3.79); IR (KBr): ν = 2948*s*, 2878*m*, 1744*vs*, 1684*m*, 1648*w*, 1522*m*, 1490*m*, 1474*m*, 1458*m*, 1398*m*, 1366*m*, 1328*w*, 1252*vs*, 1236*s*, 1194*m*, 1162*w*, 1056*m*, 1030*m* cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 9.13 (*s*, 1 H, H–36), 9.08 (*s*, 1 H, H–37), 8.02–7.99 (*m*, 2 H, H–39 + NH), 7.79–7.73 (*m*, 2 H, H–42 + H–40), 7.64 (*ddd*, *J* = 8.0, 5.8, 2.1 Hz, 1 H, H–41), 5.63 (*dd*, *J* = 3.4, 3.4 Hz, 1 H, H–12), 5.30 (*ddd*, *J* = 3.8, 3.8, 3.8 Hz, 1 H, H–2), 4.61 (*d*, *J* = 3.9 Hz, 1 H, H–3), 2.88 (*dd*, *J* = 12.4, 3.4 Hz, 1 H, H–18), 2.15 (*ddd*, *J* = 13.7, 13.7, 3.9 Hz, 1 H, H–16a), 2.02 (*s*, 3 H, H–32), 2.02 (*s*, 3 H, H–34), 2.01–1.81 (*m*, 7 H, H–11a + H–11b + H–16b + H–22a + H–22b + H–1a + H–19a), 1.76 (*ddd*, *J* = 13.8, 13.8, 3.9 Hz, 1 H, H–15a), 1.61–1.37 (*m*, 5 H, H–6a + H–6b + H–7a + H–21a + H–9), 1.37–1.27 (*m*, 4 H, H–7b + H–21b + H–1b + H–19b), 1.23 (*s*, 3 H, H–27), 1.19–1.13 (*m*, 1 H, H–15b), 1.07 (*s*, 3 H, H–25), 1.01 (*s*, 6 H, H–23 + H–29), 0.99–0.94 (*m*, 1 H, H–5), 0.98 (*s*, 3 H, H–30), 0.88 (*s*, 3 H, H–24), 0.71 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.0 (C–28), 170.9 (C–33), 170.4 (C–31), 149.4 (C–37), 145.2 (C–13), 137.2 (C–36), 130.6 (C–40), 129.8 (C–35), 128.8 (C–38), 128.5 (C–39), 128.4 (C–43), 127.4 (C–41), 123.6 (C–12), 120.0 (C–42), 78.0 (C–3), 69.7 (C–2), 55.3 (C–5), 48.1 (C–9), 48.1 (C–17), 46.8 (C–19), 43.1 (C–18), 42.6 (C–14), 42.0 (C–1), 39.7 (C–8), 37.5 (C–4), 36.8 (C–10), 34.3 (C–21), 33.1 (C–30), 33.1 (C–22), 32.5 (C–7), 30.9 (C–20), 29.2 (C–24), 27.5 (C–15), 26.1 (C–27), 24.2 (C–16), 23.8 (C–29), 23.7 (C–11), 21.4 (C–32), 21.0 (C–34), 18.0 (C–6), 17.7 (C–23), 17.4 (C–26), 16.1 (C–25) ppm; MS (ESI): *m*/*z* (%) = 683.5 ($[M+H]^+$, 100), 1365.2 ($[2M+H]^+$, 46); analysis calculated for $C_{43}H_{58}N_2O_5$ (682.93): C 75.62, H 8.56, N 4.10; found: C 75.43, H 8.65, N 3.97.

*4.2.20. 3β-Acetyloxy-urs-12-en-28-oic acid (**24**)*

Compound **24** (192 mg, 88%) was synthesized as described for compound **3** starting from **22**. The spectroscopic data were in accordance with the data from the literature.

*4.2.21. 2α, 3β, 24-Triacetyloxy-urs-12-en-28-oic acid (**25**)*

Compound **25** (209 mg, 83%) was synthesized as described for **3** starting from **23** and obtained as a white solid; m.p. 153–159 °C (lit.[29]: 151.2–154.6 °C); R_F = 0.23 (silica gel, hexane/ethyl acetate, 7:3); $[\alpha]_D$ = +34.71° (*c* = 0.35, $CHCl_3$); IR (KBr): ν = 3298*m*, 2950*s*, 2872*m*, 1748*vs*, 1698*s*, 1456*s*, 1370*s*, 1234*vs*, 1156*m*, 1144*s*, 964*m*, 918*m* cm^{-1}; ^1H NMR

(500 MHz, $CDCl_3$): δ = 5.24 (*dd*, *J* = 3.5, 3.5 Hz, 1 H, H–12), 5.16 (*ddd*, *J* = 10.9, 10.9, 4.6 Hz, 1 H, H–2), 5.08 (*d*, *J* = 10.3 Hz, 1 H, H–3), 3.85 (*d*, *J* = 11.7 Hz, 1 H, H–24a), 3.58 (*d*, *J* = 11.8 Hz, 1 H, H–24b), 2.19 (*d*, *J* = 11.3 Hz, 1 H, H–18), 2.11–1.90 (*m*, 4 H, H–11a + H–11b + H–1a + H–16a), 2.08 (*s*, 3 H, H–36), 2.02 (*s*, 3 H, H–34), 1.98 (*s*, 3 H, H–32), 1.84 (*ddd*, *J* = 13.4, 13.4, 4.1 Hz, 1 H, H–15a), 1.75–1.59 (*m*, 4 H, H–16b + H–22a + H–22b + H–9), 1.54–1.25 (*m*, 8 H, H–6a + H–6b + H–21a + H–21b + H–7a + H–7b + H–5 + H–19), 1.17–0.96 (*m*, 3 H, H–15b + H–1b + H–20), 1.10 (*s*, 3 H, H–25), 1.07 (*s*, 3 H, H–27), 0.94 (*d*, *J* = 6.3 Hz, 3 H, H–30), 0.87 (*s*, 3 H, H–23), 0.84 (*d*, *J* = 6.7 Hz, 3 H, H–29), 0.76 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 183.6 (C–28), 171.0 (C–35), 170.6 (C–31), 170.5 (C–33), 138.2 (C–13), 125.4 (C–12), 75.0 (C–3), 70.1 (C–2), 65.4 (C–24), 52.7 (C–18), 48.1 (C–17), 47.8 (C–9), 47.7 (C–5), 43.9 (C–1), 42.1 (C–14), 42.1 (C–4), 39.7 (C–8), 39.2 (C–19), 38.9 (C–20), 38.0 (C–10), 36.8 (C–22), 32.6 (C–7), 30.7 (C–21), 28.0 (C–15), 24.1 (C–16), 23.6 (C–27), 23.5 (C–11), 21.3 (C–30), 21.2 (C–32), 21.0 (C–36), 20.9 (C–34), 18.0 (C–6), 17.2 (C–25), 17.1 (C–29), 17.1 (C–26), 14.1 (C–23) ppm; MS (ESI): *m*/*z* (%) = 615.1 ($[M+H]^+$, 14), 632.2 ($[M+NH_4]^+$, 40), 637.4 ($[M+Na]^+$, 100); analysis calculated for $C_{36}H_{54}O_8$ (614.81): C 70.33, H 8.85; found: C 70.02, H 8.97.

*4.2.22. 3β-Acetyloxy-ursan-12-en-28-oic acid 5-quinolinyl amide (**26**)*

As described for **5**, compound **26** (109 mg, 87%) was obtained from **24** and 5-aminoquinoline as a white solid; m.p. 163–165 °C; R_F = 0.53 (silica gel, chloroform/ethyl acetate, 1:1); $[\alpha]_D$ = +2.98° (*c* = 0.38, $CHCl_3$); UV-vis ($CHCl_3$): λ_{max} (log ε) = 241 nm (4.44), 308 nm (3.72), 317 nm (3.72); IR (KBr): ν = 3260*s*, 2968*vs*, 2926*vs*, 2870*s*, 1736*vs*, 1684*s*, 1650*vs*, 1596*s*, 1520*s*, 1490*vs*, 1370*s*, 1320*s*, 1246*vs*, 1204*s*, 1146*m*, 1026*s*, 1006*s*, 986*s*, 968*s*, 802*s* cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): 8.91 (*dd*, *J* = 4.2, 1.5 Hz, 1 H, H–38), 8.14 (*d*, *J* = 8.4 Hz, 1 H, H–40), 8.08 (*s*, 1 H, NH), 7.99 (*d*, *J* = 7.4 Hz, 1 H, H–34), 7.92 (*d*, *J* = 8.5 Hz, 1 H, H–36), 7.67 (*dd*, *J* = 8.5, 7.7 Hz, 1 H, H–35), 7.41 (*dd*, *J* = 8.6, 4.2 Hz, 1 H, H–39), 5.54 (*dd*, *J* = 3.4, 3.4 Hz, 1 H, H–12), 4.47 (*dd*, *J* = 11.0, 4.8 Hz, 1 H, H–3), 2.19 (*d*, *J* = 10.4 Hz, 1 H, H–18), 2.13 (*ddd*, *J* = 13.6, 13.6, 4.1 Hz, 1 H, H–16a), 2.06–1.98 (*m*, 2 H, H–2a + H–22a), 2.02 (*s*, 3 H, H–32), 1.95–1.79 (*m*, 3 H, H–2b + H–16b + H–15a), 1.72 (*ddd*, *J* = 13.6, 13.6, 4.2 Hz, 1 H, H–22b), 1.65–1.23 (*m*, 11 H, H–11a + H–11b + H–1a + H–21a + H–21b + H–9 + H–19 + H–7a + H–7b + H–6a + H–6b), 1.17–0.98 (*m*, 1 H, H–15b + H–1b + H–19 + H–20), 1.15 (*s*, 3 H, H–27), 1.01 (*d*, *J* = 6.2 Hz, 3 H, H–30), 0.96 (*d*, *J* = 6.5 Hz, 3 H, H–29), 0.84 (*s*, 3 H, H–24), 0.83 (*s*, 3 H, H–25), 0.83–0.78 (*m*, 1 H, H–5), 0.81 (*s*, 3 H, H–23), 0.69 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.9 (C–28), 171.1 (C–31), 150.1 (C–38), 148.5 (C–37), 140.2 (C–

13), 133.1 (C–33), 130.0 (C–40), 129.7 (C–35), 126.5 (C–36), 126.4 (C–12), 122.6 (C–41), 120.8 (C–34), 120.7 (C–39), 80.9 (C–3), 55.4 (C–5), 54.6 (C–18), 49.5 (C–17), 47.6 (C–9), 42.8 (C–14), 40.1 (C–19), 39.7 (C–8), 39.3 (C–20), 38.4 (C–1), 37.8 (C–4), 37.7 (C–22), 36.9 (C–10), 32.9 (C–7), 31.0 (C–21), 28.2 (C–24), 28.0 (C–15), 25.2 (C–16), 23.6 (C–11), 23.6 (C–27), 23.5 (C–2), 21.4 (C–30), 21.3 (C–32), 18.2 (C–6), 17.4 (C–29), 17.4 (C–26), 16.8 (C–23), 15.6 (C–25) ppm; MS (ESI): *m*/*z* (%) = 625.5 ($[M+H]^+$, 100), 1249.3 ($[2M+H]^+$, 26); analysis calculated for $C_{41}H_{56}N_2O_3$ (624.89): C 78.80, H 9.03, N 4.48; found: C 78.64, H 8.75, N 4.29.

*4.2.23. 2α, 3β, 24-Triacetyloxy-ursan-12-en-28-oic acid 5-quinolinyl amide (**27**)*

As described for **5**, compound **27** (63 mg, 52%) was obtained from **25** and 5-aminoquinoline as a white solid; m.p. 168–172 °C; R_F = 0.49 (silica gel, chloroform/ethyl acetate, 1:1); $[\alpha]_D$ = +6.08° (*c* = 0.31, $CHCl_3$); UV-vis ($CHCl_3$): λ_{max} (log ε) = 241 nm (4.26), 306 nm (3.53), 317 nm (3.52); IR (KBr): ν = 3388*w*, 2950*s*, 2926*s*, 2870*m*, 1746*vs*, 1682*m*, 1596*m*, 1572*w*, 1522*m*, 1486*s*, 1370*s*, 1234*vs*, 1044*s*, 800 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.93 (*dd*, *J* = 4.2, 1.5 Hz, 1 H, H–42), 8.12 (*d*, *J* = 8.3 Hz, 1 H, H–44), 8.02 (*d*, *J* = 7.1 Hz, 1 H, H–38), 7.98 (*s*, 1 H, NH), 7.93 (*d*, *J* = 8.5 Hz, 1 H, H–40), 7.68 (*dd*, *J* = 8.5, 7.7 Hz, 1 H, H–39), 7.42 (*dd*, *J* = 8.6, 4.2 Hz, 1 H, H–43), 5.55 (*dd*, *J* = 3.4, 3.4 Hz, 1 H, H–12), 5.13 (*ddd*, *J* = 10.7, 10.7, 4.5 Hz, 1 H, H–2), 5.07 (*d*, *J* = 10.3 Hz, 1 H, H–3), 3.82 (*d*, *J* = 11.8 Hz, 1 H, H–24a), 3.57 (*d*, *J* = 11.9 Hz, 1 H, H–24b), 2.21 (*d*, *J* = 10.4 Hz, 1 H, H–18), 2.14 (*ddd*, *J* = 13.7, 13.7, 4.2 Hz, 1 H, H–16a), 2.10–1.89 (*m*, 5 H, H–1a + H–11a + H–11b + H–22a + H–16b), 2.08 (*s*, 3 H, H–36), 2.01 (*s*, 3 H, H–34), 1.98 (*s*, 3 H, H–32), 1.85 (*ddd*, *J* = 14.5, 14.5, 4.4 Hz, 1 H, H–15a), 1.79–1.66 (*m*, 2 H, H–22b + H–9), 1.65–1.51 (*m*, 2 H, H–19 + H–21a), 1.50–1.28 (*m*, 6 H, H–7a + H–7b + H–21b + H–6a + H–6b + H–5), 1.18–1.12 (*m*, 3 H, H–15b + H–1b + H–20), 1.17 (*s*, 3 H, H–27), 1.01 (*d*, *J* = 6.3 Hz, 3 H, H–30), 1.00 (*s*, 3 H, H–25), 0.96 (*d*, *J* = 6.5 Hz, 3 H, H–29), 0.84 (*s*, 3 H, H–23), 0.70 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.7 (C–28), 170.9 (C–35), 170.6 (C–31), 170.5 (C–33), 150.4 (C–42), 148.8 (C–31), 140.3 (C–13), 132.9 (C–37), 129.6 (C–39), 129.4 (C–44), 126.8 (C–40), 125.9 (C–12), 122.5 (C–45), 120.8 (C–43), 120.6 (C–38), 74.8 (C–3), 70.0 (C–2), 65.4 (C–24), 54.6 (C–18), 49.5 (C–17), 47.7 (C–5), 47.7 (C–9), 43.9 (C–1), 42.8 (C–14), 42.0 (C–4), 40.1 (C–19), 39.8 (C–8), 39.3 (C–20), 37.9 (C–10), 37.8 (C–22), 32.5 (C–7), 31.0 (C–21), 28.0 (C–15), 25.2 (C–16), 23.6 (C–11), 23.5 (C–27), 21.3 (C–30), 21.2 (C–32), 21.0 (C–36), 20.9 (C–34), 17.9 (C–6), 17.4 (C–26), 17.3 (C–29), 17.2 (C–25), 14.0 (C–23) ppm; MS (ESI): *m*/*z* (%)

= 741.5 ($[M+H]^+$, 100), 1482.1 ($[2M+H]^+$, 24); analysis calculated for $C_{45}H_{60}N_2O_7$ (740.97): C 72.94, H 8.16, N 3.78; found: C 72.73, H 7.97, N 3.51.

*4.2.24. 2α, 3β, 24-Triacetyloxy-ursan-12-en-28-oic acid 4-isoquinolinyl amide (**28**)*

As described for **5**, compound **28** (53 mg, 44%) was obtained from **25** and 4-aminoisoquinoline as a white solid; m.p. 173–177 °C; R_F = 0.40 (silica gel, chloroform/ethyl acetate, 1:1); $[\alpha]_D$ = -0.85° (*c* = 0.33, $CHCl_3$); UV-vis ($CHCl_3$): λ_{max} (log ε) = 289 nm (3.68), 301 nm (3.67), 324 nm (3.72); IR (KBr): ν = 3396*m*, 2948*m*, 2926*m*, 2870*m*, 1746*vs*, 1684*m*, 1626*w*, 1586*w*, 1522*m*, 1488*m*, 1456*m*, 1370*s*, 1252*vs*, 1044*s* cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 9.08 (*s*, 1 H, H–38), 9.03 (*s*, 1 H, H–39), 8.00 (*d*, *J* = 8.2 Hz, 1 H, H–41), 7.91 (*m*, 1 H, NH), 7.77–7.72 (*m*, 2 H, H–44 + H–42), 7.63 (*ddd*, *J* = 8.0, 5.9, 2.0 Hz, 1 H, H–43), 5.56 (*dd*, *J* = 3.4, 3.4 Hz, 1 H, H–12), 5.14 (*ddd*, *J* = 10.5, 10.5, 4.5 Hz, 1 H, H–2), 5.07 (*d*, *J* = 10.3 Hz, 1 H, H–3), 3.82 (*d*, *J* = 11.8 Hz, 1 H, H–24a), 3.57 (*d*, *J* = 11.8 Hz, 1 H, H–24b), 2.22 (*d*, *J* = 10.1 Hz, 1 H, H–18), 2.15 (*ddd*, *J* = 13.6, 13.6, 4.2 Hz, 1 H, H–16a), 2.10–1.91 (*m*, 5 H, H–1a + H–11a + H–11b + H–22a + H–16b), 2.08 (*s*, 3 H, H–36), 2.01 (*s*, 3 H, H–34), 1.98 (*s*, 3 H, H–32), 1.86 (*ddd*, *J* = 14.4, 14.4, 4.4 Hz, 1 H, H–15a), 1.77 (*ddd*, *J* = 13.6, 13.6, 4.3 Hz, 1 H, H–22b), 1.69 (*dd*, *J* = 11.0, 6.6 Hz, 1 H, H–9), 1.62 (*ddd*, *J* = 13.3, 6.6, 3.2 Hz, 1 H, H–21a), 1.59–1.52 (*m*, 1 H, H–19), 1.50–1.28 (*m*, 6 H, H–7a + H–7b + H–21b + H–6a + H–6b + H–5), 1.20–1.04 (*m*, 3 H, H–15b + H–1b + H–20), 1.17 (*s*, 3 H, H–27), 1.02 (*d*, *J* = 6.3 Hz, 3 H, H–30), 1.00 (*s*, 3 H, H–25), 0.97 (*d*, *J* = 6.5 Hz, 3 H, H–29), 0.85 (*s*, 3 H, H–23), 0.73 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.8 (C–28), 170.9 (C–35), 170.6 (C–31), 170.5 (C–33), 149.5 (C–39), 140.2 (C–13), 137.6 (C–38), 130.5 (C–42), 130.0 (C–37), 128.9 (C–40), 128.5 (C–41), 128.3 (C–45), 127.4 (C–43), 126.0 (C–12), 120.1 (C–44), 74.9 (C–3), 70.0 (C–2), 65.4 (C–24), 54.7 (C–18), 49.5 (C–17), 47.7 (C–5), 47.7 (C–9), 43.9 (C–1), 42.8 (C–14), 42.1 (C–4), 40.1 (C–19), 39.8 (C–8), 39.3 (C–20), 37.9 (C–10), 37.8 (C–22), 32.5 (C–7), 31.0 (C–21), 28.0 (C–15), 25.2 (C–16), 23.6 (C–11), 23.5 (C–27), 21.3 (C–30), 21.2 (C–32), 21.0 (C–36), 20.9 (C–34), 17.9 (C–6), 17.4 (C–26), 17.4 (C–29), 17.2 (C–25), 14.0 (C–23) ppm; MS (ESI): *m*/*z* (%) = 741.5 ($[M+H]^+$, 100), 763.3 ($[M+Na]^+$, 4), 1482.3 ($[2M+H]^+$, 92); analysis calculated for $C_{45}H_{60}N_2O_7$ (740.97): C 72.94, H 8.16, N 3.78; found: C 72.75, H 8.33, N 3.52.

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- Amide derivatives of augustic, 2-epi-corosolic and asiatic acid were synthesized
- They were tested for their antitumor activity using human cancer cell lines
- An augustic acid derived 4-isoquinolinyl amide showed increased cytotoxicity
- A 4-isoquinolinyl derivative of asiatic acid (**28**) gave EC_{50} = 80 nM (A2780 cells)
- The compounds act by apoptosis