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Research paper

Urea derivates of ursolic, oleanolic and maslinic acid induce apoptosis and are selective cytotoxic for several human tumor cell lines

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ABSTRACT

2,3-Di-*O*-acetyl-maslinic acid benzylamide (**5**) has previously been shown to possess high cytotoxicity for a variety of human tumor cell lines while being of low cytotoxicity to non-malignant cells. Structural modifications performed on **5** revealed that the presence of these acetyl groups in **5** and the presence of (2β,3β)-configurated centers seems necessary for obtaining high cytotoxicity combined with best selectivity between malignant cells and non-malignant mouse fibroblasts. Compounds carrying an ursane skeleton showed weaker cytotoxicity than their oleanane derived analogs. In addition, the benzylamide function in compound **5** should be replaced by a phenylurea moiety to gain better cytotoxicity while retaining and improving the selectivity. Thus, maslinic acid derived *N*-[2β,3β-di-*O*-acetyl-17β-amino-28-norolean-12-en-17-yl]phenylurea (**45**) gave best results showing EC_{50} = 0.9 μM (for A2780 ovarian cancer cells) with EC_{50} > 120 μM for fibroblasts (NIH 3T3) and triggered apoptosis while caspase-3 was not activated by this compound.

1. Introduction

Animal as well as human life seems associated with the occurrence of cancer. One of the earliest written records describing breast cancer is found in an egyptian Papyrus ("Edwin Smith") from 1600 BC. At that time and for many centuries surgery was the only treatment, later on followed by radiation, chemotherapy and now-a-days increasingly by treatment with cancer-cell specific antibodies. Although chemotherapy offers the greatest chance of cure for several types of cancer there is still an increasing need for the development of new, selective and effective drugs.

Natural products and derivatives thereof play a key role in treating cancer, and (tri)-terpenoid natural products came again in the center of scientific interest during the ever-lasting search for new cytotoxic and selective drugs. Thus, almost 40% of all scientific publications covering the chemistry/biology of triterpenoic acids (holding either a α-amyrin, a β-amyrin or a lupane skeleton) have been published not until 2010 to 2015. Oleanolic acid (**1**, **OA**, Fig. 1) and ursolic acid (**2**, **UA**) and their derivatives have been investigated in detail by several groups, and many interesting biological properties have been detected, among them antimicrobial [1,2], antifungal [3], anti-oxidative [4] and anti-inflammatory [5] as well as antitumor-active properties [5–10].

Recently, triterpenoids carrying hydroxylic groups at position C-2 and C-3 of ring A, especially maslinic acid (**3**, **MA**) moved into the focus of scientific investigations while derivatives of betulinic acid (**4**, **BA**) are of continuing interest. Although the cytotoxic properties of maslinic acid have been shown as early as 1988 [11], its mode of action remained by and large unclear [11–14]. Previously, an increase of anti-proliferative activity was achieved by derivatization at position C-28, and an EC_{50} = 0.5 μM for A2780 ovarian cancer cells was found for a 2,3-di-*O*-acetyl-maslinic acid benzylamide (EM2, **5**) [17]. This compound showed high cytotoxicity for a variety of human tumor cell lines but also rather low cytotoxicity for non-malignant mouse fibroblasts NIH 3T3 (selectivity factor approximately F = 70) [16].

Thus, compound **5** seems to be an ideal starting point for the search for highly active and tumor-cell specific compound analogs, predominantly by performing modifications in ring A (Fig. 1), in Ring E as well as by modifications at the carbonyl group. These derivatives were subjected to a sulforhodamine B assay [17] for the determination of their cytotoxic activity. Representative and most active compounds of this screening were investigated in more detail by annexin V/propidium iodide staining and by investigation of their action onto the cell-cycle.

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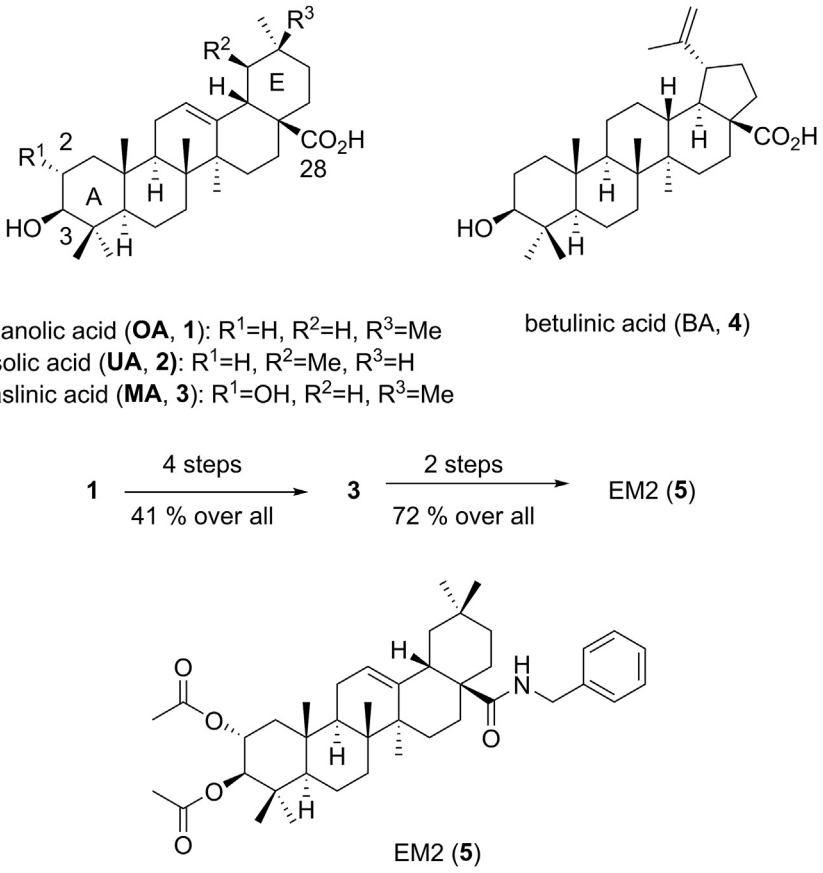


Fig. 1. Structure of representative triterpenoic acids **1**–**4** and the transformation of oleanolic acid (**1**) into maslinic acid (**3**) [20] followed by its transformation into the highly cytotoxic derivative EM2 (**5**) [15,27].

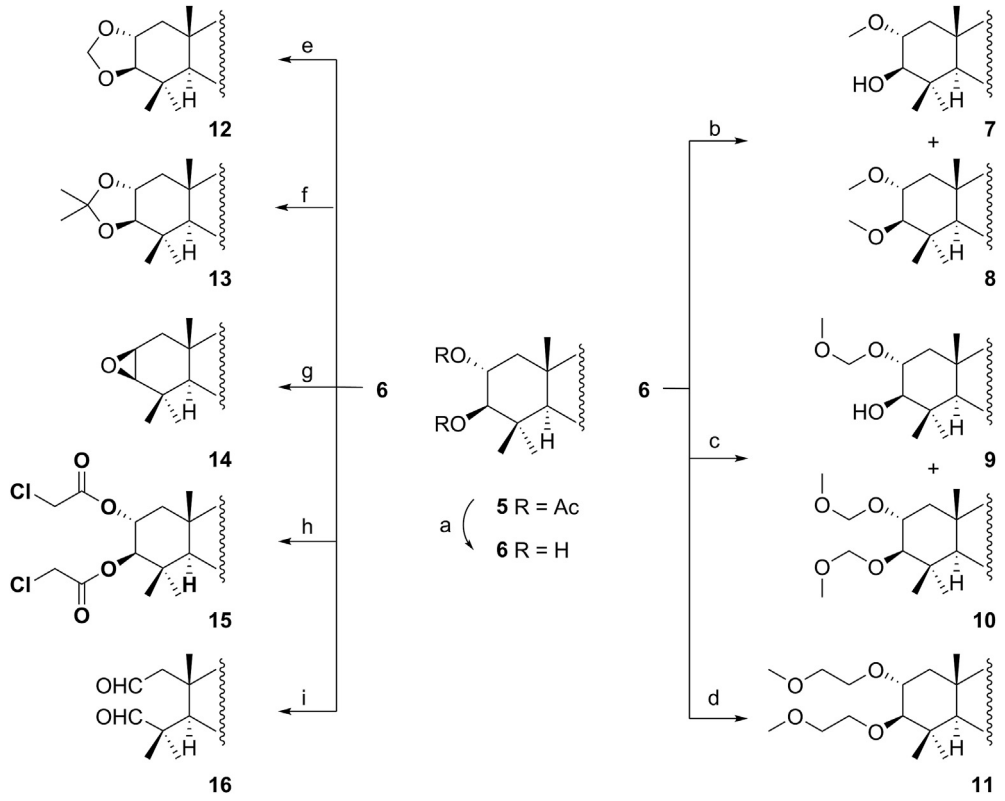
2. Results and discussion

The presence of oxygen-carrying substituents at positions C-2 and C-3 in ring A seems important for obtaining good cytotoxicity; these functionalities, however, have to be protected. Unprotected hydroxyl groups at these positions led to an approximately 4-fold decrease in cytotoxicity [15]. Our strategy to obtain C2/C3-modified derivatives of maslinic aacid (**3**) started from oleanolic acid (**1**). Thus, **3** was obtained from **1** by partial synthesis in an overall yield of 41% as previously described. This approach for obtaining large amounts of **3** seems more convenient than the extraction of **3** from olives or olive pomace [18]. Reaction of **3** with oxalyl chloride followed by a reaction with benzylamine gave known compound **6** that served as a valuable starting material for the transformations to follow (Scheme 1).

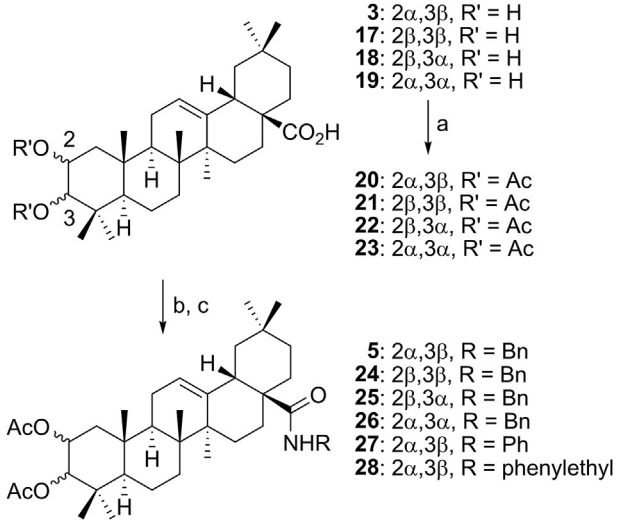
Thus, reaction of **6** with sodium hydride and methyl iodide [19] gave the 2-monomethylether **7** together with dimethyl ether **8** while no 3-monomethyl ether was formed at all (see Scheme 2). This selective methylation is probably due to steric hindrance at C (3)-OH caused by the presence of the geminal dimethyl group at position C-4. Reaction of **6** under the same conditions using 1-bromo-2-methoxyethane as the alkylating agent gave **11**. The reaction of **6** with 2,2-dimethoxymethane in the presence of catalytic amounts of *p*-TsOH led to the formation of three different products as a function of temperature and time. Thus, reaction of **6** for 6 days at room temperature gave a mixture consisting of the 2-methoxymethoxy derivative **9** together with the 2,3-dimethoxymethoxy derivative **10**, while the microwave assisted reaction at 120 °C furnished the 2,3-methylenated compound **12**. Reaction of **6** with 2,3-dimethoxypropane (in the presence of *p*-TsOH), however, gave a 91% yield of **13** within just a few minutes [20]. The epoxide **14** was synthesized following the procedure given by Garcia–Granados et al. [21] using PPh_3 and diethyl azodicarboxylate in DMF. While compound **15** was easily obtained from the reaction of **6** with chloroacetic anhydride, the formation of dialdehyde **16** required the presence of silica supported sodium periodate [22]. The presence of the two aldehyde moieties was easily shown by ^{1}H NMR-spectroscopy; the ^{1}H NMR spectrum of 16 showed the presence of a triplet at $\delta = 9.80$ ppm and a singlet at $\delta = 9.60$ ppm.

Betulinic acid (**BA**, as a standard), maslinic acid (**MA**, for comparison) and compounds **5**, **7**–**16** were submitted to SRB assays, and the results of these assays are compiled in Table 1.

For compounds **7**, **8**, **10**, **12**–**14** and **16** (Table 1) a significant decrease of the cytotoxicity was observed. In addition, these compounds also showed a diminished selectivity concerning tumor cell lines and non-malignant mouse fibroblasts. Compounds **9** and **11**, however, show similar biological activity compared to EM2 (**5**) concerning cytotoxicity and tumor-to-non-tumor selectivity. The selectivity index ($F_{SI} = EC50_{,\ NIH\ 3T3}/EC50_{,\ tumor\ cell\ line}$) is approximately 5 for both compounds and promising but still decreased as compared to compound **5**. The most active compound of this series is the bis-chloroacetate **15** showing an $EC_{50} = 2$ μM for the human breast cancer cell line MCF-7. This increase in cytotoxicity, however, is accompanied by an almost total loss in selectivity ($F_{SI} = 0.8$). This parallel previous results observed for derivatives of the triterpenoid tormentic acid [23]. As a result, derivatives carrying acetyl protecting groups at OH–C (2) and OH–C (3) produce the best results



Scheme 1. Synthesis of maslinic acid derived compounds **6**–**16**: (a) MeOH/KOH, 25 °C, 24 h, 66%; (b)NaH, MeI, THF, 0 °C → 25 °C, 5 d, 38% (for **7**), 33% (for **8**); (c) dimethoxymethane, *p*-TsOH, 25 °C, 7 d, 35% (for **9**), 40% (for **10**); (d) NaH, 1-bromo-2-methoxyethane, THF, 0 °C → 25 °C, 5 d, 58%, (e) dimethoxymethane, *p*-TsOH, 120 °C, 2 h, microwave assisted, 78%; (f) DMP, *p*-TsOH, 25 °C, 10 min, 91%; (g) PPh_3, DEAD, DMF, 0 °C → reflux, 2 d, 65%; (h) chloroacetic anhydride, TEA, DMAP, DCM, 25 °C, 20 h, 92%; (i) $NaIO_4$ on silica, DCM, 25 °C, 2 min, 98%.



Scheme 2. Synthesis of compounds **5**, **20**–**28**: (a) Ac_2O, TEA, DMAP, DCM, 25 °C, 20 h, 76–78%; (b) oxalyl chloride, TEA, DMF, DCM, 25 °C, 2 h; (c) RNH_2, TEA, DMAP, DCM, 0 °C, 5 min, 81–87%; R = Bn (**5**, **24**–**26**), Ph (**27**), phenylethyl (**28**).

in SRB assays, i.e. they combined highest cytotoxicity with best selectivity between malignant cells and non-malignant mouse fibroblasts.

In continuation of these observations, the relevance of the relative configuration at positions C-2 and C-3 of ring A was investigated in more detail. As already shown, all of the four possible diastereoisomers **3**, **17**–**19** (with respect to positions C-2 and C-3) can be synthesized very easily from commercially available oleanolic acid (**1**) [20]. Acetylation of **3**, **17**–**19** with acetic anhydride in DCM in the presence of DMAP and trimethylamine gave diacetates **20**–**23**; their treatment with oxalyl chloride/benzylamine under Schotten-Baumann conditions afforded EM2 (**5**) and analogs **24**–**26**. Reaction of **20** with aniline or 2-phenylethylamine applying similar conditions gave **27** and **28**, respectively.

The (2β,3β) configurated derivative **24** showed in the SRB assays EC_{50} values of similar magnitude as standard compound **5** but the tumor-to-non-tumor selectivity was significantly smaller than that observed for EM2. A loss of selectivity was also observed for (2α,3α)-configurated **26**; in addition, **26** showed the highest EC_{50} values of all compounds in this series. Quite the opposite, for (2β,3α)-configurated **25**, a 10-fold diminished selectivity was observed. As a result, the presence of a 3β configurated center seems important for obtaining compounds of high cytotoxicity and good-to-excellent selectivity.

In a next step, the influence of the chain length between the aromatic substituent and the amide at C-28 was investigated. Compared to EM2 (**5**) chain elongated **28** showed a decreased cytotoxicity, while shortening of the chain (as represented in phenylamide **27**) increased cytotoxicity as well as tumor-to-non-tumor cell selectivity (Table 1).

All of the derivatives described above possess an oleanane skeleton. Hence, we became interested in possible differences in bioactivity comparing molecules comprising an oleanane or an ursane skeleton. Despite all limitations results from this investigation and data from literature so far suggest that the presence of

Table 1
Cytotoxicity of selected compounds, betulinic acid (**BA**, standard) and maslinic acid (**MA**, for comparison), oleanolic acid (**OA**, for comparison) and ursolic acid (**UA**, for comparison): EC_{50} values in μM from SRB assays after 96 h of treatment; the values are averaged from three independent experiments performed each in triplicate; confidence interval CI = 95%; n.d. not detected/not determined. Human cancer cell lines: 518A2 (melanoma), FaDu (hypopharyngeal carcinoma), HT29 (colorectal adenocarcinoma), MCF7 (breast adenocarcinoma), A549 (lung adenocarcinoma), A2780 (ovarian carcinoma), SW 1736 (thyroid carcinoma); NIH 3T3: non-malignant mouse fibroblasts.

EC_{50}	518A2	FADU	HT29	MCF-7	A549	A2780	SW1736	NIH 3T3
BA	9.4 ± 0.4	15.3 ± 2.1	14.4 ± 1.5	10.2 ± 0.9	17.1 ± 1.6	8.8 ± 0.7	n.d.	16.1 ± 1.4
MA	13.7 ± 0.9	n.d.	28.8 ± 0.5	37.2 ± 1.2	23.4 ± 0.5	19.5 ± 0.8	n.d.	21.1 ± 0.2
OA	64.3 ± 4.2	75.4 ± 3.4	38.8 ± 3.1	80.0 ± 3.5	72.3 ± 1.5	14.0 ± 0.7	n.d.	76.4 ± 0.7
UA	14.7 ± 0.1	14.2 ± 2.0	10.6 ± 0.3	12.7 ± 0.1	15.5 ± 1.3	11.7 ± 0.6	n.d.	18.7 ± 1.6
5	1.5 ± 0.2	3.1 ± 0.1	4.7 ± 0.2	7.7 ± 0.5	2.5 ± 0.1	0.5 ± 0.1	n.d.	33.8 ± 3.0
7	12.6 ± 1.1	11.4 ± 1.5	10.6 ± 0.9	11.7 ± 2.1	21.5 ± 3.0	n.d.	18.1 ± 3.1	11.9 ± 1.0
8	18.1 ± 2.0	17.2 ± 1.4	14.3 ± 1.1	14.6 ± 2.4	15.3 ± 0.4	n.d.	20.5 ± 1.4	14.7 ± 1.2
9	3.2 ± 0.1	3.3 ± 0.2	5.2 ± 0.7	5.5 ± 0.6	12.8 ± 1.2	n.d.	5.4 ± 0.7	16.5 ± 1.9
10	22.1 ± 2.7	17.9 ± 2.1	15.9 ± 0.5	15.2 ± 3.0	17.3 ± 0.9	n.d.	18.2 ± 2.7	15.0 ± 1.6
11	3.5 ± 0.1	n.d.	4.9 ± 0.3	6.8 ± 1.9	4.9 ± 0.7	2.7 ± 0.9	4.6 ± 0.6	15.5 ± 2.9
12	>30	>30	20.8 ± 0.7	16.7 ± 1.7	>30	n.d.	>30	13.9 ± 3.3
13	29.8 ± 2.4	>30	25.9 ± 3.1	14.6 ± 1.7	26.4 ± 0.4	12.9 ± 1.5	>30	21.6 ± 2.3
14	15.7 ± 0.9	>30	26.6 ± 3.8	8.6 ± 2.0	25.8 ± 1.7	8.6 ± 1.1	>30	20.5 ± 4.7
15	2.1 ± 0.0	2.8 ± 1.0	4.3 ± 0.5	2.0 ± 0.5	6.5 ± 0.0	n.d.	3.3 ± 0.5	1.6 ± 0.2
16	6.0 ± 0.1	7.0 ± 0.1	8.3 ± 0.4	5.4 ± 0.1	6.9 ± 0.7	n.d.	7.5 ± 0.7	12.2 ± 0.8
20	23.1 ± 0.5	17.8 ± 0.8	25.5 ± 2.2	16.6 ± 1.5	18.9 ± 1.5	10.5 ± 0.9	n.d.	12.2 ± 0.7
21	13.8 ± 1.0	>30	18.8 ± 1.6	15.1 ± 1.3	29.1 ± 1.0	7.2 ± 0.6	>30	8.0 ± 1.0
22	11.7 ± 0.9	9.5 ± 0.5	16.5 ± 0.8	14.8 ± 0.6	15.2 ± 0.9	6.7 ± 0.7	23.4 ± 4.4	10.0 ± 0.6
23	15.3 ± 1.0	17.3 ± 0.7	21.4 ± 0.6	17.6 ± 0.6	20.4 ± 0.8	10.5 ± 0.7	22.0 ± 1.1	14.2 ± 1.1
24	0.9 ± 0.3	2.0 ± 0.3	3.7 ± 0.4	3.5 ± 1.2	5.6 ± 0.4	0.5 ± 0.2	3.4 ± 0.3	9.4 ± 1.1
25	2.3 ± 0.2	3.3 ± 0.1	5.2 ± 3.3	7.6 ± 1.0	8.8 ± 1.4	1.1 ± 0.1	5.2 ± 1.9	7.7 ± 1.0
26	5.7 ± 0.8	5.5 ± 1.1	7.7 ± 0.9	7.8 ± 0.6	15.6 ± 1.0	1.9 ± 0.3	20.7 ± 8.2	11.4 ± 0.6
27	0.7 ± 0.7	1.4 ± 0.1	2.9 ± 0.7	3.1 ± 0.5	9.5 ± 2.1	n.d.	2.9 ± 0.5	16.0 ± 1.9
28	1.2 ± 0.2	2.8 ± 0.5	6.1 ± 1.4	5.8 ± 1.0	9.2 ± 2.3	n.d.	5.2 ± 3.0	9.5 ± 3.1

acetyl groups at OH–C (2) and OH–C (3) seems as mandatory for obtaining highly active compounds as a (2β,3β)-configuration in ring A and the presence of a phenylamide rather than of a benzylamide at C-28. Hence, 2-*epi*-corsolic acid (**33**) possessing a (2β, 3β) configuration at ring A seemed an ideal starting point for these investigations. This compound, however, is expensive, and its extraction from natural sources is rather tedious and time consuming. Hence, an alternative partial synthesis of **33** was developed starting from easily accessible and cost-efficient ursolic acid (**2**). Jones oxidation [20,24] of **2** furnished 3-oxo compound **29** (Scheme 3) whose bromination with pyridinium tribromide gave a 2:1 mixture of epimeric compounds **30**/**31** [25]. Nucleophilic substitution of the bromine substituents in the presence of air gave an almost quantitative yield of enol **32** whose reduction with sodium borohydride gave (2β,3β) (**33**) in an excellent over-all yield of 38% (from **2**, after re-crystallization from ethyl acetate). Acetylation of **33** gave di-acetate **34**.

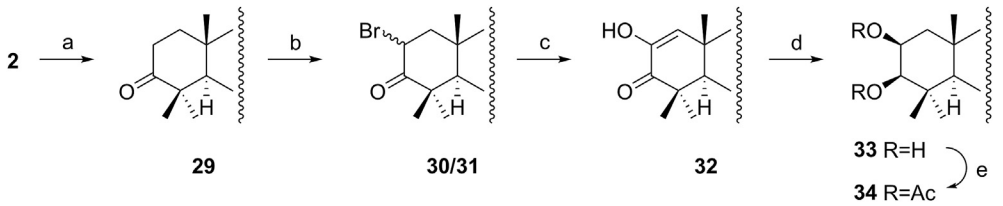
Microwave assisted reactions of **21** or **34** with diphenylphosphoryl azide at 180 °C gave isocyanates **35** and **36**, respectively (Scheme 4). The isocyanates are characterized in their IR spectra by the presence of strong absorption signals at $\nu = 2256–2270\ cm^{-1}$. And in their ^{13}C NMR spectra the signal for the N=**C**=O moiety was detected at $\delta = 122.0$ and 122.4 ppm, respectively [26].

Surprising differences in reactivity were observed for the hydrolysis reactions of the isocyanates **35** and **36**. While oleanane derived **35** gave an almost quantitative yield of amine **37** at 30 °C within 2 h, for the ursane-type isocyanate **36**, however, a complete reaction occurred only at 50 °C after 1 day of reaction. These differences in reactivity are probably due to the steric hindrance of the methyl groups in ring E in molecules of the ursane-type. Reaction of amines **37** and **38** with benzoyl chloride gave amides **41** and **42** while from the reaction of **37** and **38** with phenyl chloroformate carbamates **43** and **44** were obtained. Reaction of the amines with phenyl isocyanate yielded ureas **45** and **46**, respectively.

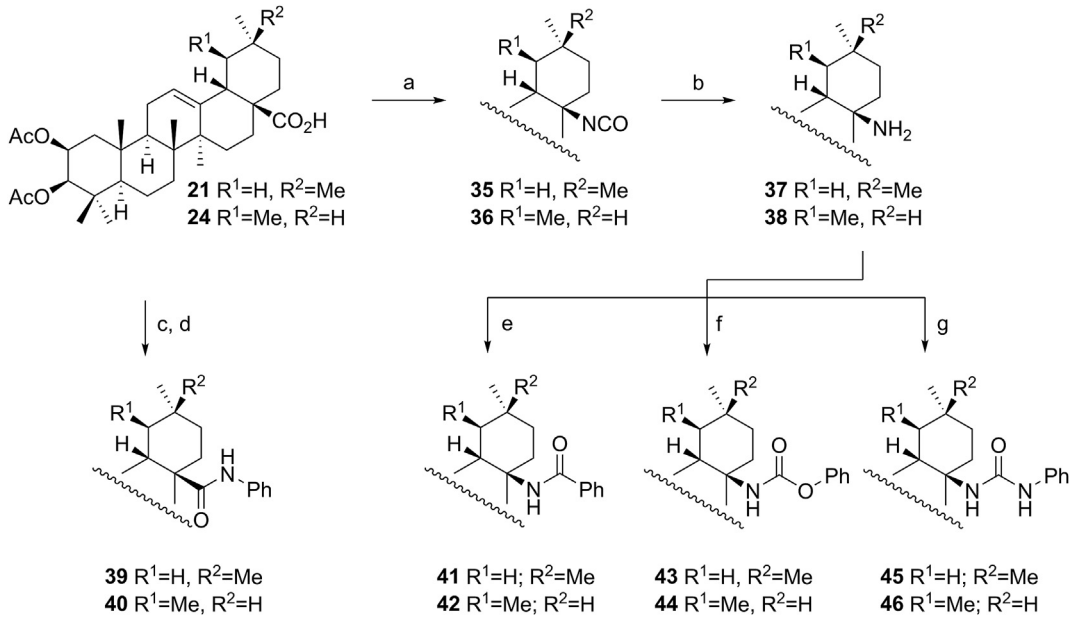
Screening of the compounds in SRB assays (Table 2) showed amides **41** and **42** of decreased cytotoxicity (compared to **39** and **40**), and for these compounds, selectivity between tumor cells and mouse fibroblasts is almost completely lost. A similar behavior was detected for carbamates **43** and **44**. Compounds **45** and **46** showed cytotoxic effects and selectivity similar to compounds **39** and **40**. By and large, ursane-derived compounds showed diminished cytotoxicity than their oleanane derived analogs.

To gain a deeper insight into the mode of action of compounds onto tumor cells, some extra experiments were performed, such as an annexin V/propidium iodide assay (Fig. 2), cell cycle evaluations (Fig. 3 A and B) as well as fluorescence microscopy (Fig. 3 C).

Thus, the cells were treated with compound **24** (10 μM, 48 h) or with compound **45** (10 μM, 24 h). The results from these assays indicate that a controlled cell death had occurred as evidenced by the presence of green fluorescent A2780 cells. Several cells showed



Scheme 3. Synthesis of compounds **29**–**34**: (a) Cr_3O/H_2SO_4, silica gel, acetone, 0 °C, 30 min, 100%; (b) pyridinium tribromide, acetic acid, 25 °C, 3 h, 100%; (c) air, NaOH (5 equiv), DMF, 60 °C, 1 h, 97%; (d) $NaBH_4$, THF/MeOH, 25 °C, 1 h, re-crystallized from ethyl acetate, 38%; (e) Ac_2O, TEA, DMAP, DCM, 25 °C, 20 h, 51%.



Scheme 4. (a) Diphenylphosphoryl azide, TEA, toluene, 180 °C, 3 h, microwaves, 76% (for **35**), 57% (for **36**); (b) HCl_{aq}, THF, 30–50 °C, 2–24 h, 76% (for **37**), 46% (for **38**); (c) oxalyl chloride, TEA, DMF, DCM, 25 °C, 2 h; (d) aniline, TEA, DMAP, DCM, 25 °C, 5 min, 86% (for **39**), 85% (for **40**); (e) benzoyl chloride, TEA, DMAP, DCM, 25 °C, 2 h, 78% (for **41**), 68% (for **42**); (f) phenyl chloroformate, TEA, DMAP, DCM 25 °C, 2 h, 92% (for **43**), 83% (for **44**); (g) phenylisocyanate, toluene, 2 h, 25 °C, 69% (for **45**), 58% (for **46**).

Table 2
Cytotoxicity of selected compounds (EC_{50} values in μM from SRB assays after 96 h of treatment; the values are averaged from three independent experiments performed each in triplicate; confidence interval CI = 95%; n.d. not detected, **MA** for comparison). Human cancer cell lines: 518A2 (melanoma), FaDu (hypopharyngeal carcinoma), HT29 (colorectal adenocarcinoma), MCF7 (breast adenocarcinoma), A549 (lung adenocarcinoma), A2780 (ovarian carcinoma), SW 1736 (thyroid carcinoma); NiH 3T3: nonmalignant mouse fibroblasts.

EC_{50}	518A2	HT29	MCF-7	A549	A2780	SW1736	NIH 3T3
MA	13.7 ± 0.9	28.8 ± 0.5	37.2 ± 1.2	23.4 ± 0.5	19.5 ± 0.8	n.d.	21.1 ± 0.2
39	2.0 ± 0.2	2.6 ± 0.5	1.8 ± 0.7	4.9 ± 0.4	1.3 ± 0.0	2.7 ± 0.8	>60
40	3.4 ± 0.1	7.3 ± 1.0	16.4 ± 2.9	8.9 ± 1.2	3.3 ± 1.3	4.4 ± 0.3	>60
41	3.5 ± 0.8	6.8 ± 1.1	16.8 ± 3.7	11.1 ± 2.0	3.1 ± 1.2	6.8 ± 2.3	12.2 ± 3.3
42	7.9 ± 0.5	11.7 ± 1.5	>30	16.4 ± 2.6	6.7 ± 1.2	14.9 ± 2.0	14.1 ± 2.1
43	4.4 ± 1.6	8.5 ± 3.2	5.8 ± 1.0	8.5 ± 1.2	2.4 ± 0.2	7.3 ± 0.9	15.4 ± 7.4
44	3.1 ± 0.9	7.6 ± 3.0	23.3 ± 6.1	10.1 ± 1.8	1.6 ± 0.4	5.5 ± 1.0	>30
45	1.2 ± 0.3	2.3 ± 2.7	2.8 ± 1.8	4.4 ± 1.7	0.9 ± 0.0	2.8 ± 1.2	>120
46	2.5 ± 0.5	16.0 ± 2.3	19.6 ± 1.6	12.4 ± 1.6	1.5 ± 0.5	6.8 ± 1.4	>120

an orange color; these cells have died by secondary necrosis. Furthermore, an annexin V/PI assay (Fig. 2) as well as a quantitative FACS experiment (Fig. 3) was performed. Therefore, A2780 cells were incubated with **24**–**26**, **43** and **45** for 24 h and 48 h, respectively. Fig. 2 depicts the results of this assay. For compounds **24**–**26** and **43**, treatment of the cells for 24 h showed only a small increase of annexin positive cells (2–5% apoptosis relative to control). On the contrary, the urea derivative **45** significantly induced controlled cell death after 24 h, and relative to control almost 33% of the A2780 cells showed apoptotic behavior. After 48 h about 65–78% of the A2780 cells carried phosphatidylserine in the outer leaf of the membrane, thus indicating an apoptotic death of these cells. Most of the dead cells (approximately 50%), however, showed apoptosis; another 20–30% of dead cell had died by a process of secondary necrosis. For the investigation of the cell cycle, A2780 cells were treated with **24**–**26**, **43** and **45** (10 μM) for 24 h. Close inspection of the results (Fig. 3) for living A2780 cells showed the presence of a weaker G1/G0 peak combined with an increase in the S phase after 24 h. An emersion of a Sub-G1 peak occurred with simultaneous decreases of G1/G0 phase and S phase (after 48 h, *cf.* suppl. part). Furthermore, a decrease of the G2/M phase was detected after 24 h. Caspase activation was determined after 24/48/72 h by using flow cytometry. As a result, the caspase assays showed no activation of effector caspase 3. Thus, a caspase-independent cell death was most likely. Based on these results we assume a cytostatic behavior of the compounds.

3. Conclusion

In this study several derivatives of 2,3-dihydroxy-triterpenoic acids were synthesized, and most of these showed low EC50 values in photometric SRB assays. Systematic variation of the protecting groups [at HO–C (2) and HO–C (3)], the absolute configuration at these centers, modifications at the carbonyl group at C-28 as well as comparison between analogs of the ursane *vs* oleanane skeleton type revealed, revealed that the presence of these acetyl groups at positions C-2 and C-3 and the presence of (2β,3β)-configurated centers seems necessary for obtaining high cytotoxicity combined with best selectivity between malignant cells and non-malignant mouse fibroblasts. An oleanane derived compounds showed better cytotoxicity than their ursane derived analogs, and the presence of a phenylurea moiety at C-28 led to a compound with improved cytotoxicity while retaining the selectivity between malignant cells and mouse fibroblasts. Thus, maslinic acid derived *N*-[2β,3β,17β)-

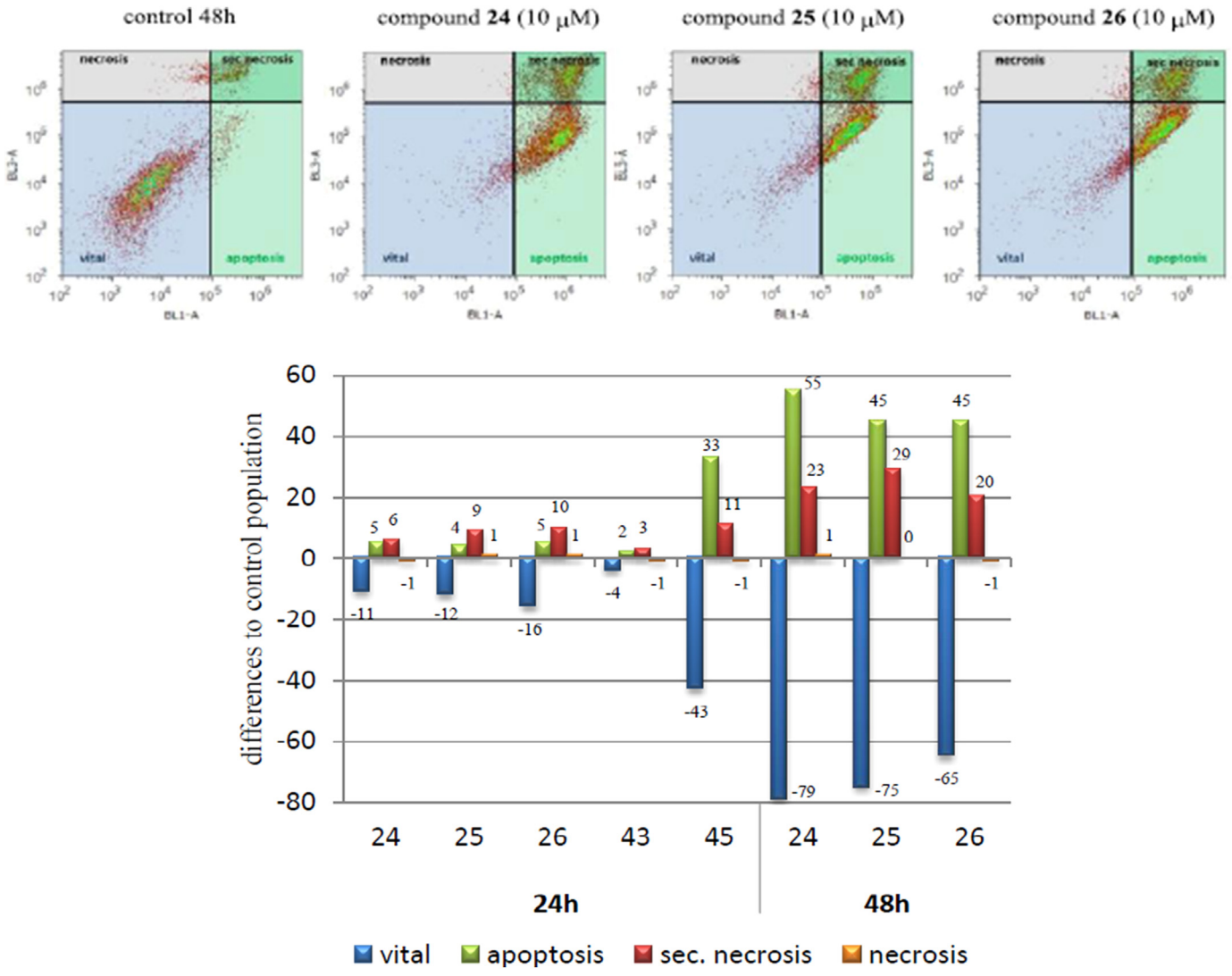


Fig. 2. Evaluation of annexin V/PI assay: treatment of A2780 cells after 24 h and 48 h with derivatives **24** (10 μM), **25** (10 μM), **26** (10 μM), **43** (10 μM), **45** (10 μM). Upper part: representative samples after 48 h treatment. Lower part: diagram with relative changes in the distribution compared to control [%], determined by Attune® Cytometric Software vl 1.2.5.

2,3-Di-*O*-acetyl-17-amino-28-norolean-12-en-17-yl]phenylurea (**45**) gave best results showing EC_{50} = 0.9 μM (for A2780 ovarian cancer cells) with EC_{50} > 120 μM for fibroblasts (NIH 3T3). This compound acts by apoptosis; its activity is caspase-3 independent.

4. Experimental part

4.1. General

Melting points are uncorrected (*Leica* hot stage microscope), NMR spectra were recorded using the Varian spectrometers Gemini 2000 or Unity 500 (δ given in ppm, *J* in Hz, internal Me_4Si, MS spectra were taken on a Finnigan MAT LCQ 7000 (electrospray, voltage 4.1 kV, sheath gas nitrogen) instrument. The optical rotation was measured on a Perkin–Elmer polarimeter at 20 °C; TLC was performed on silica gel (Merck 5554); elemental analyses were performed on a Vario EL (CHNS). The solvents were dried according to usual procedures. The purity of the compounds was determined by HPLC and found to be >98%. Ursolic acid (**1**) and oleanolic acid (**2**) were obtained from different commercial suppliers in bulk quantities; maslinic acid (**3**), EM2 (**5**), and compounds **17**–**20** were prepared as previously reported [15,18,20,27]. Microwave assisted reactions were performed in a Monowave 300 apparatus (Anton Paar, Austria). The SRB assay, the annexin V/propidium iodide staining and the FACS cell cycle investigations were performed as previously described [12,15,23,27].

4.2. Syntheses

4.2.1. 2α-Methoxy-3β-hydroxy-olean-12-en-28-oic acid benzylamide (7) and 2α,3β-dimethoxy-olean-12-en-28-oic acid benzylamide (8)

To an ice-cold solution of **6** (120 mg, 0.21 mmol) in dry THF (5 mL), sodium hydride (15 mg, 0.63 mmol) was added, and the mixture was stirred for 30 min and allowed to warm to room temperature. Methyl iodide (50 μL, 0.80 mmol) was added, and stirring at 25 °C was continued for 5 days. Et_2O (100 mL) was added, and the organic layer was washed consecutively with diluted hydrochloric acid (0.1 M, 1 × 100 mL), water (2 × 100 mL) and brine (1 × 50 mL), dried ($MgSO_4$), filtrated, and the filtrate was evaporated to dryness. The residue was subjected to column chromatography (silica gel, hexane/ethyl acetate, 8:2) to afford **7** (47 mg,

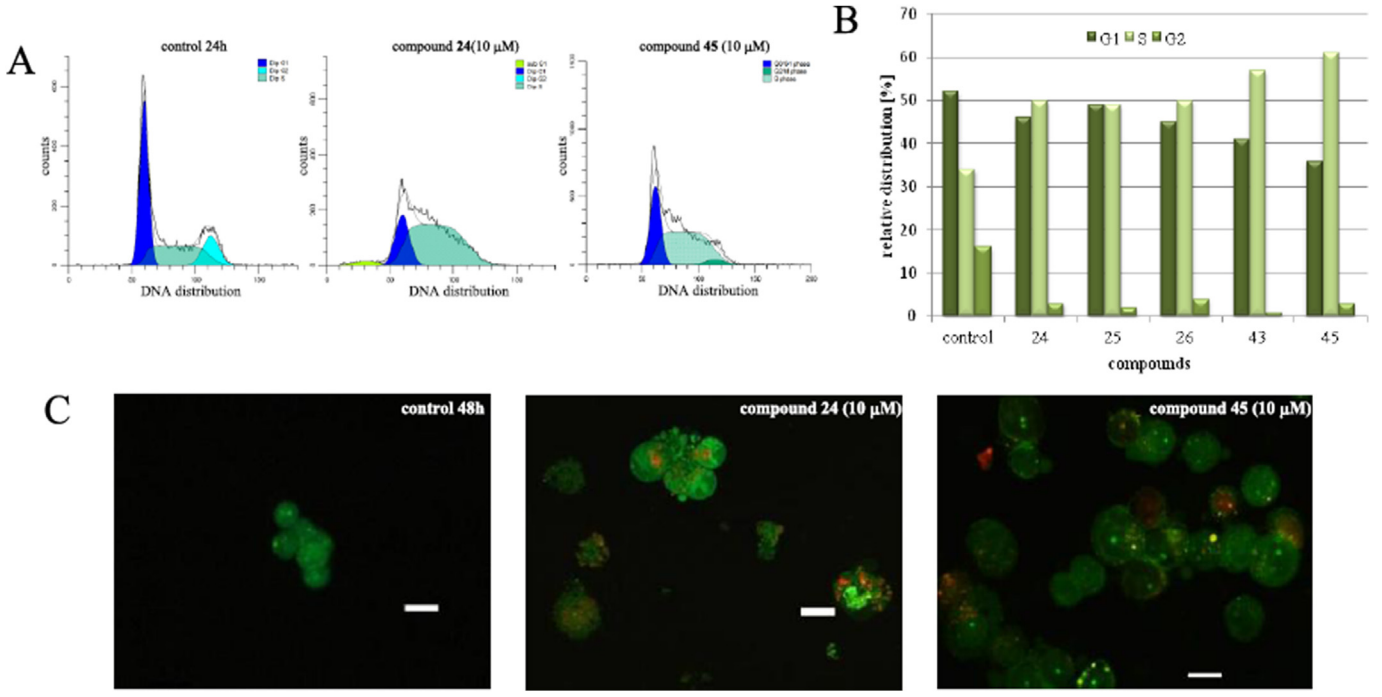


Fig. 3. (A): Representative examples for cell cycle evaluation of the living A2780 cells after 24 h with derivatives **24** (10 μM) and **45** (10 μM) via ModFit V 4.0.5. (B): Diagram with arithmetic means of the population distribution [%] of living A2780 cells treated with **24**–**26**, **43** and **45** (10 μM) for 24 h. (C) Representative fluorescence microscopic images (scale bar = 10 μm): control (A2780); treatment of A2780 cells with **24** (48 h, 10 μM) and **45** (24 h, 10 μM).

38%) and **8** (42 mg, 33%); **7**: white solid; mp 108–110 °C; R_F = 0.21 (silica gel, hexane/ethyl acetate, 8:2); $[\alpha]_D$ = −6.88° (*c* = 0.30, $CHCl_3$); IR (KBr): ν = 2944*vs*, 2878*s*, 1646*s*, 1518*s*, 1454*s*, 1388*m*, 1364*m*, 1264*m*, 1194*m*, 1092*s*, 1050*m*, 1030*m*, 698 *m* cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.35–7.31 (*m*, 2H, H–35), 7.29–7.23 (*m*, 3 H, H–34 + H–36), 6.17 (*dd*, *J* = 6.1, 4.6 Hz, 1 H, NH), 5.31 (*dd*, *J* = 3.6, 3.6 Hz, 1 H, H–12), 4.62 (*dd*, *J* = 14.7, 6.3 Hz, 1 H, H–32a), 4.15 (*dd*, *J* = 14.7, 4.4 Hz, 1 H, H–32b), 3.37 (*s*, 3 H, H–31), 3.21 (*ddd*, *J* = 11.2, 9.5, 4.3 Hz, 1 H, H–2), 3.04 (*d*, *J* = 9.5 Hz, 1 H, H–3), 2.56 (*dd*, *J* = 13.1, 4.4 Hz, 1 H, H–18), 2.05 (*dd*, *J* = 12.3, 4.3 Hz, 1 H, H–1a), 2.00 (*ddd*, *J* = 13.8, 13.8, 4.0 Hz, 1 H, H–16a), 1.94–1.80 (*m*, 2 H, H–11a + H–11b), 1.80–1.70 (*m*, 2 H, H–22a + H–19a), 1.70–1.52 (*m*, 5 H, H–16b + H–9 + H–22b + H–15a + H–6a), 1.49–1.31 (*m*, 3 H, H–7a + H–6b + H–21a), 1.29–1.13 (*m*, 3 H, H–7b + H–21b + H–19b), 1.15 (*s*, 3 H, H–27), 1.07–1.01 (*m*, 1 H, H–15b), 1.05 (*s*, 3 H, H–24), 0.93 (*s*, 3 H, H–25), 0.91 (*s*, 6 H, H–29 + H–30), 0.83 (*s*, 3 H, H–23), 0.81 (*dd*, *J* = 11.6, 1.8 Hz, 1 H, H–5), 0.72 (*dd*, *J* = 11.8, 11.8 Hz, 1 H, H–1b), 0.67 (*s*, 3 H, H–26); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 178.1 (C–28), 145.2 (C–13), 138.6 (C–33), 128.8 (C–35), 127.9 (C–34), 127.5 (C–36), 122.7 (C–12), 81.7 (C–3), 78.8 (C–2), 56.6 (C–31), 55.2 (C–5), 47.7 (C–9), 46.8 (C–19), 46.5 (C–17), 43.7 (C–32), 42.5 (C–18), 42.2 (C–14), 42.1 (C–1), 39.6 (C–8), 39.0 (C–4), 38.1 (C–10), 34.3 (C–21), 33.1 (C–30), 32.8 (C–22), 32.5 (C–7), 30.9 (C–20), 28.8 (C–24), 27.4 (C–15), 25.9 (C–27), 24.0 (C–16), 23.8 (C–29), 23.7 (C–11), 18.3 (C–6), 17.1 (C–26), 17.0 (C–23), 16.7 (C–25) ppm; MS (ESI): *m*/*z* (%) = 576.4 ($[M + H]^+$, 100), 598.6 ($[M + Na]^+$, 6), 1151.3 ($[2M + H]^+$, 82), 1173.5 ($[2M + Na]^+$, 68); analysis calculated for $C_{38}H_{57}NO_3$ (575.86): C 79.26, H 9.98, N 2.43; found: C 79.01, H 10.07, N 2.31; **8**: white solid; mp 96–97 °C; R_F = 0.42 (silica gel, hexane/ethyl acetate, 8:2); $[\alpha]_D$ = −7.61° (*c* = 0.24, $CHCl_3$); IR (KBr): ν = 2946*vs*, 2878*s*, 1644*s*, 1518*s*, 1454*s*, 1388*m*, 1364*m*, 1182*m*, 1114*s*, 1096*s*, 1016*m*, 698 *m* cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.34–7.30 (*m*, 2H, H–36), 7.29–7.21 (*m*, 3 H, H–35 + H–37), 6.18 (*dd*, *J* = 6.0, 4.6 Hz, 1 H, NH), 5.30 (*dd*, *J* = 3.5, 3.5 Hz, 1 H, H–12), 4.62 (*dd*, *J* = 14.7, 6.3 Hz, 1 H, H–33a), 4.14 (*dd*, *J* = 14.7, 4.3 Hz, 1 H, H–33b), 3.57 (*s*, 3 H, H–32), 3.42 (*s*, 3 H, H–31), 3.27 (*ddd*, *J* = 11.3, 9.6, 4.5 Hz, 1 H, H–2), 2.58 (*d*, *J* = 9.6 Hz, 1 H, H–3), 2.54 (*dd*, *J* = 12.7, 4.2 Hz, 1 H, H–18), 2.03–1.95 (*m*, 2 H, H–1a + H–16a), 1.94–1.80 (*m*, 2 H, H–11a + H–11b), 1.80–1.71 (*m*, 2 H, H–22a + H–19a), 1.70–1.48 (*m*, 5 H, H–16b + H–9 + H–22b + H–15a + H–6a), 1.47–1.28 (*m*, 3 H, H–7a + H–6b + H–21a), 1.28–1.13 (*m*, 3 H, H–7b + H–21b + H–19b), 1.14 (*s*, 3 H, H–27), 1.06–1.00 (*m*, 1 H, H–15b), 0.98 (*s*, 3 H, H–24), 0.91 (*s*, 6 H, H–29 + H–30), 0.90 (*s*, 3 H, H–25), 0.78 (*s*, 3 H, H–23), 0.78–0.73 (*m*, 2 H, H–5 + H–1b), 0.65 (*s*, 3 H, H26); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 178.2 (C–28), 145.0 (C–13), 138.6 (C–34), 128.8 (C–36), 127.9 (C–35), 127.5 (C–37), 122.9 (C–12), 93.0 (C–3), 79.7 (C–2), 62.3 (C–32), 57.8 (C–31), 55.3 (C–5), 47.7 (C–9), 46.8 (C–19), 46.5 (C–17), 44.5 (C–1), 43.7 (C–33), 42.5 (C–18), 42.2 (C–14), 40.5 (C–4), 39.6 (C–8), 37.8 (C–10), 34.3 (C–21), 33.1 (C–30), 32.8 (C–22), 32.4 (C–7), 30.9 (C–20), 28.7 (C–24), 27.5 (C–15), 25.9 (C–27), 24.0 (C–16), 23.8 (C–29), 23.7 (C–11), 18.4 (C–6), 17.4 (C–23), 17.1 (C–26), 16.7 (C–25) ppm; MS (ESI): *m*/*z* (%) = 590.3 ($[M + H]^+$, 100), 1179.3 ($[2M + H]^+$, 70), 1201.5 ($[2M + Na]^+$, 74); analysis calculated for $C_{39}H_{59}NO_3$ (589.89): C 79.41, H 10.08, N 2.37; found: C 70.26, H 10.19, N 2.16.

*4.2.2. 2α-Methoxymethoxy-3β-hydroxy-olean-12-en-28-oic acid benzylamide (**9**) and 2α,3β-dimethoxymethoxy-olean-12-en-28-oic acid benzylamide (**10**)*

To a solution of **6** (100 mg, 0.18 mmol) in dimethoxymethane (10 mL), *p*-TsOH (3 mg, 0.02 mmol) was added, and the mixture was stirred at 25 °C for 7 days. Et_2O (100 mL) was added, the organic layer was washed with water (2 × 100 mL) and brine (1 × 50 mL), dried ($MgSO_4$), filtrated, and the filtrate was evaporated to dryness. The residue was subjected to column chromatography (silica gel, hexane/ethyl acetate, 8:2) to afford compounds **9** (38 mg, 35%) and **10** (46 mg, 40%); **9**: white solid; mp 97–99 °C; R_F = 0.17 (silica gel, hexane/ethyl acetate, 8:2); $[\alpha]_D$ = −5.38° (*c* = 0.35, $CHCl_3$); IR (KBr):

ν = 2946*vs*, 1644*s*, 1520*m*, 1454*m*, 1388*m*, 1364*m*, 1212*m*, 1186*w*, 1146*m*, 1104*s*, 1040*s*, 698 *m* cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.31 (*m*, 2H, H–36), 7.29–7.23 (*m*, 3 H, H–35 + H–37), 6.17 (*dd*, *J* = 6.1, 4.7 Hz, 1 H, NH), 5.30 (*dd*, *J* = 3.6, 3.6 Hz, 1 H, H–12), 4.73 (*d*, *J* = 6.8 Hz, 1 H, H–31a), 4.69 (*d*, *J* = 6.8 Hz, 1 H, H–31b), 4.62 (*dd*, *J* = 14.7, 6.3 Hz, 1 H, H–33a), 4.14 (*dd*, *J* = 14.7, 4.4 Hz, 1 H, H–33b), 3.53 (*ddd*, *J* = 11.5, 9.4, 4.3 Hz, 1 H, H–2), 3.40 (*s*, 3 H, H–32), 3.07 (*d*, *J* = 9.5 Hz, 1 H, H–3), 2.55 (*dd*, *J* = 13.2, 4.2 Hz, 1 H, H–18), 2.03–1.95 (*m*, 2 H, H–1a + H–16a), 1.92–1.81 (*m*, 2 H, H–11a + H–11b), 1.80–1.71 (*m*, 2 H, H–22a + H–19a), 1.70–1.52 (*m*, 5 H, H–16b + H–9 + H–22b + H–15a + H–6a), 1.49–1.32 (*m*, 3 H, H–7a + H–6b + H–21a), 1.30–1.13 (*m*, 3 H, H–7b + H–21b + H–19b), 1.15 (*s*, 3 H, H–27), 1.07–1.02 (*m*, 1 H, H–15b), 1.06 (*s*, 3 H, H–24), 0.95–0.87 (*m*, 1 H, H–1b), 0.93 (*s*, 3 H, H–25), 0.90 (*s*, 6 H, H–29 + H–30), 0.83 (*s*, 3 H, H–23), 0.81 (*dd*, *J* = 11.7, 1.9 Hz, 1 H, H–5), 0.66 (*s*, 3 H, H26); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 178.1 (C–28), 145.1 (C–13), 138.6 (C–34), 128.8 (C–36), 127.9 (C–35), 127.5 (C–37), 122.8 (C–12), 96.8 (C–31), 81.5 (C–3), 78.7 (C–2), 55.8 (C–32), 55.0 (C–5), 47.6 (C–9), 46.8 (C–19), 46.5 (C–17), 44.7 (C–1), 43.7 (C–33), 42.5 (C–18), 42.3 (C–14), 39.6 (C–8), 39.3 (C–4), 38.2 (C–10), 34.3 (C–21), 33.1 (C–30), 32.8 (C–22), 32.4 (C–7), 30.9 (C–20), 29.0 (C–24), 27.4 (C–15), 25.9 (C–27), 24.0 (C–16), 23.8 (C–29), 23.7 (C–11), 18.3 (C–6), 17.1 (C–26), 17.1 (C–23), 16.7 (C–25) ppm; MS (ESI): *m*/*z* (%) = 606.4 ($[M + H]^+$, 100), 628.5 ($[M + Na]^+$, 4), 1211.3 ($[2M + H]^+$, 94), 1233.5 ($[2M + Na]^+$, 63); analysis calculated for $C_{39}H_{59}NO_4$ (605.89): C 77.31, H 9.82, N 2.31; found: C 77.08, H 9.97, N 2.03; **10**: white solid; mp 90–92 °C; R_F = 0.32 (silica gel, hexane/ethyl acetate, 8:2); $[\alpha]_D$ = 53.31° (*c* = 0.41, $CHCl_3$); IR (KBr): ν = 2946*vs*, 1646*s*, 1518*s*, 1454*s*, 1390*m*, 1364*m*, 1212*m*, 1198*m*, 1148*s*, 1106*s*, 1030*vs*, 918*s*, 698 *m* cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.34–7.30 (*m*, 2H, H–38), 7.29–7.23 (*m*, 3 H, H–37 + H–39), 6.17 (*dd*, *J* = 6.1, 4.6 Hz, 1 H, NH), 5.30 (*dd*, *J* = 3.6, 3.6 Hz, 1 H, H–12), 4.89 (*d*, *J* = 6.5 Hz, 1 H, H–33a), 4.72 (*d*, *J* = 6.4 Hz, 1 H, H–33b), 4.71 (*d*, *J* = 6.7 Hz, 1 H, H–31a), 4.67 (*d*, *J* = 6.7 Hz, 1 H, H–31b), 4.61 (*dd*, *J* = 14.7, 6.3 Hz, 1 H, H–35a), 4.14 (*dd*, *J* = 14.7, 4.4 Hz, 1 H, H–35b), 3.68 (*ddd*, *J* = 11.3, 9.6, 4.5 Hz, 1 H, H–2), 3.42 (*s*, 3 H, H–34), 3.36 (*s*, 3 H, H–32), 2.98 (*d*, *J* = 9.6 Hz, 1 H, H–3), 2.54 (*dd*, *J* = 13.0, 4.1 Hz, 1 H, H–18), 2.03–1.95 (*m*, 2 H, H–1a + H–16a), 1.92–1.80 (*m*, 2 H, H–11a + H–11b), 1.80–1.71 (*m*, 2 H, H–22a + H–19a), 1.70–1.51 (*m*, 5 H, H–16b + H–9 + H–22b + H–15a + H–6a), 1.49–1.30 (*m*, 3 H, H–7a + H–6b + H–21a), 1.29–1.13 (*m*, 3 H, H–7b + H–21b + H–19b), 1.14 (*s*, 3 H, H–27), 1.07–1.01 (*m*, 1 H, H–15b), 1.03 (*s*, 3 H, H–24), 0.93–0.85 (*m*, 1 H, H–1b), 0.93 (*s*, 3 H, H–25), 0.90 (*s*, 6 H, H–29 + H–30), 0.84 (*s*, 3 H, H–23), 0.80 (*dd*, *J* = 11.6, 1.7 Hz, 1 H, H–5), 0.65 (*s*, 3 H, H–26); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 178.1 (C–28), 145.1 (C–13), 138.5 (C–36), 128.8 (C–38), 127.9 (C–37), 127.5 (C–39), 122.8 (C–12), 99.4 (C–33), 96.4 (C–31), 89.5 (C–3), 76.2 (C–2), 56.3 (C–34), 55.5 (C–32), 55.3 (C–5), 47.6 (C–9), 46.8 (C–19), 46.5 (C–17), 45.6 (C–1), 43.7 (C–35), 42.5 (C–18), 42.2 (C–14), 39.8 (C–4), 39.5 (C–8), 37.9 (C–10), 34.3 (C–21), 33.1 (C–30), 32.8 (C–22), 32.5 (C–7), 30.9 (C–20), 28.9 (C–24), 27.4 (C–15), 25.9 (C–27), 24.0 (C–16), 23.8 (C–29), 23.7 (C–11), 18.5 (C–6), 17.8 (C–23), 17.1 (C–26), 16.6 (C–25) ppm; MS (ESI): *m*/*z* (%) = 650.3 ($[M + H]^+$, 100), 672.4 ($[M + Na]^+$, 8), 1299.3 ($[2M + H]^+$, 42), 1321.3 ($[2M + Na]^+$, 38); analysis calculated for $C_{41}H_{63}NO_5$ (649.94): C 75.77, H 9.77, N 2.16; found: C 75.52, H 9.91, N 2.04.

4.2.3. 2α,3β-Dimethoxyethoxy-olean-12-en-28-oic acid benzylamide (**11**)

To an ice-cold solution of **6** (120 mg, 0.21 mmol) in dry THF (5 mL) sodium hydride (15 mg, 0.63 mmol) was added. The mixture was stirred for 30 min at 25 °C, and 1-bromo-2-methoxyethane (80 μL, 0.85 mmol) was added. Stirring at 25 °C was continued for 5 days. Work-up as described above followed by column chromatography (silica gel, hexane/ethyl acetate, 8:2) gave **11** (84 mg, 58%) as white solid; mp 74–76 °C; R_F = 0.12 (silica gel, hexane/ethyl acetate, 8:2); $[\alpha]_D$ = 7.51° (*c* = 0.38, $CHCl_3$); IR (KBr): ν = 2944*vs*, 2874*s*, 1654*s*, 1518*m*, 1454*s*, 1388*m*, 1362*m*, 1198*m*, 1114*vs*, 1030*m*, 698 *m* cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.34–7.30 (*m*, 2H, H–40), 7.28–7.23 (*m*, 3 H, H–39 + H–41), 6.17 (*dd*, *J* = 6.2, 4.6 Hz, 1 H, NH), 5.30 (*dd*, *J* = 3.5, 3.5 Hz, 1 H, H–12), 4.62 (*dd*, *J* = 14.7, 6.3 Hz, 1 H, H–37a), 4.14 (*dd*, *J* = 14.7, 4.3 Hz, 1 H, H–37b), 4.09–4.05 (*m*, 1H, H–31a), 3.74–3.64 (*m*, 3H, H–31b + H–34a + H–34b), 3.56–3.47 (*m*, 4H, H–32a + H–32b + H–35a + H–35b), 3.43 (*ddd*, *J* = 11.4, 9.6, 4.5 Hz, 1 H, H–2), 3.37 (*s*, 3 H, H–33), 3.36 (*s*, 3 H, H–36), 2.75 (*d*, *J* = 9.5 Hz, 1 H, H–3), 2.54 (*dd*, *J* = 13.1, 4.2 Hz, 1 H, H–18), 2.03–1.94 (*m*, 2 H, H–1a + H–16a), 1.92–1.71 (*m*, 4 H, H–11a + H–11b + H–22a + H–19a), 1.70–1.48 (*m*, 5 H, H–16b + H–9 + H–22b + H–15a + H–6a), 1.47–1.28 (*m*, 3 H, H–7a + H–6b + H–21a), 1.28–1.14 (*m*, 3 H, H–7b + H–21b + H–19b), 1.13 (*s*, 3 H, H–27), 1.06–1.00 (*m*, 1 H, H–15b), 0.99 (*s*, 3 H, H–24), 0.91 (*s*, 3 H, H–30), 0.90 (*s*, 3 H, H–29), 0.89 (*s*, 3 H, H–25), 0.88–0.82 (*m*, 1 H, H–1b), 0.81 (*s*, 3 H, H–23), 0.76 (*dd*, *J* = 11.5, 1.6 Hz, 1 H, H–5), 0.64 (*s*, 3 H, H–26); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 178.1 (C–28), 145.0 (C–13), 138.6 (C–38), 128.8 (C–40), 127.9 (C–39), 127.5 (C–41), 122.9 (C–12), 91.4 (C–3), 78.6 (C–2), 73.5 (C–31), 72.7 (C–32), 72.7 (C–35), 69.5 (C–34), 59.1 (C–33), 59.1 (C–36), 55.3 (C–5), 47.6 (C–9), 46.8 (C–19), 46.5 (C–17), 44.9 (C–1), 43.7 (C–37), 42.5 (C–18), 42.2 (C–14), 40.5 (C–4), 39.5 (C–8), 37.9 (C–10), 34.3 (C–21), 33.1 (C–30), 32.8 (C–22), 32.4 (C–7), 30.9 (C–20), 28.8 (C–24), 27.4 (C–15), 25.9 (C–27), 24.0 (C–16), 23.8 (C–29), 23.7 (C–11), 18.4 (C–6), 17.7 (C–23), 17.1 (C–26), 16.6 (C–25) ppm; MS (ESI): *m*/*z* (%) = 678.3 ($[M + H]^+$, 100), 1355.3 ($[2M + H]^+$, 20); analysis calculated for $C_{43}H_{67}NO_5$ (678.00): C 76.17, H 9.96, N 2.07; found: C 75.88, H 10.11, N 1.93.

4.2.4. 2a,3b-Methylenedioxy-olean-12-en-28-oic acid benzylamide (**12**)

To a solution of **6** (50 mg, 0.09 mmol) in dimethoxymethane (10 mL) *p*-TsOH (3 mg, 0.02 mmol) was added followed by microwave irradiation (120 °C, 2 h). The mixture was diluted with Et_2O (100 mL), and the organic layer was washed with water (2 × 100 mL) and brine (1 × 50 mL), dried ($MgSO_4$), filtrated, and the filtrate was concentrated *in vacuo*. The residue was subjected to column chromatography (silica gel, hexane/ethyl acetate, 8:2) to provide **12** (40 mg, 78%) as a white solid; mp 113–116 °C; R_F = 0.41 (silica gel, hexane/ethyl acetate, 8:2); $[\alpha]_D$ = 15.08° (*c* = 0.21, $CHCl_3$); IR (KBr): ν = 2944*vs*, 2868*s*, 1644*s*, 1518*m*, 1454*m*, 1386*m*, 1364*m*, 1102*s*, 1018 *m* cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.31 (*m*, 2H, H–35), 7.29–7.23 (*m*, 3 H, H–34 + H–36), 6.16 (*dd*, *J* = 6.1, 4.6 Hz, 1 H, NH), 5.31 (*dd*, *J* = 3.6, 3.6 Hz, 1 H, H–12), 5.08 (*dd*, *J* = 10.3, 1.0 Hz, 2 H, H–31a + H–31b), 4.63 (*dd*, *J* = 14.7, 6.4 Hz, 1 H, H–32a), 4.14 (*dd*, *J* = 14.7, 4.4 Hz, 1 H, H–32b), 3.54 (*ddd*, *J* = 11.7, 9.4, 4.0 Hz, 1 H, H–2), 2.89 (*d*, *J* = 9.4 Hz, 1 H, H–3), 2.55 (*dd*, *J* = 13.1, 3.9 Hz, 1 H, H–18), 2.10 (*dd*, *J* = 11.5, 4.0 Hz, 1 H, H–1a), 2.00 (*ddd*, *J* = 13.7, 13.7, 3.8 Hz, 1 H, H–16a), 1.91–1.85 (*m*, 2 H, H–11a + H–11b), 1.80–1.72 (*m*, 2 H, H–22a + H–19a), 1.72–1.55 (*m*, 5 H, H–16b + H–9 + H–22b + H–15a + H–6a), 1.48–1.32 (*m*, 3 H, H–7a + H–6b + H–21a), 1.32–1.14 (*m*, 3 H, H–7b + H–21b + H–19b), 1.16 (*s*, 3 H, H–27), 1.08 (*s*, 3 H, H–24), 1.07–1.01 (*m*, 2 H, H–15b + H–1b), 0.97 (*s*, 3 H, H–25), 0.91 (*s*, 3 H, H–30), 0.91 (*s*, 3 H, H–29), 0.89 (*s*, 3 H, H–23), 0.83–0.79 (*m*, 1 H, H–5), 0.68 (*s*, 3 H, H–26); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 178.1 (C–28), 145.2 (C–13), 138.6 (C–33), 128.8 (C–35), 127.9 (C–34), 127.5 (C–36), 122.7 (C–12), 95.5 (C–31), 89.1 (C–3), 73.4 (C–2), 56.2 (C–5), 48.0 (C–9), 46.8 (C–19), 46.5 (C–17), 43.7 (C–34), 42.4

(C−18), 42.3 (C−14), 41.8 (C−1), 40.3 (C−4), 39.9 (C−8), 37.8 (C−10), 34.3 (C−21), 33.1 (C−30), 32.8 (C−22), 32.7 (C−7), 30.9 (C−20), 28.8 (C−24), 27.5 (C−15), 26.0 (C−27), 23.9 (C−16), 23.9 (C−11), 23.8 (C−29), 17.9 (C−6), 17.4 (C−26), 17.1 (C−25), 16.4 (C−23) ppm; MS (ESI): *m/z* (%) = 574.4 ([M + H]$^+$, 100), 596.5 ([M + Na]$^+$, 7), 1147.3 ([2M + H]$^+$, 72), 1169.5 ([2M + Na]$^+$, 82); analysis calculated for $C_{38}H_{55}NO_3$ (573.85): C 79.53, H 9.66, N 2.44; found: C 79.37, H 9.82, H 2.29.

4.2.5. 2α,3β-(Isopropylidenedioxy)-olean-12-en-28-oic acid benzylamide (**13**)

p-TsOH (3 mg, 0.02 mmol) was added to a solution of compound **6** (100 mg, 0.18 mmol) in 2,2-dimethoxypropane (10 mL). After 10 min of stirring at room temperature, Et_2O (100 mL) was added, and the organic layer was washed with water (2 × 100 mL) and brine (1 × 50 mL), dried ($MgSO_4$), filtrated, and the filtrate was evaporated to dryness followed by column chromatography (silica gel, hexane/ethyl acetate, 8:2) of the residue to afford **13** (98 mg, 91%) as a white solid; mp 122−123 °C; R_F = 0.45 (silica gel, hexane/ethyl acetate, 8:2); $[\alpha]_D$ = 29.29° (*c* = 0.38, $CHCl_3$); IR (KBr): ν = 2944*vs*, 2866*s*, 1660*s*, 1514*s*, 1454*s*, 1368*s*, 1230*s*, 1170*m*, 1004*m*, 1070*m*, 1054*s*, 854*m*, 698 *m* cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35−7.31 (*m*, 2H, H−37), 7.29−7.23 (*m*, 3 H, H−36 + H−38), 6.16 (*dd*, *J* = 6.2, 4.6 Hz, 1 H, NH), 5.30 (*dd*, *J* = 3.6, 3.6 Hz, 1 H, H−12), 4.63 (*dd*, *J* = 14.7, 6.4 Hz, 1 H, H−34a), 4.13 (*dd*, *J* = 14.7, 4.3 Hz, 1 H, H−34b), 3.69 (*ddd*, *J* = 11.7, 9.4, 4.0 Hz, 1 H, H−2), 3.03 (*d*, *J* = 9.4 Hz, 1 H, H−3), 2.54 (*dd*, *J* = 12.6, 4.2 Hz, 1 H, H−18), 2.04−1.96 (*m*, 2 H, H−1a + H−16a), 1.89−1.83 (*m*, 2 H, H−11a + H−11b), 1.79−1.72 (*m*, 2 H, H−22a + H−19a), 1.72−1.54 (*m*, 5 H, H−16b + H−9 + H−22b + H−15a + H−6a), 1.48−1.33 (*m*, 3 H, H−7a + H−6b + H−21a), 1.42 (*s*, 3 H, H−32), 1.40 (*s*, 3 H, H−33), 1.31−1.14 (*m*, 3 H, H−7b + H−21b + H−19b), 1.15 (*s*, 3 H, H−27), 1.06−0.98 (*m*, 2 H, H−15b + H−1b), 1.04 (*s*, 3 H, H−24), 0.97 (*s*, 3 H, H−25), 0.91 (*s*, 3 H, H−30), 0.91 (*s*, 3 H, H−29), 0.88 (*s*, 3 H, H−23), 0.82−0.78 (*m*, 1 H, H−5), 0.68 (*s*, 3 H, H−26); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 178.1 (C−28), 145.2 (C−13), 138.6 (C−35), 128.8 (C−37), 127.9 (C−36), 127.5 (C−38), 122.8 (C−12), 108.4 (C−31), 88.8 (C−3), 72.6 (C−2), 56.2 (C−5), 48.0 (C−9), 46.8 (C−19), 46.5 (C−17), 43.7 (C−34), 42.5 (C−18), 42.3 (C−14), 42.0 (C−1), 40.1 (C−4), 39.9 (C−8), 37.5 (C−10), 34.3 (C−21), 33.1 (C−30), 32.8 (C−22), 32.7 (C−7), 30.9 (C−20), 28.7 (C−24), 27.5 (C−15), 27.3 (C−32), 27.0 (C−33), 26.0 (C−27), 23.9 (C−16), 23.9 (C−11), 23.8 (C−29), 17.9 (C−6), 17.4 (C−26), 17.2 (C−25), 16.3 (C−23) ppm; MS (ESI): *m/z* (%) = 602.4 ([M + H]$^+$, 68), 624.5 ([M + Na]$^+$, 9), 1203.3 ([2M + H]$^+$, 50), 1225.5 ([2M + Na]$^+$, 100); analysis calculated for $C_{40}H_{59}NO_3$ (601.90): C 79.82, H 9.88, N 2.33; found: C 79.77, H 9.93, N 2.18.

4.2.6. 2β,3β-Epoxy-olean-12-en-28-oic acid benzylamide (**14**)

Compound **6** (100 mg, 0.18 mmol) was dissolved in DMF (1 mL), and PPh_3 (140 mg, 0.53 mmol) was added. The reaction mixture was stirred at 0 °C for 1 h, and a solution of diethyl azodicarboxylate (93 mg, 0.53 mmol) in DMF (0.2 mL) was slowly added. This mixture was heated under reflux for 2 h, and the solvent was removed under reduced pressure. Et_2O (100 mL) was added, and aqueous work-up as described above followed by chromatography (silica gel, hexane/ethyl acetate, 8:2) gave **14** (63 mg, 65%) as a white solid; mp 105−106 °C; R_F = 0.47 (silica gel, hexane/ethyl acetate, 8:2); $[\alpha]_D$ = 56.30° (*c* = 0.32, $CHCl_3$); IR (KBr): ν = 2950*vs*, 2868*s*, 1642*s*, 1520*s*, 1454*m*, 1386*m*, 1364*m*, 1280*w*, 1286*w*, 1240*w*, 1216*w*, 1184*w*, 840*m*, 698 *m* cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35−7.31 (*m*, 2H, H−34), 7.29−7.23 (*m*, 3 H, H−33 + H−35), 6.17 (*dd*, *J* = 6.1, 4.7 Hz, 1 H, NH), 5.32 (*dd*, *J* = 3.6, 3.6 Hz, 1 H, H−12), 4.62 (*dd*, *J* = 14.7, 6.4 Hz, 1 H, H−31a), 4.12 (*dd*, *J* = 14.7, 4.3 Hz, 1 H, H−31b), 3.23 (*ddd*, *J* = 3.9, 1.9, 1.9 Hz, 1 H, H−2), 2.82 (*d*, *J* = 4.0 Hz, 1 H, H−3), 2.53 (*dd*, *J* = 13.1, 4.0 Hz, 1 H, H−18), 2.12 (*dd*, *J* = 14.9, 1.9 Hz, 1 H, H−1a), 1.98 (*ddd*, *J* = 13.7, 13.7, 3.8 Hz, 1 H, H−16a), 1.89−1.84 (*m*, 2 H, H−11a + H−11b), 1.81−1.72 (*m*, 2 H, H−22a + H−19a), 1.71−1.51 (*m*, 3 H, H−16b + H−22b + H−15a), 1.47−1.32 (*m*, 5 H, H−9 + H−6a + H−7a + H−6b + H−21a), 1.28−1.14 (*m*, 4 H, H−7b + H−21b + H−1b + H−19b), 1.13 (*s*, 3 H, H−27), 1.08 (*s*, 3 H, H−24), 1.07−1.01 (*m*, 1 H, H−15b), 1.03 (*s*, 3 H, H−25), 1.00 (*s*, 3 H, H−23), 0.91 (*s*, 6 H, H−30 + H−29), 0.73−0.69 (*m*, 1 H, H−5), 0.67 (*s*, 3 H, H−26); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 178.1 (C−28), 144.9 (C−13), 138.6 (C−32), 128.8 (C−34), 127.9 (C−33), 127.5 (C−35), 123.1 (C−12), 61.1 (C−3), 54.4 (C−2), 52.2 (C−5), 47.8 (C−9), 46.9 (C−19), 46.6 (C−17), 43.7 (C−31), 42.6 (C−18), 42.4 (C−14), 39.7 (C−8), 38.5 (C−1), 36.9 (C−10), 34.3 (C−21), 33.2 (C−30), 32.8 (C−22), 32.5 (C−4), 32.1 (C−7), 30.9 (C−20), 30.4 (C−24), 27.4 (C−15), 25.8 (C−27), 24.0 (C−16), 23.8 (C−29), 23.6 (C−11), 20.7 (C−23), 19.8 (C−6), 16.9 (C−26), 16.8 (C−25) ppm; MS (ESI): *m/z* (%) = 544.3 ([M + H]$^+$, 98), 566.5 ([M + Na]$^+$, 14), 1087.3 ([2M + H]$^+$, 94), 1109.3 ([2M + Na]$^+$, 100); analysis calculated for $C_{37}H_{53}NO_2$ (543.82): C 81.72, H 9.82, N 2.58; found: C 81.56, H 9.93, N 2.41.

4.2.7. 2α,3β-Bis(chloroacetyloxy)-olean-12-en-28-oic acid benzylamide (**15**) (general procedure A, GP A)

To a solution of compound **6** (200 mg, 0.36 mmol) in dry DCM (20 mL), chloroacetic anhydride (246 mg, 1.44 mmol), triethylamine (164 mg, 1.62 mmol) and DMAP (5 mg, 0.04 mmol) were added, and the mixture was stirred at room temperature for 20 h. Et_2O (100 mL) was added, and the organic layer 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 the filtrate was concentrated *in vacuo*. The residue was subjected to column chromatography (silica gel, hexane/ethyl acetate, 8:2) to provide **15** (234 mg, 92%) as a white solid; mp 116−119 °C; R_F = 0.38 (silica gel, hexane/ethyl acetate 8:2); $[\alpha]_D$ = −5.04° (*c* = 0.28, $CHCl_3$); IR (KBr): ν = 3432*m*, 2948*s*, 1744*s*, 1650*m*, 1517*m*, 1454*s*, 1396*w*, 1309*s*, 1264*s*, 1185*s*, 1025*m*, 1001*s*, 751*s*, 699 *s* cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.40−7.20 (*m*, 5 H, H−37 + H−38 + H−39), 6.16 (*dd*, *J* = 5.2, 5.2 Hz, 1 H, NH), 5.31 (*dd*, *J* = 3.2, 3.2 Hz, 1 H, H−12), 5.18 (*ddd*, *J* = 11.2, 11.0, 4.5 Hz, 1 H, H−2), 4.86 (*d*, *J* = 10.3 Hz, 1 H, H−3), 4.61 (*dd*, *J* = 14.6, 6.1 Hz, 1 H, H−35a), 4.17 (*dd*, *J* = 14.6, 4.4 Hz, 1 H, H−35b), 4.05 (*s*, 1 H, H−32a), 4.05 (*s*, 1 H, H−32b), 3.96 (*s*, 2 H, H−34a + H−34b), 2.57 (dd, *J* = 12.7, 3.3 Hz, 1 H, H−18), 2.12−2.03 (m, 1 H, H−1a), 2.03−1.93 (*m*, 1 H, H−16a), 1.87−1.80 (*m*, 2 H, H−11a + H−11b), 1.81−1.53 (*m*, 7 H, H−19a + H−22a + H−16b + H−22b + H−9 + H−15a + H−6a), 1.53−1.18 (*m*, 5 H, H−7a + H−6b + H−21a + H−7b + H−21b), 1.17−1.12 (*m*, 4 H, H−19b + H−27), 1.12−1.05 (*m*, 2 H, H−1b + H−15b), 1.03 (s, 3 H, H−25), 1.01−0.96 (*m*, 1 H, H−5), 0.94 (*s*, 3 H, H−23), 0.94 (*s*, 3 H, H−24), 0.92 (*s*, 3 H, H−30), 0.92 (*s*, 3 H, H−29), 0.66 (*s*, 3 H, H−26); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.9 (C−28), 167.3 (C−31), 167.0 (C−33), 145.1 (C−13), 138.5 (C−36), 128.8 (C−38), 127.9 (C−37), 127.5 (C−39), 122.1 (C−12), 82.3 (C−3), 72.2 (C−2), 54.9 (C−5), 47.5 (C−9), 46.7 (C−19), 46.4 (C−17), 43.7 (C−1), 43.7 (C−35), 42.4 (C−18), 42.2 (C−14), 41.0 (C−32), 40.9 (C−34), 39.7 (C−4), 39.5 (C−8), 38.3 (C−10), 34.2 (C−21), 33.1 (C−30), 32.8 (C−22), 32.2 (C−7), 30.9 (C−20), 28.4 (C−24), 27.4 (C−15), 25.8 (C−27), 23.8 (C−16), 23.7 (C−29), 23.6 (C−11), 18.2 (C−6), 17.6 (C−23), 17.0 (C−26), 16.5 (C−25) ppm; MS (ESI): *m/z* (%) = 714.3 ([M + H]$^+$, 100), 736.1 ([M + Na]$^+$, 26), 1429.9 ([2M + H]$^+$, 32), 1451.3 ([2M + Na]$^+$, 52); analysis calculated for $C_{41}H_{57}Cl_2NO_5$ (714.80): C 68.89, H 8.04, N 1.96; found: C 68.64, H 7.87, N 1.79.

4.2.8. 2,3-Seco-olean-12-en-2,3-dial-28-oic acid benzylamide (**16**)

Compound **6** (100 mg, 0.18 mmol) was dissolved in DCM (30 mL) and silica supported sodium periodate (silica gel, 320 mg; sodium

periodate, 80 mg, 0.37 mmol) was added. The suspension was stirred for 2 min at 25 °C. Water (30 mL) was added, and the organic layer was washed with water (2 × 30 mL) and brine (1 × 20 mL), dried ($MgSO_4$), filtrated, and the filtrate evaporated to dryness to yield **16** (98 mg, 98%) as white solid; mp 127–129 °C; R_F = 0.24 (silica gel, hexane/ethyl acetate, 8:2); $[\alpha]_D$ = 51.38° (*c* = 0.33, $CHCl_3$); IR (KBr): ν = 3418*s*, 2950*vs*, 2872*s*, 2712*w*, 1716*s*, 1642*s*, 1518*s*, 1454*m*, 1386*m*, 1364*m*, 1030*m*, 698 *m* cm^{-1-1}; ^1H NMR (500 MHz, $CDCl_3$) δ = 9.80 (*t*, *J* = 2.2 Hz, 1 H, H–2), 9.60 (*s*, 1 H, H–3), 7.34–7.30 (*m*, 2H, H–34), 7.28–7.22 (*m*, 3 H, H–33 + H–35), 6.12 (*dd*, *J* = 5.8, 5.0 Hz, 1 H, NH), 5.29 (*dd*, *J* = 3.6, 3.6 Hz, 1 H, H–12), 4.57 (*dd*, *J* = 14.7, 6.2 Hz, 1 H, H–31a), 4.17 (*dd*, *J* = 14.7, 4.6 Hz, 1 H, H–31b), 2.58 (*dd*, *J* = 13.1, 4.0 Hz, 1 H, H–18), 2.50 (*dd*, *J* = 17.8, 2.4 Hz, 1 H, H–1a), 2.30 (*dd*, *J* = 17.8, 2.1 Hz, 1 H, H–1b), 2.21 (*dd*, *J* = 10.4, 7.2 Hz, 1 H, H–9), 2.10 (*dd*, *J* = 8.4, 5.3 Hz, 1 H, H–5), 1.99 (*ddd*, *J* = 13.7, 13.7, 3.9 Hz, 1 H, H–16a), 1.91–1.81 (*m*, 2 H, H–11a + H–11b), 1.77–1.59 (*m*, 4 H, H–19a + H–22a + H–22b + H–16b), 1.58–1.47 (*m*, 4 H, H–15a + H–6a + H–6b + H–7a), 1.39–1.14 (*m*, 4 H, H–21a + H–21b + H–7b + H–19b), 1.14 (*s*, 3 H, H–27), 1.12 (*s*, 3 H, H–24), 1.10–1.05 (*m*, 1 H, H–15b), 1.09 (*s*, 3 H, H–23), 0.95 (*s*, 3 H, H–25), 0.90 (*s*, 6 H, H–29 + H–30), 0.68 (*s*, 3 H, H–26); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 206.9 (C–3), 202.5 (C–2), 177.9 (C–28), 144.8 (C–13), 138.5 (C–32), 128.8 (C–34), 127.9 (C–33), 127.5 (C–35), 122.3 (C–12), 52.2 (C–1), 50.9 (C–4), 49.2 (C–5), 46.6 (C–19), 46.5 (C–17), 43.7 (C–31), 43.2 (C–10), 42.6 (C–14), 42.3 (C–18), 41.2 (C–9), 39.5 (C–8), 34.2 (C–21), 33.1 (C–30), 32.9 (C–22), 31.9 (C–7), 30.8 (C–20), 27.4 (C–15), 25.4 (C–27), 24.2 (C–24), 24.0 (C–16), 23.9 (C–11), 23.7 (C–29), 20.3 (C–6), 19.9 (C–23), 19.5 (C–25), 17.0 (C–26) ppm; MS (ESI): *m*/*z* (%) = 560.3 ($[M + H]^+$, 100), 1119.3 ($[2M + H]^+$, 46); analysis calculated for $C_{37}H_{53}NO_3$ (559.82): C 79.38, H 9.54, N 2.50; found: C 79.21, H 9.66, N 2.36.

4.2.9. 2β,3β-Diacetyloxy-olean-12-en-28-oic acid (*21*)

Compound **21** (185 mg, 78%) was obtained from **17** and acetic anhydride according to GP A as a white solid; mp = 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 73.21, H 9.57.

4.2.10. 2β,3α-Diacetyloxy-olean-12-en-28-oic acid (*22*)

Compound **22** (180 mg, 76%) was obtained from **18** and acetic anhydride according to GP A as a white solid; mp = 163–166 °C (lit [29].: 206–210 °C); R_F = 0.23 (silica gel, hexane/ethyl acetate, 8:2); $[\alpha]_D$ = +75.98° (*c* = 0.50, $CHCl_3$); IR (KBr): ν = 2950*s*, 2876*m*, 1746*vs*, 1696*s*, 1462*m*, 1434*m*, 1368*s*, 1252*s*, 1244*vs*, 1166*m*, 1122*w*, 1030 *s* cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 5.27 (*dd*, *J* = 3.5, 3.5 Hz, 1 H, H–12), 4.99 (*d*, *J* = 6.5 Hz, 1 H, H–3), 4.94 (*ddd*, *J* = 6.2, 6.2, 5.1 Hz, 1 H, H–2), 2.82 (*dd*, *J* = 13.6, 4.1 Hz, 1 H, H–18), 2.06 (*s*, 3 H, H–32), 2.01 (*s*, 3 H, H–34), 2.02–1.65 (*m*, 6 H, H–12a + H–11a + H–11b + H–22a + H–15a + H–1a), 1.65–1.51 (*m*, 5 H, H–19a + H–16b + H–1b + H–22b + H–9), 1.51–1.25 (*m*, 7 H, H–6a + H–6b + H–7a + H–7b + H–21a + H–21b + H–5), 1.17–1.03 (*m*, 2 H, H–19b + H–15b), 1.15 (*s*, 3 H, H–27), 1.13 (*s*, 3 H, H–25), 1.00 (*s*, 3 H, H–23), 0.92 (*s*, 3 H, H–29), 0.90 (*s*, 6 H, H–24 + H–30), 0.74 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 184.2 (C–28), 170.4 (C–31), 170.1 (C–33), 143.7 (C–13), 122.6 (C–12), 76.2 (C–3), 70.7 (C–2), 50.6 (C–5), 48.1 (C–9), 46.7 (C–17), 46.0 (C–19), 41.9 (C–14), 41.2 (C–1), 41.1 (C–18), 39.6 (C–8), 37.1 (C–4), 36.7 (C–10), 34.0 (C–21), 33.2 (C–30), 32.6 (C–22), 32.3 (C–7), 30.8 (C–20), 27.7 (C–15), 26.9 (C–24), 26.2 (C–27), 23.7 (C–29), 23.5 (C–11), 23.0 (C–16), 22.2 (C–23), 21.4 (C–34), 21.1 (C–32), 18.8 (C–6), 18.2 (C–25), 17.1 (C–26) ppm; MS (ESI): *m*/*z* (%) = 555.4 ($[M-H]^-$, 100), 1111.3 ($[2M-H]^-$, 100), 1133.6 ($[2M\text{-}2H + Na]^-$, 34); analysis calculated for $C_{34}H_{52}O_6$ (556.77): C 73.34, H 9.41; found: C 73.25, H 9.53.

4.2.11. 2α,3α-Diacetyloxy-olean-12-en-28-oic acid (*23*)

Compound **23** (180 mg, 76%) was obtained from **19** and acetic anhydride according to GP A as a white solid; mp = 151–155 °C; R_F = 0.18 (silica gel, hexane/ethyl acetate, 8:2); $[\alpha]_D$ = +28.78° (*c* = 0.36, $CHCl_3$); IR (KBr): ν = 2958*s*, 2876*m*, 1748*vs*, 1698*s*, 1462*m*, 1434*w*, 1366*m*, 1250*s*, 1234*s*, 1158*m*, 1036*m*, 1018 *m* cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 5.28 (*dd*, *J* = 3.6, 3.5 Hz, 1 H, H–12), 5.23 (*ddd*, *J* = 12.4, 4.5, 2.9 Hz, 1 H, H–2), 4.96 (*d*, *J* = 2.5 Hz, 1 H, H–3), 2.83 (*dd*, *J* = 13.9, 4.5 Hz, 1 H, H–18), 2.11 (*s*, 3 H, H–32), 2.03–1.84 (*m*, 3 H, H–11a + H–11b + H–16a), 1.96 (*s*, 3 H, H–34), 1.81–1.67 (*m*, 3 H, H–15a + H–22a + H–9), 1.66–1.53 (*m*, 4 H, H–1a + H–19a + H–16b + H–22b), 1.52–1.42 (*m*, 2 H, H–6a + H–7a), 1.39–1.05 (*m*, 8 H, H–1b + H–21a + H–21b + H–6b + H–7b + H–5 + H–19b + H–15b), 1.17 (*s*, 3 H, H–27), 1.03 (*s*, 3 H, H–25), 0.97 (*s*, 3 H, H–23), 0.93 (*s*, 3 H, H–29), 0.91 (*s*, 3 H, H–30), 0.87 (*s*, 3 H, H–24), 0.75 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 183.7 (C–28), 170.8 (C–31), 170.6 (C–33), 143.8 (C–13), 122.5 (C–12), 77.3 (C–3), 68.4 (C–2), 49.8 (C–5), 47.6 (C–9), 46.7 (C–17), 46.1 (C–19), 41.8 (C–14), 41.1 (C–18), 39.6 (C–8), 38.9 (C–1), 38.7 (C–4), 38.3 (C–10), 34.0 (C–21), 33.2 (C–30), 32.6 (C–22), 32.5 (C–7), 30.8 (C–20), 27.9 (C–24), 27.8 (C–15), 26.2 (C–27), 23.7 (C–29), 23.6 (C–11), 23.0 (C–16), 21.7 (C–23), 21.3 (C–34), 21.2 (C–32), 18.0 (C–6), 17.4 (C–26), 16.3 (C–25) ppm; MS (ESI): *m*/*z* (%) = 557.1 ($[M + H]^+$, 26), 574.2 ($[M + NH_4]^+$, 72), 579.2 ($[M + Na]^+$, 28), 1135.3 ($[2M + Na]^+$, 100); analysis calculated for $C_{34}H_{52}O_6$ (556.77): C 73.34, H 9.41; found: C 73.19, H 9.49.

4.2.12. 2β,3β-Diacetyloxy-olean-12-en-28-oic acid benzylamide (*24*) (general procedure B, GP B)

To a solution of **21** (90 mg, 0.16 mmol) in dry DCM (10 mL), oxalyl chloride (62 mg, 0.48 mmol), triethylamine (3 mg, 0.03 mmol) and DMF (2 mg, 0.03 mmol) were added. The mixture was stirred at room temperature for 2 h. The solvent was removed under reduced pressure, re-evaporated with dry THF (1 × 10 mL), and the residue was immediately dissolved in dry DCM (10 mL). The solution was cooled to 0 °C, and triethylamine (21 mg, 0.21 mmol), DMAP (2 mg, 0.02 mmol) and benzylamine (52 mg, 0.48 mmol) were added. After 5 min of stirring, Et_2O (100 mL) was added, and usual aq. work-up followed by column chromatography (silica gel, hexane/ethyl acetate, 8:2) afforded **24** (89 mg, 85%) as a white solid; mp = 120–122 °C; R_F = 0.28 (silica gel, hexane/ethyl acetate, 8:2);

$[\alpha]_D$ = +44.41° (*c* = 0.35, $CHCl_3$); IR (KBr): ν = 2948*s*, 2878*m*, 1746*vs*, 1654*m*, 1518*m*, 1454*m*, 1434*m*, 1364*s*, 1252*vs*, 1192*m*, 1160*w*, 1056*m*, 1030 *s* cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.34–7.30 (*m*, 2H, H–38), 7.28–7.23 (*m*, 3 H, H–37 + H–39), 6.17 (*dd*, *J* = 6.2, 4.7 Hz, 1 H, NH), 5.31–5.28 (*m*, 2 H, H–2 + H–12), 4.62–4.57 (*m*, 2 H, H–3 + H–35a), 4.15 (*dd*, *J* = 14.7, 4.4 Hz, 1 H, H–35b), 2.54 (*dd*, *J* = 13.0, 3.8 Hz, 1 H, H–18), 2.04 (*s*, 3 H, H–32), 2.03–1.92 (*m*, 2 H, H–1a + H–16a), 2.02 (*s*, 3 H, H–34), 1.89–1.79 (*m*, 2 H, H–11a + H–11b), 1.79–1.71 (*m*, 2 H, H–22a + H–19a), 1.70–1.44 (*m*, 7 H, H–6a + H–6b + H–16b + H–15a + H–22b + H–9 + H–7a), 1.40–1.12 (*m*, 5 H, H–1b + H–21a + H–21b + H–19b + H–7b), 1.14 (*s*, 6 H, H–27 + H–25), 1.06–1.00 (*m*, 1 H, H–15b), 1.05 (*s*, 3 H, H–23), 0.97–0.93 (*m*, 1 H, H–5), 0.90 (*s*, 3 H, H–30), 0.90 (*s*, 3 H, H–29), 0.89 (*s*, 3 H, H–24), 0.68 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 178.1 (C–28), 170.8 (C–33), 170.3 (C–31), 145.1 (C–13), 138.5 (C–36), 128.8 (C–38), 127.9 (C–37), 127.5 (C–39), 122.7 (C–12), 78.0 (C–3), 69.7 (C–2), 55.3 (C–5), 48.1 (C–9), 46.7 (C–19), 46.5 (C–17), 43.7 (C–35), 42.4 (C–18), 42.3 (C–14), 42.0 (C–1), 39.6 (C–8), 37.4 (C–4), 36.8 (C–10), 34.3 (C–21), 33.1 (C–30), 32.8 (C–22), 32.5 (C–7), 30.8 (C–20), 29.2 (C–24), 27.3 (C–15), 25.9 (C–27), 23.9 (C–16), 23.7 (C–29), 23.6 (C–11), 21.4 (C–32), 21.0 (C–34), 18.1 (C–6), 17.8 (C–23), 17.2 (C–26), 16.0 (C–25) ppm; MS (ESI): *m*/*z* (%) = 646.5 ($[M + H]^+$, 100), 668.5 ($[M + Na]^+$, 12), 1291.3 ($[2M + H]^+$, 45), 1313.6 ($[2M + Na]^+$, 28); analysis calculated for $C_{41}H_{59}NO_5$ (645.91): C 76.24, H 9.21, N 2.17; found: C 76.03, H 9.39, N 2.00.

4.2.13. 2β,3α-Diacetyloxy-olean-12-en-28-oic acid benzylamide (**25**)

Compound **25** (85 mg, 81%) was obtained from **22** according to GP B as a white solid; mp = 114–116 °C; R_F = 0.25 (silica gel, hexane/ethyl acetate, 8:2); $[\alpha]_D$ = +36.43° (*c* = 0.46, $CHCl_3$); IR (KBr): ν = 2948*s*, 2874*m*, 1744*vs*, 1654*s*, 1518*s*, 1454*m*, 1434*m*, 1368*s*, 1246*vs*, 1230*vs*, 1030*s*, 698 *m* cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.30 (*m*, 2H, H–38), 7.29–7.22 (*m*, 3 H, H–37 + H–39), 6.17 (*dd*, *J* = 5.9, 4.8 Hz, 1 H, N*H*), 5.30 (*dd*, *J* = 3.5, 3.5 Hz, 1 H, H–12), 4.98 (*d*, *J* = 6.4 Hz, 1 H, H–3), 4.92 (*ddd*, *J* = 6.1, 6.1, 4.9 Hz, 1 H, H–2), 4.61 (*dd*, *J* = 14.6, 6.2 Hz, 1 H, H–35a), 4.15 (*dd*, *J* = 14.7, 4.4 Hz, 1 H, H–35b), 2.54 (*dd*, *J* = 13.0, 3.7 Hz, 1 H, H–18), 2.06 (*s*, 3 H, H–32), 2.05–1.94 (*m*, 1 H, H–16a), 2.02 (*s*, 3 H, H–34), 1.87–1.52 (*m*, 10 H, H 11a + H 11b + H 19a + H–22a + H–22b + H–1a + H–1b + H–16b + H–9 + H–15a), 1.51–1.12 (*m*, 8 H, H–7a + H–7b + H–6a + H–6b + H–21a + H–21b + H–19b + H–5), 1.17 (*s*, 3 H, H–27), 1.09 (*s*, 3 H, H–25), 1.08–1.00 (*m*, 1 H, H–15b), 1.02 (*s*, 3 H, H–23), 0.90 (*s*, 9 H, H–30 + H–24 + H–29), 0.67 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 178.1 (C–28), 170.3 (C–31), 170.1 (C–33), 145.0 (C–13), 138.5 (C–36), 128.8 (C–38), 127.9 (C–37), 127.5 (–C39), 122.8 (C–12), 76.2 (C–3), 70.7 (C–2), 50.5 (C–5), 48.0 (C–9), 46.8 (C–19), 46.5 (C–17), 43.7 (C–35), 42.6 (C–18), 42.4 (C–14), 41.2 (C–1), 39.6 (C–8), 37.0 (C–4), 36.7 (C–10), 34.3 (C–21), 33.1 (C–30), 32.8 (C–22), 32.1 (C–7), 30.9 (C–20), 27.4 (C–15), 27.0 (C–24), 26.0 (C–27), 24.0 (C–16), 23.7 (C–29), 23.5 (C–11), 22.2 (C–23), 21.4 (C–34), 21.1 (C–32), 18.7 (C–6), 18.2 (C–25), 16.9 (C–26) ppm; MS (ESI): *m*/*z* (%) = 646.3 ($[M + H]^+$, 100), 668.5 ($[M + Na]^+$, 17), 1291.4 ($[2M + H]^+$, 36), 1313.5 ($[2M + Na]^+$, 55); analysis calculated for $C_{41}H_{59}NO_5$ (645.91): C 76.24, H 9.21, N 2.17; found: C 76.04, H 9.41, N 2.05.

4.2.14. 2α,3α-Diacetyloxy-olean-12-en-28-oic acid benzylamide (**26**)

Compound **26** (91 mg, 87%) was obtained from **23** according to GP B as a white solid; mp = 117–119 °C; R_F = 0.25 (silica gel, hexane/ethyl acetate, 8:2); $[\alpha]_D$ = −5.47° (*c* = 0.35, $CHCl_3$); IR (KBr): ν = 2946*s*, 2876*m*, 1746*vs*, 1658*m*, 1516*m*, 1454*m*, 1432*w*, 1364*m*, 1252*vs*, 1240*s*, 1036*m*, 1018 *m* cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.31 (*m*, 2H, H–38), 7.29–7.23 (*m*, 3 H, H–37 + H–39), 6.17 (*dd*, *J* = 6.3, 4.5 Hz, 1 H, N*H*), 5.31 (*dd*, *J* = 3.6, 3.6 Hz, 1 H, H–12), 5.22 (*ddd*, *J* = 12.4, 4.5, 2.8 Hz, 1 H, H–2), 4.96 (*d*, *J* = 2.3 Hz, 1 H, H–3), 4.63 (*dd*, *J* = 14.7, 6.3 Hz, 1 H, H–35a), 4.14 (*dd*, *J* = 14.7, 4.4 Hz, 1 H, H–35b), 2.55 (*dd*, *J* = 13.1, 4.0 Hz, 1 H, H–18), 2.10 (*s*, 3 H, H–32), 2.00 (*ddd*, *J* = 13.5, 13.5, 3.7 Hz, 1 H, H–16a), 1.96 (*s*, 3 H, H–34), 1.93–1.54 (*m*, 9 H, H–11a + H–11b + H–19a + H–22a + H–22b + H–9 + H–16b + H–1a + H–15a), 1.52–1.12 (*m*, 9 H, H –7a + H–7b + H–6a + H–6b + H–21a + H–21b + H–1b + H–19b + H–5), 1.20 (*s*, 3 H, H–27), 1.08–1.02 (*m*, 1 H, H–15b), 0.99 (*s*, 6 H, H–25 + H–23), 0.91 (*s*, 6 H, H–29 + H–30), 0.87 (*s*, 3 H, H–24), 0.67 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 178.1 (C–28), 170.7 (C–31), 170.6 (C–33), 145.1 (C–13), 138.6 (C–36), 128.8 (C–38), 127.9 (C–37), 127.5 (C–39), 122.8 (C–12), 77.3 (C–3), 68.3 (C–2), 49.7 (C–5), 47.5 (C–9), 46.9 (C–19), 46.5 (C–17), 43.8 (C–35), 42.5 (C–18), 42.3 (C–14), 39.7 (C–8), 38.9 (C–1), 38.5 (C–4), 38.3 (C–10), 34.3 (C–21), 33.2 (C–30), 32.8 (C–22), 32.3 (C–7), 30.9 (C–20), 27.9 (C–24), 27.5 (C–15), 26.1 (C–27), 24.0 (C–16), 23.8 (C–29), 23.6 (C–11), 21.7 (C–23), 21.3 (C–34), 21.1 (C–32), 18.0 (C–6), 17.2 (C–26), 16.4 (C–25) ppm; MS (ESI): *m*/*z* (%) = 646.4 ($[M + H]^+$, 100), 668.3 ($[M + Na]^+$, 10), 1291.2 ($[2M + H]^+$, 14), 1313.5 ($[2M + Na]^+$, 26); analysis calculated for $C_{41}H_{59}NO_5$ (645.91): C 76.24, H 9.21, N 2.17; found: C 76.11, H 9.17, N 2.29.

4.2.15. 2α,3β-Diacetyloxy-olean-12-en-28-oic acid phenylamide (**27**)

Compound **27** (95 mg, 84%) was obtained from **20** and aniline (50 μl, 0.55 mmol) according to GP B as a white solid; mp = 185–186 °C; R_F = 0.40 (silica gel, hexane/ethyl acetate, 8:2); $[\alpha]_D$ = +26.41° (*c* = 0.31, $CHCl_3$); UV–vis ($CHCl_3$): λ_{max} (log ε) = 247 nm (4.07); IR (KBr): ν = 2948*s*, 2866*m*, 1744*vs*, 1680*m*, 1598*m*, 1526*m*, 1500*m*, 1438*s*, 1368*s*, 1310*m*, 1252*vs*, 1176*w*, 1158*w*, 1042*m*, 756 *m* cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.65 (*s*, 1 H, N*H*), 7.48–7.45 (*m*, 2H, H–36), 7.32–7.27 (*m*, 2H, H–37), 7.09–7.06 (*m*, 1 H, H–38), 5.53 (*dd*, *J* = 3.5, 3.5 Hz, 1 H, H–12), 5.08 (*ddd*, *J* = 11.5, 10.5, 4.7 Hz, 1 H, H–2), 4.74 (*d*, *J* = 10.3 Hz, 1 H, H–3), 2.67 (*dd*, *J* = 12.5, 3.7 Hz, 1 H, H–18), 2.12–1.90 (*m*, 4 H, H–16a + H–11a + H–11b + H–1a), 2.05 (*s*, 3 H, H–34), 1.98 (*s*, 3 H, H–32), 1.86–1.59 (*m*, 6 H, H–19a + H–22a + H–22b + H–16b + H–15a + H–9), 1.55–1.21 (*m*, 7 H, H–6a + H–6b + H–7a + H–7b + H–21a + H–21b + H–19b), 1.19 (*s*, 3 H, H–27), 1.12–1.02 (*m*, 2 H, H–15b + H–1b), 1.03 (*s*, 3 H, H–25), 0.98–0.92 (*m*, 1 H, H–5), 0.94 (*s*, 6 H, H–29 + H–30), 0.88 (*s*, 6 H, H–23 + H–24), 0.71 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.5 (C–28), 171.0 (C–33), 170.7 (C–31), 145.3 (C–13), 138.5 (C–35), 129.1 (C–37), 124.2 (C–38), 123.0 (C–12), 119.9 (C–36), 80.7 (C–3), 70.1 (C–2), 54.9 (C–5), 47.6 (C–9), 47.3 (C–17), 46.9 (C–19), 44.1 (C–1), 42.7 (C–18), 42.4 (C–14), 39.6 (C–8), 39.5 (C–4), 38.2 (C–10), 34.3 (C–21), 33.1 (C–30), 32.6 (C–22), 32.3 (C–7), 30.9 (C–20), 28.6 (C–24), 27.5 (C–15), 25.9 (C–27), 24.2 (C–16), 23.9 (C–11), 23.7 (C–29), 21.3 (C–32), 21.0 (C–34), 18.3 (C–6), 17.7 (C–23), 17.0 (C–26), 16.6 (C–25) ppm; MS (ESI): *m*/*z* (%) = 632.4 ($[M + H]^+$, 100), 654.5 ($[M + Na]^+$, 14), 1263.3 ($[2M + H]^+$, 30); analysis calculated for $C_{40}H_{57}NO_5$ (631.88): C 76.03, H 9.09, N 2.22; found: C 75.97, H 9.23, N 1.84.

4.2.16. 2α,3β-Diacetyloxy-olean-12-en-28-oic acid ethylphenylamide (**28**)

Compound **28** (102 mg, 86%) was obtained from **20** and 2-phenylethylamine (50 μl, 0.40 mmol) according to GP B as a white solid; mp = 117–120 °C; R_F = 0.21 (silica gel, hexane/ethyl acetate, 8:2); $[\alpha]_D$ = +25.13° (*c* = 0.33, $CHCl_3$); IR (KBr): ν = 2946*s*, 2864*m*, 1744*vs*, 1660*s*, 1518*m*, 1454*m*, 1368*s*, 1252*vs*, 1232*s*, 1042*s*,

1032*s*, 700 *m* cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.34–7.30 (*m*, 2 H, H–39), 7.27–7.23 (*m*, 1 H, H–40), 7.20–7.16 (*m*, 2 H, H–38), 5.81 (*dd*, *J* = 7.5, 3.3 Hz, 1 H, N*H*), 5.08 (*ddd*, *J* = 11.5, 10.4, 4.6 Hz, 1 H, H–2), 4.93 (*dd*, *J* = 3.5, 3.5 Hz, 1 H, H–12), 4.72 (*d*, *J* = 10.4 Hz, 1 H, H–3), 3.85 (*dddd*, *J* = 13.2, 7.5, 6.4, 5.4 Hz, 1 H, H–35a), 3.09 (*dddd*, *J* = 13.2, 9.2, 5.8, 3.4 Hz, 1 H, H–35b), 2.85 (*ddd*, *J* = 13.6, 5.6, 5.6 Hz, 1 H, H–36a), 2.70 (*ddd*, *J* = 13.7, 9.0, 6.4 Hz, 1 H, H–36b), 2.29 (*dd*, *J* = 13.1, 4.2 Hz, 1 H, H–18), 2.05 (*s*, 3 H, H–34), 2.00–1.84 (*m*, 2 H, H–16a + H–1a), 1.98 (*s*, 3 H, H–32), 1.76–1.57 (*m*, 5 H, H–11a + H–11b + H–16b + H–22a + H–19a), 1.57–1.13 (*m*, 9 H, H–9 + H–22b + H–6a + H–6b + H–15a + H–7a + H–7b + H–21a + H–21b), 1.10–0.89 (*m*, 4 H, H–19b + H–1b + H–15b + H–5), 1.08 (*s*, 3 H, H–27), 0.99 (*s*, 3 H, H–25), 0.90 (*s*, 3 H, H–23), 0.88 (*s*, 3 H, H–30), 0.88 (*s*, 6 H, H–29 + H–24), 0.55 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 178.1 (C–28), 170.9 (C–33), 170.7 (C–31), 144.7 (C–13), 139.2 (C–37), 128.9 (C–38), 128.8 (C–39), 126.8 (C–40), 122.5 (C–12), 80.7 (C–3), 70.1 (C–2), 54.9 (C–5), 47.6 (C–9), 46.9 (C–19), 46.4 (C–17), 44.0 (C–1), 42.2 (C–18), 42.0 (C–14), 44.0 (C–35), 39.5 (C–8), 39.5 (C–4), 38.1 (C–10), 35.6 (C–36), 34.3 (C–21), 33.1 (C–30), 32.5 (C–22), 32.1 (C–7), 30.8 (C–20), 28.5 (C–24), 27.3 (C–15), 25.8 (C–27), 23.9 (C–16), 23.6 (C–29), 23.6 (C–11), 21.3 (C–32), 21.0 (C–34), 18.3 (C–6), 17.7 (C–23), 17.0 (C–26), 16.6 (C–25) ppm; MS (ESI): *m*/*z* (%) = 660.5 ($[M + H]^+$, 100), 682.5 ($[M + Na]^+$, 12), 1319.5 ($[2M + H]^+$, 86), 1341.6 ($[2M + Na]^+$, 72); analysis calculated for $C_{42}H_{61}NO_5$ (659.94): C 76.44, H 9.32, N 2.12; found: C 76.30, H 9.41, N 2.05.

4.2.17. 3-Oxours-12-en-28-oic acid (**29**)

Compound **29** (5.0 g, 100%) was prepared as previously described (for 3-oxoolean-12-en-28-oic acid [15]), and it was obtained as a white solid; mp = 255–258 °C (lit [30].: 250–268 °C); R_F = 0.50 (silica gel, hexane/ethyl acetate, 7:3); $[\alpha]_D$ = +80.30° (*c* = 0.41, $CHCl_3$); MS (ESI): *m*/*z* (%) = 453.5 ($[M–H]^-$, 100), 485.4 ($[M–H + MeOH]^-$, 20), 907.4 ($[2M–H]^-$, 76), 930.6 ($[2M–2H + Na]^-$, 60); analysis calculated for $C_{30}H_{46}O_3$ (454.68): C 79.25, H 10.20; found: C 79.00, H 10.38.

4.2.18. 2β-Bromo-3-oxours-12-en-28-oic acid (**30**), 2α-bromo-3-oxours-12-en-28-oic acid (**31**)

A mixture (2:1, 11.0 g, 100%) of **30** and **31** was prepared from **29** as previously described (for 2β-bromo-3-oxoolean-12-en-28-oic acid and 2α-bromo-3-oxoolean-12-en-28-oic acid [18]), and this mixture was used without any further purification.

4.2.19. 2-Hydroxy-3-oxours-1,12-dien-28-oic acid (**32**)

Compound **32** (9.80 g, 97%) was prepared from **30**/**31** as previously described (for 2-hydroxy-3-oxoolean-1,12-dien-28-oic acid [18]), and it was obtained as white solid; mp = 143–145 °C; R_F = 0.66 (silica gel, hexane/ethyl acetate, 6:4); $[\alpha]_D$ = +96.70° (*c* = 0.31, $CHCl_3$); UV–vis ($CHCl_3$): λ_{max} (log ε) = 272 nm (3.87); IR (KBr): ν = 3566*w*, 3438*m*, 2974*vs*, 2928*vs*, 2870*s*, 2644*w*, 1792*w*, *1694vs*, *1670vs*, 1650*s*, 1570*w*, 1456*s*, 1408*s*, 1382*s*, 1362*m*, 1316*m*, 1288*m*, 1238*s*, 1212*m*, 1190*m*, 1164*w*, 1146*w*, 1120*w*, 1108*w*, 1086*m*, 1054*s*, 1030*m*, 1018*w*, 968 *m* cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 6.36 (*s*, 1 H, H-−1), 5.95 (*s*, 1 H, OH–2), 5.30 (*dd*, *J* = 3.6, 3.6 Hz, 1 H, H–12), 2.22 (*d*, *J* = 11.1 Hz, 1 H, H–18), 2.18–1.97 (*m*, 3 H, H–11a + H–11b + H–16a), 1.91–1.81 (*m*, 2 H, H–9 + H–15a), 1.76–1.63 (*m*, 3 H, H–16b + H–22a + H–22b), 1.63–1.44 (*m*, 5 H, H–5 + H–6a + H–6b + H–7a + H–21a), 1.43–1.37 (*m*, 1 H, H–7b), 1.36–1.24 (*m*, 2 H, H–21b + H–19), 1.23 (*s*, 3 H, H–25), 1.21 (*s*, 3 H, H–24), 1.14–1.08 (*m*, 1 H, H–15b), 1.10 (*s*, 3 H, H–23), 1.09 (*s*, 3 H, H–27), 1.05–0.98 (*m*, 1 H, H–20), 0.95 (*d*, *J* = 6.3 Hz, 3 H, H–30), 0.85 (*s*, 3 H, H–26), 0.85 (*d*, *J* = 8.0 Hz, 3 H, H–29) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 201.2 (C–3), 183.9 (C–28), 143.9 (C–2), 138.6 (C–13), 128.5 (C–1), 125.3 (C–12), 54.0 (C–5), 52.8 (C–18), 48.2 (C–17), 44.0 (C–4), 43.1 (C–9), 42.5 (C–14), 40.3 (C–8), 39.1 (C–19), 39.0 (C–20), 38.5 (C–10), 36.8 (C–22), 32.9 (C–7), 30.7 (C–21), 28.1 (C–15), 27.4 (C–24), 24.1 (C–16), 23.7 (C–27), 23.5 (C–11), 21.9 (C–23), 21.3 (C–30), 19.9 (C–25), 18.8 (C–6), 17.7 (C–26), 17.1 (C–29) ppm; MS (ESI): *m*/*z* (%) = 469.1 ($[M + H]^+$, 100), 486.3 ($[M + NH_4]^+$, 16), 491.1 ($[M + Na]^+$, 33); analysis calculated for $C_{30}H_{44}O_4$ (468.67): C 76.88, H 9.46; found: C 76.77, H 9.52.

4.2.20. 2β,3β-Dihydroxyurs-12-en-28-oic acid = 2-epi-corosolic acid (**33**)

Compound **33** (3.70 g, 39%) was prepared from **32** as previously described for **3** [15], and it was obtained as a white solid; mp = 282–285 °C (lit [31].: 284 °C); R_F = 0.28 (silica gel, hexane/ethyl acetate, 6:4); $[\alpha]_D$ = +82.50° (*c* = 0.32, C_5H_5N); IR (KBr): ν = 3496*s*, 3436*s*, 3024*s*, 2922*vs*, 2854*s*, 2612*w*, 1706*vs*, 1458*s*, 1448*m*, 1410*m*, 1376*s*, 1362*s*, 1344*w*, 1320*m*, 1308*m*, 1286*m*, 1264*m*, 1250*m*, 1226*s*, 1200*s*, 1182*s*, 1164*m*, 1146*m*, 1114*m*, 1102*m*, 1088*m*, 1026*s*, 998*s*, 974*m*, 964*m*, 946*m*, 928*s*, 768 *m* cm^{-1}; ^1H NMR (500 MHz, pyridine-d_5): δ = 5.52 (*dd*, *J* = 3.6, 3.6 Hz, 1 H, H–12), 4.43 (*ddd*, *J* = 3.8, 3.8, 3.3 Hz, 1 H, H–2), 3.47 (*d*, *J* = 4.0 Hz, 1 H, H–3), 2.67 (*d*, *J* = 11.3 Hz, 1 H, H–18), 2.41–2.33 (*m*, 1 H, H–15a), 2.31 (*dd*, *J* = 14.1, 2.8 Hz, 1 H, H–1a), 2.20–1.93 (*m*, 6 H, H–11a + H–11b + H–16a + H–16b + H–22a + H–22b), 1.69–1.53 (*m*, 4 H, H–6a + H–6b + H–7a + H–9), 1.54–1.47 (*m*, 2 H, H–19 + H–21a), 1.53 (*s*, 3 H, H–25), 1.45–1.39 (*m*, 2 H, H–7 + H–21b), 1.39 (*s*, 3 H, H–23), 1.32–1.17 (*m*, 2 H, H–1b + H–15b), 1.29 (*s*, 3 H, H–24), 1.27 (*s*, 3 H, H–27), 1.13 (*s*, 3 H, H–26), 1.11–1.00 (*m*, 2 H, H–5 + H–20), 1.04 (*d*, *J* = 6.5 Hz, 3 H, H–29), 0.98 (*d*, *J* = 6.3 Hz, 3 H, H–30) ppm; ^{13}C NMR (125 MHz, pyridine-d_5): δ = 180.3 (C–28), 139.7 (C–13), 126.2 (C–12), 78.8 (C–3), 71.8 (C–2), 56.4 (C–5), 54.0 (C–18), 48.9 (C–9), 48.5 (C–17), 45.6 (C–1), 43.1 (C–14), 40.6 (C–8), 39.9 (C–19), 39.8 (C–20), 39.2 (C–4), 37.9 (C–22), 37.7 (C–10), 34.1 (C–7), 31.5 (C–21), 30.7 (C–24), 29.1 (C–15), 25.4 (C–16), 24.4 (C–27), 24.2 (C–11), 21.8 (C–30), 19.1 (C–6), 18.6 (C–23), 17.9 (C–29), 17.9 (C–26), 17.2 (C–25) ppm; MS (ESI): *m*/*z* (%) = 471.4 ($[M–H]^-$, 64), 943.3 ($[2M–H]^-$, 100), 965.5 ($[2M-2H + Na]^-$, 44); analysis calculated for $C_{30}H_{48}O_4$ (472.70): C 76.23, H 10.24; found: C 76.05, H 10.38.

4.2.21. 2β,3β-Diacetyloxyurs-12-en-28-oic acid (**34**)

Compound **34** (120 mg, 51%) was obtained from **33** and acetic anhydride according to GP A as a white solid; mp = 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–33), 2.02 (*s*, 3 H, H–32), 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–31), 170.4 (C–34), 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–33), 21.3 (C–30), 21.0 (C–32), 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 9.56.

4.2.22. 2β,3β-Diacetyloxy-17β-isocyanato-28-norolean-12-ene (**35**)

Compound **21** (370 mg, 0.66 mmol) was dissolved in a mixture of toluene (9 mL) and triethylamine (100 mg, 0.99 mmol), and the mixture was stirred for 15 min at room temperature. Diphenylphosphoryl azide (218 mg, 0.79 mmol) was added, and stirring was continued in a microwave reactor at 180 °C for 3 h. Et_2O (100 mL) was added, the organic layer 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 the filtrate was evaporated to dryness. Column chromatography (silica gel, hexane/ethyl acetate, 9:1) of the residue afforded **35** (280 mg, 76%) as a white solid; mp = 255–260 °C; R_F = 0.70 (silica gel, hexane/ethyl acetate, 7:3); $[\alpha]_D$ = +81.66° (*c* = 0.40, $CHCl_3$); IR (KBr): ν = 2950*m*, 2916*m*, 2866*w*, 2256*vs*, 1738*vs*, 1728*s*, 1458*w*, 1434*w*, 1400*w*, 1368*m*, 1256*vs*, 1242*s*, 1054*m*, 1028*m*, 1012 *m* cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.33–5.29 (*m*, 2 H, H−2 + H−12), 4.63 (*d*, *J* = 3.9 Hz, 1 H, H−3), 2.36 (*dd*, *J* = 13.9, 4.6 Hz, 1 H, H−18), 2.10–1.81 (*m*, 6 H, H−11a + H−11b + H−15a + H−16a + H−1a + H−22a), 2.05 (*s*, 3 H, H−32), 2.03 (*s*, 3 H, H−34), 1.70 (*ddd*, *J* = 13.6, 3.5, 3.5 Hz, 1 H, H−22b), 1.65–1.48 (*m*, 5 H, H−6a + H−6b + H−19a + H−9 + H−7a), 1.45–1.38 (*m*, 1 H, H−7b), 1.36–1.17 (*m*, 5 H, H−1b + H−21a + H−21b + H−16b + H−19b), 1.22 (*s*, 3 H, H−25), 1.14–1.05 (*m*, 1 H, H−15b), 1.12 (*s*, 3 H, H−27), 1.07 (*s*, 3 H, H−23), 1.01 (*s*, 3 H, H−26), 1.01–0.97 (*m*, 1 H, H−5), 0.96 (*s*, 3 H, H−29), 0.91 (*s*, 3 H, H−24), 0.90 (*s*, 3 H, H−30) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.9 (C−33), 170.4 (C−31), 142.9 (C−13), 124.1 (C−12), 122.0 (C−35), 78.1 (C−3), 69.7 (C−2), 62.3 (C−17), 55.4 (C−5), 49.1 (C−18), 48.2 (C−9), 47.3 (C−19), 42.1 (C−1), 41.9 (C−14), 39.9 (C−8), 37.8 (C−22), 37.5 (C−4), 36.9 (C−10), 35.6 (C−21), 32.9 (C−7), 32.8 (C−30), 30.9 (C−20), 29.3 (C−24), 27.2 (C−16), 26.8 (C−15), 25.9 (C−27), 23.9 (C−29), 23.8 (C−11), 21.4 (C−32), 21.0 (C−34), 18.2 (C−6), 17.8 (C−23), 17.2 (C−26), 16.2 (C−25) ppm; MS (ESI): *m*/*z* (%) = 576.3 ([M + Na]$^+$, 94), 1129.3 ([2M + Na]$^+$, 100); analysis calculated for $C_{34}H_{51}NO_5$ (553.77): C 73.74, H 9.28, N 2.53; found: C 73.55, H 9.40, N 2.44.

4.2.23. (2β,3β,17β)-2,3-Diacetyloxy-17-isocyanato-28-norurs-12-ene (**36**)

Following the procedure given for the preparation of **35**, compound **36** (210 mg, 57%) was synthesized starting from **34** and obtained as a white solid; mp = 92–95 °C; R_F = 0.64 (silica gel, hexane/ethyl acetate, 8:2); $[\alpha]_D$ = +71.00° (*c* = 0.29, $CHCl_3$); IR (KBr): ν = 3438*w*, 3036*w*, 2972*s*, 2934*s*, 2878*m*, 2844*m*, 2270*vs*, 1738*vs*, 1660*w*, 1654*w*, 1490*w*, 1458*m*, 1434*m*, 1400*m*, 1390*m*, 1370*s*, 1364*s*, 1342*w*, 1306*w*, 1254*vs*, 1238*vs*, 1194*m*, 1188*m*, 1158*m*, 1134*w*, 1116*w*, 1090*w*, 1056*m*, 1026*m*, 1014*m*, 976*m*, 946 *m* cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.32 (*ddd*, *J* = 4.0, 4.0, 3.4 Hz, 1 H, H−2), 5.29–5.26 (*m*, 1 H, H−12), 4.63 (*d*, *J* = 3.9 Hz, 1 H, H−3), 2.08–1.98 (*m*, 4 H, H−1a + H−11a + H−15a + H−16a), 2.05 (*s*, 3 H, H−32), 2.03 (*s*, 3 H, H−34), 1.94–1.87 (*m*, 2 H, H−11b, H−22a), 1.81–1.73 (*m*, 2 H, H−22b + H−18), 1.63–1.47 (*m*, 5 H, H−6a + H−6b + H−7a + H−9 + H−21a), 1.44–1.40 (*m*, 1 H, H−7b), 1.39–1.34 (*m*, 1 H, H−1b), 1.32–1.25 (*m*, 2 H, H−19 + H−16b), 1.24 (*s*, 3 H, H−25), 1.22–1.18 (*m*, 1 H, H−21b), 1.13–1.07 (*m*, 1 H, H−15b), 1.06 (*s*, 3 H, H−23), 1.06 (*s*, 3 H, H−26), 1.06 (*s*, 3 H, H−27), 1.04–0.95 (*m*, 2 H, H−5 + H−20), 0.93 (*d*, *J* = 6.3 Hz, 3 H, H−30), 0.91 (*s*, 3 H, H−24), 0.83 (*d*, *J* = 6.5 Hz, 3 H, H−29) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.9 (C−33), 170.4 (C−31), 138.0 (C−13), 126.8 (C−12), 122.4 (C−35), 78.1 (C−3), 69.7 (C−2), 63.0 (C−17), 60.7 (C−18), 55.4 (C−5), 48.3 (C−9), 42.3 (C−1), 42.3 (C−14), 41.9 (C−22), 41.0 (C−19), 40.1 (C−8), 39.1 (C−20), 37.5 (C−4), 36.9 (C−10), 33.2 (C−7), 31.9 (C−21), 29.3 (C−24), 28.3 (C−16), 27.3 (C−15), 23.7 (C−11), 23.4 (C−27), 21.4 (C−32), 21.0 (C−34), 20.9 (C−30), 18.2 (C−6), 17.9 (C−23), 17.5 (C−29), 17.2 (C−26), 16.4 (C−25) ppm; MS (ESI): *m*/*z* (%) = 494.2 ([M + H-HOAc]$^+$, 18), 554.1 ([M + H]$^+$, 1), 571.3 ([M + NH_4]$^+$, 52), 576.4 ([M + Na]$^+$, 29), 1129.3 ([2M + Na]$^+$, 100); analysis calculated for $C_{34}H_{51}NO_5$ (553.77): C 73.74, H 9.28, N 2.53; found: C 73.51, H 9.40, N 2.32.

4.2.24. 2β,3β-Diacetyloxy-17β-amino-28-norolean-12-ene (**37**)

To a solution of compound **35** (280 mg, 0.51 mmol) in THF (19 mL), aqueous HCl (2.53 mmol, 2 M) was added, and the mixture was stirred for 2 h at 30 °C. Et_2O (100 mL) and aqueous NaOH (2.53 mmol, 2 M) were added; usual aq. work-up followed by column chromatography (silica gel, chloroform/methanol, 9:1) provided **37** (280 mg, 76%) as a white solid; mp = 190–193 °C; R_F = 0.51 (silica gel, chloroform/methanol, 9:1); $[\alpha]_D$ = +79.27° (*c* = 0.39, $CHCl_3$); IR (KBr): ν = 3290*w*, 2950*s*, 2868*m*, 1746*vs*, 1616*w*, 1518*m*, 1464*m*, 1432*m*, 1372*s*, 1300*m*, 1248*vs*, 1196*m*, 1056*m*, 1032 *m* cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.28 (*s*, 2 H, NH_2), 5.54 (*dd*, 1 H, *J* = 3.5, 3.5 Hz, H−12), 5.32 (*ddd*, 1 H, *J* = 3.7, 3.7, 3.7 Hz, H−2), 4.62 (*d*, *J* = 3.9 Hz, 1 H, H−3), 2.62 (*dd*, *J* = 13.3, 3.8 Hz, 1 H, H−18), 2.20 (*ddd*, 1 H, *J* = 14.4, 14.4, 5.0 Hz, H−16a), 2.07–1.95 (*m*, 3 H, H−11a + H−22a + H−1a), 2.04 (*s*, 3 H, H−32), 2.03 (*s*, 3 H, H−34), 1.92–1.79 (*m*, 2 H, H−11b + H−15a), 1.79–1.46 (*m*, 7 H, H−22b + H−19a + H−16b + H−6a + H−6b + H−7a + H−9), 1.43–1.20 (*m*, 6 H, H−7b + H−21a + H−21b + H−1b + H−19b + H−15b), 1.21 (*s*, 3 H, H−25), 1.18 (*s*, 3 H, H−27), 1.06 (*s*, 3 H, H−23), 1.00 (*s*, 3 H, H−26), 1.00–0.95 (*m*, 1 H, H−5), 0.98 (*s*, 3 H, H−29), 0.92 (*s*, 3 H, H−30), 0.91 (*s*, 3 H, H−24) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.9 (C−33), 170.3 (C−31), 139.1 (C−13), 128.2 (C−12), 77.9 (C−3), 69.5 (C−2), 58.3 (C−17), 55.3 (C−5), 47.8 (C−9), 46.6 (C−19), 44.7 (C−18), 42.2 (C−1), 41.6 (C−14), 40.1 (C−8), 37.5 (C−4), 36.7 (C−10), 34.8 (C−21), 32.7 (C−30), 32.4 (C−7), 32.2 (C−22), 31.0 (C−20), 29.2 (C−24), 25.9 (C−27), 24.7 (C−15), 24.1 (C−16), 24.0 (C−11), 23.7 (C−29), 21.4 (C−32), 21.0 (C−34), 18.1 (C−6), 17.8 (C−23), 17.1 (C−26), 16.2 (C−25) ppm; MS (ESI): *m*/*z* (%) = 528.1 ([M + H]$^+$, 100); analysis calculated for $C_{33}H_{53}NO_4$ (527.78): C 75.10, H 10.12, N 2.65; found: C 75.02, H 10.31, N 2.55.

4.2.25. 2β,3β-Diacetyloxy-17β-amino-28-norurs-12-ene (**38**)

To a solution of compound **36** (280 mg, 0.51 mmol) in THF (19 mL), aqueous HCl (2.53 mmol, 2 M) was added, and the mixture was stirred for 24 h at 50 °C. Work-up as described above followed by chromatography (silica gel, chloroform/methanol, 9:1) gave **38** (123 mg, 46%) as a white solid; mp = 174–176 °C; R_F = 0.78 (silica gel, chloroform/methanol, 9:1); $[\alpha]_D$ = +69.30° (*c* = 0.32, $CHCl_3$); IR (KBr): ν = 3418*m*, 3288*m*, 2954*s*, 2872*s*, 2540*m*, 2362*w*, 2342*w*, 1982*w*, 1746*vs*, 1654*w*, 1636*w*, 1600*m*, 1558*w*, 1500*s*, 1456*s*, 1432*m*, 1392*s*, 1374*s*, 1338*m*, 1248*vs*, 1194*s*, 1158*m*, 1116*w*, 1090*m*, 1056*s*, 1030*s*, 990*m*, 970*m*, 946*m*, 752*s*, 662 *m* cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.53 (*dd*, *J* = 3.5, 3.5 Hz, 1 H, H−12), 5.33 (*ddd*, *J* = 3.8, 3.8, 3.8 Hz, 1 H, H−2), 4.62 (*d*, *J* = 3.9 Hz, 1 H, H−3), 2.23–2.08 (*m*, 3 H, H−16a + H−22a + H−22b), 2.07–1.90 (*m*, 4 H, H−1a + H−11a + H−11b + H−18), 2.05 (*s*, 3 H, H−32), 2.03 (*s*, 3 H, H−34), 1.87–1.78 (*m*, 2 H, H−15b + H−16b), 1.66–1.47 (*m*, 5 H, H−6a + H−6b + H−7a + H−9 + H−21a), 1.44–1.30 (*m*, 3 H, H−1b + H−7b + H−19), 1.29–1.17 (*m*, 2 H, H−15b + H−21b), 1.23 (*s*, 3 H, H−25), 1.16–1.09 (*m*, 1 H, H−20), 1.12 (*s*, 3 H, H−27), 1.09–0.95 (*m*, 1 H, H−5), 1.06 (*s*, 3 H, H−23), 1.02 (*s*, 3 H, H−26), 0.94 (*d*, *J* = 6.3 Hz, 3 H, H−30), 0.91 (*s*, 3 H, H−24), 0.84 (*d*, *J* = 6.5 Hz, 3 H, H−29) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.9 (C−33), 170.3 (C−31), 134.9 (C−13), 131.2 (C−12), 77.9 (C−3), 69.5 (C−2), 58.8 (C−17), 56.7 (C−18), 55.3 (C−5), 47.9 (C−9), 42.3 (C−1), 41.9 (C−14), 40.5 (C−19), 40.3 (C−8), 38.4 (C−20), 37.5 (C−4), 36.7 (C−10), 36.1

(C–22), 32.5 (C–7), 30.8 (C–21), 29.2 (C–24), 25.3 (C–15), 25.2 (C–16), 23.9 (C–11), 23.5 (C–27), 21.4 (C–32), 21.0 (C–34), 20.7 (C–30), 18.0 (C–6), 17.8 (C–23), 17.4 (C–26), 17.1 (C–29), 16.4 (C–25) ppm; MS (ESI): *m*/*z* (%) = 528.2 ([M + H]$^+$, 100); analysis calculated for $C_{33}H_{53}NO_4$ (527.78): C 75.10, H 10.12, N 2.65; found: C 75.03, H 10.34, N 2.51.

4.2.26. 2β,3β-Diacetyloxy-olean-12-en-28-oic acid phenylamide (**39**)

Compound **39** (98 mg, 86%) was obtained from **21** and aniline (50 μl, 0.55 mmol) according to GP B as a white solid; mp = 153–154 °C; R_F = 0.58 (silica gel, hexane/ethyl acetate, 7:3); $[\alpha]_D$ = +70.58° (*c* = 0.27, $CHCl_3$); UV–vis ($CHCl_3$): λ_{max} (log ε) = 246 nm (4.25); IR (KBr): ν = 2948*s*, 2878*m*, 1744*vs*, 1678*m*, 1598*m*, 1526*m*, 1500*m*, 1438*s*, 1366*m*, 1310*m*, 1250*vs*, 1194*m*, 1158*w*, 1056*m*, 1030*m*, 756 *m* cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.67 (*s*, 1 H, NH), 7.49–7.46 (*m*, 2H, H–36), 7.32–7.27 (*m*, 2H, H–37), 7.10–7.05 (*m*, 1 H, H–38), 5.54 (*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), 4.62 (*d*, *J* = 3.9 Hz, 1 H, H–3), 2.67 (*dd*, *J* = 12.8, 3.0 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), 2.03 (*s*, 3 H, H–34), 1.86–1.61 (*m*, 5 H, H–19a + H–22a + H–22b + H–16b + H–15a), 1.61–1.53 (*m*, 2 H, 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), 1.16 (*s*, 3 H, H–25), 1.09 (*ddd*, *J* = 14.1, 3.1, 3.1 Hz, 1 H, H–15b), 1.03 (*s*, 3 H, H–23), 0.99–0.95 (*m*, 1 H, H–5), 0.94 (*s*, 6 H, H–29 + H–30), 0.89 (*s*, 3 H, H–24), 0.74 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.5 (C–28), 170.9 (C–33), 170.4 (C–31), 145.3 (C–13), 138.2 (C–35), 129.0 (C–37), 124.2 (C–38), 123.2 (C–12), 119.9 (C–36), 78.0 (C–3), 69.7 (C–2), 55.3 (C–5), 48.2 (C–9), 47.3 (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), 24.2 (C–16), 23.9 (C–11), 23.7 (C–29), 21.4 (C–32), 21.0 (C–34), 18.1 (C–6), 17.8 (C–23), 17.2 (C–26), 16.2 (C–25) ppm; MS (ESI): *m*/*z* (%) = 632.3 ([M + H]$^+$, 100), 1263.1 ([2M + H]$^+$, 40); analysis calculated for $C_{40}H_{57}NO_5$ (631.88): C 76.03, H 9.09, N 2.22; found: C 75.87, H 9.17, N 2.07.

4.2.27. 2β,3β-Diacetyloxy-urs-12-en-28-oic acid phenylamide (**40**)

Compound **40** (180 mg, 85%) was obtained from **34** and aniline (100 μl, 1.1 mmol) according to GP B as a white solid; mp = 142–146 °C; R_F = 0.61 (silica gel, chloroform/hexane/ethyl acetate, 10:9:1); $[\alpha]_D$ = +47.20° (*c* = 0.34, $CHCl_3$); UV–vis ($CHCl_3$): λ_{max} (log ε) = 238 nm (4.21); IR (KBr): ν = 3404*m*, 2950*s*, 2872*m*, 1746*vs*, 1678*s*, 1600*s*, 1528*s*, 1500*s*, 1456*s*, 1438*s*, 1398*m*, 1366*s*, 1314*m*, 1292*m*, 1250*vs*, 1234*vs*, 1194*s*, 1156*m*, 1116*w*, 1078*m*, 1056*m*, 1030*s*, 972*m*, 944*m*, 754*s*, 692 *m* cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.67 (*s*, 1 H, NH), 7.45 (*d*, *J* = 7.5 Hz, 2 H, H–36), 7.32–7.27 (*m*, 2 H, H–37), 7.09–7.05 (*m*, 1 H, H–38), 5.49 (*dd*, *J* = 3.5, 3.5 Hz, 1 H, H–12), 5.32 (*ddd*, *J* = 3.7, 3.7, 3.5 Hz, 1 H, H–2), 4.62 (*d*, *J* = 3.9 Hz, 1 H, H–3), 2.08–1.94 (*m*, 6 H, H–1a + H–11a + H–11b + H–16a + H–18 + H–22a), 2.04 (*s*, 3 H, H–32), 2.03 (*s*, 3 H, H–34), 1.87–1.82 (*m*, 1 H, H–16b), 1.80–1.72 (*m*, 1 H, H–15a), 1.64–1.41 (*m*, 7 H, H–6a + H–6b + H–7a + H–9 + H–19 + H–21a + H–22b), 1.40–1.28 (*m*, 3 H, H–1b + H–7b + H–21b), 1.16 (*s*, 3 H, H–25), 1.13 (*s*, 3 H, H–27), 1.12–1.07 (*m*, 1 H, H–15b), 1.03 (*s*, 3 H, H–23), 1.01–0.93 (*m*, 2 H, H–5 + H–20), 0.98 (*d*, *J* = 5.2 Hz, 3 H, H–30), 0.93 (*d*, *J* = 6.5 Hz, 3 H, H–29), 0.89 (*s*, 3 H, H–24), 0.73 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.3 (C–28), 170.8 (C–33), 170.4 (C–31), 140.4 (C–13), 138.3 (C–35), 129.0 (C–37), 126.0 (C–12), 124.1 (C–38), 119.8 (C–36), 78.0 (C–3), 69.7 (C–2), 55.3 (C–5), 54.4 (C–18), 48.7 (C–17), 48.1 (C–9), 42.9 (C–14), 42.2 (C–1), 40.0 (C–19), 39.8 (C–8), 39.3 (C–20), 37.5 (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), 25.2 (C–16), 23.8 (C–11), 23.5 (C–27), 21.4 (C–32), 21.3 (C–30), 21.0 (C–34), 18.1 (C–6), 17.8 (C–23), 17.5 (C–29), 17.1 (C–26), 16.3 (C–25) ppm; MS (ESI): *m*/*z* (%) = 632.3 ([M + H]$^+$, 100), 654.5 ([M + Na]$^+$, 27), 970.3 ([3M + 2Na]$^{2+}$, 26), 1263.1 ([2M + H]$^+$, 23), 1285.5 ([2M + Na]$^+$, 86); analysis calculated for $C_{40}H_{57}NO_5$ (631.88): C 76.03, H 9.09, N 2.22; found: C 75.86, H 9.23, N 2.14.

4.2.28. N-[2β,3β-Diacetyloxy-17β-amino-28-norolean-12-en-17-yl]-benzamide (**41**)

Compound **37** (120 mg, 0.23 mmol) was dissolved in dry DCM (12 mL). After sequential addition of benzoyl chloride (120 mg, 0.86 mmol), triethylamine (42 mg, 0.42 mmol), and DMAP (2 mg, 0.02 mmol), the reaction mixture was stirred at room temperature for 2 h. Et_2O (50 mL) was added, the organic layer was washed with diluted HCl (0.1 M, 1 × 50 mL), water (2 × 50 mL) and brine (1 × 25 mL), dried ($MgSO_4$), filtrated, and the filtrate was evaporated to dryness. Column chromatography (silica gel, hexane/ethyl acetate, 8:2) gave **41** (112 mg, 78%) as a white solid; mp = 140–143 °C; R_F = 0.54 (silica gel, hexane/ethyl acetate, 7:3); $[\alpha]_D$ = +69.56° (*c* = 0.34, $CHCl_3$); UV–vis ($CHCl_3$): λ_{max} (log ε) = 234 nm (3.98); IR (KBr): ν = 3428*w*, 2950*s*, 2870*m*, 1746*vs*, 1670*m*, 1516*m*, 1484*m*, 1458*m*, 1436*m*, 1366*m*, 1318*m*, 1250*vs*, 1192*m*, 1056*m*, 1030 *m* cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.73–7.69 (*m*, 2 H, H–37), 7.49–7.38 (*m*, 3 H, H–39 + H–38), 5.87 (*s*, 1 H, NH), 5.40 (*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), 4.62 (*d*, *J* = 3.9 Hz, 1 H, H–3), 2.56 (*ddd*, *J* = 13.9, 3.2, 3.2 Hz, 1 H, H–22a), 2.38–2.29 (*m*, 2 H, H–18 + H–16a), 2.05–1.94 (*m*, 3 H, H–16b + H–11a + H–1a), 2.04 (*s*, 3 H, H–32), 2.03 (*s*, 3 H, H–34), 1.92–1.85 (*m*, 1 H, H–11b), 1.85–1.69 (*m*, 3 H, H–19a + H–22b + H–15a), 1.60–1.54 (*m*, 2 H, H–6a + H–9), 1.53–1.19 (*m*, 7 H, H–6b + H–7a + H–7b + H–21a + H–21b + H–1b + H–19b), 1.17 (*s*, 3 H, H–27), 1.16 (*s*, 3 H, H–25), 1.09–1.02 (*m*, 1 H, H–15b), 1.03 (*s*, 3 H, H–23), 0.99–0.94 (*m*, 1 H, H–5), 0.98 (*s*, 3 H, H–29), 0.93 (*s*, 3 H, H–30), 0.89 (*s*, 3 H, H–24), 0.80 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.9 (C–33), 170.4 (C–31), 166.2 (C–35), 143.5 (C–13), 135.5 (C–36), 131.2 (C–39), 128.6 (C–38), 126.7 (C–37), 124.6 (C–12), 78.1 (C–3), 69.7 (C–2), 57.1 (C–17), 55.3 (C–5), 48.1 (C–9), 47.5 (C–18), 46.7 (C–19), 42.1 (C–1), 42.0 (C–14), 39.8 (C–8), 37.5 (C–4), 36.8 (C–10), 35.3 (C–21), 33.0 (C–30), 32.5 (C–22), 32.4 (C–7), 30.9 (C–20), 29.2 (C–24), 26.2 (C–15), 26.0 (C–27), 24.1 (C–29), 23.8 (C–11), 22.1 (C–16), 21.4 (C–32), 21.0 (C–34), 18.1 (C–6), 17.8 (C–23), 17.2 (C–26), 16.1 (C–25) ppm; MS (ESI): *m*/*z* (%) = 632.2 ([M + H]$^+$, 100), 1285.4 ([2M + Na]$^+$, 14); analysis calculated for $C_{40}H_{57}NO_5$ (631.88): C 76.03, H 9.09, N 2.22; found: C 75.92, H 9.23, N 2.03.

4.2.29. N-[2β,3β-Diacetyloxy-17β-amino-28-norurs-12-en-17-yl]-benzamide (**42**)

Following the procedure for the preparation of **41**, compound **42** (97 mg, 68%) was synthesized from **38;** white solid; mp = 114–117 °C; R_F = 0.37 (silica gel, hexane/ethyl acetate, 8:2); $[\alpha]_D$ = +42.30° (*c* = 0.68, $CHCl_3$); UV–vis ($CHCl_3$): λ_{max} (log ε) = 234 nm (3.98); IR (KBr): ν = 3424*m*, 2926*s*, 2870*m*, 1744*vs*, 1668*m*, 1602*w*, 1580*w*, 1560*w*, 1514*m*, 1484*s*, 1456*m*, 1398*m*, 1366*m*, 1342*w*, 1318*m*, 1250*vs*, 1234*s*, 1194*m*, 1160*w*, 1090*w*, 1058*m*, 1030*m*, 710 *m* cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.70–7.68 (*m*, 2 H, H–37), 7.47–7.43 (*m*, 1 H, H–39), 7.41–7.37 (*m*, 2 H, H–38), 5.88 (*s*, 1 H, NH), 5.38 (*dd*, *J* = 3.6, 3.6 Hz, 1 H, H–12), 5.32 (*ddd*, *J* = 3.8, 3.8, 3.4 Hz, 1 H, H–2), 4.61 (*d*, *J* = 3.9 Hz, 1 H, H–3), 2.85–2.79 (*m*, 1 H, H–22a), 2.47–2.41 (*m*, 1 H, H–16a), 2.08–1.90 (*m*, 4 H, H–1a + H–11a + H–11b + H–16b), 2.04 (*s*, 3 H, H–32), 2.02 (*s*, 3 H, H–34), 1.81–1.73 (*m*, 1 H, H–15a), 1.64 (*d*, *J* = 10.8 Hz, 1 H, H–18),

1.60–1.39 (*m*, 7 H, H–6a + H–6b + H–7a + H–9 + H–19 + H–21a + H–22b), 1.38–1.22 (*m*, 3 H, H–1b + H–7b + H–21b), 1.16 (*s*, 3 H, H–25), 1.11 (*s*, 3 H, H–27), 1.09–0.98 (*m*, 2 H, H–15b + H–20), 1.02 (*s*, 3 H, H–23), 0.97 (*d*, $J = 6.2$ Hz, 3 H, H–30), 0.92–0.83 (*m*, 1 H, H–5), 0.89 (*s*, 3 H, H–24), 0.87 (*d*, $J = 6.4$ Hz, 3 H, H–29), 0.75 (*s*, 3 H, H–26 ppm; ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 170.8$ (C–33), 170.3 (C–31), 165.9 (C–35), 138.8 (C–13), 135.5 (C–36), 131.1 (C–39), 128.5 (C–38), 127.2 (C–12), 126.7 (C–37), 78.0 (C–3), 69.7 (C–2), 59.2 (C–18), 57.5 (C–17), 55.2 (C–5), 48.1 (C–9), 42.4 (C–14), 42.2 (C–1), 40.0 (C–19), 39.9 (C–8), 39.4 (C–20), 37.4 (C–4), 36.7 (C–22), 36.7 (C–10), 32.6 (C–7), 31.4 (C–21), 29.2 (C–24), 26.8 (C–15), 23.7 (C–16), 23.4 (C–27), 23.3 (C–11), 21.4 (C–32), 21.0 (C–30), 21.0 (C–34), 18.0 (C–6), 17.8 (C–23), 17.6 (C–29), 17.1 (C–26), 16.3 (C–25) ppm; MS (ESI): *m*/*z* (%) = 632.2 ($[M + H]^+$, 100), 654.3 ($[M + Na]^+$, 19), 685.7 ($[M + Na + MeOH]^+$, 8), 970.3 ($[3M + 2Na]^{2+}$, 17), 1263.3 ($[2M + H]^+$, 14), 1285.4 ($[2M + Na]^+$, 71); analysis calculated for $C_{40}H_{57}NO_5$ (631.88): C 76.03, H 9.09, N 2.22; found: C 75.81, H 9.27, N 2.00.

4.2.30. N-[2β,3β-Diacetyloxy-17β-amino-28-norolean-12-en-17-yl]-phenylcarbamate (**43**)

Following the procedure for the synthesis of **41**, compound **43** (90 mg, 92%) was obtained from **37** and phenyl chloroformate (89 mg, 0.57 mmol) as a white solid; mp = 123–125 °C; $R_F = 0.62$ (silica gel, hexane/ethyl acetate, 7:3); $[\alpha]_D = +109.64°$ ($c = 0.30$, $CHCl_3$); UV–vis ($CHCl_3$): λ_{max} (log ε) = 261 nm (2.57); IR (KBr): ν = 3426*w*, 2950*s*, 2876*m*, 1746*vs*, 1486*s*, 1366*m*, 1252*s*, 1234*s*, 1200*s*, 1164*m*, 1030*m*, 986 *m* cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.36–7.31$ (*m*, 2 H, H–38), 7.19–7.15 (*m*, 1 H, H–39), 7.10–7.05 (*m*, 1 H, H–37), 5.36 (*dd*, $J = 3.5$, 3.5 Hz, 1 H, H–12), 5.33 (*ddd*, $J = 3.7$, 3.7, 3.7 Hz, 1 H, H–2), 4.89 (*s*, 1 H, NH), 4.64 (*d*, $J = 3.9$ Hz, 1 H, H–3), 2.28–2.22 (*m*, 2 H, H–18 + H–22a), 2.05 (*s*, 3 H, H–32), 2.04 (*s*, 3 H, H–34), 2.02–1.72 (*m*, 8 H, H–16a + H–16b + H–11a + H–11b + H–15a + H–1a + H–19a + H–22b), 1.66–1.50 (*m*, 4 H, H–6a + H–6b + H–7a + H–9), 1.46–1.18 (*m*, 5 H, H–7b + H–1b + H–21a + H–21b + H–19b), 1.22 (*s*, 3 H, H–25), 1.16 (*s*, 3 H, H–27), 1.10–0.99 (*m*, 2 H, H–15b + H–5), 1.07 (*s*, 3 H, H–23), 1.03 (*s*, 3 H, H–26), 0.98 (*s*, 3 H, H–29), 0.92 (*s*, 6 H, H–24 + H–30) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 170.9$ (C–33), 170.4 (C–31), 152.6 (C–35), 151.1 (C–36), 143.1 (C–13), 129.3 (C–38), 125.2 (C–39), 124.8 (C–12), 121.9 (C–37), 78.1 (C–3), 69.7 (C–2), 55.9 (C–17), 55.4 (C–5), 48.2 (C–9), 47.0 (C–18), 46.4 (C–19), 42.1 (C–1), 41.8 (C–14), 39.9 (C–8), 37.5 (C–4), 36.9 (C–10), 35.3 (C–21), 33.0 (C–30), 32.9 (C–22), 32.6 (C–7), 30.9 (C–20), 29.3 (C–24), 26.2 (C–15), 26.1 (C–27), 24.1 (C–29), 23.8 (C–11), 22.1 (C–16), 21.4 (C–32), 21.0 (C–34), 18.1 (C–6), 17.8 (C–23), 17.1 (C–26), 16.1 (C–25) ppm; MS (ESI): *m*/*z* (%) = 648.1 ($[M + H]^+$, 22), 670.3 ($[M + Na]^+$, 28), 1317.5 ($[2M + Na]^+$, 100); analysis calculated for $C_{40}H_{57}NO_6$ (647.88): C 74.15, H 8.87, N 2.16; found: C 73.87, H 8.97, N 1.96.

4.2.31. N-[2β,3β-Diacetyloxy-17β-amino-28-norurs-12-en-17-yl]-phenylcarbamate (**44**)

Compound **44** (82 mg, 83%) was obtained as described above for **41** from **38** and phenyl chloroformate (89 mg, 0.57 mmol) as a white solid; mp = 102–104 °C; $R_F = 0.54$ (silica gel, chloroform/hexane/ethyl acetate, 10:9:1); $[\alpha]_D = +95.00°$ ($c = 0.77$, $CHCl_3$); UV–vis ($CHCl_3$): λ_{max} (log ε) = 271 nm (3.06); IR (KBr): ν = 3420*m*, 2950*s*, 2870*m*, 1746*vs*, 1606*w*, 1596*m*, 1504*m*, 1484*s*, 1456*m*, 1432*m*, 1398*m*, 1364*s*, 1344*w*, 1314*m*, 1252*s*, 1234*s*, 1198*vs*, 1162*m*, 1116*w*, 1090*w*, 1056*m*, 1042*m*, 1026*m*, 986*m*, 966*m*, 944*m*, 690 *m* cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.36–7.31$ (*m*, 2 H, H–38), 7.17 (*t*, $J = 7.4$ Hz, 1 H, H–39), 7.07 (*d*, $J = 7.7$ Hz, 2 H, H–37), 5.36–5.31 (*m*, 2 H, H–2 + H–12), 4.90 (*s*, 1 H, NH), 4.64 (*d*, $J = 3.9$ Hz, 1 H, H–3), 2.54–2.50 (*m*, 1 H, H–22a), 2.15–1.90 (*m*, 5 H, H–1a + H–11a + H–11b + H–16a + H–16b), 2.06 (*s*, 3 H, H–32), 2.04 (*s*, 3 H, H–34), 1.90–1.81 (*m*, 1 H, H–15a), 1.65–1.52 (*m*, 7 H, H–6a + H–6b + H–7a + H–9 + H–18 + H–21a + H–22b), 1.48–1.41 (*m*, 2 H, H–7b + H–19), 1.41–1.35 (*m*, 1 H, H–1b), 1.24 (*s*, 3 H, H–25), 1.23–1.18 (*m*, 1 H, H–21b), 1.13–1.04 (*m*, 1 H, H–15b), 1.11 (*s*, 3 H, H–27), 1.08 (*s*, 3 H, H–26), 1.07 (*s*, 3 H, H–23), 1.04–0.97 (*m*, 2 H, H–5 + H–20), 0.96 (*d*, $J = 6.2$ Hz, 3 H, H–30), 0.93 (*s*, 3 H, H–24), 0.86 (*d*, $J = 6.4$ Hz, 3 H, H–29) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 170.9$ (C–33), 170.5 (C–31), 155.9 (C–35), 151.1 (C–36), 138.4 (C–13), 129.3 (C–38), 127.5 (C–12), 125.2 (C–39), 122.0 (C–37), 78.1 (C–3), 69.7 (C–2), 58.8 (C–18), 56.4 (C–17), 55.3 (C–5), 48.2 (C–9), 42.3 (C–14), 42.2 (C–1), 40.1 (C–8), 40.0 (C–19), 39.3 (C–20), 37.5 (C–4), 37.1 (C–22), 36.8 (C–10), 32.9 (C–7), 31.4 (C–21), 29.3 (C–24), 26.7 (C–15), 23.7 (C–16), 23.5 (C–27), 23.3 (C–11), 21.4 (C–32), 21.0 (C–34), 20.9 (C–30), 18.1 (C–6), 17.9 (C–29), 17.6 (C–23), 17.1 (C–26), 16.3 (C–25) ppm; MS (ESI): *m*/*z* (%) = 648.1 ($[M + H]^+$, 100), 670.3 ($[M + Na]^+$, 23), 1296.2 ($[2M + H]^+$, 18), 1317.3 ($[2M + Na]^+$, 34); analysis calculated for $C_{40}H_{57}NO_6$ (647.88): C 74.15, H 8.87, N 2.16; found: C 73.96, H 9.01, N. 2.05.

4.2.32. N-[2β,3β-Diacetyloxy-17β-amino-28-norolean-12-en-17-yl]-phenylurea (**45**)

A solution of compound **37** (130 mg, 0.25 mmol) in dry toluene (10 mL) was treated with phenylisocyanate (44 mg, 0.37 mmol), and the mixture was stirred 2 h at room temperature. Et_2O (50 mL) was added, and usual aq. work-up followed by column chromatography (silica gel, hexane/ethyl acetate, 8:2) gave **45** (110 mg, 69%) as a white solid; mp = 169–172 °C; $R_F = 0.46$ (silica gel, hexane/ethyl acetate, 7:3); $[\alpha]_D = +88.50°$ ($c = 0.34$, $CHCl_3$); UV–vis ($CHCl_3$): λ_{max} (log ε) = 243 nm (4.15); IR (KBr): ν = 3402*m*, 2950*s*, 2870*m*, 1746*vs*, 1700*m*, 1664*m*, 1598*m*, 1540*s*, 1498*s*, 1438*m*, 1364*m*, 1310*m*, 1252*vs*, 1232*vs*, 1056*m*, 1030*m*, 1012 *m* cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.30–7.23$ (*m*, 4 H, H–37 + H–38), 7.06–7.01 (*m*, 1 H, H–39), 6.10 (*s*, 1 H, NH), 5.32 (*ddd*, $J = 3.7$, 3.7, 3.7 Hz, 1 H, H–2), 5.27 (*dd*, $J = 3.4$, 3.4 Hz, 1 H, H–12), 4.62 (*d*, $J = 3.9$ Hz, 1 H, H–3), 4.51 (*s*, 1 H, NH), 2.44 (*ddd*, $J = 13.8$, 3.3, 3.3 Hz, 1 H, H–22a), 2.19–2.10 (*m*, 2 H, H–18 + H–16a), 2.05 (*s*, 3 H, H–32), 2.04 (*s*, 3 H, H–34), 2.00–1.67 (*m*, 7 H, H–16b + H–11a + H–11b + H–15a + H–22b + H–1a + H–19a), 1.63–1.44 (*m*, 4 H, H–6a + H–6b + H–7a + H–9), 1.38–1.14 (*m*, 5 H, H–7b + H–21a + H–21b + H–1b + H–19b), 1.17 (*s*, 3 H, H–25), 1.13 (*s*, 3 H, H–27), 1.06 (*s*, 3 H, H–23), 1.05–0.94 (*m*, 2 H, H–15b + H–5), 0.96 (*s*, 3 H, H–29), 0.91 (*s*, 3 H, H–30), 0.91 (*s*, 3 H, H–24), 0.80 (*s*, 3 H, H–26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 170.9$ (C–33), 170.4 (C–31), 154.3 (C–35), 143.5 (C–13), 139.1 (C–36), 129.2 (C–38), 124.4 (C–12), 124.8 (C–39), 120.8 (C–37), 78.1 (C–3), 69.8 (C–2), 56.1 (C–17), 55.3 (C–5), 48.1 (C–9), 47.8 (C–18), 46.4 (C–19), 42.0 (C–1), 41.9 (C–14), 39.8 (C–8), 37.5 (C–4), 36.8 (C–10), 35.4 (C–21), 33.3 (C–22), 33.0 (C–30), 32.4 (C–7), 30.9 (C–20), 29.2 (C–24), 26.3 (C–15), 26.0 (C–27), 24.2 (C–29), 23.8 (C–11), 22.4 (C–16), 21.4 (C–32), 21.0 (C–34), 18.1 (C–6), 17.8 (C–23), 16.9 (C–26), 16.1 (C–25) ppm; MS (ESI): *m*/*z* (%) = 647.2 ($[M + H]^+$, 100), 669.3 ($[M + Na]^+$, 10), 993.7 ($[3M + 2Na]^{2+}$, 12), 1293.2 ($[2M + H]^+$, 48); analysis calculated for $C_{40}H_{58}N_2O_5$ (646.90): C 74.27, H 9.04, N 4.33; found: C 73.97, H 9.28, N 4.09.

4.2.33. N-[2β,3β-Diacetyloxy-17β-amino-28-norurs-12-en-17-yl]-phenylurea (**46**)

As described for **45**, compound **46** (93 mg, 58%) was synthesized from **38** and obtained as a white solid; mp = 173–174 °C; $R_F = 0.44$ (silica gel, hexane/ethyl acetate, 7:3); $[\alpha]_D = +69.20°$ ($c = 1.20$, $CHCl_3$); UV–vis ($CHCl_3$): λ_{max} (log ε) = 243 nm (4.17); IR (KBr): ν = 3388*m*, 3136*w*, 2950*s*, 2870*m*, 1746*vs*, 1700*s*, 1660*s*, 1600*s*,

1542*s*, 1498*vs*, 1456*s*, 1440*s*, 1398*m*, 1366*s*, 1342*m*, 1314*s*, 1290*m*, 1252*vs*, 1232*vs*, 1194*s*, 1176*m*, 1160*m*, 1116*w*, 1078*m*, 1058*s*, 1030*s*, 996*m*, 972*m*, 946*m*, 750*s*, 692*m*, 666*m*, 604 *m* cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.27–7.21$ (*m*, 4 H, H−37 + H−38), 7.04−7.00 (*m*, 1 H, H−39), 6.20 (*s*, 1 H, NH), 5.31 (*ddd*, $J = 3.7, 3.7, 3.7$ Hz, 1 H, H−2), 5.20 (*dd*, $J = 3.5, 3.5$ Hz, 1 H, H−12), 4.61 (*d*, $J = 5.4$ Hz, 1 H, H−3), 4.60 (*s*, 1 H, NH), 2.76−2.66 (*m*, 1 H, H−22a), 2.26−2.20 (*m*, 1 H, H−16a), 2.05 (*s*, 3 H, H−32), 2.03 (*s*, 3 H, H−34), 2.00−1.76 (*m*, 5 H, H−1a + H−11a + H−11b + H−15a + H−16b), 1.60−1.38 (*m*, 8 H, H−6a + H−6b + H−7a + H−9 + H−18 + H−19 + H−21a + H−22b), 1.37−1.30 (*m*, 2 H, H−1b + H−7b), 1.23−1.18 (*m*, 1 H, H−21b), 1.17 (*s*, 3 H, H−25), 1.06 (*s*, 3 H, H−27), 1.05 (*s*, 3 H, H−23), 1.04−0.99 (*m*, 1 H, H−15b), 0.99−0.92 (*m*, 2 H, H−5 + H−20), 0.94 (*d*, $J = 5.9$ Hz, 3 H, H−30), 0.90 (*s*, 3 H, H−24), 0.82 (*d*, $J = 5.8$ Hz, 3 H, H−29), 0.79 (*s*, 3 H, H−26) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 170.9$ (C−33), 170.4 (C−31), 154.2 (C−35), 139.2 (C−36), 138.8 (C−13), 129.2 (C−38), 127.1 (C−12), 123.4 (C−39), 120.9 (C−37), 78.1 (C−3), 69.7 (C−2), 59.4 (C−18), 56.5 (C−17), 55.3 (C−5), 48.1 (C−9), 42.3 (C−14), 42.2 (C−1), 40.0 (C−8), 39.9 (C−19), 39.4 (C−20), 37.5 (C−4), 37.5 (C−22), 36.7 (C−10), 32.7 (C−7), 31.5 (C−21), 29.2 (C−24), 26.8 (C−15), 23.7 (C−11 + C−16), 23.4 (C−27), 21.4 (C−32), 21.0 (C−34), 20.9 (C−30), 18.1 (C−6), 17.8 (C−23), 17.6 (C−29), 16.9 (C−26), 16.3 (C−25) ppm; MS (ESI): *m*/*z* (%) = 647.3 ($[M + H]^+$, 86), 669.3 ($[M + Na]^+$, 31), 992.3 ($[3M + 2Na]^{2+}$, 20), 1293.3 ($[2M + H]^+$, 94), 1315.4 ($[2M + Na]^+$, 100); analysis calculated for $C_{40}H_{58}N_2O_5$ (646.90): C 74.27, H 9.04, N 4.33; found: C 74.03, H 9.27, N 4.15.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.ejmech.2016.04.051.

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