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Research paper

Betulinic acid derived hydroxamates and betulin derived carbamates are interesting scaffolds for the synthesis of novel cytotoxic compounds

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ABSTRACT

The betulinic acid-derived hydroxamates **5**–**18**, the amides **19**–**24**, and betulin-derived bis-carbamates **25**–**28** as well as the carbamates **31**–**40** and **44**–**48** were prepared and evaluated for their antiproliferative activity in a photometric sulforhodamine B (SRB) assay against several human cancer cell lines and nonmalignant mouse fibroblasts (NIH 3T3). While for 3-*O*-acetyl hydroxamic acid **5** EC_{50} values as low as EC_{50} = 1.3 μM were found, *N*,*O*-bis-alkyl substituted hydroxamates showed lowered cytotoxicity (EC_{50} = 16–20 μM). In general, hydroxamic acid derivatives showed only reduced selectivity for tumor cells, except for allyl substituted compound **13** (EC_{50} = 5.9 μM for A2780 human ovarian carcinoma cells and EC_{50} > 30 μM for nonmalignant mouse fibroblasts). The cytotoxicity of betulinic acid derived amides **19**–**24** and of betulin derived bis-carbamates **25**–**28** was low, except for *N*-ethyl substituted **25**. Hexyl substituted **39** showed EC_{50} = 5.6 μM (518A2 cells) while for mouse fibroblasts EC_{50} > 30 was determined.

1. Introduction

Hydroxamic acids have been known since Lossen's discovery of oxalohydroxamic acid (Fig. 1) in 1869 [1,2]. Then and for many years to follow they were regarded as rather exotic compounds. Nowadays, they have been recognized [3] as a unique family of compounds that hold a wide spectrum of biological activities. They act as selective inhibitors of many enzymes, such as matrix metalloproteinases [4,5], hydrolases [6], ureases [7], lipoxygenase [8], tumor necrosis factor-α converting enzyme [9,10], carbonic anhydrase [11,12], ribonucleotide reductase [13,14] and many others. Their acidity is much weaker than that of structurally related carboxylic acids but the hydroxamic acid moiety may act as a bidentate ligand to chelate with several metal ions. It also controls multiple sites for potential hydrogen bond interactions with enzymes and receptors [15].

Nonspecific hydroxamic acid derivatives have been prepared starting inter alia from benzodiazepines [16], α-amino-suberic acids [17], *N*-alkylated amino acids [18] as well as from arylsulfonamides [19]. Although triterpenoic acids represent an important class of compounds bearing high potential as antitumor-active compounds [20,21], to our knowledge, there are only two reports describing a hydroxamic acid derived from glycyrrhetinic acid. These compounds (Fig. 1) acted as selective inhibitors of 11β-hydroxysteroid dehydrogenase 2; there were no data provided whether these compounds were cytotoxic.

During our continuing search for antitumor active compounds from natural products [20–22] we became interested in the synthesis of betulinic acid (**BA**, **1**, Fig. 1) derived hydroxamic acid and derivatives and their cytotoxicity. Previous studies suggested introducing a sulfamate [23,24] or carbamate [25,26] to the pentacyclic skeleton of triterpenes can significantly improve the cytotoxicity of these compounds. Thus, we decided to prepare several mono- and bis-carbamates derived from betulin (**2**, Fig. 1). Betulin as well as betulinic acid have been shown to be interesting scaffolds for developing analogs displaying various biological and medicinal properties especially potent anticancer effects [27–37].

2. Results and discussion

2.1. Chemistry

Our synthetic approach started from **BA** whose acetylation gave 3-*O*-acetyl-**BA** (**3**, Scheme 1) while from the Jones oxidation of **BA**

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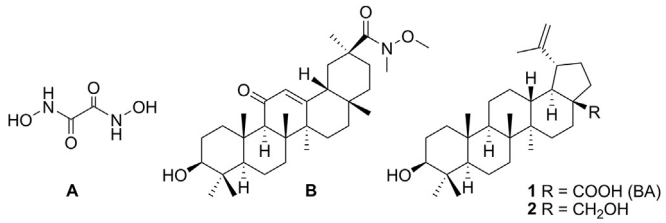


Fig. 1. Structure of Lossen's oxalohydroxamic acid (A) and a representative glycyrrhetinic acid derived hydroxamic acid (B), betulinic acid (**BA**, **1**) and betulin (**2**).

betulonic acid (**4**) was obtained [38,39]. Treatment of **3** with oxalyl chloride in DCM for 2 h at 25 °C followed by adding hydroxylammonium chloride in the presence of trimethylamine [40] provided a 68% yield of hydroxamic acid **5**. Deacetylation of **5** with potassium hydroxide in methanol gave 63% of **6** [41].

While the reaction of **1** with oxalyl chloride/hydroxylammonium chloride gave target compound **5** nicely, the reaction of **1** with propylphosphonic anhydride (T3P) or with 1,1′-carbonyldiimidazole failed to give high yields under a broad variety of different conditions [42–44].

Hydroxamic acid **5** is characterized in its ^{13}C NMR spectrum by a signal at $\delta = 175.1$ ppm being assigned to the **C**ONHOH moiety (C-28) of **5**. For comparison, C-28 was found in **3** at $\delta = 182.5$ ppm. This shifting of the resonance signal of carbonyl carbon C-28 to higher fields is typical for hydroxamic acids [45,46]. In the IR spectrum the C–O stretch vibration was detected at $\nu = 1643$ cm^{-1}.

Reaction of **3** with oxalyl chloride followed by reaction with *N*,*O*-dimethylhydroxylammonium chloride, or *N*-methylhydroxylammonium chloride or *O*-methylhydroxylammonium chloride or *O*-allylhydroxylammonium chloride in the presence of triethylamine furnished products **7**, **9**, **11** and **13**; their deacetylation yielded compounds **8**, **10**, **12** or **14**, respectively.

Under similar conditions betulonic acid (**4**) gave substituted hydroxamic acids **15**–**18**. Yields dropped slightly for these reactions because of the accompanying formation of C-3-oximes.

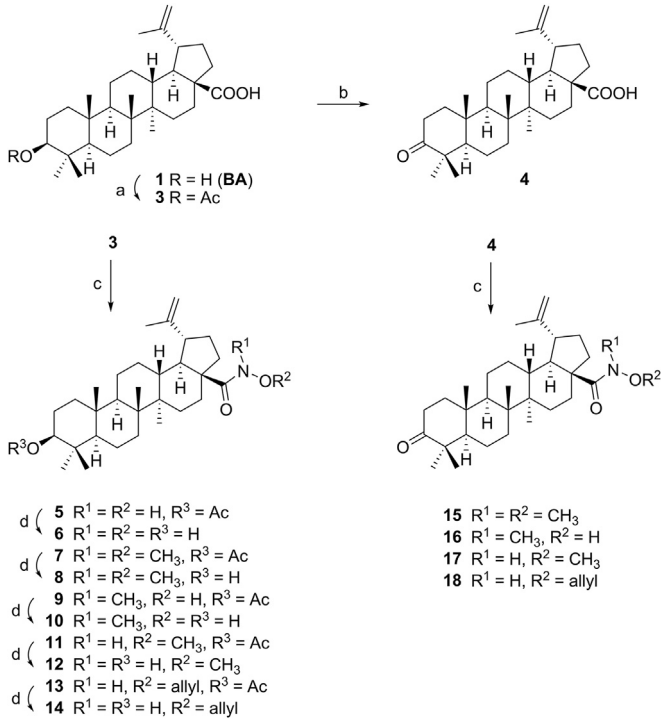
For comparison, we prepared several betulinic acid derived amides as well as betulin derived carbamates. Reaction of 3-*O*-acetyl-betulinic acid (**3**) with oxalyl chloride (Scheme 2) followed by a reaction with dry ammonia in DCM furnished amide **19** in 95% yield. Deacetylation of **19** with potassium hydroxide in methanol gave amide **20** [47,48]. In a similar way, from the reaction of **3** with oxalyl chloride and benzylamine, benzylamide **21** was obtained whose deacetylation yielded **22**; the Jones oxidation of **21** gave 3-oxo compound **23**. Following the procedure given for the synthesis of **12**, from betulonic acid (**4**) with dry ammonia in DCM 3-oxo-amide **24** [49–52] was obtained. Compound **19** is characterized in its ^{1}H NMR spectrum by the presence of a signal at $\delta = 5.55$ ppm that was assigned to the CON**H$_2$** moiety. In addition, the signal for H-19 was shifted to lower fields (compared to parent compound **3** showing $\Delta\delta = 0.08$ ppm). In the ^{13}C NMR spectrum the **C**ONH$_2$ moiety was detected at $\delta = 179.3$ ppm.

Previous studies suggested the introduction of a sulfamate [23] or carbamate [25] to the skeleton of a pentacyclic triterpenoid can significantly improve its cytotoxicity. Thus, we decided to prepare several bis-carbamates. The synthesis of these bis-carbamates **25**–**29** started from betulin (**2**, Scheme 3). While the reaction of betulin with ethyl isocyanate in refluxing chloroform for 48 h gave only low yields, the microwave assisted reaction of **2** with ethyl isocyanate in dry THF worked nicely, and 3,28-bis-*N*-ethyl-carbamate **25** was obtained in 81% isolated yield. Similarly bis-carbamates **26**–**28** were prepared.

For the synthesis of 3-*O*-acetyl-28-*N*-alkyl-carbamates **31**–**35**, 3-*O*-acetyl-betulin (**30**) was used as a starting material. Compound **30** is easily accessible from betulin; thus, diacetylation of betulin gave diacetate **29** whose selective deacetylation with KOH in MeOH/THF at 0 °C yielded 57% of monoacetate **30**.

The microwave assisted reaction of **30** with alkyl isocyanates or phenyl isocyanate allowed a quick and reliable synthesis of 3-*O*-acetylated 28-*N*-substituted carbamates **31**–**35**. From their deacetylation with potassium hydroxide in MeOH compounds **36**–**40** were obtained.

The synthesis of 3-oxo-28-*N*-alkyl-carbamates **44**–**48** (Scheme 4) started from 3-oxo-betulin **43**, and the microwave assisted reaction of **43** with alkyl isocyanates in THF gave target compounds **44**–**48** in good yields. The starting material for these reactions, **43**, was obtained from a deacetylation reaction of **42** (KOH in MeOH) in 90% isolated yield. Compound **42** was easily prepared by Jones oxidation of **41** (72% yield); the latter was made by a selective acetylation of betulin in 60% isolated yield.

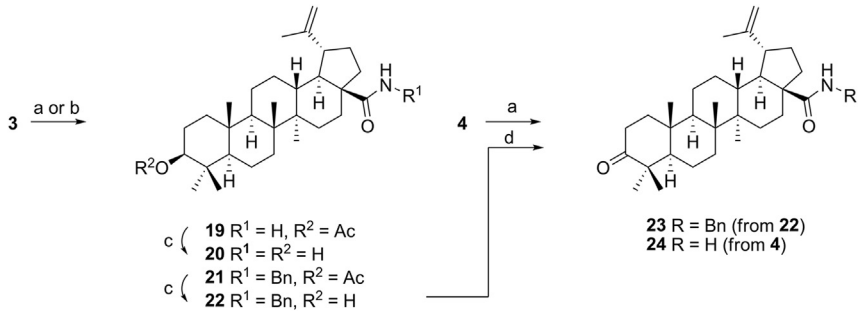


Scheme 1. Synthesis of betulinic acid derived hydroxamic acids **5**–**18**: a) Ac_2O, NEt_3, pyridine, DMAP, 12 h, 25 °C, 75%; b) Jones oxidation (4 h, 25 °C), 81%; c) oxalyl chloride, DCM, 2 h, 25 °C, then NHR^1OR^2, NEt_3, DCM, 2–12 h, 25 °C: **5** (from $NH_2OH \cdot HCl$, 68%), **7** (from HNMeOMe·HCl, 77%), **9** (from HNMeOH·HCl, 66%), **11** (from $NH_2OMe \cdot HCl$, 63%), **13** (from $NH_2OAll \cdot HCl$, 90%), **15** (from HNMeOMe·HCl, 52%), **16** (from HNMeOH·HCl, 81%), **17** (from $NH_2OMe \cdot HCl$, 45%), **18** (from $NH_2OAll \cdot HCl$, 68%); d) KOH in MeOH, 25 °C: **6** (4 d, 63%), **8** (5 d, 89%), **10** (5 d, 60%), **12** (5 d, 95%), **14** (7 d, 94%).

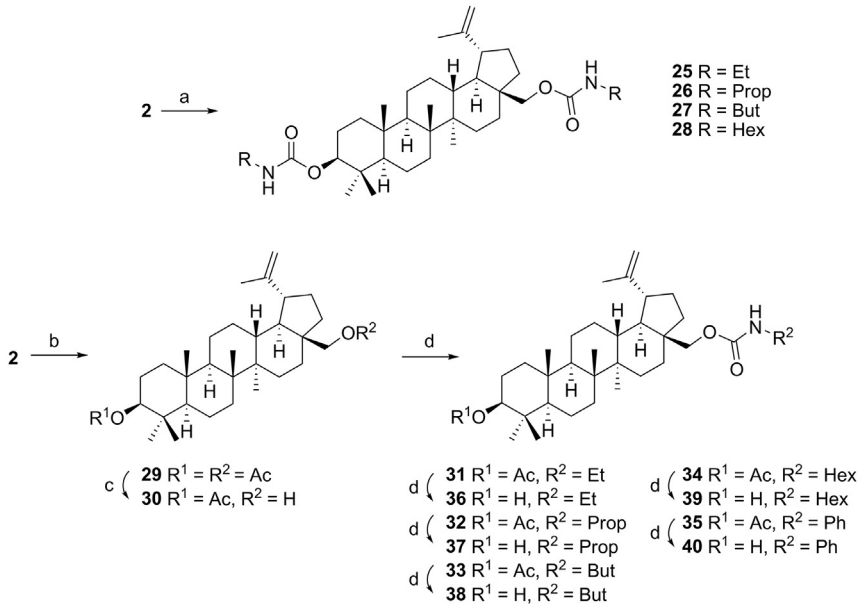
2.2. Biology

The betulinic acid-derived hydroxamates **5**–**18**, the amides **19**–**24**, and betulin-derived bis-carbamates **25**–**28** as well as the carbamates **31**–**40** and **44**–**48** were evaluated for their antiproliferative activity in a photometric sulforhodamine B (SRB) assay [53–56] against several human cancer cell lines and nonmalignant mouse fibroblasts (NIH 3T3). For comparison, betulinic acid (**1**), betulin (**2**), betulonic acid (**4**) and acetates **3**, **29** and **30** were included into this screening (Table 1).

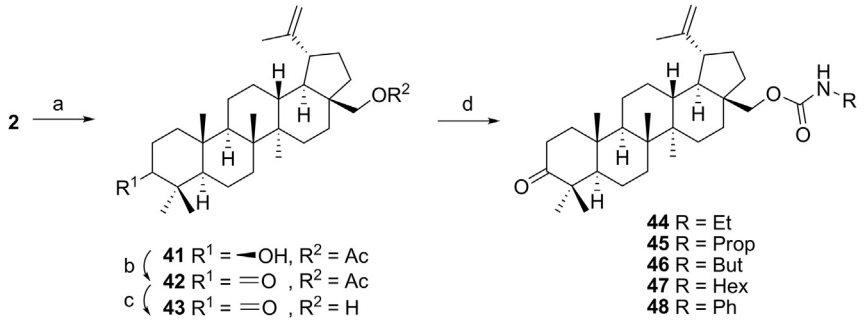
Betulin (**2**) and its diacetate **29** displayed no ($EC_{50} > 30$ μM; cut-off of the assay) cytotoxicity; low activity was found for the betulin-monoacetate **30**. Betulinic acid (**1**) is well-known for its



Scheme 2. Synthesis of betulinic or betulonic acid derived amides **19**–**24**: a) oxalyl chloride, DCM 2 h 25 °C, then NH_3, 1 h, 25 °C, 95% (for **19**) and 84% (for **24**); b) oxalyl chloride, DCM, 2 h, 25 °C, then $BnNH_2$, 1 h, reflux, 59%; c) KOH, MeOH, THF, 1 d, 25 °C, 97% (for **20**) and 92% (for **22**); d) Jones oxidation, 20 min, 25 °C, 74%; f) a) oxalyl chloride, DCM, 2 h, 25 °C, then NH_3, 1 h, 25 °C, 84%.



Scheme 3. Synthesis of betulin derived 3,28-bis-carbamates **25**–**28** and 28-mono-carbamates **31**–**40**: a) microwave assisted (7 h, 120 °C, THF, RNCO): **25** (from EtNCO, 81%), **26** (from PropNCO, 83%), **27** (from ButNCO, 81%), **28** (from HexNCO, 73%); b) Ac_2O, NEt_3, DMAP, DCM, 12 h, 25 °C, 90%; c) KOH, MeOH, THF, 0 °C, 30 min, 57%; d) KOH, MeOH, THF, 25 °C: **36** (2 d, 95%), **37** (1 d, 93%), **38** (2 d, 94%), **39** (1 d, 88%, **40** (2 d, 89%).



Scheme 4. Synthesis of 3-oxo-betulin derived 28-mono-carbamates **44**–**48**: a) Ac_2O, NEt_3, DMAP, 12 h, 25 °C, 60%; b) Jones oxidation, 40 min, 25 °C, 72%; c) KOH, MeOH, THF, 12 h, 25 °C, 90%; d) miocrowave assisted (7 h, 120 °C, THF, RNCO): **44** (from EtNCO, 68%), **45** (from PropNCO, 62%), **46** (from ButNCO, 72%), **47** (from HexNCO, 55%), **48** (from PhNCO, 85%).

cytotoxicity, and EC_{50} values between 8.8 and 17.1 μM were determined while for betulonic acid (**4**) EC_{50} values between EC_{50} = 13.1–29.0 μM were found. Betulinic acid 3-acetate **3** showed higher cytotoxicity, especially for 518A2 human melanoma cells (EC_{50} = 4.5 μM). Betulinic acid derived 3-*O*-acetyl hydroxamic acid **5** showed significantly higher cytotoxicity, and EC_{50} values as low as EC_{50} = 1.3 μM were found. Bis-alkyl substitution (as in **7**) in the hydroxamate moiety lowered cytotoxicity (EC_{50} = 16–20 μM) significantly. The presence of at least one acidic hydrogen substituent in the hydroxamic acid part seems mandatory to obtain cytotoxic compounds: Compounds **9** and **11** gave EC_{50} values between EC_{50} = 2.0–13.5 μM. For allyl-

Table 1
Cytotoxicity of betulinic acid-derived hydroxamates **5**–**18** and starting materials **1**–**4**, **29**, **30** (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%). The cell lines are human cancer cell lines: 518A2 (melanoma), A2780 (ovarian carcinoma), A549 (alveolar basal epithelial adenocarcinoma), MCF7 (breast adenocarcinoma) and non-malignant mouse fibroblasts (NIH 3T3).

	518A2	A2780	A549	MCF7	NIH 3T3
1	9.4 ± 0.7	8.8 ± 0.9	17.1 ± 1.1	10.2 ± 1.2	16.1 ± 1.4
2	>30	>30	>30	>30	>30
3	4.5 ± 0.1	18.3 ± 0.5	6.2 ± 0.4	11.0 ± 0.5	>30
4	29.0 ± 2.0	20.4 ± 1.9	25.9 ± 2.5	25.9 ± 2.0	13.1 ± 0.9
29	>30	>30	>30	>30	>30
30	15.2 ± 1.6	11.0 ± 1.3	14.0 ± 2.4	11.2 ± 1.4	>30
5	1.6 ± 0.1	1.3 ± 0.1	1.3 ± 0.1	1.4 ± 0.1	1.1 ± 0.1
6	2.4 ± 0.2	3.7 ± 0.5	5.3 ± 0.6	3.9 ± 0.6	2.0 ± 0.5
7	17.5 ± 0.6	19.3 ± 1.1	20.1 ± 1.4	16.4 ± 0.9	17.4 ± 1.1
8	7.3 ± 0.5	7.6 ± 0.3	19.0 ± 3.0	10.2 ± 1.4	7.7 ± 1.3
9	3.5 ± 0.3	2.0 ± 0.1	4.3 ± 0.7	2.3 ± 0.3	2.9 ± 0.6
10	Not soluble				
11	8.0 ± 0.6	8.9 ± 0.5	11.7 ± 2.0	13.5 ± 0.9	9.5 ± 0.5
12	5.8 ± 1.2	12.3 ± 0.9	6.9 ± 0.2	21.9 ± 0.7	15.2 ± 0.5
13	7.6 ± 0.1	5.9 ± 0.6	6.6 ± 1.5	12.2 ± 2.0	>30
14	6.7 ± 0.1	7.3 ± 0.7	4.1 ± 1.7	8.6 ± 1.0	6.1 ± 0.4
15	>30	20.7 ± 1.6	14.5 ± 1.3	18.7 ± 1.2	26.7 ± 2.0
16	6.3 ± 0.2	3.0 ± 0.2	6.0 ± 0.3	10.2 ± 0.9	5.0 ± 0.4
17	17.2 ± 1.6	12.0 ± 1.5	6.1 ± 1.1	13.8 ± 1.6	12.7 ± 1.1
18	22.4 ± 1.5	19.7 ± 2.0	25.0 ± 2.1	18.4 ± 1.9	19.7 ± 1.7

substituted **14** EC_{50} values of the same magnitude as for **11** were found (Table 2).

Deacetylated compound **6** also gave low EC_{50} values, but this compound was less active than parent **5**. Substituted hydroxamic acids **8**, **12** and **14** were of similar cytotoxicity. Despite the low EC_{50} values, hydroxamic acid derivatives showed only reduced selectivity for tumor cells, except for allyl substituted compound **13** (EC_{50} = 5.9 μM for A2780 human ovarian carcinoma cells and EC_{50} > 30 μM for nonmalignant mouse fibroblasts) (Table 3).

The cytotoxicity of amides **19**–**24**, however, was moderate; the lowest EC_{50} value was determined for 3-*O*-acetylated compounds **19** and **21**. The cytotoxicity of betulin derived bis-carbamates **25**–**28** was also low, except for *N*-ethyl substituted **25**; the same was observed for their 3-*O*-acetylated analogues **31**–**35** and their 3-oxo-analogues **44**–**48**.

Significantly improved cytotoxicity was found for carbamates **36**–**40** holding a free hydroxyl group at position C-3. While almost all of these compounds showed more or less the same cytotoxicity for tumor cell lines as well as for mouse fibroblasts, hexyl substituted **39** showed EC_{50} = 5.5 μM (518A2 cells) while for mouse fibroblasts EC_{50} > 30 was determined.

3. Conclusion

The betulinic acid-derived hydroxamates **5**–**18**, the amides **19**–**24**, and betulin-derived bis-carbamates **25**–**28** as well as the carbamates **31**–**40** and **44**–**48** were prepared and evaluated for their antiproliferative activity in a photometric sulforhodamine B (SRB) assay against several human cancer cell lines and nonmalignant mouse fibroblasts (NIH 3T3). While betulin (**2**) and its diacetate **29** exhibited no cytotoxicity, low activity was found for the betulin-monoacetate **30**. Betulinic acid 3-acetate **3** showed higher cytotoxicity than its parent compound betulinic acid, but significantly lower EC_{50} values were determined for 3-*O*-acetyl hydroxamic acid **5**, and EC_{50} values as low as EC_{50} = 1.3 μM were found. Bis-alkyl substitution in the hydroxamate moiety lowered cytotoxicity (EC_{50} = 16–20 μM). The presence of at least one acidic hydrogen substituent in the hydroxamic acid part seems mandatory to obtain cytotoxic compounds. Despite their low EC_{50} values, hydroxamic acid derivatives showed only reduced selectivity for tumor cells, except for allyl substituted compound **13** (EC_{50} = 5.9 μM for A2780 human ovarian carcinoma cells and EC_{50} > 30 μM for nonmalignant mouse fibroblasts). The cytotoxicity of betulinic acid derived amides **19**–**24** as well as of betulin derived bis-carbamates **25**–**28** was low, except for *N*-ethyl substituted **25**. While almost all of these compounds showed more or less the same cytotoxicity for tumor cell lines as well as for mouse fibroblasts, hexyl substituted **39** showed EC_{50} = 5.6 μM (518A2 cells) while for mouse fibroblasts EC_{50} > 30 was determined.

4. Experimental section

4.1. General – chemistry

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 Me4Si, 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%. Betulinic acid (**1**) and betulin (**2**) and were obtained from different commercial suppliers in bulk quantities. Microwave assisted reactions were performed in a Monowave 300 apparatus (Anton Parr, Austria).

4.2. General – biological screening

The SRB assay was performed as previously described [53–56].

4.3. Syntheses

4.3.1. (3β) 3-Acetyloxy-lup-20(29)-en-28-acid (3)

Prepared by reaction (12 h, 25 °C) of **1** (4.0 g, 8.78 mmol) with

Table 2
Cytotoxicity of betulinic acid derived amides **19**–**24** (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%). The cell lines are human cancer cell lines: 518A2 (melanoma), A2780 (ovarian carcinoma), HT29 (colorectal adenocarcinoma), MCF7 (breast adenocarcinoma), A549 (alveolar basal epithelial adenocarcinoma), HeLa (epitheloid cervix carcinoma) and non-malignant mouse fibroblasts (NIH 3T3).

	518A2	A2780	HT-29	MCF7	A549	HeLa	NIH 3T3
19	13.4 ± 1.1	5.7 ± 0.6	11.5 ± 0.7	11.1 ± 0.6	12.4 ± 1.4	12.0 ± 1.1	20.0 ± 1.3
20	9.9 ± 0.7	15.7 ± 1.4	10.2 ± 1.3	10.7 ± 0.5	8.2 ± 0.9	11.2 ± 1.2	10.7 ± 0.6
21	6.2 ± 1.3	6.2 ± 1.1	>30	>30	10.3 ± 0.8	16.9 ± 1.8	>30
22	>30	11.8 ± 1.4	–	18.0 ± 2.1	>30	>30	11.1 ± 0.9
23	>30	7.4 ± 1.1	>30	>30	>30	>30	>30
24	21.5 ± 1.9	15.6 ± 1.4	17.9 ± 1.4	10.3 ± 1.1	14.7 ± 0.9	22.9 ± 1.7	17.7 ± 1.1

Table 3
Cytotoxicity of betulin derived bis-carbamates **25**–**28** and mono-carbamates **31**–**40** and **44**–**48** (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%). The cell lines are human cancer cell lines: 518A2 (melanoma), A2780 (ovarian carcinoma), HT29 (colorectal adenocarcinoma), MCF7 (breast adenocarcinoma), A549 (alveolar basal epithelial adenocarcinoma), HeLa (epitheloid cervix carcinoma) and non-malignant mouse fibroblasts (NIH 3T3).

	518A2	A2780	HT-29	MCF7	A549	HeLa	NIH 3T3
25	12.6 ± 1.3	5.8 ± 0.6	8.3 ± 0.9	23.3 ± 2.0	10.7 ± 1.3	17.8 ± 0.9	>30
26	>30	19.4 ± 2.0	>30	>30	>30	>30	>30
27, **28**	>30	>30	>30	>30	>30	>30	>30
31	10.2 ± 1.3	11.1 ± 1.4	>30	20.4 ± 2.5	14.1 ± 1.2	17.0 ± 1.5	>30
32–**35**	>30	>30	>30	>30	>30	>30	>30
36	12.5 ± 1.6	4.6 ± 0.7	>30	12.1 ± 1.1	12.0 ± 1.6	>30	8.8 ± 1.0
37	15.9 ± 2.0	10.6 ± 1.5	16.3 ± 1.1	15.5 ± 1.4	14.2 ± 2.1	9.4 ± 0.9	7.3 ± 0.8
38	8.0 ± 1.1	7.0 ± 0.9	7.5 ± 1.0	12.5 ± 0.8	8.6 ± 0.5	10.1 ± 1.2	5.7 ± 0.7
39	5.5 ± 0.7	7.7 ± 0.9	>30	>30	12.7 ± 1.4	7.4 ± 1.1	>30
40	23.9 ± 1.4	7.2 ± 1.4	16.3 ± 2.5	24.6 ± 1.9	>30	11.5 ± 1.3	14.3 ± 2.0
44	16.6 ± 1.1	8.3 ± 0.9	11.5 ± 0.9	19.7 ± 2.5	20.3 ± 1.9	13.4 ± 1.2	4.6 ± 0.7
45–**48**	>30	>30	>30	>30	>30	>30	>30

NEt_3 (2.2 mL, 15.90 mmol), acetic anhydride (1.6 mL, 16.94 mmol) and catalytic amounts of DMAP in dry pyridine (80 mL), and **3** (3.28 g, 75%) was obtained as a colorless solid; $R_F = 0.60$ (silica gel, toluene/ethyl acetate/heptane/formic acid, 80:20:10:3); m.p.: 275–277 °C (lit.: [57] 277–278 °C; $[\alpha]_D = +20.54°$ ($c = 0.58$, $CHCl_3$) (lit.: [57] +22° ($c = 0.49$, $CHCl_3$); MS (ESI, MeOH): $m/z = 497.4$ (25%, $[M - H]^-$), 543.1 (100%, $[M + HCO_2]^-$), 995.3 (100%, $[2M - H]^-$), 1017.8 (8%, $[2M - 2H + Na]^-$).

4.3.2. Betulonic acid (*4*)

Prepared from **1** (13.1 g, 28.7 mmol) by Jones oxidation (4 h, 25 °C) as previously reported [38], followed by chromatographic workup (silica gel, hexanes/ethyl acetate, 9:1), and **4** (10.6 g, 81%) was obtained as a colorless solid; $R_F = 0.79$ (silica gel, hexanes/ethyl acetate, 7:3); m.p.: 242–244 °C (lit.: [38] 245–247 °C; $[\alpha]_D = +39.42°$ ($c = 0.64$, $CHCl_3$) (lit.: [57] $[\alpha]_D = +32°$ ($c = 0.37$, $CHCl_3$), $[\alpha]_D = +40°$ ($c = 0.86$, $CHCl_3$) [58]; MS (ESI, MeOH): $m/z = 455.2$ (100%, $[M+H]^+$), 508.9 (24%, $[M + Na + MeOH]^+$), 909.3 (16%, $[2M + H]^+$), 931.3 (46%, $[2M + Na]^+$).

4.3.3. (3β) 3-Acetyloxy-N-hydroxy-lup-20(29)-en-28-amide (*5*)

To an ice cold solution of **3** (0.39 g, 0.78 mmol) in dry DCM (25 mL), oxalyl chloride (0.40 mL, 4.70 mmol) was slowly added, and the mixture was allowed to warm to 25 °C and stirred for 2 h. The solvent was removed under diminished pressure, the residue dissolved in dry THF (20 mL), and the solvent was again removed. The residue was dissolved in dry DCM (25 mL) containing NEt_3 (0.70 mL, 5.05 mmol), and hydroxylammonium chloride (0.20 g, 2.90 mmol) was added. Stirring at 25 °C was continued for another 2 h. Usual aqueous workup gave a residue that was subjected to chromatography (silica gel, hexanes/ethyl acetate, 7:3), and **5** (0.27 g, 68%) was obtained as a colorless solid; $R_F = 0.36$ (silica gel, hexanes/ethyl acetate, 7:3); m.p.: 207–210 °C; $[\alpha]_D = +9.02°$ ($c = 0.58$, $CHCl_3$); IR (KBr): ν = 3355*br*, 3075*m*, 2943*s*, 2870*s*, 1736*s*, 1716*s*, 1643*s*, 1451*s*, 1377*s*, 1317*w*, 1265*s*, 1196*m*, 1152*w*, 1107*m*, 1066*w*, 1030*s*, 979*s*, 917*m*, 885*m* cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.93–7.70 (*m*, 2H, N*H* + O*H*), 4.73 (*s*, 1H, CH_a (29)), 4.60 (*s*, 1H, CH_b (29)), 4.50–4.42 (*m*, 1H, C*H* (3)), 3.03 (*ddd*, J = 11.1, 11.1, 4.2 Hz, 1H, C*H* (19)), 2.33 (*ddd*, J = 12.6, 12.6, 3.2 Hz, 1H, C*H* (13)), 2.03 (*s*, 3H, CH_3 (32)), 2.02–1.87 (*m*, 2H, CH_a (21) + CH_a (16)), 1.83–1.73 (*m*, 1H, CH_a (22)), 1.74–1.68 (*m*, 2H, CH_a (12) + CH_a (1)), 1.68 (*s*, 3H, CH_3 (30)), 1.66–1.28 (m, 12H, C*H* (18) + CH_2 (2) + CH_b (22) + CH_2 (7) + CH_b (16) + CH_b (21) + CH_a (15) + CH_a (11) + CH_2 (6)), 1.29–1.21 (*m*, 2H, CH_b (11) + C*H* (9)), 1.20–1.09 (*m*, 1H, CH_b (15)), 1.09–0.96 (*m*, 2H, CH_b (12) + CH_b (1)), 0.95 (*s*, 3H, CH_3 (27)), 0.93 (*s*, 3H, CH_3 (24)), 0.84 (*s*, 3H, CH_3 (26)), 0.83 (*s*, 3H, CH_3 (23)), 0.82 (*s*, 3H, CH_3 (25)), 0.80–0.74 (*m*, 1H, C*H* (5)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.1 (*C*=O, C28), 171.1 (*C*=O, C31), 150.2 (C_q, C20), 109.8 (CH_2=C, C29), 81.0 (*C*H, C3), 55.4 (*C*H, C5), 54.3 (C_q, C17), 50.4 (*C*H, C9), 50.4 (*C*H, C18), 46.9 (*C*H, C19), 42.4 (C_q, C14), 40.8 (C_q, C8), 38.4 (CH_2, C1), 38.3 (CH_2, C22), 38.0 (*C*H, C13), 37.8 (C_q, C4), 37.1 (C_q, C10), 34.3 (CH_2, C7), 32.8 (CH_2, C16), 30.7 (CH_2, C21), 29.4 (CH_2, C15), 27.9 (CH_3, C23), 25.5 (CH_2, C12), 23.7 (CH_2, C7), 21.3 (CH_3, C32), 20.8 (CH_2, C11), 19.3 (CH_3, C30), 18.2 (CH_2, C6), 16.5 (CH_3, C26), 16.2 (CH_3, C25), 16.1 (CH_3, C24), 14.6 (CH_3, C27) ppm; MS (ESI, MeOH): m/z = 514.4 (100%, $[M+H]^+$), 536.3 (30%, $[M+H]^+$), 1027.3 (50%, $[2M + H]^+$), 1049.4 (90%, $[2M + Na]^+$); analysis calcd for $C_{32}H_{51}NO_4$ (513.75): C 74.81, H 10.01, N 2.73; found: C 74.63, H 10.17, N 2.51.

4.3.4. (3β) 3-Hydroxy-N-hydroxy-lup-20(29)-en-28-amide (*6*)

To a solution of potassium hydroxide (0.28 g, 5.00 mmol) in methanol (25 mL) compound **5** (0.20 g, 0.39 mmol) was added, and stirring at 25 °C was continued for 4 days. Usual aqueous work-up followed by chromatography (silica gel, hexanes/ethyl acetate, 7:3, then 8:2, then $CHCl_3$/MeOH 9:1 followed by 10:0) gave **6** [41] (0.12 g, 63%) as an off-white solid; $R_F = 0.27$ (silica gel, hexanes/ethyl acetate, 7:3); m.p.: 188–190 °C; $[\alpha]_D = -5.30°$ ($c = 0.67$, $CHCl_3$/MeOH 5:1); IR (KBr): ν = 3252*br*, 2946*s*, 2868*m*, 1628*m*, 1466*m*, 1450*m*, 1388*m*, 1376*m*, 1256*w*, 1156*w*, 1110*w*, 1042*m*, 1030*m*, 1010*m*, 886*m* cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$/CD_3OD): δ = 4.60 (*s*, 1H, CH_a (29)), 4.47 (*s*, 1H, CH_b (29)), 3.07–3.00 (*m*, 1H, C*H* (3)), 2.96 (*ddd*, J = 10.9, 10.9, 3.8 Hz, 1H, C*H* (19)), 2.35–2.25 (*m*, 1H, C*H* (13)), 1.94–1.76 (m, 2H, CH_a (16) + CH_a (21)), 1.73–1.62 (*m*, 1H, CH_a (22)), 1.62–1.57 (*m*, 2H, CH_a (12) + CH_a (1)), 1.56 (*s*, 3H, CH_3 (30)), 1.51–1.42 (*m*, 3H, CH_2 (2) + C*H* (18)), 1.42–1.35 (*m*, 3H, CH_b (16) + CH_a (15) + CH_a (6)), 1.35–1.18 (*m*, 6H, CH_2 (7) + CH_b (21) + CH_b (22) + CH_b (6) + CH_a (11)), 1.19–1.10 (*m*, 2H, CH_b (11) + C*H* (9)), 1.07–0.96 (*m*, 1H, CH_b (15)), 0.96–0.86 (*m*, 1H, CH_b (12)), 0.84 (*s*, 3H, CH_3 (27)), 0.82 (*s*, 6H, CH_3 (23) + CH_3 (25)), 0.80–0.72 (*m*, 1H, CH_b (1)), 0.70 (*s*, 3H, CH_3 (26)), 0.62 (*s*, 3H, CH_3 (24)), 0.57–0.52 (*m*, 1H, C*H* (5)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$/CD_3OD): δ = 174.8 (*C*=O, C28), 150.7 (C_q, C20), 109.3 (CH_2=C, C29), 78.7 (*C*H, C9), 55.4 (*C*H, C5), 54.2 (C_q, C17), 50.5 (*C*H, C9), 50.4 (*C*H, C18), 46.7 (*C*H, C19), 42.3 (C_q, C14), 40.7 (C_q, C8), 38.7 (CH_2, C1), 38.2 (CH_2, C22), 37.8 (*C*H, C13), 37.1 (C_q, C4), 36.9 (C_q, C10), 34.3 (CH_2, C7), 32.6 (CH_2, C16), 30.7 (CH_2, C21), 29.3 (CH_2, C15), 27.8 (CH_3, C23), 26.9 (CH_2, C2), 25.5 (CH_2, C12), 20.8 (CH_2, C11), 19.2 (CH_3, C30), 18.2 (CH_2, C6), 16.0 (CH_3, C26), 15.9 (CH_3, C25), 15.2 (CH_3, C24), 14.5 (CH_3, C27) ppm; MS (ESI, MeOH): m/z = 472.4 (100%, $[M+H]^+$), 494.3 (6%, $[M+Na]^+$), 943.4 [20%, $[2M + H]^+$), 965.5 (60%, $[2M + Na]^+$); analysis calcd for $C_{30}H_{49}NO_3$ (471.71): C 76.39, H 10.47, N 2.97; found: C 76.21, H 10.90, N 2.76.

*4.3.5. (3β) 3-Acetyloxy-N-methoxy-N-methyl-lup-20(29)-en-28-amide (**7**)*

Following the procedure given for the synthesis of **5**, from the reaction of **3** (0.30 g, 0.60 mmol) with oxalyl chloride (0.30 mL, 3.52 mmol) in dry DCM (25 mL) for 2 h, then with NEt_3 (0.70 mL, 5.05 mmol) and *N,O*-dimethylhydroxylammonium chloride (0.12 g, 1.24 mmol) in dry DCM (25 mL) for 1 day at 25 °C followed by chromatography (silica gel, hexanes/ethyl acetate, 9:1) **7** (0.25 g, 77%) [59] was obtained as a colorless solid; $R_F = 0.72$ (silica gel, hexanes/ethyl acetate, 8:2); m.p.: 260–261 °C; $[\alpha]_D = +8.28°$ ($c = 0.66$, $CHCl_3$); IR (KBr): ν = 3441*br*, 3077*w*, 2936*s*, 2868*s*, 1737*s*, 1651*s*, 1446*m*, 1370*m*, 1327*w*, 1249*s*, 1165*w*, 1105*w*, 1029*m*, 994*m*, 976*m*, 887*m* cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 4.71 (*d*, $J = 2.4$ Hz, 1H, CH_a (29)), 4.56 (*d*, $J = 2.3$ Hz, 1H, CH_b (29)), 4.48–4.44 (*m*, 1H, *CH* (3)), 3.64 (*s*, 3H, OCH_3 (34)), 3.15 (*s*, 3H, NCH_3 (33)), 2.97 (*ddd*, J = 10.8, 10.8, 4.3 Hz, 1H, *CH* (19)), 2.71 (*ddd*, J = 12.0, 12.0, 3.6 Hz, 1H, *CH* (13)), 2.34–2.29 (*m*, 1H, CH_a (16)), 2.11–2.05 (*m*, 1H, CH_a (22)), 2.03 (*s*, 3H, CH_3 (32)), 1.84–1.75 (*m*, 1H, CH_b (16)), 1.73–1.56 (*m*, 4H, CH_a (1) + CH_a (12) + CH_2 (2)), 1.67 (*s*, 3H, CH_3 (30)), 1.56–1.50 (*m*, 1H, *CH* (9)), 1.50–1.42 (*m*, 1H, CH_a (6)), 1.42–1.20 (*m*, 10H, CH_b (6) + CH_2 (11) + CH_a (15) + CH_2 (7) + CH_b (22) + CH_2 (21) + *CH* (18)), 1.17–1.12 (*m*, CH_a (15)), 1.01–0.92 (*m*, 2H, CH_b (12) + CH_b (1)), 0.95 (*s*, 3H, CH_3 (27)), 0.93 (*s*, 3H, CH_3 (26)), 0.84 (*s*, 3H, CH_3 (25)), 0.83 (*s*, 3H, CH_3 (23)), 0.82 (*s*, 3H, CH_3 (24)), 0.80–0.76 (*m*, 1H, *CH* (5)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.1 (*C*=O, C28), 171.1 (*C*=O, C31), 151.5 (C_q, C20), 109.2 (CH_2=C, C29), 81.1 (*CH*, C3), 60.4 (OCH_3, C34), 56.2 (C_q, C17), 55.7 (*CH*, C5), 52.2 (*CH*, C9), 50.9 (*CH*, C18), 46.5 (*CH*, C19), 42.4 (C_q, C14), 40.9 (C_q, C8), 38.6 (CH_2, C1), 38.0 (C_q, C4), 37.3 (C_q, C10), 37.2 (*CH*, C13), 35.2 (CH_2, C22), 34.5 (CH_2, C7), 34.1 (NCH_3, C33), 31.2 (CH_2, C21), 31.0 (CH_2, C16), 30.1 (CH_2, C15), 28.1 (CH_3, C23), 25.8 (CH_2, C12), 23.9 (CH_2, C2), 21.4 (CH_3, C32), 21.3 (CH_2, C11), 19.7 (CH_3, C30), 18.4 (CH_2, C6), 16.6 (CH_3, C24), 16.4 (CH_3, C26), 16.3 (CH_3, C25), 14.9 (CH_3, C27) ppm; MS (ESI, MeOH): m/z = 542.5 (100%, $[M+H]^+$), 564.3 (38%, $[M+Na]^+$), 580.1 (24%, $[M + Li + MeOH]^+$), 1089.6 (40%, $[2M + Li]^+$), 1105.5 $[2M + Na]^+$); analysis calcd for $C_{34}H_{55}NO_4$ (541.80): C 75.37, H 10.37, N 2.59; found: C 75.34, H 10.51, N 2.38.

*4.3.6. (3β) 3-Hydroxy-N-methoxy-N-methyl-lup-20(29)-en-28-amide (**8**)*

Deacetylation of **7** (0.10 g, 0.18 mmol) with potassium hydroxide (0.10 g, 1.79 mmol) in MeOH/$CHCl_3$ (13 mL/3.5 mL) for 5 days at 25 °C as described above, followed by chromatography (silica gel, hexanes/ethyl acetate, 8:2) gave **8** (0.80 g, 89%) as a colorless solid; $R_F = 0.59$ (silica gel, hexanes/ethyl acetate, 7:3); m.p.: 219–220 °C; $[\alpha]_D = +4.66°$ ($c = 0.64$, $CHCl_3$); IR (KBr): ν = 3456*s*, 3078*w*, 2944*s*, 2866*s*, 1655*s*, 1621*s*, 1447*s*, 1415*m*, 1390*m*, 1357*m*, 1259*w*, 1190*m*, 1166*m*, 1109*m*, 1081*w*, 1044*m*, 1032*m*, 995*s*, 885*m* cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 4.71 (*d*, $J = 2.3$ Hz, 1H, CH_a (29)), 4.56 (*dd*, J = 2.3, 1.4 Hz, 1H, CH_b (29)), 3.65 (*s*, 3H, OCH_3 (32)), 3.17 (*dd*, $J = 11.8$, 5.4 Hz, 1H, *CH* (3)), 3.15 (*s*, 3H, NCH_3 (31)), 2.98 (*ddd*, $J = 11.1$, 11.1, 4.0 Hz, 1H, *CH* (19)), 2.71 (*ddd*, $J = 13.0$, 11.8, 3.6 Hz, 1H, *CH* (13)), 2.34–2.30 (*m*, 1H, CH_a (16)), 2.12–2.06 (*m*, 1H, CH_a (22)), 1.85–1.74 (*m*, 1H, CH_b (16)), 1.73–1.64 (*m*, 2H, CH_a (12) + CH_a (1)), 1.67 (*s*, 3H, CH_3 (30)), 1.64–1.43 (*m*, 4H, CH_2 (2) + *CH* (18) + CH_a (6)), 1.43–1.19 (*m*, 10H, CH_2 (11) + CH_b (6) + CH_2 (21) + CH_a (15) + CH_2 (7) + CH_b (22) + *CH* (9)), 1.18–1.12 (*m*, 1H, CH_b (15)), 1.00–0.94 (*m*, 1H, CH_b (12)), 0.96 (*s*, 3H, CH_3 (27)), 0.95 (*s*, 3H, CH_3 (23)), 0.94 (*s*, 3H, CH_3 (25)), 0.93–0.85 (*ddd*, $J = 13.2$, 13.2, 3.6 Hz, 1H, CH_b (1)), 0.82 (*s*, 3H, CH_3 (26)), 0.75 (*s*, 3H, CH_3 (24)), 0.69–0.66 (*m*, 1H, *CH* (5)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.1 (*C*=O, C28), 151.6 (C_q, C20), 109.2 (CH_2=C, C29), 79.2 (*CH*, C3), 60.4 (OCH_3, C32), 56.2 (C_q, C17), 55.6 (*CH*, C5), 52.3 (*CH*, C18), 51.0 (*CH*, C9), 46.5 (*CH*, C19), 42.4 (C_q, C14), 40.9 (C_q, C8), 39.0 (CH_2, C1), 38.9 (C_q, C4), 37.4 (C_q, C10), 37.2 (*CH*, C13), 35.2 (CH_2, C22), 34.6 (CH_2, C7), 34.1 (NCH_3, C31), 31.2 (CH_2, C21), 31.1 (CH_2, C16), 30.1 (CH_2, C15), 28.1 (CH_3, C23), 27.6 (CH_2, C2), 25.9 (CH_2, C12), 21.3 (CH_2, C11), 19.8 (CH_3, C30), 18.5 (CH_2, C6), 16.4 (CH_3, C26), 16.3 (CH_3, C25), 15.5 (CH_3, C24), 14.9 (CH_3, C27) ppm; MS (ESI, MeOH): $m/z = 500.5$ (100%, $[M+H]^+$), 1005.7 (28%, $[2M + Li]^+$), 1021.4 (55%, $[2M + Na]^+$); analysis calcd for $C_{32}H_{53}NO_3$ (499.77): C 76.90, H 10.69, N 2.80; found: C 76.77, H 10.84, N 2.69.

*4.3.7. (3β) 3-Acetyloxy-N-hydroxy-N-methyl-lup-20(29)-en-28-amide (**9**)*

Following the procedure for the synthesis of **5**, reaction of **3** (0.32 g, 0.64 mmol) with oxalyl chloride (0.30 mL, 3.52 mmol), then with NEt_3 (0.70 mL, 5.05 mmol) and *N*-methylhydroxylammonium chloride (0.15 g, 1.81 mmol) in dry DCM (25 mL) for 12 h at 25 °C, followed by chromatography (silica gel, hexanes/ethyl acetate, 8:2) gave **9** (0.22 g, 0.42 mmol, 66%) as a colorless solid; $R_F = 0.57$ (silica gel, hexanes/ethyl acetate, 7:3); m.p.: 226–228 °C; $[\alpha]_D = +3.52°$ (c 0.84, $CHCl_3$); IR (KBr): ν = 3302*br*, 3073*w*, 2947*s*, 2875*m*, 1736*m*, 1701*s*, 1630*s*, 1451*m*, 1390*m*, 1375*s*, 1334*w*, 1259*s*, 1271*s*, 1193*w*, 1109*w*, 1073*w*, 1029*m*, 980*m* cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.56 (*br*, 1H, O*H*), 4.74 (*d*, $J = 1.9$ Hz, 1H, CH_a (29)), 4.60 (*dd*, $J = 1.9$, 1.5 Hz, 1H, CH_b (29)), 4.49–4.44 (*m*, 1H, *CH* (3)), 3.41 (*s*, 3H, NCH_3 (33)), 2.98 (*ddd*, $J = 11.1$, 11.1, 3.9 Hz, 1H, *CH* (19)), 2.81 (*ddd*, $J = 13.0$, 13.0, 3.5 Hz, 1H, *CH* (13)), 2.11 (*ddd*, $J = 13.2$, 3.1, 3.1 Hz, 1H, CH_a (16)), 2.03 (*s*, 3H, CH_3 (32)), 1.96 (*dd*, J = 11.0, 7.8 Hz, 1H, CH_a (22)), 1.91–1.80 (*m*, 1H, CH_a (15)), 1.76–1.71 (*m*, 1H, CH_a (12)), 1.69 (*s*, 3H, CH_3 (30)), 1.67–1.57 (*m*, 4H, *CH* (18) + CH_2 (2) + CH_a (1)), 1.57–1.22 (*m*, 10H, CH_b (16) + CH_2 (6) + CH_2 (11) + CH_b (22) + CH_2 (7) + CH_b (15) + CH_a (21)), 1.16 (*ddd*, J = 13.5, 3.2, 3.2 Hz, 1H, CH_b (21)), 1.03–0.94 (*m*, 2H, CH_b (1) + CH_b (12)), 0.96 (*s*, 3H, CH_3 (27)), 0.94 (*s*, 3H, CH_3 (24)), 0.85 (*s*, 3H, CH_3 (26)), 0.83 (*s*, 3H, CH_3 (23)), 0.83 (*s*, 3H, CH_3 (25)), 0.81–0.75 (*m*, 1H, *CH* (5)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.5 (*C*=O, C28), 171.2 (*C*=O, C31), 150.9 (C_q, C20), 109.7 (CH_2=C, C29), 81.1 (*CH*, C3), 55.7 (*CH*, C5), 53.3 (C_q, C17), 52.4 (*CH*, C18), 50.9 (*CH*, C9), 46.1 (*CH*, C19), 42.2 (C_q, C14), 40.9 (C_q, C8), 38.6 (CH_2, C1), 38.4 (NCH_3, C33), 38.0 (C_q, C4), 37.3 (*CH*, C13), 37.3 (C_q, C10), 35.9 (CH_2, C22), 34.5 (CH_2, C7), 32.4 (CH_2, C16), 31.2 (CH_2, C15), 29.8 (CH_2, C21), 28.1 (CH_3, C23), 25.7 (CH_2, C12), 23.9 (CH_2, C2), 21.5 (CH_3, C32), 21.3 (CH_2, C11), 19.7 (CH_3, C30), 18.4 (CH_2, C6), 16.6 (CH_3, C26), 16.4 (CH_3, C25), 16.3 (CH_3, C24), 14.8 (CH_3, C27) ppm; MS (ESI, MeOH): m/z = 528.4 (70%, $[M+H]^+$), 550.2 (20%, $[M+Na]^+$), 1077.4 (100%, $[2M + Na]^+$); analysis calcd for $C_{33}H_{53}NO_4$ (527.78): C 75.10, H 10.12, N 2.65; found: C 75.00, H 10.21, N 2.47.

*4.3.8. (3β) 3-Hydroxy-N-hydroxy-N-methyl-lup-20(29)-en-28-amide (**10**)*

Deacetylation of **9** (0.22 g, 0.42 mmol) with potassium hydroxide (0.28 g, 5.00 mmol) in MeOH for 5 days at 25 °C, followed by chromatography gave **10** (0.12 g, 60%) as a colorless solid (only scarcely soluble in usual solvents); $R_F = 0.25$ (silica gel, hexanes/ethyl acetate, 8:2); m.p.: 258–260 °C; IR (KBr): ν = 3385*s*, 3198*m*, 3084*m*, 2956*s*, 2927*s*, 2868*s*, 1653*m*, 1607*s*, 1550*w*, 1452*m*, 1419*m*, 1384*s*, 1294*w*, 1256*w*, 1196*m*, 1107*w*, 1092*w*, 1023*m*, 982*m*, 884*m* cm^{-1}; MS (ESI, MeOH): m/z = 486.5 (100%, $[M+H]^+$), 508.4 (10%, $[M+Na]^+$), 993.6 (50%, $[2M + Na]^+$); analysis calcd for $C_{31}H_{51}NO_3$ (485.74): C 76.65, H 10.58, N 2.88; found: C 76.55, H 10.51, N 2.67.

*4.3.9. (3β) 3-Acetyloxy-N-methoxy-lup-20(29)-en-28-amide (**11**)*

Following the procedure for the synthesis of **5**, reaction of **3** (0.20 g, 0.40 mmol) with oxalyl chloride (0.20 mL, 2.35 mmol) followed by reaction with NEt_3 (0.70 mL, 5.05 mmol) and *O*-methylhydroxylammonium chloride (0.15 g, 1.81 mmol) in dry DCM (25 mL) for 5 h at 25 °C followed by chromatography (silica gel, hexanes/ethyl acetate, 7:3) gave **11** (0.13 g, 63%) as a colorless solid; R_F = 0.43 (silica gel, hexanes/ethyl acetate, 7:3); m.p.:

217–220 °C; $[\alpha]_D = +14.92°$ ($c = 0.54$, $CHCl_3$); IR (KBr): $\nu = 3639m$, 3385*m*, 3226*m*, 3071*w*, 2952*s*, 2866*m*, 1740*s*, 1654*s*, 1638*m*, 1511*w*, 1466*m*, 1448*m*, 1392*m*, 1377*m*, 1350*w*, 1317*w*, 1250*s*, 1151*w*, 1108*w*, 1084*w*, 1032*m*, 980*m*, 890*m* cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.46$ (*s*, 1H, N*H*), 4.73 (*s*, 1H, CH_a (29)), 4.60 (*s*, 1H, CH_b (29)), 4.50–4.42 (*m*, 1H, C*H* (3)), 3.75 (*s*, 3H, OCH_3 (33)), 3.11 (*ddd*, $J = 11.0$, 11.0, 4.2 Hz, 1H, C*H* (19)), 2.42 (*ddd*, $J = 12.6$, 12.6, 3.2 Hz, 1H, C*H* (13)), 2.03 (*s*, 3H, CH_3 (32)), 2.02–1.93 (*m*, 1H, CH_a (16)), 1.93–1.80 (*m*, 1H, CH_a (21)), 1.80–1.73 (*m*, 1H, CH_a (22)), 1.73–1.58 (*m*, 4H, CH_a (12) + CH_a (1) + CH_2 (2)), 1.67 (*s*, 3H, CH_3 (30)), 1.57–1.51 (*m*, 3H, C*H* (9) + CH_b (21) + CH_a (15)), 1.50–1.44 (*m*, 1H, CH_a (6)), 1.44–1.29 (*m*, 6H, CH_b (6) + CH_a (11) + CH_b (16) + CH_2 (7) + CH_b (22)), 1.29–1.20 (*m*, 2H, CH_b (11) + C*H* (18)), 1.20–1.11 (*m*, 1H, CH_b (15)), 1.01–0.90 (*m*, 2H, CH_b (12) + CH_b (1)), 0.96 (*s*, 3H, CH_3 (27)), 0.95 (*s*, 3H, CH_3 (26)), 0.84 (*s*, 3H, CH_3 (25)), 0.83 (*s*, 3H, CH_3 (23)), 0.82 (*s*, 3H, CH_3 (24)), 0.80–0.75 (*m*, 1H, C*H* (5)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 174.7$ (*C*=O, C28), 171.2 (*C*=O, C31), 150.7 (C_q, C20), 109.7 (CH_2=C, C29), 81.1 (*C*H, C3), 64.3 (OCH_3, C33), 55.6 (*C*H, C5), 54.8 (C_q, C17), 50.7 (*C*H, C9), 50.7 (*C*H, C18), 46.9 (*C*H, C19), 42.5 (C_q, C14), 41.0 (C_q, C8), 38.6 (CH_2, C1), 38.2 (*C*H_2, C22), 37.9 (C_q, C4), 37.9 (*C*H, C13), 37.3 (C_q, C10), 34.5 (*C*H_2 C7), 33.2 (*C*H_2, C21), 30.9 (*C*H_2, C16), 29.6 (*C*H_2, C15), 28.1 (*C*H_3, C23), 25.7 (*C*H_2, C12), 23.8 (*C*H_2, C2), 21.4 (*C*H_3, C32), 21.0 (*C*H_2, C11), 19.6 (*C*H_3, C30), 18.3 (*C*H_2, C6), 16.6 (*C*H_3, C24), 16.3 (*C*H_3, C26), 16.3 (*C*H_3, C25), 14.8 (*C*H_3, C27) ppm; MS (ESI, MeOH): $m/z = 528.5$ (100%, $[M+H]^+$), 550.3 (24%, $[M+Na]^+$), 1055.3 (24%, $[2M + H]^+$), 1077.40 (80%, $[2M + Na]^+$); analysis calcd for $C_{33}H_{53}NO_4$ (527.78): C 75.10, H 10.12, N 2.65; found: C 74.88, H 10.34, N 2.60.

4.3.10. (3β) 3-Hydroxy-N-methoxy-lup-20(29)-en-28-amide (**12**)

Deacetylation of **11** (0.12 g, 0.22 mmol) with potassium hydroxide (0.18 g, 3.21 mmol) in MeOH/THF (18 mL/6 mL) for 5 days at 25 °C as described above, followed by chromatography (silica gel, hexanes/ethyl acetate, 7:3) gave **12** (0.10 g, 95%) as a colorless solid; $R_F = 0.36$ (silica gel, hexanes/ethyl acetate, 7:3); m.p.: 222–224 °C; $[\alpha]_D = +3.22°$ ($c = 0.62$, $CHCl_3$); IR (KBr): $\nu = 3421m$, 3243*m*, 3082*w*, 2940*s*, 2869*m*, 1655*s*, 1464*m*, 1438*m*, 1390*m*, 1377*w*, 1256*w*, 1193*w*, 1108*w*, 1039*m*, 888*m* cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.57$ (*s*, 1H, N*H*), 4.72 (*d*, $J = 1.9$ Hz, 1H, CH_a (29)), 4.58 (*dd*, $J = 2.0$, 1.4 Hz, 1H, CH_b (29)), 3.74 (*s*, 3H, OCH_3 (31)), 3.16 (*dd*, $J = 11.3$, 4.9 Hz, 1H, C*H* (3)), 3.10 (*ddd*, $J = 11.1$, 11.1, 4.3 Hz, 1H, C*H* (19)), 2.41 (*ddd*, $J = 12.8$, 12.8, 3.6 Hz, 1H, C*H* (13)), 2.02–1.94 (*m*, 1H, CH_a (16)), 1.92–1.87 (*m*, 1H, CH_a (21)), 1.76 (*dd*, $J = 11.8$, 7.8 Hz, 1H, CH_a (22)), 1.72–1.67 (*m*, 1H, CH_a (12)), 1.66 (*s*, 3H, CH_3 (30)), 1.66–1.63 (*m*, 1H, CH_a (1)), 1.63–1.47 (*m*, 6H, CH_2 (2) + CH_a (15) + CH_b (21) + C*H* (18) + CH_a (6)), 1.47–1.30 (*m*, 6H, CH_b (6) + CH_a (11) + CH_b (16) + CH_b (22) + CH_2 (7)), 1.28–1.21 (*m*, 2H, C*H* (9) + CH_b (11)), 1.20–1.14 (*m*, 1H, CH_b (15)), 1.03–0.96 (*m*, 1H, CH_b (12)), 0.95 (*s*, 9H, CH_3 (27) + CH_3 (25) + CH_3 (25)), 0.88 (*ddd*, $J = 12.9$, 12.9, 4.1 Hz, 1H, CH_b (1)), 0.80 (*s*, 3H, CH_3 (26)), 0.74 (*s*, 3H, CH_3 (24)), 0.69–0.63 (*m*, 1H, C*H* (5)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 174.7$ (*C*=O, C28), 150.7 (C_q, C20), 109.6 (CH_2=C, C29), 79.1 (*C*H, C3), 64.3 (OCH_3, C31), 55.5 (*C*H, C5), 54.8 (C_q, C17), 50.7 (*C*H, C9), 50.7 (*C*H, C18), 46.8 (*C*H, C19), 42.5 (C_q, C14), 40.9 (C_q, C8), 39.0 (*C*H_2, C1), 38.9 (C_q, C4), 38.2 (*C*H_2, C22), 37.9 (*C*H, C13), 37.3 (C_q, C10), 34.5 (*C*H_2, C7), 33.2 (*C*H_2, C21), 30.9 (*C*H_2, C16), 29.6 (*C*H_2, C15), 28.1 (*C*H_3, C23), 27.5 (*C*H_2, C2), 25.7 (*C*H_2, C12), 21.0 (*C*H_2, C11), 19.6 (*C*H_3, C30), 18.4 (*C*H_2, C6), 16.3 (*C*H_3, C26), 16.3 (*C*H_3, C25), 15.5 (*C*H_3, C25), 14.8 (*C*H_3, C24) ppm; MS (ESI, MeOH): $m/z = 486.5$ (60%, $[M+H]^+$), 508.4 (5%, $[M+Na]^+$), 971.4 (20%, $[2M + H]^+$), 993.5 (100%, $[2M + Na]^+$); analysis calcd for $C_{31}H_{51}NO_3$ (485.74): C 76.65, H 10.58, N 2.88; found: C 76.44, H 10.67, N 2.80.

4.3.11. (3β)-3-Acetyloxy-N-allyloxy-lup-20(29)-en-28-amide (**13**)

Following the procedure for the synthesis of **5**, reaction of **3** (0.40 g, 0.80 mmol) with oxalyl chloride (0.40 mL, 4.60 mmol), followed by reaction with NEt3 (0.70 mL, 5.05 mmol) and *O*-allylhydroxylammonium chloride (0.30 g, 2.75 mmol) in dry DCM (25 mL) for 2 h at 25 °C, followed by chromatography (silica gel, hexanes/ethyl acetate, 9:1) gave **13** (0.40 g, 90%) as a colorless solid; $R_F = 0.65$ (silica gel, hexanes/ethyl acetate, 7:3); m.p.: 128–131 °C; $[\alpha]_D = +22.16°$ ($c = 0.59$, $CHCl_3$); IR (KBr): $\nu = 3260br$, 2947*s*, 1737*s*, 1644*s*, 1455*s*, 1376*s*, 1317*m*, 1245*s*, 1154*m*, 1108*m*, 1030*s*, 979*s*, 927*s*, 883*s*, 754*m*, 544*m* cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.42$ (*s*, 1H, N*H*), 5.99 (*ddt*, $J = 16.8$, 10.3, 6.4 Hz, 1H, C*H* (34)), 5.36–5.25 (*m*, 2H, CH_2, C35)), 4.72 (*s*, 1H, CH_a (29)), 4.58 (*s*, 1H, CH_b (29)), 4.50–4.43 (*m*, 1H, C*H* (3)), 4.42–4.32 (*m*, 2H, CH_2 (33)), 3.10 (*ddd*, $J = 11.0$, 11.0, 3.9 Hz, 1H, C*H* (19)), 2.42 (*ddd*, $J = 12.7$, 12.7, 3.3 Hz, 1H, C*H* (13)), 2.02 (*s*, 3H, CH_3 (32)), 2.02–1.92 (*m*, 1H, CH_a (16)), 1.92–1.84 (*m*, 1H, CH_a (21)), 1.79–1.72 (*m*, 1H), 1.66 (*s*, 3H, CH_3 (30)), 1.71–1.63 (*m*, 2H, CH_a (12) + CH_a (1)), 1.62–1.56 (*m*, 2H, CH_2 (2)), 1.55–1.49 (*m*, 3H, C*H* (18) + CH_b (21) + CH_a (15)), 1.49–1.28 (*m*, 7H, CH_2 (6) + CH_a (11) + CH_b (16) + CH_2 (7) + CH_b (22)), 1.27–1.20 (*m*, 2H, C*H* (9) + CH_b (11)), 1.19–1.10 (*m*, 1H, CH_b (15)), 1.05–0.93 (m, 2H, CH_b (12) + CH_b (1)), 0.95 (*s*, 3H, CH_3 (27)), 0.94 (*s*, 3H, CH_3 (26)), 0.83 (*s*, 3H, CH_3 (25)), 0.82 (*s*, 3H, CH_3 (23)), 0.81 (*s*, 3H, CH_3 (24)), 0.79–0.72 (*m*, 1H, C*H* (5)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 174.6$ (*C*=O, C28), 171.2 (*C*=O, C31), 150.7 (C_q, C20), 132.7 (*C*H=CH_2, C34), 120.4 (CH_2=CH, C35), 109.7 (CH_2=C, C29), 81.1 (*C*H, C3), 77.4 (*C*H_2, C33), 55.6 (*C*H, C5), 54.8 (C_q, C17), 50.7 (*C*H, C18), 50.7 (*C*H, C9), 46.8 (*C*H, C19), 42.5 (C_q, C14), 40.9 (C_q, C8), 38.5 (CH_2, C1), 38.3 (*C*H_2, C22), 37.9 (C_q, C4), 37.8 (*C*H, C13), 37.3 (C_q, C10), 34.5 (*C*H_2, C7), 33.3 (*C*H_2, C21), 30.9 (*C*H_2, C16), 29.6 (*C*H_2, C15), 28.1 (*C*H_3, C23), 25.7 (*C*H_2, C12), 23.8 (*C*H_2, C2), 21.4 (*C*H_3, C32), 21.0 (*C*H_2, C11), 19.6 (*C*H_3, C30), 18.3 (*C*H_2, C6), 16.6 (*C*H_3, C24), 16.4 (*C*H_3, C25), 16.3 (*C*H_3, C26), 14.8 (*C*H_3, C27) ppm; MS (ESI, MeOH): $m/z = 554.4$ (96%, $[M+H]^+$), 576.4 (20%, $[M+Na]^+$), 1129.5 (100%, $[2M + Na]^+$); analysis calcd for $C_{35}H_{55}NO_4$ (553.82): C 75.91, H 10.01, N 11.56; found: C 75.79, H 10.14, N 11.49.

4.3.12. (3β) 3-Hydroxy-N-allyloxy-lup-20(29)-en-28-amide (**14**)

Deacetylation of **13** (0.17 g, 0.31 mmol) with potassium hydroxide (0.17 g, 3.03 mmol) in MeOH (18 mL) and THF (7 mL) for 7 days at 25 °C as described above, followed by chromatography (silica gel, hexanes/ethyl acetate, 8:2) gave **14** (0.15 g, 94%) as a colorless solid; $R_F = 0.44$ (silica gel, hexanes/ethyl acetate, 7:3); m.p.: 129–131 °C; $[\alpha]_D = +3.36°$ ($c = 0.78$, $CHCl_3$); IR (KBr): $\nu = 3423br$, 3075*w*, 2944*s*, 2869*s*, 1655*m*, 1453*m*, 1389*m*, 1376*m*, 1279*w*, 1247*w*, 1189*w*, 1138*w*, 1107*w*, 1034*m*, 1008*m*, 983*m*, 924*m*, 883*m* cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.31$ (*s*, 1H, N*H*), 5.99 (ddt, $J = 16.8$, 10.3, 6.4 Hz, 1H, C*H* (32)), 5.37–5.27 (*m*, 2H, CH_2 (33)), 4.73 (*s*, 1H, CH_a (29)), 4.59 (*s*, 1H, CH_b (29)), 4.43–4.33 (*m*, 2H, CH_2 (31)), 3.17 (*dd*, $J = 11.3$, 4.8 Hz, 1H, C*H* (3)), 3.11 (*ddd*, $J = 11.1$, 11.1, 4.3 Hz, 1H, C*H* (19)), 2.42 (*ddd*, $J = 12.7$, 12.7, 3.5 Hz, 1H, C*H* (13)), 2.03–1.93 (*m*, 1H, CH_a (16)), 1.86 (*m*, 1H, CH_a (21)), 1.75 (*dd*, $J = 11.8$, 7.9 Hz, 1H, CH_a (22)), 1.72–1.63 (*m*, 2H, CH_a (12) + CH_a (1)), 1.67 (*s*, 3H, CH_3 (30)), 1.63–1.46 (*m*, 6H, CH_2 (2) + CH_a (15) + CH_b (21) + C*H* (18) + CH_a (6)), 1.45–1.30 (*m*, 6H, CH_b (6) + CH_a (11) + CH_b (16) + CH_2 (7) + CH_b (22)), 1.29–1.20 (*m*, 2H, C*H* (9) + CH_b (11)), 1.19–1.12 (*m*, 1H, CH_b (15)), 1.03–0.96 (*m*, 1H, CH_b (12)), 0.96 (*s*, 3H, CH_3 (23)), 0.95 (*s*, 6H, CH_3 (25) + CH_3 (27)), 0.92–0.84 (*m*, 1H, CH_b (1)), 0.81 (*s*, 3H, CH_3 (26)), 0.75 (*s*, 3H, CH_3 (24)), 0.70–0.64 (*m*, 1H, C*H* (5)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 174.6$ (*C*=O, C28), 150.7 (C_q, C20), 132.7 (*C*H=CH_2, C32), 120.5 (CH_2=CH, C33), 109.7 (CH_2=C, C29), 79.1 (*C*H, C3), 77.4 (*C*H_2, C31), 55.5 (*C*H, C5), 54.9 (C_q, C17), 50.8 (*C*H, C18), 50.7 (*C*H, C9), 46.8 (*C*H, C19), 42.5 (C_q, C14), 41.0 (C_q, C8), 39.0 (CH_2, C1), 38.9 (C_q, C4), 38.4 (*C*H_2, C22), 37.9 (*C*H, C13), 37.4 (C_q, C10), 34.6 (*C*H_2, C7), 33.4 (*C*H_2, C21), 30.9 (*C*H_2, C16), 29.6 (*C*H_2, C15), 28.1 (*C*H_3, C23), 27.6 (*C*H_2, C2), 25.8 (*C*H_2, C12), 21.0 (*C*H_2, C11), 19.6 (*C*H_3, C30), 18.4 (*C*H_2, C6), 16.4 (*C*H_3, C26), 16.3 (*C*H_3,

C25), 15.5 (*C*H$_3$, C24), 14.8 (*C*H$_3$, C27) ppm; MS (ESI, MeOH): *m/z* = 512.5 (70%, [M+H]$^+$), 534.4 (12%, [M+Na]$^+$), 1023.3 (18%, [2M + H]$^+$), 1045.6 (100%, [2M + Na]$^+$); analysis calcd for $C_{33}H_{53}NO_3$ (511.78): C 77.45, H 10.44, N 2.74; found: C 77.39, H 10.51, N 2.62.

4.3.13. 3-Oxo-N-methoxy-N-methyl-lup-20(29)-en-28-amide (**15**)

Following the procedure for the synthesis of **5**, reaction of **4** (0.25 g, 0.50 mmol) in DCM (20 mL) with oxalyl chloride (0.30 mL, 3.5 mmol), then with NEt$_3$ (0.70 mL, 5.06 mmol) and *N,O*-dimethylhydroxylammonium chloride (0.15 g, 1.55 mmol) for 12 h at 25 °C followed by chromatography (silica gel, hexanes/ethyl acetate, 9:1) gave **15** (0.13 g, 52%) as a colorless solid; R_F = 0.70 (silica gel, hexanes/ethyl acetate, 7:3); m.p.: 174–176 °C; $[\alpha]_D$ = +33.12° (*c* = 0.60, CHCl$_3$); IR (KBr): *ν* = 3398*br*, 3077*w*, 2942*s*, 2867*s*, 1709*s*, 1651*s*, 1456*s*, 1376*m*, 1356*s*, 1345*m*, 1283*w*, 1243*w*, 1168*m*, 1137*w*, 1110*m*, 1082*w*, 1022*w*, 993*s*, 881*m* cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): *δ* = 4.70 (*s*, 1H, C*H*$_a$ (29)), 4.56 (*s*, 1H, C*H*$_b$ (29)), 3.65 (*s*, 3H, OC*H*$_3$ (32)), 3.15 (*s*, 3H, NC*H*$_3$ (31)), 2.97 (*ddd*, *J* = 11.0, 11.0, 3.5 Hz, 1H, C*H* (19)), 2.75 (*ddd*, *J* = 12.9, 12.9, 3.3 Hz, 1H, C*H* (13)), 2.47 (*ddd*, *J* = 15.8, 8.2, 7.6 Hz, 1H, C*H*$_a$ (2)), 2.42–2.27 (*m*, 2H, C*H*$_b$ (2) + C*H*$_a$ (16)), 2.15–2.05 (*m*, 1H, C*H*$_a$ (22)), 1.88 (*ddd*, *J* = 13.1, 8.1, 4.6 Hz, 2H, C*H*$_a$ (1)), 1.79 (*m*, 1H, C*H*$_b$ (16)), 1.75–1.69 (*m*, 1H, C*H*$_a$ (12)), 1.67 (*s*, 3H, C*H*$_3$ (30)), 1.54 (*m*, 1H, C*H* (18)), 1.50–1.21 (*m*, 13H, C*H*$_2$ (6) + C*H*$_2$ (11) + C*H*$_2$ (21) + C*H*$_2$ (7) + C*H*$_a$ (15) + C*H*$_b$ (1) + C*H*$_b$ (22) + C*H* (5) + C*H* (9)), 1.20–1.13 (*m*, 1H, C*H*$_b$ (15)), 1.05 (*s*, 3H, C*H*$_3$ (23)), 1.00 (*s*, 3H, C*H*$_3$ (24)), 0.97 (*s*, 3H, C*H*$_3$ (25)), 0.96 (*s*, 3H, C*H*$_3$ (27)), 0.96–0.93 (*m*, 1H, C*H*$_b$ (12)), 0.91 (*s*, 3H, C*H*$_3$ (26)) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): *δ* = 218.3 (*C*=O, C3), 177.0 (*C*=O, C28), 151.4 (*C*$_q$, C20), 109.2 (*C*H$_2$=C, C29), 60.4 (OCH$_3$, C32), 56.1 (*C*$_q$, C17), 55.2 (*C*H, C5), 52.1 (*C*H, C18), 50.3 (*C*H, C9), 47.5 (*C*$_q$, C4), 46.4 (*C*H, C19), 42.4 (*C*$_q$, C14), 40.8 (*C*$_q$, C8), 39.8 (*C*H$_2$, C1), 37.3 (*C*H, C13), 37.1 (*C*$_q$, C10), 35.1 (*C*H$_2$, C22), 34.3 (*C*H$_2$, C2), 34.1 (NCH$_3$, C31), 33.8 (*C*H$_2$, C7), 31.1 (*C*H$_2$, C16), 31.0 (*C*H$_2$, C21), 30.0 (*C*H$_2$, C15), 26.7 (*C*H$_3$, C23), 25.8 (*C*H$_2$, C12), 21.8 (*C*H$_2$, C11), 21.2 (*C*H$_3$, C24), 19.8 (*C*H$_2$, C6), 19.7 (*C*H$_3$, C30), 16.1 (*C*H$_3$, C26), 16.1 (*C*H$_3$, C25), 14.8 (*C*H$_3$, C27) ppm; MS (ESI, MeOH): *m/z* = 498.5 (100%, [M+H]$^+$), 1017.6 (40%, [2M + Na]$^+$); analysis calcd for $C_{32}H_{51}NO_3$ (497.75): C 77.22, H 10.33, N 2.81; found: C 76.98, H 10.54, N 2.77.

4.3.14. 3-Oxo-N-hydroxy-N-methyl-lup-20(29)-en-28-amide (**16**)

Following the procedure for the synthesis of **5**, reaction of **4** (0.24 g, 0.53 mmol) with oxalyl chloride (0.30 mL, 3.52 mmol) followed by reaction with NEt$_3$ (0.70 mL, 5.06 mmol) and *N*-methylhydroxylammonium chloride (0.10 g, 1.20 mmol) in dry DCM (25 mL) for 12 h at 25 °C, followed by chromatography (silica gel, hexanes/ethyl acetate, 8:2) gave **16** (0.21 g, 81%) as a colorless solid; R_F = 0.25 (silica gel, hexanes/ethyl acetate, 7:3); m.p.: 214–216 °C; $[\alpha]_D$ = +21.54° (*c* = 0.70, CHCl$_3$); IR (KBr): *ν* = 3405*br*, 2942*s*, 2868*s*, 1704*m*, 1640*m*, 1595*m*, 1455*m*, 1376*m*, 1184*w*, 1104*w*, 1076*w*, 1022*w* cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): *δ* = 8.53 (*br*, 1H, O*H*), 4.73 (*s*, 1H, C*H*$_a$ (29)), 4.59 (*s*, 1H, C*H*$_b$ (29)), 3.40 (*s*, 1H, NC*H*$_3$ (31)), 2.98 (*ddd*, *J* = 11.1, 11.1, 3.6 Hz, 1H, C*H* (19)), 2.85 (*ddd*, *J* = 12.9, 12.9, 3.4 Hz, 1H, C*H* (13)), 2.53–2.44 (*m*, 1H, C*H*$_a$ (2)), 2.38 (*ddd*, *J* = 15.6, 7.5, 4.3 Hz, 1H, C*H*$_b$ (2)), 2.14 (*ddd*, *J* = 13.4, 2.8, 2.8 Hz, 1H, C*H*$_a$ (16)), 1.98 (*dd*, *J* = 10.6, 7.9 Hz, 1H, C*H*$_a$ (22)), 1.94–1.80 (*m*, 2H, C*H*$_a$ (1) + C*H*$_a$ (21)), 1.79–1.69 (*m*, 1H, C*H*$_a$ (12)), 1.68 (*s*, 3H, C*H*$_3$ (30)), 1.62 (*dd*, *J* = 11.3 Hz, 1H, C*H* (18)), 1.54 (*ddd*, *J* = 13.9, 13.9, 3.5 Hz, 1H, C*H*$_b$ (16)), 1.48–1.22 (*m*, 12H, C*H*$_2$ (6) + C*H*$_2$ (11) + C*H*$_2$ (7) + C*H*$_b$ (1) + C*H*$_b$ (22) + C*H*$_b$ (21) + C*H*$_a$ (15) + C*H* (9) + C*H* (5)), 1.17 (*ddd*, *J* = 13.5, 3.2, 3.2 Hz, 1H, C*H*$_b$ (15)), 1.05 (*s*, 3H, C*H*$_3$ (23)), 1.01 (*s*, 3H, C*H*$_3$ (24)), 0.97–0.89 (*m*, 1H, C*H*$_b$ (12)), 0.97 (*s*, 3H, C*H*$_3$ (27)), 0.97 (*s*, 3H, C*H*$_3$ (25)), 0.92 (*s*, 3H, C*H*$_3$ (26)), ppm; ^{13}C NMR (100 MHz, CDCl$_3$): *δ* = 218.4 (*C*=O, C3), 171.5 (*C*=O, C28), 150.9 (*C*$_q$, C20), 109.7 (*C*H$_2$=C, C29), 55.2 (*C*H, C5), 53.4 (*C*$_q$, C17), 52.3 (*C*H, C18), 50.3 (*C*H, C9), 47.5 (*C*$_q$, C4), 46.1 (*C*H, C19), 42.2 (*C*$_q$, C14), 40.8 (*C*$_q$, C8), 39.8 (*C*H$_2$, C1), 38.3 (NCH$_3$, C31), 37.4 (*C*H, C13), 37.1 (*C*$_q$, C10), 35.9 (*C*H$_2$, C22), 34.3 (*C*H$_2$, C2), 33.9 (*C*H$_2$, C7), 32.2 (*C*H$_2$, C16), 31.2 (*C*H$_2$, C21), 29.8 (*C*H$_2$, C15), 26.7 (*C*H$_3$, C23), 25.8 (*C*H$_2$, C12), 21.8 (*C*H$_2$, C11), 21.2 (*C*H$_3$, C24), 19.8 (*C*H$_2$, C6), 19.7 (*C*H$_3$, C30), 16.1 (*C*H$_3$, C26), 16.1 (*C*H$_3$, C25), 14.2 (*C*H$_3$, C27) ppm; MS (ESI, MeOH): *m/z* = 484.5 (100%, [M+H]$^+$), 507.5 (5%, [M+Na]$^+$), 537.8 (12%, [M + Na + MeOH]$^+$), 748.5 (80%, [3M+2Na]$^{2+}$), 989.5 (50%, [2M + Na]$^+$); analysis calcd for $C_{31}H_{49}NO_3$ (483.73): C 76.97, H 10.21, N 2.90; found: C 76.76, H 10.34, N 2.74.

4.3.15. 3-Oxo-N-methoxy-lup-20(29)-en-28-amide (**17**)

Following the procedure for the synthesis of **5**, reaction of **4** (0.25 g, 0.55 mmol) dry DCM (20 mL) with oxalyl chloride (0.4 mL, 4.70 mmol), followed by reaction with NEt$_3$ (0.75 mL, 5.42 mmol) and *O*-methylhydroxylammonium chloride (0.15 g, 1.81 mmol) in dry DCM (20 mL) for 12 h at 25 °C, followed by chromatography (silica gel, hexanes/ethyl acetate, 8:2) gave **17** (0.12 g, 45%) as a colorless solid; R_F = 0.43 (silica gel, hexanes/ethyl acetate, 7:3); m.p.: 159–162 °C; $[\alpha]_D$ = +24.32° (*c* = 0.62, CHCl$_3$); IR (KBr): *ν* = 3173*br*, 2944*s*, 2866*s*, 1708*s*, 1637*s*, 1515*m*, 1464*m*, 1376*m*, 1318*w*, 1281*w*, 1243*w*, 1195*w*, 1140*w*, 1117*w*, 1081*w*, 1046*m*, 938*m*, 886*m* cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): *δ* = 8.46 (*s*, 1H, N*H*), 4.73 (*s*, 1H, C*H*$_a$ (29)), 4.60 (*s*, 1H, C*H*$_b$ (29)), 3.75 (*s*, 3H, OC*H*$_3$ (31)), 3.11 (*ddd*, *J* = 10.9, 10.9, 3.9 Hz, 1H, C*H* (19)), 2.54–2.43 (*m*, 2H, C*H* (13) + C*H*$_a$ (2)), 2.38 (*ddd*, *J* = 15.6, 7.4, 4.3 Hz, 1H, C*H*$_b$ (2)), 2.06–1.94 (*m*, 1H, C*H*$_a$ (16)), 1.94–1.83 (*m*, 2H, C*H*$_a$ (21) + C*H*$_a$ (1)), 1.81–1.68 (m, 2H, C*H*$_a$ (22) + C*H*$_a$ (21)), 1.67 (*s*, 3H, C*H*$_3$ (30)), 1.63–1.52 (*m*, 3H, C*H*$_a$ (15) + C*H*$_b$ (21) + C*H* (18)), 1.52–1.22 (m, 11H, C*H*$_2$ (6) + C*H*$_2$ (11) + C*H*$_b$ (16) + C*H*$_2$ (7) + C*H*$_b$ (22) + C*H*$_b$ (1) + C*H* (9) + C*H* (5)), 1.21–1.15 (*m*, 1H, C*H*$_b$ (15)), 1.05 (*s*, 3H, C*H*$_3$ (23)), 1.06–1.02 (*m*, 1H, C*H*$_b$ (12)), 1.01 (*s*, 3H, C*H*$_3$ (24)), 1.00 (*s*, 3H, C*H*$_3$ (27)), 0.97 (*s*, 3H, C*H*$_3$ (25)), 0.92 (*s*, 3H, C*H*$_3$ (26)) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): *δ* = 218.3 (*C*=O, C3), 174.7 (*C*=O, C28), 150.6 (*C*$_q$, C20), 109.7 (*C*H$_2$=C, C29), 64.3 (OCH$_3$, C31), 55.2 (*C*H, C5), 54.7 (*C*$_q$, C17), 50.7 (*C*H, C18), 50.1 (*C*H, C9), 47.5 (*C*$_q$, C4), 46.8 (*C*H, C19), 42.6 (*C*$_q$, C14), 40.9 (*C*$_q$, C8), 39.8 (*C*H$_2$, C1), 38.2 (*C*H$_2$, C22), 38.0 (*C*H, C13), 37.1 (*C*$_q$, C10), 34.3 (*C*H$_2$, C2), 33.8 (*C*H$_2$, C7), 33.2 (*C*H$_2$, C21), 30.9 (*C*H$_2$, C16), 29.6 (*C*H$_2$, C15), 26.7 (*C*H$_3$, C23), 25.8 (*C*H$_2$, C12), 21.6 (*C*H$_2$, C11), 21.2 (*C*H$_3$, C24), 19.8 (*C*H$_2$, C6), 19.6 (*C*H$_3$, C30), 16.1 (*C*H$_3$, C26), 16.1 (*C*H$_3$, C25), 14.7 (*C*H$_3$, C27) ppm; MS (ESI, MeOH): *m/z* = 484.5 (100%, [M+H]$^+$), 506.3 (4%, [M+Na]$^+$), 967.3 (20%, [2M + H]$^+$), 989.6 (82%, [2M + Na]$^+$); analysis calcd for $C_{31}H_{49}NO_3$ (483.37): C 76.97, H 10.21, N 2.90; found: C 76.88, H 10.50, N 2.81.

4.3.16. 3-Oxo-N-allyloxy-lup-20(29)-en-28-amide (**18**)

Following the procedure for the synthesis of **5**, reaction of **4** (0.26 g, 0.57 mmol) with oxalyl chloride (0.3 mL, 3.52 mmol), followed by reaction with NEt$_3$ (0.75 mL, 5.42 mmol) and *O*-allylhydroxylammonium chloride (0.25 g, 2.29 mmol) in dry DCM (25 mL) for 5 h at 25 °C, followed by chromatography (silica gel, hexanes/ethyl acetate, 8:2) gave **18** (0.20 g, 68%) as a colorless solid; R_F = 0.33 (silica gel, toluene/ethyl acetate/heptane/formic acid, 80:20:30:4); m.p.: 113–115 °C; $[\alpha]_D$ = +22.88° (*c* = 0.89, CHCl$_3$); IR (KBr): *ν* = 3277*br*, 3074*w*, 2948*s*, 2868*s*, 1705*s*, 1642*s*, 1458*m*, 1376*m*, 1241*w*, 1203*w*, 1140*w*, 1115*w*, 1039*m*, 924*m*, 883*m* cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): *δ* = 8.45 (*s*, 1H, N*H*), 5.99 (*ddt*, *J* = 16.8, 10.3, 6.4 Hz, 1H, C*H* (32)), 5.37–5.24 (*m*, 2H, C*H*$_2$ (33)), 4.71 (*s*, 1H, C*H*$_a$ (29)), 4.58 (*s*, 1H, C*H*$_b$ (29)), 4.43–4.31 (*m*, 2H, C*H*$_2$ (31)), 3.10 (*ddd*, *J* = 11.0, 11.0, 3.9 Hz, 1H, C*H* (19)), 2.53–2.42 (*m*, 2H, C*H* (13) + C*H*$_a$ (2)), 2.37 (*ddd*, *J* = 15.6, 7.4, 4.3 Hz, 1H, C*H*$_b$ (2)), 2.01–1.92 (*m*, 1H, C*H*$_a$ (16)), 1.92–1.83 (*m*, 2H, C*H*$_a$ (21) + C*H*$_a$ (1)), 1.80–1.67 (*m*, 2H, C*H*$_a$ (22) + C*H*$_a$ (12)), 1.66 (*s*, 3H, C*H*$_3$ (30)), 1.60–1.50 (*m*, 3H, C*H* (18) + C*H*$_b$ (21) + C*H*$_a$ (15)), 1.49–1.21 (*m*, 11H, C*H*$_2$ (6) + C*H*$_2$ (11) + C*H*$_b$ (16) + C*H*$_2$ (7) + C*H*$_b$ (22) + C*H*$_b$ (1) + C*H* (9) + C*H* (5)),

1.19–1.14 (*m*, 1H, C*H*$_b$ (15)), 1.04 (*s*, 3H, C*H*$_3$ (23)), 1.00 (*s*, 3H, C*H*$_3$ (24)), 0.99 (*s*, 3H, C*H*$_3$ (27)), 0.95 (*s*, 3H, C*H*$_3$ (25)), 0.91 (*s*, 3H, C*H*$_3$ (26)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 218.3 (*C*=O, C3), 174.6 (*C*=O, C28), 150.6 (*C*$_q$, C20), 132.7 (*C*H=CH$_2$, C32), 120.5 (*C*H$_2$=C, C33), 109.7 (*C*H$_2$=C, C29), 77.4 (*C*H$_2$, C31), 55.1 (*C*H, C5), 54.8 (*C*$_q$, C17), 50.7 (*C*H, C18), 50.1 (*C*H, C9), 47.5 (*C*$_q$, C4), 46.7 (*C*H, C19), 42.6 (*C*$_q$, C14), 40.9 (*C*$_q$, C8), 39.8 (*C*H$_2$, C1), 38.3 (*C*H$_2$, C22), 37.9 (*C*H, C13), 37.1 (*C*$_q$, C10), 34.3 (*C*H$_2$, C2), 33.8 (*C*H$_2$, C7), 33.3 (*C*H$_2$, C21), 30.9 (*C*H$_2$, C16), 29.6 (*C*H$_2$, C15), 26.7 (*C*H$_3$, C23), 25.7 (*C*H$_2$, C12), 21.6 (*C*H$_2$, C11), 21.1 (*C*H$_3$, C24), 19.8 (*C*H$_2$, C6), 19.6 (*C*H$_3$, C30), 16.2 (*C*H$_3$, C26), 16.1 (*C*H$_3$, C25), 14.7 (*C*H$_3$, C27) ppm; MS (ESI, MeOH): *m*/*z* = 510.5 (100%, $[M+H]^+$), 532.4 (14%, $[M+Na]^+$), 784.9 (20%, $[3M + K + H]^{2+}$), 1019.3 (24%, $[2M + H]^+$), 1041.6 (84%, $[2M + Na]^+$); analysis calcd for $C_{33}H_{51}NO_3$ (509.76): C 77.75, H 10.08, N 2.75; found: C 77.59, H 10.19, N 2.63.

4.3.17. (3β) 3-Acetyloxylup-20(29)-en-28-amide (**19**)

Compound **3** (4.0 g, 8.0 mmol) was allowed to react with oxalyl chloride (3.7 g, 2.5 mL, 29.2 mmol) in dry DCM (50 mL) as described above. The volatiles were removed, and the residue was dissolved in dry DCM (50 mL). A solution of dry ammonia in DCM (satd., 50 mL) was added, and the mixture was stirred at 25 °C for 1 h. Water (50 mL) and diluted aqueous hydrochloric acid (1 N) were added until the aqueous layer showed pH = 7. The layers were separated, the aqueous layer was extracted with DCM (3 × 50 mL), the combined organic phases were dried (Na_2SO_4), and the solvent was distilled off under reduced pressure. The crude product was purified by chromatography (silica gel, hexanes/ethyl acetate, 7:3) to yield **19** (3.8 g, 95%) as a colorless solid; R_F = 0.12 (silica gel, hexanes/ethyl acetate, 8:2); m.p.: 336–338 °C (lit.: [60] 340–341 °C); $[\alpha]_D$ = +17.0° (*c* = 0.48, $CHCl_3$); IR (KBr): *ν* = 3471*m*, 3325*m*, 3202*w*, 3074*w*, 2940*s*, 2868*m*, 1742*s*, 1686*s*, 1642*s*, 1610*m*, 1449*w*, 1392*m*, 1367*s*, 1301*w*, 1242*s*, 1139*w*, 1108*w*, 1082*w*, 1025*m*, 1009*m*, 979*m*, 946*w*, 899*w*, 875*m*, 738*w*, 655*w*, 608*w*, 579*w*, 558*w*, 541*w*, 516*w* cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.53 (*br*, 2H, N*H*$_2$), 4.73 (*s*, 1H, C*H*$_a$ (29)), 4.60 (*s*, 1H, C*H*$_b$ (29)), 4.46 (*dd*, *J* = 9.7, 6.6 Hz, 1H, C*H* (3)), 3.07 (*dt*, *J* = 11.1, 4.4 Hz, 1H, C*H* (19)), 2.44 (*dt*, *J* = 12.8, 3.5 Hz, 1H, C*H* (13)), 2.03 (*s*, 3H, C*H*$_3$ (32)), 2.02–1.89 (*m*, 2H, C*H*$_a$ (16) + C*H*$_a$ (21)), 1.81 (*dd*, *J* = 11.9, 7.8 Hz, 1H, C*H*$_a$ (22)), 1.73–1.64 (*m*, 2H, C*H*$_a$ (1) + C*H*$_a$ (12)), 1.68 (*s*, 3H, C*H*$_3$ (30)), 1.63–1.52 (*m*, 5H, C*H*$_2$ (2) + C*H* (18) + C*H*$_a$ (15) + C*H*$_b$ (16)), 1.52–1.44 (*m*, 2H, C*H*$_a$ (6) + C*H*$_a$ (11)), 1.44–1.34 (*m*, 5H, C*H*$_2$ (7) + C*H*$_b$ (6) + C*H*$_b$ (21) + C*H*$_b$ (22)), 1.30–1.21 (*m*, 2H, C*H* (9) + C*H*$_b$ (11)), 1.21–1.14 (*m*, 1H, C*H*$_b$ (15)), 1.03–0.92 (*m*, 2H, C*H*$_b$ (1) + C*H*$_b$ (12)), 0.96 (*s*, 3H, C*H*$_3$ (27)), 0.95 (*s*, 3H, C*H*$_3$ (25)), 0.84 (*s*, 3H, C*H*$_3$ (23)), 0.83 (*s*, 3H, C*H*$_3$ (26)), 0.82 (*s*, 3H, C*H*$_3$ (24)), 0.78 (*m*, 1H, C*H* (5)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.3 (*C*=O, C28), 171.0 (*C*=O, C31), 150.7 (*C*=CH$_2$, C20), 109.5 (H$_2$*C*=C, C29), 80.9 (*C*H, C3), 55.8 (*C*$_q$, C17), 55.5 (*C*H, C5), 50.5 (*C*H, C9), 49.9 (*C*H, C18), 46.6 (*C*H, C19), 42.5 (*C*$_q$, C14), 40.8 (*C*$_q$, C8), 38.4 (*C*H, C13), 38.4 (*C*H$_2$, C1), 37.8 (*C*$_q$, C4), 37.7 (*C*H$_2$, C22), 37.1 (*C*$_q$, C10), 34.3 (*C*H$_2$, C7), 33.9 (*C*H$_2$, C16), 30.7 (*C*H$_2$, C21), 29.5 (*C*H$_2$, C15), 27.9 (*C*H$_3$, C23), 25.6 (*C*H$_2$, C12), 23.7 (*C*H$_2$, C2), 21.3 (*C*H$_2$, C32), 20.9 (*C*H$_2$, C11), 19.4 (*C*H$_3$, C30), 18.2 (*C*H$_2$, C6), 16.5 (*C*H$_3$, C24), 16.2 (*C*H$_3$, C26), 16.2 (*C*H$_3$, C25), 14.6 (*C*H$_3$, C27) ppm; MS (ESI, MeOH): *m*/*z* = 498.5 (34%, $[M + H]^+$), 520.4 (11%, $[M + Na]^+$), 552.0 (5%, $[M + Na + MeOH]^+$), 995.4 (100%, $[2M + H]^+$), 1017.4 (46%, $[2M + Na]^+$).

4.3.18. (3β) 3-Hydroxylup-20(29)-en-28-amide (**20**)

Deacetylation of **19** (1.78 g, 3.58 mmol) with potassium hydroxide (0.4 g, 7.16 mmol) in THF (30 mL)/MeOH (20 mL) for 1 day at 25 °C as described above, followed by chromatography (silica gel, hexanes/ethyl acetate, 7:3) gave **20** (1.57 g, 96.5%) as a colorless solid; R_F = 0.1 (silica gel, hexanes/ethyl acetate, 8:2); m.p.: 256–257 °C (lit.: [47] 254–257 °C); $[\alpha]_D$ = +2.0° (*c* = 0.3, $CHCl_3$), (lit.: [61] $[\alpha]_D$ = +6.0°, $CHCl_3$); IR (KBr): *ν* = 3422*br*, 2943*s*, 2869*m*, 1656*m*, 1451*m*, 1376*m*, 1044*w*, 883*m*, 543*w* cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.53 (*br*, 1H, N*H*$_a$), 5.43 (*br*, 1H, N*H*$_b$), 4.73 (*s*, 1H, C*H*$_a$ (29)), 4.59 (*s*, 1H, C*H*$_b$ (29)), 3.17 (*dd*, *J* = 11.1, 5.1 Hz, 1H, C*H* (3)), 3.07 (*dt*, *J* = 11.0, 4.2 Hz, 1H, C*H* (19)), 2.45 (*dt*, *J* = 12.7, 3.3 Hz, 1H, C*H* (13)), 2.03–1.89 (*m*, 2H, C*H*$_a$ (16) + C*H*$_a$ (21)), 1.80 (*dd*, *J* = 11.9, 7.8 Hz, 1H, C*H*$_a$ (22)), 1.72–1.63 (*m*, 2H, C*H*$_a$ (1) + C*H*$_a$ (12)), 1.68 (*s*, 3H, C*H*$_3$ (30)), 1.63–1.52 (*m*, 5H, C*H*$_2$ (2) + C*H* (18) + C*H*$_a$ (15) + C*H*$_b$ (16)), 1.52–1.49 (*m*, 1H, C*H*$_a$ (6)), 1.45–1.32 (*m*, 6H, C*H*$_2$ (7) + C*H*$_b$ (6) + C*H*$_a$ (11) + C*H*$_b$ (21) + C*H*$_b$ (22)), 1.30–1.21 (*m*, 2H, C*H* (9) + C*H*$_b$ (11)), 1.20–1.13 (*m*, 1H, C*H*$_b$ (15)), 1.05–0.94 (*m*, 1H, C*H*$_b$ (12)), 0.96 (*s*, 3H, C*H*$_3$ (27)), 0.95 (*s*, 3H, C*H*$_3$ (23)), 0.95 (*s*, 3H, C*H*$_3$ (25)), 0.93–0.84 (*m*, 1H, C*H*$_b$ (1)), 0.82 (*s*, 3H, C*H*$_3$ (26)), 0.75 (*s*, 3H, C*H*$_3$ (24)), 0.67 (*m*, 1H, C*H* (5)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.9 (*C*=O, C28), 150.8 (*C*=CH$_2$, C20), 109.4 (H$_2$*C*=C, C29), 79.0 (*C*H, C3), 55.8 (*C*$_q$, C17), 55.4 (*C*H, C5), 50.6 (*C*H, C9), 49.9 (*C*H, C18), 46.6 (*C*H, C19), 42.5 (*C*$_q$, C14), 40.7 (*C*$_q$, C8), 38.8 (*C*H$_2$, C1), 38.7 (*C*H$_2$, C22), 38.4 (*C*$_q$, C4), 37.7 (*C*H, C13), 37.2 (*C*$_q$, C10), 34.4 (*C*H$_2$, C7), 34.0 (*C*H$_2$, C16), 30.7 (*C*H$_2$, C21), 29.5 (*C*H$_2$, C15), 28.0 (*C*H$_3$, C23), 27.4 (*C*H$_2$, C2), 25.6 (*C*H$_2$, C12), 20.9 (*C*H$_2$, C11), 19.5 (*C*H$_3$, C30), 18.3 (*C*H$_2$, C6), 16.2 (*C*H$_3$, C25), 16.1 (*C*H$_3$, C26), 15.3 (*C*H$_3$, C24), 14.6 (*C*H$_3$, C27) ppm; MS (ESI, MeOH): *m*/*z* = 456.3 (84%, $[M + H]^+$), 911.4 (78%, $[2M + H]^+$), 933.4 (100%, $[2M + Na]^+$).

4.3.19. (3β) 3-Acetyloxylup-N-benzyl-20(29)-en-28-amide (**21**)

Following the procedure given for the synthesis of **19**, the reaction of **3** (0.35 g, 0.7 mmol) with oxalyl chloride (0.22 g, 0.15 mL, 1.8 mmol) in dry DCM (15 mL), followed by the reaction with benzylamine (0.15 g, 0.15 mL) (1 h, reflux) and chromatographic work-up (silica gel, hexanes/ethyl acetate, 8:2) gave **21** (0.24 g, 59%) as a colorless solid; R_F = 0.87 (silica gel, hexanes/ethyl acetate, 7:3); m.p.: 124–127 °C; $[\alpha]_D$ = +23.2° (*c* = 0.35, $CHCl_3$); IR (KBr): *ν* = 3425*br*, 2946*s*, 1736*m*, 1638*m*, 1517*w*, 1454*w*, 1384*m*, 1246*m*, 1028*w*, 979*w*, 882*m*, 698*w* cm^{-1}; UV–vis ($CHCl_3$): λ_{max} (log *ε*) = 253.8 (3.49) nm; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.29 (*m*, 2H, C*H* (36/36′)), 7.29–7.22 (*m*, 3H, C*H* (35/35′) + C*H* (37)), 5.89 (*br*, 1H, N*H*)), 4.74 (*s*, 1H, C*H*$_a$ (29)), 4.59 (*s*, 1H, C*H*$_b$ (29)), 4.53–4.42 (*m*, 2H, C*H* (3) + C*H*$_a$ (33)), 4.36 (*dd*, *J* = 14.7, 5.6 Hz, 1H, C*H*$_b$ (33)), 3.17 (*dt*, *J* = 11.0, 4.0 Hz, 1H, C*H* (19)), 2.49 (*dt*, *J* = 12.8, 3.5 Hz, 1H, C*H* (13)), 2.03 (*s*, 3H, C*H*$_3$ (32)), 2.02–1.94 (*m*, 2H, C*H*$_2$ (21)), 1.94–1.87 (*m*, 2H, C*H*$_2$ (16)), 1.80–1.70 (*m*, 2H, C*H*$_a$ (22) + C*H*$_a$ (12)), 1.68 (*s*, 3H, C*H*$_3$ (30)), 1.67–1.62 (*m*, 1H, C*H*$_a$ (1)), 1.62–1.51 (*m*, 3H, C*H* (18) + C*H*$_2$ (2)), 1.50–1.41 (*m*, 3H, C*H*$_b$ (22) + C*H*$_a$ (15) + C*H*$_a$ (6)), 1.40–1.28 (*m*, 7H, C*H*$_2$ (7) + C*H*$_a$ (11) + C*H*$_b$ (6)), 1.28–1.21 (*m*, 2H, C*H* (9) + C*H*$_b$ (11)), 1.15–1.08 (*m*, 1H, C*H*$_b$ (15)), 1.04–0.93 (*m*, 2H, C*H*$_b$ (1) + C*H*$_b$ (12)), 0.95 (*s*, 3H, C*H*$_3$ (27)), 0.91 (*s*, 3H, C*H*$_3$ (25)), 0.84 (*s*, 3H, C*H*$_3$ (26)), 0.83 (*s*, 3H, C*H*$_3$ (23)), 0.83 (*s*, 3H, C*H*$_3$ (24)), 0.77 (*m*, 1H, C*H* (5)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.9 (*C*=O, C28), 171.0 (*C*=O, C31), 150.8 (*C*=CH$_2$, C20), 139.2 (*C*$_q$, C34), 128.6 (*C*H, C36/36′), 127.8 (*C*H, C35/35′), 127.3 (*C*H, C37), 109.4 (H$_2$*C*=C, C29), 81.0 (*C*H, C3), 55.7 (*C*$_q$, C17), 55.5 (*C*H, C5), 50.6 (*C*H, C9), 50.2 (*C*H, C18), 46.7 (*C*H, C19), 43.3 (*C*H$_2$, C33), 42.5 (*C*$_q$, C14), 40.8 (*C*$_q$, C8), 38.4 (*C*H$_2$, C1), 38.4 (*C*H$_2$, C22), 37.8 (*C*$_q$, C4), 37.7 (*C*H, C13), 37.1 (*C*$_q$, C10), 34.4 (*C*H$_2$, C7), 33.8 (*C*H$_2$, C16), 30.9 (*C*H$_2$, C21), 29.4 (*C*H$_2$, C15), 27.9 (*C*H$_3$, C23), 25.6 (*C*H$_2$, C12), 23.7 (*C*H$_2$, C2), 21.3 (*C*H$_3$, C32), 21.0 (*C*H$_2$, C11), 19.5 (*C*H$_3$, C30), 18.2 (*C*H$_2$, C6), 16.5 (*C*H$_3$, C24), 16.2 (*C*H$_3$, C26), 16.1 (*C*H$_3$, C25), 14.6 (*C*H$_3$, C27) ppm; MS (ESI, MeOH): *m*/*z* = 588.5 (58%, $[M + H]^+$), 610.5 (26%, $[M + Na]^+$), 1175.3 (90%, $[2M + H]^+$), 1197.4 (100%, $[2M + Na]^+$); analysis calcd for $C_{39}H_{57}NO_3$ (587.87): C 79.68, H 9.77, N 2.38; found: C 79.52, H 9.85, N 2.21.

4.3.20. (3β) N-Benzyl-3-hydroxylup-20(29)-en-28-amide (**22**)

Deacetylation of **21** (210 mg, 0.36 mmol) with potassium hydroxide (0.1 g, 1.8 mmol) in THF (15 mL)/MeOH (5 mL) for 1 day at

25 °C as described above, followed by chromatography (silica gel, hexanes/ethyl acetate, 7:3) gave **22** (180 mg, 91.8%) as a colorless solid; R_F = 0.6 (silica gel, hexanes/ethyl acetate, 7:3); m.p.: 246–248 °C; $[\alpha]_D$ = +14.3° (*c* = 0.31, $CHCl_3$); IR (KBr): ν = 3496*s*, 3448*s*, 2941*s*, 2868*m*, 1634*s*, 1496*s*, 1458*m*, 1376*w*, 1319*w*, 1280*w*, 1223*w*, 1190*w*, 1105*w*, 1077*w*, 1045*w*, 892*w*, 761*w*, 702*w*, 596*w*, 496*w* cm^{-1}; UV–vis ($CHCl_3$): λ_{max} (log ε) = 258.8 (3.43) nm; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.29 (*m*, 2H, C*H* (34/34′)), 7.29–7.23 (m, 3H, C*H* (33/33′) + C*H* (35)), 5.88 (*br*, 1H, N*H*)), 4.74 (*s*, 1H, CH_a (29)), 4.59 (*s*, 1H, CH_b (29)), 4.48 (*dd*, *J* = 14.7, 5.8 Hz, 1H, CH_a (31)), 4.36 (*dd*, *J* = 14.7, 5.6 Hz, 1H, CH_b (31)), 3.17 (*m*, 2H, C*H* (19) + C*H* (3)), 2.49 (*dt*, *J* = 12.8, 3.5 Hz, 1H, C*H* (13)), 2.03–1.94 (*m*, 2H, CH_2 (21)), 1.94–1.87 (*m*, 2H, CH_2 (16)), 1.80–1.69 (*m*, 2H, CH_a (22) + CH_a (12)), 1.68 (*s*, 3H, CH_3 (30)), 1.68–1.63 (*m*, 1H, CH_a (1)), 1.62–1.54 (*m*, 3H, C*H* (18) + CH_2 (2)), 1.53–1.44 (*m*, 2H, CH_a (15) + CH_a (6)), 1.43–1.36 (*m*, 2H, CH_b (22) + CH_a (11)), 1.36–1.28 (*m*, 3H, CH_2 (7) + CH_b (6)), 1.29–1.20 (*m*, 2H, C*H* (9) + CH_b (11)), 1.16–1.08 (*m*, 1H, CH_b (15)), 1.05–0.97 (*m*, 1H, CH_b (12)), 0.96 (*s*, 3H, CH_3 (27)), 0.96 (*s*, 3H, CH_3 (23)), 0.91 (*s*, 3H, CH_3 (25)), 0.91–0.87 (*m*, 1H, CH_b (1)), 0.82 (*s*, 3H, CH_3 (26)), 0.75 (*s*, 3H, CH_3 (24)), 0.66 (*m*, 1H, C*H* (5)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.9 (*C*=O, C28), 151.0 (*C*=CH_2, C20), 139.2 (C_q, C32), 128.6 (*C*H, C34/34′), 127.8 (*C*H, C33/33′), 127.3 (*C*H, C35), 109.4 (H_2C=C, C29), 79.0 (*C*H, C3), 55.7 (C_q, C17), 55.4 (*C*H, C5), 50.7 (*C*H, C9), 50.2 (*C*H, C18), 46.7 (*C*H, C19), 43.3 (CH_2, C31), 42.5 (C_q, C14), 40.8 (C_q, C8), 38.9 (CH_2, C1), 38.7 (CH_2, C22), 38.4 (C_q, C4), 37.7 (*C*H, C13), 37.2 (C_q, C10), 34.5 (CH_2, C7), 33.8 (CH_2, C16), 30.9 (CH_2, C21), 29.5 (*C*H_2, C15), 28.0 (CH_3, C23), 27.4 (CH_2, C2), 25.7 (*C*H_2, C12), 21.0 (CH_2, C11), 19.5 (CH_3, C30), 18.3 (CH_2, C6), 16.2 (*C*H_3, C26), 16.2 (CH_3, C25), 15.4 (*C*H_3, C24), 14.7 (*C*H_3, C27) ppm; MS (ESI, MeOH): *m*/*z* = 546.5 (100%, $[M + H]^+$), 568.4 (9%, $[M + Na]^+$), 1091.4 (28%, $[2M + H]^+$), 1113.4 (52%, $[2M + Na]^+$); analysis calcd for $C_{37}H_{55}NO_2$ (545.84): C 81.42, H 10.16, N 2.57; found: C 81.39, H 10.29, N 2.43.

4.3.21. *N*-Benzyl-3-oxolup-20(29)-en-28-amide (**23**)

Jones oxidation of **22** (137 mg, 0.25 mmol) in acetone (25 mL) using freshly prepared reagent [from CrO_3 (63 mg, 0.63 mmol), sulfuric acid (62 mg, 34 μL, 0.63 mmol, 96%) and water (0.5 mL)] for 20 min, followed by usual aqueous work-up and chromatography (silica gel, hexanes/ethyl acetate, 7:3) gave **23** (100 mg, 73.5%) as a colorless solid; R_F = 0.68 (silica gel, hexanes/ethyl acetate, 7:3); m.p.: 108–111 °C; $[\alpha]_D$ = +38.3° (*c* = 0.37, $CHCl_3$), (lit.: [61] $[\alpha]_D$ = +43.0°, $CHCl_3$); IR (KBr): ν = 3396*br*, 2947*s*, 2867*m*, 1705*s*, 1640*s*, 1519*m*, 1454*m*, 1384*m*, 1241*w*, 1185*w*, 1080*w*, 986*w*, 882*w*, 724*w*, 698*w*, 583*w* cm^{-1}; UV–vis ($CHCl_3$): λ_{max} (log ε) = 259.0 (3.42) nm; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.30 (*m*, 2H, C*H* (34/34′)), 7.30–7.24 (m, 3H, C*H* (33/33′) + C*H* (35)), 5.89 (*br*, 1H, N*H*)), 4.74 (*s*, 1H, CH_a (29)), 4.60 (*s*, 1H, CH_b (29)), 4.49 (*dd*, *J* = 14.7, 5.8 Hz, 1H, CH_a (31)), 4.36 (*dd*, *J* = 14.7, 5.6 Hz, 1H, CH_b (31)), 3.18 (*dt*, *J* = 11.1, 4.3 Hz, 1H, C*H* (19)), 2.54 (*dt*, *J* = 12.8, 3.5 Hz, 1H, C*H* (13)), 2.51–2.44 (*m*, 1H, CH_a (2)), 2.48 (*ddd*, *J* = 14.7, 7.5, 2.2 Hz, 1H, CH_a (2)), 2.38 (*ddd*, *J* = 15.6, 7.5, 4.3 Hz, 1H, CH_b (2)), 2.03–1.95 (*m*, 1H, CH_a (21)), 1.94–1.85 (*m*, 2H, CH_a (1) + CH_a (16)), 1.80–1.70 (*m*, 2H, CH_a (22) + CH_a (12)), 1.68 (*s*, 3H, CH_3 (30)), 1.64–1.52 (*m*, 2H, C*H* (18) + CH_b (16)), 1.51–1.39 (*m*, 5H, CH_b (22) + CH_a (15) + CH_a (11) + CH_2 (6)), 1.39–1.33 (*m*, 5H, C*H* (9) + CH_b (1) + CH_2 (7) + CH_b (21)), 1.32–1.23 (*m*, 1H, CH_b (15) + CH_b (11)), 1.18–1.11 (*m*, 1H, C*H* (5)), 1.06 (*s*, 3H, CH_3 (23)), 1.02 (*s*, 3H, CH_3 (24)), 1.02–0.98 (*m*, 1H, CH_b (12)), 0.97 (*s*, 3H, CH_3 (27)), 0.94 (*s*, 3H, CH_3 (25)), 0.92 (*s*, 3H, CH_3 (26)) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 218.1 (*C*=O, C3), 175.8 (*C*=O, C28), 150.8 (*C*=CH_2, C20), 139.2 (C_q, C32), 128.6 (*C*H, C34/34′), 127.8 (*C*H, C33/33′), 127.3 (*C*H, C35), 109.4 (H_2C=C, C29), 55.6 (C_q, C17), 55.0 (*C*H, C5), 50.1 (*C*H, C9), 50.1 (*C*H, C18), 47.3 (C_q, C4), 46.6 (*C*H, C19), 43.3 (CH_2, C31), 42.6 (C_q, C14), 40.7 (C_q, C8), 39.7 (CH_2, C1), 38.4 (CH_2, C22), 37.8 (*C*H, C13), 36.9 (C_q, C10), 34.1 (*C*H_2, C2), 33.8 (*C*H_2, C16), 33.7 (*C*H_2, C7), 30.9 (*C*H_2, C21), 29.4 (*C*H_2, C15), 26.6 (*C*H_3, C23), 25.7 (*C*H_2, C12), 21.5 (*C*H_2, C11), 21.0 (*C*H_3, C24), 19.7 (*C*H_2, C6), 19.5 (*C*H_3, C30), 16.0 (*C*H_3, C26), 16.0 (*C*H_3, C25), 14.6 (*C*H_3, C27) ppm; MS (ESI, MeOH): *m*/*z* = 544.5 (66%, $[M + H]^+$), 566.2 (9%, $[M + Na]^+$), 1087.3 (70%, $[2M + H]^+$), 1109.4 (100%, $[2M + Na]^+$); analysis calcd for $C_{37}H_{53}NO_2$ (543.82): C 81.72, H 9.82, N 2.58; found: C 81.54, H 9.70, N 2.64.

4.3.22. 3-Oxolup-20(29)-en-28-amide (**24**)

Reaction of **4** (3.0 g, 6.61 mmol) with oxalyl chloride (3.0 g, 2 mL, 23.3 mmol) in abs. DCM (50 mL) followed by a reaction with ammonia in DCM as described above and chromatographic workup (silica gel, hexanes/ethyl acetate, 7:3) gave **24** (2.52, 84.1%) as a colorless solid; R_F = 0.21 (silica gel, hexanes/ethyl acetate, 8:2); m.p.: 155–1157 °C (lit.: [50] 156–157 °C); $[\alpha]_D$ = +32.9° (*c* = 0.37, $CHCl_3$); IR (KBr): ν = 3446*br*, 2947*s*, 2868*m*, 1703*s*, 1670*s*, 1458*m*, 1375*m*, 1204*w*, 1116*w*, 882*w*, 755*w*, 543*w* cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 5.55 (*br*, 1H, NH_a), 5.32 (*br*, 1H, NH_b), 4.74 (*s*, 1H, CH_a (29)), 4.59 (*s*, 1H, CH_b (29)), 3.08 (*dt*, *J* = 11.1, 4.4 Hz, 1H, C*H* (19)), 2.56–2.43 (*m*, 2H, C*H* (13) + CH_a (2)), 2.42–2.35 (*m*, 1H, CH_b (2)), 2.03–1.94 (*m*, 1H, CH_a (21)), 1.93–1.85 (*m*, 2H, CH_a (16) + CH_a (1)), 1.84–1.77 (*m*, 1H, CH_a (22)), 1.76–1.69 (*m*, 1H, CH_a (12)), 1.68 (*s*, 3H, CH_3 (30)), 1.62–1.53 (*m*, 3H, C*H* (9) + CH_b (16) + CH_a (15)), 1.53–1.47 (*m*, 2H, CH_a (6) + CH_b (22)), 1.46–1.34 (*m*, 7H, C*H* (18) + CH_b (1) + CH_2 (7) + CH_b (21) + CH_a (11) + CH_b (6)), 1.34–1.28 (*m*, 2H, C*H* (5) + CH_b (11)), 1.23–1.17 (*m*, 1H, CH_b (15)), 1.06 (*s*, 3H, CH_3 (23)), 1.03–0.99 (*m*, 1H, CH_b (12)), 1.01 (*s*, 3H, CH_3 (24)), 1.00 (*s*, 3H, CH_3 (25)), 0.98 (*s*, 3H, CH_3 (27)), 0.92 (*s*, 3H, CH_3 (26)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 218.1 (*C*=O, C3), 178.9 (*C*=O, C28), 150.7 (*C*=CH_2, C20), 109.4 (H_2C=C, C29), 55.8 (C_q, C17), 55.0 (*C*H, C5), 50.0 (*C*H, C18), 49.8 (*C*H, C9), 47.3 (C_q, C4), 46.5 (*C*H, C19), 42.6 (C_q, C14), 40.7 (C_q, C8), 39.6 (*C*H_2, C1), 38.3 (CH_2, C22), 37.7 (*C*H, C13), 36.9 (C_q, C10), 34.1 (*C*H_2, C2), 33.9 (*C*H_2, C16), 33.7 (*C*H_2, C7), 30.7 (*C*H_2, C21), 29.5 (*C*H_2, C15), 26.6 (*C*H_3, C23), 25.6 (*C*H_2, C12), 21.4 (*C*H_2, C11), 21.0 (*C*H_3, C24), 19.6 (*C*H_2, C6), 19.5 (*C*H_3, C30), 16.0 (*C*H_3, C26), 15.9 (*C*H_3, C25), 14.5 (*C*H_3, C27) ppm; MS (ESI, MeOH): *m*/*z* = 454.5 (59%, $[M + H]^+$), 907.3 (100%, $[2M + H]^+$), 929.5 (71%, $[2M + Na]^+$).

4.3.23. (3β) Lup-20(29)-en-3,28-bis-*N*-ethylcarbamate (**25**)

Microwave assisted reaction (7 h, 120 °C) of **2** (0.3 g, 0.68 mmol) in dry THF (5 mL) with ethyl isocyanate (0.29 g, 0.32 mL, 4.1 mmol), followed by chromatographic work-up (silica gel, hexanes/ethyl acetate, 8:2) gave **25** (0.32 g, 80.8%) as a colorless solid; R_F = 0.29 (silica gel, hexanes/ethyl acetate, 8:2); m.p.: 233–235 °C; $[\alpha]_D$ = +24.9° (*c* = 0.44, $CHCl_3$); IR (KBr): ν = 3330*br*, 2945*s*, 2870*m*, 2361*w*, 1687*s*, 1536*s*, 1449*m*, 1376*w*, 1306*m*, 1264*s*, 1142*w*, 1107*w*, 1083*w*, 1020*m*, 986*w*, 894*w*, 781*w*, 636*w* cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 4.68 (*s*, 1H, CH_a (29)), 4.65–4.51 (*br*, 2H, 2× N*H*), 4.58 (*s*, 1H, CH_b (29)), 4.34 (*dd*, *J* = 11.2, 4.0 Hz, 1H, C*H* (3)), 4.25 (*d*, *J* = 10.8 Hz, 1H, CH_a (28)), 3.83 (*d*, *J* = 10.3 Hz, 1H, CH_b (28)), 3.21 (*br*, 4H, CH_2 (32) + CH_2 (32′)), 2.4 (*dt*, *J* = 11.0, 5.8 Hz, 1H, C*H* (19)), 2.02–1.91 (*m*, 1H, CH_a (21)), 1.86–1.79 (*m*, 1H, CH_a (16)), 1.78–1.72 (*m*, 1H, CH_a (22)) 1.72–1.68 (*m*, 1H, CH_a (15)), 1.68 (*s*, 3H, CH_3 (30)), 1.68–1.64 (*m*, 1H, C*H* (13)), 1.63–1.53 (*m*, 4H, CH_a (2) + CH_a (1) + CH_2 (12)), 1.52–1.45 (*m*, 2H, CH_b (2) + C*H* (18)), 1.45–1.41 (m, 1H, CH_a (6)), 1.40–1.33 (*m*, 6H, CH_b (6) + CH_2 (11) + CH_b (21) + CH_2 (7)), 1.32–1.26 (*m*, 1H, C*H* (9)), 1.25–1.17 (*m*, 1H, CH_b (16)), 1.14 (*t*, *J* = 7.3 Hz, 3H, CH_3 (33)), 1.13 (*t*, *J* = 7.2 Hz, 3H, CH_3 (33′)), 1.09–0.95 (*m*, 3H, CH_b (15) + CH_b (22) + CH_b (1)), 1.03 (*s*, 3H, CH_3 (25)), 0.96 (*s*, 3H, CH_3 (27)), 0.88 (*s*, 3H, CH_3 (23)), 0.83 (*s*, 3H, CH_3 (26)), 0.81–0.76 (*m*, 1H, C*H* (5)), 0.80 (*s*, 3H, CH_3 (24)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.2 (*C*=O, C31), 156.9 (*C*=O, C31′), 150.4 (*C*=CH_2, C20), 109.7 (H_2C=C, C29), 80.9 (*C*H, C3), 62.8 (CH_2, C28), 55.4 (*C*H, C5), 50.3 (*C*H, C9), 48.8 (*C*H, C18), 47.7 (*C*H, C19), 46.6 (C_q, C17), 42.7 (C_q, C14), 40.9 (C_q, C8), 38.4 (CH_2, C1), 38.0 (C_q, C4), 37.5 (*C*H, C13),

37.0 (C_q, C10), 35.9 (CH_2, C32/C32′), 34.5 (CH_2, C22), 34.1 (CH_2, C7), 29.8 (CH_2, C16), 29.6 (CH_2, C21), 27.9 (CH_3, C23), 27.1 (CH_2, C15), 25.2 (CH_2, C12), 24.1 (CH_2, C2), 20.8 (CH_2, C11), 19.1 (CH_3, C30), 18.1 (CH_2, C6), 16.1 (CH_3, C24), 16.0 (CH_3, C26), 15.7 (CH_3, C25), 15.3 (CH_3, C33/C33′), 14.7 (CH_3, C27) ppm; MS (ESI, MeOH): m/z = 607.4 (37%, $[M + Na]^+$), 1169.5 (100%, $[2M + H]^+$), 1191.5 (71%, $[2M + Na]^+$); analysis calcd for $C_{36}H_{60}N_2O_4$ (584.87): C 73.93, H 10.34, N 4.79; found: C 73.77, H 10.51, N 4.69.

4.3.24. (3β) Lup-20(29)-en-3,28-bis-N-propylcarbamate (**26**)

Microwave assisted reaction (7 h, 120 °C) of **2** (0.3 g, 0.68 mmol) in dry THF (5 mL) with propyl isocyanate (0.35 g, 0.39 mL, 4.1 mmol) followed by chromatographic work-up (silica gel, hexanes/ethyl acetate, 8:2) gave **26** (0.362 g, 83.4%) as a colorless solid; R_F = 0.4 (silica gel, hexanes/ethyl acetate, 8:2); m.p.: 123–126 °C $[\alpha]_D$ = +25.5° (c = 0.32, $CHCl_3$); IR (KBr): ν = 3358*s*, 2963*s*, 2873*s*, 1717*s*, 1520s, 1458*s*, 1389*m*, 1265*s*, 1138*m*, 1106*m*, 1042*m*, 1008*m*, 976*m*, 882*w*, 774*w*, 638*w* cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 4.64–4.45 (*br*, 2H, 2× N*H*), 4.61 (*s*, 1H, CH_a (29)), 4.57 (*s*, 1H, CH_b (29)), 4.27 (*dd*, J = 7.7, 2.9 Hz, 1H, C*H* (3)), 4.19 (*d*, J = 10.6 Hz, 1H, CH_a (28)), 3.76 (*d*, J = 10.1 Hz, 1H, CH_b (28)), 3.07 (*br*, 4H, CH_2 (32) + CH_2 (32′)), 2.38 (*dt*, J = 11.1, 5.7 Hz, 1H, C*H* (19)), 1.92 (*dq*, J = 13.8, 10.5 Hz, 1H, CH_a (21)), 1.80–1.72 (*m*, 1H, CH_a (16)), 1.72–1.63 (*m*, 2H, CH_a (22) + CH_a (15)), 1.61 (*s*, 3H, CH_3 (30)), 1.62–1.54 (*m*, 4H, CH_a (2) + C*H* (13) + CH_a (1) + CH_a (12)), 1.54–1.47 (*m*, 2H, CH_b (2) + C*H* (18)), 1.47–1.40 (*m*, 5H, CH_2 (33) + CH_2 (33′) + CH_a (6)), 1.37–1.28 (*m*, 5H, CH_2 (7) + CH_b (21) + CH_a (11) + CH_b (6)), 1.25–1.20 (*m*, 1H, C*H* (9)), 1.20–1.11 (*m*, 2H, CH_b (16) + CH_b (11)), 1.03–0.92 (*m*, 3H, CH_b (22) + CH_b (15) + CH_b (12)), 0.97 (*s*, 3H, CH_3 (25)), 0.92–0.88 (*m*, 1H, CH_b (1)), 0.90 (*s*, 3H, CH_3 (27)), 0.86 (*t*, J = 7.7 Hz, 3H, CH_3 (34)), 0.85 (*t*, J = 7.7 Hz, 3H, CH_3 (34′)), 0.81 (*s*, 3H, CH_3 (23)), 0.77 (*s*, 3H, CH_3 (26)), 0.74–0.70 (*m*, 1H, C*H* (5)), 0.73 (*s*, 3H, CH_3 (24)) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.2 (*C*═O, C31), 156.9 (*C*═O, C31′), 150.3 (*C*═CH_2, C20), 109.8 (H_2C═C, C29), 81.0 (*C*H, C3), 62.9 (CH_2, C28), 55.4 (*C*H, C5), 50.3(*C*H, C9), 48.8 (*C*H, C18), 47.7 (*C*H, C19), 46.6 (C_q, C17), 42.8 (CH_2, C32/C32′), 42.7 (C_q, C14), 40.9 (C_q, C8), 38.4 (CH_2, C1), 38.0 (C_q, C4), 37.5 (*C*H, C13), 37.0 (C_q, C10), 34.6 (CH_2, C22), 34.1 (CH_2, C7), 29.8 (CH_2, C16), 29.7 (CH_2, C21), 27.9 (CH_3, C23), 27.1 (CH_2, C15), 25.2 (CH_2, C12), 24.1 (*C*H_2, C2), 23.3 (CH_2, C33/C33′), 20.8 (CH_2, C11), 19.1 (CH_3, C30), 18.2 (*C*H_2, C6), 16.5 (CH_3, C24), 16.1 (CH_3, C26), 16.0 (CH_3, C25), 14.7 (*C*H_3, C27), 11.2 (*C*H_3, C34/C34′) ppm; MS (ESI, MeOH): m/z = 612.8 (6%, $[M + H]^+$), 635.5 (26%, $[M + Na]^+$), 1125.5 (100%, $[2M + H]^+$), 1247.6 (32%, $[2M + Na]^+$); analysis calcd for $C_{38}H_{64}N_2O_4$ (612.93): C 74.46, H 10.52, N 4.57; found: C 74.39, H 10.69, N 4.50.

4.3.25. (3β) Lup-20(29)-en-3,28-bis-N-butylcarbamate (**27**)

Microwave assisted reaction (7 h, 120 °C) of **2** (0.3 g, 0.68 mmol) in dry THF (5 mL) with butyl isocyanate (0.4 g, 0.45 mL, 4.1 mmol) followed by chromatography (silica gel, hexanes/ethyl acetate, 8:2) gave **27** (0.35 g, 80.7%) as a colorless solid; R_F = 0.41 (silica gel, hexanes/ethyl acetate, 8:2); m.p.: 106–109 °C; $[\alpha]_D$ = +31.8° (c = 0.32, $CHCl_3$); IR (KBr): ν = 3364*br*, 2957*s*, 2872*m*, 2361*w*, 1709*s*, 1528*m*, 1465*m*, 1376*w*, 1247*m*, 1138*w*, 1018*w*, 883*w*, 775*w* cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 4.68 (*s*, 1H, CH_a (29)), 4.66–4.50 (*br*, 2H, 2× N*H*), 4.58 (*s*, 1H, CH_b (29)), 4.34 (*dd*, J = 11.0, 4.0 Hz, 1H, C*H* (3)), 4.26 (*d*, J = 10.9 Hz, 1H, CH_a (28)), 3.83 (*d*, J = 10.2 Hz, 1H, CH_b (28)), 3.17 (*br*, 4H, CH_2 (32) + CH_2 (32′)), 2.45 (*dt*, J = 10.9, 5.6 Hz, 1H, C*H* (19)), 2.04–1.93 (*m*, 1H, CH_a (21)), 1.86–1.79 (*m*, 1H, CH_a (16)), 1.78–1.70 (*m*, 2H, CH_a (22) + CH_a (15)), 1.69–1.61 (*m*, 4H, CH_a (1) + C*H* (13) + CH_a (12) + CH_a (2)), 1.68 (*s*, 3H, CH_3 (30)), 1.61–1.54 (*m*, 2H, C*H* (18) + CH_b (2)), 1.52–1.44 (*m*, 5H, CH_2 (33) + CH_2 (33′) + CH_a (6)), 1.44–1.38 (*m*, 6H, CH_2 (7) + CH_2 (11) + CH_b (21) + CH_b (6)), 1.38–1.32 (*m*, 4H, CH_2 (34) + CH_2 (34′)), 1.29–1.24 (*m*, 1H, C*H* (9)), 1.23–1.17 (*m*, 1H, CH_b (16)), 1.10–0.99 (*m*, 3H, CH_b (15) + CH_b (12) + CH_b (22)), 1.04 (*s*, 3H, CH_3 (25)), 0.99–0.94 (*m*, 1H, CH_b (1)), 0.97 (*s*, 3H, CH_3 (27)), 0.92 (*t*, J = 7.3 Hz, 3H, CH_3 (35)), 0.92 (*t*, J = 7.3 Hz, 3H, CH_3 (35′)), 0.88 (*s*, 3H, CH_3 (23)), 0.84 (*s*, 3H, CH_3 (26)), 0.81–0.76 (*m*, 1H, C*H* (5)), 0.80 (*s*, 3H, CH_3 (24)) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.2 (*C*═O, C31), 156.8 (*C*═O, C31′), 150.3 (*C*═CH_2, C20), 109.7 (H_2C═C, C29), 81.0 (*C*H, C3), 62.9 (CH_2, C28), 55.4 (*C*H, C5), 50.3 (*C*H, C9), 48.8 (*C*H, C18), 47.7 (*C*H, C19), 46.6 (C_q, C17), 42.7 (C_q, C14), 40.9 (C_q, C8), 40.7 (*C*H_2, C32/C32′), 38.4 (CH_2, C1), 38.0 (C_q, C4), 37.5 (*C*H, C13), 37.0 (C_q, C10), 34.6 (CH_2, C22), 34.1 (CH_2, C7), 32.1 (*C*H_2, C33/C33′), 29.8 (*C*H_2, C16), 29.7 (CH_2, C21), 27.9 (CH_3, C23), 27.1 (CH_2, C15), 25.2 (*C*H_2, C12), 24.1 (CH_2, C2), 20.8 (CH_2, C11), 19.9 (C34/C34′), 19.1 (*C*H_3, C30), 18.2 (CH_2, C6), 16.5 (*C*H_3, C24), 16.1 (*C*H_3, C26), 16.0 (*C*H_3, C25), 14.7 (*C*H_3, C27), 13.7 (*C*H_3, C35/35′) ppm; MS (ESI, MeOH): m/z = 641.1 (7%, $[M + H]^+$), 663.3 (30%, $[M + Na]^+$), 1281.4 (100%, $[2M + H]^+$), 1303.5 (24%, $[2M + Na]^+$); analysis calcd for $C_{40}H_{68}N_2O_4$ (640.98): C 74.95, H 10.69, N 4.37; found: C 74.87, H 10.82, N 4.19.

4.3.26. (3β) Lup-20(29)-en-3,28-bis-N-hexylcarbamate (**28**)

Microwave assisted reaction (7 h, 120 °C) of **2** (0.3 g, 0.68 mmol) in dry THF (5 mL) with hexyl isocyanate (0.52 g, 0.58 mL, 4.1 mmol) followed by chromatography (silica gel, hexanes/ethyl acetate, 9:1) gave **28** (0.35 g, 73.4%) as a colorless solid; R_F = 0.49 (silica gel, hexanes/ethyl acetate, 8:2); m.p.: 85–88 °C; $[\alpha]_D$ = +20.5° (c = 0.53, $CHCl_3$); IR (KBr): ν = 3347*br*, 2954*s*, 2870*m*, 2361*w*, 1700*s*, 1540*m*, 1458*m*, 1376*w*, 1247*s*, 1140*w*, 1040*w*, 1012*w*, 982*w*, 883*w*, 775*w*, 668*w* cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 4.67 (*s*, 1H, CH_a (29)), 4.64–4.59 (*br*, 2H, 2× N*H*), 4.57 (*s*, 1H, CH_b (29)), 4.34 (*dd*, J = 10.9, 3.0 Hz, 1H, C*H* (3)), 4.25 (*d*, J = 10.7 Hz, 1H, CH_a (28)), 3.82 (*d*, J = 10.4 Hz, 1H, CH_b (28)), 3.15 (*br*, 4H, CH_2 (32) + CH_2 (32′)), 2.44 (*dt*, J = 11.0, 5.9 Hz, 1H, C*H* (19)), 2.04–1.92 (*m*, 1H, CH_a (21)), 1.85–1.78 (*m*, 1H, CH_a (16)), 1.77–1.69 (*m*, 2H, CH_a (15) + CH_a (22)), 1.69–1.60 (*m*, 4H, C*H* (13) + CH_a (1) + CH_a (2) + CH_a (12)), 1.67 (*s*, 3H, CH_3 (30)), 1.60–1.53 (*m*, 2H, C*H* (18) + CH_b (2)), 1.52–1.43 (*m*, 5H, CH_2 (33) + CH_2 (33′) + CH_a (6)), 1.43–1.34 (*m*, 5H, CH_2 (7) + CH_b (6) + CH_a (11) + CH_b (21)), 1.34–1.25 (*m*, 13H, CH_2 (34) + CH_2 (34′) + CH_2 (35) + CH_2 (35′) + CH_2 (36) + CH_2 (36′) + C*H* (9)), 1.23–1.13 (*m*, 2H, CH_b (11) + CH_b (16)), 1.10–0.99 (*m*, 3H, CH_b (12) + CH_b (15) + CH_b (22)), 1.03 (*s*, 3H, CH_3 (25)), 0.98–0.92 (*m*, 1H, CH_b (1)), 0.96 (*s*, 3H, CH_3 (27)), 0.91–0.85 (*m*, 9H, CH_3 (23) + CH_3 (37) + CH_3 (37′)), 0.83 (*s*, 3H, CH_3 (26)), 0.79 (*s*, 3H, CH_3 (24)), 0.78–0.75 (*m*, 1H, C*H* (5)) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.1 (*C*═O, C31), 156.8 (*C*═O, C31′), 150.3 (*C*═CH_2, C20), 109.7 (H_2C═C, C29), 81.0 (*C*H, C3), 62.9 (CH_2, C28), 55.4 (*C*H, C5), 50.3 (*C*H, C9), 48.8 (*C*H, C18), 47.7 (*C*H, C19), 46.6 (C_q, C17), 42.7 (C_q, C14), 41.0 (CH_2, C32/C32′), 40.9 (C_q, C8), 38.4 (CH_2, C1), 38.0 (C_q, C4), 37.5 (*C*H, C13), 37.0 (C_q, C10), 34.6 (CH_2, C22), 34.1 (CH_2, C7), 31.5 (*C*H_2, C35/35′), 30.0 (CH_2, C33/C33′), 29.8 (CH_2, C16), 29.7 (*C*H_2, C21), 27.9 (CH_3, C23), 27.1 (CH_2, C15), 26.4 (CH_2, C34/34′), 25.2 (CH_2, C12), 24.1 (CH_2, C2), 22.5 (CH_2, C36/36′), 20.8 (*C*H_2, C11), 19.1 (CH_3, C30), 18.2 (CH_2, C6), 16.5 (*C*H_3, C24), 16.1 (*C*H_3, C26), 16.0 (*C*H_3, C25), 14.7 (*C*H_3, C27), 14.0 (*C*H_3, C37/37′) ppm; MS (ESI, MeOH): m/z = 697.0 (12%, $[M + H]^+$), 719.5 (34%, $[M + Na]^+$), 1394.6 (100%, $[2M + H]^+$), 1416.4 (20%, $[2M + Na]^+$); analysis calcd for $C_{44}H_{76}N_2O_4$ (697.09): C 75.81, H 10.99, N 4.02; found: C 75.69, H 11.14, N 3.94.

4.3.27. 3,28-Di-O-acetyl-betulin (**29**)

This compound was prepared from **1** (4.5 g, 10.16 mmol) by acetylation (12 h, 25 °C) with acetic anhydride (7.5 mL, 79.2 mmol), NEt_3 (15 mL, 108.2 mmol) and DMAP (0.12 g, 0.95 mmol) as previously described, followed by one re-crystallization from EtOH (30 mL) to yield **29** (4.78 g, 89.5%) as a colorless solid; R_F = 0.73 (silica gel, hexanes/ethyl acetate, 8:2); m.p.: 219–222 °C (lit.: [62] 216–218 °C); $[\alpha]_D$ = +20.7° (c = 0.36, $CHCl_3$), (lit.: [62] $[\alpha]_D$ = +19.7° ($CHCl_3$)); MS (ESI, MeOH): m/z = 467.3 (91%,

$[M + H\text{-}HOAc]^+$), 544.2 (16%, $[M + NH4]^+$), 549.4 (12%, $[M+Na]^+$), 1075.6 (10%, $[2M + Na]^+$).

*4.3.28. 3-O-Acetyl-betulin (**30**)*

Deacetylation of **29** (8.2 g, 15.6 mmol) with KOH (0.87 g, 15.6 mmol) in THF (50 mL) and MeOH (20 mL) for 30 min at 0 °C followed by usual aqueous workup and chromatography (silica gel, hexanes/ethyl acetate, 8:2) gave **30** (4.33 g, 57.4%) as a colorless solid; R_F = 0.40 (silica gel, hexanes/ethyl acetate, 8:2); m.p.: 255–258 °C (lit.: [62] 258–260 °C); $[\alpha]_D = +34.1°$ (c = 0.37, $CHCl_3$), (lit.: [62] $[\alpha]_D = +25.7°$ ($CHCl_3$)); MS (ESI, MeOH): m/z = 485.3 (8%, $[M+H]^+$), 538.9 (25%, $[M + Na + MeOH]^+$), 969.5 (18%, $[2M + H]^+$), 991.4 (100%, $[2M + Na]^+$).

*4.3.29. (3β) 3-Acetyloxylup-20(29)-en-28-N-ethylcarbamate (**31**)*

Microwave assisted reaction (7 h, 120 °C) of **30** (1.0 g, 2.1 mmol) in dry THF (5 mL) with ethyl isocyanate (0.44 g, 0.49 mL, 6.2 mmol) as described above, followed by chromatography (silica gel, hexanes/ethyl acetate, 9:1) gave **31** (1.05 g, 91.2%) as a colorless solid; R_F = 0.44 (silica gel, hexanes/ethyl acetate, 8:2); m.p.: 116–119 °C; $[\alpha]_D = +21.0°$ (c = 0.32, $CHCl_3$); IR (KBr): ν = 3424*br*, 2946*s*, 2872*m*, 1731*s*, 1641*w*, 1521*m*, 1456*m*, 1369*m*, 1245*s*, 1146*w*, 1106*w*, 1081*w*, 1026*m*, 980*w*, 883*w*, 775*w*, 548*w* cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 4.68 (*s*, 1H, CH_a (29)), 4.61 (*br*, 1H, N*H*), 4.58 (*s*, 1H, CH_b (29)), 4.46 (*dd*, J = 9.9, 6.2 Hz, 1H, C*H* (3)), 4.25 (*d*, J = 10.7 Hz, 1H, CH_a (28)), 3.82 (*d*, J = 10.7 Hz, 1H, CH_b (28)), 3.22 (*br*, 2H, CH_2 (34)), 2.44 (*dt*, J = 11.0, 5.7 Hz, 1H, C*H* (19)), 2.03 (*s*, 3H, CH_3 (32)), 2.02–1.92 (*m*, 1H, CH_a (21)), 1.86–1.76 (*m*, 1H, CH_a (16)), 1.75–1.69 (*m*, 2H, CH_a (22) + CH_a (15)), 1.68 (*s*, 3H, CH_3 (30)), 1.67–1.61 (*m*, 4H, CH_a (1) + C*H* (13) + CH_2 (12)), 1.60–1.52 (*m*, 3H, C*H* (18) + CH_2 (2)), 1.52–1.47 (*m*, 1H, CH_a (6)), 1.44–1.33 (*m*, 6H, CH_2 (7) + CH_b (21) + CH_2 (11) + CH_b (6)), 1.32–1.24 (*m*, 1H, C*H* (9)), 1.20 (*dd*, J = 12.6, 3.6 Hz, 1H, CH_b (16)), 1.14 (*t*, J = 7.2 Hz, 3H, CH_3 (35)), 1.10–0.99 (*m*, 2H, CH_b (22) + CH_b (15)), 1.03 (*s*, 3H, CH_3 (25)), 0.98–0.92 (*m*, 1H, CH_b (1)), 0.96 (*s*, 3H, CH_3 (27)), 0.84 (*s*, 3H, CH_3 (23)), 0.84 (*s*, 3H, CH_3 (26)), 0.83 (*s*, 3H, CH_3 (24)), 0.78 (*m*, 1H, C*H* (5)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.0 (*C*=O, C31), 157.0 (*C*=O, C33), 150.3 (*C*=CH_2, C20), 109.8 (H_2C=C, C29), 80.9 (*C*H, C3), 63.0 (CH_2, C28), 55.4 (*C*H, C5), 50.3 (*C*H, C9), 48.8 (*C*H, C18), 47.7 (*C*H, C19), 46.6 (C_q, C17), 42.7 (C_q, C14), 40.9 (C_q, C8), 38.4 (CH_2, C1), 37.8 (C_q, C4), 37.5 (*C*H, C13), 37.1 (C_q, C10), 35.1 (CH_2, C34), 34.5 (CH_2, C22), 34.1 (CH_2, C7), 29.8 (CH_2, C16), 29.6 (CH_2, C21), 27.9 (CH_3, C23), 27.1 (CH_2, C15), 25.2 (CH_2, C12), 23.7 (CH_2, C2), 21.3 (CH_3, C32), 20.8 (CH_2, C11), 19.1 (CH_3, C30), 18.2 (CH_2, C6), 16.5 (CH_3, C24), 16.1 (CH_3, C26), 16.0 (CH_3, C25), 15.3 (CH_3, C35), 14.7 (CH_3, C27) ppm; MS (ESI, MeOH): m/z = 555.9 (18%, $[M + H]^+$), 578.3 (15%, $[M + Na]^+$), 1111.3 (100%, $[2M + H]^+$), 1133.3 (53%, $[2M + Na]^+$); analysis calcd for $C_{35}H_{57}NO_4$ (555.83): C 75.63, H 10.34, N 2.52; found: C 75.41, H 10.47, N 2.39.

*4.3.30. (3β) 3-Acetyloxylup-20(29)-en-28-N-propylcarbamate (**32**)*

Microwave assisted reaction (7 h, 120 °C) of **30** (0.78 g, 1.6 mmol) in dry THF (5 mL) with propyl isocyanate (0.41 g, 0.45 mL, 4.8 mmol) as described above, followed by chromatography (silica gel, hexanes/ethyl acetate, 9:1) gave **32** (0.68 g, 73.6%) as a colorless solid; R_F = 0.52 (silica gel, hexanes/ethyl acetate, 8:2); m.p.: 108–111 °C; $[\alpha]_D = +29.9°$ (c = 0.34, $CHCl_3$); IR (KBr): ν = 3418*br*, 2949*s*, 2872*m*, 2362*w*, 1732*m*, 1642*w*, 1530*w*, 1461*w*, 1372*w*, 1246*m*, 1136*w*, 1106*w*, 1031*w*, 980*w*, 882*w*, 776*w*, 668*w* cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 4.68 (*s*, 1H, CH_a (29)), 4.65 (*br*, 1H, N*H*), 4.58 (*s*, 1H, CH_b (29)), 4.46 (*dd*, J = 9.9, 6.1 Hz, 1H, C*H* (3)), 4.26 (*d*, J = 10.6 Hz, 1H, CH_a (28)), 3.83 (*d*, J = 10.6 Hz, 1H, CH_b (28)), 3.14 (*br*, 2H, CH_2 (34)), 2.44 (*dt*, J = 11.1, 5.8 Hz, 1H, C*H* (19)), 2.03 (*s*, 3H, CH_3 (32)), 2.02–1.92 (*m*, 1H, CH_a (21)), 1.85–1.76 (*m*, 1H, CH_a (16)), 1.76–1.69 (*m*, 2H, CH_a (22) + CH_a (15)), 1.68 (*s*, 3H, CH_3 (30)), 1.67–1.58 (*m*, 4H, CH_a (1) + C*H* (13) + CH_2 (12)), 1.58–1.48 (*m*, 3H, CH_2 (2) + C*H* (18)), 1.44–1.34 (*m*, 3H, CH_a (6) + CH_2 (35)), 1.32–1.20 (*m*, 6H, CH_2 (7) + CH_b (21) + CH_2 (11) + CH_b (6)), 1.25–1.16 (*m*, 2H, CH_b (16) + C*H* (9)), 1.10–0.99 (*m*, 2H, CH_b (22) + CH_b (15)), 1.04 (*s*, 3H, CH_3 (25)), 0.99–0.95 (*m*, 1H, CH_b (1)), 0.96 (*s*, 3H, CH_3 (27)), 0.92 (*t*, J = 4.0 Hz, 3H, CH_3 (36)), 0.84 (*s*, 3H, CH_3 (23)), 0.84 (*s*, 3H, CH_3 (26)), 0.83 (*s*, 3H, CH_3 (24)), 0.79–0.76 (*m*, 1H, C*H* (5)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.0 (*C*=O, C31), 157.1 (*C*=O, C33), 150.3 (*C*=CH_2, C20), 109.8 (H_2C=C, C29), 80.9 (*C*H, C3), 62.9 (CH_2, C28), 55.4 (*C*H, C5), 50.3 (*C*H, C9), 48.8 (*C*H, C18), 47.7 (*C*H, C19), 46.6 (C_q, C17), 42.7 (C_q, C14), 40.9 (C_q, C8), 40.8 (CH_2, C34), 38.4 (CH_2, C1), 37.8 (C_q, C4), 37.5 (*C*H, C13), 37.1 (C_q, C10), 34.6 (CH_2, C22), 34.1 (CH_2, C7), 32.1 (CH_2, C35), 29.8 (CH_2, C16), 29.7 (CH_2, C21), 27.9 (CH_3, C23), 27.1 (CH_2, C15), 25.2 (CH_2, C12), 23.7 (CH_2, C2), 21.3 (CH_3, C32), 20.8 (CH_2, C11), 19.9 (CH_2, C36), 19.1 (CH_3, C30), 18.2 (CH_2, C6), 16.5 (CH_3, C24), 16.1 (CH_3, C26), 16.0 (CH_3, C25), 14.7 (CH_3, C27), 13.7 (CH_3, C37) ppm; MS (ESI, MeOH): m/z = 584.1 (25%, $[M + H]^+$), 606.5 (10%, $[M + Na]^+$), 1167.5 (100%, $[2M + H]^+$), 1189.5 (22%, $[2M + Na]^+$); analysis calcd for $C_{37}H_{61}NO_4$ (583.88): C 76.11, H 10.53, N 2.40; found: C 76.00, H 10.63, N 2.29.

*4.3.31. (3β) 3-Acetyloxylup-20(29)-en-28-N-butylcarbamate (**33**)*

Microwave assisted reaction (7 h, 120 °C) of **30** (1 g, 2.1 mmol) in dry THF (5 mL) with butyl isocyanate (0.61 g, 0.7 mL, 6.2 mol) as described above, followed by chromatography (silica gel, hexanes/ethyl acetate, 9:1) gave **33** (1.0 g, 83.3%) as a colorless solid; R_F = 0.57 (silica gel, hexanes/ethyl acetate, 8:2); m.p.: 94–97 °C; $[\alpha]_D = +18.6°$ (c = 0.29, $CHCl_3$); IR (KBr): ν = 3421*br*, 2951*s*, 2872*m*, 2366*w*, 1734*m*, 1636*w*, 1534*w*, 1458*w*, 1374*w*, 1245*m*, 1134*w*, 1106*w*, 1025*w*, 980*w*, 882*w*, 776*w* cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 4.68 (*s*, 1H, CH_a (29)), 4.62 (*br*, 1H, N*H*), 4.58 (*s*, 1H, CH_b (29)), 4.46 (*dd*, J = 10.3, 5.8 Hz, 1H, C*H* (3)), 4.26 (*d*, J = 10.7 Hz, 1H, CH_a (28)), 3.82 (*d*, J = 10.5 Hz, 1H, CH_b (28)), 3.17 (*br*, 2H, CH_2 (34)), 2.44 (*dt*, J = 11.1, 5.8 Hz, 1H. C*H* (19)), 2.03 (*s*, 3H, CH_3 (32)), 2.02–1.92 (*m*, 1H, CH_a (21)), 1.87–1.76 (*m*, 1H, CH_a (16)), 1.75–1.69 (*m*, 2H, CH_a (22) + CH_a (15)), 1.68 (*s*, 3H, CH_3 (30)), 1.67–1.61 (*m*, 4H, CH_a (1) + C*H* (13) + CH_2 (12)), 1.61–1.53 (*m*, 3H, CH_2 (2) + C*H* (18)), 1.52–1.44 (*m*, 3H, CH_a (6) + CH_2 (35)), 1.43–1.29 (*m*, 6H, CH_2 (7) + CH_b (21) + CH_2 (11) + CH_b (6)), 1.29–1.24 (*m*, 2H, CH_2 (36)), 1.23–1.15 (*m*, 2H, CH_b (16) + C*H* (9)), 1.10–0.99 (*m*, 2H, CH_b (22) + CH_b (15)), 1.04 (*s*, 3H, CH_3 (25)), 0.98–0.95 (*m*, 1H, CH_b (1)), 0.96 (*s*, 3H, CH_3 (27)), 0.92 (*t*, J = 4.0 Hz, 3H, CH_3 (37)), 0.84 (*s*, 3H, CH_3 (23)), 0.84 (*s*, 3H, CH_3 (26)), 0.83 (*s*, 3H, CH_3 (24)), 0.79–0.76 (*m*, 1H, C*H* (5)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.0 (*C*=O, C31), 157.1 (*C*=O, C33), 150.3 (*C*=CH_2, C20), 109.8 (H_2C=C, C29), 80.9 (*C*H, C3), 62.9 (CH_2, C28), 55.4 (*C*H, C5), 50.3 (*C*H, C9), 48.8 (*C*H, C18), 47.7 (*C*H, C19), 46.6 (C_q, C17), 42.7 (C_q, C14), 40.9 (C_q, C8), 40.8 (CH_2, C34), 38.4 (CH_2, C1), 37.8 (C_q, C4), 37.5 (*C*H, C13), 37.1 (C_q, C10), 34.6 (CH_2, C22), 34.1 (CH_2, C7), 32.1 (CH_2, C35), 29.8 (CH_2, C16), 29.7 (CH_2, C21), 27.9 (CH_3, C23), 27.1 (CH_2, C15), 25.2 (CH_2, C12), 23.7 (CH_2, C2), 21.3 (CH_3, C32), 20.8 (CH_2, C11), 19.9 (CH_2, C36), 19.1 (CH_3, C30), 18.2 (CH_2, C6), 16.5 (CH_3, C24), 16.1 (CH_3, C26), 16.0 (CH_3, C25), 14.7 (CH_3, C27), 13.7 (CH_3, C37) ppm; MS (ESI, MeOH): m/z = 584.1 (25%, $[M + H]^+$), 606.5 (10%, $[M + Na]^+$), 1167.5 (100%, $[2M + H]^+$), 1189.5 (22%, $[2M + Na]^+$); analysis calcd for $C_{37}H_{61}NO_4$ (583.88): C 76.11, H 10.53, N 2.40; found: C 76.00, H 10.63, N 2.29.

*4.3.32. (3β) 3-Acetyloxylup-20(29)-en-28-N-hexylcarbamate (**34**)*

Microwave assisted reaction (7 h, 120 °C) of **30** (1 g, 2.1 mmol) in dry THF (5 mL) with hexyl isocyanate (0.79 g, 0.9 mL, 6.2 mmol) as described above, followed by chromatography (silica gel, hexanes/ethyl acetate, 9:1) gave **34** (1.09 g, 86.5%) as a colorless solid; R_F = 0.82 (silica gel, hexanes/ethyl acetate, 8:2); m.p.: 80–82 °C; $[\alpha]_D = +19.6°$ (c = 0.43, $CHCl_3$); IR (KBr): ν = 3420*br*, 2950*s*, 2870*m*,

2362*w*, 1734*m*, 1646*w*, 1534*w*, 1457*w*, 1347*w*, 1245*m*, 1134*w*, 1106*w*, 1030*w*, 980*w*, 882*w*, 776*w*, 668*w*, 610*w* cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 4.68 (*s*, 1H, CH_a (29)), 4.62 (*br*, 1H, N*H*), 4.58 (*s*, 1H, CH_b (29)), 4.46 (*dd*, *J* = 9.4, 6.5 Hz, 1H, C*H* (3)), 4.26 (*d*, *J* = 10.8 Hz, 1H, CH_a (28)), 3.82 (*d*, *J* = 10.3 Hz, 1H, CH_b (28)), 3.16 (*br*, 2H, CH_2 (34)), 2.44 (*dt*, *J* = 11.2, 5.9 Hz, 1H, C*H* (19)), 2.03 (*s*, 3H, CH_3 (32)), 2.02–1.92 (m, 1H, CH_a (21)), 1.85–1.76 (*m*, 1H, CH_a (16)), 1.76–1.70 (*m*, 2H, CH_a (22) + CH_a (15)), 1.68 (*s*, 3H, CH_3 (30)), 1.66–1.62 (*m*, 2H, CH_a (1) + C*H* (13)), 1.61–1.53 (m, 5H, C*H* (18) + CH_2 (12) + CH_2 (2)), 1.53–1.44 (*m*, 3H, CH_2 (35) + CH_a (6)), 1.44–1.35 (*m*, 6H, CH_2 (7) + CH_b (21) + CH_2 (11) + CH_b (6)), 1.33–1.24 (*m*, 7H, C*H* (9) + CH_2 (36) + CH_2 (37) + CH_2 (38)), 1.24–1.15 (*m*, 1H, CH_b (16)), 1.08–0.99 (*m*, 2H, CH_b (22) + CH_b (15)), 1.04 (*s*, 3H, CH_3 (25)), 0.98–0.93 (*m*, 1H, CH_b (1)), 0.96 (*s*, 3H, CH_3 (27)), 0.88 (*t*, *J* = 6.4 Hz, 3H, CH_3 (39)), 0.84 (*s*, 3H, CH_3 (23)), 0.84 (*s*, 3H, CH_3 (26)), 0.83 (*s*, 3H, CH_3 (24)), 0.79–0.76 (*m*, 1H, C*H* (5)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.0 (*C*=O, C31), 157.2 (*C*=O, C33), 150.3 (*C*=CH_2, C20), 109.8 (H_2C=C, C29), 80.9 (*C*H, C3), 62.9 (CH_2, C28), 55.4 (*C*H, C5), 50.3 (*C*H, C9), 48.8 (*C*H, C18), 47.7 (*C*H, C19), 46.6 (C_q, C17), 42.7 (C_q, C14), 41.0 (CH_2, C34), 40.9 (C_q, C8), 38.4 (CH_2, C1), 37.8 (C_q, C4), 37.5 (*C*H, C13), 37.1 (C_q, C10), 34.6 (CH_2, C22), 34.1 (CH_2, C7), 31.5 (CH_2, C37), 30.0 (CH_2, C35), 29.8 (CH_2, C16), 29.7 (CH_2, C21), 27.9 (CH_3, C23), 27.1 (CH_2, C15), 26.4 (CH_2, C36), 25.2 (CH_2, C12), 23.7 (CH_2, C2), 22.5 (CH_2, C38), 21.3 (CH_3, C32), 20.8 (CH_2, C11), 19.1 (CH_3, C30), 18.2 (CH_2, C6), 16.5 (CH_3, C24), 16.1 (CH_3, C26), 16.0 (CH_3, C25), 14.7 (CH_3, C27), 14.0 (CH_3, C39) ppm; MS (ESI, MeOH): *m*/*z* = 612.2 (60%, $[M + H]^+$), 634.5 (19%, $[M + Na]^+$), 1223.6 (100%, $[2M + H]^+$), 1245.6 (26%, $[2M + Na]^+$); analysis calcd for $C_{39}H_{65}NO_4$ (611.94): C 76.55, H 10.71, N 2.29; found: C 76.37, H 10.84, N 2.19.

4.3.33. (3β) 3-Acetyloxylup-20(29)-en-28-N-phenylcarbamate (**35**)

Microwave assisted reaction (7 h, 120 °C) of **30** (1 g, 2.1 mmol) in dry THF (5 mL) with phenyl isocyanate (0.74 g, 0.67 mL, 6.2 mmol) as described above, followed by chromatography (silica gel, hexanes/ethyl acetate, 9:1) gave **35** (1.08 g, 87.1%) as a colorless solid; R_F = 0.84 (silica gel, hexanes/ethyl acetate, 7:3); m.p.: 221–223 °C; $[\alpha]_D$ = +13.2° (*c* = 0.44, $CHCl_3$); IR (KBr): ν = 3431*m*, 3080*w*, 2948*s*, 2873*m*, 1737*s*, 1647*w*, 1602*m*, 1523*s*, 1501*w*, 1442*s*, 1391*w*, 1374*m*, 1311*m*, 1246*m*, 1204*s*, 1178*w*, 1105*w*, 1084*w*, 1054*m*, 1030*m*, 978*m*, 898*w*, 872*w*, 848*w*, 757*m*, 693*w*, 545*w*, 510*w* cm^{-1}; UV–vis ($CHCl_3$): λ_{max} (log $_e$) = 236.1 (4.17) nm; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.39 (*d*, *J* = 7.9 Hz, 2H, *HC*=C (35/35′)), 7.31 (*t*, *J* = 7.9 Hz, 2H, *HC*=C (36/36′)), 7.06 (*t*, *J* = 7.3 Hz, 1H, *HC*=C (37)), 6.61 (*br*, 1H, N*H*), 4.70 (*s*, 1H, CH_a (29)), 4.60 (*s*, 1H, CH_b (29)), 4.47 (*dd*, *J* = 10.2, 5.9 Hz, 1H, C*H* (3)), 4.37 (*d*, *J* = 10.8 Hz, 1H, CH_a (28)), 3.95 (*d*, *J* = 10.8 Hz, 1H, CH_b (28)), 2.47 (*dt*, *J* = 11.0, 5.8 Hz, 1H, C*H* (19)), 2.04 (*s*, 3H, CH_3 (32)), 2.03–1.96 (*m*, 1H, CH_a (21)), 1.92–1.82 (*m*, 1H, CH_a (16)), 1.81–1.71 (*m*, 2H, CH_a (22) + CH_a (15)), 1.69 (*s*, 3H, CH_3 (30)), 1.68–1.66 (*m*, 1H, C*H* (13)), 1.66–1.59 (*m*, 3H, CH_a (1) + CH_2 (12)), 1.60–1.55 (*m*, 3H, C*H* (18) + CH_2 (2)), 1.53–1.48 (*m*, 1H, CH_a (6)), 1.46–1.36 (*m*, 6H, CH_2 (7) + CH_b (21) + CH_2 (11) + CH_b (6)), 1.33–1.19 (*m*, 2H, C*H* (9) + CH_b (16)), 1.15–1.02 (m, 2H, CH_b (22) + CH_b (15)), 1.05 (*s*, 3H, CH_3 (25)), 1.02–0.93 (*m*, 1H, CH_b (1)), 0.98 (*s*, 3H, CH_3 (27)), 0.85 (*s*, 3H, CH_3 (23)), 0.84 (*s*, 3H, CH_3 (26)), 0.84 (*s*, 3H, CH_3 (24)), 0.79–0.76 (*m*, 1H, C*H* (5)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.0 (*C*=O, C31), 154.0 (*C*=O, C33), 150.1 (*C*=CH_2, C20), 137.9 (C_q, C34), 129.0 (*C*H, C36/36′), 123.4 (*C*H, C37), 118.6 (*C*H, C35/35′), 109.9 (H_2C=C, C29), 80.9 (*C*H, C3), 63.6 (CH_2, C28), 55.4 (*C*H, C5), 50.3 (*C*H, C9), 48.8 (*C*H, C18), 47.7 (*C*H, C19), 46.6 (C_q, C17), 42.7 (C_q, C14), 40.9 (C_q, C8), 38.4 (CH_2, C1), 37.8 (C_q, C4), 37.6 (*C*H, C13), 37.1 (C_q, C10), 34.5 (CH_2, C22), 34.1 (CH_2, C7), 29.8 (CH_2, C16), 29.6 (CH_2, C21), 27.9 (CH_3, C23), 27.1 (CH_2, C15), 25.2 (CH_2, C12), 23.7 (CH_2, C2), 21.3 (CH_3, C32), 20.8 (CH_2, C11), 19.1 (CH_3, C30), 18.2 (CH_2, C6), 16.5 (CH_3, C24), 16.1 (CH_3, C26), 16.1 (CH_3, C25), 14.7 (CH_3, C27) ppm; MS (ESI, MeOH): *m*/*z* = 604.1 (6%, $[M + H]^+$), 621.0 (10%, $[M + NH_4]^+$), 626.3 (24%, $[M + Na]^+$), 1207.3 (48%, $[2M + H]^+$), 1229.3 (100%, $[2M + Na]^+$); analysis calcd for $C_{39}H_{57}NO_4$ (603.87): C 77.57, H 9.51, N 2.32; found: C 77.36, H 9.69, N 2.18.

4.3.34. (3β) 3-Hydroxylup-20(29)-en-28-N-ethylcarbamate (**36**)

Deacetylation of **31** (0.98 g, 1.77 mmol) with potassium hydroxide (0.25 g, 5.3 mmol) in THF (30 mL) and MeOH (10 mL) for 2 days at 25 °C as described above, followed by chromatography (silica gel, hexanes/ethyl acetate, 7:3) gave **36** (0.86 g, 94.5%) as a colorless solid; R_F = 0.13 (silica gel, hexanes/ethyl acetate, 8:2); m.p.: 223–225 °C; $[\alpha]_D$ = +10.1° (*c* = 0.29, $CHCl_3$); IR (KBr): ν = 3432*br*, 2938*s*, 1689*m*, 1640*w*, 1536*w*, 1458*w*, 1375*w*, 1248*m*, 1024*w*, 883*m*, 543*w* cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 4.67 (*s*, 1H, CH_a (29)), 4.62 (*br*, 1H, N*H*), 4.57 (*s*, 1H, CH_b (29)), 4.24 (*d*, *J* = 10.8 Hz, 1H, CH_a (28)), 3.83 (*d*, *J* = 10.5 Hz, 1H, CH_b (28)), 3.21 (*br*, 2H, CH_2 (32)), 3.17 (*dd*, *J* = 11.2, 5.0 Hz, 1H, C*H* (3)), 2.44 (*dt*, *J* = 11.1, 5.8 Hz, 1H, C*H* (19)), 1.98 (*ddd*, *J* = 19.5, 11.4, 7.0 Hz, 1H, CH_a (21)), 1.86–1.72 (*m*, 3H, CH_a (15) + CH_a (16) + CH_a (22)), 1.72–1.54 (*m*, 5H, C*H* (18) + C*H* (13) + CH_a (1) + CH_a (2) + CH_a (12)), 1.67 (*s*, 3H, CH_3 (30)), 1.54–1.48 (*m*, 2H, CH_b (2) + CH_a (6)), 1.44–1.33 (m, 5H, CH_2 (7) + CH_b (6) + CH_a (11) + CH_b (21)), 1.29–1.17 (*m*, 3H, C*H* (9) + CH_b (11) + CH_b (16)), 1.13 (*t*, *J* = 7.2 Hz, 3H, CH_3 (33)), 1.10–0.99 (*m*, 3H, CH_b (12) + CH_b (15) + CH_b (22)), 1.03 (*s*, 3H, CH_3 (25)), 0.96 (*s*, 3H, CH_3 (27)), 0.96 (*s*, 3H, CH_3 (23)), 0.89 (*dt*, *J* = 12.8, 4.4 Hz, 1H, CH_b (1)), 0.81 (*s*, 3H, CH_3 (26)), 0.75 (*s*, 3H, CH_3 (24)), 0.67–0.65 (*m*, 1H, C*H* (5)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.0 (*C*=O, C31), 150.3 (*C*=CH_2, C20), 109.7 (H_2C=C, C29), 79.0 (*C*H, C3), 62.9 (CH_2, C28), 55.3 (*C*H, C5), 50.4 (*C*H, C9), 48.8 (*C*H, C18), 47.7 (*C*H, C19), 46.6 (C_q, C17), 42.7 (C_q, C14), 40.9 (C_q, C8), 38.8 (C_q, C4), 38.7 (CH_2, C1), 37.5 (*C*H, C13), 37.1 (C_q, C10), 35.9 (CH_2, C32), 34.6 (CH_2, C22), 34.2 (CH_2, C7), 29.8 (CH_2, C16), 29.7 (CH_2, C21), 28.0 (CH_3, C23), 27.4 (CH_2, C2), 27.1 (CH_2, C15), 25.2 (CH_2, C12), 20.8 (CH_2, C11), 19.1 (CH_3, C30), 18.3 (CH_2, C6), 16.1 (CH_3, C26), 16.0 (CH_3, C25), 15.3 (CH_3, C24), 15.3 (CH_3, C33), 14.7 (CH_3, C27) ppm; MS (ESI, MeOH): *m*/*z* = 514.1 (14%, $[M + H]^+$), 536.4 (6%, $[M + Na]^+$), 1027.5 (100%, $[2M + H]^+$), 1049.4 (96%, $[2M + Na]^+$); analysis calcd for $C_{33}H_{55}NO_3$ (513.79): C 77.14, H 10.79, N 2.73; found: C 77.04, H 10.90, N 2.59.

4.3.35. (3β) 3-Hydroxylup-20(29)-en-28-N-propylcarbamate (**37**)

Deacetylation of **32** (0.53 g, 0.93 mmol) with potassium hydroxide (0.10 g, 1.8 mmol) in THF (5 mL)/MeOH (5 mL) for 1 day as decribed above, followed by chromatography (silica gel, hexanes/ethyl acetate, 8:2) gave **37** (0.46 g, 93.0%) as a colorless solid; R_F = 0.26 (silica gel, hexanes/ethyl acetate, 8:2); m.p.: 111–114 °C; $[\alpha]_D$ = +10.5° (*c* = 0.31, $CHCl_3$); IR (KBr): ν = 3456*br*, 2941*s*, 2869*s*, 2362*w*, 1702*s*, 1528*m*, 1460*m*, 1375*w*, 1244*m*, 1106*w*, 1045*m*, 883*w*, 668*w* cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 4.68 (*s*, 1H, CH_a (29)), 4.64 (*br*, 1H, N*H*), 4.58 (*s*, 1H, CH_b (29)), 4.25 (*d*, *J* = 10.7 Hz, 1H, CH_a (28)), 3.84 (*d*, *J* = 10.6 Hz, 1H, CH_b (28)), 3.18 (*dd*, *J* = 11.2, 5.0 Hz, 1H, C*H* (3)), 3.14 (*br*, 2H, CH_2 (32)), 2.44 (*dt*, *J* = 11.1, 5.7 Hz, 1H, C*H* (19)), 2.03–1.92 (*m*, 1H, CH_a (21)), 1.87–1.79 (*m*, 1H, CH_a (16)), 1.79–1.69 (*m*, 2H, CH_a (22) + CH_a (15)), 1.67 (*s*, 3H, CH_3 (30)), 1.66–1.61 (*m*, 3H, CH_a (1) + C*H* (13) + CH_a (12)), 1.61–1.55 (*m*, 3H, C*H* (18) + CH_2 (2)), 1.55–1.47 (*m*, 3H, CH_2 (33) + CH_a (6)), 1.44–1.33 (*m*, 5H, CH_2 (7) + CH_b (21) + CH_a (11) + CH_b (6)), 1.29–1.17 (*m*, 3H, C*H* (19) + CH_b (16) + CH_b (11)), 1.10–0.99 (*m*, 3H, CH_b (22) + CH_b (15) + CH_b (12)), 1.04 (*s*, 3H, CH_3 (25)), 0.97 (*s*, 3H, CH_3 (23)), 0.96 (*s*, 3H, CH_3 (27)), 0.92 (*t*, *J* = 7.3 Hz, 3H, CH_3 (34)), 0.89–0.84 (*m*, 1H, CH_b (1)), 0.82 (*s*, 3H, CH_3 (26)), 0.75 (*s*, 3H, CH_3 (24)), 0.69–0.66 (*m*, 1H, C*H* (5)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.2 (*C*=O, C31), 150.3 (*C*=CH_2, C20), 109.7 (H_2C=C, C29), 79.0 (*C*H, C3), 63.0 (CH_2, C28), 55.3 (*C*H, C5), 50.4 (*C*H, C9), 48.8 (*C*H, C18), 47.7 (*C*H, C19), 46.6 (C_q, C17), 42.8 (CH_2, C32), 42.7 (C_q, C14), 40.9 (C_q, C8), 38.8 (C_q, C4), 38.7 (CH_2, C1), 37.5 (*C*H, C13), 37.1 (C_q, C10), 34.6 (CH_2, C22), 34.2 (CH_2, C7), 29.9 (CH_2, C16), 29.7 (CH_2, C21), 28.0 (CH_3, C23), 27.4 (CH_2, C2), 27.1 (CH_2,

C15), 25.2 (*C*H$_2$, C12), 23.3 (*C*H$_2$, C33), 20.8 (*C*H$_2$, C11), 19.1 (*C*H$_3$, C30), 18.3 (*C*H$_2$, C6), 16.1 (*C*H$_3$, C26), 16.0 (*C*H$_3$, C25), 15.3 (*C*H$_3$, C24), 14.7 (*C*H$_3$, C27), 11.2 (*C*H$_3$, C34) ppm; MS (ESI, MeOH): m/z = 528.1 (14%, [M + H]$^+$), 1055.4 (100%, [2M + H]$^+$), 1077.5 (72%, [2M + Na]$^+$); analysis calcd for $C_{34}H_{57}NO_3$ (527.82): C 77.37, H 10.88, N 2.65; found: C 77.15, H 10.91, N 2.52.

4.3.36. (3β) 3-Hydroxylup-20(29)-en-28-N-butylcarbamate (**38**)

Deacetylation of **33** (0.23 g, 0.39 mmol) with potassium hydroxide (0.11 g, 2.0 mmol) in THF (10 mL)/MeOH (5 mL) for 2 days at 25 °C as described above, followed by chromatography (silica gel, hexanes/ethyl acetate, 8:2) gave **38** (0.2 g, 94.0%) as a colorless solid; R_F = 0.39 (silica gel, hexanes/ethyl acetate, 8:2); m.p.: 100–102 °C; $[\alpha]_D$ = +11.6° (c = 0.43, $CHCl_3$); IR (KBr): ν = 3456*br*, 2941*s*, 2870*s*, 2362*w*, 1700*m*, 1638*w*, 1522*w*, 1458*m*, 1374*w*, 1248*w*, 1136*w*, 1106*w*, 1047*w*, 984*w*, 882*w*, 774*w*, 638*w* cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.68 (*s*, 1H, C*H*$_a$ (29)), 4.62 (*br*, 1H, N*H*), 4.58 (*s*, 1H, C*H*$_b$ (29)), 4.25 (*d*, J = 10.9 Hz, 1H, C*H*$_a$ (28)), 3.82 (*d*, J = 10.5 Hz, 1H, C*H*$_b$ (28)), 3.18 (*m*, 3H, C*H*$_2$ (32) + C*H* (3)), 2.45 (*dt*, J = 11.0, 5.7 Hz, 1H, C*H* (19)), 2.03–1.92 (*m*, 1H, C*H*$_a$ (21)), 1.86–1.76 (*m*, 1H, C*H*$_a$ (16)), 1.76–1.69 (*m*, 2H, C*H*$_a$ (22) + C*H*$_a$ (15)), 1.67 (*s*, 3H, C*H*$_3$ (30)), 1.66–1.61 (*m*, 3H, C*H*$_a$ (1) + C*H* (13) + C*H*$_a$ (12)), 1.61–1.55 (*m*, 3H, C*H*$_2$ (2) + C*H* (18)), 1.54–1.44 (*m*, 3H, C*H*$_a$ (6) + C*H*$_2$ (33)), 1.43–1.36 (*m*, 5H, C*H*$_2$ (7) + C*H*$_b$ (21) + C*H*$_a$ (11) + C*H*$_b$ (6)), 1.36–1.30 (*m*, 2H, C*H*$_2$ (34)), 1.29–1.17 (*m*, 3H, C*H*$_b$ (16) + C*H* (9) + C*H*$_b$ (11)), 1.10–1.00 (*m*, 3H, C*H*$_b$ (22) + C*H*$_b$ (15) + C*H*$_b$ (12)), 1.04 (*s*, 3H, C*H*$_3$ (25)), 0.96 (*s*, 3H, C*H*$_3$ (23)), 0.96 (*s*, 3H, C*H*$_3$ (27)), 0.92 (*t*, J = 7.3 Hz, 3H, C*H*$_3$ (35)), 0.89–0.84 (*m*, 1H, C*H*$_b$ (1)), 0.82 (*s*, 3H, C*H*$_3$ (26)), 0.76 (*s*, 3H, C*H*$_3$ (24)), 0.69–0.66 (*m*, 1H, C*H* (5)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.1 (*C*=O, C31), 150.3 (*C*=CH$_2$, C20), 109.7 (H$_2$*C*=C, C29), 79.0 (*C*H, C3), 62.9 (*C*H$_2$, C28), 55.3 (*C*H, C5), 50.4 (*C*H, C9), 48.8 (*C*H, C18), 47.7 (*C*H, C19), 46.6 (*C*$_q$, C17), 42.7 (*C*$_q$, C14), 40.9 (*C*$_q$, C8), 40.8 (*C*H$_2$, C32), 38.8 (*C*$_q$, C4), 38.7 (*C*H$_2$, C1), 37.5 (*C*H, C13), 37.1 (*C*$_q$, C10), 34.6 (*C*H$_2$, C22), 34.2 (*C*H$_2$, C7), 32.1 (*C*H$_2$, C33), 29.8 (*C*H$_2$, C16), 29.7 (*C*H$_2$, C21), 28.0 (*C*H$_3$, C23), 27.4 (*C*H$_2$, C2), 27.1 (*C*H$_2$, C15), 25.2 (*C*H$_2$, C12), 20.8 (*C*H$_2$, C11), 19.9 (*C*H$_2$, C34), 19.1 (*C*H$_3$, C30), 18.3 (*C*H$_2$, C6), 16.1 (*C*H$_3$, C26), 16.0 (*C*H$_3$, C25), 15.3 (*C*H$_3$, C24), 14.7 (*C*H$_3$, C27), 13.7 (*C*H$_3$, C35) ppm; MS (ESI, MeOH): m/z = 542.1 (14%, [M + H]$^+$), 1083.5 (100%, [2M + H]$^+$), 1105.5 (22%, [2M + Na]$^+$); analysis calcd for $C_{35}H_{59}NO_3$ (541.85): C 77.58, H 10.98, N 2.58; found: C 77.40, H 11.14, N 2.41.

4.3.37. (3β) 3-Hydroxylup-20(29)-en-28-N-hexylcarbamate (**39**)

Deacetylation of **34** (0.27 g, 0.56 mmol) with potassium hydroxide (0.1 g, 1.8 mmol) in THF (10 mL)/MeOH (5 mL) for 1 day as described above, followed by chromatography (silica gel, hexanes/ethyl acetate, 8:2) gave **39** (0.22 g, 87.5%) as a colorless solid; R_F = 0.32 (silica gel, hexanes/ethyl acetate, 8:2); m.p.: 95–97 °C; $[\alpha]_D$ = +11.7° (c = 0.41, $CHCl_3$); IR (KBr): ν = 3456*br*, 2940*s*, 2869*s*, 1702*s*, 1642*w*, 1523*m*, 1456*m*, 1375*w*, 1248*m*, 1106*w*, 1045*m*, 883*w*, 637*w* cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.68 (*s*, 1H, C*H*$_a$ (29)), 4.63 (*br*, 1H, N*H*), 4.57 (*s*, 1H, C*H*$_b$ (29)), 4.25 (*d*, J = 10.4 Hz, 1H, C*H*$_a$ (28)), 3.83 (*d*, J = 10.4 Hz, 1H, C*H*$_b$ (28)), 3.17 (*m*, 3H, CH$_2$ (32) + C*H* (3)), 2.44 (*dt*, J = 11.0, 5.7 Hz, 1H, C*H* (19)), 2.06–1.92 (m, 1H, C*H*$_a$ (21)), 1.79 (*dd*, J = 17.5, 9.3 Hz, 1H, C*H*$_a$ (16)), 1.76–1.69 (*m*, 2H, C*H*$_a$ (22) + C*H*$_a$ (15)), 1.67 (*s*, 3H, C*H*$_3$ (30)), 1.66–1.61 (*m*, 3H, C*H*$_a$ (1) + C*H* (13) + C*H*$_a$ (12)), 1.61–1.51 (*m*, 4H, C*H* (18) + C*H*$_2$ (2) + C*H*$_a$ (6)), 1.51–1.44 (*m*, 2H, C*H*$_2$ (33)), 1.44–1.36 (*m*, 5H, C*H*$_2$ (7) + C*H*$_b$ (21) + C*H*$_a$ (11) + C*H*$_b$ (6)), 1.34–1.23 (*m*, 7H, C*H* (9) + C*H*$_2$ (34) + C*H*$_2$ (35) + C*H*$_2$ (36)), 1.23–1.14 (*m*, 2H, C*H*$_b$ (11) + C*H*$_b$ (16)), 1.09–1.01 (*m*, 3H, C*H*$_b$ (22) + C*H*$_b$ (15) + C*H*$_b$ (12)), 1.03 (*s*, 3H, C*H*$_3$ (25)), 0.96 (*s*, 3H, C*H*$_3$ (23)), 0.96 (*s*, 3H, C*H*$_3$ (27)), 0.93–0.87 (*m*, 1H, C*H*$_b$ (1)), 0.88 (*t*, J = 6.7 Hz, 3H, C*H*$_3$ (37)), 0.82 (*s*, 3H, C*H*$_3$ (26)), 0.75 (*s*, 3H, C*H*$_3$ (24)), 0.69–0.66 (*m*, 1H, C*H* (5)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.2 (*C*=O, C31), 150.3 (*C*=CH$_2$, C20), 109.7 (H$_2$*C*=C, C29), 79.0 (*C*H, C3), 62.9 (*C*H$_2$, C28), 55.3 (*C*H, C5), 50.4 (*C*H, C9), 48.8 (*C*H, C18), 47.7 (*C*H, C19), 46.6 (*C*$_q$, C17), 42.7 (*C*$_q$, C14), 41.1 (*C*H$_2$, C32), 40.9 (*C*$_q$, C8), 38.8 (*C*$_q$, C4), 38.7 (*C*H$_2$, C1), 37.5 (*C*H, C13), 37.1 (*C*$_q$, C10), 34.6 (*C*H$_2$, C22), 34.2 (*C*H$_2$, C7), 31.5 (*C*H$_2$, C35), 30.0 (*C*H$_2$, C33), 29.8 (*C*H$_2$, C16), 29.7 (*C*H$_2$, C21), 28.0 (*C*H$_3$, C23), 27.4 (*C*H$_2$, C2), 27.1 (*C*H$_2$, C15), 26.4 (*C*H$_2$, C34), 25.2 (*C*H$_2$, C12), 22.5 (*C*H$_2$, C36), 20.8 (*C*H$_2$, C11), 19.1 (*C*H$_3$, C30), 18.3 (*C*H$_2$, C6), 16.1 (*C*H$_3$, C26), 16.0 (*C*H$_3$, C25), 15.3 (*C*H$_3$, C24), 14.7 (*C*H$_3$, C27), 14.0 (*C*H$_3$, C37) ppm; MS (ESI, MeOH): m/z = 570.1 (12%, [M + H]$^+$), 592.3 (4%, [M + Na]$^+$), 1139.5 (100%, [2M + H]$^+$), 1161.5 (60%, [2M + Na]$^+$); analysis calcd for $C_{37}H_{63}NO_3$ (569.90): C 77.98, H 11.14, N 2.46; found: C 77.77, H 11.29, N 2.27.

4.3.38. (3β) 3-Hydroxylup-20(29)-en-28-N-phenylcarbamate (**40**)

Deacetylation of **35** (1 g, 1.8 mmol) with potassium hydroxide (0.4 g, 7.16 mmol) in THF (30 mL)/MeOH (20 mL) for 2 days at 25 °C as described above, followed by chromatography (silica gel, hexanes/ethyl acetate, 7:3) gave **40** (0.83 g, 89.2%) as a colorless solid; R_F = 0.28 (silica gel, hexanes/ethyl acetate, 8:2); m.p.: 233–234 °C; $[\alpha]_D$ = +7.2° (c = 0.27, $CHCl_3$); IR (KBr): ν = 3511*br*, 2945*s*, 2867*m*, 1721*s*, 1602*m*, 1550*s*, 1503*w*, 1446*s*, 1385*w*, 1316*w*, 1228*s*, 1086*m*, 1070*m*, 1031*w*, 984*w*, 886*w*, 751*m*, 692*w* 506*w* cm^{-1}; UV–vis ($CHCl_3$): λ_{max} (log ε) = 235.8 (4.06) nm; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39 (*d*, J = 7.9 Hz, 2H, *H*C=C (33/33′)), 7.31 (*t*, J = 7.9 Hz, 2H, *H*C=C (34/34′)), 7.06 (*t*, J = 7.3 Hz, 1H, *H*C=C (35)), 6.63 (*br*, 1H, N*H*), 4.70 (*s*, 1H, C*H*$_a$ (29)), 4.60 (*s*, 1H, C*H*$_b$ (29)), 4.37 (*d*, J = 10.7 Hz, 1H, C*H*$_a$ (28)), 3.96 (*d*, J = 10.8 Hz, 1H, C*H*$_b$ (28)), 3.18 (dd, J = 11.1, 5.0 Hz, 1H, C*H* (3)), 2.47 (*dt*, J = 11.0, 5.8 Hz, 1H, C*H* (19)), 2.02 (*ddd*, J = 19.2, 13.9, 10.5 Hz, 1H, C*H*$_a$ (21)), 1.93–1.82 (*m*, 1H, C*H*$_a$ (16)), 1.81–1.72 (*m*, 2H, C*H*$_a$ (22) + C*H*$_a$ (15)), 1.69 (*s*, 3H, C*H*$_3$ (30)), 1.68–1.55 (*m*, 4H, C*H* (18) + C*H*$_a$ (1) + C*H* (13) + C*H*$_a$ (12)), 1.55–1.44 (*m*, 3H, C*H*$_2$ (2) + C*H*$_a$ (6)), 1.44–1.36 (*m*, 5H, C*H*$_2$ (7) + C*H*$_b$ (21) + C*H*$_a$ (11) + C*H*$_b$ (6)), 1.32–1.22 (*m*, 3H, C*H* (9) + C*H*$_b$ (16) + C*H*$_b$ (11)), 1.15–1.02 (*m*, 2H, C*H*$_b$ (22) + C*H*$_b$ (15)), 1.05 (*s*, 3H, C*H*$_3$ (25)), 1.01–0.95 (*m*, 1H, C*H*$_b$ (12)), 0.98 (*s*, 3H, C*H*$_3$ (27)), 0.97 (*s*, 3H, C*H*$_3$ (23)), 0.90 (*dt*, J = 12.9, 4.3 Hz, 1H, C*H*$_b$ (1)), 0.83 (*s*, 3H, C*H*$_3$ (26)), 0.76 (*s*, 3H, C*H*$_3$ (24)), 0.69–0.66 (*m*, 1H, C*H* (5)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.1 (*C*=O, C31), 150.1 (*C*=CH$_2$, C20), 137.9 (*C*$_q$, C32), 129.0 (*C*H, C34/34′), 123.4 (*C*H, C35), 118.6 (*C*H, C33/33′), 109.8 (H$_2$*C*=C, C29), 79.0 (*C*H, C3), 63.5 (*C*H$_2$, C28), 55.3 (*C*H, C5), 50.4 (*C*H, C9), 48.9 (*C*H, C18), 47.7 (*C*H, C19), 46.6 (*C*$_q$, C17), 42.7 (*C*$_q$, C14), 40.9 (*C*$_q$, C8), 38.9 (*C*$_q$, C4), 38.7 (*C*H$_2$, C1), 37.6 (*C*H, C13), 37.2 (*C*$_q$, C10), 34.6 (*C*H$_2$, C22), 34.2 (*C*H$_2$, C7), 29.8 (*C*H$_2$, C16), 29.6 (*C*H$_2$, C21), 28.0 (*C*H$_3$, C23), 27.4 (*C*H$_2$, C2), 27.1 (*C*H$_2$, C15), 25.2 (*C*H$_2$, C12), 20.8 (*C*H$_2$, C11), 19.2 (*C*H$_3$, C30), 18.3 (*C*H$_2$, C6), 16.1 (*C*H$_3$, C26), 16.1 (*C*H$_3$, C25), 15.3 (*C*H$_3$, C24), 14.8 (*C*H$_3$, C27) ppm; MS (ESI, MeOH): m/z = 579.1 (6%, [M + NH$_4$]$^+$), 584.3 (6%, [M + Na]$^+$), 1123.4 (48%, [2M + H]$^+$), 1146.5 (44%, [2M + Na]$^+$); analysis calcd for $C_{37}H_{55}NO_3$ (561.84): C 79.10, H 9.87, N 2.49; found: C 79.03, H 10.02, N 2.33.

4.3.39. 28-O-Acetyl-betulin (**41**)

Acetylation of **2** (15.0 g, 33.88 mmol) in DCM (100 mL) with acetic anhydride (3.2 mL, 33.88 mmol) in the presence of NEt_3 (4.3 mL) and DMAP (0.24 g, 1.96 mmol) as previously described, followed by usual workup and chromatography (silica gel, hexanes/ethyl acetate, 8:2) gave **41** (9.87 g, 60.4%) as a colorless solid; R_F = 0.40 (silica gel, hexanes/ethyl acetate, 8:2); m.p.: 216–217 °C (lit.: [63] 214–215 °C); $[\alpha]_D$ = +11.1° (c = 0.39, $CHCl_3$), (lit.: [64] $[\alpha]_D$ = +10.3° ($CHCl_3$)); MS (ESI, MeOH): m/z = 467.3 (100%, [M + H−H$_2$O]$^+$), 485.1 (4%, [M+H]$^+$), 991.4 (16%, [2M + Na]$^+$).

4.3.40. 28-Acetyloxy-lup-20(29)-en-3-one (**42**)

Jones oxidation of **41** (3.0 g, 6.22 mmol) for 40 min at 25 °C as previously described, followed by usual aqueous workup and chromatography (silica gel, hexanes/ethyl acetate, 8:2) gave **42**

(2.14 g, 71.6%) as a colorless solid; R_F = 0.73 (silica gel, hexanes/ethyl acetate, 8:2); m.p.: 91–94 °C (lit.: [65] 77–79 °C); $[\alpha]_D$ = +37.1° (*c* = 0.35, $CHCl_3$), (lit.: [66] $[\alpha]_D$ = +38.0° ($CHCl_3$)); MS (ESI, MeOH): *m/z* = 483.2 (26%, $[M+H]^+$), 505.3 (8%, $[M+Na]^+$), 536.8 (10%, $[M + Na + MeOH]^+$), 965.1 (12%, $[2M + H]^+$), 987.3 (70%, $[2M + Na]^+$).

*4.3.41. 28-Hydroxy-lup-20(29)en-3-one (**43**)*

Deacetylation of 42 (2.1 g, 4.36 mmol) with KOH (0.61 g, 10.9 mmol) in THF (20 mL) and MeOH (10 mL) for 12 h at 25 °C as described above, followed by usual workup and chromatography (silica gel, hexanes/ethyl acetate, 8:2) gave 43 (1.73 g, 90.4%) as a colorless solid; R_F = 0.45 (silica gel, hexanes/ethyl acetate, 8:2); m.p.: 103–105 °C (lit.: [67] 94–96 °C); $[\alpha]_D$ = +45.0° (*c* = 0.40, $CHCl_3$), (lit.: [67] $[\alpha]_D$ = +52.7° ($CHCl_3$)); MS (ESI, MeOH): *m/z* = 423.1 (31%, $[M + H-H_2O]^+$), 441.2 (46%, $[M+H]^+$), 881.4 (29%, $[2M + H]^+$), 903.4 (100%, $[2M + Na]^+$).

*4.3.42. 3-Oxo-lup-20(29)-en-28-N-ethylcarbamate (**44**)*

Microwave assisted reaction (7 h, 120 °C) of **43** (0.3 g, 0.682 mmol) in dry THF (5 mL) with ethyl isocyanate (0.15 mg, 0.16 mL, 2.05 mmol) as described above, followed by chromatography (silica gel, hexanes/ethyl acetate, 8:2) gave **44** (0.237 g, 68.0%) as a colorless solid; R_F = 0.32 (silica gel, hexanes/ethyl acetate, 8:2); m.p.: 83–86 °C; $[\alpha]_D$ = +34.7° (*c* = 0.32, $CHCl_3$); IR (KBr): *ν* = 3441*s*, 2945*s*, 2870*m*, 1706*s*, 1639*m*, 1523*w*, 1458*m*, 1384*w*, 1243*m*, 1138*w*, 1112*w*, 1080*w*, 1023*m*, 882*w*, 774*w* cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* = 4.68 (*s*, 1H, CH_a (29)), 4.60 (*br*, 1H, N*H*), 4.58 (*s*, 1H, CH_b (29)), 4.26 (*d*, *J* = 10.7 Hz, 1H, CH_a (28)), 3.83 (*d*, *J* = 10.9 Hz, 1H, CH_b (28)), 3.22 (*br*, 2H, CH_2 (32)), 2.53–2.43 (*m*, 2H, *CH* (19) + CH_a (2)), 2.37 (*ddd*, *J* = 15.7, 7.4, 4.5 Hz, 1H, CH_b (2)), 2.05–1.94 (*m*, 1H, CH_a (21)), 1.92–1.86 (*m*, 1H, CH_a (1)), 1.81–1.71 (*m*, 3H, CH_a (22) + CH_a (16) + CH_a (15)), 1.68 (*s*, 3H, CH_3 (30)), 1.68–1.64 (*m*, 2H, *CH* (13) + CH_a (12)), 1.62–1.56 (*m*, 1H, *CH* (18)), 1.49–1.39 (*m*, 4H, CH_2 (6) + CH_2 (7)), 1.36–1.30 (*m*, 4H, *CH* (9) + CH_b (1) + CH_b (21) + CH_a (11)), 1.28–1.26 (*m*, 1H, *CH* (5)), 1.25–1.20 (*m*, 2H, CH_b (11) + CH_b (16)), 1.14 (*t*, *J* = 7.2 Hz, 3H, CH_3 (33)), 1.08 (*s*, 3H, CH_3 (25)), 1.06 (*s*, 3H, CH_3, (23)), 1.05–1.00 (*m*, 3H, CH_b (22) + CH_b (15) + CH_b (12)), 1.02 (*s*, 3H, CH_3 (24)), 0.98 (*s*, 3H, CH_3 (27)), 0.93 (*s*, 3H, CH_3 (26)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 218.0 (*C*=O, C3), 157.0 (*C*=O, C31), 150.2 (*C*=CH_2, C20), 109.8 (H_2C=C, C29), 62.8 (CH_2, C28), 55.0 (*CH*, C5), 49.8 (*CH*, C9), 48.7 (*CH*, C18), 47.6 (*CH*, C19), 47.3 (C_q, C4), 46.6 (C_q, C17), 42.8 (C_q, C14), 40.8 (C_q, C8), 39.6 (CH_2, C1), 37.6 (*CH*, C13), 36.9 (C_q, C10), 36.1 (CH_2, C32), 34.5 (CH_2, C22), 34.1 (CH_2, C2), 33.5 (CH_2, C7), 29.8 (CH_2, C16), 29.6 (CH_2, C21), 27.1 (CH_2, C15), 26.5 (CH_3, C23), 25.2 (CH_2, C12), 21.3 (CH_2, C11), 21.0 (CH_3, C24), 19.6 (CH_2, C6), 19.1 (CH_3, C30), 15.9 (CH_3, 25), 15.8 (CH_3, C26), 15.3 (CH_3, C33), 14.7 (CH_3, C27) ppm; MS (ESI, MeOH): *m/z* = 512.1 (100%, $[M + H]^+$), 529.1 (7%, $[M + NH_4]^+$), 534.3 (17%, $[M + Na]^+$), 1023.5 (100%, $[2M + H]^+$), 1025.5 (64%, $[2M + Na]^+$); analysis calcd for $C_{33}H_{53}NO_3$ (511.78): C 77.45, H 10.44, N 2.74; found: C 77.39, H 10.51, N 2.57.

*4.3.43. 3-Oxo-lup-20(29)-en-28-N-propylcarbamate (**45**)*

Microwave assisted reaction (7 h, 120 °C) of **43** (0.29 g, 0.659 mmol) in dry THF (5 mL) with propyl isocyanate (0.17 g, 0.19 mL, 1.98 mmol) as described above, followed by chromatography (silica gel, hexanes/ethyl acetate, 8:2) gave **45** (0.216 g, 62.0%) as a colorless solid; R_F = 0.35 (silica gel, hexanes/ethyl acetate, 8:2); m.p.: 87–91 °C; $[\alpha]_D$ = +34.5° (*c* = 3.4, $CHCl_3$); IR (KBr): *ν* = 3406*s*, 2958*s*, 2870*m*, 1706*s*, 1642*w*, 1530*w*, 1459*m*, 1384*w*, 1236*m*, 1138*w*, 1112*w*, 1044*w*, 1004*w*, 882*w*, 776*w* cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* = 4.72–4.64 (*br*, 1H, N*H*), 4.67 (*s*, 1H, CH_a (29)), 4.57 (*s*, 1H, CH_b (29)), 4.26 (*d*, *J* = 10.8 Hz, 1H, CH_a (28)), 3.82 (*d*, *J* = 10.7 Hz, 1H, CH_b (28)), 3.13 (*br*, 2H, CH_2 (32)), 2.53–2.42 (*m*, 2H, *CH* (19) + CH_a (2)), 2.37 (*ddd*, *J* = 15.6, 7.5, 4.4 Hz, 1H, CH_b (2)), 2.07–1.93 (*m*, 1H, CH_a (21)), 1.92–1.82 (*m*, 1H, CH_a (1)), 1.82–1.69 (*m*, 3H, CH_a (16) + CH_a (22) + CH_a (15)), 1.67 (*s*, 3H, CH_3 (30)), 1.69–1.55 (*m*, 4H, *CH* (13) + CH_2 (12) + *CH* (18)), 1.54–1.47 (*m*, 2H, CH_2 (33)), 1.47–1.33 (*m*, 8H, CH_2 (6) + CH_2 (7) + CH_a (11) + CH_b (21) + CH_b (1) + *CH* (9)), 1.25 (*m*, 3H, *CH* (5) + CH_b (11) + CH_b (16)), 1.10–0.99 (*m*, 2H, CH_b (22) + CH_b (15)), 1.07 (*s*, 3H, CH_3 (25)) 1.05 (*s*, 3H, CH_3, (23)), 1.01 (*s*, 3H, CH_3 (24)), 0.97 (*s*, 3H, CH_3, (27)), 0.9 (*s*, 3H, CH_3 (26)), 0.91 (*t*, *J* = 2.0 Hz, 3H, CH_3 (34)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 218.0 (*C*=O, C3), 157.1 (*C*=O, C31), 150.2 (*C*=CH_2, C20), 109.8 (H_2C=C, C29), 62.8 (CH_2, C28), 55.0 (*CH*, C5), 49.7 (*CH*, C9), 48.7 (*CH*, C18), 47.6 (*CH*, C19), 47.3 (C_q, C4), 46.6 (C_q, C17), 43.3 (CH_2, C32), 42.7 (C_q, C14), 40.8 (C_q, C8), 39.6 (CH_2, C1), 37.6 (*CH*, C13), 36.9 (C_q, C10), 34.5 (CH_2, C22), 34.1 (CH_2, C2), 33.5 (CH_2, C7), 29.8 (CH_2, C16), 29.6 (CH_2, C21), 27.1 (CH_2, C15), 26.5 (CH_3, C23), 25.2 (CH_2, C2), 23.2 (CH_2, C33), 21.3 (CH_2, C11), 21.0 (CH_3, C24), 19.6 (CH_2, C6), 19.1 (CH_3, C30), 15.9 (CH_3, 25), 15.8 (CH_3, C26), 14.7 (CH_3, C27), 11.2 (CH_3, C34) ppm; MS (ESI, MeOH): *m/z* = 526.2 (40%, $[M + H]^+$), 548.4 (6%, $[M + Na]^+$), 1051.6 (100%, $[2M + H]^+$], 1073.6 (46%, $[2M + Na]^+$); analysis calcd for $C_{34}H_{55}NO_3$ (525.81): C 77.66, H 10.54, N 2.66; found: C 77.51, H 10.69, N 2.50.

*4.3.44. 3-Oxo-lup-20(29)-en-28-N-butylcarbamate (**46**)*

Microwave assisted reaction (7 h, 120 °C) of **43** (0.28 g, 0.682 mmol) in dry THF (5 mL) with butyl isocyanate (0.2 g, 0.23 mL, 2.05 mmol) as described above, followed by chromatography (silica gel, hexanes/ethyl acetate, 8:2) gave **46** (0.246 g, 72.0%) as a colorless solid; R_F = 0.51 (silica gel, hexanes/ethyl acetate, 8:2); m.p.: 84–86 °C; $[\alpha]_D$ = +32.4° (*c* = 3.65, $CHCl_3$); IR (KBr): *ν* = 3416*s*, 2956*s*, 2870*m*, 1706*s*, 1642*w*, 1530*m*, 1460*m*, 1384*w*, 1245*m*, 1136*w*, 1112*w*, 1052*w*, 1021*m*, 882*w*, 776*w* cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* = 4.68 (*s*, 1H, CH_a (29)), 4.64 (*br*, 1H, N*H*), 4.58 (*s*, 1H, CH_b (29)), 4.26 (*d*, *J* = 10.5 Hz, 1H, CH_a (28)), 3.83 (*d*, *J* = 10.5 Hz, 1H, CH_b (28)), 3.17 (*br*, 2H, CH_2 (32)), 2.55–2.42 (*m*, 2H, *CH* (19) + CH_a (2)), 2.38 (*ddd*, *J* = 15.5, 7.4, 4.3 Hz, 1H, CH_b (2)), 2.07–1.93 (*m*, 1H, CH_a (21)), 1.92–1.83 (*m*, 1H, CH_a (1)), 1.82–1.69 (*m*, 3H, CH_a (16) + CH_a (22) + CH_a (15)), 1.69–1.54 (*m*, 4H, *CH* (13) + CH_2 (12) + *CH* (18)), 1.67 (*s*, 3H, CH_3 (30)), 1.53–1.41 (*m*, 6H, CH_2 (33) + CH_2 (6) + CH_2 (7)), 1.41–1.33 (*m*, 5H, CH_2 (11) + CH_b (21) + CH_b (1) + *CH* (9)), 1.32–1.17 (*m*, 4H, *CH* (5) + CH_b (16) + CH_2 (34)), 1.11–1.05 (*m*, 2H, CH_b (22) + CH_b (15)), 1.07 (*s*, 3H, CH_3 (25)), 1.06 (*s*, 3H, CH_3 (23)), 1.02 (*s*, 3H, CH_3 (24)), 0.97 (*s*, 3H, CH_3 (27)), 0.94 (*s*, 3H, CH_3 (26)), 0.92 (*t*, *J* = 7.7 Hz, 3H, CH_3 (35)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 218.0 (*C*=O, C3), 157.2 (*C*=O, C31), 150.2 (*C*=CH_2, C20), 109.8 (H_2C=O, C29), 62.8 (CH_2, C28), 55.0 (*CH*, C5), 49.7 (*CH*, C9), 48.8 (*CH*, C18), 47.6 (*CH*, C19), 47.3 (C_q, C4), 46.6 (C_q, C17), 42.8 (C_q, C14), 40.8 (C_q, C8), 40.8 (CH_2, C32), 39.1 (CH_2, C1), 37.6 (*CH*, C13), 36.9 (C_q, C10), 34.5 (CH_2, C22), 34.1 (CH_2, C2), 33.5 (CH_2, C7), 32.1 (CH_2, C33), 29.8 (CH_2, C16), 29.6 (CH_2, C21), 27.1 (CH_2, C15), 26.5 (CH_3, C23), 25.2 (CH_2, C12), 21.3 (CH_2, C11), 21.0 (CH_3, C24), 19.9 (CH_2, C34), 19.6 (CH_2, C6), 19.1 (CH_3, C30), 15.9 (CH_3, C25), 15.9 (CH_3, C26), 14.7 (CH_3, C27), 13.7 (CH_3, C35) ppm; MS (ESI, MeOH): *m/z* = 540.2 (72%, $[M + H]^+$), 562.5 (8%, $[M + Na]^+$), 1079.5 (100%, $[2M + H]^+$), 1101.5 (49%, $[2M + Na]^+$); analysis calcd for $C_{35}H_{57}NO_3$ (539.83): C 77.87, H 10.64, N 2.59; found: C 77.61, H 10.83, N 2.41.

*4.3.45. 3-Oxo-lup-20(29)-en-28-N-hexylcarbamate (**47**)*

Microwave assisted reaction (7 h, 120 °C) of **43** (0.29 g, 0.66 mmol) in dry THF (5 mL) with hexyl isocyanate (0.25 g, 0.29 mL, 1.98 mmol) as described above, followed by chromatography (silica gel, hexanes/ethyl acetate, 8:2) gave **47** (0.205 g, 55.1%) as a colorless solid; R_F = 0.57 (silica gel, hexanes/ethyl acetate, 8:2); m.p.: 76–79 °C; $[\alpha]_D$ = +29.8° (*c* = 0.52, $CHCl_3$); IR (KBr):

ν = 3397*m*, 2951*s*, 2869*s*, 1706*s*, 1640*w*, 1522*m*, 1458*m*, 1384*w*, 1243*m*, 1138*w*, 1112*w*, 1041*w*, 1018*w*, 882*w*, 776*w*, 580*w* cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 4.68 (*s*, 1H, CH_a (29)), 4.63 (*br*, 1H, N*H*), 4.58 (*s*, 1H, CH_b (29)), 4.26 (*d*, *J* = 10.7 Hz, 1H, CH_a (28)), 3.83 (*d*, *J* = 10.8 Hz, 1H, CH_b (28)), 3.17 (*br*, 2H, CH_2 (32)), 2.54–2.42 (*m*, 2H, C*H* (19) + CH_a (2)) 2.38 (*ddd*, *J* = 15.6, 7.5, 4.3 Hz, 1H, CH_b (2)), 2.00 (*m*, 1H, CH_a (21)), 1.93–1.83 (*m*, 1H, CH_a (1)), 1.83–1.69 (*m*, 3H, CH_a (16) + CH_a (22) + CH_a (15)), 1.67 (*s*, 3H, CH_3 (30)), 1.69–1.54 (*m*, 4H, C*H* (13) + CH_2 (12) + C*H* (18)), 1.54–1.40 (*m*, 6H, CH_2 (33) + CH_2 (6) + CH_2 (7)), 1.39–1.31 (*m*, 4H, C*H* (9) + CH_b (1) + CH_b (21) + CH_a (11)), 1.30–1.26 (*m*, 7H, CH_2 (34) + CH_2 (36) + CH_2 (35) + C*H* (5)), 1.26–1.16 (*m*, 2H, CH_b (11) + CH_b (16)), 1.07 (s, 3H, CH_3 (25)), 1.06 (*s*, 3H, CH_3 (23)) 1.12–0.95 (*m*, 2H, CH_b (22) + CH_b (15)), 1.02 (*s*, 3H, CH_3 (24)), 0.97 (*s*, 3H, CH_3 (27)), 0.92 (*s*, 3H, CH_3 (26)), 0.88 (*t*, *J* = 6.5 Hz, 3H, CH_3 (37)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 218.0 (*C*=O, C3), 157.1 (*C*=O, C31), 150.2 (*C*=CH_2, C20), 109.8 (H_2C=C, C29), 62.8 (CH_2, C28), 55.0 (*C*H, C5), 49.8 (*C*H, C9), 48.8 (*C*H, C18), 47.6 (*C*H, C19), 47.3 (C_q, C4), 46.6 (C_q, C17), 42.8 (C_q, C14), 41.1 (CH_2, C32), 40.8 (C_q, C8), 39.6 (CH_2, C1), 37.6 (*C*H, C13), 36.9 (C_q, C10), 34.5 (CH_2, C22), 34.1 (CH_2, C2), 33.5 (CH_2, C7), 31.5 (CH_2, C35), 30.0 (CH_2, C33), 29.8 (CH_2, C6), 29.7 (CH_2, C21), 27.1 (CH_2, C15), 26.5 (CH_3, C23), 26.4 (CH_2, C34), 25.2 (CH_2, C12), 22.5 (CH_2, C36), 21.3 (CH_2, C11), 21.0 (CH_3, C24), 19.6 (CH_2, C6), 19.1 (CH_3, C30), 15.9 (CH_3, C25), 15.8 (CH_3, C26), 14.7 (CH_3, C27), 14.0 (CH_3, C37) ppm; MS (ESI, MeOH): *m*/*z* = 568.1 (30%, $[M + H]^+$), 590.5 (4%, $[M + Na]^+$), 1135.6 (100%, $[2M + H]^+$), 1157.8 (32%, $[2M + Na]^+$); analysis calcd for $C_{37}H_{61}NO_3$ (567.89): C 78.25, H 10.83, N 2.47; found: C 78.01, H 10.97, N 2.38.

4.3.46. 3-Oxo-lup-20(29)-en-28-N-phenylcarbamate (**48**)

Microwave assisted reaction (7 h, 120 °C) of **43** (0.3 g, 0.682 mmol) in dry THF (5 mL) with phenyl isocyanate (0.24 g, 0.22 mL, 2.05 mmol) as described above, followed by chromatography (silica gel, hexanes/ethyl acetate, 8:2) gave **48** (0.325 g, 85.3%) as a colorless solid; R_F = 0.53 (silica gel, hexanes/ethyl acetate, 8:2); m.p.: 200–202 °C; $[\alpha]_D$ = +23.3° (*c* = 0.46, $CHCl_3$); IR (KBr): ν = 3443*s*, 2945*s*, 2868*m*, 2362*w*, 2344*w*, 1734*s*, 1700*s*, 1602*m*, 1540*m*, 1442*m*, 1386*w*, 1374*w*, 1216*m*, 1057*w*, 1030*w*, 882*w*, 752*w*, 692*w* cm^{-1}; UV–vis ($CHCl_3$): λ_{max} (log ε) = 234.4 (4.23) nm; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.39 (*d*, *J* = 7.9 Hz, 2H, *HC*=C (33/33′)), 7.31 (*t*, *J* = 7.8 Hz, 2H, *HC*=C (34/34′)), 7.06 (*t*, *J* = 7.3 Hz, 1H, *HC*=C (35)), 6.63 (*br*, 1H, N*H*), 4.70 (*s*, 1H, CH_a (29)), 4.60 (*s*, 1H, CH_b (29)), 4.38 (*d*, *J* = 10.8 Hz, 1H, CH_a (28)), 3.96 (*d*, *J* = 10.7 Hz, 1H, CH_b (28)), 2.55–2.43 (*m*, 2H, C*H* (19) + CH_a (2)), 2.39 (*ddd*, *J* = 15.6, 7.4, 4.2 Hz, 1H, CH_b (2)), 2.10–1.95 (*m*, 1H, CH_a (21)), 1.95–1.80 (*m*, 3H, CH_a (1) + CH_a (22) + CH_a (16)), 1.78–1.57 (*m*, 4H, CH_a (15) + CH_a (12) + C*H* 13 + C*H* (18)), 1.69 (*s*, 3H, CH_3 (30)), 1.55–1.35 (*m*, 8H, CH_2 (7) + CH_2 (6) + CH_b (21) + CH_a (11) + CH_b (1) + C*H* (9)), 1.35–1.22 (*m*, 3H, C*H* (5) + CH_b (11) + CH_b (16)), 1.14–1.04 (*m*, 3H, CH_b (22) + CH_b (15) + CH_b (12)) 1.09 (*s*, 3H, CH_3 (25)), 1.07 (*s*, 3H, CH_3 (23)), 1.03 (*s*, 3H, CH_3 (24)), 0.99 (*s*, 3H, CH_3 (27)), 0.94 (*s*, 3H, CH_3 (26)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 218.5 (*C*=O, C3), 154.0 (*C*=O, C31), 150.0 (*C*=CH_2, C20), 137.9 (C_q, C32), 129.1 (*C*H, C34/34′), 123.4 (*C*H, C35), 118.6 (*C*H, C33/33′), 109.9 (H_2C=C, C29), 63.5 (CH_2, C28), 55.0 (*C*H, C5), 49.7 (*C*H, C9), 48.8 (*C*H, C18), 47.6 (*C*H, C19), 47.4 (C_q, C4), 46.6 (C_q, C17), 42.8 (C_q, C14), 40.8 (C_q, C8), 39.6 (CH_2, C1), 37.7 (*C*H, C13), 36.9 (C_q, C10), 34.5 (CH_2, C22), 34.2 (CH_2, C2), 33.5 (CH_2, C7), 29.8 (CH_2, C16), 29.6 (CH_2, C21), 27.1 (CH_2, C15), 26.6 (CH_3, C23), 25.2 (CH_2, C12), 21.3 (CH_2, C11), 21.1 (CH_3, C24), 19.6 (CH_2, C6), 19.2 (CH_3, C30), 15.9 (CH_3, C25), 15.9 (CH_3, C26), 14.7 (CH_3, C27) ppm; MS (ESI, MeOH): *m*/*z* = 560.0 (12%, $[M + H]^+$), 582.3 (34%, $[M + Na]^+$), 613.3 (10%, $[M + Na + MeOH]^+$), 1119.3 (58%, $[2M + H]^+$), 1141.5 (100%, $[2M + Na]^+$); analysis calcd for $C_{37}H_{53}NO_3$ (559.82): C 79.38, H 9.54, N 2.50; found: C 79.13, H 9.61, N 2.43.

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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.2015.10.043.

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