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Mediterranean Journal of Chemistry

Mediterranean Journal of Chemistry **2022**, 12(2), 188-200

Triterpenoid cholinesterase inhibitors that might improve gait disturbances in Parkinson's disease patients

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Abstract: Parkinson's disease (PD) is the second most common neurodegenerative disease. Besides rigidity and tremor, patients often suffer from gait disturbance. Treatment with cholinesterase inhibitors (ChEI) has been shown to improve gait speed. Thus, the triterpene acids oleanolic acid and ursolic acid have been used as starting materials for the synthesis of compounds intended to act as inhibitors of the enzymes acetylcholinesterase (AChE) and butyrylcholinesterase (BChE). The parent compounds were acetylated and converted via isocyanates and amines into a series of amides, while the isocyanates were also used as starting materials for the synthesis of several urea derivatives. Screening of the compounds with the cholinesterases showed them to be good to moderate inhibitors, with ursolic acid derived isocyanate being a superior mixed-type dual inhibitor for both enzymes holding K_i values in the low μM concentration range. The data from the experiments parallel the results from molecular modeling calculations. In addition, this compound is remarkably stable in an aqueous solution and undergoes decarboxylative hydrolysis to the corresponding amine only at 50 °C after several hours.

Keywords: Ursolic acid; Oleanic acid; Acetylcholinesterase; Butyrylcholinestase; Parkinson's disease.

1. Introduction

Inhibitors of the enzyme acetylcholinesterase are usually seen in connection with Alzheimer's disease [1-12]. However, it is often overlooked that the second most common neurodegenerative disease is Parkinson's disease (PD). PD mainly affects the motoric behavior of patients, which manifests itself in rigidity, tremor, bradykinesia, and gait disturbance [13-16]. However, the last symptom cannot be reduced either by dopaminergic replacement therapy or traditional subthalamic deep brain stimulation. In individual cases, the latter therapy even leads to a worsening of the clinical picture. In a recent meta-study, however, it was revealed that treatment with cholinesterase inhibitors (ChEI) might improve gait speed [17]. In previous work, we showed that some derivatives of triterpenoic acids are characterized by relatively low cytotoxicity but at the same time, proved to be good inhibitors of the enzymes acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) [18-30]. In this regard, some iminium salts [19] and diazabicyclo [3.2.2.]nonane-substituted derivatives [18], but also those derived from dehydroabietylamines [26,30], were found to be excellent inhibitors of the enzyme BChE esterase. In contrast, some derivatives, particularly those derived from platanic acid, [20] were suitable inhibitors for AChE.

As exemplified by the AChE inhibitor rivastigmine, Carbamates have been investigated very often due to their ability to inhibit this enzyme. Since amides can be regarded as bioisosteric replacements of carbamates, amides have also been studied [31-33] in this context, while urea functionality is inherent [34] in numerous bioactive compounds. Since we were looking for improved inhibitors, we decided to extend our studies to amide and urea derivatives of ursolic and oleanolic acids, respectively.

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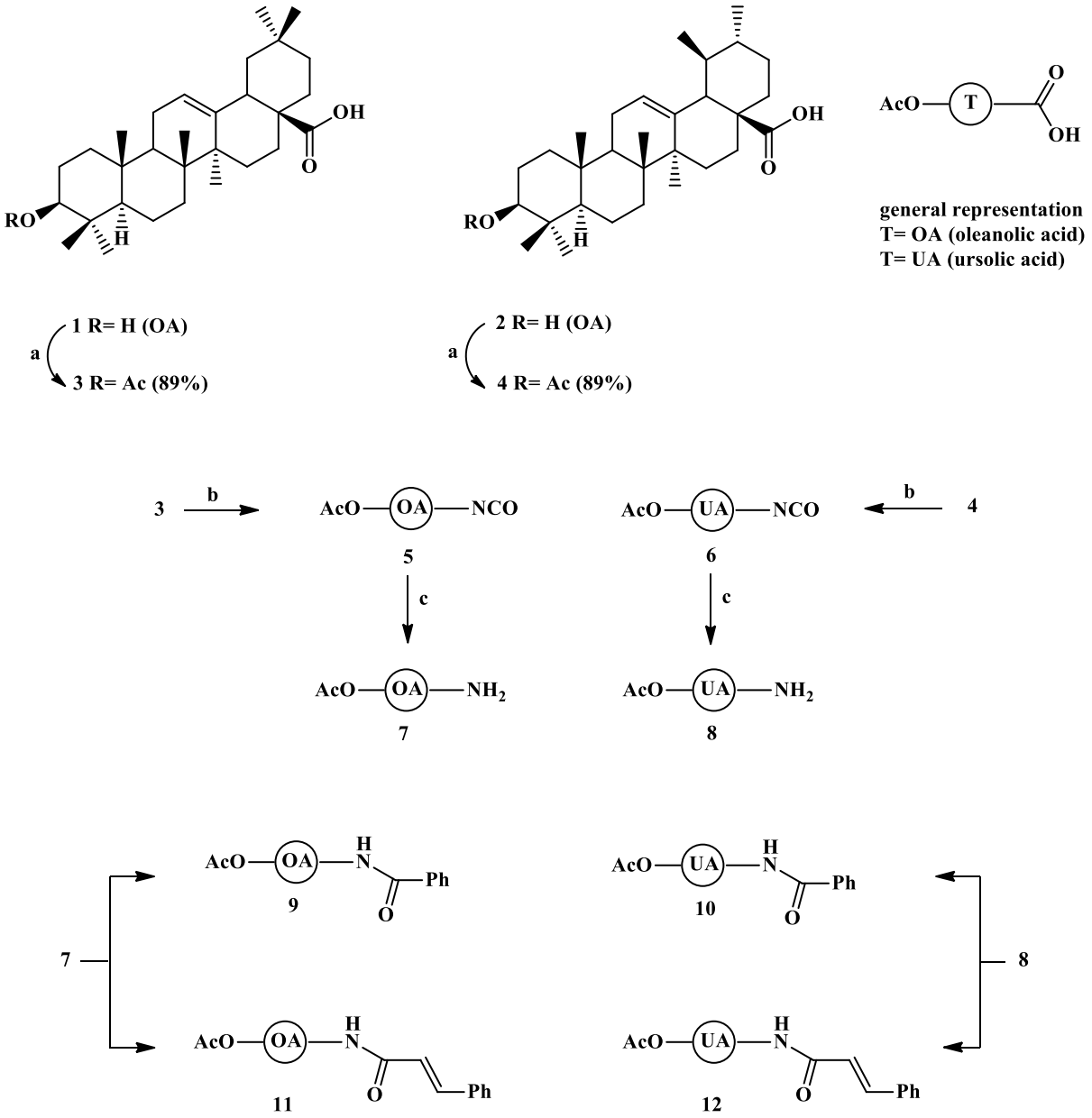
DOI: http://dx.doi.org/10.13171/mjc02211021650csuk

Received Septeber 26, 2022
Accepted October 22, 2022
Published November 2, 2022

2. Results and Discussion

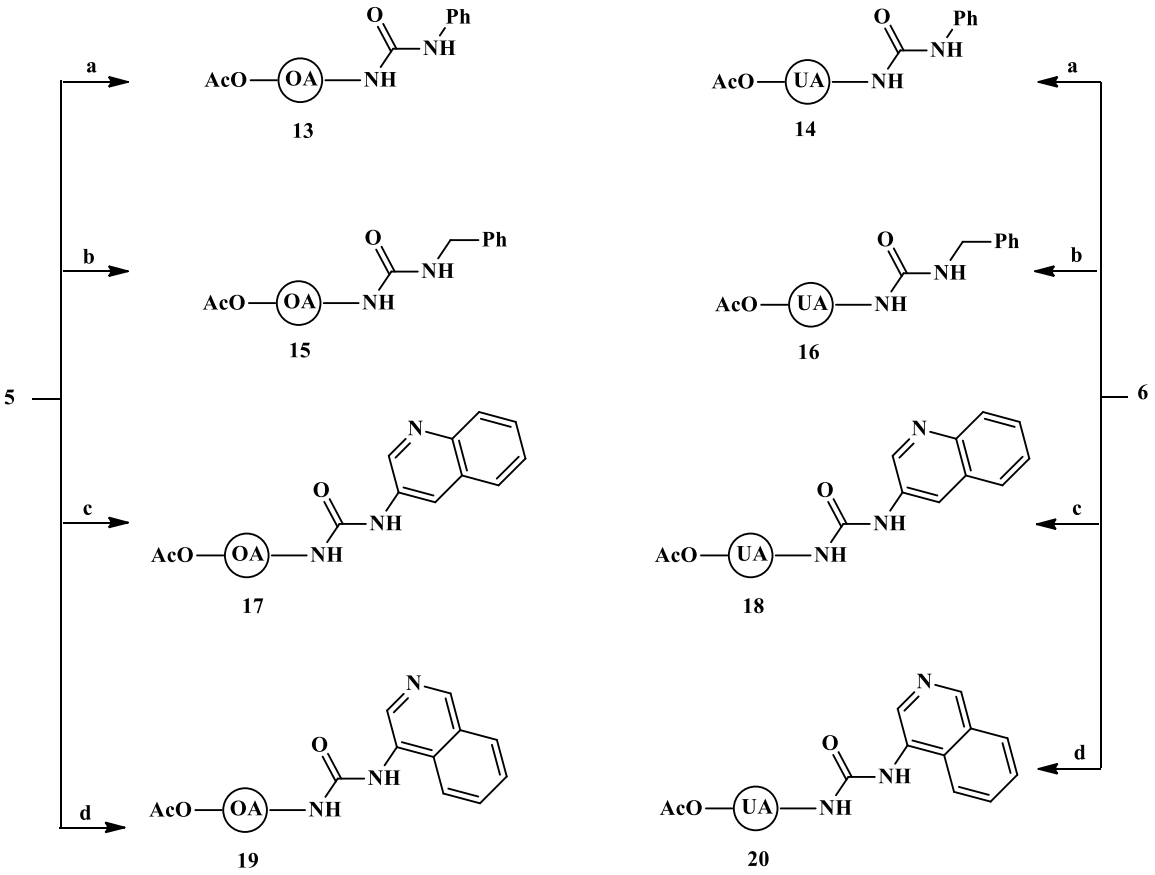
The starting point of the syntheses was oleanolic acid (**OA**, **1**, Scheme 1) and ursolic acid (**UA**, **2**), which were converted into the known [35] acetates **3** and **5**. Treatment of **3** and **5** with diphenylphosporylazide [36] in the presence of triethylamine in toluene gave in good yields the isocyanates **5** and **6**, whose hydrolysis led to the amines **7** and **8** [37], respectively.



Scheme 1. Synthesis of **OA** (**1**) and **UA** (**2**) derived amides **9**–**12**; reactions and conditions: a) Ac_2O, pyridine, DMAP (cat.), 21°C, 3h: 89% of **3** and 90% of **4**; b) DPPA, NEt_3, toluene, 21°C, 12 h: 96% of **5** and 96% of **6**; c) aq. HCl, THF, 50°C, 24 h: 47% of **7** and 90% of **8**; d) BzCl, cat. NEt_3, DMAP (cat.), DCM, 21 °C, 2 h: 86 % of **9** and quant. yield of **10**; cinnamic acid, $(COCl)_2$, DMF (cat), then DCM, NEt_3, DMAP, 21 °C, 2 h: 89% of **11** and 68% of **12**

Hydrolysis of the isocyanates proceeded very slowly at room temperature; within 48 h (21°C, pH = 7) only trace amounts of the amines could be detected by TLC. However, hydrolysis succeeded at 50 °C in a THF/aq. HCl mixture within one day. Benzoylation of **7** and **8** gave the benzamides **9** and **10**, while reaction with cinnamic acid chloride afforded the target compounds **11** and **12**, respectively.

Isocyanates **5** and **6** also provided the starting material for synthesizing urea derivatives (Scheme 2). The reaction of **5** and **6** with aniline gave the phenylurea **13** and **14**, while with benzylamine, the benzylurea **15** and **16** were obtained in quantitative yield. The microwave-assisted reaction of **5** and **6** with 3-amino-quinoline and 4-amino-isoquinoline gave the derivatives **17**–**20**, albeit in reduced yields.



Scheme 2. Synthesis of ureas **13**–**20**: aniline, NEt_3, toluene, 21°C, 12 h: 46% of **13** and 81% of **14**; b) $BnNH_2$, NEt_3, toluene, 21°C, 12 h: quant yields of **15** and **16**; c) 3-amino-quinoline, NEt_3, 90°C, 5 h (microwave-assisted): 50% of **17** and 30% of **18**; 4-amino-isoquinoline, NEt_3, 90°C, 5 h (microwave-assisted): 35% of **19** and 30% of **20**

The compounds were subjected to Ellman's assays to establish their activity as inhibitors for AChE and BChE. The results from these experiments are summarized in Table 1.

Table 1. Results from Ellman's assays for compounds **6**, **9**-**20** (compounds **5**, **7,** and **8** were not soluble under the assay conditions); all experiments were performed in triplicate with three technical replicas each; concentration of the inhibitor 10 μM.

Compound	Inhibition *ee*AChE [%]	Inhibition *eq*BChE [%]
6	94.8 ± 0.2	96.2 ± 0.1
9	82.1 ± 0.2	69.9 ± 0.2
10	83.9 ± 1.8	68.1 ± 0.5
11	81.4 ± 0.2	75.8 ± 1.0
12	83.7 ± 0.2	77.3 ± 0.1
13	77.1 ± 0.2	70.1 ± 0.4
14	79.4 ± 0.3	67.5 ± 0.8
15	81.2 ± 0.5	69.7 ±0.9
16	83.4 ± 0.5	71.9 ± 0.3
17	67.1 ± 0.3	57.4 ± 0.1
18	90.9 ± 0.1	77.2 ± 2.0
19	62.8 ± 0.4	44.6 ± 1.1
20	59.7 ± 0.3	43.1 ± 0.3
Galantamine	86.4 ± 0.3	42.7 ± 0.4

To better understand these results, molecular modeling calculations were performed. For the enzyme AChE is concerned, for compound **6** all conformations showed optimal docking with the interactions to Ile287 and Arg289 or Trp84. In particular, the oxygen of the ester served as a hydrogen acceptor to Arg289, resulting in an energy gain of -2.8 kcal/mol. Their distance was calculated with 2.1 Å. Compound **6** has the best score in docking. The main reason is most probably the size of this molecule.

Consequently, the improved and unhindered movement within the binding pocket allows optimal positioning of the molecule to the amino acids of the enzyme. Thus, the distances are smaller to the essential amino acids isoleucine, arginine, tryptophan, and ligand/receptor interactions are tight. A depiction is found in Fig. 2 (left).

Extra measurements employing compounds **6**, **11**, **12**, **14**–**16,** and **18** showed them to act as mixed-type inhibitors. The respective K_i and K_i' values have been compiled in Table 2. The Dixon, Cornish-Bowden, and Lineweaver-Burk plots are depicted in Fig. 1.

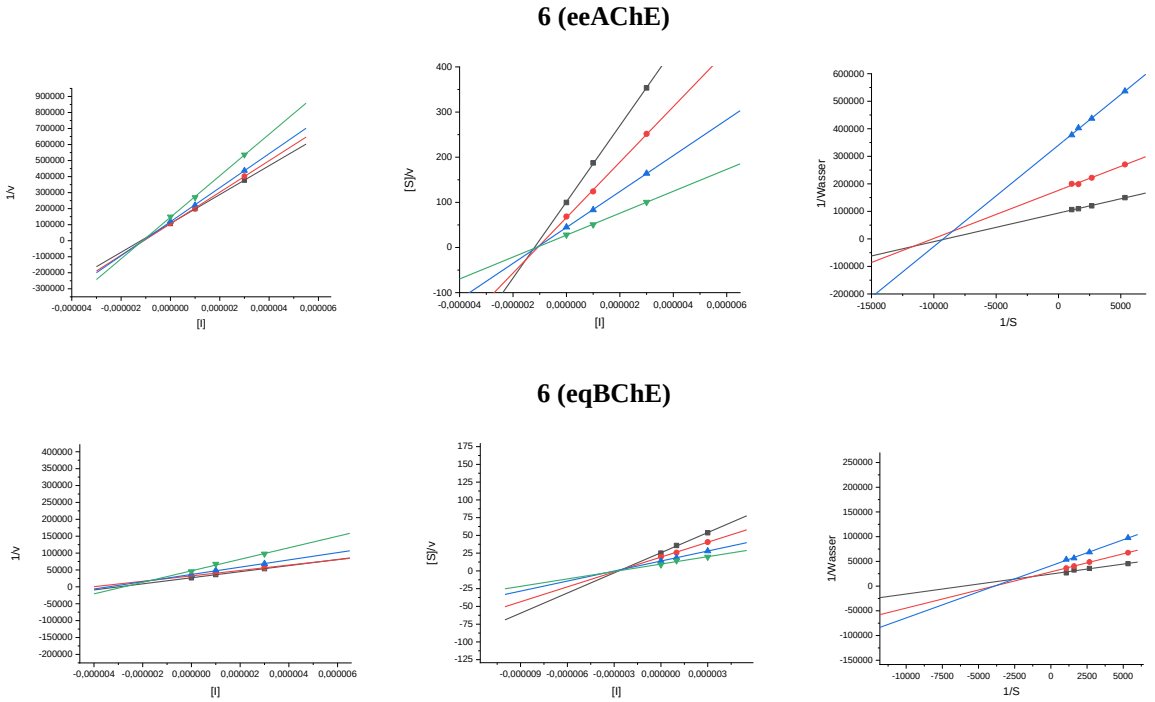


Figure 1. Dixon (left), Cornish-Bowden (middle), and Lineweaver-Burk (right) plots for **6**, eeAChE and eqBChE

Compounds **14**–**16** exhibited somewhat similar inhibition percentage values. This is also reflected in their docking results. Thus, **16** shows the molecule's optimal positioning in the enzyme's active site. In contrast, for **15**, several donor/acceptor interactions (compared to **16**) are missing, and the distances between ligand and receptor are larger than in **16**. This is probably due to the different orientations of the methyl groups at positions C-19 and C-20, respectively.

Table 2. Inhibition constants (μM) for compounds **6**, **11**, **12**, **14-16**, and **18**.

	eeAChE		**eqBChE**	
	K_i	**K_i'**	**K_i**	**K_i'**
6	1.02 ± 0.24	1.19 ± 0.17	1.63 ± 0.08	2.57 ± 0.14
11	3.02 ± 0.6	4.13 ± 0.25	10.30 ± 0.72	17.40 ±2.0
12	2.88 ± 1.3	4.00 ± 0.47	14.71 ± 1.3	15.35 ± 0.9
14	13.29 ± 1.55	26.99 ± 2.99	6.21 ± 0.44	3.90 ± 0.49
15	2.10 ± 0.09	3.08 ± 0.02	8.91 ± 0.64	15.90 ± 2.12
16	2.89 ± 0.50	3.92 ± 0.24	13.1 ± 1.75	7.50 ± 1.26
18	5.41 ± 0.15	4.58 ± 0.05	5.09 ± 0.28	4.19 ± 0.29

Compound **14** showed two interactions. On the one hand, nitrogen (N37) served as a hydrogen donor to Ser122, and oxygen (O33) served as a hydrogen acceptor to Gly355. This resulted in an energy gain of -1.4 kcal/mol. On the other hand, in compound **15** the oxygen served as a hydrogen acceptor for Arg289, resulting in a distance of 2.62 Å and an energy gain of -1.8 kcal/mol. The calculation for compound **16** showed four interactions. The interaction between the oxygen of the ester and Arg289 is particularly stabilizing. With a distance of 2.4 Å, an energy gain of -2.4 kcal/mol can be assumed. In addition, residue Ile287 stabilizes the same oxygen with an energy gain of -0.5 kcal/mol. Furthermore, the interaction as a hydrogen acceptor for Gly188 and Ser122 had a positive effect with an energy gain of -2.4 kcal/mol. Thus, the ranking from the calculations perfectly meets the experimental results.

The difference in the skeleton [ursolic (**18**) vs. oleanolic (**17**, **19**)] can also be seen upon comparing compounds **17**–**19**. The orientation of the methyl groups of molecules holding an oleanolic acid backbone resulted in a greater distance to the amino acids of the enzyme. Compound **19** was even slightly outside of the binding pocket. Here, too, the result of the experiment can be explained by the calculations.

Similar results have been obtained for the molecular modeling employing the enzyme BChE. Again, for compound **6** all conformations (Fig. 2, right) showed optimal docking, with the interaction with Gly116 being of particular influence. The oxygen of the isocyanate might serve as a hydrogen acceptor from the glycine's nitrogen, or the isocyanate's nitrogen serves as a hydrogen acceptor for the glycine. These interactions result in an energy gain of -1.7 kcal/mol and -1.3 kcal/mol, respectively. The close positioning of the amino acids of the binding pocket to the structure should also be emphasized. Compound **6** has the best score in docking again, the main reason being the size of the molecule.

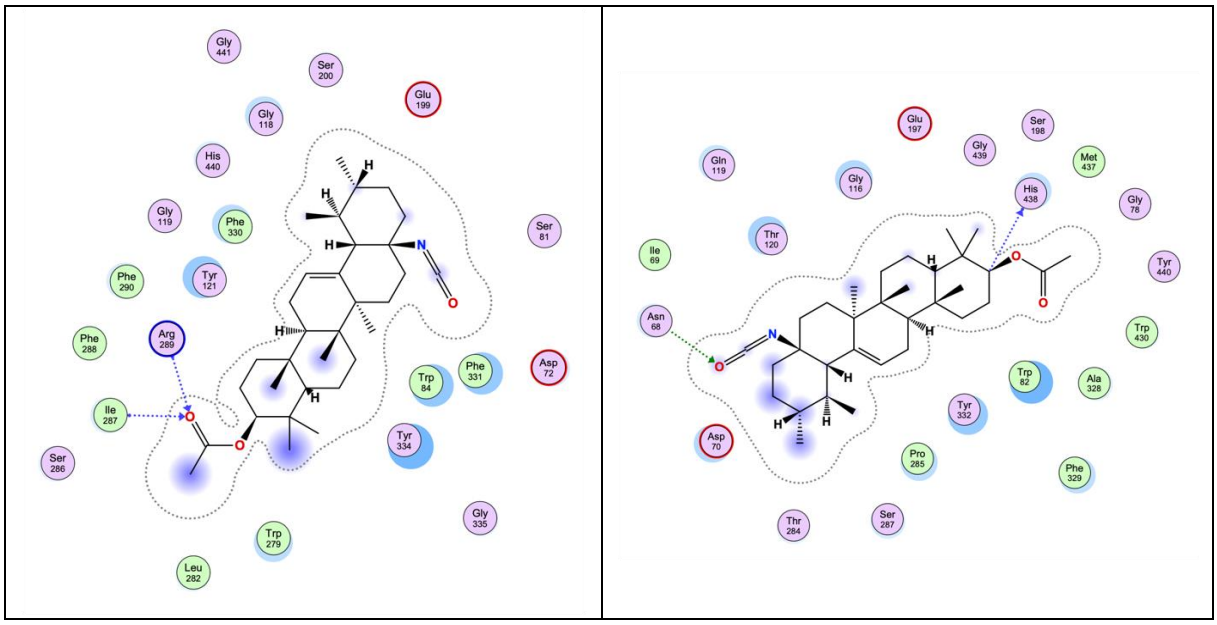


Figure 2. Depiction of the results from the modeling for compound **6** and enzymes AChE (left) and BChE (right)

For compounds **14**–**16**, very similar inhibition percentages have been determined. This is also reflected in their docking results. Again, **16** has the best docking result, identical to that calculated for **15**. Due to the larger binding pocket of BChE (as compared to AChE), the steric effect between ursolic acid and oleanolic acid is not as pronounced as with AChE. The results for compounds **17**–**19** and BChE parallel those obtained for the enzyme AChE. Here, too, the experiment results are sufficiently supported by the calculations. The results from the experiments can be explained quite well by the docking calculations. However, these results must also conclude that rather small structural changes trigger different binding behavior. Consequently, the library of compounds studied here is too small to perform meaningful SAR.

3. Conclusion

Parkinson's disease (PD) is the second most common neurodegenerative disease. Besides rigidity and tremor, patients often suffer from gait disturbance. Treatment with cholinesterase inhibitors (ChEI) are beneficial in improving gait speed. Thus, triterpenoic acids oleanolic acid and ursolic were used as starting materials for the synthesis of compounds intended to act as inhibitors of the enzymes acetylcholinesterase (AChE) and butyrylcholinesterase (BChE). The parent compounds were acetylated and converted via isocyanates and amines into a series of amides while the isocyanates were used as starting materials for the synthesis of several urea derivatives. Screening of the compounds with the esterases showed them to be good to moderate inhibitors with an ursolic acid

derived isocyanate being a superior mixed-type dual inhibitor for both enzymes holding K_i values in the low μM concentration range. The data from the experiments parallel the results from molecular modeling calculations. In addition, this compound is remarkably stable in an aqueous solution and undergoes decarboxylative hydrolysis to the corresponding amine only at 50 °C after several hours.

Acknowledgements

We would like to thank Th. Schmidt for measuring the MS spectra, Dr. D. Ströhl, Y. Schiller, and S. Ludwig for the NMR spectra. Many thanks are also due to M. Schneider for measuring the IR, UV/vis spectra, and microanalyses.

4. Experimental

NMR spectra were recorded using the Varian spectrometers (Darmstadt, Germany) DD2 and VNMRS (400 and 500 MHz, respectively). MS spectra were taken on an Advion expression LCMS mass spectrometer (Ithaca, NY, USA; positive ion polarity mode, solvent: methanol, solvent flow: 0.2 mL/min, spray voltage: 5.17 kV, source voltage: 77 V, APCI corona discharge: 4.2 μA, capillary temperature: 250°C, capillary voltage: 180 V, sheath gas: N_2). Thin-layer chromatography was performed on pre-coated silica gel plates supplied by Macherey-Nagel (Düren, Germany). IR spectra were recorded on a Spectrum 1000 FT-IR-spectrometer from Perkin Elmer (Rodgau, Germany). The UV/Vis-spectra were recorded on a Lambda 14 spectrometer from Perkin Elmer (Rodgau, Germany); optical rotations were measured at 20°C using a JASCO-P2000 instrument (JASCO Germany GmbH, Pfungstadt, Germany) The melting points were determined using a Leica hot stage microscope Galen III (Leica Biosystems, Nussloch, Germany) and are uncorrected. The solvents were dried according to the usual procedures. Microanalyses were performed with an Elementar Vario EL (CHNS) instrument (Elementar Analysensysteme GmbH, Elementar-Straße 1, D-63505, Langenselbold, Germany). The Ellman's assays have been performed as previously described. The crystal structures of the AChE (PDB = 4EY6) and BuChE (PDB = 4BDS) were retrieved from the protein databank (rcsb.org).

Oleanoic acid (1) and ursolic acid (2)
These compounds were obtained from Betulinines (Strbrna Skalice, Czech Republic) and used as received.

3-*O*-Acetyl-oleanolic acid (3) and 3-*O*-acetyl-ursolic acid (4)
The compounds were prepared as previously described [35].

3*β*-Acetyloxy-17*β*-isocyanato-28-norolean-12-ene (5)
To a solution of **3** (330 mg, 0.66 mmol) in toluene (10 mL)/Et_3N (0.14 mL, 100 mg, 1.0 mmol) diphenyl phosphoryl azide (0.17 mL, 218 mg, 0.8 mmol) was added, and the reaction mixture was stirred for 12 h at 21°C. Usual aqu. work-up followed by column chromatography (SiO_2, hexanes/ethyl acetate, 97:3) gave **5** (310 mg, 96%) as a white solid; m.p. 198–200°C (decomp.); R_F = 0.68 (hexanes/ethyl acetate, 9:1); $[\alpha]_D$ = +72.3° (*c* 0.20, $CHCl_3$);
IR (ATR): $\tilde{\nu}$ = 575*w*, 608*w*, 652*w*, 658*w*, 868*w*, 900*w*, 950*w*, 959*w*, 971*w*, 986*m*, 1010*m*, 1027*m*, 1096*w*, 1185*w*, 1212*w*, 1246*vs*, 1363*m*, 1371*m*, 1378*m*, 1387*w*, 1441*w*, 1464*w*, 1730*m*, 2250*s*, 2932*m*, 2943*m*, 2970*w* cm^{-1};
^1H NMR (500 MHz, $CDCl_3$): δ = 5.34–5.27 (m, 1H, 12-H), 4.53–4.45 (m, 1H, 3-H), 2.36 (dd, *J* = 13.7, 4.5 Hz, 1H, 18-H), 2.04 (d, *J* = 2.4 Hz, 3H, 32-H_3), 2.03–1.85 (m, 3H, 11-H_a+16-H_a+16-H_b), 1.69 (m, 2H, 2-H_a+15-H_a), 1.67–1.50 (m, 8H, 1-H_a+1-H_b+6-H_b+9-H+11-H_b+19-H_a+22-H_a+22-H_b), 1.50–1.15 (m, 6H, 2-H_b+6-H_a+7-H_a+7-H_b+19-H_b+21-H_a), 1.10 (s, 3H, 27-H_3), 1.07 (m, 1H, 15-H_b), 0.94 (s, 3H, 25-H_3), 0.92 (s, 3H, 30-H_3), 0.90 (s, 3H, 29-H_3), 0.86 (m, 6H, 23-H_3+24-H_3), 0.82 (s, 1H, 5-H), 0.77 (s, 3H, 26-H_3) ppm;
^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.1 (C-31), 143.1 (C-13), 124.1 (C-28), 123.1 (C-12), 80.8 (C-3), 62.0 (C-17), 55.3 (C-5), 48.9 (C-18), 47.3 (C-1), 45.7 (C-9), 41.7 (C-19), 39.4 (C-8), 38.2 (C-22), 37.7 (C-4), 36.8 (C-10), 35.4 (C-21), 32.9 (C-30), 32.5 (C-7), 32.3 (C-2), 30.6 (C-20), 28.1 (C-24), 27.3 (C-15), 25.9 (C-27), 23.4 (C-29), 23.3 (C-11), 23.0 (C-16), 21.4 (C-32), 18.2 (C-6), 16.8 (C-26), 16.7 (C-23), 15.4 (C-25) ppm;
MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* = 1013.6 (25%, $[2M+Na]^+$);
analysis calcd for $C_{32}H_{49}NO_3$ (495.75): C 77.53, H 9.96, N 2.83; found: C 77.40, H 10.15, N 2.75.

3*β*-Acetyloxy-17*β*-isocyanato-28-norurs-12-ene (6)
Following the procedure given for the synthesis of **5**, **6** (310 mg, 96%) was obtained from **4** (330 mg, 0.67 mmol) as a white solid; m.p. 180–182°C (decomp.); R_F = 0.67 (hexanes/ethyl acetate, 9:1); $[\alpha]_D$ = +63.8° (*c* 0.21, $CHCl_3$);
IR (ATR): $\tilde{\nu}$ = 575*w*, 662*w*, 864*w*, 901*w*, 977*m*, 985*m*, 1005*m*, 1026*m*, 1245*vs*, 1370*m*, 1388*w*, 1456*w*, 1729*s*, 2238*s*, 2254*s*, 2929*m* cm^{-1};
^1H NMR (500 MHz, $CDCl_3$): δ = 5.27 (m, *J* = 3.9 Hz, 1H, 12-H), 4.53–4.46 (m, 1H, 3-H), 2.14 (dd, *J* = 11.3, 1.9 Hz, 1H, 9-H), 2.04 (s, 3H, 32-H_3), 1.96–1.90 (m, 3H, 11-H_a+16-H_a+22-H_a), 1.78–1.73 (m, 8H, 18-H+22-H_b+1-H_a+2-H_a+2-H_b+11-H_b+21-H_a+6-H_a), 1.53 (s, 1H, 7-H_a), 1.44–1.17 (m, 5H, 6-H_b+7-H_b+16-H_b+19-H+16-H_b+21-H_b), 1.11–1.05 (m, 3H, 1-H_b+15-H_a+15-H_b), 1.04 (s, 3H, 27-H_3), 1.03 (s, 3H, 23-H_3), 0.98 (s, 1H, 20-H), 0.94 (s, 3H,

29-H_3), 0.93 (s, 3H, 30-H_3), 0.88 (s, 3H, 24-H_3), 0.85 (s, 3H, 25-H_3), 0.83 (s, 1H, 5-H), 0.78 (s, 3H, 26-H_3) ppm;
^{13}C NMR (126 MHz, $CDCl_3$): δ = 170.8 (C-31), 137.6 (C-13), 126.7 (C-12), 126.1 (C-28), 80.7 (C-3), 60.5 (C-18), 55.4 (C-5), 52.6 (C-9), 41.8 (C-14), 41.7 (C-22), 40.9 (C-19), 39.9 (C-10), 39.5 (C-18), 38.9 (C-20), 38.2 (C-1), 37.7 (C-4), 36.4 (C-2), 33.0 (C-7), 31.8 (C-21), 28.3 (C-16), 28.2 (C-24), 27.3 (C-15), 24.1 (C-17), 23.3 (C-11), 23.0 (C-27), 21.3 (C-32), 20.8 (C-30), 18.2 (C-6), 17.5 (C-23), 16.9 (C-26), 16.6 (C-25), 15.7 (C-29) ppm;
MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* = 1013.5 (28%, $[2M+Na]^+$);
analysis calcd for $C_{32}H_{49}NO_3$ (495.75): C 77.53, H 9.96, N 2.83; found: C 77.37, H 10.24, N 2.69.

3*β*-Acetyloxy-17*β*-amino-28-norolean-12-ene (7)
A solution of **5** (250 mg, 0.5 mmol) in THF (15 mL) and aqu. HCl (2 M,1.2 mL, 2.5 mmol) was stirred for 1 day at 50°C. Usual aqu. work-up followed by chromatography (SiO_2, $CHCl_3$/MeOH, 95:5) gave **7** (110 mg, 47%) as a white solid; m.p. 215-217°C (decomp.); R_F = 0.50 ($CHCl_3$/MeOH, 9:1); $[\alpha]_D$ = +84.0° (*c* 0.05, $CHCl_3$);
IR (ATR): $\tilde{\nu}$ = 660*w*, 816*m*, 968*w*, 987*m*, 1004*m*, 1026*m*, 1244*vs*, 1364*m*, 1388*w*, 1463*w*, 1733*s*, 2856*w*, 2946*m* cm^{-1};
^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.40 (t, *J* = 3.6 Hz, 1H, 12-H), 4.55–4.43 (m, 1H, 3-H), 4.15–4.06 (m, 2H, 28-NH_2), 2.32 (m, 1H, 9-H), 2.12 (m, 1H, 15-H_a), 2.04 (s, 3H, 32-H_3), 1.88 (d, *J* = 3.6 Hz, 1H, 11-H_a), 1.79 (m, 2H, 2-H_a+16-H_a), 1.74–1.28 (m, 16H, 1-H_a+2-H_b+19-H_a+19-H_b+21-H_a+1-H_b+6-H_a+6-H_b+11-H_b+18-H+21-H_b+22-H_a+22-H_b+7-H_a+7-H_b+15-H_b), 1.20–1.14 (m, 1H, 16-H_b), 1.12 (s, 3H, 27-H_3), 0.98 (s, 3H, 29-H_3), 0.96 (s, 3H, 26-H_3), 0.95 (s, 3H, 25-H_3) 0.90 (s, 3H, 30-H_3), 0.87 (s, 3H, 24-H_3), 0.86 (s, 3H, 23-H_3), 0.85–0.80 (m, 1H, 5-H) ppm;
^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.1 (C-31), 141.5 (C-13), 125.8 (C-12), 80.9 (C-3), 55.2 (C-5), 54.5 (C-17), 47.5 (C-9), 47.4 (C-18), 47.2 (C-19), 41.4 (C-14), 39.9 (C-8), 38.1 (C-1), 37.7 (C-4), 36.9 (C-10), 35.3 (C-7), 34.6 (C-21), 32.9 (C-30), 32.4 (C-22), 31.0 (C-20), 28.1 (C-24), 25.8 (C-16), 25.7 (C-27), 25.1 (C-15), 23.9 (C-29), 23.6 (C-2), 23.5 (C-11), 21.2 (C-32), 18.2 (C-6), 17.0 (C-26), 16.7 (C-23), 15.6 (C-5) ppm;
MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* = 470.6 (55%, $[M+H]^+$);
analysis calcd for $C_{31}H_{51}NO_2$ (469.75): C 79.26, H 10.94, N 2.98; found: C 78.95, H 11.11, N 2.74.

3*β*-Acetyloxy-17*β*-amino-28-norurs-12-ene (8)
Compound **8** (843 mg, 90%) was obtained from **6** (1.0 g, 2.0 mmol) as a colorless solid; m.p. 220-220°C (decomp.); R_F = 0.50 ($CHCl_3$/MeOH, 9:1); $[\alpha]_D$ = +66.3° (*c* 0.051, $CHCl_3$);
IR (ATR): $\tilde{\nu}$ = 781*w*, 830*w*, 841*w*, 970*m*, 985*m*, 1004*m*, 1023*m*, 1244*vs*, 1368*m*, 1387*w*, 1456*w*, 1733*s*, 2855*w*, 2911*m*, 2924*m*, 2957*w*, 2978*w* cm^{-1};
^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.32 (t, *J* = 3.7 Hz, 1H, 12-H), 4.52–4.47 (m, 1H, 3-H), 3.10 (s, 2H, 28-NH_2), 2.09–2.07 (m, 1H, 16-H_a), 2.03 (s, 3H, 32-H_3), 1.96–1.91 (m, 1H, 11-H_a), 1.91–1.82 (m, 2H, 2-H_a+15-H_a), 1.77–1.72 (m, 2H, 22-H_a+2-H_b), 1.67–1.61 (m, 3H, 1-H_a+1-H_b+11-H_b), 1.58–1.50 (m, 6H, 6-H_a+7-H_a+9-H+18-H+21-H_a+22-H_b), 1.42–1.35 (m, 2H, 6-H_b+7-H_b), 1.33–1.27 (m, 1H, 19-H), 1.27–1.20 (m, 2H, 16-H_b+21-H_b), 1.13–1.06 (m, 1H, 15-H_b), 1.08 (s, 3H, 27-H_3), 1.00 (s, 3H, 23-H_3), 1.02–0.95 (m, 1H, 20-H), 0.97 (s, 3H, 29-H_3), 0.93–0.92 (m, 3H, 30-H_3), 0.87 (s, 3H, 24-H_3), 0.86 (s, 3H, 25-H_3), 0.83–0.78 (m, 1H, 5-H), 0.80 (s, 3H, 26-H_3) ppm;
^{13}C NMR (126 MHz, $CDCl_3$): δ = δ 170.8 (C-31), 137.5 (C-13), 128.1 (C-12), 80.9 (C-3), 60.4 (C-18), 55.3 (C-5), 53.2 (C-17), 47.5 (C-9), 41.9 (C-14), 40.6 (C-19), 39.9 (C-18), 39.8 (C-22), 39.0 (C-20), 38.4 (C-1), 37.6 (C-4), 36.8 (C-10), 32.7 (C-7), 31.4 (C-21), 28.0 (C-24), 27.8 (C-16), 25.9 (C-15), 23.7 (C-2), 23.5 (C-11), 23.1 (C-27), 21.3 (C-32), 20.9 (C-30), 18.3 (C-6), 17.3 (C-26), 17.1 (C-23), 16.7 (C-25), 15.7 (C-29) ppm;
MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* = 470.5 (45%, $[M+H]^+$);
analysis calcd for $C_{31}H_{51}NO_2$ (469.75): C 79.26, H 10.94, N 2.98; found: C 79.12, H 11.15, N 2.77.

***N*-[3*β*-Acetyloxy-17*β*-amino-28-norolean-12-en-17-yl]-benzamide (9)**
The reaction of **7** (110 mg, 0.23 mmol) with benzoyl chloride (0.1 mL, 0.86 mmol) in dry DCM (4 mL) in the presence of NEt_3/DMAP (cat. amounts) for 2 h at 21°C followed by aq. work-up and chromatography (SiO_2, hexanes/ethyl acetate, 9:1) gave **9** (109 mg, 86%) as a colorless solid; m.p. 260-263°C (decomp.); R_F = 0.25 (hexanes/ethyl acetate, 9:1); $[\alpha]_D$ = +45.1° (*c* 0.20, $CHCl_3$);
IR (ATR): $\tilde{\nu}$ = 478*w*, 505*w*, 676*w*, 691*w*, 709*m*, 970*w*, 986*m*, 1004*m*, 1014*m*, 1027*m*, 1217*w*, 1244*vs*, 1318*w*, 1366*m*, 1387*w*, 1434*w*, 1446*w*, 1463*m*, 1482*m*, 1512*m*, 1666*m*, 1733*m*, 2872*w*, 2946*m* cm^{-1};
^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.74–7.68 (m, 2H, 35-H+39-H), 7.49–7.36 (m, 3H, 37-H+36-H+38-H), 5.87 (s, 1H, 28-H), 5.40 (t, *J* = 3.6 Hz, 1H, 12-H), 4.52–4.45 (m, 1H, 3-H), 2.60–2.52 (m, 1H, 22-H_a), 2.37–2.28 (m, 2H, 9-H+16-H_a), 2.04 (s, 3H, 32-H_3), 2.07–1.69 (m, 7H, 16-H_b+11-H_a+2-H_a+19-H_a+2-H_b+15-H_a+21-H_a), 1.65–1.24 (m, 9H, 1-H_a+11-H_b+18-H+6-H_a+22-H_b+6-H_b+7-H_a+7-H_b+21-H_b), 1.26–1.18 (m, 1H, 19-H_b), 1.17 (s, 3H, 27-H_3), 1.09–1.00 (m, 2H, 1-H_b+15-H_b), 0.98 (s, 3H, 29-H_3), 0.93 (s, 3H, 30-H_3), 0.91 (s, 3H, 23-H_3), 0.85 (s, 3H, 24-H_3), 0.86–0.81 (m, 1H, 5-H), 0.83 (s, 3H, 25-H_3), 0.77 (s, 3H, 26-H_3) ppm;
^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.1 (C-31), 166.0 (C-33), 143.1 (C-13), 135.3 (C-34), 131.1 (C-37), 128.5 (C-36+C-38), 126.7 (C-35+C-39), 124.6 (C-12), 80.9 (C-3), 56.8 (C-17), 55.2 (C-5), 47.5 (C-9), 47.3 (C-18), 46.7 (C-19), 41.7

(C-14), 39.6 (C-8), 38.0 (C-1), 37.7 (C-4), 36.9 (C-20), 35.0 (C-7), 32.9 (C-30), 32.4 (C-21+ C-22), 30.8 (C-10), 28.0 (C-24), 26.3 (C-15), 25.7 (C-27), 23.9 (C-29), 23.5 (C-11), 23.4 (C-2), 21.9 (C-16), 21.3 (C-32), 18.2 (C-6), 16.9 (C-26), 16.5 (C-25), 15.3 (C-23) ppm;
MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* = 574.6 (81%, $[M+H]^+$), 1169.7 (100%, $[2M+Na]^+$);
analysis calcd for $C_{38}H_{55}NO_3$ (573.86): C 79.53, H 9.66, N 2.44; found: C 79.41, H 9.79, N 2.24.

***N*-[3*β*-Acetyloxy-17*β*-amino-28-norurs-12-en-17-yl]-benzamide (10)**

The synthesis of **10** (160 mg, 100%) was accomplished from **8** (122 mg, 0.26 mmol) following the procedure given for **9**; m.p. 248–250°C (decomp.); R_F = 0.26 (hexanes/ethyl acetate, 9:1); $[\alpha]_D$ = +24.8° (*c* 0.22, $CHCl_3$);
IR (ATR): $\tilde{\nu}$ = 522*m*, 529*m*, 539*m*, 609*w*, 667*w*, 693*m*, 715*s*, 801*w*, 985*m*, 991*w*, 1005*w*, 1025*m*, 1246*vs*, 1291*m*, 1320*m*, 1368*m*, 1452*m*, 1483*m*, 1510*m*, 1579*w*, 1601*w*, 1666*s*, 1730*s*, 2852*w*, 2927*w*, 3412*w* cm^{-1};
^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.72–7.65 (m, 2H, 35-H+39-H), 7.50–7.42 (m, 2H, 36-H+38-H), 7.39 (dd, *J* = 8.2, 6.7 Hz, 1H, 37-H), 5.91 (s, 1H, 28-H), 5.38 (t, *J* = 3.6 Hz, 1H, 12-H), 4.48 (dd, *J* = 10.8, 4.9 Hz, 1H, 3-H), 2.87–2.79 (m, 1H, 22-H_a), 2.46–2.39 (m, 1H, 16-H_a), 2.04 (s, 3H, 32-H_3), 2.02–1.99 (m, 1H, 16-H_b), 1.99–1.96 (m, 1H, 11-H_a), 1.80–1.72 (m, 1H, 15-H_a), 1.67–1.61 (m, 3H, 1-H_a+11-H_b+18-H), 1.57–1.54 (m, 2H, 9-H+21-H_a), 1.54–1.51 (m, 1H, 22-H_b), 1.51–1.48 (m, 2H, 6-H_a+19-H), 1.48–1.46 (m, 1H, 7-H_a), 1.35–1.22 (m, 3H, 6-H_b+7-H_b+21-H_b), 1.11 (s, 3H, 27-H_3), 1.09–1.06 (m, 1H, 15-H_b), 1.05 (d, *J* = 2.3 Hz, 1H, 1-H_b), 1.13–0.98 (m, 1H, 20-H), 0.96 (s, 3H, 29-H_3), 0.91 (s, 3H, 23-H_3), 0.87 (s, 3H, 30-H_3), 0.85 (s, 3H, 24-H_3), 0.82 (s, 3H, 25-H_3), 0.81–0.80 (m, 1H, 5-H), 0.72 (s, 3H, 26-H_3) ppm;
^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.1 (C-31), 165.8 (C-33), 138.5 (C-13), 135.3 (C-34), 131.1 (C-37), 128.4 (C-36), 128.3 (C-38), 127.3 (C-12), 126.6 (C-35+C-39), 80.9 (C-3), 59.1 (C-18), 57.5 (C-17), 55.1 (C-5), 47.5 (C-9), 42.0 (C-14), 39.9 (C-19), 39.6 (C-8), 39.3 (C-20), 38.2 (C-1), 37.5 (C-4), 36.8 (C-10), 36.4 (C-22), 32.4 (C-7), 31.3 (C-21), 28.1 (C-24), 26.7 (C-15), 23.6 (C-2), 23.5 (C-11), 23.2 (C-16), 23.1 (C-27), 21.3 (C-32), 20.8 (C-29), 18.1 (C-6), 17.6 (C-30), 16.8 (C-26), 16.6 (C-25), 15.5 (C-23) ppm;
MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* = 574.4 (100%, $[M+H]^+$), 1170.2 (33%, $[2M+Na]^+$);
analysis calcd for $C_{38}H_{55}NO_3$ (573.86): C 79.53, H 9.66, N 2.44; found: C 79.43, H 9.92, N 2.31.

***N*-[3*β*-Acetyloxy-17*β*-amino-28-norolean-12-en-17-yl]-cinnamic acid amide (11)**

The reaction of cinnamic acid chloride (58.5 mg, 0.35 mmol, freshly prepared from cinnamic acid and oxalyl chloride), NEt_3 (0.06 mL) with **7** (150 mg, 0.32 mmol) in dry DCM (10 mL) in the presence of DMAP (cat.) followed by usual aq. work-up and chromatography (SiO_2, hexanes/ethyl acetate, 9:1) gave **11** (170 mg, 89%) as a white solid; m.p. 143–145°C; R_F = 0.20 (hexanes/ethyl acetate, 9:1); $[\alpha]_D$ = +50.8° (*c* 0.23, $CHCl_3$)
IR (ATR): $\tilde{\nu}$ = 472*m*, 491*m*, 568*m*, 686*m*, 710*m*, 763*m*, 972*m*, 985*m*, 1004*m*, 1026*m*, 1217*m*, 1244*vs*, 1336*m*, 1365*m*, 1387*w*, 1449*m*, 1463*m*, 1504*m*, 1537*m*, 1625*m*, 1662*m*, 1673*m*, 1733*m*, 2872*w*, 2946*m* cm^{-1};
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65–7.63 (m, 1H, 39-H), 7.62–7.59 (m, 1H, 35-H), 7.51–7.43 (m, 2H, 38-H+40-H), 7.36–7.31 (m, 2H, 37-H+41-H), 6.34 (d, *J* = 15.5 Hz, 1H, 34-H), 5.52 (s, 1H, 28-H), 5.41–5.35 (m, 1H, 12-H), 4.53–4.44 (m, 1H, 3-H), 2.48 (d, *J* = 13.8 Hz, 1H, 22-H_a), 2.28–2.24 (m, 2H, 9-H+16-H_a), 2.04 (s, 3H, 32-H_3), 2.02–1.96 (m, 1H, 16-H_b), 1.96–1.16 (m, 16H, 2-H_a+11-H_a+2-H_b+15-H_a+19-H_a+22-H_b+1-H_a+11-H_b+6-H_a+18-H+21-H_a+6-H_b+7-H_a+7-H_b+19-H_b+21-H_b), 1.15 (s, 3H, 27-H_3), 1.09–1.00 (m, 2H, 1-H_b+15-H_b), 0.97 (s, 3H, 30-H_3), 0.94 (s, 3H, 23-H_3), 0.92 (s, 3H, 29-H_3), 0.87 (s, 3H, 25-H_3), 0.86 (s, 3H, 24-H_3), 0.89–0.81 (m, 1H, 5-H), 0.84 (s, 3H, 26-H_3) ppm;
^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.1 (C-31), 165.3 (C-33), 142.9 (C-13), 141.3 (C-35+C-39), 134.8 (C-36), 129.8 (C-37), 128.8 (C-41), 127.8 (C-38+C-40), 124.9 (C-12), 120.8 (C-34), 80.8 (C-3), 57.4 (C-17), 55.3 (C-5), 47.5 (C-18), 47.1 (C-9), 46.3 (C-19), 41.6 (C-14), 39.6 (C-8), 38.1 (C-1), 37.7 (C-4), 36.9 (C-20), 35.0 (C-7), 32.8 (C-29), 32.2 (C-22), 32.1 (C-21), 30.7 (C-10), 28.0 (C-24), 26.2 (C-15), 25.9 (C-27), 24.0 (C-30), 23.6 (C-2), 23.4 (C-11), 21.3 (C-16), 21.2 (C-32), 18.1 (C-6), 16.8 (C-26), 16.6 (C-25), 15.4 (C-23) ppm;
MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* = 599.4 (95%, $[M-H]^-$);
analysis calcd for $C_{40}H_{57}NO_3$ (599.90): C 80.09, H 9.58, N 2.33; found: C 79.79, H 9.81, N 2.05.

***N*-[3*β*-Acetyloxy-17*β*-amino-28-norurs-12-en-17-yl]-cinnamic acid amide (12)**

Following the procedure given for **11**, from **8** (150 mg, 0.32 mmol), **12** (131 mg, 68%) was obtained as a white solid; m.p. 155–158°C; R_F = 0.26 (hexanes/ethyl acetate, 9:1); $[\alpha]_D$ = +45.0° (*c* 0.22, $CHCl_3$););
IR (ATR): $\tilde{\nu}$ = 480*w*, 496*w*, 565*m*, 687*w*, 713*m*, 763*m*, 972*m*, 985*m*, 1005*m*, 1026*m*, 1220*m*, 1244*vs*, 1341*m*, 1369*m*, 1450*m*, 1504*m*, 1537*m*, 1622*m*, 1659*m*, 1733*m*, 2870*w*, 2924*m*, 2947*m* cm^{-1};
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61–7.58 (m, 1H, 39-H), 7.57–7.55 (m, 1H, 35-H), 7.49–7.43 (m, 2H, 38-H+40-H), 7.36–7.30 (m, 2H, 37-H+41-H), 6.30 (s, 1H, 28-H), 6.26 (s, 1H, 34-H), 5.37–5.32 (m, 1H, 12-H), 4.53–4.45 (m, 1H, 3-H), 2.81–2.72 (m, 1H, 22-H_a), 2.39–2.31 (m, 1H, 16-H_a), 2.03 (s, 3H, 32-H_3), 2.01–1.90 (m, 3H, 2-H_a+11-H_a+16-H_b), 1.78–1.21 (m, 15H, 2-H_b+15-H_a+1-H_a+1-H_b+11-H_b+6-H_a+7-H_a+9-H+18-H+19-H+21-H_a+22-H_b+6-H_b+7-H_b+21-H_b), 1.10 (s, 3H, 27-H_3), 1.10–1.04 (m, 1H, 15-H_b), 0.95 (s, 6H, 23-H_3+30-H_3), 0.94 (s,

1H, 20-H), 0.90 (s, 3H, 25-H_3), 0.86 (s, 3H, 29-H_3), 0.86 (s, 3H, 24-H_3), 0.84 (s, 3H, 26-H_3), 0.82–0.81 (m, 1H, 5-H) ppm;
^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.1 (C-31), 164.9 (C-33), 140.8 (C-35+C-39), 138.3 (C-13), 135.2 (C-36), 129.4 (C-37), 128.7 (C-41), 127.9 (C-38), 127.4 (C-12+C-40), 1.5 (C-34), 80.8 (C-3), 58.9 (C-18), 57.5 (C-17), 55.3 (C-5), 47.4 (C-9), 41.9 (C-14), 39.9 (C-19), 39.8 (C-8), 39.2 (C-20), 38.3 (C-1), 37.7 (C-4), 36.8 (C-10), 36.7 (C-22), 32.4 (C-7), 31.3 (C-21), 28.0 (C-24), 26.7 (C-15), 23.5 (C-11), 23.3 (C-27), 23.2 (C-2), 23.0 (C-16), 21.3 (C-32), 20.8 (C-30), 18.1 (C-6), 17.5 (C-29), 16.8 (C-26), 16.7 (C-25), 15.5 (C-23) ppm;
MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* = 601.4 (100%, $[M+H]^+$);
analysis calcd for $C_{40}H_{57}NO_3$ (599.90): C 80.09, H 9.58, N 2.33; found: C 79.93, H 9.72, N 2.25.

***N*-[3*β*-Acetyloxy-17*β*-amino-28-norolean-12-en-17-yl]-phenyl urea (13)**
The reaction of **5** (124 mg, 0.25 mmol) in dry toluene (10 mL) with aniline (0.37 mmol, 34 µl), in the presence of NEt_3 (1 mL) at 21°C for 12 h, followed by usual aq. work-up and chromatography (SiO_2, $CHCl_3$) gave **13** (68 mg, 46%) as a colorless solid; m.p. 221–223°C (decomp.); R_F = 0.20 ($CHCl_3$); $[\alpha]_D$ = +52.5° (*c* 0.23, $CHCl_3$);
IR (ATR): $\tilde{\nu}$ = 478*m*, 505*m*, 609*m*, 652*m*, 665*m*, 692*s*, 748*s*, 897*w*, 968*m*, 986*m*, 1009*m*, 1026*s*, 1096*w*, 1215*s*, 1244*vs*, 1310*m*, 1365*m*, 1440*m*, 1464*m*, 1498*s*, 1543*s*, 1599*m*, 1659*m*, 1693*m*, 1698*m*, 1732*m*, 2872*w*, 2946*m*, 3375*w* cm^{-1};
^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.30–7.21 (m, 1H, 38-H), 7.29–7.23 (m, 2H, 36-H+40-H), 7.03 (m, 2H, 37-H+39-H), 6.10 (s, 1H, 28-H), 5.38–5.23 (m, 1H, 12-H), 4.52–4.46 (m, 2H, 34-H+3-H), 2.47–2.39 (m, 1H, 22-H_a), 2.19–2.09 (m, 2H, 9-H+16-H_a), 2.04 (s, 3H, 32-H_3), 1.97–1.45 (m, 11H, 2-H_a+16-H_b+11-H_a+19-H_a+15-H_a+1-H_a+2-H_b+11-H_b6-H_a+18-H+21-H_a), 1.41–1.35 (m, 1H, 6-H_b), 1.36–1.27 (m, 3H, 7-H_a+21-H_b+22-H_b), 1.29–1.23 (m, 1H, 7-H_b), 1.20–1.15 (m, 1H, 19-H_b), 1.13 (s, 3H, 27-H_3), 1.09–0.98 (m, 2H, 1-H_b+15-H_b), 0.96 (s, 3H, 29-H_3), 0.91 (s, 3H, 23-H_3), 0.91 (s, 3H, 30-H_3), 0.86 (s, 3H, 24-H_3), 0.85 (s, 3H, 25-H_3), 0.86–0.82 (m, 1H, 5-H), 0.75 (s, 3H, 26-H_3) ppm;
^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.1 (C-31), 154.3(C-33), 143.1 (C-13), 138.9 (C-35), 129.1 (C-38), 124.6 (C-12), 123.4 (C-37+C-39), 120.9 (C-36+C-40), 80.8 (C-3), 56.0 (C-17), 55.2 (C-5), 47.5 (C-9), 47.4 (C-18), 46.3 (C-19), 41.5 (C-14), 39.6 (C-8), 38.1 (C-1), 37.7 (C-4), 36.8 (C-20), 35.2 (C-7), 33.1 (C-22), 32.9 (C-30), 32.3 (C-21), 30.8 (C-10), 28.0 (C-24), 26.2 (C-15), 25.7 (C-27), 24.0 (C-29), 23.6 (C-2), 23.5 (C-11), 22.3 (C-16), 21.2 (C-32), 18.0 (C-6), 16.7 (C-26), 16.7 (C-25), 15.3 (C-23) ppm;
MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* = 587.3 (100%, $[M-H]^-$);
analysis calcd for $C_{38}H_{56}N_2O_3$ (588.88): C 77.51, H 9.59, N 4.76; found: C 77.30, H 9.71, N 4.52.

***N*-[3*β*-Acetyloxy-17*β*-amino-28-norurs-12-en-17-yl]-phenyl urea (14)**
Following the synthesis of **13**, **14** (237 mg, 81%) was prepared from **6** (248 mg, 0.5 mmol) and obtained as a white solid; m.p. 149–151°C (decomp.); R_F = 0.25 ($CHCl_3$); $[\alpha]_D$ = +50.4° (*c* 0.25, $CHCl_3$);
IR (ATR): $\tilde{\nu}$ = 504*m*, 667*m*, 692*s*, 748*s*, 968*m*, 985*m*, 1005*m*, 1026*m*, 1244*vs*, 1314*m*, 1370*m*, 1440*m*, 1454*m*, 1467*m*, 1498*vs*, 1542*s*, 1600*m*, 1659*m*, 1731*m*, 2870*w*, 2924*m*, 2947*m*, 3374*w* cm^{-1};
^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.30–7.27 (m, 3H, 37-H+39-H+38-H), 7.23–7.22 (m, 2H, 36-H+40-H), 5.22–5.15 (m, 1H, 12-H), 4.81 (s, 1H, 28-H), 4.52–4.46 (m, 1H, 3-H), 4.27 (s, 1H, 34-H), 2.61–2.52 (m, 1H, 22-H_a), 2.18–2.10 (m, 1H, 16-H_a), 2.03 (s, 3H, 32-H_3), 1.96–1.73 (m, 4H, 16-H_b+11-H_a+2-H_a+15-H_a), 1.61 (m, 2H, 1-H_a+11-H_b), 1.52 (s, 1H, 6-H_a), 1.57–1.45 (m, 4H, 2-H_b+7-H_a+9-H+21-H_a), 1.43–1.31 (m, 5H, 19-H+22-H_b+6-H_b+18-H+21-H_b), 1.23–1.14 (m, 1H, 7-H_b), 1.11–1.05 (m, 1H, 1-H_b), 1.04 (s, 3H, 27-H_3), 1.03–0.97 (m, 1H, 15-H_b), 0.96–0.95 (m, 1H, 20-H_b), 0.93 (s, 3H, 23-H_3), 0.92 (s, 6H, 29-H_3+30-H_3), 0.87 (s, 3H, 24-H_3), 0.86 (s, 3H, 25-H_3), 0.84–0.83 (m, 1H, 5-H), 0.80 (s, 3H, 26-H_3) ppm;
^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.1 (C-31), 157.2 (C-33), 139.3 (C-35), 138.6 (C-13), 128.6 (C-39), 128.5 (C-37), 127.4 (C-38), 127.3 (C-36), 127.2 (C-40), 127.0 (C-12), 80.9 (C-3), 59.1 (C-18), 56.4 (C-17), 55.1 (C-5), 47.5 (C-9), 42.0 (C-14), 39.8 (C-19), 39.7 (C-8), 39.2 (C-20), 38.3 (C-1), 37.7 (C-4), 37.6 (C-22), 36.8 (C-10), 32.6 (C-21), 31.4 (C-7), 28.1 (C-24), 26.7 (C-15), 23.8 (C-16), 23.5 (C-2), 23.4 (C-11), 23.2 (C-27), 21.3 (C-32), 20.9 (C-29), 18.1 (C-6), 17.5 (C-26), 16.9 (C-25), 16.6 (C-30), 15.5 (C-23) ppm;
MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* = 589.3 (100%, $[M+H]^+$);
analysis calcd for $C_{38}H_{56}N_2O_3$ (588.88): C 77.51, H 9.59, N 4.76; found: C 77.41, H 9.73, N 4.57.

***N*-[3*β*-Acetyloxy-17*β*-amino-28-norolean-12-en-17-yl]-benzyl urea (15)**
The reaction of **5** (248 mg, 0.5 mmol) in dry toluene (10 mL) with benzylamine (81 µl, 79.3 mg, 0.74 mmol) in the presence of NEt_3 (1.2 mL) at 21°C for 12 h followed by usual aqu. work-up and chromatography (SiO_2, $CHCl_3$) gave **15** (316 mg, 100%) as a colorless solid; m.p. 159–161°C; R_F = 0.08 ($CHCl_3$); $[\alpha]_D$ = +51.1° (*c* 0.21, $CHCl_3$
IR (ATR): $\tilde{\nu}$ = 594*w*, 609*w*, 652*w*, 664*w*, 698*m*, 743*m*, 968*w*, 986*m*, 1013*m*, 1026*m*, 1243*vs*, 1302*w*, 1365*m*, 1454*m*, 1463*m*, 1497*m*, 1547*m*, 1550*m*, 1638*m*, 1735*m*, 2946*m*, 3361*w* cm^{-1};
^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34–7.31 (m, 2H, 38-H+40-H), 7.30 (s, 1H, 39-H), 7.29–7.21 (m, 2H, 37-H+41-H), 5.26–5.21 (m, 1H, 12-H), 5.17 (s, 1H, 28-H), 4.52–4.45 (m, 1H, 3-H), 4.38–4.21 (m, 3H, 34-H+35-H_a+35-H_b), 2.34–2.26 (m, 1H, 22-H_a),

2.09–2.00 (m, 2H, 9-H+16-H_a), 2.04 (s, 3H, 32-H_3), 1.94–1.88 (m, 1H, 16-H_b), 1.89–1.83 (m, 2H, 2-H_a+11-H_a), 1.78–1.67 (m, 3H, 2-H_b+15-H_a+ 19-H_a), 1.64–1.19 (m, 10H, 11-H_b+1-H_a+18-H+ 22-H_b+6-H_a+21-H_a+6-H_b+21-H_b+7-H_a+7-H_b), 1.16–1.12 (m, 1H, 19-H_b), 1.11 (s, 3H, 27-H_3), 1.09–0.96 (m, 2H, 1-H_b+15-H_b), 0.93 (s, 3H, 23-H_3), 0.89 (s, 3H, 29-H_3), 0.88 (s, 3H, 30-H_3), 0.87 (s, 3H, 24-H_3), 0.86 (s, 3H, 25-H_3), 0.92–0.81 (m, 1H, 5-H), 0.84 (s, 3H, 26-H_3) ppm;
^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.1 (C-31), 157.4 (C-33), 143.0 (C-13), 138.7 (C-36), 128.6 (C-38+C-40), 127.5 (C-39), 126.8 (C-37+C-41), 124.4 (C-12), 80.9 (C-3), 56.2 (C-17), 55.3 (C-5), 47.6 (C-9), 47.5 (C-18), 46.3 (C-19), 44.6 (C-35), 41.7 (C-14), 39.6 (C-8), 38.1 (C-1), 37.7 (C-4), 36.8 (C-20), 35.3 (C-7), 33.3 (C-22), 32.8 (C-30), 32.3 (C-21), 30.7 (C-10), 28.0 (C-24), 26.2 (C-15), 25.7 (C-27), 23.9 (C-29), 23.6 (C-2), 23.5 (C-11), 22.5 (C-16), 21.4 (C-32), 18.2 (C-6), 16.9 (C-26), 16.7 (C-25), 15.4 (C-23) ppm;
MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* = 603.3 (100%, $[M+H]^+$);
analysis calcd for $C_{39}H_{58}N_2O_3$ (602.90): C 77.70, H 9.70, N 4.65; found: C 77.46, H 9.85, N 4.53.

_N_-[3β-Acetyloxy-17β-amino-28-norurs-12-en-17-yl]-benzyl urea (16)
Following the procedure given for **15**, **16** (394 mg, 100%) was synthesized from **6** (248 mg, 0.5 mmol) and obtained as a white solid; m.p. 156–158°C; R_F = 0.17 ($CHCl_3$); $[\alpha]_D$ = +42.8° (*c* 0.15, $CHCl_3$);
IR (ATR): $\tilde{\nu}$ = 594*w*, 609*w*, 652*w*, 664*w*, 698*m*, 743*m*, 968*w*, 986*m*, 1013*m*, 1026*m*, 1243*vs*, 1302*w*, 1365*m*, 1454*m*, 1463*m*, 1497*m*, 1547*m*, 1550*m*, 1638*m*, 1735*m*, 2946*m*, 3361*w* cm^{-1};
^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.26–7.19 (m, 2H, 37-H+41-H), 7.18–7.12 (m, 2H, 38-H+40-H), 7.02–6.95 (m, 1H, 39-H), 6.60 (s, 1H, 28-H), 5.20–5.15 (m, 1H, 12-H), 4.75 (s, 1H, 34-H), 4.51–4.44 (m, 1H, 3-H), 3.41–3.22 (m, 1H, 35-H_a), 3.16–3.02 (m, 1H, 35-H_b), 2.69–2.61 (m, 1H, 22-H_a), 2.24–2.17 (m, 1H, 16-H_a), 2.04 (s, 3H, 32-H_3), 1.96–1.86 (m, 3H, 2-H_a+11-H_a+16-H_b), 1.85–1.75 (m, 1H, 15-H_a), 1.66–1.56 (m, 2H, 1-H_a+11-H_b), 1.55–1.47 (m, 6H, 2-H_b+6-H_a+7-H_a+9-H+21-H_a+22-H_b), 1.44–1.41 (m, 2H, 18-H+19-H), 1.37–1.28 (m, 2H, 6-H_b+ 21-H_b), 1.27–1.13 (m, 1H, 7-H_b), 1.12–1.04 (m, 1H, 1-H_b), 1.05 (s, 3H, 27-H_3), 1.04–0.98 (m, 1H, 15-H_b), 0.93 (s, 3H, 29-H_3), 0.90 (s, 3H, 23-H_3), 0.86 (s, 3H, 24-H_3), 0.85 (s, 3H, 30-H_3), 0.81 (s, 3H, 25-H_3), 0.80 (s, 1H, 5-H), 0.79 (s, 3H, 26-H_3) ppm;
^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.1 (C-31), 154.4 (C-33), 139.2 (C-36), 138.4 (C-13), 129.0 (C-40), 128.9 (C-41), 127.0 (C-12), 123.0 (C-39), 120.4 (C-37+C-38), 80.8 (C-3), 59.1 (C-18), 56.4 (C-17), 55.3 (C-5), 47.5 (C-9), 41.8 (C-14), 40.9 (C-35), 39.7 (C-19), 39.7 (C-8), 39.2 (C-20), 38.4 (C-1), 37.7 (C-4), 37.4 (C-22), 36.8 (C-10), 32.7 (C-21), 31.4 (C-7), 28.0 (C-24), 26.7 (C-15), 23.7 (C-16), 23.5 (C-2), 23.4 (C-11), 23.2 (C-27), 21.3 (C-32), 20.8 (C-29), 18.2 (C-6), 17.5 (C-25), 16.7 (C-26), 16.6 (C-30), 15.5 (C-23) ppm;
MS (ESI, MeOH/$CHCl_3$ 4:1): *m/z* = 603.1 (100%, $[M+H]^+$);
analysis calcd for $C_{39}H_{58}N_2O_3$ (602.90): C 77.70, H 9.70, N 4.65; found: C 77.52, H 9.92, N 4.49.

_N_-[3β-Acetyloxy-17β-amino-28-norolean-12-en-17-yl]-3-quinolyl urea (17)
The reaction of **5** (248 mg, 0.5 mmol) in dry toluene (10 mL) with 3-amino-quinoline (107 mg, 0.74 mmol) in the presence of NEt_3 (1.2 mL) at 90°C in a microwave reactor for 5 h followed by usual aq. work-up and chromatography (SiO_2, hexanes/ethyl acetate, 3:1) gave **17** (160 mg, 50%) as a colorless solid; m.p. 177–179°C; R_F = 0.15 (hexanes/ethyl acetate, 3:1); $[\alpha]_D$ = +60.1° (*c* 0.15, $CHCl_3$);
IR (ATR): $\tilde{\nu}$ = 475*m*, 610*m*, 662*m*, 749*m*, 781*m*, 897*m*, 968*m*, 986*m*, 1009*m*, 1026*m*, 1183*m*, 1211*s*, 1243*vs*, 1302*m*, 1364*m*, 1464*m*, 1489*m*, 1523*m*, 1547*m*, 1609*w*, 1702*m*, 1734*m*, 2872*w*, 2945*m*, 3391*vw* cm^{-1};
^{1}H NMR (500 MHz, $CDCl_3$): δ = 10.61 (s, 1H, 34-H), 9.66 (d, *J* = 2.3 Hz, 1H, 40-H), 9.16 (s, 1H, 36-H), 8.36 (d, *J* = 8.5 Hz, 1H, 44-H), 7.96 (d, *J* = 8.3 Hz, 1H, 41-H), 7.78 (t, *J* = 7.7 Hz, 1H, 43-H), 7.73 (t, *J* = 7.6 Hz, 1H, 42-H), 5.78 (s, 1H, 28-H), 5.46–5.41 (m, 1H, 12-H), 4.52–4.45 (m, 1H, 3-H), 2.44–2.31 (m, 1H, 22-H_a), 2.14–2.09 (m, 1H, 16-H_a), 2.11–2.07 (m, 1H, 9-H), 2.04 (s, 3H, 32-H_3), 2.06–2.02 (m, 1H, 22-H_b), 2.00–1.92 (m, 1H, 15-H_a), 1.91–1.83 (m, 1H, 16-H_b), 1.85–1.81 (m, 1H, 11-H_a), 1.80–1.79 (m, 1H, 2-H_a), 1.79–1.76 (m, 1H, 19-H_a), 1.64–1.56 (m, 3H, 1-H_a+11-H_b+ 18-H), 1.66–1.54 (m, 1H, 2-H_b), 1.52–1.46 (m, 2H, 6-H_a+21-H_a), 1.41–1.32 (m, 3H, 6-H_b+7-H_a+21-H_b), 1.28–1.25 (m, 1H, 7-H_b), 1.24–1.22 (m, 1H, 19-H_b), 1.18 (s, 3H, 27-H_3), 1.12–1.05 (m, 2H, 1-H_b+15-H_b), 1.05 (s, 3H, 29-H_3), 0.94 (s, 3H, 23-H_3), 0.93 (s, 3H, 30-H_3), 0.89 (s, 3H, 25-H_3), 0.86 (s, 3H, 24-H_3), 0.85–0.82 (m, 1H, 5-H), 0.80 (s, 3H, 26-H_3) ppm;
^{13}C NMR (126 MHz, $CDCl_3$): δ = (126 MHz, $CDCl_3$): δ = 171.1 (C-31), 154.2 (C-33), 142.8 (C-13), 137.1 (C-38), 135.1 (C-36), 132.9 (C-35), 131.0 (C-43), 130.1 (C-39), 129.9 (C-42), 129.3 (C-40), 128.2 (C-41), 124.3 (C-12), 120.7 (C-44), 80.8 (C-3), 56.3 (C-17), 55.3 (C-5), 47.7 (C-9), 47.5 (C-18), 46.7 (C-19), 41.5 (C-14), 39.8 (C-8), 38.2 (C-1), 37.7 (C-4), 36.8 (C-20), 35.5 (C-7), 33.0 (C-22), 32.9 (C-30), 32.7 (C-21), 30.9 (C-10), 28.0 (C-24), 26.2 (C-15), 25.9 (C-27), 24.2 (C-29), 23.8 (C-2), 23.5 (C-11), 22.3 (C-16), 21.4 (C-32), 18.3 (C-6), 16.7 (C-25), 16.7 (C-26), 15.4 (C-23) ppm;
MS (ESI, MeOH/$CHCl_3$ 4:1): m/z = 640.9 (100%, $[M+H]^+$);
analysis calcd for $C_{41}H_{57}N_3O_3$ (639.93): C 76.95, H 8.98, N 6.57; found: C 76.81, H 9.13, N 6.41.

_N_-[3β-Acetyloxy-17β-amino-28-norurs-12-en-17-yl]-3-quinolyl urea (18)
As described for **17**, **18** (100 mg, 30%) was obtained from **6** (248 mg, 0.5 mmol) as a white solid; m.p.

148–150°C (decomp.) R_F = 0.30 (hexanes/ethyl acetate, 2:1); $[\alpha]_D$ = +34.3° (*c* 0.06, $CHCl_3$);
IR (ATR): $\tilde{\nu}$ = 471*m*, 607*m*, 653*m*, 664*m*, 724*m*, 752*m*, 768*m*, 803*m*, 900*m*, 968*m*, 985*m*, 1007*m*, 1025*s*, 1094*m*, 1188*m*, 1244*vs*, 1365*m*, 1455*m*, 1519*m*, 1546*m*, 1704*m*, 1733*m*, 2854*m*, 2923*s*, 3318*w* cm^{-1};
^1H NMR (500 MHz, $CDCl_3$): δ = 9.97 (s, 1H, 34-H), 9.44 (s, 1H, 40-H), 9.07 (s, 1H, 36-H), 8.29 (d, *J* = 8.4 Hz, 1H, 44-H), 7.89 (d, *J* = 8.2 Hz, 1H, 41-H), 7.73 (t, *J* = 8.6, 6.9, 1.4 Hz, 1H, 43-H), 7.67 (t, *J* = 7.6 Hz, 1H, 42-H), 5.54 (s, 1H, 28-H), 5.40 (t, *J* = 3.6 Hz, 1H, 12-H), 4.52–4.44 (m, 1H, 3-H), 2.47–2.41 (m, 1H, 22-H), 2.18–2.11 (m, 1H, 16-H_a), 2.11–2.00 (m, 1H, 16-H_b), 2.04 (s, 3H, 32-H_3), 2.01–1.89 (m, 2H, 2-H_a+11-H_a), 1.86–1.80 (m, 1H, 18-H), 1.80–1.69 (m, 1H, 22-H_b), 1.65–1.57 (m, 2H, 1-H_a+11-H_b), 1.57–1.51 (m, 3H, 2-H_b+7-H_a+9-H), 1.50–1.44 (m, 3H, 6-H_a+19-H+21-H_a), 1.44–1.38 (m, 1H, 15-H_a), 1.39–1.33 (m, 1H, 21-H_b), 1.32–1.19 (m, 2H, 6-H_b+7-H_b), 1.11 (s, 3H, 27-H_3), 1.09–1.06 (m, 2H, 1-H_b+15-H_b), 1.02 (s, 3H, 30-H_3), 0.96 (s, 1H, 20-H), 0.95 (s, 3H, 29-H_3), 0.87 (s, 3H, 25-H_3), 0.85 (s, 3H, 23-H_3), 0.84 (s, 3H, 24-H_3), 0.83–0.81 (m, 1H, 5-H), 0.80 (s, 3H, 26-H_3) ppm;
^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.1 (C-31), 153.8 (C-33), 138.7 (C-13), 137.5 (C-36), 135.6 (C-38), 134.8 (C-35), 130.4 (C-43), 129.7 (C-39), 129.5 (C-42), 127.9 (C-40+C-41), 127.6 (C-12), 122.1 (C-44), 80.8 (C-3), 58.1 (C-18), 56.9 (C-17), 55.2 (C-5), 47.6 (C-9), 45.3 (C-14), 41.9 (C-8), 39.8 (C-19), 39.1 (C-20), 38.5 (C-1), 37.6 (C-4), 37.3 (C-22), 32.8 (C-21), 31.5 (C-7), 29.5 (C-10), 28.0 (C-24), 26.9 (C-15), 24.4 (C-16), 23.7 (C-2), 23.5 (C-11), 23.4 (C-27), 21.3 (C-32), 20.8 (C-29), 18.2 (C-6), 17.6 (C-25), 17.1 (C-30), 16.7 (C-26), 15.6 (C-23) ppm;
MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* = 640.5 (100%, $[M+H]^+$);
analysis calcd for $C_{41}H_{57}N_3O_3$ (639.93): C 76.95, H 8.98, N 6.57; found: C 76.73, H 9.19, N 6.35.

***N*-[3*β*-Acetyloxy-17*β*-amino-28-norolean-12-en-17-yl]-4-isoquinolyl urea (19)**
As described above, from **5** (24.8 mg, 0.05 mmol) and 4-amino-quinoline (10.7 mg, 0.074 mmol), **19** (12.2 mg, 35%) was obtained as a colorless solid; m.p. 177–180°C (decomp.); R_F = 0.05 (hexanes/ethyl acetate, 3:1); $[\alpha]_D$ = +44.1° (*c* 0.03, $CHCl_3$);
IR (ATR): $\tilde{\nu}$ = 476*m*, 500*m*, 524*m*, 661*m*, 752*m*, 779*m*, 847*m*, 901*w*, 970*m*, 986*m*, 1006*m*, 1026*s*, 1096*m*, 1243*vs*, 1365*m*, 1430*m*, 1463*m*, 1534*s*, 1612*w*, 1707*m*, 1731*m*, 2874*w*, 2945*m*, 3277*w* cm^{-1};
^1H NMR (500 MHz, $CDCl_3$): δ = 9.69 (s, 1H, 34-H), 9.18 (s, 1H, 38-H), 8.85–8.79 (m, 2H, 36-H+44-H), 8.01 (d, *J* = 8.3 Hz, 1H, 41-H), 7.90 (t, *J* = 7.9 Hz, 1H, 43-H), 7.69 (t, *J* = 7.6 Hz, 1H, 42-H), 7.02 (s, 1H, 28-H), 5.32 (t, *J* = 3.7 Hz, 1H, 12-H), 4.51–4.44 (m, 1H, 3-H), 2.81 (s, 1H, 22-H_a), 2.07–1.85 (m, 5H, 16-H_a+9-H+ 22-H_b+15-H_a+16-H_b), 2.03 (s, 3H, 32-H_3), 1.85–1.80 (m, 1H, 19-H_a), 1.80–1.71 (m, 2H, 2-H_a+11-H_a), 1.66–1.52 (m, 4H, 1-H_a+2-H_b+ 11-H_b+18-H), 1.50–1.44 (m, 2H, 6-H_a+21-H_a), 1.38–1.34 (m, 3H, 6-H_b+7-H_a+21-H_b), 1.28–1.22 (m, 2H, 7-H_b+19-H_b), 1.16–1.12 (s, 3H, 27-H_3), 1.08–1.03 (m, 2H, 1-H_b+15-H_b), 1.01 (s, 3H, 30-H_3), 0.98 (s, 3H, 29-H_3), 0.89 (s, 3H, 25-H_3), 0.87 (s, 3H, 23-H_3), 0.84 (s, 3H, 24-H_3), 0.85–0.82 (m, 1H, 5-H), 0.80 (s, 3H, 26-H_3) ppm;
MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* = 640.6 (100%, $[M+H]^+$);
analysis calcd for $C_{41}H_{57}N_3O_3$ (639.93): C 76.95, H 8.98, N 6.57; found: C 76.75, H 9.15, N 6.41.

***N*-[3*β*-Acetyloxy-17*β*-amino-28-norurs-12-en-17-yl]-4-isoquinolyl urea (20)**
As described above, for **19**, **20** (110 mg, 30%) was obtained from **6** (248 mg, 0.5 mmol) as a white solid; m.p. 176–179°C (decomp.) R_F = 0.06 (hexanes/ethyl acetate, 3:1); $[\alpha]_D$ = +21.9° (*c* 0.04, $CHCl_3$);
IR (ATR): $\tilde{\nu}$ = 416*m*, 459*s*, 479*s*, 522*s*, 577*s*, 660*s*, 750*s*, 772*s*, 830*s*, 1026*s*, 1094*m*, 1244*vs*, 1292*m*, 1370*m*, 1402*m*, 1432*m*, 1455*m*, 1538*s*, 1657*m*, 1729*m*, 2871*m*, 2925*m*, 3174*w*, 3314*w* cm^{-1};
^1H NMR (500 MHz, $CDCl_3$): δ = 9.00 (s, 1H, 34-H), 8.71 (s, 1H, 36-H), 8.61 (s, 1H, 38-H), 8.09–7.99 (m, 1H, 44-H), 7.94 (t, *J* = 8.2 Hz, 1H, 41-H), 7.77–7.65 (m, 1H, 43-H), 7.65–7.55 (m, 1H, 42-H), 6.94 (s, 1H, 28-H), 5.00 (s, 1H, 12-H), 4.51–4.38 (m, 1H, 3-H), 2.67–2.61 (m, 1H, 22-H_a), 2.20–2.10 (m, 1H, 16-H_a), 2.04 (s, 3H, 32-H_3), 1.95–1.85 (m, 1H, 16-H_b), 1.84–1.73 (m, 3H, 2-H_a+11-H_a+15-H_a), 1.60–1.57 (m, 2H, 2-H_b+11-H_b), 1.56–1.52 (m, 2H, 1-H_a+ 22-H_b), 1.53–1.46 (m, 1H, 7-H_a), 1.45 (s, 1H, 6-H_a), 1.47–1.38 (m, 3H, 9-H+18-H+21-H_a), 1.40–1.33 (m, 1H, 19-H), 1.31–1.27 (m, 1H, 21-H_b), 1.29–1.25 (m, 1H, 6-H_b), 1.18–1.14 (m, 1H, 7-H_b), 1.01 (s, 3H, 27-H_3), 0.99 (s, 3H, 30-H_3), 0.98–0.97 (m, 2H, 1-H_b+15-H_b), 0.92–0.90 (m, 4H, 20-H+29-H_3), 0.87 (s, 3H, 23-H_3), 0.84 (s, 3H, 24-H_3), 0.82 (s, 3H, 25-H_3), 0.78–0.77 (m, 1H, 5-H), 0.74 (s, 3H, 26-H_3) ppm;
^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.0 (C-31), 154.4 (C-33), 137.9 (C-13), 137.4 (C-38), 131.4 (C-35), 130.9 (C-43), 129.9 (C-40), 128.7 (C-39), 127.9 (C-41), 127.8 (C-42), 127.1 (C-12), 122.4 (C-36), 121.7 (C-44), 80.8 (C-3), 58.9 (C-18), 56.6 (C-17), 55.2 (C-5), 47.4 (C-9), 46.3 (C-14), 41.9 (C-8), 39.8 (C-19), 39.1 (C-20), 38.3 (C-1), 37.6 (C-4), 37.2 (C-22), 32.6 (C-21), 31.4 (C-7), 29.7 (C-10), 28.0 (C-24), 26.7 (C-15), 23.9 (C-16), 23.5 (C-2), 23.3 (C-11), 23.1 (C-27), 21.3 (C-32), 20.7 (C-29), 18.0 (C-6), 17.3 (C-26), 16.8 (C-30), 16.7 (C-25), 15.4 (C-23) ppm;
MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* = 640.6 (100%, $[M+H]^+$);
analysis calcd for $C_{41}H_{57}N_3O_3$ (639.93): C 76.95, H 8.98, N 6.57; found: C 76.73, H 9.11, N 6.41.

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