SYNTHESIS OF BETULONIC ACID AMIDES

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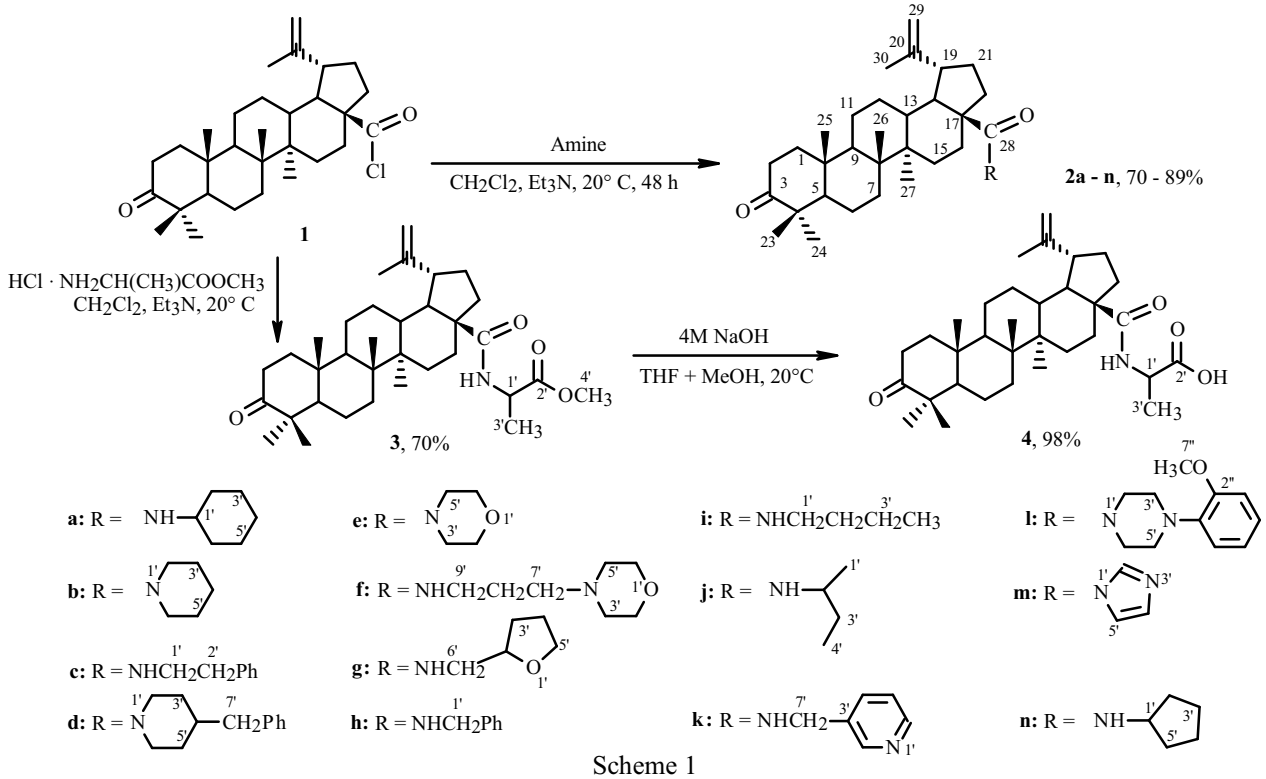
Betulonic acid amides of interest as potential biologically active compounds were prepared.

Key words: betuloic acid, amides, NMR spectra.

Derivatives of betulonic acid containing various substituents on C-28 are known to possess various types of biological activity [1, 2]. Thus, amides, peptides, and hydrazides of betulonic acid exhibit antiviral (including anti-HIV) [3-5], immunostimulating [5], and antitumor activity [6]. It was demonstrated [7] that derivatives of betulonic acid containing ω-amino acids are active indicators of apoptosis in leucocytes and hepatocarcinoma cells *in vitro*. Furthermore, amides containing β-alanine exhibit antioxidant activity and can lower the toxicity of antitumor preparations [8]. In the search for biologically active compounds, we synthesized new amides of betulonic acid for subsequent studies of their pharmacological properties.

The reaction of betulonic acid chloride **1** with various amines produced compounds **2a-n** with the corresponding secondary or tertiary amine group on C-28 (Scheme 1). The reaction was carried out at room temperature in anhydrous CH_2Cl_2 in the presence of triethylamine. The yields of products were 70-89%. The isolated betulonic acid amides were chromatographed over Al_2O_3 in order to obtain analytically pure samples. Amide **3** with the methyl ester of α-alanine on C-28, alkaline hydrolysis of which smoothly gave amino-acid derivative **4**, was synthesized analogously (Scheme 1).



Scheme 1

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TABLE 1. ^{13}C NMR Spectra of Amides **2a**-**n**, **3**, **4** (δ, ppm)

C atom	**2a**	**2b**	**2c**	**2d**	**2e**	**2f**	**2g**	**2h**
C-1	39.46 t	39.47	39.43	39.42	39.43	39.44	39.38	39.40
C-2	33.93 t	33.92	33.95	33.85	33.88	33.91	33.89	33.86
C-3	217.74 d	217.76	217.98	217.56	217.70	217.61	217.98	217.75
C-4	47.10 s	47.08	47.12	47.01	47.05	47.07	47.06	47.03
C-5	54.85 d	54.90	54.81	54.85	54.85	54.86	54.71	54.75
C-6	19.46 t	19.46	19.44	19.42	19.47	19.47	19.40	19.43
C-7	33.57 t	33.51	33.47	33.46	33.48	33.57	33.47	33.38[a]
C-8	40.56 s	40.41	40.47	40.37	40.39	40.54	40.41	40.46
							40.43	
C-9	49.83 d	50.05	49.78	50.01	49.97	49.85	49.73	49.78
							49.75	
C-10	36.74 s	36.74	36.71	36.69	36.70	36.74	36.65	36.66
C-11	21.32 t	21.52	21.23	21.47	21.44	21.31	21.21	21.25
							21.24	
C-12	25.48 t	25.52	25.39	25.47	25.43	25.46	25.36	25.44
							25.38	
C-13	37.69 d	36.80	37.53	36.75	36.75	37.51	37.50	37.48
							37.53	
C-14	42.33 s	41.74	42.30	42.75	41.71	42.32	42.28	42.28
							42.37	
C-15	29.19 t	29.66	29.15	29.61	29.54	29.25	29.11	29.17
							29.17	
C-16	33.57 t	33.51	33.47	33.46	33.48	33.57	33.40	33.49[a]
C-17	55.22 s	54.44	55.42	54.40	54.24	55.29	55.37	55.35
							55.47	
C-18	49.96 d	52.59	49.78	52.52	52.36	49.97	49.71	49.92
							49.87	
C-19	46.67 d	45.49	46.49	45.44	45.37	46.44	46.40	46.35
							46.49	
C-20	150.76 s	151.24	150.64	151.11	150.84	150.71	150.67	150.62
C-21	30.75 t	31.22	30.60	31.18	31.06	30.72	30.58	30.64
							30.62	
C-22	38.27 t	35.72	38.12	35.68	35.60	38.22	38.16	38.13
							38.20	
C-23	26.44 q	26.42	26.40	26.40	26.39	26.44	26.36	26.41
C-24	20.81 q	20.79	20.83	20.75	20.77	20.81	20.76	20.77
C-25	15.80[a] q	15.76[a]	15.78[a]	15.72	15.73[a]	15.71	15.72	15.70
							15.74	
C-26	15.74[a] q	15.71[a]	15.74[a]	15.66	15.67[a]	15.86	15.61	15.70
							15.69	
C-27	14.38 q	14.39	14.32	14.35	14.35	14.35	14.30	14.31
							14.31	
C-28	174.90 t	172.97	175.88	172.98	173.39	175.95	175.94	175.70
							175.97	
C-29	109.09 t	108.79	109.21	108.81	109.03	109.10	109.13	109.12
C-30	19.33 q	19.51	19.26	19.48	19.49	19.30	19.22	19.28
C-1′	47.52 d		35.66	44.45[a]				42.96
C-2′	32.76[b] t	32.25	40.11	32.05[b]	66.71	66.63	77.77	
							77.90	
C-3′	24.73[c] t	26.02		38.16	32.14	53.68	28.22	
							28.29	
C-4′	25.48 t	24.56		32.36[b]			25.63	
							25.69	
C-5′	24.80[c] t	26.02		44.85[a]	32.14	53.68	67.84	
							67.89	

TABLE 1. (continued)

C atom	**2a**	**2b**	**2c**	**2d**	**2e**	**2f**	**2g**	**2h**
C-6′	33.08[b] t	32.25		42.75	66.71	66.63	42.25	
C-7′						57.78		
C-8′						25.03		
C-9′						38.80		
Ar			126.28	125.72				126.94
			128.43	127.98				127.40
			128.51	128.78				128.30
			138.92	139.76				139.05

C atom	**2i**	**2j**	**2k**	**2l**	**2m**	**2n**	**3**	**4**
C-1	39.38	39.47	39.38	39.44	39.36	39.49	39.15	39.38
C-2	33.83	33.92	33.86	33.88	33.80	34.00	33.66	33.86
C-3	217.63	217.67	217.85	217.67	217.51	217.77	217.51	218.86
C-4	46.99	47.08	47.02	47.05	47.01	47.17	46.83	47.11
C-5	54.76	54.85	54.72	54.87	54.69	54.86	54.49	54.71
C-6	19.40	19.46	19.39	19.42	19.30	19.47	19.15	19.40
C-7	33.48	33.57	33.28[a]	33.49	33.27	33.54[a]	33.07	33.38
								33.42
C-8	40.45	40.56	40.44	40.41	40.33	40.56	40.21	40.47
C-9	49.77	49.86	49.74	50.01	49.74	49.84	49.49	49.72
C-10	36.65	36.74	36.65	36.71	36.63	36.76	36.42	36.66
C-11	21.24	21.32	21.23	20.77	21.23	21.31	20.96	21.22
C-12	25.41	25.50	25.40	25.48	25.20	25.47	25.12	25.38
C-13	37.50	37.58	37.47	36.77	36.76	37.65	37.18	37.54
							37.28	37.59
C-14	42.25	42.34	42.25	41.73	41.89	42.35	41.99	42.26
							42.06	42.32
C-15	29.15	29.48	29.15	29.58	29.42	29.19	28.78	29.08
							28.88	29.13
C-16	33.48	33.57	33.44[a]	33.49	32.82	33.68[a]	33.13	33.26
							33.19	33.32
C-17	55.27	55.27	55.37	54.36	57.37	55.19	55.05	55.39
C-18	49.90	50.00	49.87	52.47	51.13	49.93	49.44	49.66
							49.55	49.78
C-19	46.42	46.53	46.30	45.42	44.93	46.64	46.13	46.38
C-20	150.67	150.76	150.46	150.99	149.40	150.84	150.30	150.37
							150.36	150.43
C-21	30.64	30.74	30.60	31.13	30.37	30.75	30.26	30.49
							30.32	30.55
C-22	38.17	38.28	38.04	35.75	36.63	38.16	37.58	37.85
							37.90	38.17
C-23	26.39	26.45	26.40	26.40	26.30	26.44	26.13	26.41
C-24	20.72	20.80	20.74	21.48	20.72	20.86	20.53	20.78
C-25	15.66	15.75	15.70[b]	15.73	15.71	15.76[b]	15.48	15.71
C-26	15.66	15.75	15.58[b]	15.73	15.48	15.79[b]	15.28	15.51
							15.39	15.59
C-27	14.28	14.36	14.28	14.38	14.33	14.41	14.04	14.30
							14.09	14.33

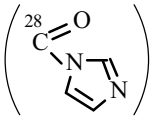
TABLE 1. (continued)

C atom	**2i**	**2j**	**2k**	**2l**	**2m**	**2n**	**3**	**4**
C-28	175.69	175.07	176.13	173.25	172.61	175.5	175.28	176.21
							175.49	176.51
C-29	108.99	109.06	109.18	108.93	109.93	109.16	108.88	109.24
							108.97	109.32
C-30	19.25	19.35	19.26	19.49	19.15	19.35	18.98	19.22
							19.03	19.25
C-1′	38.63	20.15				39.49	47.34	47.70
		20.45						47.60
C-2′	31.67	45.80		32.30	137.24	32.73[c]	173.40	176.81
		45.82					173.42	176.85
C-3′	19.87	29.16		50.75		23.59[d]	17.51	17.49
		29.24					17.83	17.83
C-4′	13.49	10.31			129.56	23.62[d]	51.87	
							51.91	
C-5′				50.75	117.32	33.09[c]		
C-6′				32.30				
C-7′			40.44					
C-7″				55.19				
Ar			123.26	111.28				
			134.93	118.08				
			135.44	120.82				
			148.18	123.14				
			148.72	140.53				
				152.05				

[a,b,c,d]Chemical shifts denoted with the same letters could possibly be switched within the same column.

TABLE 2. Physical Chemical Properties and Yields of **2a-n**, **3**, **4**

Compound	Yield, %	[α], deg, (*c*)	Empirical formula	M^+	
				found	calc.
2a	74	+22 (3.6)	$C_{36}H_{57}NO_2$	535.43718	535.43890
2b	84	+21 (5.2)	$C_{35}H_{55}NO_2$	521.42281	521.42326
2c	72	+31 (5.3)	$C_{38}H_{55}NO_2$	557.42227	557.42326
2d	87	+8 (3.6)	$C_{42}H_{61}NO_2$	611.46932	611.47020
2e	73	+23 (4.2)	$C_{34}H_{53}NO_3$	523.40126	523.40252
2f	75	+26 (3.6)	$C_{37}H_{60}N_2O_3$	580.46206	580.46037
2g	86	+33 (4.5)	$C_{35}H_{55}NO_3$	537.42134	537.41817
2h	80	+43 (4.8)	$C_{37}H_{53}NO_2$	543.40625	543.40761
2i	70	+29 (4.1)	$C_{34}H_{55}NO_2$	509.42338	509.42326
2j	85	+29 (3.5)	$C_{34}H_{55}NO_2$	509.42404	509.42326
2k	83	+26 (4.3)	$C_{36}H_{52}N_2O_2$	544.40151	544.40286
2l	77	+21 (3.4)	$C_{41}H_{60}N_2O_3$	628.45614	628.46037
2m	89	+7 (4.5)	$C_{33}H_{48}N_2O_2$	409.34248*	409.34702*
2n	78	+30 (5.1)	$C_{35}H_{55}NO_2$	521.42281	521.42326
3	70	+30 (4.4)	$C_{34}H_{53}NO_4$	539.39779	539.39743
4	98	+36 (3.7)	$C_{33}H_{51}NO_4$	525.38163	525.38178

*Fragment ion M – 

The compositions and structures of **2a-n**, **3**, and **4** were confirmed by elemental analysis and mass, IR, and NMR spectra. Thus, IR spectra of the synthesized compounds lacked an absorption band at 1804 cm^{-1} corresponding to carbonyl stretching vibrations of COCl and contained bands for stretching vibrations of CONH in the range 1625-1644 cm^{-1} (amide band I) and 3346-3489 cm^{-1} (*trans*-associated NH). PMR and ^{13}C NMR spectra of **2a-n**, **3**, and **4** agreed completely with their structures. Resonances of H and C atoms in NMR spectra of **2a-n**, **3**, and **4** were assigned based on two-dimensional NMR spectra of **2d**, **f**, **g**, **i**, **m**, and **4** using literature data for betulonic acid and its amino-acid derivatives [9, 10]. We verified the resonances for H-2′ (8.23 ppm) and H-4′ (7.00 ppm) (protons of the imidazole ring) of **2m**, for which chemical shifts at 7.01 and 8.25 ppm, respectively, were assigned [11]. Resonances of certain atoms in the NMR spectra of **2g**, **j**, **3**, and **4** were doubled because we used the corresponding amines, including the methyl ester of α-alanine, as a mixture of optical isomers (D and L).

Table 1 lists the ^{13}C NMR spectra of **2a-n**.

EXPERIMENTAL

NMR spectra in $CDCl_3$ were recorded on Bruker AC-200 and AM-400 instruments at operating frequencies 200.13 and 400.13 MHz for ^1H and 50.32 and 100.61 MHz for ^{13}C. The multiplicity of signals in ^{13}C NMR spectra was determined by standard procedures for recording spectra with *J*-modulation (JMOD) and with off-resonance proton decoupling. 2D NMR ^1H—^1H (COSY) and ^{13}C—^1H (COSY 125 Hz, COLOC 7 Hz) spectra of **2d**, **e**, **g**, **h**, **j**, and **n** in $CDCl_3$ were recorded on a Bruker DRX-500 instrument at operating frequency 500.13 MHz for ^1H and 125.76 MHz for ^{13}C using standard Bruker programs. The internal standards were resonances of $CDCl_3$ solvent (δ_C 76.90) and residual protons (δ_H 7.24 ppm). Mass spectra were obtained in a Finnigan MAT 8200 high-resolution mass spectrometer at ionizing potential 70 eV. Specific rotation ($[\alpha]_{580}$) was measured on a Polamat A polarimeter in $CHCl_3$ at room (20-25°C) temperature. Elemental analyses were performed on a Carlo Erba 1106 CHN-analyzer.

The course of reactions and purity of products were monitored using TLC on Silufol UV-254 plates and $CHCl_3$:CH_3CN (30:1) for **2a-c**, **d**, **g**, **h-i**, **m**, **n**, **3**, and **4**; $CHCl_3$:CH_3OH (20:1), **2e-f** and **j-l**. Spots were developed by spraying with H_2SO_4 (20%) followed by heating to 100°C.

Betulonic acid chloride (**1**) was prepared by the literature method [9]. Table 2 lists the physical chemical properties of **2a-n**, **3**, and **4** (yields, constants, mass spectra). The compounds were obtained as amorphous powders. Elemental analyses of **2a-n**, **3**, and **4** agreed with those calculated.

General Method for Synthesizing Amides 2a-n, 3. A solution of betulonic acid chloride (**1**, 1 g, 2.12 mmol) in dry CH_2Cl_2 (60 mL) was treated with amine (4.24 mmol) and distilled triethylamine (8.48 mmol, 1.19 mL). The mixture was stored at room temperature for 48 h, periodically stirred, washed with HCl (10%) and water, dried over anhydrous $MgSO_4$, and evaporated. The resulting compound was chromatographed over Al_2O_3 (activity II) using CH_2Cl_2 and dried over P_2O_5.

***N*-[3-Oxolup-20(29)-en-28-oyl]cyclohexylamine (2a).** PMR spectrum (δ, ppm, J/Hz): 0.86 (3H, s, Me), 0.91 (3H, s, Me), 0.92 (3H, s, Me), 0.95 (3H, s, Me), 1.00 (3H, s, Me), 1.61 (3H, s, Me-30), 3.10 (1H, td, J_1 = 11.2, J_2 = 3.8, H-19), 3.69 (1H, m, H-1′), 4.52 and 4.67 (2H, both br.s, H-29), 5.43 (1H, d, J = 8.3, CONH) (only characteristic proton resonances are given).

***N*-[3-Oxolup-20(29)-en-28-oyl]piperidine (2b).** PMR spectrum (δ, ppm): 0.85 (3H, s, Me), 0.90 (3H, s, Me), 0.91 (3H, s, Me), 0.94 (3H, s, Me), 0.99 (3H, s, Me), 1.61 (3H, s, Me-30), 2.91 (2H, m, H-13,19), 3.45 (4H, m, H-2′,2′,6′,6′), 4.50 and 4.65 (2H, both br.s, H-29) (only characteristic proton resonances are given).

***N*-[3-Oxolup-20(29)-en-28-oyl]-2-phenylethylamine (2c).** IR spectrum (KBr, ν, cm^{-1}): 1639 (CONH), 1704 (C=O), 3392 (CONH). PMR spectrum (δ, ppm, J/Hz): 0.88 (3H, s, Me), 0.91 (6H, s, 2Me), 0.98 (3H, s, Me), 1.02 (3H, s, Me), 1.63 (3H, s, Me-30), 2.40 (3H, m, H-2,1′,1′), 2.78 (2H, m, H-2,13), 3.20 (1H, td, J_1 = 11.9, J_2 = 4.8, H-19), 3.48 (2H, m, H-2′,2′), 4.54 and 4.68 (2H, both br.s, H-29), 5.66 (1H, t, J = 5.3, CONH), 7.15-7.29 (5H, m, Ph) (only characteristic proton resonances are given).

***N*-[3-Oxolup-20(29)-en-28-oyl]-4-benzylpiperidine (2d).** PMR spectrum (δ, ppm, J/Hz): 0.89 (3H, s, Me-25), 0.91 (1H, m, H-12), 0.93 (3H, s, Me-27), 0.95 (3H, s, Me-26), 0.99 (3H, s, Me-24), 1.03 (3H, s, Me-23), 1.07 (2H, m, H-3′,5′), 1.13 (1H, m, H-15), 1.24-1.46 (12H, m, H-1,5,6,6,7,7,9,11,11,15,21,22), 1.46 (1H, m, H-16), 1.52 (1H, t, J = 11.2, H-18), 1.60-1.76 (4H, m, H-12,3′,4′,5′), 1.65 (3H, s, Me-30), 1.85 (2H, m, H-1,21), 1.92 (1H, m, H-22), 2.07 (1H, dt, J_1 = 13.3, J_2 = 3.4, H-16), 2.36 (1H, m, H-2), 2.43 (1H, m, H-2), 2.51 (2H, d, J = 7.2, H-7′), 2.64 (2H, m, H-2′,6′), 2.92 (1H, ddd, J_1 = 13.1, J_2 = 11.4,

J_3 = 3.6, H-13), 2.97 (1H, td, J_1 = 11.0, J_2 = 3.9, H-19), 4.32 (2H, m, H-2′,6′), 4.54 and 4.69 (2H, both br.s, H-29), 7.09 (2H, m, $2H_o$), 7.15 (1H, m, H_p), 7.23 (2H, m, $2H_m$).

***N*-[3-Oxolup-20(29)-en-28-oyl]morpholine (2e).** PMR spectrum (δ, ppm): 0.85 (3H, s, Me), 0.91 (6H, s, 2Me), 0.96 (3H, s, Me), 0.99 (3H, s, Me), 1.61 (3H, s, Me-30), 2.88 (2H, m, H-13,19), 3.55 (8H, m, H-2′,2′,3′,3′,5′,5′,6′,6′), 4.51 and 4.65 (2H, both br.s, H-29) (only characteristic proton resonances are given).

***N*-[3-Oxolup-20(29)-en-28-oyl]-3-morpholinopropylamine (2f).** IR spectrum (KBr, ν, cm^{-1}): 1638 (CONH), 1699 (C=O), 3357, 3489 (CONH). PMR spectrum (δ, ppm, J/Hz): 0.83 (3H, s, Me-25), 0.89 (6H, s, Me-26,27), 0.91 (1H, m, H-12), 0.93 (3H, s, Me-24), 0.98 (3H, s, Me-23), 1.07 (1H, dt, J_1 = 13.2, J_2 = 3.2, H-15), 1.15-1.52 (14H, m, H-1,5,6,6,7,7,9,11,11,15,16,18,21,22), 1.59 (3H, s, Me-30), 1.60-1.68 (4H, m, H-12,22,8′,8′), 1.82 (1H, m, H-1), 1.87 (1H, m, H-21), 1.90 (1H, m, H-16), 2.31 (1H, m, H-2), 2.35-2.43 (7H, m, H-2,3′,3′,5′,5′,7′,7′), 2.46 (1H, ddd, J_1 = 13.0, J_2 = 11.5, J_3 = 3.8, H-13), 3.07 (1H, td, J_1 = 11.2, J_2 = 4.5, H-19), 3.24 (2H, td, J_1 = 6.4, J_2 = 5.1, H-9′,9′), 3.64 (4H, t, J = 4.7, H-2′,2′,6′,6′), 4.50 and 4.65 (2H, both br.s, H-29), 6.76 (1H, t, J = 5.1, CONH).

***N*-[3-Oxolup-20(29)-en-28-oyl]tetrahydrofurfurylamine (2g).** PMR spectrum (δ, ppm, J/Hz): 0.86 (3H, s, Me-25), 0.91 (6H, s, Me-26,27), 0.93 (1H, m, H-12), 0.95 (3H, s, Me-24), 1.00 (3H, s, Me-23), 1.11 (1H, m, H-15), 1.18-1.55 (15H, m, H-1,5,6,6,7,7,9,11,11,15,16,18,21,22,3′), 1.62 (3H, s, Me-30), 1.63-1.75 (2H, m, H-12,22), 1.79-1.95 (6H, m, H-1,16,21,4′,4′,3′), 2.33 (1H, m, H-2), 2.42 (2H, m, H-2,13), 3.07 (1H, m, H-19), 3.07, 3.17, 3.45, 3.53 (2H, m, H-6′,6′), 3.69 and 3.79 (2H, m, H-5′,5′), 3.89 (1H, m, H-2′), 4.52 and 4.67 (2H, both br.s, H-29), 5.92 and 5.95 (1H, t, J = 7.1, CONH).

***N*-[3-Oxolup-20(29)-en-28-oyl]benzylamine (2h).** PMR spectrum (δ, ppm, J/Hz): 0.86 (3H, s, Me), 0.88 (3H, s, Me), 0.92 (3H, s, Me), 0.96 (3H, s, Me), 1.01 (3H, s, Me), 1.64 (3H, s, Me-30), 3.13 (1H, td, J_1 = 11.2, J_2 = 3.5, H-19), 4.35 (2H, ABX, J_1 = 15.1, J_2 = 5.8, H-1′,1′), 4.54 and 4.68 (2H, both br.s, H-29), 6.19 (1H, t, J = 4.6, CONH), 7.23 (5H, m, Ph) (only characteristic proton resonances are given).

***N*-[3-Oxolup-20(29)-en-28-oyl]-*n*-butylamine (2i).** PMR spectrum (δ, ppm, J/Hz): 0.84 (3H, s, Me-25), 0.85 (3H, t, J = 10.3, Me-4′), 0.90 (6H, s, Me-26,27), 0.92 (1H, m, H-12), 0.94 (3H, s, Me-24), 0.99 (3H, s, Me-23), 1.09 (1H, m, H-15), 1.15-1.45 (17H, m, H-1,5,6,6,7,7,9,11,11,15,16,21,22,2′,2′,3′,3′), 1.49 (1H, m, H-18), 1.60 (3H, s, Me-30), 1.66 (2H, m, H-12,22), 1.82 (1H, m, H-1), 1.88 (2H, m, H-16,21), 2.32 (1H, m, H-2), 2.42 (2H, m, H-2,13), 3.08 (2H, m, H-19,1′), 3.22 (1H, m, H-1′), 4.51 and 4.65 (2H, both br.s, H-29), 5.73 (1H, t, J = 5.3, CONH).

***N*-[3-Oxolup-20(29)-en-28-oyl]-*sec*-butylamine (2j).** IR spectrum (KBr, ν, cm^{-1}): 1625 (CONH), 1709 (C=O), 3346 (CONH). PMR spectrum (δ, ppm, J/Hz): 0.85 (3H, s, Me), 0.91 (3H, s, Me), 0.92 (3H, s, Me), 0.95 (3H, s, Me), 0.99 (3H, s, Me), 1.61 (3H, s, Me-30), 3.09 (1H, td, J_1 = 12.1, J_2 = 3.8, H-19), 3.83 (1H, m, H-2′), 4.51 and 4.65 (2H, both br.s, H-29), 5.34 (1H, d, J = 8.1, CONH) (only characteristic proton resonances are given).

***N*-[3-Oxolup-20(29)-en-28-oyl]pyridin-3-yl-methylamine (2k).** PMR spectrum (δ, ppm, J/Hz): 0.79 (3H, s, Me), 0.81 (3H, s, Me), 0.88 (3H, s, Me), 0.92 (3H, s, Me), 0.96 (3H, s, Me), 1.59 (3H, s, Me-30), 3.06 (1H, td, J_1 = 12.2, J_2 = 3.8, H-19), 4.33 (2H, ABX, J_1 = 15.5, J_2 = 5.6, H-7′,7′), 4.51 and 4.65 (2H, both br.s, H-29), 6.55 (1H, t, J = 4.6, CONH), 7.16, 7.58, 8.41 (1H, 1H, 2H, heterocycle) (only characteristic proton resonances are given).

***N*-[3-Oxolup-20(29)-en-28-oyl]-4-(2-methoxyphenyl)piperazine (2l).** PMR spectrum (δ, ppm, J/Hz): 0.87 (3H, s, Me), 0.93 (3H, s, Me), 0.94 (3H, s, Me), 0.96 (3H, s, Me), 1.01 (3H, s, Me), 1.64 (3H, s, Me-30), 2.96 (6H, m, H-13,19,3′,3′,5′,5′), 3.73 (4H, m, H-2′,2′,6′,6′), 3.81 (3H, s, H-7″), 4.53 and 4.68 (2H, both br.s, H-29), 6.77-7.02 (4H, m, Ar) (only characteristic proton resonances are given).

***N*-[3-Oxolup-20(29)-en-28-oyl]-1-imidazole (2m).** PMR spectrum (δ, ppm, J/Hz): 0.85 (3H, s, Me-25), 0.87 (3H, s, Me-26), 0.93 (6H, s, Me-24,27), 0.94 (1H, m, H-12), 0.97 (3H, s, Me-23), 1.09-1.45 (12H, m, H-1,5,6,6,7,7,9,11,11,15,15,21), 1.62 (3H, s, Me-30), 1.65 (1H, m, H-22), 1.69 (1H, m, H-18), 1.71 (1H, m, H-12), 1.74 (1H, m, H-16), 1.78 (1H, m, H-21), 1.82 (1H, m, H-1), 2.22 (1H, m, H-22), 2.32 (1H, m, H-2), 2.37 (1H, m, H-16), 2.40 (1H, m, H-2), 2.65 (1H, ddd, J_1 = 13.0, J_2 = 11.7, J_3 = 3.6, H-13), 2.88 (1H, td, J_1 = 11.2, J_2 = 4.8, H-19), 4.56 and 4.68 (2H, both br.s, H-29), 7.00 (1H, br.s, H-4′), 7.49 (1H, br.s, H-5′), 8.23 (1H, br.s, H-2′).

***N*-[3-Oxolup-20(29)-en-28-oyl]cyclopentylamine (2n).** PMR spectrum (δ, ppm, J/Hz): 0.89 (3H, s, Me), 0.94 (3H, s, Me), 0.95 (3H, s, Me), 0.98 (3H, s, Me), 1.03 (3H, s, Me), 1.65 (3H, s, Me-30), 3.13 (1H, td, J_1 = 11.2, J_2 = 4.2, H-19), 4.14 (1H, m, H-1′), 4.55 and 4.70 (2H, both br.s, H-29), 5.44 (1H, d, J = 7.0, CONH) (only characteristic proton resonances are given).

Methyl Ester of *N*-[3-Oxolup-20(29)-en-28-oyl]-D,L-α-aminopropionic Acid (3). IR spectrum (KBr, ν, cm^{-1}): 1644 (CONH), 1704 (C=O), 1744 ($COOCH_3$), 3395 (CONH). PMR spectrum (δ, ppm, J/Hz): 0.85 (3H, s, Me), 0.90 (3H, s, Me),

0.94 (6H, s, 2Me), 0.99 (3H, s, Me), 1.61 (3H, s, Me-30), 3.04 (1H, td, J_1 = 11.1, J_2 = 4.0, H-19), 3.68 (3H, s, Me-4′), 4.46 (1H, m, H-1′), 4.52 and 4.66 (2H, both br.s, H-29), 6.06 and 6.12 (1H, both d, J_1 = 7.1, CONH) (only characteristic proton resonances are given).

***N*-[3-Oxolup-20(29)-en-28-oyl]-D,L-α-aminopropionic Acid (4).** A solution of **3** (0.54 g, 1 mmol) in CH_3OH (10 mL) and THF (5 mL) under Ar at 0°C was treated with NaOH solution (2 mL, 8 mmol, 4 M), stored at room temperature for 1 d, and poured into ice mixed with HCl. The resulting precipitate was filtered off, washed with water, and dried over P_2O_5 to afford **4** (0.52 g, 98%) as an amorphous powder. IR spectrum (KBr, ν, cm^{-1}): 1641 (CONH), 1706 (C=O), 3430 (CONH). PMR spectrum (δ, ppm, J/Hz): 0.89 and 0.90 (3H, s, Me-25), 0.94 and 0.95 (3H, s, Me-26), 0.96 (3H, s, Me-27), 0.97 (1H, m, H-12), 1.00 (3H, s, Me-24), 1.04 (3H, s, Me-23), 1.14-1.41 (12H, m, H-1,5,6,6,7,7,9,11,11,15,21,22), 1.43 and 1.45 (3H, d, J = 7.0, H-3′), 1.47-1.62 (3H, m, H-15,16,18), 1.66 (3H, s, Me-30), 1.67-2.01 (5H, m, H-1,12,16,21,22), 2.33-2.52 (3H, m, H-2,2,13), 3.07 (1H, td, J_1 = 11.2, J_2 = 4.0, H-19), 4.51 (1H, m, H-1′), 4.58 and 4.71 (2H, both br.s, H-29), 6.05 and 6.11 (1H, both d, J_1 = 7.0, CONH), 8.84 (1H, broad, COOH).

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