Synthesis of lupane triterpenoids with triphenylphosphonium substituents and studies of their antitumor activity

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New derivatives of lupane triterpenoids, *viz.*, 20,29-dihydrobetulinic and 3-*epi*-20,29-dihydrobetulinic acid derivatives containing triphenylphosphonium fragments as substituents were synthesized. These compound considerably exceed betulinic acid in antitumor activity.

Key words: lupane triterpenoids, betulinic acid, triphenylphosphonium compounds, anticancer compounds.

Native pentacyclic lupane triterpenoids (betulin, betulinic acid) and their synthetic derivatives are an important class of biologically active compounds with a wide range of biological and pharmacological effects. Lupane triterpenoids are of special interest due to their antitumor and antiviral properties.[1—3] In 1995, betulinic acid was discovered to exhibit high cytotoxicity toward human melanoma by the induction of the cancer cells apoptosis (ED_{50} 1.1—4.8 μg mL^{-1}).[4,5] Later, this natural compound was reported to display antitumor activity toward other types of malignant cells.[6,7] Betulinic acid and its certain synthetic derivatives belong to a group of mitocanes, *i.e.*, anticancer compounds whose biological targets are mitochondria.[8] This compound promotes accumulation of active oxygen-containing particles in the cancer cell mitochondria, that leads to the increase in the mitochondria membrane penetrability and induction of cell apoptosis independent of their p53-status.[7,9,10]

In the series of mitochondrion-targeted antitumor compounds, the most promising results were obtained when small positively charged molecules were used, in particular, the molecules conjugated with a lipophilic membrane-penetrating triphenylphosphonium cation.[11,12] From the literature data,[13—16] it follows that compounds containing triphenylphosphonium cation are promising ionic molecules for the targeted delivery of neutral biologically active compounds into cancer cell mitochondria, including antitumor agents possessing prooxidant properties and destabilizing mitochondrion membranes. Betulinic acid and its semi-synthetic derivatives, undoubtedly, belong to such compounds. At the same time, there are no literature data on the synthesis of phosphonium salts of lupane pentacyclic triterpenoids and on the studies of their cytotoxic effect toward cancer cells.

Results and Discussion

Synthesis. The present studies are devoted to the development of efficient methods for the conversion of dihydrobetulinic (**1**) and 3-*epi*-dihydrobetulinic acids (**2**) to the earlier unknown triphenylphosphonium salts **3**—**8** and to the *in vitro* studies of cytotoxic effect of the latter on the Ehrlich carcinoma and mastocytoma P-815 cancer cell lines.

The key intermediates in the synthesis of the target phosphonium salts **3**—**8** (Scheme 1), *i.e.* 2-β-allyl-substituted methyl- and benzyldihydrobetulonates **12** and **13**, were obtained based on betulonic acid **9** available from betulin,[17] which was transformed into compounds **10** and **11** using typical procedures.[18,19]

Dihydrobetulonates **12** and **13** were obtained by the reaction of deprotonated ketones **10** and **11** with allyl bromide in 1,2-dimethoxyethane under the kinetic control conditions according to the method reported by us earlier[20] (see Scheme 1). The reduction of the keto group in compounds **12** and **13** with $NaBH_4$ or L-selectride gives their 2-hydroxy derivatives, which are necessary for subsequent transformations into triphenylphosphonium salts (Scheme 2). The studies of this reaction allowed us to reveal a considerable influence of the C(2)-allylic fragment on stereochemistry of the reduction process of 3-keto group in ring *A*. Thus, in contrast to the highly stereose-

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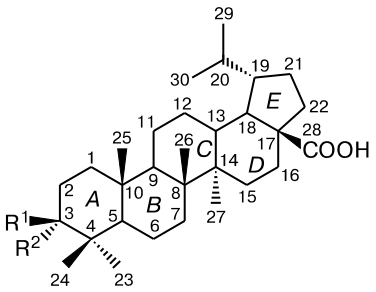
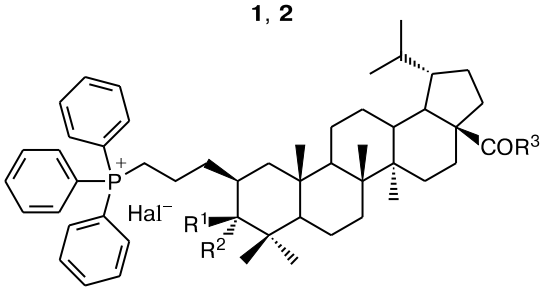


1, **2**



3—8

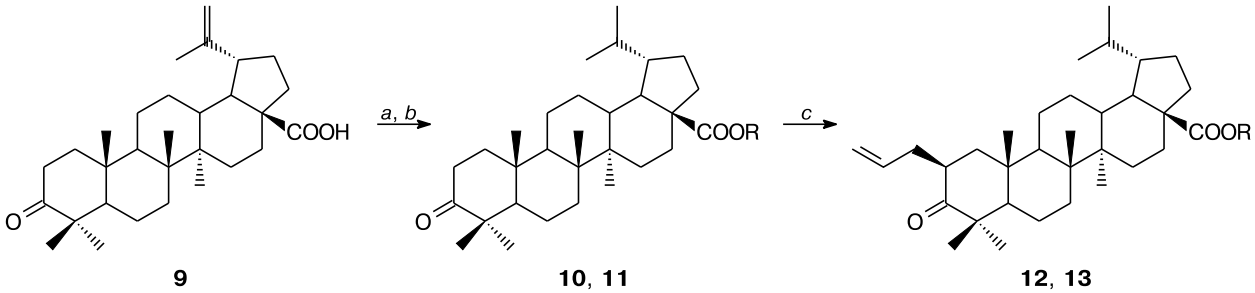
Compound	R^1	R^2	R^3	Hal
1	OH	H	—	—
2	H	OH	—	—
3	OAc	H	OMe	Br
4	H	OAc	OMe	Br
5	OH	H	OMe	I
6	H	OH	OMe	I
7	OAc	H	OH	Br
8	OAc	H	OBn	I

lective transformation of betulonic acid into betulinic acid (3β-OH : 3α-OH = 94 : 6),[17,21] the reaction of compounds **12** and **13** with $NaBH_4$ in the MeOH—$CHCl_3$ or MeOH—THF solvent systems led to a mixture of epimers **14** and **15** with a slight predominance of the 3β-epimer (3β-OH : 3α-OH = 68 : 32). The spin-spin coupling constant ($^3J_{H(2),H(3)}$ = 10 Hz) of proton H(3) with the axial proton H(2) (the axial position of the latter was established earlier[20]) in the ^1H NMR spectra of compounds **14** and **15** indicates the axial position of proton H(3) and, consequently, β-orientation of the OH-group (in α-epimer **16**, the spin-spin coupling constant $^3J_{H(2),H(3)}$ = 1.5—2 Hz). The stereoselectivity of the reaction was considerably increased by using $NaBH_4$ modified with $CeCl_3 \cdot 7H_2O$.[22] In this case, 3β-epimers **14** and **15** were obtained with 95—96% selectivity. The authors of the work[22,23] explain the stereospecificity of the reduction of ketones with the reagent $NaBH_4$—$CeCl_3 \cdot 7H_2O$ by the formation of a complex of the cerium ion with the carbonyl oxygen atom, that promotes the "axial" attack by the hydride anion on the ketone with subsequent formation of an equatorial alcohol.

The influence of the allylic substituent in compounds **12** and **13** was found to exist also when a bulky reducing agent lithium tri(*sec*-butyl)borohydride (L-selectride) was used. The reaction of dihydrobetulonate **12** with L-selectride led to 3α-alcohol **16** with high selectivity (3α-OH : 3β-OH = 96 : 4), that considerably differed from the results of reduction of betulonic acid with L-selectride.[24] The obtained alcohols **14**, **16** and their acetates **17—19** were converted into phosphonium salts **3—8** in good yields (see Scheme 2). To achieve this, the double bond in compounds **14** and **16—19** was hydroborated, the primary alcohols **20**, **21**, and **24** were converted to iodides **25—27** upon the action of iodine in the presence of imidazole and triphenylphosphine, whereas alcohols **22—24** were converted to bromides **31—33** through the step of the corresponding mesylates **28—30**. The reaction of halide **25—27**, **31**, **32**, and **34** with excess of triphenylphosphine in refluxing toluene gave the target triphenylphosphonium salts **3—8** (see Scheme 2).

The structures of all the compounds obtained were confirmed by 1D (^1H, ^{13}C, APT, ^{31}P), 2D homo- (COSY, NOESY) and hetero-NMR-experiments (HSQC, HMBC). The ^{13}C NMR spectra of compounds **3—34** are given in Tables 1—3. In the ^{31}P NMR spectra of salts **3—8**, the signals for the phosphorus atom were observed in the region δ 23.37—24.34 indicative for phosphonium salts.[25]

Scheme 1

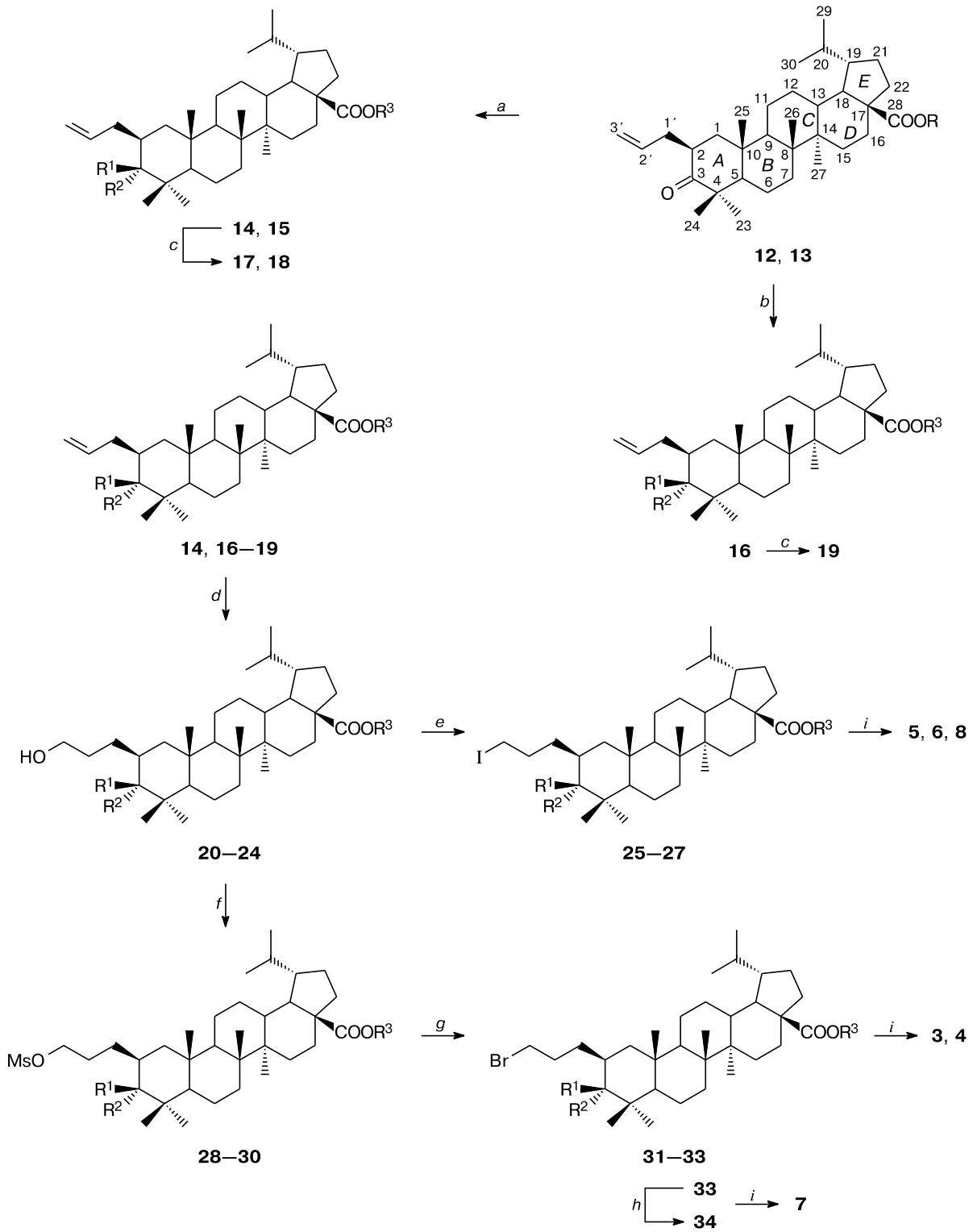


9 **10**, **11** **12**, **13**

R = Me (**10**,**12**), Bn (**11**,**13**)

Reagents and conditions: *a*. H_2, Pd/C, MeOH—THF (50 : 50), 20 °C, 94%; *b*. CH_2N_2, Et_2O, 20 °C, yield 89%, or BnCl, DMF, K_2CO_3, 55 °C, yield 92%; *c*. $KN(SiMe_3)_2$, Et_3B, C_3H_5Br, dimethoxyethane, 20 °C, Ar, 77—79%.

Scheme 2



R = Me (**12**), OBn (**13**); R^1 = OH, R^2 = H, R^3 = Me (**14**, **20**, **25**); R^1 = OH, R^2 = H, R^3 = Bn (**15**); R^1 = H, R^2 = OH, R^3 = Me (**16**, **21**, **26**); R^1 = OAc, R^2 = H, R^3 = Me (**17**, **22**, **28**, **31**); R^1 = OAc, R^2 = H, R^3 = Bn (**18**, **24**, **27**, **30**, **33**); R^1 = H, R^2 = OAc, R^3 = Me (**19**, **23**, **29**, **32**); R^1 = OAc, R^2 = H, R^3 = H (**34**)

Reagents and conditions: *a*. $NaBH_4$, $CeCl_3 \cdot 7H_2O$, MeOH—THF, −30 °C→20 °C, Ar; *b*. L-Selectride, THF, −78 °C→20 °C, Ar; *c*. Ac_2O, Py, DMAP, 20 °C; *d*. $BH_3 \cdot$THF, THF, 20 °C, Ar; *e*. I_2, PPh_3, imidazole, THF, 0 °C; *f*. MsCl, Py, CH_2Cl_2, DMAP, 20 °C; *g*. LiBr, Me_2CO, reflux, Ar; *h*. Pd/C, Et_2O; *i*. PPh_3, CH_3Ph, reflux, Ar.

Table 1. ^{13}C NMR spectra (δ, *J*/Hz) of compounds **3—8** and **12—14**

Atom or group	**3**	**4**	**5**	**6**	**7**	**8**	**12**	**13**	**14**
1	44.18	40.81	44.22	44.36	44.14	44.16	46.86	46.86	44.14
2	34.22	32.24	34.34	32.09	34.23	34.20	41.50	41.49	35.34
3	82.84	78.42	82.61	77.43	82.92	82.80	216.97	217.19	82.61
4	38.82	37.34	39.29	37.28	38.85	38.84	48.30	48.30	39.12
5	55.17	49.93	55.25	48.86	55.16	55.15	57.95	57.25	55.49
6	18.30	17.96	18.51	19.33	18.30	18.30	19.34	19.34	18.49
7	32.51	34.15	34.52	34.91	32.52	32.47	34.16	34.14	34.36
8	40.71	41.42	40.69	40.66	40.73	40.69	40.76	40.74	40.69
9	50.22	49.93	50.14	51.17	50.19	50.23	49.86	49.87	50.32
10	37.26	37.67	37.28	36.76	37.40	37.23	37.35	37.33	37.89
11	20.96	20.69	20.95	21.27	20.93	20.97	21.17	21.16	20.90
12	23.00	22.79	23.01	22.87	23.02	23.01	25.27	25.28	22.97
13	38.01	38.07	38.12	38.13	38.11	37.93	38.09	38.01	38.09
14	42.53	42.62	42.55	42.53	42.58	42.54	42.65	42.66	42.53
15	29.58	29.65	29.63	29.65	29.61	29.47	29.63	29.52	29.63
16	32.03	32.14	32.05	32.02	32.07	31.97	32.06	32.00	32.06
17	56.96	57.00	56.99	57.02	56.77	56.93	56.95	56.92	56.95
18	48.90	48.89	48.92	48.86	48.72	48.89	48.92	48.91	48.93
19	44.27	44.22	44.21	44.18	44.30	44.27	44.19	44.17	45.03
20	28.15	27.75	28.52	33.45	28.17	28.15	26.84	26.87	28.43
21	29.80	29.65	29.77	29.74	29.79	29.80	29.75	29.76	29.72
22	37.10	37.65	37.13	36.76	37.13	37.09	37.29	37.27	37.17
23	26.82	26.75	26.94	26.92	26.81	26.84	22.96	22.98	26.94
24	16.94	21.28	16.91	22.76	16.94	15.82	21.74	21.75	16.22
25	17.08	16.77	16.93	16.83	17.08	17.09	16.12	16.06	16.82
26	15.95	16.00	15.96	16.38	16.07	16.98	16.04	15.99	15.97
27	14.71	14.84	14.71	14.72	14.71	14.70	14.67	14.67	14.69
28	176.83	176.95	176.89	176.88	181.81	175.97	176.70	175.97	176.82
29	22.75	23.00	22.76	22.99	22.75	22.73	22.76	22.74	22.74
30	14.53	14.65	15.01	14.59	14.52	14.10	14.55	14.52	14.64
1′	32.97 ($^1J_{C,P}$ = 15)	33.42 ($^1J_{C,P}$ = 16)	34.54 ($^1J_{C,P}$ = 16)	33.10 ($^1J_{C,P}$ = 16)	33.03 ($^1J_{C,P}$ = 15)	33.10 ($^1J_{C,P}$ = 15)	34.55	34.56	37.29
2′	19.09 ($^1J_{C,P}$ = 4)	20.12 ($^1J_{C,P}$ = 4)	20.38 ($^1J_{C,P}$ = 4)	19.95 ($^1J_{C,P}$ = 4)	19.08 ($^1J_{C,P}$ = 3)	19.02 ($^1J_{C,P}$ = 3)	136.78	136.93	137.52
3′	22.98 ($^1J_{C,P}$ = 66)	23.06 ($^1J_{C,P}$ = 68)	23.48 ($^1J_{C,P}$ = 48)	22.51 ($^1J_{C,P}$ = 68)	22.99 ($^1J_{C,P}$ = 50)	23.35 ($^1J_{C,P}$ = 49)	116.29	116.18	116.05
OMe	51.17	51.15	51.16	51.89	—	—	51.18	—	51.15
Me<u>C</u>O	171.52	171.39	—	—	171.55	171.51	—	—	—
<u>Me</u>CO	21.41	21.61	—	—	21.38	21.40	—	—	—
OCH_2Ph	—	—	—	—	—	65.61	—	65.63	—
Ph	118.47 (d, $^1J_{C,P}$ = 85); 130.50 (d, $^1J_{C,P}$ = 12); 133.74 (d, $^2J_{C,P}$ = 10); 134.95 (br.s)	118.43 (d, $^1J_{C,P}$ = 85); 130.44 (d, $^1J_{C,P}$ = 12); 132.08 (d, $^1J_{C,P}$ = 10); 134.91 (br.s)	118.50 (d, $^1J_{C,P}$ = 85); 130.50 (d, $^1J_{C,P}$ = 13); 133.76 (d, $^1J_{C,P}$ = 10); 135.05 (br.s)	118.40 (d, $^1J_{C,P}$ = 85); 130.60 (d, $^1J_{C,P}$ = 13); 132.71 (d, $^1J_{C,P}$ = 10); 135.15 (br.s)	118.44 (d, $^1J_{C,P}$ = 84); 130.50 (d, $^3J_{C,P}$ = 12); 133.74 (d, $^2J_{C,P}$ = 9); 134.97 (br.s)	118.18 (d, $^1J_{C,P}$ = 85); 130.50 (d, $^3J_{C,P}$ = 12); 133.69 (d, $^2J_{C,P}$ = 10); 128.01, 128.23, 128.44, 135.09, 136.52	—	128.02, 128.27, 128.47, 136.58	—

Pharmacological studies. Cytotoxic effect of phosphonium salts on the Ehrlich carcinoma and mastocytoma P-815 cancer cell lines was studied *in vitro*. Betulinic acid was a comparison compound. The mastocytoma P-815 and Ehrlich carcinoma cell lines were used for the study of antitumor activity. Ehrlich carcino-

Table 2. ^{13}C NMR spectra (δ, *J*/Hz) of compounds **15—24**

Atom or group	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**
1	44.18	39.99	44.19	44.18	40.47	44.18	40.69	44.20	40.89	44.19
2	35.40	32.88	34.33	34.32	32.65	34.39	32.65	34.32	32.25	34.32
3	82.76	78.37	83.72	83.73	77.36	82.62	78.45	83.84	79.95	83.85
4	39.13	38.08	38.89	38.89	37.96	39.15	38.08	38.83	37.83	38.82
5	55.48	48.96	55.35	55.35	50.11	55.47	49.01	55.28	50.12	55.28
6	18.49	18.24	18.37	18.37	18.23	18.52	18.21	18.37	18.02	18.37
7	34.36	34.30	33.30	33.31	34.22	34.54	34.30	33.10	34.22	33.10
8	40.71	40.91	40.75	40.74	40.74	40.71	40.91	40.76	41.14	40.75
9	50.37	50.12	50.29	50.31	50.15	50.37	50.10	50.34	50.12	50.36
10	37.93	37.87	37.31	37.27	37.66	37.31	37.68	37.30	37.67	37.28
11	20.92	20.78	20.93	20.93	20.75	20.94	20.78	20.97	20.75	20.97
12	22.98	22.97	22.96	22.98	22.96	22.98	22.98	22.98	22.98	22.98
13	38.06	38.30	38.09	38.02	38.08	38.07	38.25	38.09	38.08	38.03
14	42.59	42.63	42.56	42.57	42.64	42.55	42.63	42.57	42.65	42.58
15	29.55	29.63	29.63	29.53	29.68	29.63	29.63	29.63	29.68	29.53
16	32.05	32.09	32.08	32.02	32.11	32.09	32.10	32.08	32.12	32.03
17	56.97	57.01	56.98	56.96	56.99	56.98	57.02	56.99	57.00	56.97
18	48.95	48.96	48.94	48.94	48.95	48.93	48.95	48.93	48.94	48.93
19	45.08	44.21	44.96	44.97	44.19	45.20	44.22	44.74	44.21	44.75
20	28.41	28.58	28.18	28.19	27.59	28.51	28.65	28.24	27.70	28.24
21	29.76	29.73	29.74	29.75	29.74	29.73	29.73	29.74	29.74	29.75
22	37.20	37.32	37.13	37.27	37.31	37.13	37.32	37.09	37.32	37.08
23	26.98	26.92	26.90	26.93	26.92	26.94	26.90	26.87	26.90	26.90
24	15.86	21.87	16.93	15.86	21.06	16.29	20.78	16.92	21.07	15.87
25	16.84	16.74	17.08	17.08	16.70	16.84	16.78	17.08	16.76	17.08
26	16.20	16.01	15.99	16.94	16.02	15.97	16.01	15.99	16.04	16.93
27	14.60	14.71	14.68	14.67	14.85	14.69	14.72	14.68	14.85	14.67
28	176.80	176.88	176.76	176.85	176.32	176.92	176.94	176.64	177.31	176.70
29	22.75	22.77	22.76	22.74	22.76	22.76	22.77	22.76	22.77	22.75
30	14.68	14.69	14.56	14.53	14.56	14.63	14.69	14.57	14.66	14.53
1′	37.30	37.74	37.27	37.12	37.47	29.63	29.15	29.65	28.80	29.65
2′	137.56	137.55	136.86	136.87	136.85	28.68	30.17	28.11	30.35	28.11
3′	116.11	115.74	116.00	116.00	116.02	63.61	63.22	63.15	63.00	63.16
OMe	—	51.13	51.15	—	51.15	51.17	51.15	51.17	51.17	—
Me<u>C</u>O	—	—	171.30	171.20	171.20	—	—	171.30	171.30	172.43
<u>Me</u>CO	—	—	21.10	21.10	21.60	—	—	21.11	21.59	21.10
Me—S	—	—	—	—	—	—	—	—	—	—
OCH_2Ph	65.61	—	—	65.60	—	—	—	—	—	65.60
Ph	128.00, 128.25, 128.46, 136.63	—	—	127.99, 128.25, 128.45, 136.87	—	—	—	—	—	127.99, 128.25, 128.45, 138.40

ma was supported *in vivo* in the BALB/c mice line by intraperitoneal transplantation method. Mastocytoma P-815 was supported *in vitro*. The animals were kept in compliance with the rules of laboratory practice (GLP, Good Laboratory Practice) and the order of the Ministry of Health of Russian Federation No. 267 dated by 19.06.2003 "On approval of the rules of laboratory practice".

To determine antitumor activity, the tumor cells were cultured in 96-pit round-bottom plates in the concentration of $2 \cdot 10^4$ mL^{-1} at 37 °C in CO_2 atmosphere (5%) and absolute humidity over 48 h in the presence of compounds under study in different dilutions. Four hours before stopping the incubation, 1-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT, Merck Biosciences) was added into the pits.[26] After the incubation was stopped, the supernatant was removed, the precipitate was dissolved in DMSO, and absorption was measured using light solutions with the wavelength of 530 nm on a Uniplan spectrophotometer (PIKON Ltd.).

Table 3. ^{13}C NMR spectra (δ, *J*/Hz) of compounds **25—34**

Atom or group	**25**	**26**	**27**	**28**	**29**	**30**	**31**	**32**	**33**	**34**
1	44.20	40.32	44.19	44.20	40.87	44.19	44.20	40.90	44.19	44.18
2	34.79	32.10	34.31	34.30	32.11	34.29	34.31	32.13	34.30	34.30
3	82.66	78.53	83.56	83.46	79.36	83.47	83.56	79.64	83.57	83.58
4	39.16	38.06	38.85	38.85	37.82	38.85	38.85	37.87	38.85	38.86
5	55.38	48.95	55.23	55.26	50.05	55.26	55.25	50.08	55.24	55.23
6	18.52	18.26	18.36	18.36	17.99	18.36	18.36	18.00	18.36	18.34
7	34.36	34.29	32.77	32.90	34.18	32.90	32.89	34.22	32.89	32.91
8	40.73	40.91	40.76	40.77	41.10	40.75	40.77	41.09	40.75	40.77
9	50.37	50.10	50.34	50.33	50.09	50.35	50.32	50.08	50.34	50.27
10	37.32	37.69	37.28	37.30	37.67	37.27	37.30	37.68	37.27	37.41
11	20.96	20.79	20.98	20.98	20.75	20.97	20.98	20.77	20.98	20.93
12	22.97	22.78	22.98	22.97	22.97	22.97	22.97	22.97	22.97	22.97
13	38.13	38.31	38.02	38.08	38.05	38.01	38.09	38.09	38.02	38.25
14	42.58	42.63	42.59	42.58	42.64	42.59	42.57	42.66	42.58	42.61
15	29.64	29.63	29.53	29.62	29.66	29.52	29.63	29.69	29.52	29.64
16	32.11	31.37	32.03	32.08	31.98	32.02	32.08	31.82	32.02	32.06
17	56.98	57.01	56.96	56.97	56.98	56.95	56.98	57.00	56.96	56.83
18	48.95	48.95	48.93	48.92	48.92	48.92	48.93	48.96	48.93	48.75
19	45.07	44.21	44.94	44.65	44.19	44.66	44.86	44.22	44.87	44.86
20	28.43	28.58	28.24	28.21	27.67	28.21	28.23	27.65	28.23	28.24
21	29.75	29.74	29.76	29.74	29.73	29.75	29.75	29.75	29.76	29.73
22	37.19	37.32	37.13	37.13	37.31	37.11	37.13	37.32	37.12	37.16
23	26.93	26.89	26.91	26.86	26.86	26.89	26.88	26.89	26.90	26.83
24	16.14	20.79	15.87	16.92	21.01	16.93	16.93	21.04	16.94	16.91
25	16.85	16.79	17.07	17.05	16.75	17.05	17.07	16.77	17.06	17.05
26	15.99	16.02	16.95	15.99	16.02	15.87	16.00	16.04	15.87	16.10
27	14.69	14.72	14.68	14.68	14.84	14.67	14.69	14.66	14.67	14.67
28	176.88	176.89	176.00	176.86	176.85	175.99	176.86	177.55	176.00	182.56
29	22.76	22.78	22.75	22.76	22.76	22.74	22.76	22.78	22.74	22.73
30	14.64	14.71	14.54	14.56	14.66	14.53	14.56	14.85	14.53	14.56
1′	29.63	34.18	30.73	27.96	28.57	27.96	29.98	30.27	29.99	30.00
2′	30.97	32.09	33.25	26.18	26.71	26.18	30.87	31.38	30.87	30.88
3′	7.50	7.28	7.15	70.27	70.26	70.26	34.02	34.13	34.00	34.00
OMe	51.17	51.15	—	51.16	51.16	—	51.17	51.16	—	—
Me<u>C</u>O	—	—	171.26	171.29	171.07	171.27	171.30	171.02	171.27	171.32
<u>Me</u>CO	—	—	21.14	21.04	21.58	21.04	21.09	21.59	21.08	21.08
Me—S	—	—	—	37.40	37.35	37.41	—	—	—	—
OCH_2Ph	—	—	65.61	—	—	65.60	—	—	65.60	—
Ph	—	—	127.99, 128.25, 128.46, 136.60	—	—	127.99, 128.25, 128.45, 136.59	—	—	127.99, 128.25, 128.45, 136.60	—

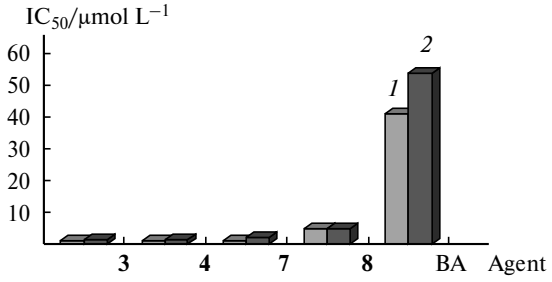


Fig. 1. Cytotoxic effect of betulinic acid (BA) and salts **3**, **4**, **7**, and **8** on mastocytoma P-815 (*1*) and Ehrlich carcinoma (*2*) tumor cells.

As it follows from the experimental results (Table 4, Fig. 1), all the salts under study **3**, **4**, **7**, and **8** considerably (by 34—40 times) exceeded betulinic acid in antitumor activity.

In conclusion, we developed an efficient approach to the synthesis of earlier unknown phosphonium-containing lupane triterpenoids possessing high cytotoxic activity. The availability of the starting plant-originated metabolites (betulin, betulonic and betulinic acids) and high yields in all the steps of the synthesis make this approach promising for the preparation of a large group of pentacyclic triterpene conjugates with phosphonium cations as potential antitumor agents.

Table 4. Cytotoxic effect of phosphonium salts **3**, **4**, **7**, **8** and betulinic acid (BA) on the P-815 (in the numerator) and Ehrlich tumor cells (in the denominator) (% of viable cells) (X±SE)[a]

Concentration of compound/μg mL^{-1}	**3**	**4**	**7**	**8**	BA
—[b]	—	—	100.0±2.2 100.0±2.4	—	—
0.1	98.6±4.2 95.5±1.2	96.1±3.8 95.1±4.9	97.5±4.5 98.6±2.6	97.6±2.3 98.1±3.8	89.3±4.1 93.3±4.4
1	59.7±3.7[c,d] 73.4±5.02[c,d]	53.8±5.0[c,d] 71.7±3.62[c,d]	60.0±4.5[c,d] 73.4±2.32[c,d]	89.1±6.1 99.8±4.8	102.8±6.0 96.8±3.1
10	−6.8±2.9[c,d] −3.9±4.62[c,d]	−3.5±1.6[c,d] −1.3±2.02[c,d]	−11.2±3.7[c,d] 16.0±2.22[c,d]	13.4±4.4[c,d] 10.8±1.12[c,d]	62.8±1.1[c] 57.3±4.2[c]
25	7.8±6.6[c,d] 7.2±4.82[c,d]	3.8±1.0[c,d] −3.8±2.22[c,d]	−2.8±3.2[c,d] 5.4±2.62[c,d]	2.2±4.2[c,d] 1.2±2.32[c,d]	34.3±5.0[c] 50.4±2.4[c]
50	8.3±2.8[c,d] −2.1±7.92[c,d]	5.0±1.6[c,d] 0.2±1.92[c,d]	7.2±3.7[c,d] −5.2±5.02[c,d]	4.6±2.2[c,d] 0.1±4.02[c,d]	30.5±2.9[c] 40.5±2.6[c]
IC_{50}[e]/μmol L^{-1}	1.20 1.37	1.15 1.35	1.10 2.30	4.79 4.70	41.00 54.00

[a] X is the average value of the experimental data, SE is the standard error.
[b] Control.
[c] The differences with the control are reliable, $p < 0.05$.
[d] The differences with the corresponding concentration of betulinic acid are reliable, $p < 0.05$.
[e] IC_{50} is the concentration causing a half-maximal inhibition of viable cells.

Experimental

IR spectra were recorded on a Specord IR-75 spectrometer for neat samples or for solutions in $CHCl_3$. ^1H, ^{13}C, and ^{31}P NMR spectra were recorded on a Bruker Avance-400 spectrometer (^1H, 400.13 MHz; ^{13}C, 100.62 MHz; ^{31}P, 161.98 MHz) using Me_4Si as an internal standard and $CDCl_3$ as a solvent. Mass spectra were recorded on a Bruker-Autoflex III instrument in the MALDI-TOF regime with recording positive ions and using 2,5-dihydroxybenzoic and α-cyano-4-hydroxycinnamic acids as matrices. Optical rotation was measured on a Perkin—Elmer-141 polarimeter. Specific rotation is given in deg mL g^{-1} dm^{-1}, the concentration of solutions is given in g (100 mL)$^{-1}$. Elemental analysis was performed on a Karlo Erba 1106 analyzer. Sorbfil plates (Sorbpolimer, Krasnodar, Russia) were used for TLC, visualizing with anisaldehyde. Silica gel L (50—160 μm, KSKG) was used for column chromatography. The following reagents were used in the work: $BH_3 \cdot THF$ (1 *M* solution in THF), BEt_3 (1 *M* solution in THF), $KN(SiMe_3)_2$ (1 *M* solution in THF), L-selectride, $CeCl_3 \cdot 7H_2O$, DME (dimethoxyethane), allyl bromide (Aldrich). Hexane, THF, and DME were refluxed and distilled over sodium. Compounds **12** and **13** were synthesized according to the method described earlier.[20] Betulonic acid was obtained from betulin according to the known procedures.[17,27] The carboxylic function in compound **33** was deblocked according to the typical procedure.[19] Compounds **14**—**16** were acetylated according to the standard procedure. Acetates **17**—**19** were purified by chromatography.

Methyl 2β-allyl-3-oxo-20,29-dihydrobetulonate (12). A 1 *M* solution of $KN(SiMe_3)_2$ in THF (0.55 mL, 0.55 mmol) was added to a solution of compound **10** (0.42 mmol) in DME (2.50 mL) at ~20 °C under argon with stirring. After 15 min, a 1 *M* solution of Et_3B in THF (0.55 mL, 0.55 mmol) was added to the mixture and this was stirred for 1 h, followed by addition of a solution of allyl bromide (0.1 g, 0.84 mmol) in DME (1 mL). The reaction mixture was stirred for 4 h (TLC monitoring), then neutralized with 3 *M* HCl, diluted with H_2O (1.5 mL), and extracted with EtOAc (4×10 mL). The combined extracts were dried with $MgSO_4$. The residue was concentrated and subjected to chromatography on a column with SiO_2 (eluent hexane—EtOAc) to obtain compound **12** (0.15 g, 65%) as white crystals, m.p. 84—86 °C (EtOH), $[\alpha]_D^{20}$ −36.0 (*c* 0.35, $CHCl_3$). Found (%): C, 80.03; H, 10.61. $C_{34}H_{54}O_3$. Calculated (%): C, 79.95; H, 10.66. IR, ν/cm^{-1}: 1728 (C=O). ^1H NMR, δ: 0.76, 0.87 (both d, 3 H each, H(29), H(30), J = 6 Hz); 0.91 (m, 1 H, $H^a_{eq}(1)$); 0.95, 0.98, 1.06, 1.07, 1.11 (all s, 3 H each, H(23)—H(27)); 1.13—2.25 (m, 21 H, CH, CH_2 in pentacyclic skeleton and 1 H, H(20)); 1.98 (dt, 1 H, H(1′), ^2J = 15 Hz, ^3J = 7 Hz); 2.10 (dd, 1 H, $H^b_{ax}(1)$, ^2J = 13 Hz, ^3J = 6 Hz); 2.55 (m, 1 H, H(1′)); 2.72 (m, 1 H, H(2)); 3.67 (s, 3 H, OMe); 5.00—5.05 (m, 2 H, H(3′)); 5.76 (m, 1 H, H(2′)). MS, m/z: 533.4 $[M + Na]^+$, 549.4 $[M + K]^+$. $C_{34}H_{54}O_3$. Calculated, m/z: 533.4 $[M + Na]^+$, 549.4 $[M + K]^+$.

Benzyl 2β-allyl-3-oxo-20,29-dihydrobetulonate (13) was obtained similarly to compound **12**. The yield was 67%. White crystals, m.p. 132—134 °C (EtOH), $[\alpha]_D^{20}$ −21.9 (*c* 0.70, $CHCl_3$). Found (%): C, 81.93; H, 9.91. $C_{40}H_{58}O_3$. Calculated (%): C, 81.86; H, 9.96. IR, ν/cm^{-1}: 1726 (C=O). ^1H NMR, δ: 0.75, 0.86 (both d, 3 H each, H(29), H(30), J = 7 Hz); 0.81, 0.93, 1.06, 1.07, 1.09 (all s, 3 H each, H(23)—H(27)); 0.90 (m, 1 H, $H^a_{eq}(1)$); 1.12—2.27 (m, 21 H, CH, CH_2 in pentacyclic skeleton and 1 H, H(20)); 1.97 (dt, 1 H, H(1′), ^2J = 15 Hz, ^3J = 7 Hz); 2.10 (dd, 1 H, $H^b_{ax}(1)$, ^2J = 13 Hz, ^3J = 6 Hz); 2.57 (m, 1 H, H(1′)); 2.71 (m, 1 H, H(2)); 4.99—5.05 (m, 2 H, H(3′)); 5.13 (m, 2 H, OCH_2Ph); 5.78 (m, 1 H, H(2′)); 7.28—7.39 (m, 5 H, Ph). MS, m/z: 609.4 $[M + Na]^+$. $C_{40}H_{58}O_3$. Calculated, m/z: 609.4 $[M + Na]^+$.

Methyl 2β-allyl-3β-hydroxy-20,29-dihydrobetulinate (14). A solution of $CeCl_3 \cdot 7H_2O$ (0.15 g, 0.4 mmol) in a mixture of THF—methanol (1 : 1, 1 mL) was added dropwise to a solution of compound **12** (0.3 mmol) in a mixture of THF—methanol (1 : 2, 7.5 mL) cooled to −30 °C (Ar). Then, $NaBH_4$ (0.023 g, 0.6 mmol) was added in small portions over 5 min, the temperature was raised to ~20 °C and the mixture was stirred at this temperature for 2 h (TLC monitoring). Then, the reaction mixture was neutralized with 5% aqueous HCl and extracted with ethyl acetate (3×10 mL). The extract was washed with saturated aq. $NaHCO_3$ and water, dried with $MgSO_4$, and the solvent was evaporated *in vacuo*. The residue was purified by column chromatography on SiO_2 (eluent hexane—EtOAc) to obtain compound **14**(0.11 g, 74%) as white crystals, m.p. 90—92 °C (EtOH), $[\alpha]_D^{20}$ −4.7 (*c* 0.45, $CHCl_3$). Found (%): C, 79.69; H, 10.57. $C_{34}H_{56}O_3$. Calculated (%): C, 79.63; H, 11.01. IR, ν/cm^{-1}: 1726 (C=O), 3450 (OH). ^{1}H NMR, δ: 0.55 (t, 1 H, $H^a_{eq}(1)$, J = 12 Hz); 0.72, 0.83 (both d, 3 H each, H(29), H(30), J = 7 Hz); 0.76, 0.83, 0.89, 0.93, 0.96 (all s, 3 H each, H(23)—H(27)); 1.13—2.21 (m, 22 H, CH, CH_2 in pentacyclic skeleton and 1 H, H(20)); 1.73 (m, 1 H, $H^b_{ax}(1)$); 1.91 (dt, 1 H, H(1′), ^2J = 15 Hz, ^3J = 7 Hz); 2.48 (m, 1 H H(1′)); 2.85 (d, 1 H, H(3), J = 10 Hz); 3.63 (s, 3 H, COOMe); 4.98—5.04 (m, 2 H, H(3′)); 5.81 (m, 1 H, H(2′)). MS, *m/z*: 512.4 $[M]^+$. $C_{34}H_{56}O_3$. Calculated, *m/z*: 512.4 $[M]^+$.

Benzyl 2β-allyl-3β-hydroxy-20,29-dihydrobetulinate (15) was obtained similarly to compound **14**. The yield was 72%. White crystals, m.p. 76—78 °C (EtOH), $[\alpha]_D^{20}$ −19.3 (*c* 0.60, $CHCl_3$). Found (%): C, 81.64; H, 10.21. $C_{40}H_{60}O_3$. Calculated (%): C, 81.58; H, 10.27. IR, ν/cm^{-1}: 1726 (C=O), 3500 (OH). ^{1}H NMR, δ: 0.58 (t, 1 H, $H^a_{eq}(1)$, J = 12 Hz); 0.75, 0.86 (both d, 3 H each, H(29), H(30), J = 7 Hz); 0.76, 0.79, 0.84, 0.95, 0.99 (all s, 3 H each, H(23)—H(27)); 1.11—2.24 (m, 22 H, CH, CH_2 in pentacyclic skeleton and 1 H, H(20)); 1.70 (m, 1 H, $H^b_{ax}(1)$); 1.97 (dt, 1 H, H(1′), ^2J = 15 Hz, ^3J = 7 Hz); 2.48 (m, 1 H, H(1′)); 2.89 (d, 1 H, H(3), J = 10 Hz); 5.02—5.16 (m, 2 H, H(3′)); 5.09—5.13 (m, 2 H, OCH_2Ph); 5.80—5.91 (m, 1 H, H(2′)); 7.31—7.37 (m, 5 H, Ph). MS, *m/z*: 611.4 $[M + Na]^+$, 627.3 $[M + K]^+$. $C_{40}H_{60}O_3$. Calculated, *m/z*: 611.4 $[M + Na]^+$, 627.4 $[M + K]^+$.

Methyl 2β-allyl-3α-hydroxy-20,29-dihydrobetulinate (16). A 1 *M* solution of L-selectride in THF(2.4 mL, 2.4 mmol) was added to a solution of compound **12** (0.41 g, 0.8 mmol) in THF (15 mL) cooled to −78 °C (Ar) with stirring. The solution was stirred for 2 h at ~20 °C, followed by the addition of a 2 *M* aq. NaOH (18 mL) and 30% aq. H_2O_2 (4 mL) and stirring for another 1 h. The mixture was concentrated to a small volume and extracted with EtOAc (4×10 mL). The organic phase was washed with water, dried with $MgSO_4$, and the solvent was evaporated *in vacuo*. The residue was purified by column chromatography on SiO_2 (eluent hexane—EtOAc) to obtain compound **16** (0.28 g, 68%) as white crystals, m.p. 84—86 °C (EtOH), $[\alpha]_D^{20}$ −0.54 (*c* 1.66, $CHCl_3$). Found (%): C, 79.72; H, 10.59. $C_{34}H_{56}O_3$. Calculated (%): C, 79.63; H, 11.01. IR, ν/cm^{-1}: 1729 (C=O), 3450 (OH). ^{1}H NMR, δ: 0.75, 0.86 (both d, 3 H each, H(29), H(30), J = 7 Hz); 0.83, 0.85, 0.91, 0.95, 0.96 (all s, 3 H each, H(23)—H(27)); 1.12—2.30 (m, 24 H, CH, CH_2 in pentacyclic skeleton, 1 H, H(20) and 2 H, H(1′)); 3.21 (br.s, 1 H, H(3)); 3.65 (s, 3 H, COOMe); 5.00—5.07 (m, 2 H, H(3′)); 5.81 (m, 1 H, H(2′)). MS, *m/z*: 512.4 $[M]^+$. $C_{34}H_{56}O_3$. Calculated, *m/z*: 512.4 $[M]^+$.

Methyl 3β-acetoxy-2β-allyl-20,29-dihydrobetulinate (17). The yield was 95%. White crystals, m.p. 208—210 °C (EtOH), $[\alpha]_D^{20}$ −29.6 (*c* 1.15, $CHCl_3$). Found (%): C, 77.98; H, 10.49. $C_{36}H_{58}O_4$. Calculated (%): C, 77.93; H, 10.54. IR, ν/cm^{-1}: 1734 (C=O). ^{1}H NMR, δ: 0.63 (t, 1 H, $H^a_{eq}(1)$, J = 12 Hz); 0.75, 0.85 (both d, 3 H each, H(29), H(30), J = 7 Hz); 0.82, 0.84, 0.88, 0.92, 0.95 (all s, 3 H each, H(23)—H(27)); 1.10—2.30 (m, 22 H, CH, CH_2 in pentacyclic skeleton, 1 H, H(20) and 2 H, H(1′)); 1.73 (m, 1 H, $H^b_{ax}(1)$); 2.09 (s, 3 H, Me (OAc)); 3.66 (s, 3 H, OMe); 4.47 (d, 1 H, H(3), J = 11 Hz); 4.95—5.00 (m, 2 H, H(3′)); 5.68—5.75 (m, 1 H, H(2′)). MS, *m/z*: 577.5 $[M + Na]^+$. $C_{36}H_{58}O_4$. Calculated, *m/z*: 577.4 $[M + Na]^+$.

Benzyl 3β-acetoxy-2β-allyl-20,29-dihydrobetulinate (18). The yield was 87%. White crystals, m.p. 74—76 °C (EtOH), $[\alpha]_D^{20}$ −25.9 (*c* 0.36, $CHCl_3$). Found (%): C, 80.01; H, 9.87. $C_{42}H_{62}O_4$. Calculated (%): C, 79.95; H, 9.90. IR, ν/cm^{-1}: 1732 (C=O). ^{1}H NMR, δ: 0.63 (t, 1 H, $H^a_{eq}(1)$, J = 12 Hz); 0.75, 0.86 (both d, 3 H each, H(29), H(30), J = 7 Hz); 0.76, 0.84, 0.85, 0.87, 0.94 (all s, 3 H each, H(23)—H(27)); 1.08—2.28 (m, 22 H, CH, CH_2 in pentacyclic skeleton, 1 H, H(20) and 2 H, H(1′)); 1.69 (m, 1 H, $H^b_{ax}(1)$); 2.09 (s, 3 H, Me (OAc)); 4.47 (d, 1 H, H(3), J = 11 Hz); 4.96—5.00 (m, 2 H, H(3′)); 5.12 (m, 2 H, OCH_2Ph); 5.69—5.75 (m, 1 H, H(2′)); 7.31—7.37 (m, 5 H, Ph). MS, *m/z*: 653.4 $[M + Na]^+$. $C_{42}H_{62}O_4$. Calculated, *m/z*: 653.4 $[M + Na]^+$.

Methyl 3α-acetoxy-2β-allyl-20,29-dihydrobetulinate (19). The yield was 87%. White crystals, m.p. 182—184 °C (EtOH), $[\alpha]_D^{20}$ −24.2 (*c* 0.19, $CHCl_3$). Found (%): C, 77.99; H, 10.47. $C_{36}H_{58}O_4$. Calculated (%): C, 77.93; H, 10.54. IR, ν/cm^{-1}: 1731 (C=O). ^{1}H NMR, δ: 0.75, 0.85 (both d, 3 H each, H(29), H(30), J = 7 Hz); 0.82, 0.84, 0.88, 0.92, 0.99 (all s, 3 H each, H(23)—H(27)); 1.14—2.30 (m, 24 H, CH, CH_2 in pentacyclic skeleton, 1 H, H(20) and 2 H, H(1′)); 2.10 (s, 3 H, Me (OAc)); 3.66 (s, 3 H, OMe); 4.77 (br.s, 1 H, H(3)); 4.95—4.99 (m, 2 H, H(3′)); 5.77—5.85 (m, 1 H, H(2′)). MS, *m/z*: 577.5 $[M + Na]^+$. $C_{36}H_{58}O_4$. Calculated, *m/z*: 577.4 $[M + Na]^+$.

Methyl 3β-hydroxy-2β-(3-hydroxypropyl)-20,29-dihydrobetulinate (20). A 1 *M* solution of $BH_3 \cdot THF$ in THF (0.86 mL, 0.86 mmol) was added to a stirred solution of compound **14** (0.43 mmol) in anhydrous THF (5 mL) at ~20 °C (Ar). After 3 h, the reaction mixture was cooled to 0 °C, followed by a careful dropwise addition of 10% aq. NaOH (1 mL) and 30% aq. H_2O_2 (1 mL). The reaction mixture was stirred for 1 h at ~20 °C, neutralized with 3 *M* HCl, and extracted with ethyl acetate (3×20 mL). The combined organic phases were washed with brine and dried with $MgSO_4$, the solvent was evaporated *in vacuo*. The residue was purified by column chromatography on SiO_2 (eluent hexane—EtOAc) to obtain compound **20** (0.17 g, 76%) as white crystals, m.p. 111—113 °C (EtOH), $[\alpha]_D^{20}$ −40 (*c* 0.28, $CHCl_3$). Found (%): C, 76.82; H, 10.12. $C_{34}H_{58}O_4$. Calculated (%): C, 76.93; H, 11.01. IR, ν/cm^{-1}: 1730 (C=O), 3334 (OH). ^{1}H NMR, δ: 0.57 (t, 1 H, $H^a_{eq}(1)$, J = 12 Hz); 0.77, 0.75 (both d, 3 H each, H(29), H(30), J = 7 Hz); 0.84, 0.85, 0.92, 0.95, 0.98 (all s, 3 H each, H(23)—H(27)); 1.16—2.29 (m, 22 H, CH, CH_2 in pentacyclic skeleton, 1 H, H(20), 2 H, H(1′), 2 H, H(2′)); 1.70 (m, 1 H, $H^b_{ax}(1)$); 3.64 (br.m, 2 H, H(3′)); 3.65 (s, 3 H, OMe); 2.84 (d, 1 H, H(3), J = 10 Hz). MS, *m/z*: 553.4 $[M + Na]^+$, 569.3 $[M + K]^+$. $C_{34}H_{58}O_4$. Calculated, *m/z*: 553.4 $[M + Na]^+$, 569.4 $[M + K]^+$.

Methyl 3α-hydroxy-2β-(3-hydroxypropyl)-20,29-dihydrobetulinate (21) was obtained similarly to compound **20** from com-

pound **16**. The yield was 78%. White crystals, m.p. 92—94 °C (EtOH), $[\alpha]_D^{20}$ −24 (*c* 0.28, $CHCl_3$). Found (%): C, 76.87; H, 10.14. $C_{34}H_{58}O_4$. Calculated (%): C, 76.93; H, 11.01. IR, ν/cm^{-1}: 1726 (C=O), 3363 (OH). ^{1}H NMR, δ: 0.76, 0.87 (both d, 3 H each, H(29), H(30), *J* = 7 Hz); 0.82, 0.85, 0.89, 0.91, 0.95 (all s, 3 H each, H(23)—H(27)); 1.11—2.23 (m, 24 H, CH, CH_2 in pentacyclic skeleton, 1 H, H(20), 2 H, H(1′), 2 H, H(2′)); 3.50 (t, 2 H, H(3′), *J* = 5 Hz); 3.66 (s, 3 H, OMe); 3.23 (s, 1 H, H(3)). MS, *m/z*: 553.4 $[M + Na]^+$. $C_{34}H_{58}O_4$. Calculated, *m/z*: 553.4 $[M + Na]^+$.

Methyl 3β-acetoxy-2β-(3-hydroxypropyl)-20,29-dihydrobetulinate (22) was obtained similarly to compound **20** from compound **17**. The yield was 71%. White crystals, m.p. 114—116 °C (EtOH), $[\alpha]_D^{20}$ −28.9 (*c* 1.05, $CHCl_3$). Found (%): C, 75.57; H, 10.49. $C_{36}H_{60}O_5$. Calculated (%): C, 75.48; H, 10.56. IR, ν/cm^{-1}: 1732 (C=O), 3446 (OH). ^{1}H NMR, δ: 0.68 (t, 1 H, $H^a_{eq}(1)$, *J* = 12 Hz); 0.75, 0.86 (both d, 3 H each, H(29), H(30), *J* = 7 Hz); 0.81, 0.83, 0.88, 0.92, 0.95 (all s, 3 H each, H(23)—H(27)); 1.12—2.29 (m, 22 H, CH, CH_2 in pentacyclic skeleton, 1 H, H(20), 2 H, H(1′), 2 H, H(2′)); 1.69 (m, 1 H, $H^b_{ax}(1)$); 2.10 (s, 3 H, Me (OAc)); 3.55 (m, 2 H, H(3′)); 3.66 (s, 3 H, OMe); 4.46 (d, 1 H, H(3), *J* = 11 Hz). MS, *m/z*: 595.4 $[M + Na]^+$, 611.4 $[M + K]^+$. $C_{36}H_{60}O_5$. Calculated, *m/z*: 595.4 $[M + Na]^+$, 611.4 $[M + K]^+$.

Methyl 3α-acetoxy-2β-(3-hydroxypropyl)-20,29-dihydrobetulinate (23) was obtained similarly to compound **20** from compound **19**. The yield was 74%. White crystals, m.p. 104—106 °C (EtOH), $[\alpha]_D^{20}$ −20.2 (*c* 0.22, $CHCl_3$). Found (%): C, 75.54; H, 10.51. $C_{36}H_{60}O_5$. Calculated (%): C, 75.48; H, 10.56. IR, ν/cm^{-1}: 1731 (C=O), 3445 (OH). ^{1}H NMR, δ: 0.76, 0.88 (both d, 3 H each, H(29), H(30), *J* = 7 Hz); 0.82, 0.87, 0.89, 0.92, 1.00 (all s, 3 H each, H(23)—H(27)); 1.10—2.26 (m, 24 H, CH, CH_2 in pentacyclic skeleton, 1 H, H(20), 2 H, H(1′), 2 H, H(2′)); 2.10 (s, 3 H, Me (OAc)); 3.59 (t, 2 H, H(3′), *J* = 6 Hz); 3.66 (s, 3 H, OMe); 4.77 (br.s, 1 H, H(3)). MS, *m/z*: 595.5 $[M + Na]^+$, 611.4 $[M + K]^+$. $C_{36}H_{60}O_5$. Calculated, *m/z*: 595.4 $[M + Na]^+$, 611.4 $[M + K]^+$.

Benzyl 3β-acetoxy-2β-(3-hydroxypropyl)-20,29-dihydrobetulinate (24) was obtained similarly to compound **20** from compound **18**. The yield was 79%. White crystals, m.p. 74—76 °C (EtOH), $[\alpha]_D^{20}$ −23.2 (*c* 0.46, $CHCl_3$). Found (%): C, 77.80; H, 9.89. $C_{42}H_{64}O_5$. Calculated (%): C, 77.73; H, 9.94. IR, ν/cm^{-1}: 1730 (C=O). ^{1}H NMR, δ: 0.65 (t, 1 H, $H^a_{eq}(1)$, *J* = 12 Hz); 0.75, 0.86 (both d, 3 H each, H(29), H(30), *J* = 7 Hz); 0.77, 0.81, 0.85, 0.87, 0.94 (all s, 3 H each, H(23)—H(27)); 1.08—2.32 (m, 22 H, CH, CH_2 in pentacyclic skeleton, 1 H, H(20), 2 H, H(1′), 2 H, H(2′)); 1.69 (m, 1 H, $H^b_{ax}(1)$); 2.10 (s, 3 H, Me (OAc)); 3.57 (m, 2 H, H(3′)); 4.46 (d, 1 H, H(3), *J* = 11 Hz); 5.12 (m, 2 H, OCH_2Ph); 7.32—7.39 (m, 5 H, Ph). MS, *m/z*: 649.9 $[M + H]^+$, 671.3 $[M + Na]^+$. $C_{42}H_{64}O_5$. Calculated, *m/z*: 649.7 $[M + H]^+$, 671.4 $[M + Na]^+$.

Methyl 3β-hydroxy-2β-(3-iodopropyl)-20,29-dihydrobetulinate (25). Triphenylphosphine (0.22 g, 0.84 mmol), imidazole (0.12 g, 1.17 mmol), and crystalline iodine (0.19 g, 0.75 mmol) were added to a solution of compound **20** (0.35 mmol) in anhydrous THF (6 mL) at 0 °C (Ar) with stirring and the mixture was stirred for 1 h at 0 °C (TLC monitoring). After the reaction reached completion, the solution was diluted with ethyl acetate (10—15 mL) and the solvent was evaporated *in vacuo*. The residue was purified by column chromatography on SiO_2 (eluent hexane—EtOAc) to obtain compound **25** (0.13 g, 57%) as white crystals, m.p. 97—99 °C (EtOH), $[\alpha]_D^{28}$ −39.3 (*c* 0.28, $CHCl_3$). Found (%): C, 63.85; H, 8.79; I, 19.69. $C_{34}H_{57}O_3I$. Calculated (%): C, 63.74; H, 8.97; I, 19.81. IR, ν/cm^{-1}: 757 (CH_2—I), 1727 (C=O). ^{1}H NMR, δ: 0.58 (t, 1 H, $H^a_{eq}(1)$, *J* = 12 Hz); 0.75, 0.88 (both d, 3 H each, H(29), H(30), *J* = 7 Hz); 0.78, 0.86, 0.92, 0.96, 0.99 (all s, 3 H each, H(23)—H(27)); 1.13—2.26 (m, 22 H, CH, CH_2 in pentacyclic skeleton, 1 H, H(20), 2 H, H(1′), 2 H, H(2′)); 1.71 (m, 1 H, $H^b_{ax}(1)$); 3.19 (m, 2 H, H(3′)); 3.67 (s, 3 H, OMe); 2.85 (d, 1 H, H(3), *J* = 12 Hz).

Methyl 3α-hydroxy-2β-(3-iodopropyl)-20,29-dihydrobetulinate (26) was obtained similarly to compound **25** from compound **21**. The yield was 73%. White crystals, m.p. 86—88 °C (EtOH), $[\alpha]_D^{28}$ −28.4 (*c* 0.28, $CHCl_3$). Found (%): C, 63.81; H, 8.75; I, 19.69. $C_{34}H_{57}O_3I$. Calculated (%): C, 63.74; H, 8.97; I, 19.81. IR, ν/cm^{-1}: 757 (CH_2—I), 1728 (C=O). ^{1}H NMR, δ: 0.76, 0.87 (both d, 3 H each, H(29), H(30), *J* = 7 Hz); 0.83, 0.85, 0.91, 0.96, 0.98 (all s, 3 H each, H(23)—H(27)); 1.12—2.24 (m, 24 H, CH, CH_2 in pentacyclic skeleton, 1 H, H(20), 2 H, H(1′), 2 H, H(2′)); 3.19 (m, 2 H, H(3′)); 3.66 (s, 3 H, OMe); 3.21 (br.s, 1 H, H(3)).

Benzyl 3β-acetoxy-2β-(3-iodopropyl)-20,29-dihydrobetulinate (27) was obtained similarly to compound **25** from compound **24**. The yield was 94%. White crystals, m.p. 69—71 °C (EtOH), $[\alpha]_D^{28}$ −13.2 (*c* 0.28, $CHCl_3$). Found (%): C, 66.39; H, 8.42; I, 16.68. $C_{42}H_{63}O_4I$. Calculated (%): C, 66.48; H, 8.37; I, 16.72. IR, ν/cm^{-1}: 756 (CH_2—I), 1731 (C=O). ^{1}H NMR, δ: 0.66 (t, 1 H, $H^a_{eq}(1)$, *J* = 12 Hz); 0.75, 0.87 (both d, 3 H each, H(29), H(30), *J* = 7 Hz); 0.76, 0.82, 0.83, 0.86, 0.94 (all s, 3 H each, H(23)—H(27)); 1.09—2.28 (m, 22 H, CH, CH_2 in pentacyclic skeleton, 1 H, H(20), 2 H, H(1′), 2 H, H(2′)); 1.73 (m, 1 H, $H^b_{ax}(1)$); 2.13 (s, 3 H, Me (OAc)); 3.14 (t, 2 H, H(3′), *J* = 7 Hz); 4.45 (d, 1 H, H(3), *J* = 11.2 Hz); 5.09—5.16 (m, 2 H, OCH_2Ph); 7.28—7.35 (m, 5 H, Ph).

Methyl 3β-acetoxy-2β-(3-mesyloxypropyl)-20,29-dihydrobetulinate (28). Pyridine (0.06 g, 0.77 mmol) and DMAP (0.03 g, 0.25 mmol) were added to compound **22** (0.44 mmol) dissolved in CH_2Cl_2 (2 mL) and the mixture was cooled to 0 °C, followed by a dropwise addition of a solution of methanesulfonyl chloride (0.07 g, 0.65 mmol) in CH_2Cl_2 (1 mL) and stirring for 24 h at ~20 °C (TLC monitoring). Then, a cold 5% aq. HCl was added to the reaction mixture, which was extracted with ethyl acetate (3×10 mL). The extract was washed with saturated aq. $NaHSO_3$, water, dried with $MgSO_4$, and the solvent was evaporated *in vacuo*. The residue was purified by column chromatography on SiO_2 (eluent hexane—EtOAc) to obtain compound **28** (0.27 g, 93%) as white crystals, m.p. 98—100 °C (EtOH), $[\alpha]_D^{20}$ −40.1 (*c* 0.18, $CHCl_3$). Found (%): C, 68.33; H, 9.55; S, 4.96. $C_{37}H_{62}O_7S$. Calculated (%): C, 68.27; H, 9.60; S, 4.93. IR, ν/cm^{-1}: 1358 (S=O), 1730 (C=O). ^{1}H NMR, δ: 0.66 (t, 1 H, $H^a_{eq}(1)$, *J* = 12 Hz); 0.76, 0.86 (both d, 3 H each, H(29), H(30), *J* = 7 Hz); 0.81, 0.83, 0.88, 0.92, 0.95 (all s, 3 H each, H(23)—H(27)); 1.10—2.25 (m, 22 H, CH, CH_2 in pentacyclic skeleton, 1 H, H(20), 2 H, H(1′), 2 H, H(2′)); 1.69 (m, 1 H, $H^b_{ax}(1)$); 2.11 (s, 3 H, Me (OAc)); 3.00 (s, 3 H, OMs); 3.66 (s, 3 H, OMe); 4.18 (t, 2 H, H(3′), *J* = 6 Hz); 4.45 (d, 1 H, H(3), *J* = 11 Hz). MS, *m/z*: 673.3 $[M + Na]^+$, 689.3 $[M + K]^+$. $C_{37}H_{62}O_7S$. Calculated, *m/z*: 673.4 $[M + Na]^+$, 689.4 $[M + K]^+$.

Methyl 3α-acetoxy-2β-(3-mesyloxypropyl)-20,29-dihydrobetulinate (29) was obtained similarly to compound **28** from compound **23**. The yield was 87%. White crystals, m.p. 90—92 °C (EtOH), $[\alpha]_D^{20}$ −22.1 (*c* 0.24, $CHCl_3$). Found (%): C, 68.35;

H, 9.56; S, 4.97. $C_{37}H_{62}O_7S$. Calculated (%): C, 68.27; H, 9.60; S, 4.93. IR, ν/cm^{-1}: 1357 (S=O), 1729 (C=O). ^{1}H NMR, δ: 0.75, 0.85 (both d, 3 H each, H(29), H(30), J = 7 Hz); 0.81, 0.86, 0.88, 0.91, 0.99 (all s, 3 H each, H(23)—H(27)); 1.10—2.24 (m, 24 H, CH, CH_2 in pentacyclic skeleton, 1 H, H(20), 2 H, H(1′), 2 H, H(2′)); 2.10 (s, 3 H, Me (OAc)); 3.00 (s, 3 H, OMs); 3.65 (s, 3 H, OMe); 4.11—4.20 (m, 2 H, H(3′)); 4.75 (br.s, 1 H, H(3)). MS, m/z: 673.5 $[M + Na]^+$, 689.5 $[M + K]^+$. $C_{37}H_{62}O_7S$. Calculated, m/z: 673.4 $[M + Na]^+$, 689.4 $[M + K]^+$.

Benzyl 3β-acetoxy-2β-(3-mesyloxypropyl)-20,29-dihydrobetulinate (30) was obtained similarly to compound **28** from compound **24**. The yield was 90%. White crystals, m.p. 78—80 °C (EtOH), $[\alpha]_D^{20}$ −22.3 (c 0.26, $CHCl_3$). Found (%): C, 70.81; H, 9.00; S, 4.45. $C_{43}H_{66}O_7S$. Calculated (%): C, 71.04; H, 9.15; S, 4.41. IR, ν/cm^{-1}: 1358 (S=O), 1730 (C=O). ^{1}H NMR, δ: 0.67 (t, 1 H, H^a_{eq}(1), J = 12 Hz); 0.76, 0.86 (both d, 3 H each, H(29), H(30), J = 7 Hz); 0.77, 0.81, 0.83, 0.87, 0.94 (all s, 3 H each, H(23)—H(27)); 1.08—1.91 (m, 22 H, CH, CH_2 in pentacyclic skeleton, 1 H, H(20), 2 H, H(1′), 2 H, H(2′)); 1.68 (m, 1 H, H^b_{ax}(1)); 2.11 (s, 3 H, Me (OAc)); 3.01 (s, 3 H, OMs); 4.18 (t, 2 H, H(3′), J = 6 Hz); 4.45 (d, 1 H, H(3), J = 11 Hz); 5.12 (m, 2 H, OCH_2Ph); 7.28—7.37 (m, 5 H, Ph).

Methyl 3β-acetoxy-2β-(3-bromopropyl)-20,29-dihydrobetulinate (31). Lithium bromide (0.07 g, 0.8 mmol) was added to a solution of mesylate **28** (0.42 mmol) in anhydrous acetone (12 mL). The mixture was refluxed for 3 h (TLC monitoring) and cooled, a residue formed was filtered and washed with acetone (2 mL). A combined filtrate was concentrated *in vacuo*. The residue was purified by column chromatography on SiO_2 (eluent hexane—EtOAc) to obtain compound **31** (0.21 g, 79%) as white crystals, m.p. 92—94 °C (EtOH), $[\alpha]_D^{20}$ +19.2 (c 1.50, $CHCl_3$). Found (%): C, 68.21; H, 9.35; Br, 12.72. $C_{36}H_{59}O_4Br$. Calculated (%): C, 68.01; H, 9.35; Br, 12.57. IR, ν/cm^{-1}: 1732 (C=O). ^{1}H NMR, δ: 0.66 (t, 1 H, H^a_{eq}(1), J = 12 Hz); 0.76, 0.86 (both d, 3 H each, H(29), H(30), J = 7 Hz); 0.81, 0.83, 0.88, 0.92, 0.95 (all s, 3 H each, H(23)—H(27)); 1.13—2.25 (m, 22 H, CH, CH_2 in pentacyclic skeleton, 1 H, H(20), 2 H, H(1′), 2 H, H(2′)); 1.66 (m, 1 H, H^b_{ax}(1)); 2.11 (s, 3 H, Me (OAc)); 3.36 (t, 2 H, H(3′), J = 7 Hz); 3.66 (s, 3 H, OMe); 4.46 (d, 1 H, H(3), J = 11 Hz). MS, m/z: 634.1 $[M]^+$. $C_{36}H_{59}O_4Br$. Calculated, m/z: 634.3 $[M]^+$.

Methyl 3α-acetoxy-2β-(3-bromopropyl)-20,29-dihydrobetulinate (32) was obtained similarly to compound **31** from compound **29**. The yield was 78%. White crystals, m.p. 84—86 °C (EtOH), $[\alpha]_D^{20}$ +20.9 (c 0.46, $CHCl_3$). Found (%): C, 68.10; H, 9.29; Br, 12.61. $C_{36}H_{59}O_4Br$. Calculated (%): C, 68.01; H, 9.35; Br, 12.57. IR, ν/cm^{-1}: 1731 (C=O). ^{1}H NMR, δ: 0.76, 0.87 (both d, 3 H each, H(29), H(30), J = 7 Hz); 0.83, 0.88, 0.89, 0.93, 1.01 (all s, 3 H each, H(23)—H(27)); 1.11—2.28 (m, 24 H, CH, CH_2 in pentacyclic skeleton, 1 H, H(20), 2 H, H(1′), 2 H, H(2′)); 2.10 (s, 3 H, Me (OAc)); 3.28—3.40 (m, 2 H, H(3′)); 3.65 (s, 3 H, OMe); 4.76 (br.s, 1 H, H(3)). MS, m/z: 634.2 $[M]^+$. $C_{36}H_{59}O_4Br$. Calculated, m/z: 634.3 $[M]^+$.

Benzyl 3β-acetoxy-2β-(3-bromopropyl)-20,29-dihydrobetulinate (33) was obtained similarly to compound **31** from compound **30**. The yield was 81%. White crystals, m.p. 86—88 °C (EtOH), $[\alpha]_D^{20}$ −30.5 (c 0.21, $CHCl_3$). Found (%): C, 70.91; H, 8.88; Br, 11.25. $C_{42}H_{63}O_4Br$. Calculated (%): C, 70.86; H, 8.92; Br, 11.22. IR, ν/cm^{-1}: 1732 (C=O). ^{1}H NMR, δ: 0.67 (t, 1 H, H^a_{eq}(1), J = 12 Hz); 0.75, 0.87 (both d, 3 H each, H(29), H(30), J = 7 Hz); 0.76, 0.82, 0.83, 0.86, 0.94 (all s, 3 H each, H(23)—H(27)); 1.11—2.28 (m, 22 H, CH, CH_2 in pentacyclic skeleton, 1 H, H(20), 2 H, H(1′), 2 H, H(2′)); 1.67 (m, 1 H, H^b_{ax}(1)); 2.12 (s, 3 H, Me (OAc)); 3.36 (t, 2 H, H(3′), J = 7 Hz); 4.45 (d, 1 H, H(3), J = 11 Hz); 5.12 (m, 2 H, OCH_2Ph); 7.28—7.35 (m, 5 H, Ph). MS, m/z: 735.4 $[M + Na]^+$. $C_{42}H_{63}O_4Br$. Calculated, m/z: 735.4 $[M + Na]^+$.

3β-Acetoxy-2β-(3-bromopropyl)-20,29-dihydrobetulinic acid (34) was obtained from compound **33** according to a typical procedure.[19] The yield was 97%. White crystals, m.p. 184—186 °C (EtOH), $[\alpha]_D^{20}$ −34.4 (c 0.42, $CHCl_3$). Found (%): C, 67.70; H, 9.19; Br, 12.78. $C_{35}H_{57}O_4Br$. Calculated (%): C, 67.61; H, 9.24; Br, 12.85. IR, ν/cm^{-1}: 1731 (C=O), 3366 (OH). ^{1}H NMR, δ: 0.69 (t, 1 H, H^a_{eq}(1), J = 12 Hz); 0.77, 0.87 (both d, 3 H each, H(29), H(30), J = 7 Hz); 0.78, 0.83, 0.89, 0.95, 0.97 (all s, 3 H each, H(23)—H(27)); 1.10—2.29 (m, 22 H, CH, CH_2 in pentacyclic skeleton, 1 H, H(20), 2 H, H(1′), 2 H, H(2′)); 1.68 (m, 1 H, H^b_{ax}(1)); 2.12 (s, 3 H, Me (OAc)); 3.36 (t, 2 H, H(3′), J = 7 Hz); 4.47 (d, 1 H, H(3), J = 11 Hz). MS, m/z: 643.4 $[M + Na]^+$. $C_{35}H_{57}O_4Br$. Calculated, m/z: 643.3 $[M + Na]^+$.

Methyl 3β-acetoxy-2β-(3-triphenylphosphoniopropyl)-20,29-dihydrobetulinate bromide (3). A mixture of bromide **31** (0.24 mmol), toluene (10 mL), and Ph_3P (0.72 mmol) was refluxed for 32 h (TLC monitoring). The solution was cooled and the solvent was evaporated *in vacuo*. A solid product obtained was washed with hot hexane (2×7 mL), dissolved in EtOAc (2 mL) and diluted with hexane (8 mL). The precipitate was filtered off to obtained compound **3** (0.20 g, 94%) as white crystals, m.p. 165—167 °C (EtOH), $[\alpha]_D^{20}$ −22.3 (c 0.95, $CHCl_3$). IR, ν/cm^{-1}: 1727 (C=O). ^{1}H NMR, δ: 0.46 (t, 1 H, H^a_{eq}(1), J = 12 Hz); 0.74, 0.76 (both d, 3 H each, H(29), H(30), J = 7 Hz); 0.75, 0.77, 0.79, 0.87, 0.89 (all s, 3 H each, H(23)—H(27)); 1.17—2.22 (m, 22 H, CH, CH_2 in pentacyclic skeleton, 1 H, H(20), 2 H, H(1′), 2 H, H(2′)); 1.65 (m, 1 H, H^b_{ax}(1)); 2.06 (s, 3 H, Me(OAc)); 3.63 (s, 3 H, OMe); 3.82 (m, 2 H, H(3′)); 4.30 (d, 1 H, H(3), J = 11 Hz); 7.70—7.87 (m, 15 H, Ph) ^{31}P NMR, δ: 24.00. MS, m/z: 817.4 $[M - Br]^+$. $C_{54}H_{74}O_4BrP$. Calculated, m/z: 817.5 $[M - Br]^+$.

Methyl 3α-acetoxy-2β-(3-triphenylphosphoniopropyl)-20,29-dihydrobetulinate bromide (4) was obtained similarly to compound **3** from bromide **32**. The yield was 89%. White crystals, m.p. 170—172 °C (EtOH), $[\alpha]_D^{20}$ +0.2 (c 0.42, $CHCl_3$). IR, ν/cm^{-1}: 1726 (C=O). ^{1}H NMR, δ: 0.75, 0.86 (both d, 3 H each, H(29), H(30), J = 7 Hz); 0.77, 0.78, 0.80, 0.88, 0.97 (all s, 3 H each, H(23)—H(27)); 1.02—2.30 (m, 24 H, CH, CH_2 in pentacyclic skeleton, 1 H, H(20), 2 H, H(1′), 2 H, H(2′)); 2.10 (s, 3 H, Me (OAc)); 3.46, 4.01 (both m, 2 H, H(3′)); 3.64 (s, 3 H, OMe); 4.54 (br.s, 1 H, H(3)); 7.64—7.81 (m, 15 H, Ph). ^{31}P NMR, δ: 23.77. MS, m/z: 817.5 $[M - Br]^+$. $C_{54}H_{74}O_4BrP$. Calculated, m/z: 817.5 $[M - Br]^+$.

Methyl 3β-hydroxy-2β-(3-triphenylphosphoniopropyl)-20,29-dihydrobetulinate iodide (5) was obtained similarly to compound **3** by the reaction of iodide **25** with Ph_3P for 16 h. The yield was 21%. White crystals, m.p. 124—126 °C (EtOH), $[\alpha]_D^{20}$ −21 (c 0.22, $CHCl_3$). IR, ν/cm^{-1}: 1724 (C=O). ^{1}H NMR, δ: 0.48 (t, 1 H, H^a_{eq}(1), J = 12 Hz); 0.75, 0.87 (both d, 3 H each, H(29), H(30), J = 7 Hz); 0.74, 0.76, 0.79, 0.85, 0.88 (all s, 3 H each, H(23)—H(27)); 1.13—2.30 (m, 22 H, CH, CH_2 in pentacyclic skeleton, 1 H, H(20), 2 H, H(1′), 2 H, H(2′)); 1.65 (m, 1 H, H^b_{ax}(1)); 2.89 (d, 1 H, H(3), J = 10 Hz); 3.60 (m, 2 H, H(3′)); 3.64 (s, 3 H, OMe); 7.60—7.90 (m, 15 H, Ph). ^{31}P NMR, δ: 24.08. MS, m/z: 775.4 $[M - I]^+$. $C_{52}H_{72}O_3IP$. Calculated, m/z: 775.5 $[M - I]^+$.

Methyl 3α-hydroxy-2β-(3-triphenylphosphoniopropyl)-20,29-dihydrobetulinate iodide (6) was obtained similarly to compound **5** from iodide **26**. The yield was 23%. White crystals, m.p. 142—144 °C (EtOH), $[\alpha]_D^{20}$ –1 (*c* 0.20, $CHCl_3$). IR, ν/cm^{-1}: 1725 (C=O). ^{1}H NMR, δ: 0.75, 0.87 (both d, 3 H each, H(29), H(30), *J* = 7 Hz); 0.76, 0.79, 0.85, 0.88, 0.93 (all s, 3 H each, H(23)—H(27)); 1.13—1.80 (m, 24 H, CH, CH_2 in pentacyclic skeleton, 1 H, H(20), 2 H, H(1′), 2 H, H(2′)); 3.56 (m, 2 H, H(3′)); 3.64 (s, 3 H, OMe); 5.15 (br.s, 1 H, H(3)); 7.67—7.89 (m, 15 H, Ph). ^{31}P NMR, δ: 24.34. MS, *m/z*: 775.3 $[M - I]^+$. $C_{52}H_{72}O_3IP$. Calculated, *m/z*: 775.5 $[M - I]^+$.

3β-Acetoxy-2β-(3-triphenylphosphoniopropyl)-20,29-dihydrobetulinic acid bromide (7) was obtained similarly to compound **3** from bromo acid **34**. The yield was 81%. White crystals, m.p. 206—208 °C (EtOH), $[\alpha]_D^{20}$ –25.4 (*c* 0.24, $CHCl_3$). IR, ν/cm^{-1}: 1726 (C=O). ^{1}H NMR, δ: 0.47 (t, 1 H, $H^a_{eq}(1)$, *J* = 12 Hz); 0.74, 0.86 (both d, 3 H each, H(29), H(30)); 0.71, 0.73, 0.80, 0.85, 0.88 (all s, 3 H each, H(23)—H(27)); 1.12—2.21 (m, 22 H, CH, CH_2 in pentacyclic skeleton, 1 H, H(20), 2 H, H(1′), 2 H, H(2′)); 1.68 (m, 1 H, $H^b_{ax}(1)$); 2.03 (s, 3 H, Me (OAc)); 3.62—3.75 (m, 2 H, H(3′)); 4.29 (d, 1 H, H(3), *J* = 11 Hz); 7.28 (br.s, 1 H, COOH); 7.47—7.98 (m, 15 H, Ph). ^{31}P NMR, δ: 24.15. MS, *m/z*: 803.4 $[M - Br]^+$. $C_{53}H_{72}O_4BrP$. Calculated, *m/z*: 803.5 $[M - Br]^+$.

Benzyl 3β-acetoxy-2β-(3-triphenylphosphoniopropyl)-20,29-dihydrobetulinate iodide (8) was obtained similarly to compound **5** from iodide **27**. The yield was 78%. White crystals, m.p. 148—150 °C (EtOH), $[\alpha]_D^{20}$ –17.9 (*c* 0.24, $CHCl_3$). IR, ν/cm^{-1}: 1728 (C=O). ^{1}H NMR, δ: 0.47 (t, 1 H, $H^a_{eq}(1)$, *J* = 12 Hz); 0.70, 0.86 (both d, 3 H each, H(29), H(30)); 0.71, 0.74, 0.77, 0.86, 0.88 (all s, 3 H each, H(23)—H(27)); 1.04—2.27 (m, 22 H, CH, CH_2 in pentacyclic skeleton, 1 H, H(20), 2 H, H(1′), 2 H, H(2′)); 1.65 (m, 1 H, $H^b_{ax}(1)$); 2.07 (s, 3 H, Me (OAc)); 3.53—3.66 (m, 2 H, H(3′)); 4.31 (d, 1 H, H(3), *J* = 11 Hz); 5.05—5.13 (m, 2 H, OCH_2Ph); 7.29—7.85 (m, 20 H, Ph). ^{31}P NMR, δ: 24.11. MS, *m/z*: 893.5 $[M - I]^+$. $C_{60}H_{78}O_4IP$. Calculated, *m/z*: 893.6 $[M - I]^+$.

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