ISSN 1068-1620, Russian Journal of Bioorganic Chemistry, 2007, Vol. 33, No. 6, pp. 584–588. © Pleiades Publishing, Inc., 2007.
Original Russian Text © O.B. Flekhter, N.I. Medvedeva, O.S. Kukovinets, L.V. Spirikhin, E.G. Galkin, F.Z. Galin, D.G. Golovanov, N.I. Pavlova, O.V. Savinova, E.I. Boreko, G.A. Tolstikov, 2007, published in Bioorganicheskaya Khimiya, 2007, Vol. 33, No. 6, pp. 629–634.

Synthesis and Antiviral Activity of Lupane Triterpenoids with Modified Cycle E

O. B. Flekhter[a,1], N. I. Medvedeva[a], O. S. Kukovinets[a], L. V. Spirikhin[a], E. G. Galkin[a], F. Z. Galin[a], D. G. Golovanov[b], N. I. Pavlova[c], O. V. Savinova[c], E. I. Boreko[c], and G. A. Tolstikov[d]

[a] *Institute of Organic Chemistry, Ufa Scientific Center, Russian Academy of Sciences, pr. Oktyabrya 71, Ufa, 450054 Bashkortostan, Russia*

[b] *Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, ul. Vavilova 28, Moscow, 117813 Russia*

[c] *State Research Institute of Epidemiology and Microbiology, Minsk, Belarus*

[d] *Vorozhtsov Institute of Organic Chemistry, Siberian Division, Russian Academy of Sciences, pr. Akademika Lavrent'eva 9, Novosibirsk, 630090 Russia*

Received October 30, 2006; in final form, March 6, 2007

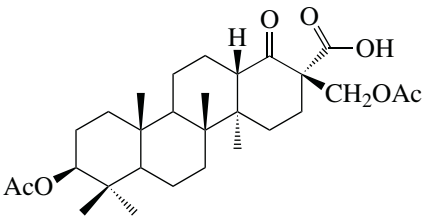
Abstract—A reductive transformation of the peroxide products of ozonolysis of derivatives of 3β-*O*-acetyl-22(17⟶28)-*abeo*-lupa-17(28),20(29)-diene and the subsequent intramolecular ketalization led to a compound with a trioxane fragment. This is a new approach to a skeletal modification of triterpenoid cycle E. An activity of the synthesized compounds was found toward the viruses of type A influenza and herpes simplex.

Key words: lupane triterpenoids, ozonolysis, antiviral activity

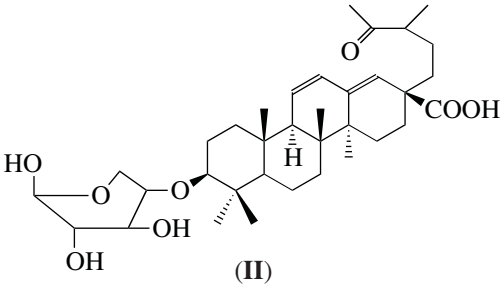
DOI: 10.1134/S1068162007060088

INTRODUCTION

Modification of cycle E in triterpenoids is a prospective approach to the synthesis of compounds with a pronounced pharmacological activity.[2] Oxidation of the 18(19)-lupene triterpenoids with ruthenium oxide demonstrated that 18-oxo-19,20,21,29,30-pentanoracid (**I**) exhibits a high anticancer activity [1]. Glycoside of the E-*seco*-ursane type (**II**) isolated from the *Ilex crenata* exhibits a strong antiallergenic effect. Its antiinflammatory activity is ten times higher than that of glycyrrhizic acid [2].



(**I**)



(**II**)

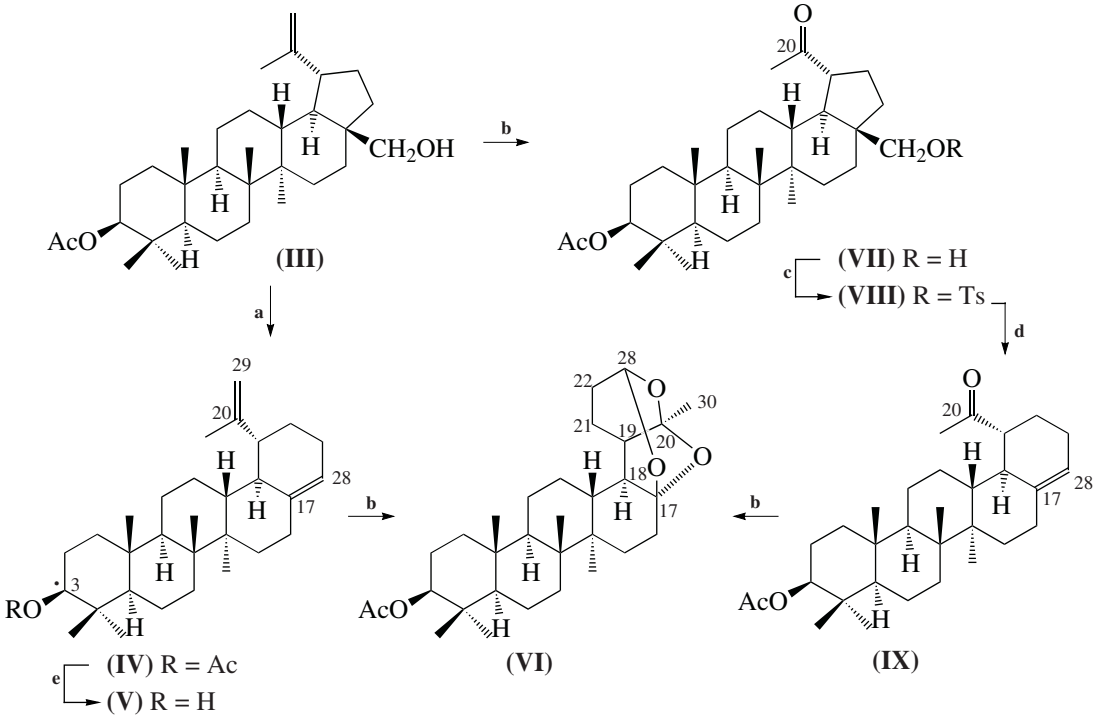
RESULTS AND DISCUSSION

Derivatives of 22(17⟶28)-*abeo*-lupa-17(28),20(29)-diene, easily preparable from betulin, are interesting subjects for skeletal transformations in triterpenoid cycle E. For example, 3β-*O*-acetyl-

[1] Corresponding author; phone/fax: (3472) 35-6066; e-mail: obf@anrb.ru.

[2] Abbreviations: MTC, maximum tolerated concentration; HSV, herpes simplex virus; PFU, plague-forming unit; TCID, tissue cytopathogenic infecting dose.

22(17⟶28)-*abeo*-lupa-17(28),20(29)-diene (**IV**) was synthesized from 3β-*O*-acetylbetulin (**III**) by heating at 100°C in pyridine in the presence of $POCl_3$ according to the method described in [3] (scheme). The target product (**IV**) was formed in 73% yield and crystallized as needles of 1–1.5 cm in length. Its structure followed from X-ray data (figure). Resonances from protons and carbon atoms of compound (**IV**) in its NMR spectra were completely attributed using two-dimensional spectroscopy and CH-correlation (CH-CORR). Deacetylation of (**IV**) was achieved in methanol in the presence of 5% KOH, and 3β-hydroxyderivative (**V**) was obtained in 73% yield.

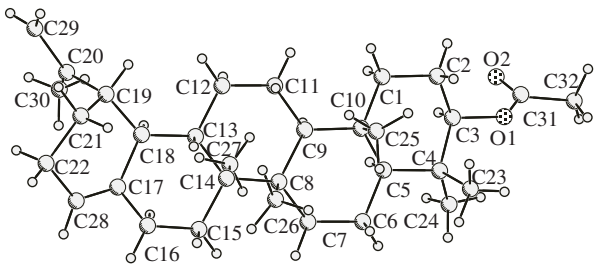


Conditions: (**a**) $POCl_3/C_5H_5N$, 2 h, 100°C; (**b**) O_3, CH_2Cl_2/methanol, –60°C, zinc/acetic acid or Me_2S; (**c**) *p*-TosCl, C_5H_5N, 48 h, 20°C; (**d**) NaOAc, 2 h, 100°C; (**e**) 5% KOH/methanol.

Scheme.

We tried to carry out an oxidative cleavage of the endocyclic bond of acetate (**IV**) to prepare E-*seco*-derivative, but a nontrivial product was synthesized by exhaustive ozonolysis in the CH_2Cl_2–methanol solution at –60°C. Compound (**VI**) with molecular mass of 500.345 with a composition of $C_{31}H_{48}O_5$ according to its mass spectrum was obtained. Resonances at δ 104.5, 94.8, and 105.5 were observed in its ^{13}C NMR spectrum. They correspond to the carbon atoms connected to oxygen atoms (–C17–O–C28–O–C20–O–). Resonance from H28 looked as a doublet at 5.41 ppm (*J* 6.2 Hz) in the ^1H NMR spectrum. These results indicate the presence of a ketal fragment in ozonolysis product (**VI**). Formation of compound (**VI**) from acetate (**IV**) can be explained by spontaneous intramolecular cyclization with the predominant formation of zwitter ion and carbonyl functional groups at C17 and C20 atoms.

We tried to confirm the structure of product (**VI**) by elucidation of the character of derivatives that could be obtained by ozonolysis of 20-oxo-22(17⟶28)-*abeo*-29-norlup-17(28)-ene (**IX**), which was prepared from3β-*O*-acetylbetulin by ozonolysis of norketone (**VII**), followed by solvolysis of tosylate (**VIII**) by the method [4]. As expected, the ozonolysis of ketone (**IX**) with the subsequent reduction of the peroxide products



Structure of 3β-*O*-acetyl-22(17⟶28)-*abeo*-lupa-17(28),20(29)-diene (**IV**).

Antiviral activity of triterpenoids (**IV**)–(**VI**)

Compound	FPV		HSV-1	
	EC_{50} (I_{95}), μM EC_{90} (I_{95}), μM	MTC/EC_{50} MTC/EC_{90}	EC_{50} (I_{95}), μM EC_{90} (I_{95}), μM	MTC/EC_{50} MTC/EC_{90}
(IV)	164.50 (249.82–108.30)	2.52	>207.15	<1
	1371.10 (2082.37–902.78)	0.3		
(V)	33.80 (58.06–19.68)	1.81	12.77 (14.75–11.05)	19.19
	169.29 (290.78–98.55)	0.36		9.67
(VI)	56.18 (79.06–39.91)	14.23	>799.44	<1
	472.61 (665.17–335.78)	1.69		

Note: I_{95} is a confidence interval.

resulted in the product whose physicochemical and spectral characteristics were identical to those of (**VI**).

This result is not anomalous and probably arises from the original structure of the starting compound, which contains an isopropylidenecyclohexene fragment. The ozonolysis of naphthalene, 3-carene, and a number of steroids is known to give such nontrivial products [5–7]. Note that compounds with such fragments occur in nature. For example, the tetranortriterpenoid fragmalin, belonging to melecyanins of the *Melia* plant family, has a similar structure, and can exhibit anticancer properties.

Thus, a compound with a trioxane fragment was prepared by reductive conversion of the peroxide products of ozonolysis of the derivatives of 3β-*O*-acetyl-22(17⟶28)-*abeo*-lupa-17(28),20(29)-diene as a result of intramolecular ketalization. This is a new approach to a skeletal modification of cycle E in lupane triterpenoids.

The results of studies of antiviral activity of triterpenoids (**IV**)–(**VI**) are given in the table. Among the studied compounds, 3β-hydroxy-22(17⟶28)-*abeo*-lupa-17(28),20(29)-diene (**V**) had the highest activity against the herpes simplex virus. The decrease in the virus titer in the presence of (**V**) taken at the maximum tolerate concentration (245.1 μM) and at a lower concentration close to MTC proved to be 1.6 log $TCID^*_{50}$//ml. The MTC/EC_{50} and MTC/EC_{90} values for (**V**) indicate a sufficiently wide range of nontoxic concentrations exhibiting the antiviral effect. Compounds (**IV**) and (**VI**) were inactive toward HSV-1. Compounds (**IV**)–(**VI**) similarly inhibited the reproduction of the FPV influenza virus, but only (**VI**) at the concentrations of 799.4 (MTC) and 399.7 μM decreased the virus titer by the value more than 1 log PFU/ml. These results confirms the possibility of inhibition of the influenza virus reproduction by the betulin derivatives, which has earlier been demonstrated [8, 9].

EXPERIMENTAL

TLC was carried out on Silufol plates (Chemapol, Czech Republic) in 20 : 1 of chloroform–methanol mixture. The substance spots were detected by the treatment with 5% phosphotungstic acid solution in ethanol with the subsequent heating at 100–120°C for 2–3 min. ^1H and ^{13}C NMR spectra (δ, ppm, *J*, Hz) were recorded on a Bruker AM-300 spectrometer (300 and 75.5 MHz, respectively) in $CDCl_3$ using $SiMe_4$ as an internal standard. Optical rotation was measured on a Perkin-Elmer 241 MC polarimeter in a tube of 1 dm in length. Mass spectra were recorded on a ThermoFinnigan MAT 95 XP spectrometer. Mps were determined on a Boetius device. An Ozon-2K ozonator was used for the ozonation. 3β-*O*-Acetylbetulin (**III**) was prepared by the procedure [10].

3β-*O*-Acetyl-22(17⟶28)-*abeo*-lupa-17(28),20(29)-diene (IV). Freshly distilled $POCl_3$ (4 ml) was added to a solution of 3β-*O*-acetylbetulin (**III**) (0.43 g, 1 mmol) in anhydrous pyridine (10 ml). The reaction mixture was heated with a backflow condenser on a water bath for 2 h and carefully poured out on ice (50 g). The precipitate was filtered, washed with water, and dried. The product was purified on a column with Al_2O_3 eluted with benzene. Compound (**IV**) was obtained as white needle crystals of 1–1,5-cm in length in yield of 0.31 g (73%); R_f 0.75, mp 200°C; $[\alpha]_D^{20}$ –0.35° (*c* 2, CH_2Cl_2); ^1H NMR: 0.75 (1 H, m, H5), 0.79 (3 H, s, H26), 0.80 (3 H, s, H23), 0.83 (3 H, s, H25), 0.90 (3 H, s, H24), 0.95–0.97 (2 H, m, H1a and H15a), 1.00 (3 H, s, H27), 1.65–1.67 (2 H, m, H1b and H15b), 1.05 and 1.40 (2 H, m, H11), 1.30–1.37 (7 H, m, H2a, H7, H9, H18, and H22), 1.45–1.55 (5 H, m, H2b, H6, and H12), 1.70 (3 H, s, H30), 1,82–1.85 (2 H, m, H21), 1.95–1.98 and 2.15–2.17 (2H, both m, H16), 2.00–2.05 (2 H, m, H13 and H19), 2.02 (3 H, s, OAc), 4.65 and 4.72 (2 H, both d, *J* 0.8, H29), 4.45 (1 H, dd, *J* 5.5 and 10.5, H3), 5.30 (1 H, t, *J* 4.0, H28); ^{13}C NMR: 14.8 (C25), 15.8 (C27), 16.3 (C26), 16.4 (C30), 18.2 (C6), 21.3 (C11), 21.8 ($OCO\underline{C}H_3$), 22.3 (C24), 23.5 (C2), 23.7 (C12), 26.5 (C22), 27.8 (C21), 27.9 (C23), 32.7 (C15), 33.7 (C7),

34.1 (C16), 37.0 (C10), 37.8 (C4), 38.5 (C1), 40.9 (C8), 40.9 (C19), 42.3 (C14), 44.0 (C13), 46.1 (C18), 50,4 (C9), 55.4 (C5), 80.9 (C3), 108.9 (C29), 118.3 (C28), 141.5 (C17), 150.6 (C20), 170.8 ($O\underline{C}OCH_3$).

X-Ray analysis of (IV): crystals ($C_{32}H_{50}O_2$, M 466.72) are monoclinic, a 13.061(4), b 6.579 (1), and c 31.284 (9) Å, $\beta = 90.65(3)°$, $V = 2688.1(13)$ Å^3 at 120 K, spatial group $C2$, Z 4 (Z' = 1), d_{calc} = 1.153 g/cm^{-3}, $\mu(MoK\alpha)$ = 0.69 cm^{-1}, F(000) = 1032. Intensities of 8106 reflections were measured at 120 K on a Smart 1000 CCD diffractometer ($\lambda(MoK\alpha)$ = 0.71072 Å, ω-scans, $2\theta < 47°$), 3544 Independent reflections (R_{int} = 0.0308) were used for further decoding and refinement of the structure. The experimental data were processed and averaged using the SAINT Plus program complex [11]. The account for absorption was carried out semiempirically according to equivalent reflections by the SADABS program [12]. The structure was decoded by the direct method and sequential syntheses of electron density. All the atoms, except for hydrogen atoms, were localized from difference syntheses of the electron density. Positions of the hydrogen atoms were geometrically calculated. The refinement was carried out according to F^2_{hkl} in anisotropic approximation for non-hydrogen atoms, positions of the hydrogen atoms were fixed. The final value of reliability factors was $R1$ = 0.0624 (calculated according to F_{hkl} for 2959 reflections with $I > 2s(I)$), wR2 = 0.1690, the number of refined parameters was 314, and GOF = 1.062. The calculations were carried out using the SHELXTL 5.10 program complex [13]. Coordinates of the atoms and temperature factors were deposited in the Cambridge Bank of Structural Data (CCDC 290282; http://www.ccdc.cam.ac.uk/products/csd/request/).

3β-Hydroxy-22(17⟶28)-*abeo*-lupa-17(28),20(29)-diene (V). A 5% solution of KOH in methanol (5 ml) was added to a solution of (**IV**) (0.77 g, 2 mmol) in methanol (10 ml) and stirred for 2 h. The reaction mixture was poured into 5% HCl (50 ml). The precipitate was filtered, washed with water, dried, and purified on a column withAl_2O_3 eluted with chloroform. Yield of (**V**) was 0.56 g (73%); R_f 0.48; mp 175–177°C; $[\alpha]_D^{20}$ –18° (c 2, CH_2Cl_2); ^{1}H NMR: 0.83, 0.85, 0.86, 0.94, and 1.04 (15 H, all s, CH_3), 1.10–1.90 (25 H, m, CH_2, CH), 1.76 (3 H, s, H30), 3.20–3.30 (1 H, m, H3), 4.65 and 4.73 (2 H both broadened s, H29), 5.35 (2 H, broadened s, H28); ^{13}C NMR: 14.8, 15.3, 15.8, 16.2, 18.2, 21.2, 21.9, 22.3, 23.5, 26.2, 27.3, 27.7, 28.0, 32.7, 33.7, 34.1, 37.1, 38.7, 40.8, 40.9, 42.2, 43.9, 46.0, 50.4, 55.3, 78.9 (C3), 108.8 (C29), 118.4 (C28), 141.4 (C17), 150.6 (C20). Found, %: C 87.18, H 9.12. Calc. for C 9.12. $C_{30}H_{48}O$ (M_r 520.884), %: C 87.62, H 9.31.

3β-*O*-Acetyl-20-oxo-22(17⟶28)-*abeo*-29-norlup-17(28)-ene (IX). Ozonated oxygen was passed through a solution of 3β-*O*-acetylbetulin (**III**) (0.94 g, 2 mmol) in CH_2Cl_2 (50 ml) until ozone began to exit out of a flask. The solution was cooled to 0°C, diluted with glacial acetic acid (10 ml), and zinc powder (1 g) was added. The reaction mixture was stirred for 1 h, and the zinc powder was filtered off. The filtrate was washed with the saturated solution of Na_2CO_3 (3 × 20 ml) and water (3 × 20 ml), dried with Na_2SO_4, and purified on a column with Al_2O_3 eluted with chloroform. 3β-*O*-Acetyl-28-hydroxy-20-oxo-29-norlupane (**VII**) was obtained as a white substance in yield 0.77 g (82%); R_f 0.48; mp 141–143°C; $[\alpha]_D^{20}$ +0.02° (c 1.0, CH_2Cl_2); ^{1}H NMR: 0.84, 0.85, 1.00, and 1.01 (15 H, all s, 5 CH_3), 1.10–2.00 (m, CH_2, CH), 2.04 (3 H, s, OAc), 2.16 (3 H, s, H30), 3.25 and 3.78 (2 H, both d, J 11.0, H28), 4.46 (1 H, dd, J 5.8 and 10.5, H3). Found, %: C 79.67, H 10.08. Calc. for C 10.08. $C_{31}H_{48}O_3$ (M_r 468.717), %: C 79.46, H 10.36. *p*-TosCl (1.30 g) was added to a solution of (**VII**) (0.94 g, 2 mmol) in anhydrous pyridine (50 ml). The reaction mixture was stirred for 48 h at room temperature and poured out into 5% solution of HCl (150 ml). The precipitate was filtered, washed, and dried. 3β-*O*-Acetyl-20-oxo-29-norlup-28-*O*-tosylate (**VIII**) was obtained as a yellow substance in yield 0.83 g (88%); R_f 0.88; mp 134–136°C; $[\alpha]_D^{20}$ +12.5° (c 2.0, CH_2Cl_2); ^{1}H NMR: 0.78, 0.83, 0.87, and 0.95 (15 H, all s, 5 CH_3), 1.00–2.00 (m, CH_2 and CH), 2.05 (3 H, s, OAc), 2.13 (3 H, s, H30), 3.65 and 4.00 (2 H, both d, J 95, H28), 4.40–4.50 (1H, m, H3), 7.35 and 7.80 (4H, both d, aromatic H). Found, %: C 71.15, H 8.55, S 5.27. Calc. for $C_{38}H_{56}O_6S$ (M_r 626.888), %: C 70.89, H 8.68, S 5.11. NaOAc (2.8 g) was added to a solution of (**VIII**) (1.25 g, 2 mmol) in acetic acid (100 ml). The reaction mixture was refluxed for 2 h and poured into cool water (200 ml). The precipitate was filtered, washed with water, dried, and purified by a column chromatography on Al_2O_3 with a chloroform elution. Compound (**IX**) was obtained as white crystals; yield 1.12 g (90%); R_f 0.75; mp 121–123°C; $[\alpha]_D^{20}$ +6.7° (c 3.0, CH_2Cl_2); ^{1}H NMR: 0.82, 0.85, 0.92, and 1.04 (15 H, all s, 5 CH_3), 1.10–2.00 (m, CH_2 and CH), 2.07 (3 H, s, OAc), 2.17 (3 H, s, H30), 4.47 (1 H, dd, J 5.5 and 10.5, H3), 5.38 (2 H, broadened s, H28); ^{13}C NMR: 14.5, 15.7, 16.3, 16.4, 18.1, 21.2, 21.3, 23.6, 24.5, 26.8, 27.7, 27.9, 28.4, 32.2, 32.9, 34.0, 36.9, 37.7, 38.4, 38.5, 40.7, 41.9, 46.0, 50.2, 53.5, 55.3, 80.8 (C3), 117.9 (C28), 140.6 (C17), 170.9, 211.5 (C20). Found, %: C 79.67, H 10.05. Calc. for C 10.05. $C_{31}H_{48}O_3$ (M_r 468.717), %: C 79.46, H 10.36.

(4*R*)-10-Acetyloxy-4,5,9,9,13,24-hexamethyl-23,25,26-trioxaheptacyclo[20.3.1.0^{1,18}.0^{4,17}.0^{5,14}.0^{8,13}. 0^{19,24}]hexacosane (VI). a. Excess of ozonated oxygen was passed through a solution of (**VI**) (2 mmol) in a 1 : 1 dichloromethane–methanol mixture (50 ml) at – 60°C. The reaction was monitored by TLC. After the completeness of reaction, the reaction mixture was heated to 0°C. The peroxide products were reduced by two methods. The first method consisted in

the treatment of the reaction mixture with zinc powder (1 g, 0.0154 g-atoms) in glacial acetic acid (10 ml) under stirring at 0°C for 1 h. The zinc powder was filtered off, and the filtrate was washed with a saturated solution of Na_2CO_3 (3 × 20 ml) and water (3 × 20 ml), dried with Na_2SO_4, and evaporated in a vacuum. According to the second method, Me_2S (0.2 ml, 0.17 g, 2.75 mmol) was added, and the reaction mixture was stirred for 2 h at room temperature and filtered. The filtrate was washed with 5% NaCl (3 × 20 ml) and water (3 × 20 ml), dried with Na_2SO_4, and evaporated in a vacuum. The residues obtained by both methods were purified on columns with Al_2O_3 eluted with chloroform. Compound (**VI**) was obtained as a white substance in yield of 0.60 g (71%); R_f 0.40; mp 159°C; $[\alpha]_D^{20}$ +23.3° (*c* 0.67; CH_2Cl_2); ^{1}H NMR: 0.83, 0.84, 0.87, 0.90, and 0.94 (15 H, all s, $5CH_3$), 1.00–2.00 (m, CH_2 and CH), 1.47 (3 H, s, H30), 2.04 (3 H, s, OAc), 4.47 (1 H, dd, *J* 6.0 and 10.0, H3), 5.41 (2 H, d, *J* 6.2, H28); ^{13}C NMR: 13.6, 15.6, 16.4, 16.6, 17.9, 18.7, 21.2, 21.3, 23.6, 23.7, 25.8. 26.5, 27.5, 27.9, 28.4, 33.8, 37.1, 37.7, 38.6, 40.1, 40.4, 41.9, 46.4, 50.8, 51.2, 55.5, 80.8, 94.8 (C28), 104.5 (C17), 105,5 (C20), 171.0. Found, %: C 74.54, H 9.93. Calc. for $C_{31}H_{48}O_5$ (M_r 500.345 according to the mass spectrum), %: C 74.47, H 9.78.

b. Compound (**IX**) (2 mmol) was ozonated as described above. Yield of (**VI**) after the purification by column chromatography was 0.65 g (78%). Its physicochemical properties and spectral characteristics were the same as those for the compound obtained by procedure **a**.

Antiviral properties of compounds (IV)–(VI) were studied on a cell culture with the A/FPV/Rostock/34 (H7N1) influenza virus and with HSV-1, IC strain, as described previously [14, 15]. Antiviral activity toward the influenza virus A was studied on a culture of fibroblasts of chicken embryos by the method of plague reduction. Studies with HSV-1 were carried out on a cell line of human rabdomyosarcoma (RD). The result was evaluated according to a development delay of the cytopathogenic effect of the virus. The studied substances were preliminarily dissolved in 10% ethanol, and serial twofold dilutions in a supporting medium (medium 199, Sigma, United States) were prepared. A decrease in the virus titer in comparison with control, 50% and 90% effective concentrations (EC_{50} and EC_{90}) of the studied substances, and the ratio of their MTC to their EC_{50} (MTC/ES_{50}) and to EC_{90} (MTC/EC_{90}, the selectivity index) were calculated as quantitative criteria of the observed antiviral effect. MTCs of the compounds were determined after the incubation with the uninfected cell culture for 72 h at 37°C.

ACKNOWLEDGMENTS

This study was supported by the Russian Foundation for Basic Research, project no. 05-03-32832 and by the grant of the President of Russian Federation for Support of Young Scientists and Leading Scientific Schools, project no. NSh-1589.2006.3, and by the UNESCO grant (IBSP/4-VN-01).

REFERENCES

1. Sarek, J., Klinot, J., Dzubak, B., Klinotova, E., Noskova, V., Krecek, V., Korinkova, G., Thomson, J.O., Janostakova, A., Wang, S., and Parsons, S., *J. Med. Chem.*, 2003, vol. 46, pp. 5402–5415.
2. Kakuno, T., Yoshikawa, K., and Arihara, S., *Tetrahedron Lett.*, 1997, vol. 32, pp. 3535–3538.
3. Anjaneyulu, A.S.R., Narayana, M., Sree, A., and Murty, S., *Indian J. Chem.,* 1980, vol. 19B, pp. 735–738.
4. Fuchino, H., Nozawa, O., and Tanaka, N., *Chem. Pharm. Bull.*, 1994, vol. 42, pp. 1745–1749.
5. Krstic, N.M., Lirenc, L.B., Pavlovic, V.D., Tinant, B., and Declercq, J.P., *J. Chem. Res.*, 2002, no. 8, pp. 392–394.
6. Kukovinez, O.S., Odinokov, V.N., Tolstikov, G.A., Lindeman, S.V., Struchkov, Y.T., Kosnikov, A.Y., and Khalilov, L.M., *Tetrahedron Lett.*, 1985, vol. 26, pp. 5843–5844.
7. Kukovinets, O.S., Kasradze, V.G., Galin, F.Z., Spirikhin, L.V., Zainullin, R.A., Kislitsin, M.I., Abdullin, M.I., Kunakova, R.V., and Tolstikov, G.A., *Zh. Org. Khim.,* 2002, vol. 38, pp. 536–543.
8. Boreko, E.I., Pavlova, N.I., Savinova, O.V., Nikolaeva, S.N., Flekhter, O.B., Phyzhova, N.S., and Nikandrov, V.N., *News Biomed. Sci.*, 2002, no. 3, pp. 86–91.
9. Pavlova, N.I., Savinova, O.V., Nikolaeva, S.N., Boreko, E.I., and Flekhter, O.B., *Fitoterapia*, 2003, vol. 74, pp. 489–492.
10. Vesterberg, K.A. and Vesterberg, R., *Arkiv. Kem. Mineral Geology,* 1926, vol. 9, p. 17.
11. *SMART. Bruker Molecular Analysis Research Tool*, vol. 5.059, Bruker AXS, Madison, WI, USA, 1998.
12. Sheldrick, G.M., *SADABS*, Bruker AXS Inc, Madison, WI-53719, USA, 1997.
13. Sheldrick, G.M., *SHELXTL-97, Version 5.10*, Bruker AXS Inc., Madison, WI-53719, USA, 1998.
14. Boreko, E.I., Pavlova, N.I., and Votyakov, V.I., *Vopr. Virusol.*, 1999, no. 3, pp. 115–119.
15. Boreko, E.I., Pavlova, N.I., Zaitseva, G.V., and Mikhailopulo, I.A., *Vopr. Virusol.*, 2001, no. 5, pp. 40–42.