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Synthesis of Heterocyclic Derivatives of Abietane

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Abstract—The methods of synthesis of some new derivatives of abietane including pyridines and indoles fused with diterpene skeleton were described.

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In recent years interest in abietane diterpene was renewed due to versatile biological activity found in its derivatives. In nature, were found anticancer diterpenoids [1, 2] and drugs against leishmaniasis [3, 4]. Activators of potassium channels [5], hypocholesterolemic [6], anticancer [7] and antiulcer [8] substances, plant growth regulators [9], compounds with antimicrobial activity [10–12] were found among the synthetic derivatives of abietane.

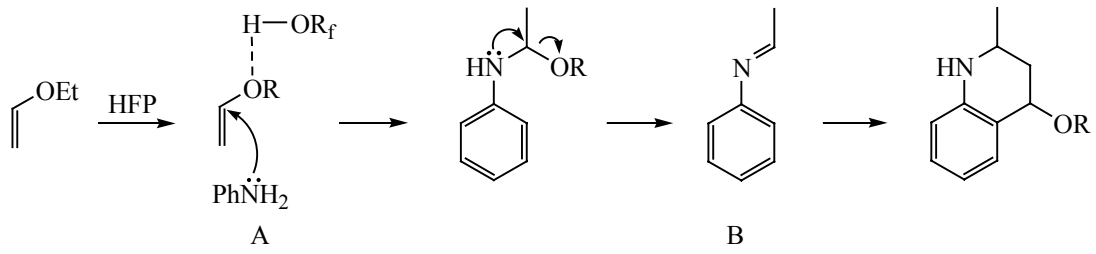
Dehydroabietic acid as a natural product was found in the galipot of a number of coniferous species [13] and can be separated from the mixture of resin acids through ethanolamine salt. Dehydroabietic acid can also be produced by dehydrogenation of levopimaric, palustric acids or by disproportionation of abietic or other resin acids. In developing the concept of the use of renewable natural raw materials for producing chiral reagents and reagents for asymmetric synthesis [14–16], we suggested one possible way to utilize a waste of a pine rosin: a synthesis of some heterocyclic derivatives of dehydroabietic acid from pyridines and indoles with diterpene skeleton using Povarov reaction [17–22].

The aim of this work is to study Povarov reaction with acetaldehyde and trifluoroacetaldehyde. Since Schiff bases of aliphatic aldehydes are unstable and prone to trimerization, we used an approach described in [23], when vinyl ethyl ether was used instead of acetaldehyde in the presence of Lewis acid. 1,1,1,3,3,3-Hexafluoropropanol-2 (HFP) acts analogously [24, 25] (Scheme 1).

As a result a nucleophilic attack of amine occurs at α-atom of a double bond with removal of ethanol and formation of ethylidene derivative (B) entering further in Povarov reaction according a usual scheme. Thus, application of HFP and 2,2,2-trifluoroethanol (TFE) allows using vinyl ethyl ether instead of acetaldehyde without employing catalysts [26]. It should be noted that in recent years fluorinated alcohols (TFE and HFP) have found wide application to organic synthesis due to their specific feature: large ionizing power, low nucleophility and high acidity [25, 27].

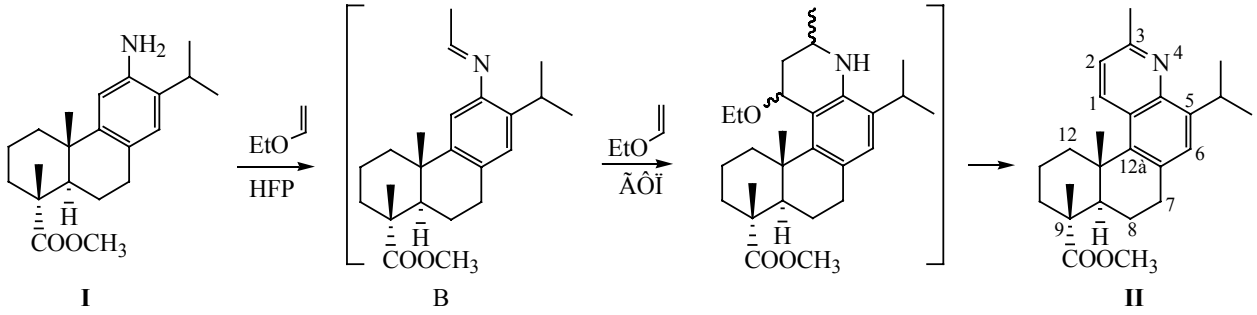
We stated that compound **II** was formed on condensation of the methyl ether of 12-aminohydroabietic acid

Scheme 1.



A B

Scheme 2.



(**I**) with two equivalents of ethyl vinyl ether in HFP in 60 % yield. Intermediate tetrahydroquinoline easily lost ethanol and was oxidized in air to compound **II** in releasing (Scheme 2).

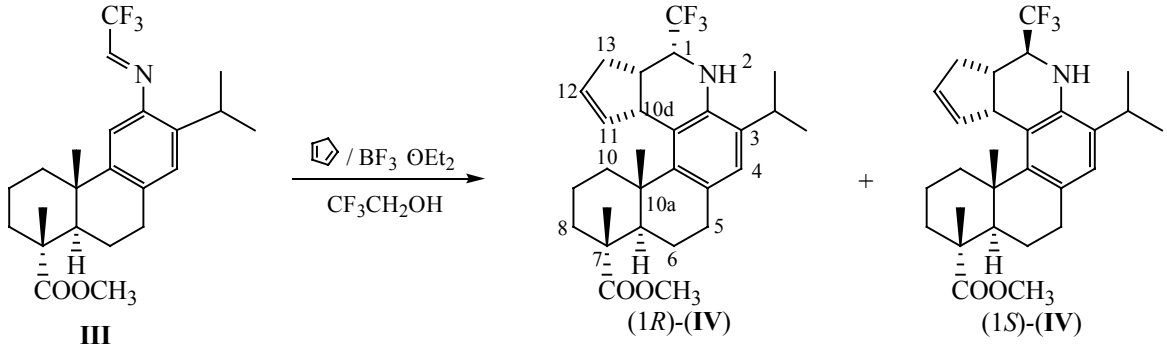
Two doublet signals with coupling constant J = 9.3 Hz in ^{1}H NMR spectra of compound **II** at δ 8.81 and 8.07 ppm belonging to protons at atoms C(1) and C(2), respectively, and also a signal in the form of a singlet of protons of methyl group at C(3) atom at δ 2.67 ppm point to the presence of an aromatic structure in the formed ring.

It is known that some 2-trifluoromethyl substituted quinolines demonstrate activity malaricidal and against leishmaniasis [28]. The Povarov's reaction was described for imines based on trifluoroacetaldehyde in [29, 30]. The Schiff base (**III**) that was introduced into a reaction of cyclopentadiene in the presence of 15 % mol boron trifluoride etherate was prepared to synthesize compounds with trifluoromethyl group at α-carbon atom of the heterocycle of amine **I**. As a result we produced compound **IV** with 17% yield as a blend of (1*R*)- and (1*S*)-diastereomers of about 1 : 1 ratio according to ^{1}H NMR data (Scheme 3).

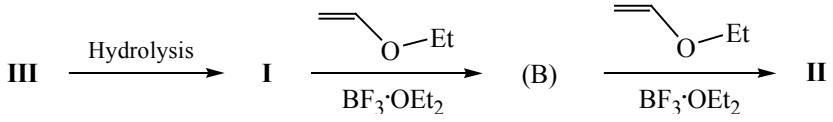
Reaction of imine **III** with ethyl vinyl ether in 3,3,3-trifluoroethanol was peculiar: Instead of trifluoromethyl-substituted product with 53% yield we obtained methyl-substituted quinoline (**II**) that was confirmed by a peak of a molecular ion with m/z = 379 in its mass spectrum. Apparently, the hydrolysis of imine **III** to amine **I** occurs and then the synthesis proceeds similarly to producing of compound **II** described above (Scheme 4).

Afterward we developed preparative techniques for O-methylation and O-benzylation of 18-hydroxyabieta-8,11,13-trienes (**Va, Vb**) to 18-methoxy- or 18-benzyloxyabieta-8,11,13-trienes (**VIa**, **VIb**) and (**VIIa**, **VIIb**) and then we produced their 7-oxo-derivatives (**VIIIa**, **VIIIb**) and (**IXa**, **IXb**). Compounds (**VI–IX**) can be used as syntons in organic synthesis.

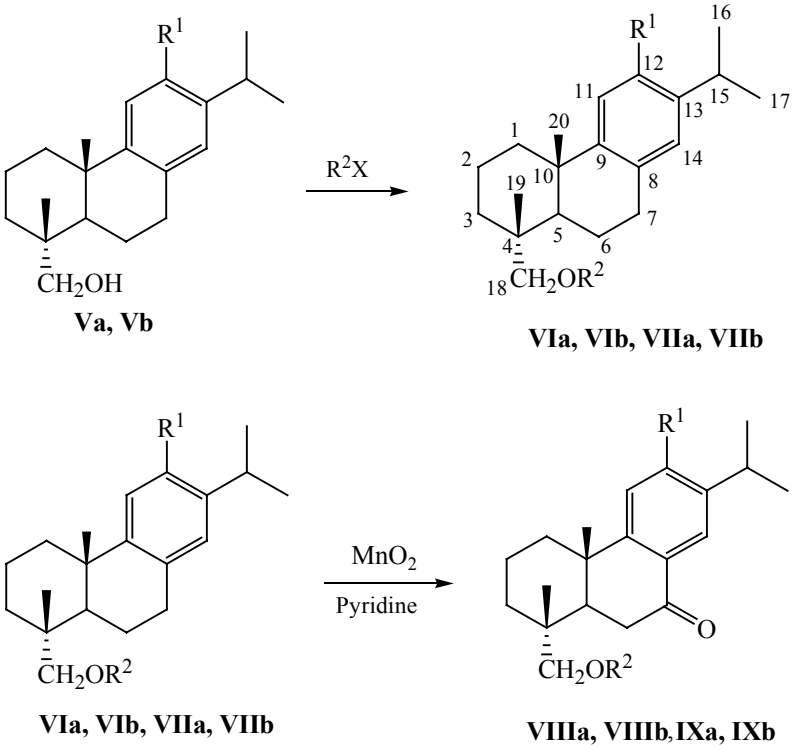
Scheme 3.



Scheme 4.



Scheme 5.



Va, Vb

VIa, VIb, VIIa, VIIb

VIa, VIb, VIIa, VIIb

VIIIa, VIIIb, IXa, IXb

(**V**)–(**IX**): R^1 – H (**a**), Br (**b**); R^2 – Me (**VI**), (**VIII**), CH_2Ph (**VII**), (**IX**).

We tested two techniques for alkylation of compounds **Va, Vb**: an interaction of sodium alcoholate generated from sodium hydride with alkyl halides (technique A) and alkylation under condition of interphase catalysis (technique B). We noted that an increase in temperature more than 25°C on the stage of alcoholate formation was resulted in a partial reduction of brominr atom in compound **Vb** by molecular hydrogen (Scheme 5).

7-Oxo-derivatives of abietane (**VIIIa**, **VIIIb**) (**IXa**, **IXb**) were synthesized by oxidizing **VIa**, **VIIa** with $KMnO_4$–Al_2O_3 mixture in acetone [31] or $MnSO_4$–$KMnO_4$ in pyridine [32]. The first method gives good yield (up to 80 %) only for charges in a range of 1–10 mmol, while the yield falls for loads in the range of 10–50 mmol, in this case an application of the second method is more reasonable.

As s result of further studies of [33, 34] we synthesized indoles condensed with the abietane skeleton

Starting from compound **VIIIa** we obtained intermediate hydrazone **X** that according to Fischer reaction was converted in indole **XI**.

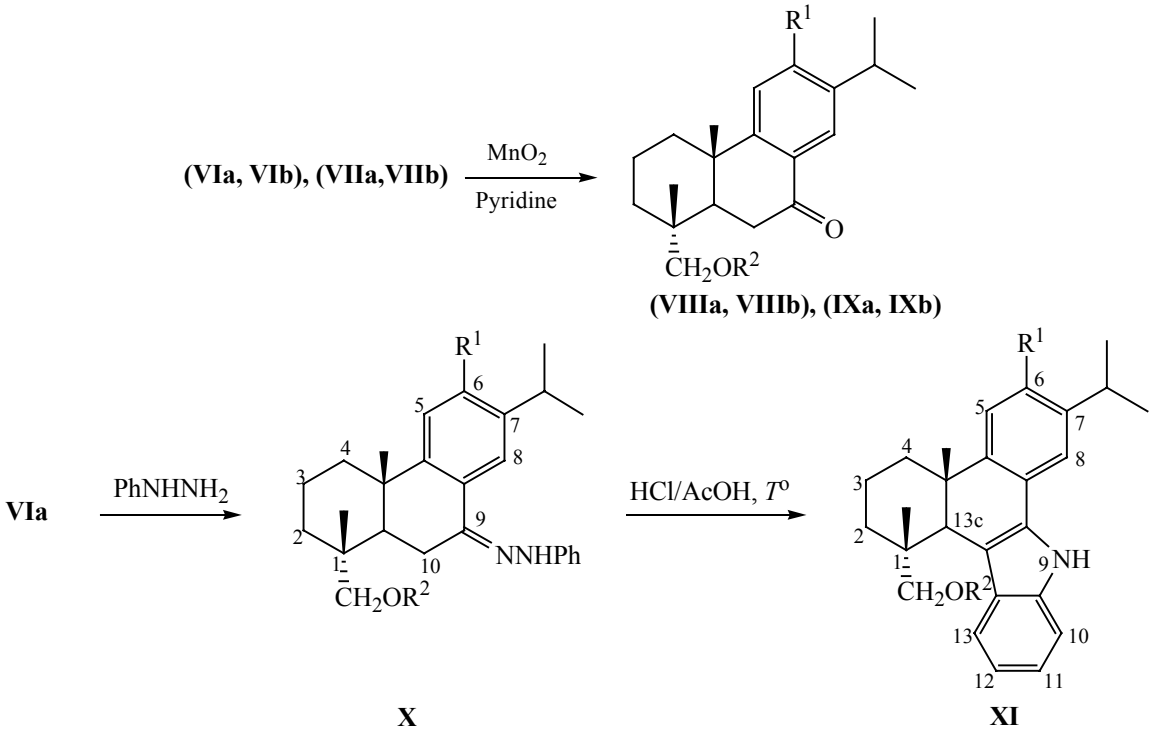
Thus, we showed that a nature of the functional group at C^{18} atom of abietic system did not affect the indolization possibility.

EXPERIMENTAL

The melting temperatures were measured with an Optimelt MPA100 (Stanford Research Systems). IR spectra were recorded with a Specord M-80 instrument in liquid paraffin.

^1H and ^{13}C NMR are recorded in $CDCl_3$ or DMSO-d_6 on Varian Mercury+300 at 300 and 75 MHz, respectively. To record ^1H NMR spectra we used internal reference GMDS, and the solvent in the case of ^{13}C NMR recording. Assignment of signals in ^1H and ^{13}C NMR spectra were made on the basis of data in [21, 35, 36]. A specific rotation was measured by a Perkin-Elmer 341 device, the value of $[\alpha]_D$ were given in units of deg g^{-1} cm^2. Chromato-mass spectra were received on an Agilent Technologies 5975B Network instrument (EC, 70 eV), connected to an Agilent Technologies 6890N chromatograph, capillary column HP-5MS 3000 × 0.25 mm, evaporator temperature 240°C with temperature programming within 20–40 deg min^{-1}, carrier gas helium. Column chromatography was performed on silica gel (Silicagel 60 with particle size 0.035–0.070 mm of "Merck"), a solvent mixture

Scheme 6.



of hexane–ethyl acetate was as eluent. Monitoring the progress of reactions and purity of products was carried out by TLC in the system hexane–ethyl acetate (10 : 1) with silufol (unless specified) or silasorb with developing by solution of phosphorus-molybdic acid in ethanol at heating to 100–150°C. Elemental analysis was performed on a Leco CHNS 9321P instrument. We used sodium hydride, trifluoroacetaldehyde, vinyl ethyl ether, 2,2,2-trifluoroethanol and 1,1,1,3,3,3-hexafluoropropylene-2-propanol of Lancaster Co. (Alfa Aesar).

Methyl ester of (8a*R*,9*R*,12a*S*)-5-isopropyl-3,9,12a-trimethyl-7,8,8a,9,10,11,12,12a-octahydronaphtho[1,2-*f*]quinoline-9-carboxylic acid (II). Ethyl vinyl ether (0.0065 g: 0.0086 ml, 0.09 mmol) dropwise was added at stirring to a solution of 0.01 g (0.03 mmol) of methyl ether of 12-aminodehydroabietic acid (**I**) synthesized according to [20] in 10 ml of 1,1,1,3,3,3-hexafluoro-2-propanol. The reaction monitoring was conducted by TLC in hexane–ethylacetate system of 9 : 1 ratio. The solvent was distilled under a vacuum, 10 ml of saturated aqueous $NaHCO_3$ and 20 ml of ethyl acetate were added to the residue, the organic layer was separated, washed with a saturated solution of NaCl, dried over $MgSO_4$. The reaction product was purified by column chromatography on silica gel (hexane–ethyl acetate, 20 : 1). Pale yellow transparent oil. Yield 60%. ^{1}H NMR spectrum, δ, ppm: 1.31 (d, 3H, H_3C, J = 6.6 Hz), 1.32 (d, 3H, CH_3, J = 6.6 Hz), 1.33 s (3H, H_3C), 1.65 s (3H, H_3C), 1.42–1.91 m (7H, H_2C^8, H_2C^{10}, H_2C^{11}, $H_{ax}C^{12}$), 2.23 m (1H, HC^{8a}), 2.67 s (3H, H_3CAr), 2.76–3.13 m (3H, H_2C^7, $H_{equiv}C^{12}$), 3.69 s (3H, OCH_3), 4.21–4.28 m (1H, HCAr), 7.15 s (1H, HC^6), 8.07 d (1H, HC^2, J = 9.3 Hz), 8.81 d (1H, HC^1, J = 9.3 Hz). Found, %: C 78.98, H 8.72, N 3.55. $C_{25}H_{33}NO_2$. Calculated, %: C 79.11, H 8.76, N 3.69.

Methyl ester of (1*R*,4a*S*,10a*R*)-1,4a-dimethyl-7-isopropyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-6-[(*E*)-(2,2,2-trifluoroethylidene)amino]-1-carboxylic acid (III). To a solution of 0.82 g (2.5 mmol) of compound **I** in 40 ml of toluene was added 0.134 g (2.5 mmol) 75% solution of CF_3CHO in water and about 200 mg of molecular sieves 4Å. The blend was stirred for 3 h at room temperature, then the molecular sieves was separated, a volatile matter was distilled by a vacuum water-jet pump. The obtained yellowish oil without treatment was immediately used in compounds **IV** synthesis.

Methyl ester of (1*RS*,6a*R*,7*R*,10a*S*,10d*R*,13a*S*)-7,10a-dimethyl-2,5,6,6a,7,8,9,10,10a,10d,13,13a-

dodecahydro-3-isopropyl-1-(trifluoromethyl)-1*H*-cyclopentane[*c*]naphtho[1,2-*f*]quinoline-7-carboxylic acid [the mixture of diastereomers (1*R*)-(IV) and (1*S*)-(IV)]. Shciff bases **III** [82 mg (0.20mM)] were dissolved in 10 ml of 2,2,2-trifluoroethanol. After 3.8 ml (4.3 mg, 0.03 mmol) of boron trifluoride etherate was added, and stirred for 10 min, then 75 ml (40 mg, 0.6 mmol) of freshly distilled cyclopentadiene was dropwise added. Separation was performed as in the case of compound **II**. Yellow-brown oil. Yield 17%. The ^{1}H NMR spectrum of (1*R*)-(**IV**)-diastereomer, δ, ppm: 1.14 d (3H, CH_3, J = 6.9 Hz), 1.18 d (3H, CH_3, J = 6.9 Hz), 1.31 s (3H, CH_3), 1.43 s (3H, CH_3), 1.38–1.89 m (7H, H_2C^6, H_2C^8, H_2C^9, $H_{ax}C^{10}$), 2.18–2.33 m (3H, HC^{6a}, H_2C^{13}), 2.71–3.35 m (6H, HC^1, H_2C^5, $H_{equiv}C^{10}$, HC^{13a}, HCAr), 3.65 s (3H, OCH_3), 4.89–4.92 m (1H, HC^{10d}), 5.16–5.17 m (1H, HC^{11}), 5.67–5.71 m (1H, HC^{12}), 6.69 s (1H, HC^4). ^{1}H NMR spectrum of (1*S*)-(**IV**)-diastereomer, δ, ppm: 1.14 d (3H, CH_3, J = 6.9 Hz), 1.18 d (3H, CH_3, J = 6.9 Hz), 1.27 s (3H, CH_3), 1.46 s (3H, CH_3), 1.38–1.89 m (7H, H_2C^6, H_2C^8, H_2C^9, $H_{ax}C^{10}$), 2.18–2.33 m (3H, HC^{6a}, H_2C^{13}), 2.71–3.35 m (6H, HC^1, H_2C^5, $H_{equiv}C^{10}$, HC^{13a}, HCAr), 3.68 s (3H, OCH_3), 4.80–4.83 m (1H, HC^{10d}), 5.39–5.42 m (1H, HC^{11}), 5.84–5.86 m (1H, HC^{12}), 6.74 s (1H, HC^4). Found (for the misture of diastereomers) (%): C 70.75, H 7.84, N 2.67. $C_{28}H_{36}F_3NO_2$. Calculated, %:C 70.71, H 7.63, N 2.95.

12-Bromo-18-hydroxyabieta-8,11,13-triene (Vb). It was prepared by reduction of methyl ester of 12-bromodehydroabietic acid [37] with the aid of $LiAlH_4$ in THF, mp 112–114°C (MeOH–water) (according to [38] mp 116°C). Yield 66%. $[\alpha]_D^{26}$ +59.0 (*c* 1, $CHCl_3$). R_f 0.16. IR spectrum, ν, cm^{-1}: 3300 br (OH in H-bond); 1500, 1320, 1060, 1040, 1015. ^{1}H NMR spectrum (300 MHz, DMSO-d_6), δ, ppm: 0.81 s (3H, $C^{20}H_3$), 1.11 d (3H, CH_3, J = 6.6 Hz), 1.14 d (3H, CH_3, J = 6.6 Hz), 1.16 s (3H, $C^{19}H_3$), 1.32–1.74 m (8H, H_2C^1, C^2H_2, H_2C^3, H_2C^6), 2.15 m (1H, C^5H), 2.77 m (2H, C^7H_2), 3.14 d (1H, $C\underline{H}_2OH$, J = 11.1 Hz), 3.19 m (1H, $C^{15}H$), 3.40 d (1H, $C\underline{H}_2OH$, J = 11.1 Hz), 6.84 s (1H, $C^{14}H$), 7.30 s (1H, $C^{11}H$). ^{13}C NMR spectrum (75 MHz, $CDCl_3$), δ, ppm: 15.34, 16.46, 16.60, 20.75, 20.92, 23.07, 27.50, 32.97, 35.35, 35.78, 36.30, 41.49, 70.00, 119.33, 124.95, 126.55, 132.49, 141.75, 147.34.

18-Methoxyabieta-8,11,13-triene (VIa) (method A). 18-Hydroxyabieta-8,11,13-triene (**Va**) (obtained according to [39], colorless oil, mp 163°C/0.2 mm Hg) [16.35 g (57.2 mM)] was dissolved in 100 ml of dry DMSO (especially pure, dried by annealed molecular sieves 4Å). A flask with the mixture was blew with argon and in argon flow 1.56 g (65 mmol) of sodium hydride (obtained from 2.60 g of 60% suspension of NaH in mineral oil by dry hexane processing) was quickly added. The mixture was stirred at 40°C to complete the alcoholate formation (~ 1 h), then cooled to 20°C, and after 4.02 ml (9.23 g, 65 mmol) of iodomethane dropwise added within 10 min. After 4 h stirring another 1.5 ml of MeI was added and stirred for 2 h, then 5 ml of ethanol and 5 ml of water were cautiously dropwise added, DMSO was distilled by the vacuum water-jet pump (temperature 80°C), 150 ml of water and 150 ml of ethyl acetate were added to the residue, the organic layer was separated, the aqueous layer was extracted with 60 ml of ethyl acetate, the organic layers were washed with saturated NaCl solution and dried over magnesium sulfate. After distillation of the solvent the residue [pale-yellow oil, yield 15.37 g (90%)] without additional purification was directed to the oxidation stage. For identification about 2 g of oil was purified by silica gel column (hexane–ethyl acetate, 10 : 1); R_f 0.80. A colorless oil (colorless oil according to [40]). ^{1}H NMR spectrum coincided with the data of [40].

12-Bromo-18-methoxyabieta-8,11,13-triene (VIb) was synthesized according to method A from 14.16 g (39 ммоль) of compound Vb, 1.7 g (40.5 ммоль) of 60% suspension of NaH in 100 ml of dry THF and 9.8 g (4.5 ml, 69 mM) of iodomethane. Purification was carried out by silica gel column (hexane–ethyl acetate, 10 : 1); R_f 0.9. Yield 8.43 g (57%). Colorless prisms from methanol, mp 112–113°C. $[\alpha]_D^{22}$ +96.3 (*c* 1, $CHCl_3$). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 0.80 s (3H, $C^{20}H_3$), 1.13 s (3H, $C^{19}H_3$), 1.15 s (3H, $C^{16}H_3$), 1.19 s (3H, $C^{17}H_3$), 1.30–1.76 m (7H, $H_{ax}C^1$, H_2C^2, H_2C^3, H_2C^6), 2.16 m (1H, $H_{equiv}C^1$), 2.71 m (1H, HC^5), 2.77 m (2H, H_2C^7), 2.87 d (1H, $C\underline{H}_2OH$, J = 10.2 Hz), 3.12 d (1H, $C\underline{H}_2OH$, J = 10.2 Hz), 3.20 m (1H, HC^{15}), 3.22 s (3H, CH_3O), 6.83 s (1H, $HC^{14}H$), 7.29 s (1H, HC^{11}). Found, %: C 66.17, H 8.28. $C_{21}H_{31}BrO$. Calculated, %: C 66.49, H 8.24.

18-Benzyloxyabieta-8,11,13-triene (VIIa) (method B). A mixture of 9.36 g (32.7 mM) of compound **Va**, 5.64 g (3.92 ml, 33 mM) of benzyl bromide, 40 ml dichloromethane, 14.50 g (25 mM) of tetrabutylammonium sulfate, and 23 ml of 50% KOH was intensively stirred for 6 h (monitoring by TLC), 100 ml of dichloromethane and 300 ml of water were added, the organic layer was separated, washed until neutral medium, dried over $MgSO_4$, the solvent was distilled. By chromatography

of the residue on silica gel (hexane–ethyl acetate, 10 : 1) 2.07 g (16%) of compound **VIIa** was obtained in the form of a thick colorless oil, R_f 0.78. $[\alpha]_D^{22}$ +24.4 (*c* 1.84, $CHCl_3$). IR spectrum, ν, cm^{-1}: 1600 $(C=C)_{arom}$. ^1H NMR spectrum (DMSO-d_6) δ, ppm: 0.80 s (3H, $C^{20}H_3$), 1.12 s (3H, $C^{19}H_3$), 1.15 d (6H, $C^{16}H_3$ and $C^{17}H_3$, J = 7 Hz), 1.19–1.37 m (2H, H_2C^1), 1.55–1.77 m (6H, H_2C^2, H_2C^3, H_2C^6), 2.17 m (1H, HC^5), 2.75 m (1H, $HC^{15}H$), 2.77 m (2H, H_2C^7), 2.91 d (1H, HC^{18}, J = 11.1 Hz), 3.21 d (1H, HC^{18}, J = 11.1 Hz), 4.34 d (1H, $OC\underline{H}_2Ph$, J = 12.4 Hz), 4.42 d (1H, $OC\underline{H}_2Ph$, J = 12.4 Hz), 6.80 d (1H, HC^{14}, ^4J = 1.2 Hz), 6.89 dd(1H, HC^{12}, ^4J = 1.2 Hz, ^3J = 8.4 Hz), 7.09 d (1H, HC^{11}, ^3J = 8.4 Hz), 7.13–7.22 m (5H, Ph). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 15.95, 16.84, 17.01, 22.04, 23.47, 28.36, 31.48, 33.92, 35.43, 35.61, 36.50, 42.14, 71.22, 77.69, 121.76, 122.34, 124.80, 125.36, 126.24, 132.92, 137.02, 143.34, 145.52. Found, %: C 86.28, H 9.57. $C_{27}H_{36}O$. Calculated, %: C 86.12, H 9.64.

12-Bromo-18-benzyloxyabieta-8,11,13-triene (VIIb) (method A). Compound **Va** 2.95 g (7.7 mmol) was dissolved in 30 ml of dimethylacetamide and 0.184 g of 60% suspension of NaH in mineral oil was added in the argon flow, the mixture was stirred for 30 min, then within 20 minutes the solution of 1.32 g (0.92 ml, 7.7 mmol) of benzyl bromide in 3 ml of dry toluene was added. The mixture was heated with stirring at 70°C for 5 h, and another 0.15 g of NaH and after 0.5 h 0.46 g of benzyl bromide in 2 ml of toluene were added with the following heating to 70°C for 3 h. The reaction mixture was poured into 500 ml of water, extracted with ether (70 ml, 5 times). Essential extracts were washed with twice 50 ml of saturated solution of NaCl, dried over $MgSO_4$, the residue from the distillation of the solvent was chromatographed on silica gel (hexane–ethyl acetate, 10 : 1), R_f 0.60. Yield 1.47 g (40%), colorless waxy substance, mp 72–78°C, $[\alpha]_D^{26}$ +54.4 (*c* 1, $CHCl_3$). IR spectrum, ν, cm^{-1}: 1600, 1300, 1205, 1110, 1070, 1040, 960, 900, 880. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 0.79 s (3H, $C^{20}H_3$), 1.12 d (6H, $C^{16}H_3$ and $C^{17}H_3$, J = 6.3 Hz), 1.19 s (3H, $C^{19}H_3$), 1.32 m (2H, H_2C^1), 1.52–1.72 m (6H, H_2C^2, H_2C^3, H_2C^6), 2.12 m (1H, HC^5), 2.72 m (2H, H_2C^7), 2.90 d (1H, HC^{18}, J = 8.7 Hz), 3.17 m (1H, $HC^{15}H$), 3.22 d (1H, $HC^{18}H$, J = 8.7 Hz), 4.40 m (2H, $OC\underline{H}_2Ph$), 6.84 s (1H, HC^{14}), 7.26 m (5H, Ph), 7.30 s (1H, HC^{11}). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 15.96 (C^{20}), 16.67 (C^{19}), 16.77 (C^2), 20.88 (C^{16}), 21.05 (C^{17}), 23.36 (C^6), 27.83 (C^{15}), 30.36 (C^7), 33.78 (C^3), 35.52 (C^{10}), 35.60 (C^1), 36.38 (C^5), 41.71 (C^4), 71.23 (C^{18}), 77.45 ($O\underline{C}H_2Ph$), 119.40, 125.02, 125.40, 126.29, 126.76, 127.07, 132.77, 136.38, 141.68, 147.64. Found, %: C 71.18, H 7.64, Br 16.88. $C_{27}H_{35}BrO$. Calculated, %: C 71.20, H 7.75, Br 16.54.

18-Methoxy-7-oxoabieta-8,11,13-triene (VIIIa). Oxidation was carried out by method suggested in [32].

Compound **VIa** [15.37 g (51 mmol)] was dissolved in 270 ml of pyridine, 20.5 g of $MnSO_4 \cdot H_2O$ and 32.5 g $KMnO_4$ were added, the mixture was heated in a boiling water bath (the temperature in the flask 85–90°C) for 6 h, monitoring by TLC (R_f 0.6). After completion of the reaction precipitate of MnO_2 was filtered through a layer of Al_2O_3 (5 cm) and washed with its 300 ml of ethanol, the ethanol and pyridine were distilled off under a vacuum, the residue was dissolved in 300 ml of ethyl acetate, washed with water and 5% HCl to extinction of pyridine smell, and dried over $MgSO_4$, the solvent was distilled off, the oily residue was chromatographed on silica gel (hexane–ethyl acetate, 10 : 1). Yield 9.6 g (60%). Colorless prisms from ethanol, mp 115–116°C, $[\alpha]_D^{17}$ +41.1 (*c* 1, $CHCl_3$). UR spectrum, ν, cm^{-1} (liquid paraffin): 1670 (C=O), 1600 (C=C), 1300, 1270, 1250, 1195, 1175, 1105, 1030, 985, 935, 845. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.86 s (3H, $C^{20}H_3$), 1.16 d (6H, $C^{16}H_3$ and $C^{17}H_3$, J = 6.6 Hz), 1.17 s (3H, $C^{19}H_3$), 1.27–1.76 m (5H, $H_{ax}C^1$, H_2C^2, H_2C^3), 2.22 m (2H, $H_{equiv}C^1$ and $H_{ax}C^6$), 2.58 m (2H, HC^5 and $H_{equiv}C^6$), 2.77 d (1H, HC^{18}, J = 11.1 Hz), 2.87 m (1H, HC^{15}), 3.09 d (1H, HC^{18}, J=11.1 Hz), 3.17 s (3H, OCH_3), 7.21 d (1H, HC^{11}, ^3J = 8.1 Hz), 7.30 dd (1H, HC^{12}, ^3J = 8.1 Hz, ^4J = 2.1 Hz), 7.79 d (1H, HC^{14}, ^4J = 2.1 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 15.6, 16.3, 21.8, 21.9, 31.6, 33.5, 35.2, 34.0, 35.5, 40.7, 57.1 (OCH_3), 79.3 (OCH_2), 121.7, 122.8, 128.8, 130.4, 144.5, 151.7, 197.7 (C=O). Found, %: C 80.18, H 9.60. $C_{21}H_{30}O_2$. Calculated, %: C 80.21, H 9.62.

12-Bromo-7-oxo-18-methoxy-7-oxoabieta-8,11,13-triene (VIIIb) was obtained analogous to compound **VIIIa**. Yield 52%, mp 135–136°C (colorless prisms from ethanol). $[\alpha]_D^{22}$ +71.4 (*c* 1, $CHCl_3$). IR spectrum, ν, cm^{-1} (liquid paraffin): 1675 (C=O), 1590 (C=C), 1245, 1105, 995, 920. ^1H NMR spectrum ($CDCl_3$) δ, ppm: 0.87 s (3H, $C^{20}H_3$), 1.16 d (3H, CH_3, J = 6.9 Hz), 1.18 s (3H, $C^{19}H_3$), 1.20 d (3H, CH_3, J = 6.9 Hz), 1.28–1.78 m (5H, $H_{ax}C^1$, H_2C^2, H_2C^3), 2.20 m (2H, $H_{equiv}C^1$ and $H_{ax}C^6$), 2.56 m (2H, HC^5 and $H_{equiv}C^6$), 2.78 d (1H, HC^{18}, J = 9 Hz), 3.09 d (1H, HC^{18}, J = 9 Hz), 3.19 s (3H, OCH_3), 3.25 m (1H, HC^{15}), 7.47 s (1H, HC^{11}), 7.83 s (1H, HC^{14}).

Found, %: C 64.33, H 7.29. $C_{21}H_{29}BrO_2$. Calculated, %: C 64.12, H 7.43.

18-Benzyloxy-7-oxoabieta-8,11,13-triene (IXa) was obtained by oxidation of compound **VIIa** analogous to compound **VIIIa**. Yield 22%, mp 80–83°C, $[\alpha]_D^{25}$ –1.6 (*c* 0.5, $CHCl_3$), R_f 0.20 (silasorb). In iodine vapor the substance gave characteristic orange-yellow color very quickly disappearing in air. IR soectrum, ν, cm^{-1}: 1715 (C=O), 1675, 1605, 1275, 1250, 1180, 1120, 1070, 1030, 990, 975, 935, 910, 840, 830. ^{1}H NMR spectrum (DMSO-d_6) δ, ppm: 1.07 s (3H, $C^{20}H_3$), 1.19 d (6H, $C^{16}H_3$ and $C^{17}H_3$, *J* = 6.9 Hz), 1.24 s (3H, $C^{19}H_3$), 1.47–1.55 m (5H, $H_{ax}C^1$, H_2C^2, H_2C^3), 1.75 m (2H, $H_{equiv}C^1$, $H_{ax}C^6$), 2.21 m (1H, $H_{equiv}C^6$), 2.32 m (1H, HC^5), 2.71 m (2H, HC^{18}), 2.86 m (1H, HC^{15}), 3.93 d (1H, $OC\underline{H}_2Ph$, *J* = 10.8 Hz); 4.45 d (1H, $OC\underline{H}_2Ph$, *J* = 10.8 Hz), 7.26 d (1H, HC^{11}, *J* = 8.4 Hz), 7.35 m (3H, Ph), 7.47 m (1H, Ph), 7.81 d (1H, HC^{14}, *J* = 1.8 Hz), 7.90 m (2H, HC^{12}, H_{arom}). Found, %: C 82.99, H 8.75. $C_{27}H_{34}O_2$. Calculated, %: C 83.03, H 8.77.

12-Bromo-18-benzyloxy-7-oxoabieta-8,11,13-triene (IXb) was obtained analogous to compound **IXa**. It was purified by silica gel column (hexane–ethyl acetate, 10 : 1). Yield 28%. It was recrystallized from ethyl acetate; mp 144–146°C. $[\alpha]_D^{25}$ +37.4 (*c* 1, $CHCl_3$), R_f 0.18 (silasorb). This substance as well as compound **IXa**, gave in iodine vapor characteristic orange-yellow color very quickly disappearing in air. IR spectrum, ν, cm^{-1} (liquid paraffin): 1720 (C=O), 1680, 1595, 1310, 1275, 1250, 1205, 1170, 1115, 1060, 1045, 1030, 975, 935. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.06 s (3H, $C^{20}H_3$), 1.17 d (6H, $C^{16}H_3$, $C^{17}H_3$, *J* = 7 Hz), 1.23 s (3H, $C^{19}H_3$), 1.42–1.56 m (5H, $H_{ax}C^1$, H_2C^2, H_2C^3), 1.75 m (2H, $H_{equiv}C^1$, $H_{ax}C^6$), 2.18 m (1H, $H_{экв}C^6$), 2.26 m (1H, HC^5), 2.67 m (2H, HC^{18}), 3.26 m (1H, HC^{15}), 3.92 d (1H, $OC\underline{H}_2Ph$, *J* = 11.1 Hz), 4.04 d (1H, $OC\underline{H}_2Ph$, *J* = 11.1 Hz), 7.35 t (2H, 3',5'-H, *J* = 7.8 Hz), 7.45 t (1H, 4'-H, *J* = 7.8 Hz), 7.49 s (1H, HC^{14}), 7.84 s (1H, HC^{11}), 7.91 d (2H, 2',6'-H, *J* = 7.8 Hz). Спектр ЯМР ^{13}C ($CDCl_3$), δ, ppm: 15.44 (C^{20}), 16.10 (C^{19}), 20.71(C^{16}), 20.74 (C^{17}), 21.97 (C^2), 30.73(C^{15}), 33.61(C^6), 34.10 (C^3), 35.17 (C^{10}), 35.45 (C^1), 35.83 (C^5), 41.97 (C^4), 70.28 (C^{18}), 94.20 ($O\underline{C}H_2Ph$), 123.77, 126.42, 126.50, 127.61, 128.16, 129.49, 131.04, 143.79, 152.25, 164.39, 195.84 (C^7=O). Found, %: C 68.94, H 7.12, Br 16.90. $C_{27}H_{33}BrO_2$. Calculated, %: C 69.08, H 7.09, Br 17.02.

(*E*)-1-[(1*R*,4a*S*)-1,4a-Dimethyl-7-isopropyl-1-methoxymethyl-2,3,4,4a,10,10a-hexahydrophenanthrene-9(1*H*)-ylidene]-2-phenylhydrazine (X). To a solution of 0.5 g (1.59 mmol) of compound **VIIIa** in 5 ml of ethanol 0.17 g (0.154 ml, 1.59 mmol) of phenylhydrazine and 2 drops of HCl (conc) were added. The mixture was boiled for 5 min and kept for 12 h. The precipitated yellow crystals of phenylhydrazone were filtered off and dried; mp 134–136°C. Yield 0.27 g (42%). IR spectrum (liquid paraffin), ν, cm^{-1}: 3300 br (NH in H-bond), 1595 (C=C), 1335, 1300 sl, 1255, 1200, 1140, 1095, 1060, 1030, 970, 930, 880, 820 s. ^{1}H NMR spectrum, δ, ppm: 0.98 s (3H, CH_3), 1.03 s (3H, CH_3), 1.21 d (3H, CH_3, *J* = 6.6 Hz), 1.22 d (3H, CH_3, *J* = 6.6 Hz), 1.32–2.63 m (5H, H_2C^2, H_2C^3, $H_{ax}C^4$), 1.94 dd (1H, $H_{ax}C^{10}$), 2.20 m (1H, $H_{equiv}C^4$), 2.37 dd (1H, HC^{10a}), 2.60 dd (1H, $H_{equiv}C^{10}$), 2.83 m (1H, HCAr), 2.89 d (1H, $\underline{H}_2COMe$, *J* = 9.3 Hz), 3.16 d (1H, $\underline{H}_2COMe$, *J* = 9.3 Hz), 3.22 s (3H, OCH_3), 6.81 m (1H, H_{arom}), 7.04–7.27 [m, 6H, HC(5), HC(6), $4H_{arom}$], 7.33 br.s (1H, NH), 7.89 s [1H, HC(8)]. $C_{27}H_{36}N_2O$. The exact data of elemental analysis were not determined due to non-stability of the compound.

(1*R*,4a*S*)-1,4a-Dimethyl-7-isopropyl-1-methoxymethyl-2,3,4,4a,10,10a-hexahydro-1*H*-dibenzo[*a,c*]carbazol (XI). Hydrazone (**X**) (0.3 g, 0.74 mmol) was dissolved in 5 ml of glacial acetic acid, 1 ml of HCl(conc.) was added and the mixture was boiled for 5 h, then poured into 30 ml of water, and brought to pH 7 by dry $NaHCO_3$, the precipitate was filtered off, dried and chromatographed on silica gel (hexane–ethyl acetate, 10 : 1), R_f 0.50. Yield 70 mg, mp 183–184°C (from aqueous ethanol), $[\alpha]_D^{21}$ +84.7 (*c* 0.15, $CHCl_3$). IR spectrum, ν, cm^{-1}: 3340 br (NH in H-bond), 1600 (C=C). ^{1}H NMR spectrum, δ, ppm: 0.95 s (3H, CH_3), 1.24 d (3H, CH_3, *J* = 6.9 Hz), 1.25 d (3H, CH_3, *J* = 6.9 Hz), 1.42 s (3H, CH_3), 1.33–1.87 m (5H, H_2C^2, H_2C^3, $H_{ax}C^4$), 2.22 m (1H, $H_{equiv}C^4$), 2.88 m (1H, HCAr), 2.92 s (1H, HC^{13c}), 3.25 d (1H, $\underline{H}_2COMe$, *J* = 8.7 Hz), 3.26 s (3H, OCH_3), 3.95 d (1H, $\underline{H}_2COMe$, *J* = 8.7 Hz), 7.08 m (3H, H_{arom}), 7.21 m (2H, H_{arom}), 7.37 d (HC^6, *J* = 8.4 Hz), 7.67 d (1H, HC^5, *J* = 8.4 Hz), 8.39 br.s (1H, NH). Found, %: C 83.62, H 8.57, N 3.55. $C_{27}H_{36}N_2O$. Calculated, %: C 83.68, H 8.58, N 3.61.

CONCLUSION

(1) It is shown that in the fluorinated alcohols vinyl ethyl ether acts as the equivalent of acetaldehyde and can be introduced into condensation with methyl ester of 12-aminodehydroabietic acid with the formation of

pyridine (**II**), annelated with the abietane skeleton.

(2) An interaction of methyl ester of 12-amino-dehydroabietic acid with trifluoroacetaldehyde and cyclopentadiene in Povarov's reaction leads to derivatives of cyclopentenoquinoline containing diterpene fragment.

(3) Preparative techniques for the synthesis of some 7-oxoderivatives of 18-methoxy- and 18-benzyloxyabieta-8 ,11,13-triene were developed.

(4) Based on the 18-methoxy-7-oxoabieta-8 ,11,13-triene we synthesized his phenylhydrazone and by Fischer reaction obtained indol annelated with abietane skeleton.

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