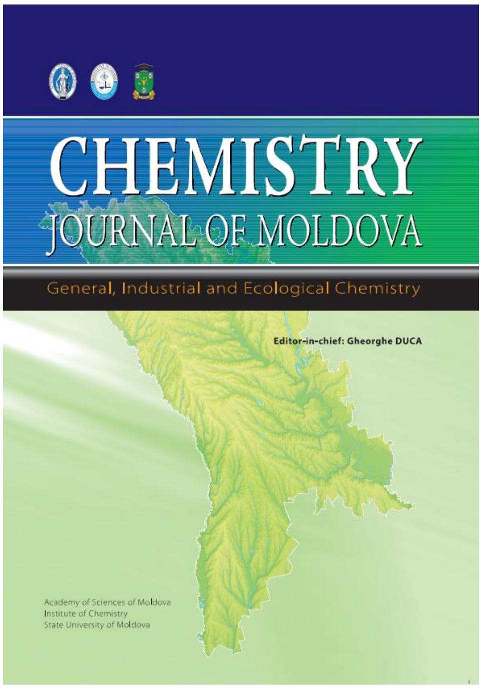

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Abstract. The main purpose of this research was the synthesis of highly functionalized derivatives of (+)-larixol by combination of classical and nonconventional method, like dye-sensitized photooxidation with preservation of outside chain. As a result, a series of four new cycle B derivatives of (+)-larixol were obtained, including products of photooxidative dehydrogenation and [2+4] cycloaddition of singlet oxygen, compounds **7** and **8**, respectively. The structure of all synthesized compounds was fully confirmed by spectral method (IR, ^{1}H and ^{13}C NMR) and for compound **8** containing endoperoxide functional group, additionally by single crystal X-ray diffraction analysis.

Keywords: (+)-larixol, enolacetylation, dye-sensitized photooxidation, reduction, X-ray analysis.

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Introduction

The isolation of the larixyl acetate from the oleoresin of European larch (*Larix europea* D.C.), contributed to the development of the chemistry of (+)-larixol (**1**) [1]. In the next two decades, different groups of researchers contributed to the establishment of absolute stereochemistry of (+)-larixol (**1**) [1-5]. At the same time larixol (**1**) was identified in Siberian larch (*L. sibirica* Labd.) [6].

Until now, many syntheses based on (+)-larixol (**1**) and its C_6 acetate are known, most of them being focused on the degradation of the side chain with the formation of norlabdanic derivatives [7-17]. Unlike the syntheses mentioned above, only a few are known based on (+)-larixol **1**, which proceed with the preservation of the side chain or its regrouping through allylic transpositions and with functionalization in cycle B. In one of them, the synthesis of (-)-borjatriol [18], a natural compound with pronounced anti-inflammatory activity was reported [19,20]. Another paper describes the synthesis of (+)-6β-isovaleryloxylabda-8,13-diene-7α,15-diol [21], a strong natural repellent [22,23]. The results of recent biological tests, which have highlighted antimicrobial, anti-mildew, antifungal, antioxidant, cytotoxic, antilarval, anti-inflammatory, neuroprotective, TRPC6 control activities of vegetal extracts containing (+)-larixol (**1**) and larixyl acetate (**2**), or of their pure forms were reported by author [24].

The aim of this work was the synthesis of derivatives with an advanced degree of functionalization of the B cycle and preservation of the side chain, based on (+)-larixol (**1**), by combining classical and unconventional synthesis methods, such as sensitized photooxidation.

Experimental

Generalities

The following reagents and solvents were used in the research: *N*,*N*-dimethylacetamide (DMA), petroleum ether (PE), ethyl acetate (EtOAc), acetyl chloride (AcCl), diethyl ether (Et_2O), isopropenyl acetate (≥-OAc), *p*-toluenesulphonic acid (*p*-TsOH), acetone, *meso*-tetraphenylporphyrine (H_2tpp), pyridinium chlorochromate (PCC) and dichloromethane (DCM). Reagents and solvents were purchased from Sigma-Aldrich and used without further purification.

Melting points (m.p) were determined on a Boetius hot stage apparatus and are uncorrected. *Optical rotations* measurements were performed on a JASCO DIP 370 polarimeter with a 1 dm microcell, in $CHCl_3$. *IR spectra* were obtained on a Spectrum 100 FT-IR spectrometer using ATR technique. *^{1}H and ^{13}C NMR* (400 and 100 MHz, respectively) and COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC, and DEPT spectra were acquired on a Bruker Avance DRX 400 spectrometer in $CDCl_3$. Chemical shifts are given in parts per million values in δ scale with the residual solvent protons and carbon atoms as internal standard (7.26 ppm and 77.0 ppm) and coupling constants (*J*) in Hertz. *HRMS analyses* were performed on a Thermo Scientific Orbitrap Fusion Tribrid mass spectrometer fitted with an EASY-Max NG heated electrospray source operating in negative or positive HESI mode. Ion source voltage was 3.5 and –2.5 kV for positive and negative mode, respectively. Temperatures of ion transfer tube and vaporizer were 300 and 60°C, and auxiliary and sheath gases were set at 3 and 6 arbitrary units, respectively.

Crystallographic measurements for **8** were carried out with an Oxford-Diffraction XCALIBUR Eos CCD diffractometer equipped with a source of graphite-monochromated Mo-K_α radiation. The crystal was placed 40 mm from the CCD detector and 575 frames were measured each for 60 s over 1 scan width. The unit cell determination and data integration were carried out using the CrysAlisPro package from Oxford Diffraction [25]. The structure was solved with program SHELXT using the intrinsic phasing method and refined by the full-matrix least-squares method on F^2 with SHELXL [26,27]. Olex2 was used as an interface to the SHELX programs [28]. Non-hydrogen atoms were refined anisotropically. Hydrogen atoms were added in idealized positions and refined using a riding model. In the absence of significant anomalous scattering, the absolute configuration could not be reliably determined, so that the Friedel pairs were merged and any reference to the Flack parameter was removed. The molecular plots were obtained with the Olex2 program. Selected crystallographic data and structure refinement details are provided in Tables S1, S2 and S3 in Supplementary material and the corresponding CIF-files. The supplementary crystallographic data can be obtained free of charge from the Cambridge CrystallographicData Centre No. CCDC-2312910 (12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223–336-033; or deposit@ccdc.ca.ac.uk.)

Progress of reactions and purity of products were examined by TLC on Merck silica gel 60 plates, eluent PE/EtOAc. The chromatograms visualization was achieved by treatment with concd H_2SO_4 and heating at 80°C for 5 min or using UV lamp (254 or 365 nm). Column chromatography was carried out on Across silica gel (60-200 mech) using petroleum ether (PE) (b.p. 40°-60°C) and the gradient mixture of PE with EtOAc. Solutions in organic solvents were dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure.

***Oxidation of (+)-larixol* (1)**

The oxidation of (+)-larixol (**1**) was performed to previously described procedures [15]. After workup and flash column chromatography corresponding exocyclic ketone **2** was obtained in 95%, as a colourless oil, $[\alpha]_{20}^{D}$ +75.7° (c 2.0, $CHCl_3$) (lit. $[\alpha]_{20}^{D}$ +74.6° (c 3.0) [15]; $[\alpha]_{20}^{D}$ +76.0° (c 0.84) [28]). The spectral data of *(4S,4aR,8aS)-4-((S)-3-hydroxy-3-methylpent-4-enyl)-4a,8,8-trimethyl-3-methylene-octahydro-naphthalen-1(2H)-one* ***(2)*** are in accordance with those reported before [15].

The isomerization of exocyclic ketone **2** into trisubstituted ketone **3** was performed according to previously described procedures [15]. After workup and flash column chromatography corresponding ketone **3** was obtained in 98%, as light-yellow oil, $[\alpha]_{20}^{D}$ +65.2° (c 2.5) (lit. $[\alpha]_{20}^{D}$ +43.5° (c 3.6) [15]). The spectral data of *(4S,4aR,8aS)-4-((S)-3-hydroxy-3-methylpent-4-enyl)-3,4a,8,8-tetramethyl-4a,5,6,7,8,8a-hexahydronaphthalen-1(4H)-one* ***(3)*** are in accordance with those reported before [15].

***Acetylation of hydroxyketone* 3**

To a solution of ketone **3** (0.93 g, 3.07 mmol) in DMA (13 mL) at 5°C dropwise AcCl (3.0 mL, 41.0 mmol) was added in 50 min. The reaction mixture was stirred at room temperature for 64 h, after that diluted with water (50 mL) and extracted with Et_2O (3×50 mL). Diethyl ether extract was washed consecutively with water (50 mL), solution of 5% H_2SO_4 (20 mL), brine (20 mL), water (2×50 mL) and dried over anhydrous Na_2SO_4. After solvent removal, the crud product (1.25 g) was subjected to flash chromatography on silica gel (eluent PE/EtOAc 96:4), to give *(S)-3-methyl-5-((1S,4aS,8aR)-2,5,5,8a-tetramethyl-4-oxo-1,4,4a,5,6,7,8,8a-octahydronaph-thalen-1-yl)pent-1-en-3-yl acetate* ***(4)***. Yield (1.12 g, 92%), as white crystals, m.p. 101°C (from EP), $[\alpha]_{20}^{D}$ +34.1° (c 0.1, $CHCl_3$). IR (ν, cm^{-1}) 2910, 1721, 1648, 1444, 1360, 1240, 1108, 915, 862. ^1H NMR: δ 5.94 (1H, dd, *J*= 17.6, 10.8, 14-C*H*), 5.73 (1H, dt, *J*= 1.3, 7-C*H*), 5.17 (1H, d, *J*= 17.6, 15-CH_2), 5.13 (1H, dd, *J*= 10.8, 15-CH_2), 2.20-2.14 (1H, m, CH_2), 2.01 (1H, s, 5-C*H*), 2.00 (3H, s, O*Ac*), 1.98 (1H, s, 9-C*H*), 1.87 (3H, t, *J*= 1.3, 17-CH_3), 1.80-1.75 (2H, m, CH_2), 1.53 (3H, s, 16-CH_3), 1.49-1.16 (5H, m, CH_2), 1.13 (3H, s, 18-CH_3), 1.12-1.09 (2H, m, CH_2), 1.09 (3H, s, 19-CH_3), 0.81 (3H, s, 20-CH_3). ^{13}C NMR: δ 200.3 (C-6), 169.7 (OAc), 158.7 (C-8), 141.4 (C-14), 128.4 (C-7), 113.5 (C-15), 82.8 (C-13), 63.4 (C-5), 56.6 (C-9), 43.0 (C-10), 42.9 (C-3), 42.1 (C-12), 38.3 (C-1), 33.4 (C-19), 32.3 (C-4), 23.5 (C-16), 21.9 (OAc), 21.8 (C-17), 21.3 (C-18), 21.1 (C-2), 18.1 (C-11), 14.6 (C-20). Mass-spectrum, m/z (%): Calcd: 346.48912. $C_{22}H_{34}O_3$. Found: 286.24948 (M+, -60).

***Enolacetilation of ketoacetate* 4**

To a solution of ketoacetate **4** (900 mg, 2.6 mmol) in isopropenyl acetate (20 mL) *p*-toluenesulphonic acid (20 mg) was added and reaction mixture was termostated under nitrogen in an oil bath at 109°C for 13h. Then it was diluted with water (20 mL) and extracted with Et_2O (3×30 mL). Organic extract was washed consecutively with solution of 5% $NaHCO_3$ (20 mL), water (3×20 mL) and dried over anhydrous Na_2SO_4. After solvent removal under reduced pressure crud product (1.0 g) was purified by column chromatography on silica gel (eluent: PE/EtOAc 95:5) to give the following compounds:

*(S)-5-((4aS,8aS)-4-Acetoxi-2,5,5,8a-tetrametil-4a,5,6,7,8,8a-hexahidronaftalen-1-il)-3-metilpent-1-en-3-il acetate (**5**)*. Yield (500 mg, 49%), as white crystals, m.p. 55-56°C (from PE), $[\alpha]^{D}_{20}$ -119.7° (c 0.7, $CHCl_3$). IR (*ν*, cm^{-1}) 2970, 1750, 1673, 1480, 1390, 1260, 1210, 1058, 940, 910. ^{1}H NMR: *δ* 5.95 (1H, dd, *J*= 17.6, 10.7, 14-C*H*), 5.52 (1H, d, *J*= 3.0, 7-C*H*), 5.14 (1H, dd, *J*= 12.8, 0.9, 15-C*H₂*), 5.12 (1H, dd, *J*= 6.4, 0.9, 15-C*H₂*), 2.35 (1H, d, *J*= 3.0, H-5), 2.16 (3H, s, OAc), 2.15-2.11 (1H, m, C*H₂*), 2.00 (3H, s, OAc), 2.07-2.02 (2H, m, C*H₂*), 1.78-1.70 (1H, m, C*H₂*), 1.67 (3H, s, 17-C*H₃*), 1.55 (3H, s, 16-C*H₃*), 1.35-129 (2H, m, C*H₂*), 1.14-1.07 (2H, m, C*H₂*), 1.04 (3H, s, 19-C*H₃*), 1.02 (3H, s, 18-C*H₃*), 0.94 (3H, s, 20-C*H₃*). ^{13}C NMR: *δ* 169.7 (OAc), 169.0 (OAc), 141.4 (C-9), 141.3 (C-14), 128.2 (C-6), 123.9 (C-8), 118.4 (C-7), 113.2 (C-15), 82.2 (C-13), 54.3 (C-5), 43.6 (C-3), 41.4 (C-10), 39.9 (C-12), 35.2 (C-1), 34.6 (C-19), 33.0 (C-4), 23.4 (C-16), 22.9 (C-18), 21.9 ($COCH_3$), 21.7 ($COCH_3$), 18.6 (C-2), 17.7 (C-17), 18.1 (C-11), 16.2 (C-20). Mass-spectrum, m/z (%): Calcd: 388.26136. $C_{22}H_{36}O_4$. Found: 388.26057.

Next eluted compound was: *(S)-5-((1S,8aR)-4-Acetoxi-2,5,5,8a-tetrametil-1,5,6,7,8,8a-hexahidronaftalen-1-il)-3-metilpent-1-en-3-il acetate* (**6**). Yield (420 mg, 41%), as an oil, $[\alpha]^{D}_{20}$ -112.0° (c 0.04, $CHCl_3$). IR (*ν*, cm^{-1}) 2960, 1754, 1665, 1476, 1385, 1225, 1068, 940, 913. ^{1}H NMR: *δ* 5.94 (1H, dd, *J*= 10.9, 4.5, 14-C*H*), 5.37 (1H, dd, *J*= 2.8, 1.4, 7-C*H*), 5.14 (1H, d, *J*= 10.9, 15-C*H₂*), 5.11 (1H, d, *J*= 4.5, 15-C*H₂*), 2.21-2.14 (2H, m, C*H₂*), 2.13 (3H, s, OAc), 2.07 (1H, s, 9-C*H*), 2.04-2.00 (2H, m, C*H₂*), 1.99 (3H, s, OAc), 1.82 (3H, t, *J*= 1.7, 17-C*H₃*), 1.53 (3H, s, 16-C*H₃*), 1.36-1.27 (2H, m, C*H₂*), 1.18 (3H, s, 19-C*H₃*), 1.14-1.12 (2H, m, C*H₂*), 1.11 (3H, s, 18-C*H₃*), 1.04-0.90 (2H, m, C*H₂*), 0.89 (3H, s, 20-C*H₃*). ^{13}C NMR: *δ* 169.8 (OAc), 169.3 (OAc), 141.4 (C-14), 138.4 (C-8), 134.6 (C-5), 120.7 (C-7), 128.1 (C-6), 82.8 (C-13), 51.2 (C-9), 42.0 (C-12), 41.8 (C-3), 40.2 (C-10), 38.2 (C-1), 33.5 (C-4), 31.9 (C-19), 28.8 (C-18), 23.7 (C-16), 22.1 (OAc), 21.4 (OAc), 20.9 (C-17), 20.8 (C-2), 18.4 (C-11), 17.3 (C-20). Mass-spectrum, m/z (%): Calcd: 388.26136. $C_{22}H_{36}O_4$. Found: 388.26057.

***General procedure for dye-sensitized photooxidation of enolacetates* 5 *and* 6**

To a solution of enolacetate **5** or **6** (388, 1 mmol) in acetone (100 mL) a catalytic amount of meso-tetraphenylporphyrine (H_2tpp) (20 mg) was added and obtained mixture was incubated in an acetone/dry ice bath at -78°C for 12 hours (TLC control). The reaction mixtures were irradiated with 2 lamps (60 W) during the full reaction time with a constant oxygen bubbling. Then the solvent was removed at the reduced pressure and crude reaction products were purified separately on column chromatography on silica gel (eluent: PE/EtOAc, 90:10), to give dienone **7** and endoperoxide **8**.

*(S)-3-methyl-5-((R)-2,5,5,8a-tetramethyl-3-oxo-3,5,6,7,8,8a-hexahydronaphthalen-1-yl)pent-1-en-3-yl acetate (**7**)*. Yield (282 mg, 82%), colourless oil, $[\alpha]^{D}_{20}$ -91.3° (c 0.06, $CHCl_3$). IR (ATR) (*ν*, cm^{-1}) 2980, 1740, 1625, 1605, 1380, 1360, 1240, 1160. ^{1}H NMR: *δ* 6.08 (1H, d, *J*= 1.2, H-6), 5.84 (1H, dd, *J*= 17.6, 10.8, 14-C*H*), 5.11 (1H, dd, *J*= 5.2, 0.8, 15-C*H₂*), 5.07 (1H, d, *J*= 11.5, 0.8, 15-C*H₂*), 2.27-2.08 (2H, m, C*H₂*), 2.00 (3H, s, OAc), 1.90 (3H, d, *J*= 0.8, 17-C*H₃*), 1.65-1.56 (2H, m, C*H₂*), 1.45 (3H, s, 16-C*H₃*), 1.39-1.33 (2H, m, C*H₂*) 1.31 (3H, s, 18-C*H₃*), 1.29 (3H, s, 19-C*H₃*), 1.22 (3H, s, 20-C*H₃*), 1.13-1.08 (2H, m, C*H₂*), 0.90-0.85 (2H, m, C*H₂*). ^{13}C NMR: *δ* 185.9 (C-7), 169.7 (OAc), 160.1 (C-5), 158.4 (C-9), 141.5 (C-14), 141.2 (C-8), 130.4 (C-6), 113.5 (C-15), 82.3 (C-13), 45.9 (C-10), 41.6 (C-3), 34.9 (C-1), 33.7 (C-4), 31.1 (C-12), 28.6 (C-19), 28.0 (C-17), 27.3 (C-11), 25.4 (C-18), 23.6 (C-16), 22.1 (OAc), 19.0 (C-2), 18.8 (C-20).

*(S)-5-((1R,2S,4aR,8aR)-4-acetoxy-2,5,5,8a-tetramethyl-2,5,6,7,8,8a-hexahydro-1H-2,4a-epidioxynaphthalen-1-yl)-3-methylpent-1-en-3-yl acetate (**8**)*. Yield (327 mg, 78%), colourless oil, $[\alpha]^{D}_{20}$ -123.5° (c 0.09, $CHCl_3$). IR (ATR) (*ν*, cm^{-1}) 2993, 1754, 1735, 1611, 1382, 1358, 1242, 1168, 1110. ^{1}H NMR: *δ* 6.11 (1H, s, 7-C*H*), 5.93 (1H, dd, *J*= 17.6, 10.9, 14-C*H*), 5.14 (1H, d, *J*= 10.5, 15-C*H₂*), 5.11 (1H, d, *J*= 4.1, 15-C*H₂*), 2.21 (3H, s, OAc), 1.99 (3H, s, OAc), 1.90-1.65 (6H, m, C*H₂*), 1.52 (3H, s, 16-C*H₃*), 1.36 (3H, s, 17-C*H₃*), 1.34 (3H, s, 18-C*H₃*), 1.23-1.14 (2H, m,

C*H*$_2$), 1.15 (3H, s, 19-C*H*$_3$), 1.00 (3H, s, 20-C*H*$_3$), 0.92-0.86 (2H, m, C*H*$_2$). ^{13}C NMR: δ 169.9 (OAc), 167.2 (OAc), 150.9 (C-6), 141.5 (C-14), 117.7 (C-7), 113.5 (C-15), 84.9 (C-5), 82.9 (C-13), 78.7 (C-8), 55.5 (C-9), 42.9 (C-10), 40.6 (C-12), 38.1 (C-3), 37.8 (C-1), 36.2 (C-4), 28.8 (C-19), 26.7 (C-17), 23.4 (C-16), 22.2 (OAc), 21.9 (OAc), 21.8 (C-11), 21.0 (C-18), 18.5 (C-20), 18.1 (C-20).

Crystallographic studies. Single-crystal X-ray diffraction data were measured on an Oxford-Diffraction XCALIBUR Eos CCD diffractometer supplied with a source of graphite-monochromated Mo-Kα radiation.

Results and discussion

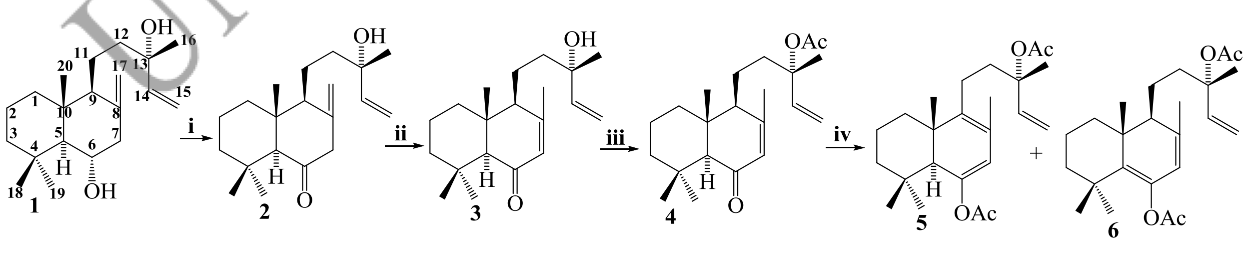
The starting compound, (+)-larixol (**1**), was isolated from commercially available Larch oleoresine by the method proposed by Lagnel, B. *et al*. [14]. Initially, it was oxidized to the exocyclic ketone **2**, which was further isomerized into ketone **3** according to the method described by the authors [15]. The spectral data of compounds **2** and **3** are in accordance with those reported before [15]. The tertiary C_{13} bonded hydroxyl group was protected by acetylation under standard conditions to give ketoacetate **4** (Scheme 1).

In the IR spectrum of compound **4**, absorption bands are characteristic to the ester group at 1721 and 1240 cm^{-1} and to conjugated carbonyl group at 1648 cm^{-1}. The structure of acetate **4** was confirmed by proton spectrum which contained a singlet of the methyl protons from the ester group at 2.00 ppm and those from C_{16} position at 1.53 ppm, and also by triplet of the methyl protons from the C_{17} position at 1.87 ppm. The structure of this compound is also confirmed by signals of protons bonded to the double bonds C_7-C_8 doublet of triplets at 5.73 ppm, C_{14}-C_{15} as doublet of doublets at 5.94 ppm, doublets and doublets of doublets at 5.17 and 5.13 ppm. The ^{13}C NMR spectrum completes the spectral data with signals of quaternary carbon C_6 at 200.3 ppm, carbonyl from acetate group at 169.7 ppm, C_8 at 158.7 ppm and C_{13} at 82.8 ppm, signals of tertiary carbons C_5 at 63.4 ppm, C_9 at 56.6 ppm, C_7 at 128.4 ppm and C_{14} at 141.4 ppm, but also the signal of the methylene carbon C_{15} at 113.5 ppm.

Next, the ketoacetate **4** was subjected to the enolacetylation reaction under standard conditions [29], obtaining the previously undescribed enolacetates **5** and **6** in 49% and 41% yields, respectively (Scheme 1).

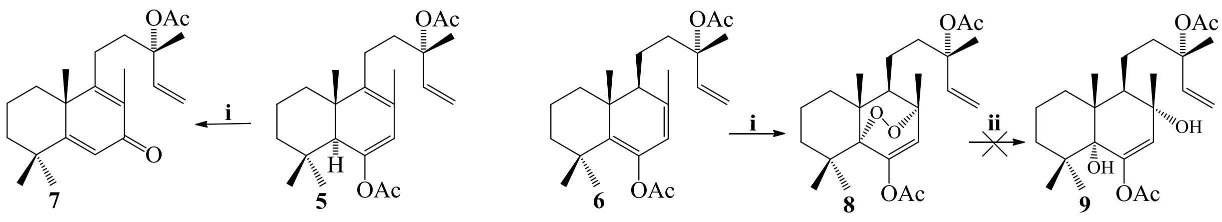
In the IR spectra of compounds **5** and **6**, there are absorption bands characteristic to acetate groups at 1754, 1750, 1260 and 1225 cm^{-1}, and double bonds at 1673 and 1665 cm^{-1}. The proton spectrum of compound **5** includes the singlets of protons from the acetate groups at 2.16 and 2.00 ppm. In the spectrum are present, also, the signals of the proton located at the double bonds C_7 at 5.52 ppm and those of methyl C_{17} at 1.67 ppm. The structure was also confirmed by the ^{13}C NMR spectrum through the signals of the quaternary carbon atoms from the acetate groups at 169.7 and 169.0 ppm, C_9 at 141.4 ppm, C_8 at 123.9 ppm and those of the tertiary carbons C_7 at 118.4 ppm and C_6 at 128.2 ppm.

In the ^{1}H NMR spectrum of compound **6**, there are singlets of the protons from the acetate groups at 2.13 and 1.99 ppm. In the spectrum there are the signal of the proton located at the double bonds C_7 at 5.37 ppm and methyl C_{17} at 1.82 ppm. The carbon spectrum includes the signals of the quaternary carbon atoms from the acetate groups at 169.8 and 169.3 ppm, C_8 at 138.4 ppm, C_5 at 134.6 ppm and those of the tertiary carbons C_7 at 120.7 ppm and C_6 at 128.1 ppm.



Reagents and conditions: i. PCC, DCM, AcOH, 3Å, r.t., 75 min, 95%; ii. MeONa, MeOH, H_2O_2, r.t., 1 h, 98%; iii. AcCl, DMA, 50 min, 5°C, then r.t., 64 h, 92%; iv. Isopropenyl acetate, *p*-TsOH, N_2, 109°C, 13 h, **5** (49%) and **6** (41%).

Scheme 1. Synthesis labdanic derivatives of (+)-larixol (1).



Reagents and conditions: i. O_2, *hν*, H_2tpp, DCM, 12 h, **7** (82%) and **8** (78%); ii. Thiourea, MeOH, 1.5 h.

Scheme 2. Sensitized photooxygenation of enolacetates 5 and 6.

Compounds **5** and **6**, due to the conjugated diene systems, represent suitable substrates for sensitized photooxidation reactions, which were carried out under the conditions described in Scheme 2.

Compounds **7** and **8** were isolated from the photooxygenation reaction products of compounds **5** and **6**. Dienone **7** is a product of photooxidative dehydrogenation of compound **5**, which follows the mechanism described in source [30], and endoperoxide **8** is a product of the [2+4] cycloaddition of the singlet oxygen to the conjugated diene system from the molecule **6**.

In the ^{1}H NMR spectrum of compound **7**, includes the signals of methyl protons of the acetate group at 2.00 ppm. Also, in the spectrum are the signals of the proton located at the double bonds C_6 at 6.10 ppm and C_{17} at 1.90 ppm. In the carbon spectrum, there are the signals of the quaternary carbon atoms from the acetate group at 169.7 ppm, C_7 at 185.9 ppm, C_5 at 160.1 ppm and C_8 at 141.2 ppm and this of the tertiary carbon C_6 at 130.4 ppm.

The proton spectrum of compound **8** includes the singlet signals of the methyl protons C_{17} at 1.36 ppm and those of the acetate groups at 2.21 and 1.99 ppm. In the spectrum, there are the signals of the protons located at the double bond C_7 at 6.11 ppm. The structure is also confirmed by the ^{13}C NMR spectrum through the signals of the quaternary carbon atoms from the acetate groups at 169.9 and 167.2 ppm, and of the tertiary ones C_8 at 78.7 ppm, C_7 at 117.7 ppm and C_6 at 150.9 ppm.

The structure and chemical composition of **8** was confirmed by single crystal X-ray diffraction method. Accordingly, to X-ray crystallography, it crystalizes in Sohnke $P2_1$ apace group with one molecule in the asymmetric unit. No co-crystallized solvate molecules were found in the crystal. A view of the molecular structure is shown in Figure 1, while the crystal data, details and geometric parameters are summarized in Tables S1, S2 and S3.

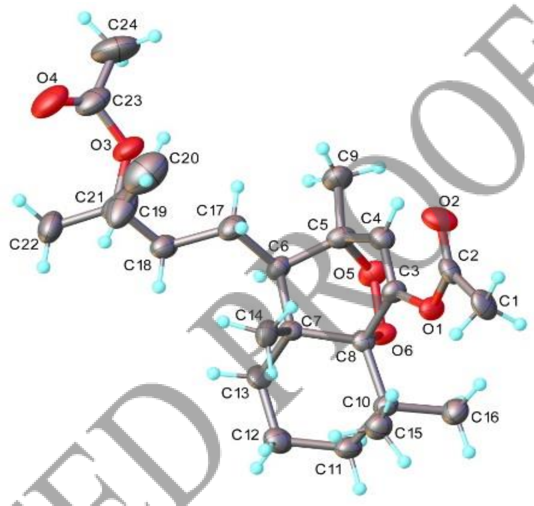


Figure 1. X-ray molecular structure of **8** with atom labeling and thermal ellipsoids at 50% level.

Next the endoperoxide **8** was reduced with thiourea in methanol [13], but the expected (+)-larixol derivative **9** was unstable and decomposed during column chromatography on silica gel (Scheme 2).

Conclusions

Thus, based on intermediates **2-4** obtained from (+)-larixol (**1**), with preservation of the side chain, for the first time, syntheses of cycle B polyfunctionalized labdanic derivatives **4-8**, were carried out including by non-conventional methods, such as sensitized photooxidation. Single-crystal X-ray diffraction results confirmed the structure and chemical composition of compound **8**. In turn, the reported C_{5-9} functionalized compounds, can serve as intermediates for the synthesis of new labdane diterpenoids with the involvement of some outside chain transformations.

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