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Eleuthesides and Their Analogs: VII.* Synthesis of Menthane Derivatives by the Diels–Alder Reaction of Levoglucosenone with (2*E*,4*E*)-Hexa-2,4-dien-1-yl Acetate

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Abstract—The Diels–Alder reaction of levoglucosenone with (2*E*,4*E*)-hexa-2,4-dien-1-yl acetate was used to synthesize chiral functionalized derivatives of isopropyl(methyl)cyclohexene fused to a carbohydrate fragment.

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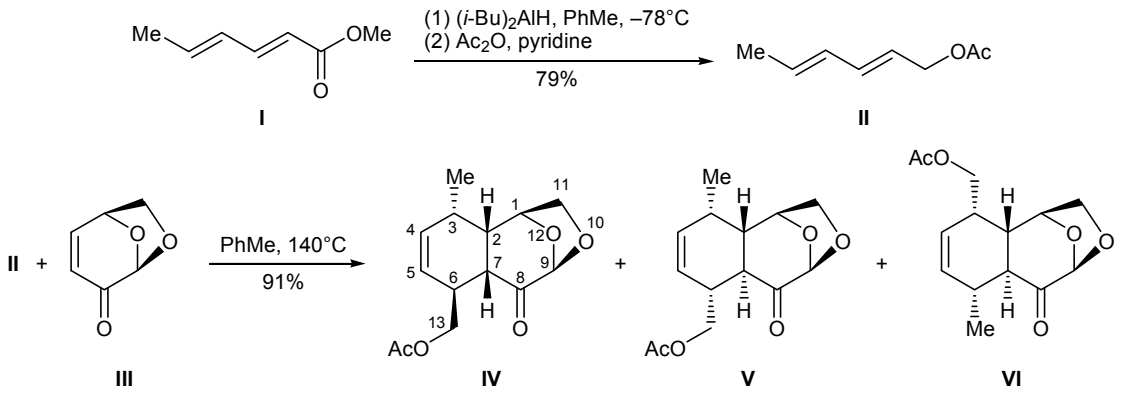
Menthane fragment constitutes a structural unit of many terpenoids and some alkaloids exhibiting diverse and in some cases unusual biological activity [2, 3]. Development of methods for the synthesis of functionalized menthane derivatives is promising from the viewpoints of both extension of the series of such compounds and studying the effect of menthane fragment on the activity of other pharmacophoric groups. Nowadays, the presence of a menthane fragment in molecules of natural compounds indicates only their biogenetic specificity.

Syntheses of eleuthesides involve mainly monoterpenoids, such as (*R*)- and (*S*)-carvones [4, 5] and (–)-α-phellandrene [6], and sesquiterpenoid (+)-δ-cadinol [7]. In the present work we made an attempt to obtain a chiral functionalized menthane derivative via Diels–Alder reaction of levoglucosenone with (2*E*,4*E*)-hexa-2,4-dien-1-yl acetate (**II**).

Diene **II** was synthesized from sorbic acid which was converted into methyl ester [8, 9], ester **I** was reduced with (*i*-Bu)$_2$AlH to (2*E*,4*E*)-hexa-2,4-dien-1-ol, and the latter was treated with acetic anhydride in pyridine. Hexadienyl acetate **II** was brought into Diels–Alder reaction with levoglucosenone (**III**) in toluene at 140°C under pressure, which led to the formation of three isomeric adducts **IV**–**VI**; the ratio (**IV**/**V**)–**VI** was 34 : 66 (Scheme 1). We failed to separate compounds **IV** and **V** by column chromatography on silica gel.

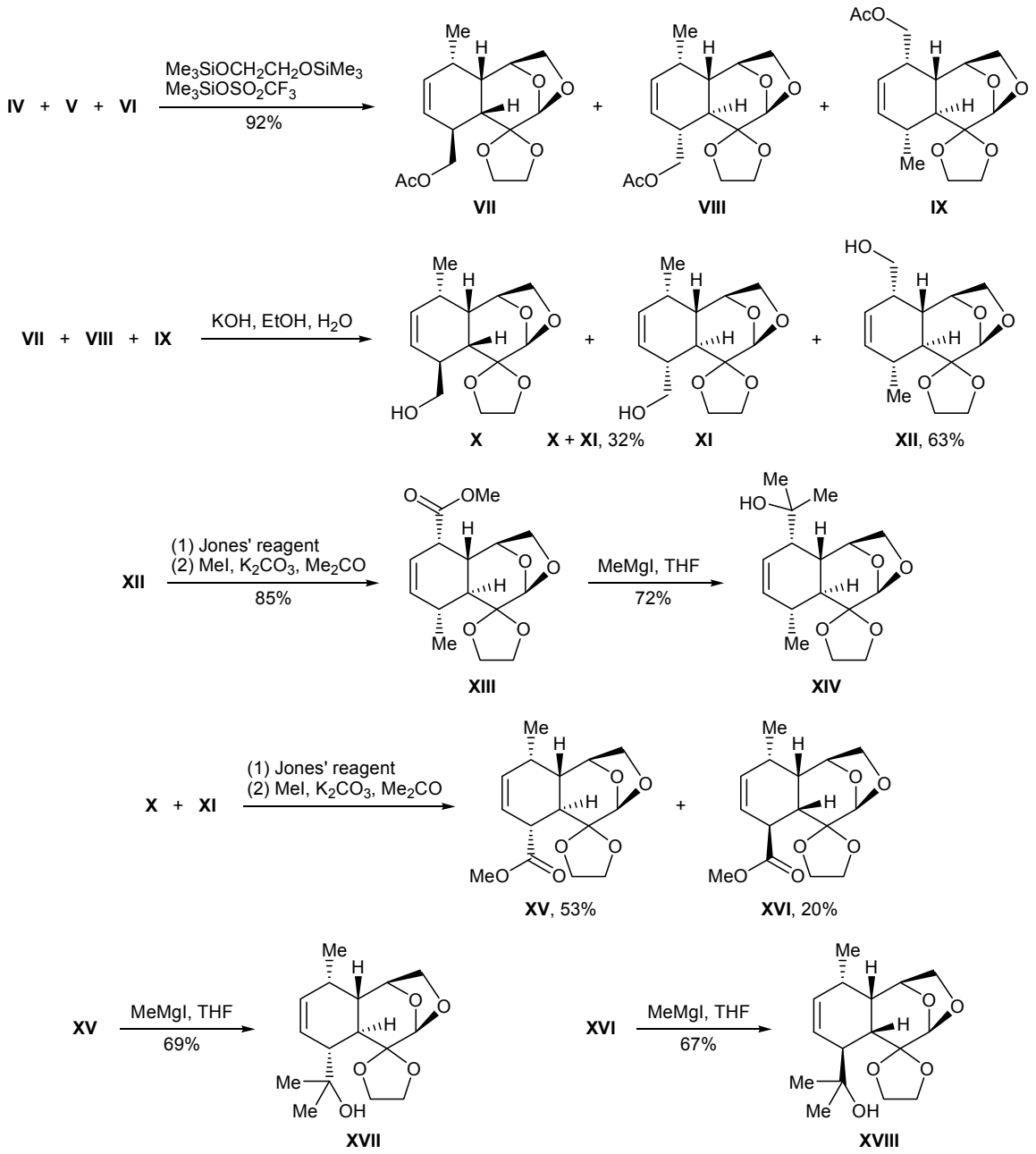
The structure of **IV**–**VI** was determined on the basis of their ^{1}H and ^{13}C NMR spectra. Protonated carbon atoms in molecule **IV** were assigned using

Scheme 1.



* For communication VI, see [1].

Scheme 2.



COSY and HSQC techniques. The nuclear Overhauser effects observed for the 11-*endo*-H proton, on the one hand, and 2-H and 7-H, on the other, as well as the vicinal coupling constants $^3J_{2,7} = 6.6$ and $^3J_{2,3} = 7.3$ Hz, indicated 2*S*,7*R* configuration of **IV** and *syn* orientation of 3-H and 7-H with respect to 2-H. The *S* configuration of C^3 and C^6 was proved by the observation of Me/1-H and 13-H_B/2-H correlation peaks in the NOESY spectrum.

The *S* configuration of C^2 in **VI** follows from the NOE between 11-*endo*-H and 2-H, while the vicinal coupling constants $^3J_{7,2} = {}^3J_{7,6} = 11.5$ Hz prove *anti* orientation of 2-H and 6-H with respect to 7-H; the coupling constant $^3J_{2,3} = 4.0$ Hz corresponds to *syn* orientation of 2-H and 3-H. The NOESY spectrum of **VI** revealed correlations between 13-H and 1-H, 13-H and 7-H, and 2-H and 6-H, which additionally confirmed 7*S*,2*S*,3*S*,6*R* configuration of asymmetric centers in molecule **VI**.

Compound **V** displayed in the ^{1}H NMR spectrum the vicinal coupling constants $^3J_{7,2} = 11.5$ and $^3J_{7,6} = 10.0$ Hz, indicating *anti* orientation of 2-H and 6-H

with respect to 7-H, and the coupling constant $^3J_{2,3}$ = 4.8 Hz conformed with the *syn* arrangement of 2-H and 3-H. In the NOESY spectrum of **V**, protons of the methyl group showed correlations with 1-H and 7-H.

It was surprising that the cycloaddition of hexadienyl acetate **II** to levoglucosenone (**III**) gave compounds **V** and **VI** with *trans*-junction of the rings. This is the first example of epimerization of the Diels–Alder adduct of levoglucosenone with diene during the process. Presumably, intramolecular hydrogen bond formed in the initial *cis* adduct due to strong proximity of the substituent on C^6 to the ketone carbonyl oxygen atom favors epimerization and stabilizes the conformation with equatorial substituents. Analogous pattern was observed when levogucosenone adduct with piperylene was treated with HCl–MeOH, which involved rupture of the 1,6-anhydro bridge [10].

To advance further toward construction of the menthene ring, the ketone group in adducts **IV**–**VI** was protected by treatment with 1,2-bis(trimethylsiloxy)ethane in the presence of a catalytic amount of trimethylsilyl trifluoromethanesulfonate [11]. The hydrolysis of acetates **VII**–**IX** thus obtained gave alcohols **X**–**XII**. By column chromatography on silica gel we isolated pure alcohol **XII**, whereas alcohols **X** and **XI** were not separated.

The subsequent Jones' oxidation of **XII** afforded the corresponding carboxylic acid which was converted into methyl ester **XIII** by the action of methyl iodide in acetone in the presence of potassium carbonate. By reaction of **XIII** with methylmagnesium iodide in tetrahydrofuran we obtained tertiary alcohol **XIV** in which the menthene ring is fused to carbohydrate fragment (Scheme 2). Analogous transformations performed with a mixture of alcohols **X** and **XI** led to a mixture of esters **XV** and **XVI** which can be readily separated by chromatography on silica gel. Pure esters **XV** and **XVI** were treated with methylmagnesium iodide in THF to obtain alcohols **XVII** and **XVIII** with completed menthene fragment.

To conclude, we have synthesized chiral functionalized derivatives of menthane fused to a carbohydrate fragment, which are promising as intermediate products for the preparation of biologically active natural compounds.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM-300 spectrometer at 300 and 75.47 MHz, respectively, as well as on a Bruker Avance III spectrometer at 500 MHz (^{1}H), using $CDCl_3$ as solvent unless otherwise stated. The IR spectra were measured on Shimadzu IR Prestige-21 and Bruker Tensor 27 instruments from films or Nujol mulls. The mass spectra were obtained on a Hewlett Packard HP 5973 mass-selective detector coupled with an HP 6890 gas chromatograph. The optical rotations were determined on a Perkin Elmer-341 polarimeter. Analytical TLC was performed on Sorbfil PTSKh-AF-A plates manufactured by *Sorbpolimer* closed corporation (Krasnodar, Russia). The melting points were measured on a Boetius PHMK 05 melting point apparatus.

(2*E*,4*E*)-Hexa-2,4-dien-1-yl acetate (II). A solution of 66 mL (0.357 mol) of 73% $(i\text{-Bu})_2$AlH in 150 mL of toluene was cooled to –78°C, and a solution of 15.0 g (0.119 mol) of methyl (2*E*,4*E*)-hexa-2,4-dienoate (**I**) in 50 mL of toluene was added under argon. The mixture was stirred for 2 h at –40°C, 48 mL (0.595 mol) of pyridine and 56 mL (0.595 mol) of acetic anhydride were slowly added dropwise, and the mixture was allowed to warm up to room temperature. When the reaction was complete (TLC), the mixture was cooled to 0°C, treated with 50 mL of ethanol, stirred for 30 min, and treated with 5% aqueous HCl until gel disappeared. The organic phase was separated, the aqueous phase was extracted with ethyl acetate (3 × 150 mL), the extracts were combined with the organic phase and dried over $MgSO_4$, the solvent was distilled off on a rotary evaporator, and the residue was distilled under reduced pressure. Yield 13.1 g (79%), oily material, bp 55–60°C (5 mm), R_f 0.66 (petroleum ether–EtOAc, 5:1). ^{1}H NMR spectrum, δ, ppm: 1.89 d (3H, CH_3, $^3J_{Me,5}$ = 7.6 Hz), 2.02 s (3H, OAc), 4.52 d (2H, 1-H, $^3J_{1,2}$ = 6.6 Hz), 5.50 m (1H, 2-H), 5.65 m (1H, 5-H), 5.95 d.d (1H, 4-H, $^3J_{4,5}$ = 12.0, $^3J_{4,3}$ = 10.3 Hz), 6.15 d.d (1H, 3-H, $^3J_{3,2}$ = 14.7, $^3J_{3,4}$ = 10.3 Hz). ^{13}C NMR spectrum, δ_C, ppm: 17.73 (CH_3), 20.54 (CH_3), 64.59 (C^1), 123.45 (C^5), 130.21 (C^4), 130.76 (C^2), 134.54 (C^3).

Diels–Alder reaction of diene II with levoglucosenone (III). A high-pressure reactor was charged with a solution of 2.00 g (14.3 mmol) of ester **II** and 1.28 g (10.2 mol) of levoglucosenone (**III**) in 10 mL of anhydrous toluene. The mixture was heated for 15 h at 140°C and evaporated on a rotary evaporator, and the residue was subjected to chromatography on silica gel to isolate 2.47 g (91%) of a mixture of adducts **IV**/**V** and **VI** at a ratio of 34:66.

(1*S*,2*S*,3*S*,6*S*,7*R*,9*R*)- and (1*S*,2*S*,3*S*,6*R*,7*S*,9*R*)-(3-Methyl-8-oxo-10,12-dioxatricyclo[7.2.1.0^{2,7}]dodec-4-en-6-yl)methyl acetate (IV/V). Oily material,

R_f 0.35 (petroleum ether–ethyl acetate, 3:1), $[\alpha]_D^{20}$ = –15.5° (*c* = 1.0, $CHCl_3$). The ratio **IV**/**V** was 1:3 according to the ^1H NMR data.

Compound **IV**. ^1H NMR spectrum (C_6D_6), δ, ppm: 0.65 d (3H, CH_3, $^3J_{Me,3}$ = 7.1 Hz), 1.45 d.d (1H, 2-H, $^3J_{2,3}$ = 7.3, $^3J_{2,7}$ = 6.6 Hz), 1.56 s (3H, OAc), 2.35 m (1H, 3-H), 2.92 d (1H, 7-H, $^3J_{7,2}$ = 6.6 Hz), 3.13 m (1H, 6-H), 3.49 d.d (1H, 11-*endo*-H, ^2J = 7.6, $^3J_{11\text{-}endo,1}$ = 5.1 Hz), 3.57 d (1H, 11-*exo*-H, ^2J = 7.6 Hz), 3.67 d.d (1H, 13-H_A, ^2J = 10.9, $^3J_{13A,6}$ = 4.8 Hz), 3.78 d.d (1H, 13-H_B, ^2J = 10.9, $^3J_{13B,6}$ = 8.4 Hz), 3.99 d (1H, 1-H, $^3J_{1,11\text{-}endo}$ = 5.1 Hz), 5.20 s (1H, 9-H), 5.32 m (2H, 4-H, 5-H). ^{13}C NMR spectrum (C_6D_6), δ_C, ppm: 19.42 (CH_3), 19.98 (OAc), 27.91 (C^3), 30.63 (C^6), 40.99 (C^7), 45.77 (C^2), 65.65 (C^{13}), 66.81 (C^{11}), 74.59 (C^1), 101.71 (C^9), 122.98 (C^4), 133.82 (C^5), 170.04 (Me**C**=O), 200.23 (C^8). Mass spectrum: *m*/*z* 266.2 $[M]^+$. $C_{14}H_{18}O_5$. Calculated: *M* 266.1154.

Compound **V**. ^1H NMR spectrum (C_6D_6), δ, ppm: 1.03 d (3H, CH_3, $^3J_{Me,6}$ = 6.8 Hz), 1.70 d.d.d (1H, 2-H, $^3J_{2,7}$ = 11.6, $^3J_{2,3}$ = 4.8, $^3J_{2,1}$ = 1.4 Hz), 2.12 s (3H, Ac), 2.48 m (1H, 3-H), 2.62 m (1H, 6-H), 2.72 d.d (1H, 7-H, $^3J_{7,2}$ = 11.5, $^3J_{7,6}$ = 10.0 Hz), 3.62 m (2H, 11-H), 3.73 m (1H, 13-H_B), 3.84 m (1H, 13-H_A), 4.60 d.d (1H, 1-H, $^3J_{1,11\text{-}endo}$ = 3.6 Hz), 5.17 s (1H, 9-H), 5.60 d (1H, 5-H, $^3J_{5,4}$ = 10.2 Hz), 5.90 d.d.d (1H, 4-H, $^3J_{4,5}$ = 10.2, $^3J_{4,3}$ = 5.6, $^4J_{4,6}$ = 2.2 Hz). ^{13}C NMR spectrum (C_6D_6), δ_C, ppm: 19.98, 20.38, 24.59, 33.54, 39.59, 44.38, 65.65, 66.74, 74.80, 101.61, 124.76, 131.72, 170.04, 200.23. Mass spectrum: *m*/*z* 266.2 $[M]^+$. $C_{14}H_{18}O_5$. Calculated: *M* 266.1154.

(1*S*,2*S*,3*S*,6*R*,7*S*,9*R*)-(6-Methyl-8-oxo-10,12-dioxatricyclo[7.2.1.0^{2,7}]dodec-4-en-3-yl)methyl acetate (VI). Oily material, R_f 0.33 (petroleum ether–ethyl acetate, 3:1), $[\alpha]_D^{20}$ = +54.9° (*c* = 1.0, $CHCl_3$). ^1H NMR spectrum, δ, ppm: 1.14 d (3H, CH_3, $^3J_{Me,6}$ = 6.6 Hz), 1.83 d.d.d (1H, 2-H, $^3J_{2,7}$ = 11.5, $^3J_{2,3}$ = 4.0, $^3J_{2,1}$ = 1.3 Hz), 2.11 s (3H, Ac), 2.37 d.d (1H, 7-H, $^3J_{7,2}$ = 11.5, $^3J_{7,6}$ = 11.5 Hz), 2.45 m (1H, 6-H), 2.72 m (1H, 3-H), 3.62 d (1H, 11-*exo*-H, ^2J = 7.1 Hz), 3.82 d.d (1H, 11-*endo*-H, ^2J = 7.1, $^3J_{11\text{-}endo,1}$ = 5.2 Hz), 4.18 d.d (1H, 13-H_B, ^2J = 11.7, $^3J_{13B,3}$ = 4.9 Hz), 4.42 d.d (1H, 13-H_A, ^2J = 11.7, $^3J_{13A,3}$ = 6.8 Hz), 4.90 d.d (1H, 1-H, $^3J_{1,11\text{-}endo}$ = 5.2, $^3J_{1,2}$ = 1.3 Hz), 5.15 s (1H, 9-H), 5.60 d.d (1H, 5-H, $^3J_{5,4}$ = 9.7, $^3J_{5,6}$ = 1.0 Hz), 5.67 d.d.d (1H, 4-H, $^3J_{4,5}$ = 9.7, $^3J_{4,3}$ = 5.0, $^4J_{4,6}$ = 1.7 Hz). ^{13}C NMR spectrum, δ_C, ppm: 20.82 (CH_3), 21.01 (**C**H_3CO), 31.54 (C^6), 38.05 (C^3), 41.18 (C^2), 43.07 (C^7), 63.97 (C^{13}), 71.15 (C^{11}), 73.61 (C^1), 99.09 (C^9), 125.19 (C^4), 135.74 (C^5), 170.76 (CH_3**C**=O), 207.04 (C^8). Mass spectrum: *m*/*z* 266.2 $[M]^+$. $C_{14}H_{18}O_5$. Calculated: *M* 266.1154.

Acetates VII–IX. A solution of 0.300 g (1.13 mmol) of acetate mixture **IV**–**VI** in 10 mL of methylene chloride was cooled to 0°C, 0.41 mL (1.69 mmol) of 1,2-bis(trimethylsiloxy)ethane and 0.006 mL (0.034 mmol) of trimethylsilyl trifluoromethanesulfonate were added, and the mixture was stirred for 5 h at room temperature. The mixture was neutralized with a saturated solution of sodium hydrogen carbonate, the aqueous phase was extracted with ethyl acetate (3×30 mL), the extract was dried over $MgSO_4$, the solvent was distilled off on a rotary evaporator, and the residue was subjected to chromatography on silica gel to isolate 0.321 g (92%) of an oily mixture of acetates **VII**–**IX**.

(1′*S*,2′*S*,3′*S*,6′*S*,7′*R*,9′*R*)-{3′-Methyl-10′,12′-dioxaspiro[1,3-dioxolane-2,8′-tricyclo[7.2.1.0^{2,7}]dodec-4′-en]-6′-yl}methyl acetate (VII). R_f 0.29 (petroleum ether–ethyl acetate, 2:1). ^1H NMR spectrum, δ, ppm: 1.06 d (3H, CH_3, *J* = 7.1 Hz), 1.40 m (1H, 2-H), 2.06 s (3H, Ac), 2.37 d (1H, 7-H, $^3J_{7,2}$ = 5.8 Hz), 2.43 m (1H, CH), 2.63 m (1H, CH), 3.80–4.10 m (8H, CH_2O), 4.61 d (1H, 1-H, $^3J_{1,11}$ = 4.5 Hz), 5.00 s (2H, 9-H), 5.52 m (1H, 5-H, *J* = 10.0, 6.8, 3.1 Hz), 5.67 m (1H, 4-H). ^{13}C NMR spectrum, δ_C, ppm: 19.47, 20.43, 27.85, 33.48, 35.15, 41.62, 60.16, 65.76, 66.15, 67.38, 73.82, 100.36, 108.65, 126.01, 132.02, 170.56.

(1′*S*,2′*S*,3′*S*,6′*R*,7′*S*,9′*R*)-{3′-Methyl-10′,12′-dioxaspiro[1,3-dioxolane-2,8′-tricyclo[7.2.1.0^{2,7}]dodec-4′-en]-6′-yl}methyl acetate (VIII). ^1H NMR spectrum, δ, ppm: 1.08 d (3H, CH_3, *J* = 6.9 Hz), 1.62–1.78 m (2H, CH), 2.02 s (3H, Ac), 2.42 m (1H, CH), 2.66 m (1H, CH), 3.59 d (1H, 11-H, *J* = 7.0 Hz), 3.69 m (1H, 11-H), 3.80–4.10 m (6H, CH_2O), 4.60 d (1H, 1-H, *J* = 4.6 Hz), 5.04 s (1H, 9-H), 5.52 m (1H, 5-H, *J* = 9.8, 1.2 Hz), 5.77 d.d.d (1H, 4-H, *J* = 9.8, 5.5, 2.3 Hz). ^{13}C NMR spectrum, δ_C, ppm: 20.85, 21.08, 30.27, 33.03, 36.23, 41.16, 64.68, 65.76, 65.90, 71.04, 73.47, 101.93, 108.49, 127.80, 132.81, 170.69.

(1′*S*,2′*S*,3′*S*,6′*R*,7′*S*,9′*R*)-{6′-Methyl-10′,12′-dioxaspiro[1,3-dioxolane-2,8′-tricyclo[7.2.1.0^{2,7}]dodec-4′-en]-3′-yl}methyl acetate (IX). ^1H NMR spectrum, δ, ppm: 1.02 d (3H, CH_3, *J* = 7.0 Hz), 1.65 d.d.d (1H, 2-H, *J* = 12.5, 4.9, 2.1 Hz), 1.73 d.d (1H, 7-H, *J* = 12.5, 10.0 Hz), 2.08 s (3H, Ac), 2.28 m (1H, CH), 2.52 m (1H, CH), 3.62 d (1H, 11-H, *J* = 7.0 Hz), 3.70 m (1H, 11-H), 3.81–3.95 m (2H, CH_2), 3.96–4.12 m (4H, CH_2, 13-H), 4.35 d.d (1H, 1-H, *J* = 4.5, 2.1 Hz), 5.04 s (1H, 9-H), 5.53 m (1H, 5-H, *J* = 9.8,

1.2 Hz), 5.61 d.d.d (1H, 4-H, J = 9.8, 5.3, 2.2 Hz). ^{13}C NMR spectrum, δ_C, ppm: 21.08, 22.72, 31.50, 37.19, 38.35, 41.11, 62.61, 65.90, 66.36, 71.19, 72.65, 102.35, 108.75, 124.92, 136.64, 170.43, 170.73.

Hydrolysis of acetates VII–IX. Acetate mixture **VII–IX**, 0.267 g (0.861 mmol), was dissolved in 10 mL of ethanol, 4 mL of a solution prepared from 4.0 g of potassium hydroxide, 20 mL of water, and 40 mL of ethanol was added dropwise, and the mixture was stirred for 1 h and neutralized with 3% aqueous HCl to pH 7. The aqueous phase was extracted with ethyl acetate (3×20 mL), the extracts were combined, washed with brine, and dried over $MgSO_4$, the solvent was distilled off on a rotary evaporator, and the residue was subjected to chromatography on silica gel to isolate 0.074 g (32%) of alcohol mixture **X/XI** and 0.146 g (63%) of alcohol **XII**.

(1′*S*,2′*S*,3′*S*,6′*S*,7′*R*,9′*R*)- and (1′*S*,2′*S*,3′*S*,6′*R*,-7′*S*,9′*R*)-{3′-Methyl-10′,12′-dioxaspiro[1,3-dioxolane-2,8′-tricyclo[7.2.1.0^{2,7}]dodec-4′-en]-6′-yl}-methanol (X/XI). Stereoisomer ratio 3:1 (according to the ^{1}H NMR data). Crystalline material, mp 100–103°C, R_f 0.4 (petroleum ether–ethyl acetate, 1:1), $[\alpha]_D^{20}$ = +0.3° (c = 1.0, $CHCl_3$). IR spectrum, ν, cm^{-1}: 2930, 1458, 1391, 1197, 1096, 1026, 932, 737.

Isomer **X**. ^{1}H NMR spectrum, δ, ppm: 1.03 d (3H, CH_3, $^3J_{Me,6}$ = 7.2 Hz), 1.93 m (1H, 2-H), 2.21 d (1H, 7-H, $^3J_{7,2}$ = 6.0 Hz), 2.43 m (2H, 3-H), 2.74 m (2H, 6-H), 3.54 d.d (1H, 13-H$_B$, ^2J = 11.3, $^3J_{13B,6}$ = 3.5 Hz), 3.68 m (1H, 13-H$_A$), 3.83–4.15 m (6H, 11-H, CH_2), 4.68 d (1H, 1-H, $^3J_{1,11\text{-}endo}$ = 5.1 Hz), 4.98 s (1H, 9-H), 5.54 m (1H, 5-H), 5.80 d.d.d (1H, 4-H, $^3J_{4,5}$ = 9.9, $^3J_{4,3}$ = 5.2, $^4J_{4,6}$ = 2.1 Hz). ^{13}C NMR spectrum, δ_C, ppm: 21.27 (CH_3), 31.65 (C^3), 34.40 (C^6), 37.37 (C^7), 38.29 (C^2), 63.19 (C^{13}), 64.57 (C$^{4'}$), 64.74 (C$^{5'}$), 71.35 (C^1), 74.25 (C^{11}), 100.38 (C^9), 106.98 (C^8), 126.45 (C^4), 133.29 (C^5). Mass spectrum: m/z 268.13 $[M]^+$. $C_{14}H_{20}O_5$. Calculated: M 268.1310.

Isomer **XI**. ^{1}H NMR spectrum, δ, ppm: 1.02 d (3H, CH_3, $^3J_{Me,6}$ = 7.0 Hz), 1.72 d.d.d (1H, 2-H, $^3J_{2,7}$ = 12.3, $^3J_{2,3}$ = 4.7, $^3J_{2,1}$ = 1.2 Hz), 1.81 d.d (1H, 7-H, $^3J_{7,2}$ = 12.3, $^3J_{7,6}$ = 9.6 Hz), 2.42 m (2H, 3-H, 6-H), 3.57 d (1H, 11-*exo*-H, ^2J = 6.8 Hz), 3.71 d.d (1H, 11-*endo*-H, ^2J = 6.8, $^3J_{11\text{-}endo,1}$ = 4.6 Hz), 3.75 m (1H, 13-H$_A$), 3.90 d.d (1H, 13-H$_B$, ^2J = 11.0, $^3J_{13B,3}$ = 6.4 Hz), 3.91–4.13 m (4H, 4′-H, 5′-H), 4.78 d.d (1H, 1-H, $^3J_{1,11\text{-}endo}$ = 4.6, $^3J_{1,2}$ = 1.2 Hz), 5.06 s (1H, 9-H), 5.53 d.d (1H, 5-H, $^3J_{5,4}$ = 9.9, $^3J_{5,6}$ = 1.2 Hz), 5.80 d.d.d (1H, 4-H, $^3J_{4,5}$ = 9.9, $^3J_{4,3}$ = 5.2, $^4J_{4,6}$ = 2.1 Hz). ^{13}C NMR spectrum, δ_C, ppm: 21.06 (CH_3), 31.42 (C^3), 37.17 (C^6), 40.95 (C^7), 41.10 (C^2), 62.45 (C$^{4'}$), 62.94 (C$^{5'}$), 65.78 (C^{13}), 71.14 (C^1), 72.61 (C^{11}), 102.01 (C^9), 108.56 (C^8), 125.53 (C^4), 136.16 (C^5). Mass spectrum: m/z 268.13 $[M]^+$. $C_{14}H_{20}O_5$. Calculated: M 268.1310.

(1′*S*,2′*S*,3′*S*,6′*R*,7′*S*,9′*R*)-{6′-Methyl-10′,12′-dioxaspiro[1,3-dioxolane-2,8′-tricyclo[7.2.1.0^{2,7}]dodec-4′-en]-3′-yl}methanol (XII). Crystalline substance, mp 122–124°C, R_f 0.5 (petroleum ether–ethyl acetate, 1:1), $[\alpha]_D^{20}$ = +8.3° (c = 1.0, $CHCl_3$). IR spectrum, ν, cm^{-1}: 2952, 1464, 1377, 1209, 1093, 1042, 911, 761. ^{1}H NMR spectrum, δ, ppm: 1.10 d (3H, CH_3, $^3J_{Me,3}$ = 7.0 Hz), 1.72 d.d.d (1H, 2-H, $^3J_{2,7}$ = 12.2, $^3J_{2,3}$ = 4.9, $^3J_{2,1}$ = 1.5 Hz), 2.12 d.d (1H, 7-H, $^3J_{7,2}$ = 12.2, $^3J_{7,6}$ = 10.1 Hz), 2.29 m (1H, 3-H), 2.52 m (1H, 6-H), 3.65 d (1H, 11-*exo*-H, ^2J = 6.5 Hz), 3.72 d.d (1H, 11-*endo*-H, ^2J = 6.5, $^3J_{11\text{-}endo,1}$ = 4.4 Hz), 3.73 m (1H, 13-H$_A$), 3.83–4.15 m (5H, 13-H$_B$, 4′-H, 5′-H), 4.35 d.d (1H, 1-H, $^3J_{1,11\text{-}endo}$ = 4.4, $^3J_{1,2}$ = 1.5 Hz), 5.09 s (1H, 9-H), 5.52 d.d (1H, 5-H, $^3J_{5,4}$ = 9.9, $^3J_{5,6}$ = 2.0 Hz), 5.82 d.d.d (1H, 4-H, $^3J_{4,5}$ = 9.9, $^3J_{4,3}$ = 5.5, $^4J_{4,6}$ = 2.4 Hz). ^{13}C NMR spectrum, δ_C, ppm: 26.67 (CH_3), 30.30 (C^3), 33.27 (C^6), 39.53 (C^2), 41.35 (C^7), 62.65 (C^{13}), 65.40 (C$^{4'}$), 65.66 (C$^{5'}$), 71.35 (C^{11}), 73.62 (C^1), 101.72 (C^9), 108.78 (C^8), 128.91 (C^4), 133.49 (C^5). Mass spectrum: m/z 268.13 $[M]^+$. $C_{14}H_{20}O_5$. Calculated: M 268.1310.

Methyl (1′*S*,2′*R*,3′*S*,6′*R*,7′*S*,9′*R*)-6′-methyl-10′,12′-dioxaspiro[1,3-dioxolane-2,8′-tricyclo-[7.2.1.0^{2,7}]dodec-4′-ene]-3′-carboxylate (XIII). A solution of 0.200 g (0.746 mmol) of alcohol **XII** in 10 mL of acetone was cooled to 0°C, 1.4 mL of Jones' reagent (a solution of 26.72 g of CrO_3 in 23 mL of concentrated sulfuric acid was diluted with water to a volume of 100 mL) was added dropwise under stirring, and the mixture was stirred until the initial compound disappeared (TLC). The mixture was then treated with 6 mL of isopropyl alcohol and filtered, and the filtrate was neutralized with a saturated solution of sodium hydrogen carbonate. The aqueous phase was extracted with ethyl acetate (3×30 mL), the combined extracts were dried over $MgSO_4$ and evaporated, the residue was dissolved in 10 mL of acetone, 0.206 g (1.492 mmol) of calcined potassium carbonate and 0.23 mL (3.73 mmol) of methyl iodide were added, and the mixture was stirred at room temperature. When the reaction was complete, the mixture was filtered, and the precipitate was washed with diethyl ether. The filtrate was combined with the washings and evaporated on a rotary evaporator, and the residue was purified by chromatography on silica gel. Yield 0.188 g (85%), crystalline substance, mp 85–87°C, R_f 0.7 (petroleum

ether–ethyl acetate, 1:1). $[\alpha]_D^{20}$ = +51.5° (*c* = 1.0, $CHCl_3$). IR spectrum, ν, cm^{-1}: 2955, 1735, 1194, 1097, 967, 946. ^1H NMR spectrum, δ, ppm: 1.08 d (3H, CH_3, $^3J_{Me,6}$ = 7.0 Hz), 1.68 d.d.d (1H, 2-H, $^3J_{2,7}$ = 12.4, $^3J_{2,3}$ = 5.5, $^3J_{2,1}$ = 2.4 Hz), 2.20 d.d (1H, 7-H, $^3J_{7,2}$ = 12.4, $^3J_{7,6}$ = 9.8 Hz), 2.45 m (1H, 6-H), 3.20 d.d.d (1H, 3-H, $^3J_{3,2}$ = 5.5, $^3J_{3,4}$ = 5.0, $^4J_{3,5}$ = 1.7 Hz), 3.60 d (1H, 11-*exo*-H, ^2J = 6.9 Hz), 3.65 d.d (1H, 11-*endo*-H, ^2J = 6.9, $^3J_{11\text{-}endo,1}$ = 3.6 Hz), 3.73 s (3H, OMe), 3.89–4.11 m (4H, 4′-H, 5′-H), 4.47 d.d (1H, 1-H, $^3J_{1,11\text{-}endo}$ = 3.6, $^3J_{1,2}$ = 2.4 Hz), 5.04 s (1H, 9-H), 5.58 d.d.d (1H, 4-H, $^3J_{4,5}$ = 9.8, $^3J_{4,3}$ = 5.0, $^4J_{4,6}$ = 2.1 Hz), 5.65 d.d (1H, 5-H, $^3J_{5,4}$ = 9.8, $^4J_{5,3}$ = 1.7 Hz). ^{13}C NMR spectrum, δ_C, ppm: 20.65 (CH_3), 30.78 (C^6), 36.95 (C^3), 39.85 (C^2), 44.81 (C^7), 51.83 (OMe), 62.56 ($C^{4'}$), 65.78 ($C^{5'}$), 70.92 (C^1), 73.22 (C^{11}), 101.86 (C^9), 108.53 (C^8), 120.82 (C^4), 137.83 (C^5), 170.05 (C=O). Mass spectrum: *m*/*z* 296.2 $[M]^+$. $C_{15}H_{20}O_6$. Calculated: *M* 296.1259.

2-{(1′*S*,2′*S*,3′*S*,6′*R*,7′*S*,9′*R*)-6′-Methyl-10′,12′-dioxaspiro[1,3-dioxolane-2,8′-tricyclo[7.2.1.0^{2,7}]dodec-4′-en]-3′-yl}propan-2-ol (XIV). A solution of 0.153 g (0.517 mmol) of ester **XIII** in 10 mL of THF was cooled to 0°C, 1.91 mL of a 2.7 M solution of methylmagnesium iodide in diethyl ether was added dropwise under stirring in an argon atmosphere, and the mixture was allowed to warm up to room temperature and stirred until the initial compound disappeared (TLC). The mixture was treated with 3% aqueous HCl to dissolve gel and extracted with ethyl acetate (3×40 mL), the combined extracts were washed with brine and dried over $MgSO_4$, the solvent was distilled off, and the residue was purified by chromatography on silica gel. Yield 0.110 g (72%), crystalline substance, mp 126–130°C, $[\alpha]_D^{20}$ = +0.4° (*c* = 1.0, $CHCl_3$), R_f 0.15 ($CHCl_3$–EtOAc, 10:1). IR spectrum, ν, cm^{-1}: 2985, 2360, 1457, 1169, 943, 796. ^1H NMR spectrum, δ, ppm: 1.05 d (3H, CH_3, $^3J_{Me,6}$ = 7.0 Hz), 1.36 s (3H, CH_3), 1.38 s (3H, CH_3), 1.63 br.s (1H, OH), 1.75 d.d.d (1H, 2-H, $^3J_{2,7}$ = 12.9, $^3J_{2,3}$ = 5.2, $^3J_{2,1}$ = 2.2 Hz), 2.20 d.d (1H, 7-H, $^3J_{7,2}$ = 12.9, $^3J_{7,6}$ = 9.5 Hz), 2.41 m (1H, 3-H), 2.45 m (1H, 6-H), 3.63 d (1H, 11-*exo*-H, ^2J = 6.8 Hz), 3.69 d.d (1H, 11-*endo*-H, ^2J = 6.8, $^3J_{11\text{-}endo,1}$ = 4.7 Hz), 3.89–4.13 m (4H, 4′-H, 5′-H), 5.05 s (1H, 9-H), 5.43 d.d (1H, 1-H, $^3J_{1,11\text{-}endo}$ = 4.7, $^3J_{1,2}$ = 2.2 Hz), 5.60 d.d (1H, 5-H, $^3J_{5,4}$ = 10.1, $^4J_{5,3}$ = 1.7 Hz), 5.67 d.d.d (1H, 4-H, $^3J_{4,5}$ = 10.1, $^3J_{4,3}$ = 5.4, $^4J_{4,6}$ = 2.1 Hz). ^{13}C NMR spectrum, δ_C, ppm: 21.04 (CH_3), 28.29 (CH_3), 31.01 (C^6), 31.76 (CH_3), 37.45 (C^3), 42.57 (C^2), 47.28 (C^7), 62.47 ($C^{4'}$), 65.78 ($C^{5'}$), 71.67 (C^{13}), 72.43 (C^{11}), 74.33 (C^1), 101.83 (C^9), 108.81 (C^8), 125.53 (C^4), 136.49 (C^5). Mass spectrum: *m*/*z* 296.16 $[M]^+$. $C_{16}H_{24}O_5$. Calculated: *M* 296.1623.

Methyl (1′*S*,2′*S*,3′*S*,6′*R*,7′*R*,9′*R*)- and (1′*S*,2′*S*,3′*S*,6′*S*,7′*S*,9′*R*)-3′-methyl-10′,12′-dioxaspiro[1,3-dioxolane-2,8′-tricyclo[7.2.1.0^{2,7}]dodec-4′-ene]-6′-carboxylates XV and XVI were synthesized as described above for compound **XIII** from 0.324 g (1.21 mmol) of alcohol mixture **X/XI**. Yield 0.190 g (53%) (**XV**) and 0.072 g (20%) (**XVI**).

Compound **XV**. Colorless crystals, mp 105–107°C, $[\alpha]_D^{20}$ = –93.1° (*c* = 1.0, $CHCl_3$), R_f 0.3 (petroleum ether–ethyl acetate, 2:1). IR spectrum, ν, cm^{-1}: 2961, 1735, 1245, 1086, 1014, 918. ^1H NMR spectrum, δ, ppm: 1.16 d (3H, CH_3, $^3J_{Me,3}$ = 7.1 Hz), 1.62 d.d.d (1H, 2-H, $^3J_{2,7}$ = 12.6, $^3J_{2,3}$ = 5.0, $^3J_{2,1}$ = 1.6 Hz), 2.34 m (1H, 3-H), 2.54 d.d (1H, 7-H, $^3J_{7,2}$ = 12.6, $^3J_{7,6}$ = 10.5 Hz), 3.28 d.d (1H, 6-H, $^3J_{6,7}$ = 10.5, $^4J_{6,4}$ = 2.5 Hz), 3.62 d (1H, 11-*exo*-H, ^2J = 6.8 Hz), 3.64 s (3H, OMe), 3.73 d.d (1H, 11-*endo*-H, ^2J = 6.8, $^3J_{11\text{-}endo,1}$ = 5.0 Hz), 3.80–3.89 m (2H, 4′-H), 4.02 d.d (2H, 5′-H, $^3J_{5',4'}$ = 5.7, 7.1 Hz), 4.36 d.d (1H, 1-H, $^3J_{1,11\text{-}endo}$ = 5.0, $^3J_{1,2}$ = 1.6 Hz), 5.03 s (1H, 9-H), 5.44 d.d (1H, 5-H, $^3J_{5,4}$ = 9.8, $^4J_{5,3}$ = 1.3 Hz), 5.83 d.d.d (1H, 4-H, $^3J_{4,5}$ = 9.8, $^3J_{4,3}$ = 5.6, $^4J_{4,6}$ = 2.5 Hz). ^{13}C NMR spectrum, δ_C, ppm: 14.65 (CH_3), 32.68 (C^7), 32.78 (C^3), 40.25 (C^2), 43.12 (C^6), 51.99 (OMe), 63.73 ($C^{4'}$), 66.06 ($C^{5'}$), 70.97 (C^{11}), 73.16 (C^1), 102.71 (C^9), 108.17 (C^8), 123.30 (C^5), 134.02 (C^4), 174.86 (C=O). Mass spectrum: *m*/*z* 296.2 $[M + H]^+$. $C_{15}H_{20}O_6$. Calculated: *M* 296.1259.

Compound **XVI**. Colorless crystals, mp 133–135°C, $[\alpha]_D^{20}$ = –73.2° (*c* = 1.0, $CHCl_3$), R_f 0.55 (petroleum ether–ethyl acetate, 2:1). IR spectrum, ν, cm^{-1}: 2981, 1731, 1322, 1176, 1110, 1012, 930. ^1H NMR spectrum (C_6D_6), δ, ppm: 0.95 d (3H, CH_3, $^3J_{Me,3}$ = 7.3 Hz), 2.25 m (1H, 6-H), 2.30 m (1H, 7-H), 2.32 m (1H, 2-H), 3.35 s (3H, OMe), 3.28–3.40 m (4H, 4′-H, 5′-H), 3.55 m (2H, 11-H), 4.09 m (1H, 3-H), 4.54 s (1H, 1-H), 5.05 s (1H, 9-H), 5.60 d.d.d (1H, 5-H, $^3J_{5,4}$ = 9.9, $^3J_{5,6}$ = 3.6, $^4J_{5,3}$ = 3.6 Hz), 5.83 d.d.d (1H, 4-H, $^3J_{4,5}$ = 9.9, $^3J_{4,3}$ = 5.6, $^4J_{4,6}$ = 2.3 Hz). ^{13}C NMR spectrum, δ_C, ppm: 22.68 (CH_3), 27.05 (C^6), 35.13 (C^2), 38.38 (C^7), 41.52 (C^3), 51.54 (OMe), 64.61 ($C^{4'}$), 66.19 ($C^{5'}$), 67.25 (C^{11}), 75.24 (C^1), 100.76 (C^9), 107.38 (C^8), 123.62 (C^4), 132.62 (C^5), 174.50 (C=O). Mass spectrum: *m*/*z* 296.2 $[M + H]^+$. $C_{15}H_{20}O_6$. Calculated: *M* 296.1259.

2-{(1′*S*,2′*S*,3′*S*,6′*R*,7′*R*,9′*R*)-3′-Methyl-10′,12′-dioxaspiro[1,3-dioxolane-2,8′-tricyclo[7.2.1.0^{2,7}]dodec-4′-en]-6′-yl}propan-2-ol (XVII) was synthesized from

ester **XV** as described above for compound **XIV**. Yield 69%, crystalline substance, mp 113–115°C, R_f 0.27 ($CHCl_3$–EtOAc, 10:1), $[\alpha]_D^{20}$ = +5.5° (*c* = 1.0, $CHCl_3$). IR spectrum, ν, cm^{-1}: 2966, 1467, 1373, 1114, 1061, 943, 752. ^1H NMR spectrum, δ, ppm: 1.06 d (3H, CH_3, $^3J_{Me,3}$ = 6.9 Hz), 1.06 s (3H, CH_3), 1.27 s (3H, CH_3), 1.67 d.d.d (1H, 2-H, $^3J_{2,7}$ = 12.8, $^3J_{2,3}$ = 4.5, $^3J_{2,1}$ = 3.0 Hz), 2.20 m (1H, 3-H), 2.27 d.d (1H, 7-H, $^3J_{7,2}$ = 12.8, $^3J_{7,6}$ = 8.5 Hz), 2.58 d.d.d (1H, 6-H, $^3J_{6,7}$ = 8.5, $^3J_{6,5}$ = 3.3, $^4J_{6,4}$ = 1.9 Hz), 3.60 d (1H, 11-*exo*-H, ^2J = 6.5 Hz), 3.70 d.d (1H, 11-*endo*-H, ^2J = 6.5, $^3J_{11\text{-}endo,1}$ = 4.1 Hz), 3.90–4.14 m (4H, 4′-H, 5′-H), 4.29 d.d (1H, 1-H, $^3J_{1,11\text{-}endo}$ = 4.1, $^3J_{1,2}$ = 3.0 Hz), 5.07 s (1H, 9-H), 5.53 d.d (1H, 5-H, $^3J_{5,4}$ = 9.9, $^3J_{5,6}$ = 3.3 Hz), 5.87 d.d.d (1H, 4-H, $^3J_{4,5}$ = 9.9, $^3J_{4,3}$ = 6.4, $^4J_{4,6}$ = 1.9 Hz). ^{13}C NMR spectrum, δ_C, ppm: 13.91 (CH_3), 25.16 (C^6), 30.28 (CH_3), 30.28 (CH_3), 32.22 (C^3), 41.75 (C^2), 46.81 (C^7), 63.10 ($C^{4'}$), 65.32 ($C^{5'}$), 71.16 (C^{13}), 71.94 (C^{11}), 74.26 (C^1), 101.88 (C^9), 109.23 (C^8), 128.67 (C^4), 132.84 (C^5). Mass spectrum: *m*/*z* 281.13 $[M - CH_3]^+$. $C_{16}H_{24}O_5$. Calculated: *M* 296.1623.

2-{(1′*S*,2′*S*,3′*S*,6′*S*,7′*S*,9′*R*)-3′-Methyl-10′,12′-dioxaspiro[1,3-dioxolane-2,8′-tricyclo[7.2.1.0^{2,7}]dodec-4′-en]-6′-yl}propan-2-ol (XVIII) was synthesized from ester **XVI** as described above for compound **XIV**. Yield 67%, crystalline substance, mp 210–213°C, R_f 0.4 ($CHCl_3$–EtOAc, 10:1), $[\alpha]_D^{20}$ = –24.6° (*c* = 1.0, $CHCl_3$). IR spectrum, ν, cm^{-1}: 2969, 1249, 1116, 1043, 910, 756. ^1H NMR spectrum, δ, ppm: 1.00 d (3H, CH_3, $^3J_{Me,3}$ = 7.2 Hz), 1.13 s (3H, CH_3), 1.38 s (3H, CH_3), 2.09 m (1H, 2-H), 2.20 d (1H, 7-H, $^3J_{7,2}$ = 6.5 Hz), 2.26 m (1H, 3-H), 2.67 m (1H, 6-H), 3.78–4.07 m (6H, 11-H, 4′-H, 5′-H), 4.95 s (1H, 9-H), 5.20 d (1H, 1-H, $^3J_{1,11}$ = 5.4), 5.54 d.d.d (1H, 5-H, $^3J_{5,4}$ = 10.4, $^3J_{5,6}$ = 2.9, $^4J_{5,3}$ = 1.0 Hz), 5.78 d.d.d (1H, 4-H, $^3J_{4,5}$ = 10.4, $^3J_{4,3}$ = 5.5, $^4J_{4,6}$ = 1.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 21.47 (CH_3), 24.80 (CH_3), 25.91 (C^6), 30.35 (CH_3), 34.28 (C^3), 38.26 (C^2), 44.20 (C^7), 64.48 ($C^{4'}$), 65.92 ($C^{5'}$), 67.48 (C^{13}), 74.04 (C^{11}), 76.91 (C^1), 100.08 (C^9), 106.57 (C^8), 126.13 (C^4), 131.71 (C^5). Mass spectrum: *m*/*z* 281.13 $[M - CH_3]^+$. $C_{16}H_{24}O_5$. Calculated: *M* 296.1623.

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