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Eleuthesides and Their Analogs: VIII.* Preparation of Menthane Derivatives from Levoglucosenone and (2*E*,4*E*)-6-Methylhepta-2,4-dienyl Acetate by Diels—Alder Reaction

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Abstract—Synthesis of chiral functionalized menthane derivatives was carried out by Diels–Alder reaction from levoglucosenone and (2*E*,4*E*)-6-methylhepta-2,4-dienyl acetate.In extension of research [1] on development of preparation methods for polyfunctional menthane derivatives we explored the possibility of an isopropyl group direct introduction in the course of Diels–Alder reaction.

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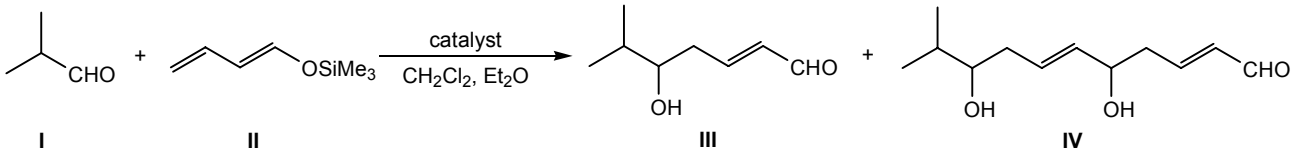
For the preparation of the corresponding diene we studied the condensation conditions of isobutyric aldehyde (**I**) and siloxybutadiene (**II**) [2] leading to the formation of 5-hydroxy-6-methylhept-2-enal (**III**). The use of $TiCl_4$ as catalyst resulted in the formation of trace amounts of aldehyde **III**, but its yields were increased at the addition of Et_3N [3]. More appropriate catalyst for siloxybutadiene (**II**) condensation proved to be $BF_3 \cdot Et_2O$ [4]. However in the reaction of equimolar quantities of reagents compound **IV** formed in 30% yield, a product of repeated addition of siloxybutadiene to adduct **III**. Utilization of the triple excess of isobutyric aldehyde allowed increasing the yield of aldehyde **III** up to 67% and reducing the yield of compound **IV** to 7% (Table 1, Scheme 1).

The dehydration of alcohol **III** to obtain dienal **V** was carried out in the systems 10% solution of HCl–dichloroethane [5], TsOH–CH_2Cl_2, Py·HCl–toluene–DMF [6]. The most efficient procedure resulting in the predominant formation of *trans, trans*-diene **V** (4*E*/4*Z* 94 : 6) was boiling of alcohol **III** in the system Py·HCl–toluene–DMF. The reduction of the carbonyl group in aldehyde **V** was performed by treating with $(i\text{-Bu})_2AlH$, and the subsequent acetylation of the hydroxy group to obtain acetate **VI** was carried out with a mixture Ac_2O–Py (Scheme 2).

Diene **VI** whose reactivity was tested in the reaction with maleic anhydride turned out to be sufficiently active. At boiling in toluene for 4 h the cycloaddition proceeded stereospecifically affording the only product **VII** (Scheme 3) in 74% yield; the relative configuration of compound **VII** was established from ^1H and ^{13}C NMR spectra.

Adduct **VII** possesses a *cis*-junction of the rings. The vicinal constants $^3J_{3a,4}$ 6.4, $^3J_{3a,7a}$ 9.5, and $^3J_{7a,7}$ 5.9 Hz

Scheme 1.



I **II** **III** **IV**

* For communication VII, see [1].

Table 1. Yields of condensation products of isobutyric aldehyde (**I**) and siloxybutadiene (**II**) depending on reaction conditions

Run no.	Catalyst (equiv.)	Ratio **I**/**II** (equiv.)	*T*, °C	Time, h	Yield, %	
					III	**IV**
1	$TiCl_4$, Et_3N (1.1)	1.5	–40	5	32	–
2	$BF_3 \cdot Et_2O$ (1)	1.1	–78	2	44	30
3	$BF_3 \cdot Et_2O$ (1.5)	2	–78	1	56	11
4	$BF_3 \cdot Et_2O$ (1.5)	3	–78	1	67	7

show the *syn*-position of protons H^4, H^{3a}, H^7, and H^{7a}. Correlation peaks H^4/H^7, H^4/H^{7a}, and H^7/H^{3a} in the NOESY spectrum indicate the 3a*S*,4*S*,7*R*,7a*R*-coordination of the centers.

6-Methylhepta-2,4-dienyl acetate (**VI**) unlike hexa-2,4-dienyl acetate [1] was as expected less reactive in the cycloaddition with levoglucosenone (**VIII**). This process was carried out at heating either in toluene or without solvent. The reaction proceeded regiospecifically and stereoselectively affording two diastereomeric acetates. To isolate from the mixture the diastereomeric acetates possessing chromatographic mobility close to that of levoglucosenone we subjected them to hydrolysis into alcohols **IX** and **X** (Scheme 4), whose ratio measured by ^1H NMR spectra varied in the range 1 : 4–1 : 5 (Table 2).

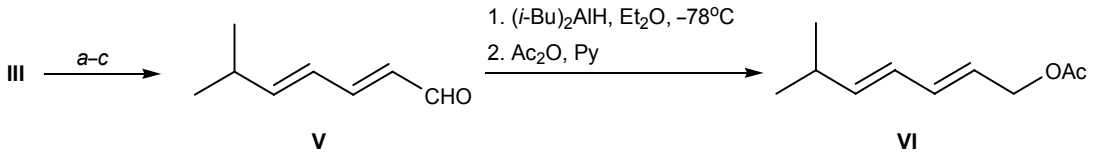
The increased reaction time led to levoglucosenone consumption, but did not affect the ratio of adducts **IX** and **X** (Table 2, runs nos. *1*, *2*, *7*, *8*). Increased diene quantity resulted in growing conversion and yield of the adducts. At the temperature increase to 200°C the yield decreased. In the absence of solvents the same trend was observed, but the reaction time was shorter. The best results were obtained at the use in the Diels–Alder reaction of the five-fold excess of acetoxydiene **VI** with respect to levoglucosenone (**VIII**).

The structure of adducts was established from ^1H and ^{13}C NMR spectra. The signal positions of the protonated carbon atoms in compound **IX** were established from the analysis of spectra COSY and HSQC. The 2*S*- and 7*R*-configurations are demonstrated by the correlation peaks H^{11endo}/H^2 and H^{11endo}/H^7 in the NOESY spectra. The vicinal constants $^3J_{2,3}$ 8.0 and $^3J_{2,7}$ 7.0 Hz indicate the *syn*-location of protons H^3 and H^7 with respect to H^2. The absence of a constant $^3J_{7,6}$ permits a conclusion that the torsion angle $H^7C^7C^6H^6$ is close to 90° which is possible at the *S*-configuration of the center C^6. Besides in the NOESY spectrum the correlation peaks appear between H^{14}/H^7, H^{14}/H^2, and H^{13}/H^1 proving the 2*S*,3*S*,6*S*,7*R*-configuration of these centers.

In compounds **X** the *S*-configuration of C^2 center is confirmed by the correlation peak H^{11endo}/H^2 in the NOESY spectra. The vicinal constants $^3J_{7,2}$ 11.7 and $^3J_{7,6}$ 10.2 Hz show the *anti*-location of protons H^2 and H^6 with respect to H^7, and the constant $^3J_{2,3}$ 4.6 Hz indicates the *syn*-location of atoms H^2 and H^3. The NOESY spectrum contains the correlation peaks H^2/H^6, H^7/H^1, H^7/H^{13}, and H^7/H^{14}, proving the 2*S*,3*S*,6*R*,7*S*-configuration of these centers.

In order to optimize the conditions of the Diels–Alder reaction between levoglucosenone (**VIII**) and diene **VI** we studied this process at superhigh pressure. The cycloaddition at 10000 at and 100°C in toluene (Scheme 5) resulted in total consumption of levoglucosenone within 6 h, but the selectivity of the cycloaddition reduced: we isolated from the reaction mixture five adducts **XI**–**XV**. At the pressure decreased to 6000 at the yields of adducts **XI**–**XV** grew, and the side product, dimer **XVI**, was detected in trace quantity. The reaction performed without solvent unexpectedly gave two adducts **XI** and **XV** having a *trans*-junction of the six-membered rings; levoglucosenone dimer (**XVI**) proved to be the main product [7] (Table 3).

Scheme 2.



V **VI**

a. 10% HCl, $C_2H_4Cl_2$, 55°C; *b*. TsOH, CH_2Cl_2, boiling; *c*. Py·HCl, toluene, DMF, boiling.

Table 2. Yield and the ratio of adducts **IX** and **X** depending on reaction conditions

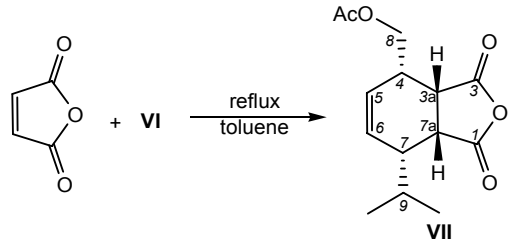
Run no.	Ratio **VI**/**VIII** (equiv.)	Conditions	Conversion, %	Overall yield, % (ratio **IX**–**X**)
1	1.3	160°C, toluene, 100 h	72	24 (1 : 4)
2	1.3	160°C, toluene, 150 h	86	23 (1 : 4)
3	2	160°C, toluene, 50 h	49	29 (1 : 4)
4	5	160°C, toluene, 75 h	73	47 (1 : 4)
5	5	200°C, toluene, 15 h	100	18
6	1.3	160°C, 75 h	91	27 (1 : 5)
7	2	160°C, 24 h	63	33 (1 : 5)
8	2	160°C, 36 h	82	20 (1 : 5)
9	5	160°C, 24 h	90	54 (1 : 5)

The structure of adducts was established from the ^{1}H and ^{13}C NMR spectra, the structure of compounds **XIV** and **XV** was additionally confirmed by hydrolysis into alcohols **IX** and **X**.

The position of isopropyl group at C^3 and acetoxymethyl group at C^6 in compound **XI** is indicated by cross-peaks H^2/C^{14}, H^7/C^{13}, H^{13A}/C^7, and H^{13B}/C^7 in HMBC spectra. The vicinal constants $^3J_{7,2}$ 12.0 and $^3J_{7,6}$ 10.2 Hz show the *anti*-location of protons H^2 and H^6 with respect to H^7. The presence of NOE was informative for confirming the 6*R*-configuration. The signal of H^6 at 2.71 ppm has a NOE with H^2 (1.82 ppm) which in its turn interacts with H^{11endo}. The β-orientation of H^3 proton is indicated by the presence of NOE H^{14}/H^1, and also by the interaction between the protons of the methyl group and H^1, H^7.

The HMBC of compound **XII** contained cross-peaks H^2/C^{14}, H^7/C^{13}, H^{13A}/C^7, and H^{13B}/C^7 analogously to the spectra of compound **XI**. The vicinal constant $^3J_{7,2}$ 6.9 Hz indicates the *syn*-location of atoms H^2 and H^7.

Scheme 3.



The 3*S*-configuration is suggested by the presence of NOE H^{14}/H^1. The presence of NOE H^{11endo}/H^2, H^{11endo}/H^7 and H^7/H^{13} confirms the 6*S*,7*R*-configuration.

HMBC spectra of compound **XIII** contain cross-peaks H^2/C^{13}, H^7/C^{14}, H^{14}/C^7, and H^{13}/C^2. The vicinal constant $^3J_{7,2}$ 7.0 Hz indicates the *syn*-location of atoms H^2 and H^7. The *anti*-position of H^2 and H^3 is confirmed by the constant $^3J_{2,3}$ 9.1 Hz. The presence of NOE H^{13B}/H^7, H^1/H^3, H^2/H^{14}, and H^2 with the protons of the methyl group proves the 2*S*,3*R*,6*S*,7*R*-configuration.

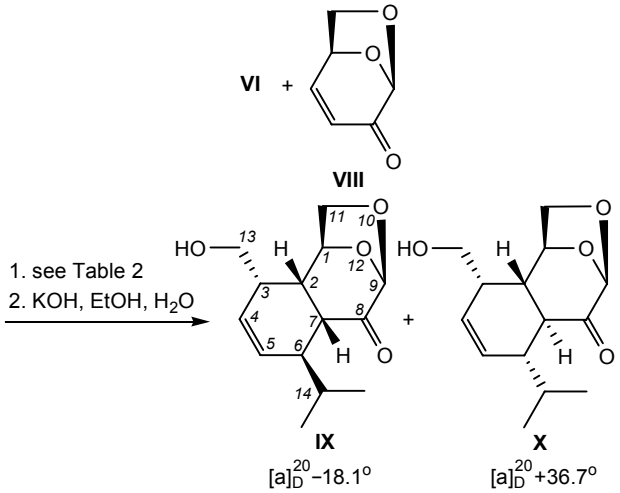
Hence a method was developed for the preparation of menthane derivatives fused with carbohydrate fragment based on Diels–Alder reaction between levoglucosenone and (2*E*,4*E*)-6-methylhepta-2,4-dienyl acetate.

EXPERIMENTAL

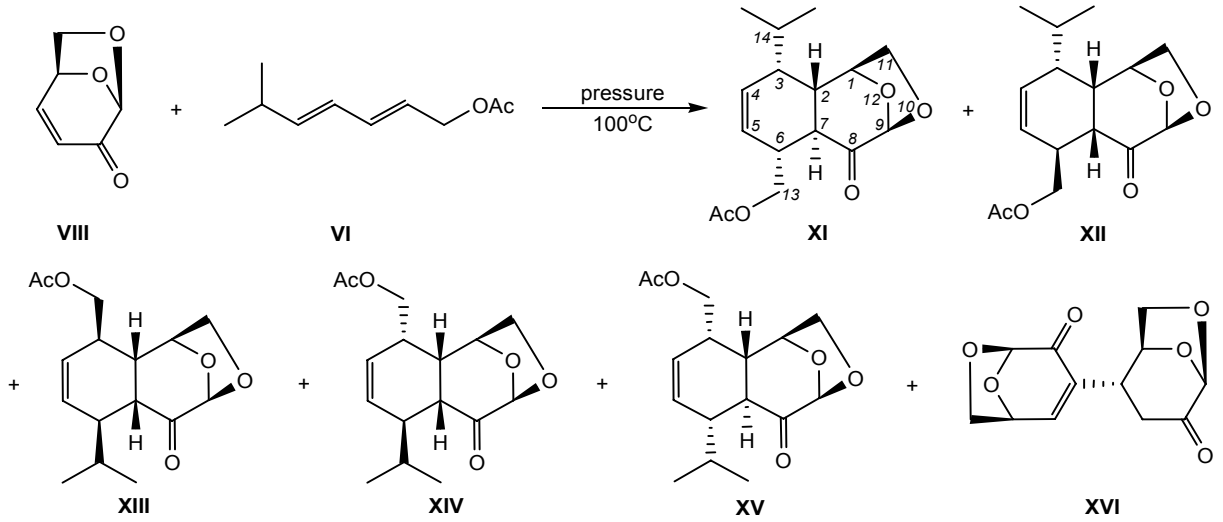
^{1}H and ^{13}C NMR spectra were registered on a spectrometer Bruker AM-300 at operating frequencies 300 (^{1}H) and 75.47 (^{13}C) MHz and on a spectrometer Bruker Avance III, 500 MHz, solvent $CDCl_3$ if not indicated otherwise. IR spectra were recorded on spectrophotometers Shimadzu IRPrestige-21 or Bruker Tensor 27 (from films or mulls in mineral oil). Mass spectra were measured on a GC-MS instrument Hewlett Packard, chromatograph HP 6890 with a mass-selective detector HP 5973. Optical rotation was determined on a polarimeter Perkin Elmer-341. Analytic TLC was carried out on Sorbfil plates of the grade PTSKh-AF-A ("Sorbpolymer" Co., Krasnodar). The melting points were measured on a Boëtius 05 heating block.

(*E*)-5-Hydroxy-6-methylhept-2-enal (III) and **(2*E*,6*E*)-5,9-dihydroxy-10-methylundeca-2,6-di-**

Scheme 4.



Scheme 5.



eneal (IV). *a*. To a solution of 4.25 mL (38.7 mmol) of $TiCl_4$ in 50 mL of CH_2Cl_2 at –78°C was added dropwise 5.44 mL (38.7 mmol) of Et_3N. The mixture was stirred for 5 min, 5.00 g (35.2 mmol) of siloxybutadiene (**II**) was added, and the stirring at –78°C was continued for 30 min 4.78 mL (52.8 mmol) of isobutyric aldehyde (**I**) was added, the reaction mixture was warmed to –40°C, and it was stirred for 5 h. The reaction mixture was diluted with 20 mL of saturated NH_4Cl solution. The reaction products were extracted into dichloromethane (3 × 50 mL), the combined organic solutions were washed with saturated solution of $NaHCO_3$, with water, and dried with $MgSO_4$. The solvent was distilled off, the residue was chromatographed on SiO_2. Yield of compound **III** 1.60 g (32%).

b. To a solution of 3.00 g (21.12 mmol) of siloxybutadiene (**II**) in 50 mL of a mixture CH_2Cl_2–Et_2O, 9 : 1, was added at –78°C 5.6 mL (63.4 mmol) of isobutyric aldehyde (**I**) and 4.0 mL (31.6 mmol) of $BF_3{\cdot}Et_2O$. The mixture was stirred for 1 h at –78°C, then diluted with 10 mL of 1 M HCl solution and was left standing till it warmed to 0°C, then it was treated with saturated $NaHCO_3$ solution and water. The organic layer was separated and washed with water. The product was extracted from the water layer with dichloromethane (3 × 50 mL). The combined organic solutions were dried with $MgSO_4$. The solvent was distilled off, the residue was chromatographed to obtain 2.01 g (67%) of alcohol **III** and 0.157 g (7%) of diol **IV**. The reaction was similarly carried out at the other reagents ratios (Table 1).

Compound III. Oily substance. R_f 0.3 (petroleum ether–EtOAc, 3 : 1). IR spectrum, cm^{-1}: 2962, 1691, 1469, 1386, 1145, 1033, 975. ^1H NMR spectrum, δ, ppm: 0.81 d (3H, CH_3, *J* 6.7 Hz), 0.82 d (3H, CH_3, *J* 6.8 Hz), 1.58 m (1H, H^6), 2.31 d.d.d (1H, H^4, *J* 16.0, 8.9, 7.2 Hz), 2.37 d.d.d (1H, H^4, *J* 16.0, 7.2, 3.7 Hz), 3.57 d.d.d (1H, H^5, *J* 8.9, 5.5, 3.7 Hz), 6.20 d.d (1H, H^2, *J* 15.6, 7.9 Hz), 6.95 t.d (1H, H^3, *J* 15.6, 7.2 Hz), 9.55 d (1H, H^1, *J* 7.9 Hz). ^{13}C NMR spectrum, δ, ppm: 17.32 (CH_3), 18.81 (CH_3), 33.71 (C^6), 37.52 (C^4), 76.79 (C^5), 134.71 (C^2), 155.72 (C^3), 194.06 (C^1). Mass spectrum: *m/z* 143.1 $[M + H]^+$. $C_8H_{14}O_2$. M_{calc} 142.0994.

Compound IV. Oily substance. R_f 0.3 (petroleum ether–EtOAc, 1 : 1). Mixture of diastereomers. IR spectrum, cm^{-1}: 3402, 2956, 1693, 1417, 1139, 1029, 972. ^1H NMR spectrum, δ, ppm: 0.75–0.86 m (6H, CH_3), 0.81 d (3H, CH_3, *J* 6.7 Hz), 1.57 m (1H, H^9), 1.94 m (1H, H^{8A}), 2.15 m (1H, H^{8B}), 2.47 m (2H, C^4H_2), 3.27 m (1H, H^9), 4.70 m (1H, H^5), 5.50 t.d (1H, H^7, *J* 15.4,

Table 3. Yields of adducts **XI–XV** depending on reaction conditions

Run no.	Ratio **VI**/**VIII** (equiv.)	Time, h	Pressure, at	Solvent	Yield, %			
					XI	**XII** + **XIII** (ratio)	**XIV** + **XV** (ratio)	**XVI**
1	2	6	10 000	Toluene	13	5 (2:5)	30 (1:2)	19
2	2	5	10 000	Without solvent	5	–	16 (XV)	37
3	2	9	6 000	Toluene	7	8 (3:8)	47 (1:2)	1

6.7 Hz), 5.61 d.d 1H, $H^{6'}$, *J* 15.4, 7.7 Hz) 5.65 d.d (1H, $H^{6''}$, *J* 15.4, 7.4 Hz), 6.08 d.d (1H, H^2, *J* 15.6, 7.9 Hz), 6.80 t.d (1H, H^3, *J* 15.6, 7.2 Hz), 9.40 d (1H, H^1, *J* 7.9 Hz). ^{13}C NMR spectrum, δ, ppm: 17.65 (CH_3), 17.80 (CH_3), 18.55 (CH_3), 18.68 (CH_3), 33.11 (C^{10}), 33.39 (C^{10}), 36.72 (C^8), 36.89 (C^8), 40.19 (C^4), 40.25 (C^4), 70.90 (C^5), 71.20 (C^5), 75.81 (C^9), 75.98 (C^9), 129.13 (C^7), 129.95 (C^7), 134.49 (C^6), 134.62 (C^2), 134.72 (C^2), 154.85 (C^3), 194.23 (C^1). Mass spectrum: *m/z* 212.1 $[M]^+$. $C_{12}H_{20}O_3$. M_{calc} 212.1412.

(2*E*,4*E*)-6-Methylhepta-2,4-dieneal (V). *a*. To a solution of 2.00 g (14.1 mmol) of alcohol **III** in 40 mL of 1,2-dichloroethane was added 40 mL of 10% HCl solution, then the two-phase system at vigorous stirring was heated at 55°C and stirred for 6 h. On cooling to room temperature the mixture was cautiously neutralized with a saturated solution of $NaHCO_3$. The organic layer was separated, the reaction products were extracted from the water phase with dichloromethane (2 × 30 mL). The combined organic solutions were washed with water and dried with $MgSO_4$. The solvent was distilled off, the residue was chromatographed. Yield 1.01 g (58%).

b. A mixture of 1.36 g (9.58 mmol) of alcohol **III** with 0.04 g (3 mol%) of TsOH in 10 mL of dichloromethane was boiled with a Dean–Stark trap for 5 h. The solvent was distilled off, the residue was chromatographed. Yield 0.70 g (59%).

c. A mixture of 13.60 g (95.8 mmol) of alcohol **III** with 0.11 g (1 mol%) of Py·HCl in 50 mL of a mixture toluene–DMF, 4 : 1, was boiled for 30 min. The solvent was distilled off, the residue was distilled in a vacuum collecting the fraction boiling at 55–65°C (5 mmHg). Yield 8.91 g (75%). A mixture of 4*E*- and 4*Z*-isomers, 94 : 6. Crystalline substance, mp 50–52°C, R_f 0.7 (petroleum ether–EtOAc, 10 : 1). IR spectrum, cm^{-1}: 2960, 1734, 1683, 1265, 1114, 1045, 738. ^1H NMR spectrum (4*E*), δ, ppm: 0.93 d (3H, CH_3, *J* 6.8 Hz), 0.94 d (3H, CH_3, *J* 6.8 Hz), 1.83 m (1H, H^6), 6.07 d.d (1H, H^2, *J* 15.3, 8.1 Hz), 6.24 d.d (1H, H^5, *J* 15.3, 6.3 Hz), 6.27 d.d (1H, H^4, *J* 15.3, 8.9 Hz), 7.07 d.d (1H, H^3, *J* 15.3, 8.1 Hz), 9.53 d (1H, H^1, *J* 8.1 Hz). ^{13}C NMR spectrum, δ, ppm: 20.93 (CH_3), 20.93 (CH_3), 31.68 (C^6), 125.77 (C^4), 130.18 (C^2), 153.19 (C^3), 153.67 (C^5), 193.86 (C^1). Mass spectrum: *m/z* 124.1 $[M]^+$. $C_8H_{12}O$. M_{calc} 124.0888.

(2*E*,4*E*)-6-Methylhepta-2,4-dienyl acetate (VI). In an argon atmosphere to a solution of 10.00 g (80.6 mmol) of aldehyde **V** in 300 mL of Et_2O at –78°C was slowly added 21.6 mL (88.7 mmol) of 73% solution of $(i\text{-Bu})_2AlH$ in toluene. The mixture was stirred for 1 h at –78°C, then 20 mL (241.8 mmol) of pyridine and 23 mL (241.8 mmol) of Ac_2O was added. The reaction mixture was left to warm to 0°C and it was stirred for another 2 h. 30 mL of EtOH was added dropwise, and the mixture was neutralized with 10% solution of HCl. The reaction products were extracted from the water phase with petroleum ether (2 × 100 mL), the combined organic solutions were dried with $MgSO_4$. The solvent was distilled off, the residue was distilled in a vacuum collecting the fraction of bp 80–90°C (5 mmHg). Yield 10.84 g (80%). Crystalline substance, mp 50–53°C, R_f 0.5 (petroleum ether–EtOAc, 5 : 1). IR spectrum, cm^{-1}: 2960, 1734, 1471, 1377, 1232, 1099, 1024, 746. ^1H NMR spectrum, δ, ppm: 0.98 d (6H, CH_3, *J* 6.7 Hz), 2.03 s (3H, CH_3), 2.31 m (1H, H^6), 4.55 d (2H, H^1, *J* 6.7 Hz), 5.61 d.d (1H, H^5, *J* 15.3, 6.8 Hz), 5.67 t.d (1H, H^2, *J* 15.3, 6.7 Hz), 5.95 d.d (1H, H^4, *J* 15.3, 10.4 Hz), 6.21 d.d (1H, H^3, *J* 15.3, 10.4 Hz). ^{13}C NMR spectrum, δ, ppm: 20.89 (CH_3), 22.09 (CH_3), 22.09 (CH_3), 31.03 (C^6), 64.91 (C^1), 123.98 (C^2), 126.08 (C^4), 135.17 (C^3), 143.59 (C^5), 170.75 (Ac). Mass spectrum: *m/z* 111.1 $[M - OAc]^+$. $C_{10}H_{16}O_2$. M_{calc} 168.1150.

(±)-[(3a*S*,4*S*,7*R*,7a*R*)-7-Isopropyl-1,3-dioxo-1,3,3a,4,7,7a-hexahydroisobenzofuran-4-yl]-methyl acetate (VII). A mixture of 0.030 g (0.31 mmol) of maleic anhydride and 0.077 g (0.46 mmol) of diene **VI** in 10 mL of anhydrous toluene was boiled for 4 h. The reaction mixture was evaporated, the residue was chromatographed on SiO_2. Yield 0.060 g (74%). Crystalline substance, mp 80–82°C, R_f 0.24 (petroleum ether–AcOEt, 5 : 1). IR spectrum, cm^{-1}: 1842, 1774, 1739, 1473, 1369, 1249, 1037, 979, 932. ^1H NMR spectrum, δ, ppm: 1.03 d (3H, $C^{11}H_3$, $^3J_{11,9}$ 6.6 Hz), 1.14 d (3H, $C^{10}H_3$, $^3J_{10,9}$ 6.4 Hz), 1.80 m (1H, H^7), 2.08 s (3H, Ac), 2.21 m (1H, H^9), 2.63 m (1H, H^4), 3.54 d.d (1H, H^{3a}, $^3J_{3a,7a}$ 9.5, $^3J_{3a,4}$ 6.4 Hz), 3.61 d.d (1H, H^{7a}, $^3J_{7a,3a}$ 9.5, $^3J_{7a,7}$ 5.9 Hz), 4.45 d.d (1H, H^{8A}, $^2J_{8A,8B}$ 11.2, $^3J_{8A,4}$ 7.6 Hz), 4.56 d.d (1H, H^{8B}, $^2J_{8B,8A}$ 11.2, $^3J_{8B,4}$ 7.7 Hz), 5.86 d.d.d (1H, H^5, $^3J_{5,6}$ 9.2, $^3J_{5,4}$ 3.3, $^4J_{5,7}$ 3.3 Hz), 6.03 d.d.d (1H, H^6, $^3J_{6,5}$ 9.2, $^3J_{6,7}$ 3.4, $^4J_{6,4}$ 3.4 Hz). ^{13}C NMR spectrum, δ, ppm: 20.82 ($C^{10}H_3$), 20.87 (Ac), 21.94 ($C^{11}H_3$), 27.81 (C^9), 35.30 (C^4), 42.90 (C^{7a}), 43.22 (C^{3a}), 44.25 (C^7), 63.39 (C^8), 129.36 (C^5), 134.47 (C^6), 170.78 (CO), 170.95 (CO), 171.25 (CO). Mass spectrum: *m/z* 224.1 $[M - Ac + H]^+$. $C_{14}H_{18}O_5$. M_{calc} 266.1154.

Reaction of levoglucosenone (VIII) and diene VI. *a*. A solution of 0.550 g (1.3 equiv.) [0.840 g (2 equiv.) or 2.1 g (5 equiv.)] of diene **VI**, 0.315 g (2.5 mol) of levoglucosenone (**VIII**), and several crystals of ionol in 10 mL of anhydrous toluene was heated in a pressure reactor (reaction time and temperature are listed in Table 2). The reaction mixture was evaporated, the residue was dissolved in 5 mL of ethanol and hydrolyzed with a mixture of 4 g of KOH, 40 mL of EtOH, 20 mL of H_2O. On completion of the reaction (TLC monitoring) the mixture was neutralized with 3% HCl solution. The reaction product was extracted from the water layer with ethyl acetate (3 × 30 mL). The combined organic solutions were dried with $MgSO_4$ and evaporated on a rotary evaporator. The residue was chromatographed on SiO_2. Compounds **IX** and **X** were isolated.

b. A mixture of 0.550 g (1.3 equiv.) [0.840 g (2 equiv.) or 2.1 g (5 equiv.)] of diene **VI**, 0.315 g (2.5 mol) of levoglucosenone (**VIII**), and several crystals of ionol was heated in a pressure reactor (reaction time is listed in Table 2). The reaction mixture was dissolved in 5 mL of ethanol and hydrolyzed with a mixture of 4 g of KOH, 40 mL of EtOH, 20 mL of H_2O. On completion of the reaction (TLC monitoring) the mixture was neutralized with 3% HCl solution. The reaction product was extracted from the water layer with ethyl acetate (3 × 30 mL). The combined organic solutions were dried with $MgSO_4$ and evaporated on a rotary evaporator. The residue was chromatographed on SiO_2. Compounds **IX** and **X** were isolated.

c. A solution of 0.118 g (0.94 mmol) of levoglucosenone (**VIII**), 0.310 g (1.87 mmol) of diene **VI**, and several crystal of ionol in 1.5 mL of anhydrous toluene were heated in a pressure reactor at 100°C and a pressure of 10000 at for 6 h. The reaction mixture was evaporated, the residue was chromatographed on SiO_2. We obtained 0.036 g (13%) of adduct **XI**, 0.014 g (5%) of a mixture of adducts **XII** and **XIII**, 0.083 g (30%) of a mixture of adducts **XIV** and **XV**, 0.022 g (19%) of dimer **XVI**. The ratio of adducts **XII–XIII** is 2 : 5, of adducts **XIV–XV** is 1 : 2, according to ^{1}H NMR data.

d. A mixture of 0.236 g (1.87 mmol) of levoglucosenone (**VIII**), 0.620 g (3.71 mmol) of diene **VI**, and several crystals of ionol were heated in a pressure reactor at 100°C and 10000 at for 5 h. The reaction mixture was chromatographed on SiO_2 to obtain 0.028 g (5%) of adduct **XI**, 0.088 g (16%) of adduct **XV**, and 0.087 g (37%) of dimer **XVI**.

e. A solution of 0.314 g (2.49 mmol) of levoglucosenone (**VIII**), 0.830 g (4.98 mmol) of diene **VI**, and some ionol crystals in 3 mL of anhydrous toluene was heated in a pressure reactor at 100°C and a pressure of 6000 at for 9 h. The reaction mixture was evaporated, the residue was chromatographed on SiO_2. We obtained 0.051 g (7%) of adduct **XI**, 0.058 g (8%) of a mixture of adducts **XII** and **XIII**, 0.344 g (47%) of a mixture of adducts **XIV** and **XV**, 0.003 g (1%) of dimer **XVI**. The ratio of adducts **XII–XIII** is 3 : 8, of **XIV–XV** 1 : 2, according to ^{1}H NMR data.

(1*S*,2*S*,3*S*,6*S*,7*R*,9*R*)-3-(Hydroxymethyl)-6-isopropyl-10,12-dioxatricyclo[7.2.1.0^{2,7}]dodec-4-en-8-one (IX). Oily substance, $[\alpha]_D^{20}$ –18.1° (*c* 1.0, $CHCl_3$), R_f 0.3 (petroleum ether–AcOEt, 3 : 1). ^{1}H NMR spectrum, δ, ppm: 0.90 d (3H, C^{16}H$_3$, $^3J_{16,14}$ 6.7 Hz), 0.92 d (3H, C^{15}H$_3$, $^3J_{15,14}$ 6.7 Hz), 1.61 m (1H, H^{14}), 2.44 d.d.d (1H, H^2, $^3J_{2,3}$ 8.0, $^3J_{2,7}$ 7.0, $^3J_{2,1}$ 1.3 Hz), 2.59 m (2H, H^3, H^6), 3.04 d (1H, H^7, $^3J_{7,2}$ 7.0 Hz), 3.66 d.d (1H, H^{13B}, $^2J_{13B,13A}$ 11.0, $^3J_{13B,3}$ 3.4 Hz), 3.74 d.d (1H, H^{13A}, $^2J_{13A,13B}$ 11.0, $^3J_{13A,3}$ 4.4 Hz), 4.08 d.d (1H, H^{11endo}, $^2J_{11endo,11exo}$ 7.5, $^3J_{11endo,1}$ 5.2 Hz), 4.19 d (1H, H^{11exo}, $^2J_{11exo,11endo}$ 7.5 Hz), 4.81 d.d (1H, H^1, $^3J_{1,11endo}$ 5.2, $^3J_{1,2}$ 1.4 Hz), 5.12 s (1H, H^9), 5.56 d.d.d (1H, H^4, $^3J_{4,5}$ 10.3, $^3J_{4,3}$ 1.7, $^4J_{4,6}$ 1.7 Hz), 5.88 d.d.d (1H, H^5, $^3J_{5,4}$ 10.3, $^3J_{5,6}$ 4.7, $^4J_{5,3}$ 2.3 Hz). ^{13}C NMR spectrum, δ, ppm: 20.27 (C^{16}H$_3$), 20.60 (C^{15}H$_3$), 32.44 (C^{14}), 35.99 (C^6), 36.49 (C^3), 41.26 (C^7), 41.99 (C^2), 64.99 (C^{13}), 69.71 (C^{11}), 75.69 (C^1), 101.61 (C^9), 126.52 (C^4), 130.87 (C^5), 202.26 (C=O). Mass spectrum: *m/z* 252.1 $[M]^+$. $C_{14}H_{20}O_4$. M_{calc} 252.1362.

(1*S*,2*S*,3*S*,6*R*,7*S*,9*R*)-3-(Hydroxymethyl)-6-isopropyl-10,12-dioxatricyclo[7.2.1.0^{2,7}]dodec-4-en-8-one (X). Oily substance, $[\alpha]_D^{20}$ +36.7° (*c* 1.0, $CHCl_3$), R_f 0.28 (petroleum ether–AcOEt, 3 : 1). ^{1}H NMR spectrum, δ, ppm: 0.65 d (3H, C^{16}H$_3$, $^3J_{16,14}$ 7.0 Hz), 1.04 d (3H, C^{15}H$_3$, $^3J_{15,14}$ 7.0 Hz), 1.79 d.d.d (1H, H^2, $^3J_{2,7}$ 11.7, $^3J_{2,3}$ 4.6, $^3J_{2,1}$ 1.2 Hz), 2.20 m (1H, H^{14}), 2.43 d.d.d (1H, H^6, $^3J_{6,7}$ 10.2, $^3J_{6,14}$ 4.4, $^3J_{6,5}$ 4.4 Hz), 2.58 m (1H, H^3), 2.78 d.d (1H, H^7, $^3J_{7,2}$ 11.7, $^3J_{7,6}$ 10.2 Hz), 3.57 d (1H, H^{11exo}, $^2J_{11exo,11endo}$ 7.1 Hz), 3.79 d.d (1H, H^{11endo}, $^2J_{11endo,11exo}$ 7.1, $^3J_{11endo,1}$ 5.0 Hz), 3.83 d.d (1H, H^{13B}, $^2J_{13B,13A}$ 11.3, $^3J_{13B,3}$ 4.4 Hz), 3.93 d.d (1H, H^{13A}, $^2J_{13A,13B}$ 11.3, $^3J_{13A,3}$ 6.7 Hz), 5.06 d.d (1H, H^1, $^3J_{1,11endo}$ 5.0, $^3J_{1,2}$ 1.2 Hz), 5.14 s (1H, H^9), 5.69 d.d (1H, H^4, $^3J_{4,5}$ 10.2, $^4J_{4,6}$ 2.2 Hz), 5.80 d.d.d (1H, H^5, $^3J_{5,4}$ 10.2, $^3J_{5,6}$ 4.4, $^4J_{5,3}$ 2.2 Hz). ^{13}C NMR spectrum, δ, ppm: 14.59 (C^{16}H$_3$), 21.23 (C^{15}H$_3$), 28.45 (C^{14}), 38.75 (C^7), 40.85 (C^3), 41.37 (C^2), 41.74 (C^6), 62.72 (C^{13}), 71.23 (C^{11}), 73.85 (C^1), 99.08 (C^9), 127.94 (C^4), 129.39 (C^5),

208.17 (C=O). Mass spectrum: *m/z* 252.1 $[M]^+$. $C_{14}H_{20}O_4$. M_{calc} 252.1362.

{(1*S*,2*S*,3*S*,6*R*,7*S*,9*R*)-3-Isopropyl-8-oxo-10,12-dioxatricyclo[7.2.1.0^{2,7}]dodec-4-en-6-yl}methyl acetate (XI). Oily substance, R_f 0.3 (petroleum ether–AcOEt, 3 : 1), $[\alpha]_D^{20}$ +10.6° (*c* 1.0, $CHCl_3$). IR spectrum, cm^{-1}: 2960, 1735, 1467, 1368, 1247, 1101, 1036, 904. ^{1}H NMR spectrum, δ, ppm: 1.00 d (3H, C^{16}H$_3$, $^3J_{16,14}$ 6.7 Hz), 1.13 d (3H, C^{15}H$_3$, $^3J_{15,14}$ 6.8 Hz), 1.82 d.d.d (1H, H^2, $^3J_{2,7}$ 12.0, $^3J_{2,3}$ 5.3, $^3J_{2,1}$ 1.6 Hz), 2.00 s (3H, Ac), 2.21 m (1H, H^{14}), 2.27 m (1H, H^3), 2.71 m (1H, H^6), 2.82 d.d (1H, H^7, $^3J_{7,2}$ 12.0, $^3J_{7,6}$ 10.2 Hz), 3.62 d (1H, H^{11endo}, $^2J_{11endo,11exo}$ 7.0 Hz), 3.81 d.d (1H, H^{11exo}, $^2J_{11exo,11endo}$ 7.0, $^3J_{11exo,1}$ 4.9 Hz), 4.19 d.d (1H, H^{13A}, $^2J_{13A,13B}$ 10.9, $^3J_{13A,6}$ 4.9 Hz), 4.38 d.d (1H, H^{13B}, $^2J_{13B,13A}$ 10.9, $^3J_{13B,6}$ 3.3 Hz), 4.78 d.d (1H, H^1, $^3J_{1,11exo}$ 4.9, $^3J_{1,2}$ 1.6 Hz), 5.17 s (1H, H^9), 5.65 d (1H, H^5, $^3J_{5,4}$ 10.1 Hz), 5.85 d.d.d (1H, H^4, $^3J_{4,5}$ 10.1, $^3J_{4,3}$ 5.5, $^4J_{4,6}$ 2.2 Hz). ^{13}C NMR spectrum, δ, ppm: 20.46 (C^{16}H$_3$), 20.99 (Ac), 24.12 (C^{15}H$_3$), 28.52 (C^{14}), 36.53 (C^6), 37.82 (C^7), 42.27 (C^2), 43.43 (C^3), 65.94 (C^{13}), 71.55 (C^{11}), 73.78 (C^1), 99.13 (C^9), 129.09 (C^5), 129.44 (C^4), 171.06 (Ac), 207.13 (C=O). Mass spectrum: *m/z* 266.1 $[M - C_2H_5 + H]^+$. $C_{16}H_{22}O_5$. M_{calc} 294.1467.

{(1*S*,2*S*,3*S*,6*S*,7*R*,9*R*)-3-Isopropyl-8-oxo-10,12-dioxatricyclo[7.2.1.0^{2,7}]dodec-4-en-6-yl}methyl acetate (XII). Oily substance, R_f 0.37 (petroleum ether–AcOEt, 3 : 1). IR spectrum, cm^{-1}: 2960, 1738, 1465, 1387, 1231, 1107, 1037, 896. ^{1}H NMR spectrum, δ, ppm: 0.75 d (3H, CH_3, *J* 6.8 Hz), 1.03 d (3H, CH_3, *J* 6.9 Hz), 1.91 m (1H, H^{14}), 2.04 s (3H, Ac), 2.29 m (1H, H^2), 2.43 m (1H, H^3), 2.71 m (1H, H^6), 3.05 d (1H, H^7, *J* 6.9 Hz), 3.91 d.d (1H, H^{13A}, *J* 9.8, 8.7 Hz), 4.19 d.d (1H, H^{13B}, *J* 9.8, 4.8 Hz), 4.07 m (2H, H^{11}), 4.68 d (1H, H^1, *J* 4.9 Hz), 5.11 s (1H, H^9), 5.68 m (2H, H^4, H^5). ^{13}C NMR spectrum, δ, ppm: 16.72 (C^{15}H$_3$), 20.94 (Ac), 21.14 (C^{16}H$_3$), 28.33 (C^{14}), 30.40 (C^6), 38.78 (C^3), 40.68 (C^7), 41.70 (C^2), 65.33 (C^{13}), 67.29 (C^{11}), 75.30 40.68 (C^7), 41.70 (C^2), 65.33 (C^{13}), 67.29 (C^{11}), 75.30 (C^1), 101.52 (C^9), 124.52 (C^4), 128.58 (C^5), 171.14 (Ac), 201.30 (C=O). Mass spectrum: *m/z* 294.1 $[M]^+$. $C_{16}H_{22}O_5$. M_{calc} 294.1467.

{(1*S*,2*S*,3*R*,6*S*,7*R*,9*R*)-6-Isopropyl-8-oxo-10,12-dioxatricyclo[7.2.1.0^{2,7}]dodec-4-en-3-yl}methyl acetate (XIII). Oily substance, R_f 0.37 (petroleum ether–AcOEt, 3 : 1). IR spectrum, cm^{-1}: 2960, 1738, 1465, 1387, 1231, 1107, 1037, 896. ^{1}HNMR spectrum, δ, ppm: 0.89 d (3H, C^{16}H$_3$, $^3J_{16,14}$ 6.8 Hz), 0.90 d (3H, C^{15}H$_3$, $^3J_{15,14}$ 6.7 Hz), 1.62 m (1H, H^{14}), 2.04 s (3H, Ac), 2.24 d.d.d (1H, H^2, $^3J_{2,3}$ 9.1, $^3J_{2,7}$ 7.0, $^3J_{2,1}$ 1.6 Hz), 2.61 m (1H, H^6), 2.71 m (1H, H^3), 3.01 d (1H, H^7, $^3J_{7,2}$ 7.0 Hz), 4.05 d (1H, H^{11endo}, $^2J_{11endo,11exo}$ 7.7 Hz), 4.05 d.d (1H, H^{11exo}, $^2J_{11exo,11endo}$ 7.7, $^3J_{11exo,1}$ 5.1 Hz), 4.16 d.d (1H, H^{13A}, $^2J_{13A,13B}$ 11.2, $^3J_{13A,3}$ 6.4 Hz), 4.19 d.d (1H, H^{13B}, $^2J_{13B,13A}$ 11.2, $^3J_{13B,3}$ 4.8 Hz), 4.75 d.d (1H, H^1, $^3J_{1,11exo}$ 5.1, $^3J_{1,2}$ 1.6 Hz), 5.12 s (1H, H^9), 5.56 d.d.d (1H, H^4, $^3J_{4,5}$ 10.3, $^3J_{4,3}$ 2.1, $^4J_{4,6}$ 2.1 Hz), 5.79 d.d.d (1H, H^5, $^3J_{5,4}$ 10.3, $^3J_{5,6}$ 4.8, $^3J_{5,3}$ 2.5 Hz). ^{13}C NMR spectrum, δ, ppm: 20.08 (C^{15}H$_3$), 20.43 (C^{16}H$_3$), 20.81 (Ac), 32.36 (C^{14}), 33.70 (C^3), 35.63 (C^6), 41.15 (C^7), 42.39 (C^2), 65.93 (C^{13}), 67.31 (C^{11}), 75.23 (C^1), 101.59 (C^9), 126.27 (C^4), 129.60 (C^5), 170.99 (Ac), 201.57 (C=O). Mass spectrum: *m/z* 206.1 $[M - OAc - Et]^+$. $C_{16}H_{22}O_5$. M_{calc} 294.1467.

{(1*S*,2*S*,3*S*,6*S*,7*R*,9*R*)-6-Isopropyl-8-oxo-10,12-dioxatricyclo[7.2.1.0^{2,7}]dodec-4-en-3-yl}methyl acetate (XIV). Oily substance, R_f 0.4 (petroleum ether–AcOEt, 1 : 1). IR spectrum, cm^{-1}: 2960, 1733, 1464, 1368, 1242, 1037, 895. ^{1}H NMR spectrum, δ, ppm: 0.87 d (3H, C^{16}H$_3$, $^3J_{16,14}$ 6.6 Hz), 0.97 d (3H, C^{15}H$_3$, $^3J_{15,14}$ 6.5 Hz), 1.53 m (1H, H^{14}), 2.06 s (3H, Ac), 2.44 m (1H, H^2), 2.65 m (2H, H^3, H^6), 3.20 d.d (1H, H^7, $^3J_{7,2}$ 6.6, $^3J_{7,6}$ 3.7 Hz), 3.59 d.d (1H, H^{11endo}, $^2J_{11endo,11exo}$ 7.4, $^3J_{11endo,1}$ 5.1 Hz), 4.06 d (1H, H^{11exo}, $^2J_{11exo,11endo}$ 7.4 Hz), 4.27 d.d (1H, H^{13B}, $^2J_{13B,13A}$ 11.0, $^3J_{13B,3}$ 5.9 Hz), 4.39 m (1H, H^{13A}), 4.82 d.d (1H, H^1, $^3J_{1,11endo}$ 5.3, $^3J_{1,2}$ 1.4 Hz), 4.94 s (1H, H^9), 5.62 d.d.d (1H, H^4, $^3J_{4,5}$ 9.6, $^3J_{4,3}$ 2.7, $^4J_{4,6}$ 2.7 Hz), 6.00 d.d.d (1H, H^5, $^3J_{5,4}$ 9.6, $^3J_{5,6}$ 2.9, $^4J_{5,3}$ 2.9 Hz). Mass spectrum: *m/z* 266.1 $[M - C_2H_5 + H]^+$. $C_{16}H_{22}O_5$. M_{calc} 294.1467.

{(1*S*,2*S*,3*S*,6*R*,7*S*,9*R*)-6-Isopropyl-8-oxo-10,12-dioxatricyclo[7.2.1.0^{2,7}]dodec-4-en-3-yl}methyl acetate (XV). Oily substance, R_f 0.4 (petroleum ether–AcOEt, 1 : 1), $[\alpha]_D^{20}$ +48.4° (*c* 1.0, $CHCl_3$). IR spectrum, cm^{-1}: 2960, 1733, 1464, 1368, 1242, 1037, 895. ^{1}H NMR spectrum, δ, ppm: 0.63 d (3H, C^{16}H$_3$, $^3J_{16,14}$ 6.8 Hz), 1.02 d (3H, C^{15}H$_3$, $^3J_{15,14}$ 6.8 Hz), 1.76 d.d.d (1H, H^2, $^3J_{2,7}$ 11.9, $^3J_{2,3}$ 4.7, $^3J_{2,1}$ 1.3 Hz), 2.08 s (3H, Ac), 2.17 m (1H, H^{14}), 2.40 m (1H, H^6), 2.60 d.d (1H, H^7, $^3J_{7,2}$ 11.9, $^3J_{7,6}$ 10.4 Hz), 2.67 m (1H, H^3), 3.56 d (1H, H^{11endo}, $^2J_{11endo,11exo}$ 7.2 Hz), 3.77 d.d (1H, H^{11exo}, $^2J_{11exo,11endo}$ 7.2, $^3J_{11exo,1}$ 4.8 Hz), 4.15 d.d (1H, H^{13A}, $^2J_{13A,13B}$ 11.6, $^3J_{13A,3}$ 5.1 Hz), 4.34 d.d (1H, H^{13B}, $^2J_{13B,13A}$ 11.6, $^3J_{13B,3}$ 7.0 Hz), 4.87 d.d (1H, H^1, $^3J_{1,11exo}$ 4.8, $^3J_{1,2}$ 1.3 Hz), 5.11 s (1H, H^9), 5.67 d (1H, H^5, $^3J_{5,4}$ 10.1 Hz), 5.76 d.d.d (1H, H^4, $^3J_{4,5}$ 10.1, $^3J_{4,3}$ 5.6, $^4J_{4,6}$ 2.1 Hz). ^{13}C NMR spectrum, δ, ppm: 16.28 (C^{16}H$_3$), 21.08 (Ac), 21.26 (C^{15}H$_3$), 28.57 (C^{14}), 37.96 (C^3), 38.49 (C^7), 41.36 (C^2), 41.88 (C^6), 64.15 (C^{13}), 71.29 (C^{11}), 73.83 (C^1), 99.17 (C^9), 127.58 (C^4),

129.62 (C^5), 170.90 (Ac), 207.64 (C=O). Mass spectrum: *m/z* 266.1 $[M - C_2H_5 + H]^+$. $C_{16}H_{22}O_5$. M_{calc} 294.1467.

(1*S*,5*R*)-3-{(1*S*,2*R*,5*R*)-4-Oxo-6,8-dioxabicyclo-[3.2.1]octan-2-yl}-6,8-dioxabicyclo[3.2.1]oct-2-en-4-one (XVI). ^{1}H NMR spectrum, δ, ppm: 2.23 d (1H, $H^{3'}$, *J* 16.92 Hz), 2.97 d.d (1H, $H^{3'}$, *J* 16.92, 8.82 Hz), 3.43 d (1H, $H^{2'}$, *J* 8.82 Hz), 3.72 d (1H, H^7, *J* 6.62 Hz), 3.90 d.d (1H, H^7, *J* 6.62, 4.41 Hz), 4.05 d.d (1H, $H^{7'}$, *J* 8.09, 5.15 Hz), 4.10 d (1H, $H^{7'}$, *J* 8.09 Hz), 4.53 d (1H, $H^{1'}$, *J* 5.15 Hz), 5.01 d.d (1H, H^1, *J* 5.14, 4.41 Hz), 7.11 d (1H, H^2, *J* 5.14 Hz).

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