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Synthesis of (2*S*,3*S*,4*S*)-2,3-*O*-Isopropylidene-4-(methoxycarbonylmethyl)cyclopentan-1-one

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Abstract—(2S,3*S*,4*S*)-2,3-*O*-Isopropylidene-4-(methoxycarbonylmethyl)cyclopentan-1-one was synthesized starting from D-ribose through methyl (Z)-3-(5-acetyl-2,2-acetoxyacetyl-2,2-dimethyl-1,3-dioxolan-4-yl)prop-2-enoate which was subjected to cyclization in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene, followed by decarboxylation.

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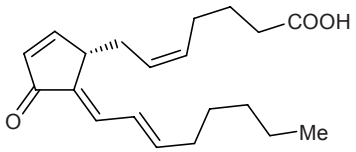
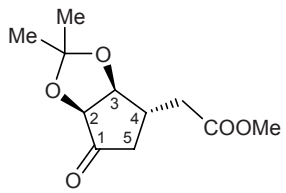
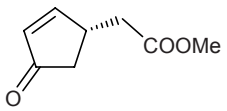
Chiral cyclopentenone derivatives of sugars are used as key building blocks in the synthesis of prostanoids, carbanucleosides, etc. [1–5]. Among these compounds, cyclopentenone prostaglandins attract specific interest. For example, *in vivo* metabolite of prostaglandin D_2 (PGD_2), 15-deoxy-$\Delta^{12,14}$-prostaglandin J_2 (**I**), is a potent natural ligand for peroxisome proliferator-activated receptors (PPARs). The latter are known to induce apoptosis, control transcription of a series of viral genes, inhibit enzymes responsible for triggering of inflammation processes, etc. [6, 7]. Molecule **I** contains a cross-conjugated trienone system and, unlike other prostanoids, only one chiral center (C^8). The synthesis of compound **I** was described in [8, 9].



I



II

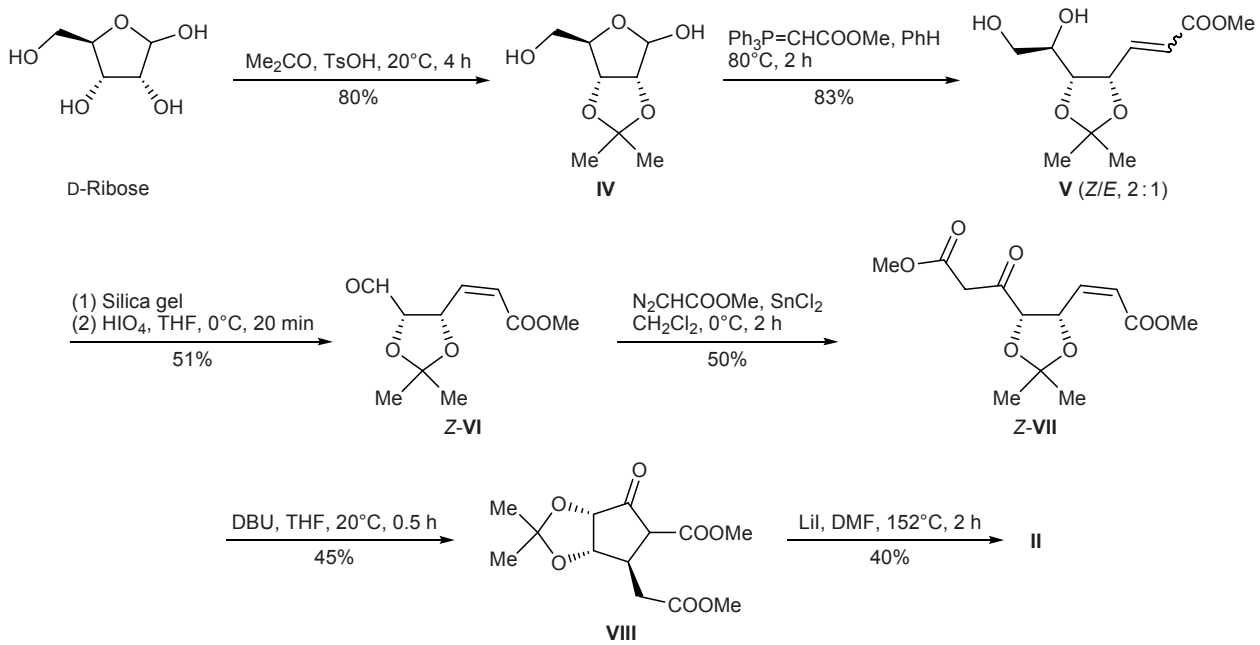


III

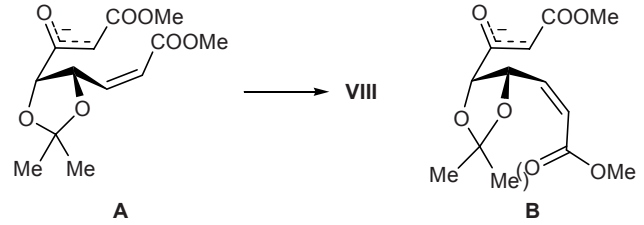
In the present work we have developed a scheme for stereoselective synthesis of optically active cyclopentanone building block **II**, starting from D-ribose. The configuration of the chiral center in molecule **II** is the same as in 15-deoxy-$\Delta^{12,14}$-prostaglandin J_2. Acetonide **II** can also be regarded as a structural isoster of cyclopentenone **III** (a more obvious precursor of **I**) with protected double bond. The developed approach is based on intramolecular carbocyclization according to Michael. In order to build up the "acceptor" molecular fragment, known D-ribose acetonide **IV** [10] was treated with methyl (triphenyl-λ^5-phosphanylidene)-acetate [11] in benzene. The reaction gave oily olefin **V** as a mixture of *Z* and *E* isomers at a ratio of 2:1 (according to the ^{1}H NMR data). This step could be accompanied by facile intramolecular Michael cyclization of compound **V** with formation of furanose-like products. In keeping with published data [12], addition of trace amounts of benzoic acid makes it possible to avoid side cyclization process. The reaction selectivity can be improved toward increased fraction of the *Z* isomer of **V** by carrying out the Wittig reaction in methylene chloride as solvent [13].

The "donor" fragment was built up as follows. Isomeric diols **V** were separated into individual *Z* and *E* isomers by chromatography on silica gel, and the pure isomers were converted into the corresponding aldehydes **VI** via oxidative cleavage with HIO_4 in THF at 0°C. The reaction of *Z*-**VI** with methyl diazoacetate [14] in the presence of anhydrous tin(II) chloride as catalyst (CH_2Cl_2, 0°C) [15] gave compound *Z*-**VII**. According to the ^{1}H and ^{13}C NMR and IR data, diester *Z*-**VII** exists as a mixture of ketone and enol tautomers.

Scheme 1.



The β-keto ester fragment in molecule **VII** is capable of readily losing a proton to generate the corresponding carbanion which undergoes intramolecular anionotropic cyclization following the allowed 5-*exo*-trig path according to Baldwin [16]. Isomer *Z*-**VII** gives rise to stereochemically unambiguous products. By analogy with the radical process [17], among two possible transition states **A** and **B**, state **A** leading to compound **VIII** should be preferred.



As might be expected, the cyclization of *Z*-**VII** in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (THF, 20°C) in 0.5 h afforded 45% of diester **VIII**. The cyclization product was isolated as a mixture of diastereoisomers with respect to C^4, which cannot be separated by chromatography. Each isomer exists in the enol form, as follows from the ^{1}H NMR spectra which contain two downfield signals ($\delta \approx 10$ ppm) from the enolic hydroxy proton with an intensity ratio of 85:15. The major stereoisomer has 3,4-*trans*-configuration, and the cyclopentane ring therein adopts mainly a *twist* conformation ($^4T_3$) where the dihedral angle $H^3C^3C^4H^4$ approaches 90° ($J_{3,4}$ = 0.9 Hz; the corresponding coupling constant for the 3,4-*cis* isomer is much greater, 6 Hz).

In the final step, diester **VIII** was subjected to decarboxylation by the action of lithium iodide in boiling dimethylformamide (150°C, 2 h). According to the ^{1}H and ^{13}C NMR data, ester **II** was isolated as a mixture of two diastereoisomers at C^4 at a ratio of 9:1, the major isomer having *trans* configuration. The conformational equilibrium of compound **II** is displaced toward the structure with pseudoaxial orientation of the substituent on C^4. The substituents on C^3 and C^4 occupy pseudoaxial positions, and the dihedral angles between the equatorial C^3–H/C^4–H and C^4–H/C^5–H_{eq} bonds are close to 90°; therefore, no coupling is observed between these protons. The dihedral angle between the C^4–H and C^5–H_{ax} bonds is about 30° ($J_{4,5\text{-}ax}$ = 9.5 Hz). In the *cis* isomer of **II**, conformational mobility of the cyclopentane ring is restricted, so that conformations characterized by two dihedral angles close to 90° for the corresponding protons are less probable.

Analogous transformations of the *E* isomer of aldehyde **VI** are not selective, and they are not discussed in the present article.

EXPERIMENTAL

The IR spectra were recorded on UR-20 and Specord M-80 spectrometers from samples prepared as thin films or dispersed in mineral oil. The ^{1}H and ^{13}C

NMR spectra were recorded on a Bruker AM-300 spectrometer at 300.13 and 75.47 MHz, respectively, using chloroform-*d* as solvent and reference (δ 7.27, δ_C 77.00 ppm). The progress of reactions was monitored by thin-layer chromatography on Silufol plates using petroleum ether–ethyl acetate or methylene chloride–methanol as eluent; spots were detected by treatment with a 10% solution of *p*-methoxybenzaldehyde in ethanol with addition of sulfuric acid.

2,3-*O*-Isopropylidene-β-D-ribofuranose (IV). D-Ribose, 1.00 g (6.66 mmol), was dispersed in 20 ml of anhydrous acetone, 0.11 g (0.66 mmol) of *p*-toluenesulfonic acid was added, and the mixture was stirred for 4 h at room temperature (TLC). Triethylamine, 0.3 ml, was then added, and the mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel using methylene chloride (200:1) as eluent to isolate 1.01 g (80%) of acetonide **IV**, R_f 0.38 (CH_2Cl_2–MeOH, 9:1). IR spectrum, ν, cm^{-1}: 1080 (C–O), 1145 (O–C–O), 3380 (OH). ^1H NMR spectrum, δ, ppm: 1.25 s (3H, Me), 1.45 s (3H, Me), 3.52 m (1H, 5-H_A), 3.70 m (1H, 5-H_B), 4.30 br.s (1H, 5-OH), 4.33 br.s (1H, 4-H), 4.52 d (1H, 3-H, $^3J_{3,2}$ = 6.0 Hz), 4.76 d (1H, 2-H, $^3J_{2,3}$ = 6.0 Hz), 5.36 d (1H, 1-H, $^3J_{1,OH}$ = 5.6 Hz), 5.6 d (1H, 1-OH, $^3J_{OH,1}$ = 5.6 Hz). ^{13}C NMR spectrum, δ_C, ppm: 24.62 (Me), 26.27 (Me), 63.40 (C^5), 81.58 (C^2), 86.63 (C^3), 87.53 (C^4), 102.61 (C^1), 112.11 (OCO). Found, %: C 50.67; H 7.35. $C_8H_{14}O_5$. Calculated, %: C 50.52; H 7.42.

Reaction of acetonide IV with methyl (triphenyl-λ^5-phosphanylidene)acetate. Methyl (triphenyl-λ^5-phosphanylidene)acetate [11], 0.26 g (0.79 mmol), was added in portions to a solution of 0.10 g (0.53 mmol) of acetonide **IV** in 4 ml of anhydrous benzene. The mixture was stirred for 2 h on heating under reflux (TLC) and concentrated under reduced pressure. The residue was recrystallized from *tert*-butyl methyl ether, the precipitate of triphenylphosphine oxide was filtered off, the mother liquor was concentrated, and the residue was subjected to column chromatography on silica gel using petroleum ether–chloroform–methanol (50:50:3) as eluent to isolate 0.07 g (55%) of *Z*-**V** and 0.035 g (28%) of *E*-**V**.

Methyl (*Z*)-3-{(4*S*,5*R*)-5-[(1*S*)-1,2-dihydroxyethyl)]-2,2-dimethyl-1,3-dioxolan-4-yl}prop-2-enoate (*Z*-V). R_f 0.39 ($CHCl_3$–MeOH, 97:3; 3 successive elutions). IR spectrum, ν, cm^{-1}: 874 (*cis*-HC=CH), 1180 (O–C–O), 1648 (*cis*-HC=CH), 1714 (C=O), 3430 (OH). ^1H NMR spectrum, δ, ppm: 1.38 s (3H, Me), 1.50 s (3H, Me), 2.50 t (1H, 2″-OH, $J_{OH,2''A} = J_{OH,2''B}$ = 5.7 Hz), 3.42 d (1H, 1″-OH, $J_{OH,1''}$ = 3.1 Hz), 3.6–3.8 m (3H, 1″-H, 2″-H), 3.75 s (3H, OMe), 4.33 d.d (1H, 5′-H, $J_{5',4'}$ = 6.6, $J_{5,1''}$ = 7.9 Hz), 5.54 d.d (1H, 4′-H, $J_{4',5'}$ = 6.6, $J_{4',3}$ = 8.2 Hz), 6.02 d (1H, 2-H, $J_{2,3}$ = 11.5 Hz), 6.29 d.d (1H, 3-H, $J_{3,4'}$ = 8.2, $J_{3,2}$ = 11.5 Hz). ^{13}C NMR spectrum, δ_C, ppm: 25.32 (Me), 26.76 (Me), 52.01 (OMe), 64.06 ($C^{2''}$), 70.12 ($C^{1''}$), 74.60 ($C^{5'}$), 79.09 ($C^{4'}$), 109.55 (OCO), 121.75 (C^2), 146.17 (C^3), 167.42 (C^1).

Methyl (*E*)-3-{(4*S*,5*R*)-5-[(1*S*)-1,2-dihydroxyethyl)]-2,2-dimethyl-1,3-dioxolan-4-yl}prop-2-enoate (*E*-V). R_f 0.23 ($CHCl_3$–MeOH, 97:3; 3 successive elutions). IR spectrum, ν, cm^{-1}: 934 (*trans*-HC=CH), 1168 (*trans*-C=C), 1714 (C=O), 3394 (OH). ^1H NMR spectrum, δ, ppm: 1.35 s (3H, Me), 1.46 s (3H, Me), 3.30 br.s (1H, OH), 3.70 m (3H, 1″-H, 2″-H), 3.73 s (3H, OMe), 4.16 d.d (1H, 5′-H, $J_{5',4'}$ = 7.3, $J_{5',1''}$ = 8.0 Hz), 4.36 d.d (1H, 4′-H, $J_{4',3}$ = 4.4, $J_{4',5'}$ = 7.3 Hz), 5.30 s (1H, 1″-OH), 6.15 d (1H, 2-H, $J_{2,3}$ = 15.6 Hz), 7.08 d.d (1H, 3-H, $J_{3,4'}$ = 4.4, $J_{3,2}$ = 15.6 Hz). ^{13}C NMR spectrum, δ_C, ppm: 24.66 (Me), 27.01 (Me), 51.28 (OMe), 63.95 ($C^{2''}$), 69.52 ($C^{1''}$), 76.08 ($C^{5'}$), 77.28 ($C^{4'}$), 109.06 (OCO), 121.11 (C^2), 143.99 (C^3), 166.78 (C^1). Found, %: C 53.58; H 7.41. $C_{11}H_{18}O_6$. Calculated, %: C 53.65; H 7.37.

Oxidation of isomeric diols *Z*-V and *E*-V with HIO_4. A solution of 0.22 g (0.97 mmol) of $HIO_4 \cdot 2H_2O$ in 5 ml of THF was added to a solution of 0.16 g (0.65 mmol) of diol *Z*-**V** in 3 ml of THF, cooled to 0°C, and the mixture was stirred for 20 min (TLC). The mixture was diluted with ethyl acetate, washed with saturated aqueous solutions of $NaHCO_3$ and NaCl, dried over Na_2SO_4, and concentrated. The residue was subjected to column chromatography on silica gel using petroleum ether–ethyl acetate (9:1) to isolate 0.07 g (51%) of aldehyde *Z*-**VI**. Diol *E*-**V** was oxidized following a similar procedure. The yield of *E*-**VI** was 0.12 g (86%).

Methyl (*Z*)-3-[(4*S*,5*S*)-5-formyl-2,2-dimethyl-1,3-dioxolan-4-yl]prop-2-enoate (*Z*-VI). R_f 0.46 (petroleum ether–ethyl acetate, 1:1). IR spectrum, ν, cm^{-1}: 826 (*cis*-HC=CH), 1720 (C=O), 1732 (C=O). ^1H NMR spectrum, δ, ppm: 1.44 s (Me), 1.60 s (Me), 3.75 s (OMe), 4.80 d.d (1H, 5′-H, $J_{5',1''}$ = 1.9, $J_{5',4'}$ = 7.7 Hz), 5.82 d.d.d (1H, 4′-H, $J_{4',2}$ = 1.9, $J_{4',3}$ = 6.8, $J_{4',5'}$ = 7.7 Hz), 6.00 d.d (1H, 2-H, $J_{2,4'}$ = 1.9, $J_{2,3}$ = 11.5 Hz), 6.23 d.d (1H, 3-H, $J_{3,4'}$ = 6.8, $J_{3,2}$ = 11.5 Hz), 9.5 d (1H, 1″-H, $J_{1'',5'}$ = 1.9 Hz). ^{13}C NMR spectrum, δ_C, ppm: 25.11 (Me), 27.21 (Me), 51.70 (OMe), 75.70

($C^{5'}$), 81.86 ($C^{4'}$), 111.39 (OCO), 122.58 (C^3), 143.70 (C^2), 165.80 (C^1), 199.17 ($C^{1''}$).

Methyl (*E*)-3-[(4*S*,5*S*)-5-formyl-2,2-dimethyl-1,3-dioxolan-4-yl]prop-2-enoate (*E*-VI). R_f 0.26 (petroleum ether–ethyl acetate, 1:1). IR spectrum, ν, cm^{-1}: 982 (*trans*-HC=CH), 1720 (C=O), 1738 (C=O). ^1H NMR spectrum, δ, ppm: 1.40 s (3H, Me), 1.57 s (3H, Me), 3.68 s (3H, OMe), 4.48 d.d (1H, 5′-H, $J_{5',1''}$ = 2.8, $J_{5',4'}$ = 7.6 Hz), 5.00 d.d.d (1H, 4′-H, $J_{4',2}$ = 1.7, $J_{4',3}$ = 6.2, $J_{4',5'}$ = 7.6 Hz), 6.12 d.d (1H, 2-H, $J_{2,4'}$ = 1.7, $J_{2,3}$ = 15.8 Hz), 6.79 d.d (1H, 3-H, $J_{3,4'}$ = 6.2, $J_{3,2}$ = 15.8 Hz), 9.43 d (1H, 1″-H, $J_{1'',5'}$ = 2.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 25.07 (Me), 27.03 (Me), 51.65 (OMe), 76.42 ($C^{4'}$), 81.79 ($C^{5'}$), 111.71 (OCO), 123.04 (C^2), 140.00 (C^3), 165.67 (C^1), 200.00 ($C^{1''}$). Found, %: C 56.19; H 6.46. $C_{10}H_{14}O_5$. Calculated, %: C 56.07; H 6.59.

Methyl (*Z*)-3-[(4*S*,5*S*)-5-(3-methoxy-3-oxopropanoyl)-2,2-dimethyl-1,3-dioxolan-4-yl]prop-2-enoate (*Z*-VII). A solution of 0.126 g (1.26 mmol) of methyl diazoacetate [12] in 3 ml of anhydrous methylene chloride was added dropwise over a period of 1 h to a mixture of 0.27 g (1.26 mmol) of *cis*-aldehyde *Z*-**VI** and 0.024 g (0.126 mmol) of $SnCl_2$ in 5 ml of anhydrous methylene chloride while stirring at 0°C under argon. The mixture was stirred for an additional 1 h (TLC) and subjected to flash chromatography. The eluate was concentrated under reduced pressure, and the residue was purified by column chromatography using petroleum ether–ethyl acetate (95:5) as eluent. Yield 0.175 g (50%), R_f 0.42 (petroleum ether–ethyl acetate, 8:2; 2 successive elutions). IR spectrum, ν, cm^{-1}: 874 (*cis*-HC=CH), 1710 (C=O), 1725 (C=O), 3620 (OH).

Methyl (*Z*)-3-[(4*S*,5*R*)-5-(3-methoxy-3-oxopropanoyl)-2,2-dimethyl-1,3-dioxolan-4-yl]prop-2-enoate (*Z*-VII, ketone tautomer). ^1H NMR spectrum, δ, ppm: 1.41 s (3H, Me), 1.61 s (3H, Me), 3.38 d (1H, 2″-H_A, $J_{A,B}$ = 16.3 Hz), 3.54 d (1H, 2″-H, $J_{B,A}$ = 16.3 Hz), 3.70 s (3H, OMe), 3.74 s (3H, OMe), 4.88 d (1H, 5′-H, $J_{5',4'}$ = 8.1 Hz), 5.88 d.d (1H, 4′-H, $J_{4',3}$ = 7.2, $J_{4',5'}$ = 8.1 Hz), 5.95 d (1H, 2-H, $J_{2,3'}$ = 11.4 Hz), 6.20 d.d (1H, 3-H, $J_{3,4'}$ = 7.2, $J_{3,2}$ = 11.4 Hz). ^{13}C NMR spectrum, δ_C, ppm: 24.57 (Me), 26.55 (Me), 46.82 ($C^{2''}$), 51.62 (OMe), 52.18 (OMe), 75.44 ($C^{5'}$), 82.45 ($C^{4'}$), 111.22 (OCO), 122.89 (C^2), 142.97 (C^3), 165.74 (C^1), 173.18 ($C^{3''}$), 201.02 ($C^{1''}$).

Methyl (*Z*)-3-{(4*R*,5*S*)-5-[(*Z*)-1-hydroxy-3-methoxy-3-oxoprop-1-en-1-yl]-2,2-dimethyl-1,3-dioxolan-4-yl}prop-2-enoate (*Z*-VII, enol tautomer). ^1H NMR spectrum, δ, ppm: 1.41 s (3H, Me), 1.59 s (3H, Me), 3.71 s (3H, OMe), 3.72 s (3H, OMe), 4.82 d (1H, 5′-H, $J_{5',4'}$ = 7.3 Hz), 5.20 s (1H, 2″-H), 5.85 d (1H, 2-H, $J_{2,3'}$ = 11.6 Hz), 5.87 d.d (1H, 4′-H, $J_{4',3}$ = 7.2, $J_{4',5'}$ = 7.3 Hz), 6.22 d.d (1H, 3-H, $J_{3,4'}$ = 7.2, $J_{3,2}$ = 11.6 Hz), 11.7 s (1H, 1′-OH). ^{13}C NMR spectrum, δ_C, ppm: 24.79 (Me), 26.66 (Me), 51.26 (OMe), 51.45 (OMe), 75.10 ($C^{4'}$), 77.62 ($C^{5'}$), 88.40 ($C^{2''}$), 110.56 (OCO), 121.74 (C^2), 144.15 (C^3), 167.13 (C^1), 172.61 ($C^{3''}$), 173.17 ($C^{1''}$). Found, %: C 54.65; H 6.23. $C_{13}H_{18}O_7$. Calculated, %: C 54.54; H 6.34.

Cyclization of diester *Z*-VII. 1,8-Diazabicyclo-[5.4.0]undec-7-ene, 50.074 g (0.48 mmol), was added to a solution of 0.14 g (0.48 mmol) of *Z*-**VII** in 4 ml of anhydrous THF under stirring at room temperature. The mixture was stirred for 30 min (TLC) and concentrated on a rotary evaporator. The residue was subjected to column chromatography on silica gel using petroleum ether–ethyl acetate (9:1 to 7:3) as eluent. Yield of **VIII** 0.063 g (45%), R_f 0.24 ($CHCl_3$–MeOH, 9:1). IR spectrum, ν, cm^{-1}: 1745 (C=O), 3615 (OH).

Methyl (3a*S*,4*R*,5R*S*,6a*S*)-4-(2-methoxy-2-oxoethyl)-2,2-dimethyl-6-oxotetrahydro-3a*H*-cyclopenta[*d*][1,3]dioxole-5-carboxylate (VIII). ^1H NMR spectrum, δ, ppm: major isomer (4*S*)-**VIII**: 1.37 s (3H, Me), 1.44 s (3H, Me), 2.49 d.d (1H, 1′-H_A, $^3J_{A,4}$ = 8.2, $^2J_{A,B}$ = 16.1 Hz), 2.76 d.d (1H, 1′-H_B, $^3J_{B,4}$ = 3.8, $^2J_{B,A}$ = 16.1 Hz), 3.33 d.d (1H, 4-H, $^3J_{4,B}$ = 3.8, $^3J_{4,A}$ = 8.2 Hz), 3.68 s (3H, OMe), 3.82 s (3H, OMe), 4.52 d (1H, 2-H, $^3J_{2,3}$ = 5.8 Hz), 5.10 d (1H, 3-H, $^3J_{3,2}$ = 5.8 Hz), 10.1 s (1H, OH); minor isomer (4*R*)-**VIII**: 1.35 s (3H, Me), 1.42 s (3H, Me), 2.63 d.d (1H, 1′-H_A, $^3J_{A,4}$ = 8.0, $^2J_{A,B}$ = 16.0 Hz), 2.93 d.d (1H, 1′-H_B, $^3J_{B,4}$ = 4.0, $^2J_{B,A}$ = 16.0 Hz), 3.40 d.d.d (1H, 4-H, $^3J_{4,B}$ = 4.0, $^3J_{4,3}$ = 6.0, $^3J_{4,A}$ = 8.0 Hz), 3.72 s (3H, OMe), 3.79 s (3H, OMe), 4.80 t (1H, 3-H, $^3J_{3,2}$ = 6.0, $^3J_{3,4}$ = 6.0 Hz), 4.94 d (1H, 2-H, $^3J_{2,3}$ = 6.0 Hz), 10.25 s (1H, OH). Found, %: C 54.65; H 6.31. $C_{13}H_{18}O_7$. Calculated, %: C 54.54; H 6.34.

Decarboxylation of compound VIII. Compound **VIII**, 0.06 g (0.2 mmol), was dissolved in 5 ml of DMF, 0.056 g (0.42 mmol) of lithium iodide was added, and the mixture was heated for 2 h at the boiling point (TLC). The mixture was cooled to room temperature, diluted with ethyl acetate, washed with water and a saturated aqueous solution of NaCl, dried over Na_2SO_4, and evaporated. The residue was subjected to column chromatography on silica gel using petroleum ether–ethyl acetate (9:1) as eluent to isolate 0.02 g (40%) of compound **II**, R_f 0.20 (petroleum ether–ethyl acetate, 7:3). IR spectrum, ν, cm^{-1}: 1715 (C=O), 1740 (C=O).

Methyl [(3a*S*,4R*S*,6a*S*)-2,2-dimethyl-6-oxotetrahydro-3a*H*-cyclopenta[*d*][1,3]dioxol-4-yl]acetate (II). ^{1}H NMR spectrum, δ, ppm: major isomer (4*S*)-**II**: 1.34 s (3H, Me), 1.44 s (3H, Me), 2.12 br.d (1H, 5-H$_A$, $^2J_{A,B}$ = 17.7 Hz), 2.78 m (1H, 4-H), 2.85 d.d (1H, 5-H$_B$, $^3J_{B,4}$ = 9.5, $^2J_{B,A}$ = 17.7 Hz), 2.3–2.5 m (3H, 1′-H, 5-H$_A$), 2.7–2.9 m (2H, 5-H$_B$, 4-H), 3.68 s (3H, OMe), 4.28 d (1H, 2-H, $J_{2,3}$ = 5.4 Hz), 4.46 d (1H, 3-H, $J_{3,2}$ = 5.4 Hz); minor isomer (4*R*)-**II**: 1.35 s (3H, Me), 1.41 s (3H, Me), 2.3–2.9 m (3H, 1′-H, 4-H), 3.73 s (3H, OMe), 4.23 d (1H, 2-H, $J_{2,3}$ = 5.0 Hz), 4.79 t (1H, 3-H, $J_{3,2}$ = $J_{3,4}$ = 5.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: major isomer (4*S*)-**II**: 24.80 (Me), 26.86 (Me), 33.92 (C$^{1'}$), 37.35 (C^4), 39.66 (C^5), 51.93 (OMe), 78.68 (C^3), 81.88 (C^2), 112.15 (OCO), 171.91 (C$^{2'}$), 212.71 (C^1); minor isomer (4*R*)-**II**: 25.13 (Me), 29.00 (Me), 31.60 (C$^{1'}$), 34.31 (C^4), 38.96 (C^5), 51.08 (OMe), 77.20 (C^3), 80.06 (C^2), 109.50 (OCO), 171.91 (C$^{2'}$), 212.05 (C^1). Found, %: C 57.76; H 7.12. $C_{11}H_{16}O_5$. Calculated, %: C 57.88; H 7.07.

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