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Efficient Synthesis of (1*R*,4*S*,6*R*)-4-Isopropenyl-1,3,3-trimethyl-7-oxabicyclo[4.1.0]heptan-2-one

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Abstract—A simple and convenient one-pot synthesis of (1*R*,4*S*,6*R*)-4-isopropenyl-1,3,3-trimethyl-7-oxabicyclo[4.1.0]heptan-2-one was developed consisting in a thermodynamic methylation of carvone (NaH, MeI, THF, 20°C) followed by the epoxidation with alkalinized hydrogen peroxide. The reduction of the obtained epoxyketone with sodium borohydride proceeded stereoselectively to give a β-alcohol. The attempts to convert its isopropenyl fragment into an acetate group by a rearrangement of products or intermediates of the oxidative fragmentation resulted only in obtaining intermediate acyl derivatives.

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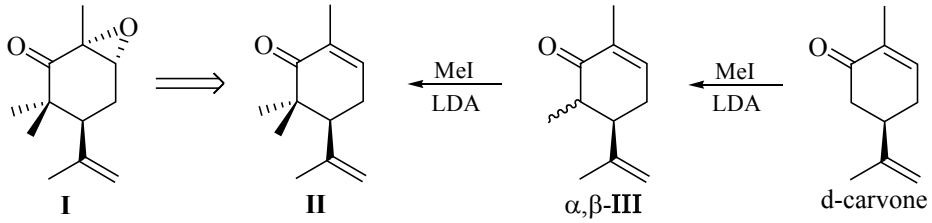
Among chiral matrices from natural sources (sugars, amino acids, monoterpenes etc.) d-carvone is attractive by its availability, inexpensiveness, and unique topology providing a possibility of a fast preparation of variously functionalized cyclohexane block-synthons. A number of these synthons and descriptions of their application in targeted syntheses were mentioned in recent publications [1–5].

We report here on a simple one-pot synthesis of new *gem*-dimethyl-containing cyclohexane block **I** from d-carvone, and on some its reactions. Cyclohexane fragments with the *gem*-dimethyl group are present in the structure of many naturally occurring compounds, in particular, in diterpenoids of the types of atisane [6], tapsane [7], spongnane [8], valeriananes A–C [9], taxoids [10] etc. [11].

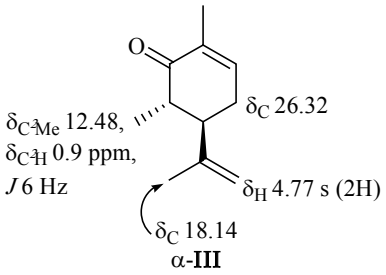
As the precursor of the target block **I** we selected the known 6,6-dimethylcarvone [12] which fundamentally like carvone [13] could be selectively epoxidized with alkaline hydrogen peroxide. The introduction of the *gem*-dimethyl group into the carvone structure was performed by the alkylation of its kinetic enolate with MeI to obtain monomethyl derivative **III** with repeating subsequently the same alkylation as described in [12].

Because of the necessity to use organometallic compounds (BuLi, LDA), to work in an inert atmosphere and at low temperature, of the prolonged alkylation stages (~12 h) the above procedure for the synthesis of compound **II** is impractical and inconvenient. We developed a version of the synthesis of compound **I** where the key stage of carvone methylation occurred under the conditions of the thermodynamic control by excess MeI using as the

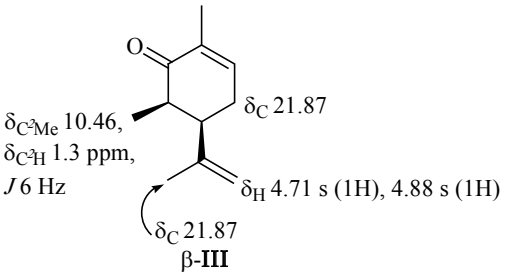
Scheme 1.



base NaH in the medium of THF–HMPA, 4 : 1, at room temperature. The reaction mixture was stirred for 10 h, then the crude product was filtered through a bed of silica gel. The products obtained are difficult to separate on SiO_2. According to the ^1H NMR data the mixture contained two main compounds, 6,6-dimethylcarvone and residual HMPA in about equal quantity. Therewith the fraction of the minor side products of the mono- and polyalkylation is also significant, but the precise quantitative estimation of their amount is difficult. The analytically pure sample of compound **II** was successfully prepared by the repeated chromatography of the mixture on a longer column packed with SiO_2. Therewith the compound less retained on silica gel than compound **II** proved to be the monomethylated product, and the present more polar compounds were not isolated. One of the possible minor compounds necessary for its identification in the mixture, the epimers of 6-methylcarvones (**III**), were prepared by procedure [14] through the kinetic alkylation of the carvone enolate with MeI. The formed 6-methylcarvone was an isomeric mixture of 6α- and 6β-methylcarvones in the ratio ~4 : 1 (from the ^1H NMR spectrum according to the integral intensity of the different signals of 6-Me). For the assignment of epimers **III** the doublet signals of the 6-methyl group are characteristic. The signal of the β-epimer is located upfield, besides, the signal of the methylene group of the α-(**III**) is a two-proton singlet, whereas the methylene group of β-(**III**) gives rise to two separate singlets.



α-**III**



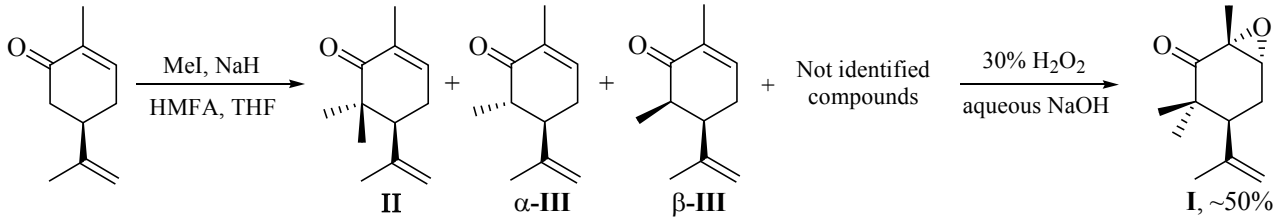
β-**III**

The comparison of the ^1H NMR spectra of the obtained mixture of the products of carvone methylation under the conditions of the thermodynamic control and of the spectrum of the methylcarvones from the model synthesis indicated the presence of the main compound **II**, minor α-(**III**) and β-(**III**) in the ratio 4 : 1, and unidentified compounds (presumably products of C^4- and O-alkylation) (Scheme 2). As seen, the ratio of isomers of the methylcarvones is approximately the same as in the products of the kinetic alkylation. The problem of isolation of individual compound **II** for using it in further reactions found an unexpected solution in the stage of the epoxidation with the alkaline hydrogen peroxide. Into this reaction we brought the mixture of compounds **II**, **III**, and the others hoping that the arising epoxy compounds would have higher R_f values and would be suitable for the separation by the column chromatography on SiO_2.

However as a result of the reaction we isolated a single individual reaction product **I**. The expected epoxide **IV** was not detected. Apparently epoxide **IV** originating from monomethyl derivative **III** and the other epoxy byproducts unlike compound **I** enolized under the reaction conditions and thus initiated intermolecular condensation processes involving compounds **III** and **IV** or led to the formation of more polar compounds of type **VI** through Faworsky intermediate **V** [15] (Scheme 3).

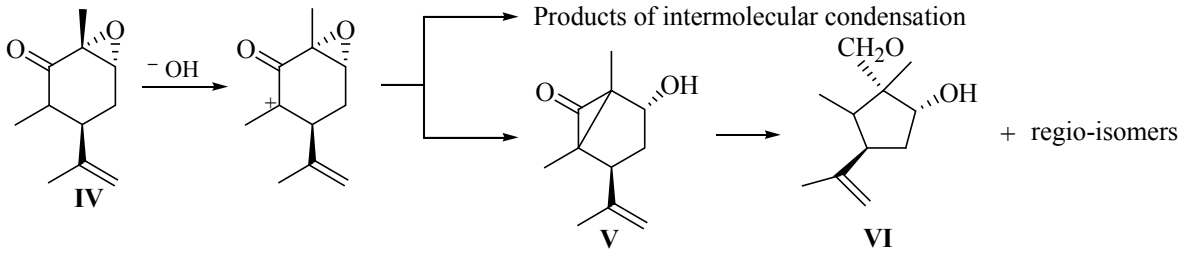
As a whole, this "self-cleaning" reaction simplified the isolation of epoxide **I**, and the elaborated route carvone → (**I**) turned out to be convenient for the pre-

Scheme 2.



II α-**III** β-**III** **I**, ~50%

Scheme 3.

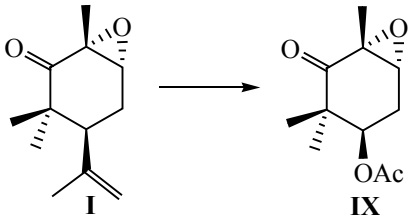


parative accumulation of a considerable quantity of this compound.

After development of the efficient synthetic way to epoxide **I** we studied its reduction with $NaBH_4$ and oxidation aiming at possible conversion of its isopropenyl fragment into an acetate group. The reduction of ketone **I** with $NaBH_4$ in MeOH occurred with a good stereoselectivity with the predominant formation of β-alcohol **VII** (Scheme 4).

The content of the minor α-alcohol **VII** was no more than 3–5%, and it was easily removed by chromatography of the mixture on SiO_2. The assumed stereochemistry of the chiral center C^2 in β-(**VII**) was confirmed by the NOE data for methyl ketone **XI** obtained from its acetate β-(**VIII**) (see the figure).

We further planned to obtain from compound **I** block **IX** promising for further application.



In the case of methyl-free analogs of compound **I** two approaches were used for the conversion of the propenyl function into the acetyl group, involving the Criegee rearrangement of ozonides [16, 17] or oxidation by Baeyer–Villiger method of methyl ketones obtained by oxidative cleavage of the propenyl part of the substrate [18].

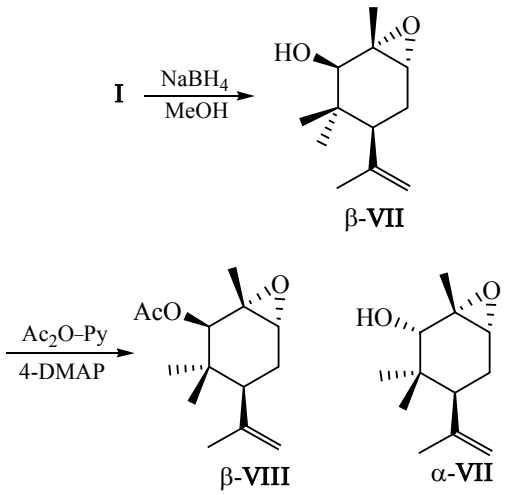
Both versions of the Criegee rearrangement of ozonides were tested on epoxiketone **I** and epoxyacetate **VIII**. However in both cases only methyl ketones **X** and **XI** were obtained (Scheme 5). We also failed to carry out the Baeyer–Villiger oxidation of methyl ketones **X** and **XI** with the use of *m*-CPBA at 20°C in CH_2Cl_2.

The application of more severe conditions (the oxidation with *m*-CPBA in boiling dichloroethane) resulted in a mixture of compounds, and the oxidation of compound **X** with the use of CF_3CO_3H (prepared as described in [19]) afforded hydration product **XII**.

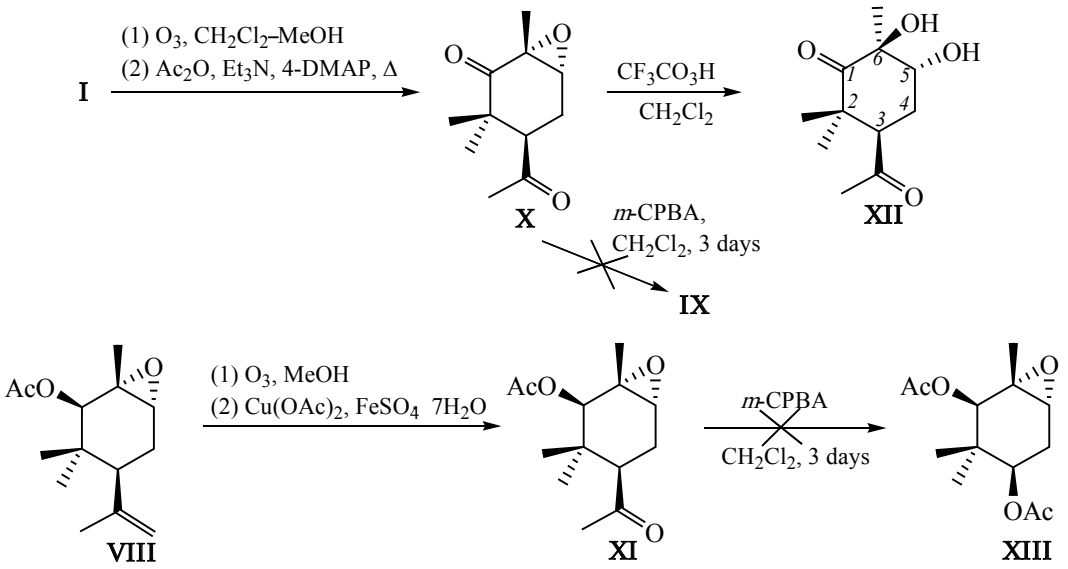
As seen, the lack of the expected products (acetates) in the Criegee rearrangement of the ozonides obtained from epoxy derivatives **I** and **VIII**, and also in the products of Baeyer–Villiger oxidation of methyl ketones **X** and **XI** with *m*-CPBA demonstrated the impeding of the desired reactions by the *gem*-dimethyl groups in the substrates. Evidently in the Criegee intermediates **XIV** leading to the acetates **IX** and **XIII** the migration of the functionalized cyclohexane substituent does not occur, and only the ejection of methyl peroxyacetyl takes place (Scheme 6).

In the absence of the *gem*-dimethyl substituents at C^6, namely, in carvone proper, the conversion of the isopropenyl group into the acetyl group can be readily performed by oxidation with *m*-CPBA of diketone **XV** obtained by the ozonolytic cleavage of known epoxide **XVI** [20].

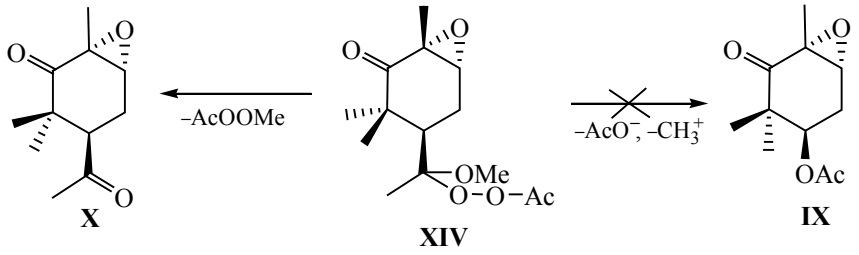
Scheme 4.

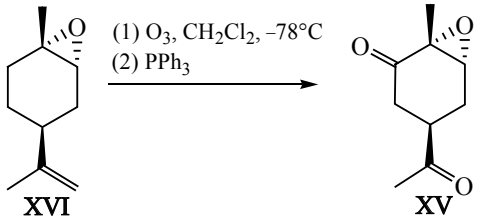


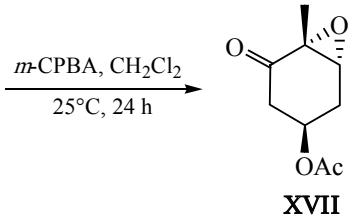
Scheme 5.



Scheme 6.







Thus we described here the preparatively convenient method of the synthesis of new functionalized *gem*-dimethyl-containing cyclohexane block from the d-carvone.

EXPERIMENTAL

IR spectra were recorded on a spectrophotometer Shimadzu IR Prestige-21 from thin films. ^{1}H and ^{13}C NMR spectra were registered on a spectrometer Bruker AM-300 at operating frequencies 300.13 and 75.47 MHz respectively, internal eference TMS. Optical rotation was measured on a polarimeter Perkin Elmer-341. Mass spectra were obtained on instruments Thermo Finnigan MAT 95XP (ionizing chamber temperature 200°C, sample admission at temperature 5–270°C, heating rate 22 deg/min) and Shimadzu LCMS-2010 (chemical ionization at atmospheric pressure) electrons energy 20eV with registration of positive and negative ions. Liquid mobile phase MeOH–water, 1 : 1, flow rate 0.03 or 0.05 ml/min. The reaction progress was monitored by TLC on Sorbfil plates (Russia), spots visualized with acidified solution of anise aldehyde.

(1*R*,4*S*,6*R*)-4-Isopropenyl-1,3,3-trimethyl-7-oxabicyclo[4.1.0]heptan-2-one (I). To a solution of

5.0 g (33.3 mmol) of *R*-carvone in 50 ml of THF–HMPA mixture, 4 : 1, at 20°C was added 6.48 g (272.11 mmol) of 55% NaH and 38.8 ml (272.11 mmol) of MeI, and the reaction mixture was stirred for 10 h. To the reaction mixture 5 ml of saturated water solution of NH_4Cl was added and then the mixture was diluted with 200 ml of EtOAc, the organic phase was washed in succession with saturated solutions of $NaHCO_3$ and NaCl, dried with Na_2SO_4, and evaporated. The residue was filtered through a bed of SiO_2, the elution with a mixture petroleum ether–EtOAc, 20 : 1. We obtained 10.5 g of the mixture of alkylation products and HMPA. To the solution of 10 g of the obtained mixture, 8.85 ml of 30% solution of H_2O_2 in 75 ml of MeOH cooled to 0°C was added 11 ml of 4.0 N NaOH solution, and the reaction mixture was stirred for 15 min at this temperature and then 10 h at room temperature. The reaction mixture was diluted with 45 ml of H_2O, extracted with CH_2Cl_2 (3 × 10 ml), the combined organic extracts were dried with $MgSO_4$, and evaporated. The residue was subjected to column chromatography on SiO_2 (eluent petroleum ether–EtOAc, 5 : 1). Yield 3.0 g (50%), colorless oily substance, $[\alpha]_D^{20}$ +77.7° (*c* 1.995, $CHCl_3$). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.96 s and 1.09 s (6H, *gem*-CH_3), 1.41 s (3H, CH_3), 1.75 s (3H, CH_3), 2.12–2.18 m (2H, CH_2), 2.54 d.d (1H, H^4, *J* 9.6, *J* 6.6 Hz), 3.37 t (1H, OCH, *J* 2.0 Hz), 4.73 s (1H) and 4.95 s (1H, =CH_2). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 16.59 (CH_3), 19.71 and 24.36 (*gem*-CH_3), 23.09 (CH_2), 26.79 (CH_2), 42.79 (C^4), 45.99 (C^3), 57.35 (C^1), 60.49 (C^6), 111.68 (=CH_2), 144.26 (C$^{1'}$), 209.11 (C^2). Mass spectrum, *m/z* (I_{rel}, %): 194 $[M]^+$ (2), 179 $[M - CH_3]^+$ (12), 166 $[M - CO]^+$ (12), 151 (23), 110 (35), 85 (46), 81 (100). Found, %: C 73.89; H 9.22. $C_{12}H_{18}O_2$. Calculated, %: C 74.19; H 9.34. *M* 194.27.

(5*S*)-5-Isopropenyl-2,6,6-trimethylcyclohex-2-en-1-one (II). The analytically pure sample of compound **II** was obtained by the repeated chromatography on column packed with SiO_2 of 0.5 g of crude mixture obtained by the methylation in the preceding experiment (eluent petroleum ether–EtOAc, 20 : 1, 15 : 1, 10 : 1). Colorless oily substance, $[\alpha]_D^{20}$ –9.3° (*c* 1.11, $CHCl_3$) {$[\alpha]_D^{25}$ +1.8° (*c* 3.8, $CHCl_3$) [12]}. IR spectrum, ν, cm^{-1}: 2970, 2924, 1701, 1670, 1451, 1377, 1358, 1201, 1039, 895, 842. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.02 s and 1.12 s (6H, *gem*-CH_3), 1.69 s (3H, CH_3), 1.75 s (3H, CH_3), 2.42 m (2H, CH, CH_2), 2.52 d.d (1H, CH_2, *J* 5.4, *J* 7.6 Hz), 4.76 s (1H) and 4.86 s (1H, =CH_2), 6.61 m (1H, =CH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 16.05 (CH_3), 18.21 and 24.45 (*gem*-CH_3), 20.35 (CH_3), 31.21 (C^4), 44.64 (C^6), 50.62 (C^5), 113.21 (=CH_2), 134.79 (C^2), 143.39 (C^3), 145.69 (C$^{1'}$), 201.77 (C^1). Found, %: C 80.48; H 10.03. $C_{12}H_{18}O$. Calculated, %: C 80.85; H 10.18.

(5*R*,5*S*)-5-Isopropenyl-2,6-dimethylcyclohex-2-en-1-one α-(III). IR spectrum, ν, cm^{-1}: 2953, 1674, 1645, 1436, 1365, 894. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.02 d (3H, CH_3, *J* 6.0 Hz), 1.68 s (3H, CH_3), 1.74 s (3H, CH_3), 2.20–2.45 m (2H) and 2.66 m (1H, CH, CH_2), 4.71 br.s (2H, =CH_2), 6.65 m (1H, H^3). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 12.48 (CH_3), 16.09 (CH_3), 18.14 (CH_3), 31.17 (C^4), 44.20 (C^6), 50.61 (C^5), 113.14 (=CH_2), 133.62 (C^2), 143.27 (C^3), 145.58 (C$^{1'}$), 201.41 (C^1).

(5*R*,6*R*)-5-Isopropenyl-2,6-dimethylcyclohex-2-en-1-one β-(III). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.89 d (3H, CH_3, *J* 6.0 Hz), 1.67 s (3H, CH_3), 1.74 s (3H, CH_3), 2.20–2.40 m (3H, CH, CH_2), 4.71 s and 4.88 s (2H, =CH_2), 6.65 m (1H, H^3). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 10.46 (CH_3), 15.92 (CH_3), 21.87 (CH_3), 26.32 (C^4), 42.98 (C^5), 44.80 (C^6), 111.52 (=CH_2), 134.69 (C^2), 143.90 (C^3), 144.80 (C$^{1'}$), 203.17 (C^1).

(1*S*,4*S*,6*R*)-4-Isopropenyl-1,3,3-trimethyl-7-oxabicyclo[4.1.0]heptan-2-ol (VII). To a dispersion of 0.15 g (3.95 mmol) of $NaBH_4$ in 5 ml of MeOH cooled to 0°C was added a solution of 0.25 g (1.30 mmol) of compound **I** in 3 ml of MeOH, and the reaction mixture was stirred at this temperature till complete consumption of the initial compound (TLC monitoring). The 2 ml of H_2O was added to the reaction mixture, methanol was evaporated, and the residue was extracted with $CHCl_3$ (4 × 5 ml). The combined extracts were washed with brine, dried with $MgSO_4$, and evaporated. The residue was subjected to chromatography on SiO_2 (eluent EtOAc–petroleum ether, 1 : 5) to obtain 0.16 g (64%) of oily compound β-(**VII**) with a small (~5%) impurity of alcohol α-(**VII**). $[\alpha]_D^{20}$ –8.1° (*c* 2.17, $CHCl_3$). IR spectrum, ν, cm^{-1}: 3408, 3078, 1722, 1445, 1444, 1375, 1207, 1080, 1061, 1031, 985, 974, 897, 882, 788, 731. Main β-isomer. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.82 s and 0.89 s (6H, *gem*-CH_3), 1.35 s (3H, CH_3), 1.74 s (3H, CH_3), 1.98 m (3H, CH, CH_2), 2.10 br.s (1H, OH), 3.09 s (1H, H^6), 3.42 d (1H, H^2, *J* 4.2 Hz), 4.72 s (1H) and 4.88 t (1H, =CH_2, *J* 1.3, *J* 1.6 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 13.38 (CH_3), 20.04 and 24.99 (*gem*-CH_3), 24.44 (CH_3), 27.94 (CH_2), 37.21 (C^3), 44.12 (C^4), 60.04 (C^1), 61.35 (C^6), 78.54 (C^2), 113.49 (=CH_2), 145.75 (C$^{1'}$). Minor α-isomer. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.84 s and 0.91 s (6H, *gem*-CH_3), 1.37 s (3H, CH_3), 1.76 s (3H, CH_3), 1.87 d (1H, CH, *J* 2.2 Hz), 1.98 m (1H, CH_2) and

1.99 d (1H, CH_2, *J* 1.9 Hz), 2.10 br.s (1H, OH), 3.09 s (1H, H^6), 3.42 d (1H, H^2, *J* 4.2 Hz), 4.72 s (1H) and 4.88 t (1H, $=CH_2$, *J* 1.3, *J* 1.6 Hz).

(1*R*,2*R*,4*S*,6*R*)-4-Isopropenyl-1,3,3-trimethyl-7-oxabicyclo[4.1.0]hept-2-yl acetate (VIII). To a stirred solution of 0.1 g (0.51 mmol) of alcohol **VII** in 5 ml of pyridine was added 0.29 ml (2.55 mmol) of acetic anhydride and 1 mg of DMAP, and the reaction mixture was stirred till complete consumption of the initial compound (TLC monitoring) (~20 h). Then the reaction mixture was diluted with 5 ml of ice water, extracted with $CHCl_3$, the extracts were dried with $MgSO_4$ and evaporated. The obtained substance was subjected to column chromatography on SiO_2 (eluent EtOAc–petroleum ether, 1 : 4). Yield 0.12 g (98%). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.77 s and 0.89 s (6H, *gem*-CH_3), 1.20 s (3H, CH_3), 1.75 s (3H, CH_3), 2.14 s (3H, $COCH_3$), 1.98 m (3H, CH, CH_2), 3.09 s (1H, H^6), 4.75 s (2H, $=CH_2$), 4.91 s (1H, H^2). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.52 (CH_3), 19.73 and 24.68 (*gem*-CH_3), 20.82 (CH_3), 24.55 (CH_3), 27.92 (CH_2), 36.51 (C^3), 43.75 (C^4), 58.49 (C^1), 60.75 (C^6), 78.85 (C^2), 113.94 ($=CH_2$), 145.22 ($C^{1'}$), 170.36 (Ac). Found, %: C 70.13; H 9.19. $C_{14}H_{22}O_3$. Calculated, %: C 70.56; H 9.30.

(1*R*,4*R*,6*R*)-4-Acetyl-1,3,3-trimethyl-7-oxabicyclo[4.1.0]heptan-2-one (X). Through a solution of 0.2 g (1.03 mmol) of compound **I** in 20 ml of the mixture of anhydrous methanol and dichloromethane, 1 : 5, at –70°C while stirring was passed the ozone-oxygen mixture till the solution turned blue. The excess O_3 was flushed from the reaction mixture by the argon flow, the reaction mixture was heated to room temperature and evaporated. The residue was dissolved in 10 ml of benzene, 1 ml of Ac_2O, 0.7 ml of triethylamine, and 2 mg of DMAP were added, the mixture was stirred for 30 min at room temperature and then boiled for 7 h. The mixture was cooled, diluted with H_2O, the water layer was extracted with EtOAc, the combined organic solutions were washed with 5% HCl, then with brine, dried with $MgSO_4$, and evaporated. The residue was subjected to column chromatography on SiO_2 (eluent EtOAc–petroleum ether, 1 : 5) Yield 0.1 g (50%). Colorless oily substance, $[\alpha]_D^{20}$ +18.8° (*c* 1.16, $CHCl_3$). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.03 s (3H, CH_3), 1.20 s and 1.42 s (6H, *gem*-CH_3), 2.18 s (3H, CH_3), 2.19–2.26 m (2H, CH_2), 2.99 d.d (1H, H^4, *J* 9.05, *J* 5.4 Hz), 3.35 t (1H, H^6, *J* 2.3 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 16.31 (CH_3), 20.09 and 22.98 (*gem*-CH_3), 23.73 (CH_2), 32.14 (CH_3), 50.02 (C^4), 44.18 (C^3), 57.47 (C^1), 59.81 (C^6), 206.59 ($C^{1'}$), 209.44 (C^2). Mass spectrum, *m/z* (I_{rel}, %): 196 $[M]^+$ (4), 168 $[M - CO]^+$ (8), 153 $[M - CH_3CO]^+$ (10), 125 $[M - CO - CH_3CO]^+$ (22), 111 (10), 83 (49), 43 (100). Found, %: C 67.66; H 8.34. $C_{11}H_{16}O_3$. Calculated, %: C 67.32; H 8.22. *M* 196.25.

(1*R*,2*R*,4*R*,6*R*)-4-Acetyl-1,3,3-trimethyl-7-oxabicyclo[4.1.0]hept-2-yl acetate (XI). Through a solution of 0.15 g (0.63 mmol) of compound **VIII** in 20 ml of the mixture of anhydrous methanol and dichloromethane in the presence of 10 mg of $NaHCO_3$ at –40°C while stirring was passes the ozone-oxygen mixture till the solution turned blue. The excess O_3 was flushed from the reaction mixture by the argon flow, at –40°C 0.25 g (1.27 mmol) of $Cu(OAc)_2$ was added, the reaction mixture was stirred for 15 min, 0.21 g (0.76 mmol) of $FeSO_4 \cdot 7H_2O$ was added, the mixture was warmed to room temperature, and the stirring was continued for 18 h. Then 5 ml of water was added, methanol was evaporated, the residue was extracted with EtOAc, the organic phase was washed in succession with saturated solutions of $NaHCO_3$ and NaCl, dried with $MgSO_4$, and evaporated. The residue was subjected to column chromatography on SiO_2 (eluent EtOAc–petroleum ether, 1 : 5). Yield 0.015 g (47%). Colorless oily substance, $[\alpha]_D^{20}$ –84.8° (*c* 0.885, $CHCl_3$). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.87 s and 0.97 s (6H, *gem*-CH_3), 1.20 s (3H, CH_3), 2.14 s (3H, $COCH_3$), 2.17 s (3H, $COCH_3$), 1.99 d.d (1H, CH_2, *J* 15.0, *J* 5.2 Hz) and 2.59 d.d (1H, CH_2, *J* 5.2, *J* 11.9 Hz), 2.09 m (1H, CH), 3.09 s (1H, H^6), 4.75 c (1H, H^2). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.38 (CH_3), 19.49 and 24.86 (*gem*-CH_3), 20.68 (CH_3), 24.40 (CH_3), 33.10 (CH_2), 35.98 (C^3), 48.92 (C^4), 58.46 (C^1), 59.96 (C^6), 77.50 (C^2), 170.50 (Ac), 210.21 (C=O). Found, %: C 65.45; H 8.30. $C_{13}H_{20}O_4$. Calculated, %: C 64.98; H 8.39.

(3*R*,5*R*,6*S*)-3-Acetyl-5,6-dihydroxy-2,2,6-trimethylcyclohexan-1-one (XII). To 1.5 ml of CH_2Cl_2 at 0°C was added 0.02 ml of H_2O_2, 0.1 ml of trifluoroacetic anhydride, the mixture was stirred for 10 min, then a solution was added of 0.03 g of epoxide **X** in 0.5 ml of CH_2Cl_2, and the stirring was continued for 10–15 min at this temperature. The reaction mixture was diluted with CH_2Cl_2, was washed in succession with saturated solutions of $NaHCO_3$ and NaCl, dried with $MgSO_4$, and evaporated. The residue was subjected to column chromatography on SiO_2 (eluent EtOAc–petroleum ether, 1 : 5). Yield 0.015 g (47%). Colorless oily substance, $[\alpha]_D^{20}$ +16.4° (*c* 0.787, $CHCl_3$). ^{1}H NMR spectrum ($CDCl_3$), δ,

ppm: 1.10 s (3H, CH_3), 1.28 s and 1.35 s (6H, *gem*-CH_3), 2.07 d.d (1H, CH_2, *J* 5.4, *J* 3.1 Hz), 2.14 d.d (1H, CH_2, *J* 11.8, *J* 5.2 Hz), 2.22 s (3H, CH_3), 2.98 d.d (1H, H^3, *J* 5.4, *J* 3.4 Hz), 2.62 br.s (1H, OH), 3.93 d.d (1H, H^5, *J* 5.4, *J* 11.9 Hz), 4.13 br.s (1H, OH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 21.91 and 26.22 (*gem*-CH_3), 23.73 (CH_3), 27.26 (C^4), 30.95 (CH_3), 44.16 (C^2), 56.63 (C^3), 73.07 (C^5), 79.92 (C^6), 209.88 (C^1), 214.65 ($C^{1'}$).

(1*R*,4*R*,6*R*)-4-Acetyl-1-methyl-7-oxabicyclo-[4.1.0] heptan-2-one (XV). Through a solution of 2 g (12.0 mmol) of epoxycarvone **XVI** obtained from d-(–)-carvone [20] in 40 ml of MeOH at –78°C while stirring was passed the ozone-oxygen mixture till the solution turned blue. The excess O_3 was flushed from the reaction mixture by the argon flow, 3.30 g (12.6 mmol) of PPh_3 was added, the temperature was raised to ambient, and the stirring was continued for 3 h. Then the solvent was distilled off, and the residue was distilled at 128–130°C (4 mm Hg). Yield 1.29 g (64%). Viscous light-yellow fluid. IR spectrum, ν, cm^{-1}: 2984, 2934, 1712. ^1H NMR spectrum ($CDCl_3$) δ, ppm: 1.38 s (3H, CH_3), 1.91–1.99 m (1H, CH_2), 2.15 s (3H, CH_3), 2.19–2.25 m (1H, CH_2), 2.44–2.48 m (1H, CH_2), 2.59 d.d (1H, CH_2, *J* 3.2, *J* 18.1 Hz), 3.04–3.13 m (1H, H^6), 3.42–3.43 m (1H, H^4). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 15.06 (CH_3), 25.80 (C^5), 28.23 (CH_3), 37.53 (C^3), 41.83 (C^4), 58.96 (C^1), 60.55 (C^6), 203.84 (C=O), 208.23 (C=O).

(1*R*,4*R*,6*R*)-1-Methyl-2-oxo-7-oxabicyclo-[4.1.0] hept-4-yl acetate (XVII). To a solution of 0.5 g (2.98 mmol) of epoxide **XV** in 30 ml of CH_2Cl_2 was added 5.9 g (23.8 mmol) of 70% *m*-CPBA, the mixture was stirred for 48h at room temperature. Then 1.5 ml of Me_2S was added, the reaction mixture was washed with a saturated solution of $NaHCO_3$, and extracted with CH_2Cl_2. The extract was evaporated, the residue was subjected to column chromatography on SiO_2 (eluent EtOAc–petroleum ether, 1 : 1). Yield 0.36 g (66%). Colorless crystals, mp 84–86°C, $[\alpha]_D^{20}$ +18.1° (*c* 1.98, $CHCl_3$). IR spectrum, ν, cm^{-1}: 1740, 1720, 1242, 1040. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.44 s (3H, CH_3), 2.03 s (3H, CH_3), 2.10–2.16 m (1H, CH_2), 2.33 d.d (1H, CH_2, *J* 6.2, *J* 15.7 Hz), 2.54 d.d (1H, CH_2, *J* 4.4, *J* 15.9 Hz), 2.96 d.d (1H, CH_2, *J* 3.54, *J* 15.7 Hz), 3.44 s (1H, H^6), 5.24–5.26 m (1H, H^4). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.67 (CH_3), 20.99 (CH_3), 29.37 (C^5), 40.84 (C^3), 59.38 (C^1), 61.81 (C^6), 69.40 (C^4), 169.83 (C=O), 203.97 (C^2). Found, %: C 59.01; H 6.80. $C_9H_{12}O_4$. Calculated, %: C 58.69; H 6.57.

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