Synthetic approaches to homochiral bicyclo[5.2.1]decanes based on *d*-camphor

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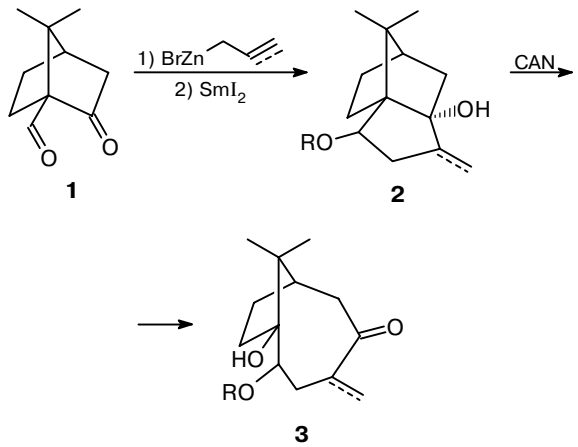
The Reformatsky reaction of bornanic enone (10-nor-1-vinylcamphor) with ethyl iodoacetate followed by iodocyclization afforded tricyclic iodolactone. Fragmentation of the latter initiated by $HgO—I_2$ gave rise to bicyclic iodoxolactone. Attempts to perform cyclization of this iodoxolactone analogously to intramolecular alkylation of CH-acids with halogen-containing electrophiles failed.

Key words: bornenone, the Reformatsky reaction, iodolactonization, hypoiodite, fragmentation, bicyclic lactone.

Previously, we have used ketopinic aldehyde (**1**) as the starting compound for the synthesis of new *ortho*-fused tricyclic bornane derivatives (**2**) whose further fragmentation afforded bicyclic compounds (**3**)[1,2] (Scheme 1). The latter are of interest as potential chiral synthetic blocks for the construction of taxoids.[3,4]

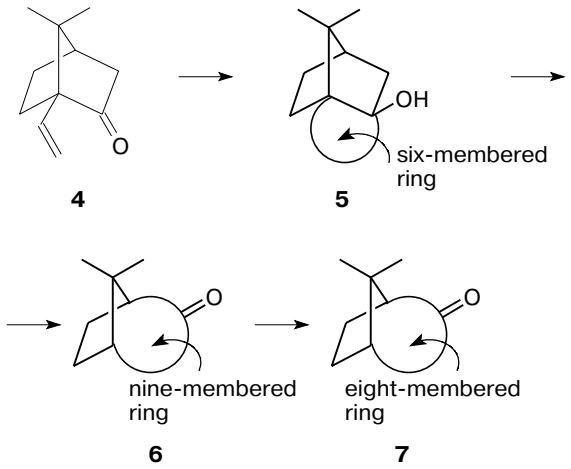
Scheme 1



CAN is cerium ammonium nitrate

However, this approach to compounds **3** has essential limitations[2] in the stage of annelation of dione **1** giving rise to sterically strained tricyclic derivatives **2**. Hence, in the present work we examined the effectiveness of alternative approaches to functionalized bicyclo[5.2.1]decanes analogous to compounds of the type **3**. In particular, starting from the available ketone (**4**)[5] we intended to construct tricyclic structures (**5**), which are sterically less hindered than **2**, and to perform subsequent transformation of compounds **5** into bicycles (**6**) followed by contraction of the nine-membered ring of the latter to the eight-membered ring (transformation **6** → **7**) (Scheme 2).

Scheme 2



Results and Discussion

The procedure developed by us for the synthesis (Scheme 3) of one of representatives of compounds **5**, *viz.*, of lactone (**10**), involves the formation of hydroxy ester (**8**) from ketone **4** by the Reformatsky reaction, saponification of **8** yielding acid (**9**), and iodolactonization of the latter. In this approach to tricyclic compound **10**, the specific features of the preparation of Reformatsky adduct **8** is worthy of note. Attempts to synthesize hydroxy ester **8** even under forced conditions[6] (activated Zn—Cu or Zn—Ag pairs, ethyl bromoacetate, THF or DMF, heating) failed. The slow formation of hydroxy ester **8** was observed only in benzene with the use of non-distilled ICH_2CO_2Et (apparently, traces of I_2 that

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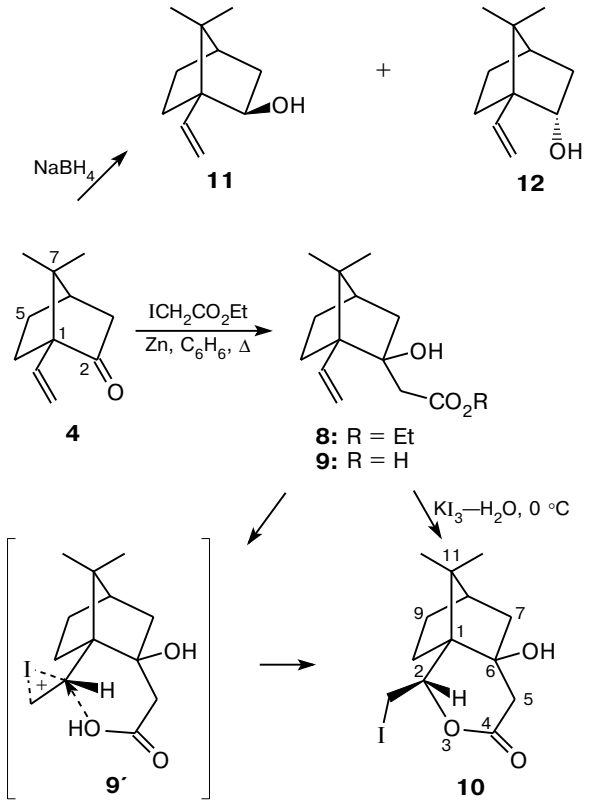
present acted as a promoter) and a Zn powder. However, the formation of compound **8** ceased when the conversion of ketone **4** reached 60—70%. Fortunately, no by-products formed in the course of this rather prolonged process. Due to the fact that the mobilities of ketone **4** and reaction product **8** on SiO_2 are comparable, it was difficult to separate these compounds by column chromatography. Hence, the initial ketone was regenerated from the (**4** + **9**) mixture in the stage of alkaline hydrolysis by extraction with ethyl acetate.

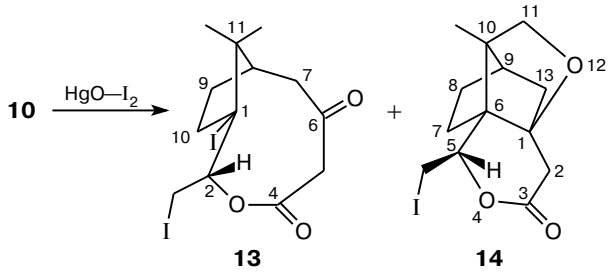
Scheme 3



In the stage of the Reformatsky reaction, the attack of the nucleophile ($IZnCH_2CO_2Et$) from the sterically less hindered α-side of molecule **4** led to the stereospecific formation of *exo*-alcohol **8** (for analogous examples, see Refs. 7—9). In this connection, it should be noted that even a non-stereodifferentiating reducing agent, such as $NaBH_4$, reacted with ketone **4** to give predominantly *exo*-alcohol (**11**) (**11** : **12** = 9 : 1). Iodolactonization of acid **9** also appeared to proceed streospecifically giving rise to lactone **10** *via* probable intermediate **9′**. The stereochemistry of the new chiral center was confirmed by NOE experiments performed for one of transformation products of lactone **10** (see below).

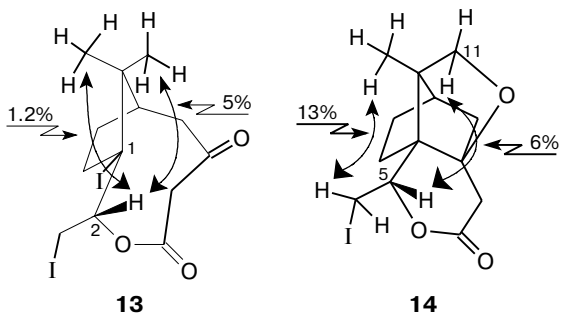
Once tertiary alcohol **10** has been prepared according to a rather feasible procedure, we turned to the examination of the possibilities of its fragmentation. Cerium ammonium nitrate (CAN) used for performing the conversion **2** → **3** did not initiate the expected reaction in the case of compound **10**. The application of a feasible procedure to the generation of alkoxyl radicals *via* hypoiodites[10] proved to be successful. In this case, lactone **10** was rapidly converted into a mixture of compounds **13** and **14** in a ratio of 3 : 1 in a total yield of 85% (Scheme 4). The reaction of lactone **10** with $Pb(OAc)_4$—I_2 proceeded analogously. The formation of by-product **14** in the course of fragmentation of lactone **10** can be considered as an unusual example of C(8)-functionalization of camphor.[11]

Scheme 4



The structure of compound **14** was confirmed by the data from 2D correlation NMR spectra (^1H—^1H and ^{13}C—^1H). Thus based of the ^{13}C—^1H correlation spectra, the two-proton multiplet signal at δ 3.32 (^1H) and the signal at δ 3.16 (^{13}C) were assigned to the CH_2I group. Analogously, the signal for the proton of the C(5)H group (δ 4.78, dd) in the ^1H NMR spectrum has a cross-peak with the doublet signal for the C(5) atom at δ 80.07 in the ^{13}C NMR spectrum. The doublet signals at δ 3.71 and 3.59 in the ^1H NMR spectrum were assigned to the $C(11)H_2$ fragment based on the presence of cross-peaks with the triplet signal for C(11) at δ 70.82.

In addition, the structures of compounds **13** and **14** were confirmed by ^1H NMR spectroscopy. The data from NOE experiments indicate that the protons of the CH_2I group in compound **14** are located in proximity to the methyl group. Irradiation of the methine proton at the C(5) atom gave NOE for *endo*-C(11)H. The results of the NOE experiments also confirmed the (*R*) configuration of the C(2) chiral center of compound **13** and, consequently, the (*S*) configuration of this center in its precursor, *viz.*, in lactone **10**.



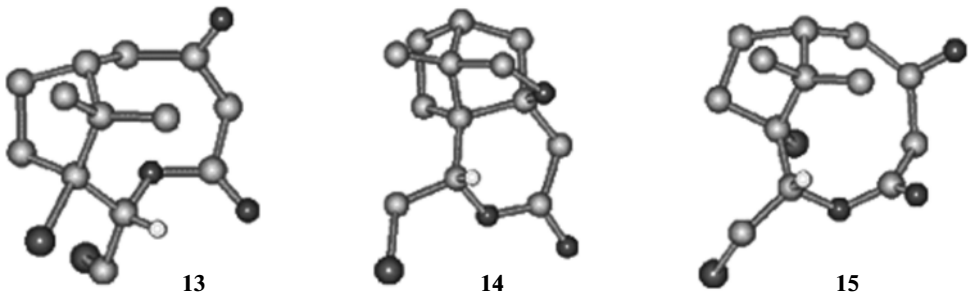


Fig. 1. Low-energy conformers of compounds **13—15**.

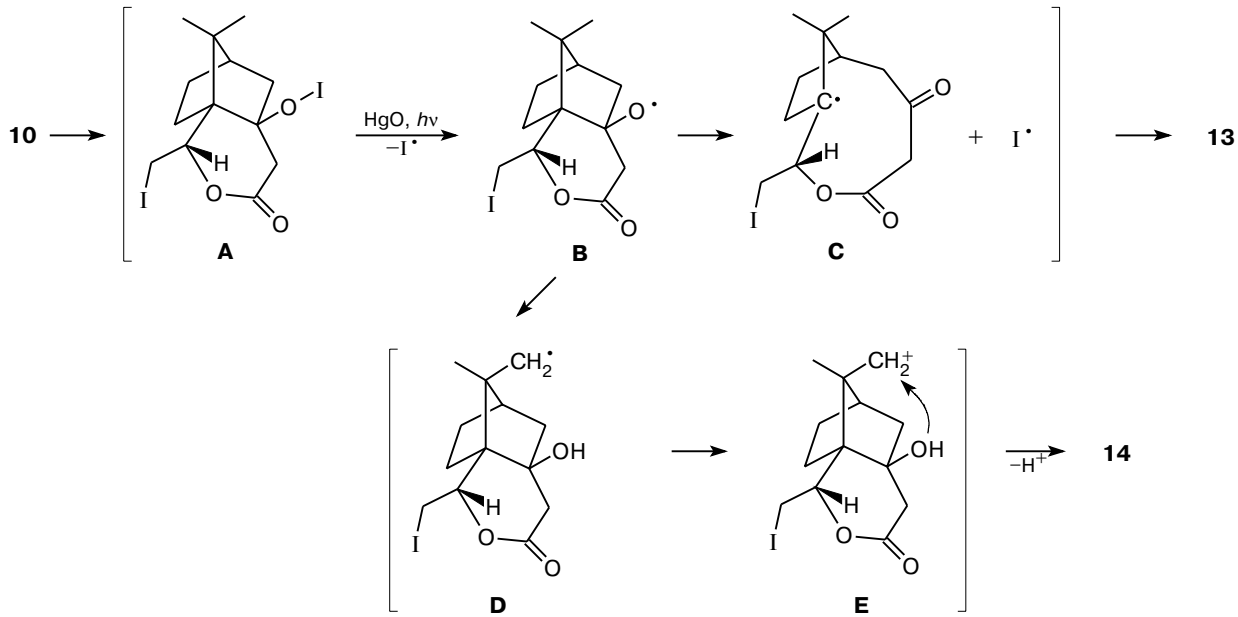
The data from the NOE experiments for compound **13** are indicative of the *exo* orientation of the I atom at C(1). According to the results of calculations by the MNDO method (HyperChem), the distances between the H—C(2) fragment and the *endo*- and *exo*-C(11) methyl groups in the minimum-energy conformation of compound **13** have different values (2.58 and 4.08 Å, respectively), whereas these distances in the low-energy conformer of the *endo*-C(1)—I diastereomer (structure **15**) differ only slightly (2.97 and 2.88 Å, respectively). The nuclear Overhauser effects on the CH_3 groups observed for compound **13** upon irradiation of H—C(2) are sufficiently different, which provides evidence in favor of the proposed structure.

Bicyclic lactone **13** is of particular interest. The signal for one of the bridging *gem*-dimethyl groups in its ^{13}C NMR spectrum has an extraordinarily large downfield shift. This signal was not observed in the region δ 18—22 typical of such compounds. The 2D heteronuclear $^{13}C—^{1}H$ correlation NMR spectrum of compound **13** demonstrated that the signals at δ 1.05 (^{1}H) and 18.89 (^{13}C) belong to one methyl group, whereas the signals at δ 1.40 (^{1}H) and 42.37 (^{13}C) belong to another methyl group. Noteworthy are the upfield shifts of the signals for CH_3 and C(7) in the ^{13}C NMR spectrum of compound **14** (for example, $\delta_{C(10)} = 16$; for comparison, the signal for this C atom in lactone **10** is observed at δ 25), which are associated with further flattening of the molecule and an increase in the steric *gauche* interactions of the C(7) atom with CH_2I and the O atom of the ester group (Fig. 1).

The probable mechanism of formation of compounds **13** and **14** is shown in Scheme 5.

In the $HgO—I_2$ system, alcohol **10** rapidly produced hypoiodite **A** from which the key alkoxyl radical **B** was smoothly formed upon irradiation. The homolytic cleavage of the bridging C—C—O bond afforded radical **C**. In spite of the rigidity of bicyclic structure **C**, its radical center underwent inversion giving rise to sterically favorable *exo*-C(1)—I derivative **13**. Due to the short distance between the O-centered radical and the *syn*-methyl group in intermediate **B**, the abstraction of the proton proceeded as a concurrent reaction to generate new radical **D**, which was oxidized to form cation **E**. The latter

Scheme 5

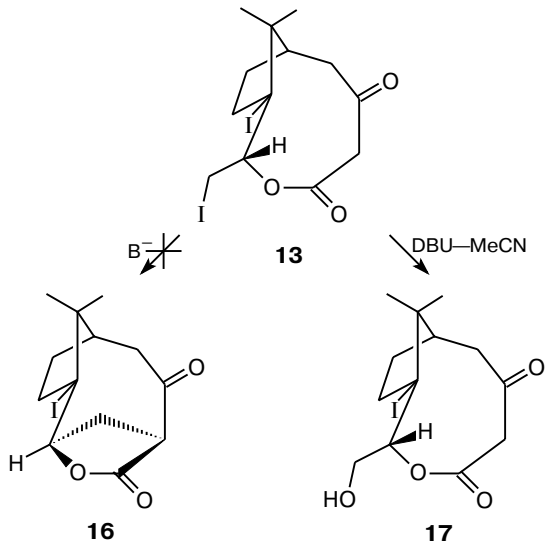


underwent intramolecular cyclization with elimination of H^+ giving tetracyclic compound **14**.

In the final stage of the present investigation, we attempted to perform the contraction of the nine-membered ring to the eight-membered ring suggested in Scheme 1 with the aim of preparing compounds of the type **7**. The resulting iodomethyllactone **13** seemed to be a suitable substrate for controlled intramolecular alkylation involving the CH_2I group and the methylene group of the β-oxoester fragment.

Analysis of the molecular model of compound **13** demonstrated that the intramolecular attack of the C(5)-carbanion on the CH_2I substituent can occur and requires only insignificant conformational changes in its nine-membered fragment. However, attempts to perform the transformation **13** → **16** with the use of NaH as a base in THF at 0 °C afforded a complex mixture of unidentified products, whereas the reaction with the use of DBU in MeCN in air led only to hydrolysis of the iodomethyl group of molecule **13** to form hydroxy oxo lactone **17** (Scheme 6).

Scheme 6



To summarize, it should be noted that we failed to obtain the desired compounds of the type **7**. Nevertheless, the strategy and the realized fragmentation of compound **10** yielding macrocyclic lactone **13** are of obvious synthetic interest. Probable alternative approaches to the desired compounds based on lactone **10** are being examined at our laboratory.

Experimental

The IR spectra were recorded on a UR-20 spectrophotometer in a thin layer or as a suspension. The ^1H and ^{13}C NMR spectra were measured on a Bruker AM-300 spectrometer (300 MHz for ^1H and 75.47 MHz for ^{13}C) in $CDCl_3$ with Me_4Si as the internal standard. Column chromatography was carried out on silica gel L 100/160 (Lachema). The TLC analysis was performed with the use of chromatographic Silufol plates. The optical rotation was measured on a Perkin—Elmer instrument. The mass spectra (EI) were recorded on an MX-1320 instrument (70 eV); the temperature of the ionization chamber was 60—90 °C.

(1*S*,2*S*,4*R*)-2-Carboxymethyl-2-hydroxy-7,7-dimethyl-1-vinylbicyclo[2.2.1]heptane (9). ICH_2CO_2Et (39.09 g, 182.66 mmol) was added to a mixture of ketone **4** (10.00 g, 60.89 mmol) and Zn (16.66 g, 182.66 mg-at.) in benzene (300 mL). The reaction mixture was refluxed with stirring for 8 h, cooled, and treated with 10% H_2SO_4 (30 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc. The combined extracts were dried with Na_2SO_4 and concentrated. Chromatography of the residue on SiO_2 (hexane—ethyl acetate, 10 : 1) afforded a mixture of **ethyl [(1*S*,2*S*,4*R*)-2-hydroxy-7,7-dimethyl-1-vinylbicyclo[2.2.1]hept-2-yl]acetate (8)** and the initial ketone, R_f = 0.82 (hexane—ethyl acetate, 7 : 3). **Compound 8**. ^1H NMR, δ: 6.15 (dd, 1 H, HC=, J = 17.7 and 11.0 Hz); 5.20 (dd, 1 H, H_2C=, J = 11.0 and 2.1 Hz); 4.97 (dd, 1 H, H_2C=, J = 17.7 and 2.1 Hz); 4.10 (q, 2 H, CH_2CH_3, J = 7.1 Hz); 3.85 (s, 1 H, OH); 2.50 (d, 1 H, CH_2CO_2, J = 14.1 Hz); 2.43 (d, 1 H, CH_2CO_2, J = 14.1 Hz); 2.20 (m, 2 H); 1.70 (m, 1 H); 1.45 (m, 4 H); 1.25 (t, 3 H, $CH_2C\underline{H}_3$, J = 7.2 Hz); 1.20 (s, 3 H, CH_3); 0.78 (s, 3 H, CH_3). ^{13}C NMR, δ: 14.08, 20.94, and 21.63 (all CH_3); 25.40 (C(5)); 26.50 (C(6)); 43.45 ($\underline{C}H_2CO_2$); 45.59 (C(4)); 47.05 (C(3)); 50.70 (C(7)); 58.76 (C(1)); 60.58 ($\underline{C}H_2O$); 80.39 (C(2)); 116.59 and 136.28 (CH_2=CH); 173.31 (CO_2). The resulting oily mixture (**4** + **8**) was dissolved in MeOH (20 mL) and a 0.25 *M* aqueous solution of NaOH (20 mL) was added. The reaction mixture was stirred at 20 °C. The course of the reaction was monitored by TLC. After completion of the reaction, the mixture was diluted with water, MeOH was evaporated, and the aqueous layer was extracted with EtOAc. The extract was concentrated and ketone **4** was obtained in a yield of 3 g. The aqueous layer was acidified with 10% H_2SO_4 to pH 3 and extracted with EtOAc. The combined extracts were dried with Na_2SO_4 and concentrated. Compound **9** was obtained in a yield of 7.51 g (55%). Found (%): C, 69.53; H, 8.86. $C_{13}H_{20}O_3$. Calculated (%): C, 69.61; H, 8.99. R_f = 0.38 (hexane—ethyl acetate, 7 : 3), m.p. 85—86 °C, $[\alpha]_D^{15}$ −37 (*c* 10, $CHCl_3$). IR, ν/cm^{-1}: 1640, 1720, 3430. ^1H NMR, δ: 6.14 (dd, 1 H, HC=, J = 17.8 and 11.0 Hz); 5.19 (dd, 1 H, H_2C=, J = 11.0 and 2.4 Hz); 5.02 (dd, 1 H, H_2C=, J = 17.8 and 2.4 Hz); 3.35 (br.s, CO_2H); 2.43 (d, 1 H, CH_2CO_2, J = 14.1 Hz); 2.50 (d, 1 H, CH_2CO_2, J = 14.1 Hz); 2.20 (m, 1 H); 2.05 (br.s, 1 H, OH); 1.70—1.82 (m, 3 H); 1.58 (d, 1 H, C(3)H_a, J = 13.2 Hz); 1.40 (m, 1 H); 1.23 (s, 3 H, CH_3); 1.10 (m, 1 H); 0.88 (s, 3 H, CH_3). ^{13}C NMR, δ: 20.32 and 21.14 (both CH_3); 24.78 (C(5)); 25.85 (C(6)); 42.07 ($\underline{C}H_2CO_2$); 45.43 (C(4)); 46.14 (C(3)); 50.03 (C(7)); 58.42 (C(1)); 79.28 (C(2)); 115.61 and 136.36 (CH_2=CH); 174.17 (CO_2).

(1*R*,2*S*,6*S*,8*R*)-2-Iodomethyl-11,11-dimethyl-4-oxo-3-oxatricyclo[6.2.1.0^{1,6}]undecan-6-ol (10). A solution of KI (43.96 g, 264.80 mmol) and I_2 (21.48 g, 84.63 mmol) in water (50 mL) was added to a solution of compound **9** (5.4 g, 27.86 mmol) and NaOH (1.05 g, 30.24 mmol) in water (250 mL) neutralized with 10% H_2SO_4 to pH 7 at 0 °C. The resulting dark reaction mixture was stirred at 0 °C for 30 min and $CHCl_3$ (100 mL) was added. Then solid $Na_2S_2O_3$ was added portionwise until the solution became colorless. The product was extracted with $CHCl_3$ (3×100 mL). The combined extracts were washed with a saturated aqueous solution of NaCl, dried with Na_2SO_4, filtered, and concentrated. The residue was purified on SiO_2 (hexane—ethyl acetate, 10 : 1). The yield of lactone **10** was

6.0 g (62%). Found (%): C, 44.36; H, 5.35; I, 36.45. $C_{13}H_{19}IO_3$. Calculated (%): C, 44.59; H, 5.47; I, 36.24. R_f = 0.21 (hexane—ethyl acetate, 7 : 3), m.p. 126—127 °C, $[\alpha]_D^{20}$ +33 (*c* 10, $CHCl_3$). IR, ν/cm^{-1}: 1720, 3430. ^{1}H NMR, δ: 5.18 (dd, 1 H, C(2)H, *J* = 10.3 and 2.3 Hz); 3.40 (dd, 1 H, CH_2I, *J* = 10.5 and 2.3 Hz); 3.25 (t, 1 H, CH_2I, *J* = 10.5 Hz); 3.00 (br.s, 1 H, OH); 2.84 (d, 1 H, CH_2CO_2, *J* = 18.4 Hz); 2.73 (d, 1 H, CH_2CO_2, *J* = 18.4 Hz); 2.10 (m, 1 H); 1.70—1.80 (m, 3 H); 1.45 (d, 1 H, C(7)H_a, *J* = 11.7 Hz); 1.30 (m, 1 H); 1.28 (s, 3 H, CH_3); 1.10 (m, 1 H); 1.05 (s, 3 H, CH_3). ^{13}C NMR, δ: 3.96 (CH_2I); 22.41 and 22.57 (both CH_3); 23.46 (C(9)); 25.91 (C(10)); 44.45 (C(5)); 44.80 (C(7)); 47.91 (C(8)); 48.33 (C(11)); 53.93 (C(1)); 78.34 (C(2)); 81.34 (C(6)); 17.05 (C(4)).

(*1S*,2*R*,4*R* and 1*S*,2*S*,4*R*)-7,7-Dimethyl-1-vinylnorbornan-2-ols (11 and 12). A solution of compound **4** (1 g, 6.09 mmol) in EtOH (10 mL) was added to a solution of $NaBH_4$ (0.23 g, 6.09 mmol) in EtOH (20 mL). The mixture was stirred for 3 h. After standard workup, epimers **11** and **12** were isolated by column chromatography on SiO_2 (hexane—ethyl acetate, 10 : 1). Alcohols **11** and **12** were obtained in yields of 0.88 g (87%) and 0.09 g (9%), respectively. **Compound 11.** R_f = 0.74 (hexane—ethyl acetate, 7 : 3), $[\alpha]_D^{20}$ −40 (*c* 5, $CHCl_3$). IR, ν/cm^{-1}: 1640, 3430. ^{1}H NMR, δ: 5.80 (dd, 1 H, *J* = 17.5 and 10.9 Hz), 5.20 (dd, 1 H, *J* = 1.8 and 10.9 Hz), 5.05 (dd, 1 H, *J* = 1.8 and 17.5 Hz) (CH=CH_2); 4.30 (m, C(2)H); 2.30 and 2.00 (both m, 1 H each); 1.50—1.85 (m, 4 H); 1.30 (m, 1 H); 1.05 (dd, 1 H, C(6)H, *J* = 3.5 and 13.3 Hz); 0.93 and 0.83 (both s, 3 H each, CH_3). ^{13}C NMR, δ: 18.95 and 20.48 (both CH_3); 22.68 (C(5)); 28.19 (C(6)); 38.28 (C(3)); 45.67 (C(4)); 49.94 (C(7)); 56.79 (C(1)); 75.06 (C(2)); 116.32 and 138.21 (CH=CH_2). MS, *m/z*: 166 $[M]^{+\cdot}$, 148 $[M - H_2O]^{+\cdot}$ (maximum); 133 $[M - H_2O - CH_3]^{+\cdot}$. **Compound 12,** R_f = 0.66 (hexane—ethyl acetate, 7 : 3). $[\alpha]_D^{20}$ +32 (*c* 5, $CHCl_3$). IR, ν/cm^{-1}: 1640, 3410. ^{1}H NMR, δ: 6.00 (dd, 1 H, *J* = 11.0 and 17.8 Hz), 5.26 (dd, 1 H, *J* = 2.0 and 11.0 Hz), 5.10 (dd, 1 H, *J* = 2.0 and 17.8 Hz) (CH=CH_2); 3.70 (dd, 1 H, 2-H, *J* = 3.7 and 7.7 Hz); 2.10 (br.s, 1 H, OH); 1.60—1.85 (m, 6 H); 1.05 (m, 1 H); 1.10 and 0.87 (both s, 3 H each, CH_3). ^{13}C NMR, δ: 20.42 and 20.60 (both CH_3); 27.15 (C(5)); 29.95 (C(6)); 40.33 (C(3)); 45.55 (C(4)); 47.60 (C(7)); 5.63 (C(1)); 80.30 (C(2)); 116.80 and 137.00 (CH=CH_2).

(1*S*,2*R*,8*R*)-1-Iodo-2-iodomethyl-11,11-dimethyl-3-oxabicyclo[6.2.1]undecane-4,6-dione (13) and (1*S*,5*S*,6*S*,9*R*,10*S*)-5-iodomethyl-10-methyl-4,12-dioxatetracyclo[7.3.1.0^{1,6}.0^{6,10}]tridecan-3-one (14). A mixture of lactone **10** (1.00 g, 2.86 mmol), HgO (8.53 g, 39.41 mmol), and I_2 (8.55 g, 33.70 mmol) in CCl_4 (150 mL) was refluxed and irradiated with UV light (a PRK-4 ultraviolet lamp) for 5 min and then filtered. The filtrate was concentrated and the residue was chromatographed on SiO_2 (hexane—ethyl acetate, 10 : 1). Compounds **13** and **14** were obtained in yields of 0.88 g (65%) and 0.23 g (23%), respectively. **Compound 13.** Found (%): C, 32.73; H, 3.90; I, 53.30. $C_{13}H_{17}IO_3$. Calculated (%): C, 32.80; H, 3.81; I, 53.31. R_f = 0.78 (hexane—ethyl acetate, 7 : 3), m.p. 98—100 °C, $[\alpha]_D^{20}$ +22 (*c* 10, $CHCl_3$). IR, ν/cm^{-1}: 1710, 1765. ^{1}H NMR, δ: 5.42 (dd, 1 H, C(2)H, *J* = 1.8 and 9.0 Hz); 4.32 (dd, 1 H, CH_2I_2, *J* = 1.8 and 11.0 Hz); 3.44 (d, 1 H, C(5)H_a, *J* = 17.0 Hz); 3.41 (dd, 1 H, CH_2I, *J* = 9.0 and 11.0 Hz); 3.38 (d, 1 H, C(5)H_b, *J* = 17.0 Hz); 2.80 (m, 1 H); 2.40—2.60 (m, 4 H); 1.90 and 1.75 (both m, 1 H each); 1.40 and 1.05 (both s, 3 H each, CH_3). ^{13}C NMR, δ: 4.96 (CH_2I); 18.89 (CH_3); 27.13 (C(9)); 36.46 (C(10)); 42.03 (C(8)); 42.37 (CH_3); 42.80 (C(7)); 50.58 (C(5)); 51.10 (C(11)); 67.33 (C(1)); 79.94 (C(2)); 165.53 (C(4)); 201.90 (C(6)). MS, *m/z*: 476 $[M]^+$, 348 [M − HI], 331, 321 $[M - HI - I^-]^+$, 203, 179, 169, 128 $[HI]^+$, 127 $[I]^+$. **Compound 14.** Found (%): C, 44.69; H, 4.85; I, 36.63. $C_{13}H_{17}IO_3$. Calculated (%): C, 44.84; H, 4.92; I, 36.45. R_f = 0.22 (hexane—ethyl acetate, 7 : 3), m.p. 108—110 °C, $[\alpha]_D^{20}$ +92 (*c* 10, $CHCl_3$). IR, ν/cm^{-1}: 1120, 1735. ^{1}H NMR, δ: 4.78 (d, 1 H, C(5)H, *J* = 9.8 Hz); 3.71 (d, 1 H_a, CH_2O, *J* = 8.6 Hz); 3.59 (d, 1 H_b, CH_2O, *J* = 8.6 Hz); 3.32 (dd, 1 H_b, CH_2I, *J* = 9.8 and 2.3 Hz); 3.25 (dd, 1 H_a, CH_2I, *J* = 9.8 and 2.3 Hz); 2.86 and 2.67 (both d, 1 H each, C(2)H, *J* = 18.9 Hz); 1.70—2.05 (m, 4 H); 1.10—1.40 (m, 3 H); 1.05 (s, 3 H, CH_3). ^{13}C NMR, δ: 3.16 (CH_2I); 13.26 (CH_3); 16.72 (C(7)); 29.11 (C(8)); 34.20 (C(2)); 39.65 (C(13)); 44.86 (C(9)); 53.67 (C(6)); 54.75 (C(10)); 70.82 (C(11)); 80.07 (C(5)); 87.46 (C(1)); 168.74 (CO_2).

(1*S*,2*R*,8*R*)-2-Hydroxymethyl-1-iodo-11,11-dimethyl-3-oxabicyclo[6.2.1]undecane-4,6-dione (17). A solution of compound **13** (200 mg, 0.42 mmol) and DBU (0.13 mL, 0.84 mmol) in MeCN (10 mL) was stirred at 20 °C for 2 days. Then the reaction solution was concentrated and the residue was chromatographed on SiO_2 (hexane—ethyl acetate, 10 : 1). Oily compound **17** was obtained in a yield of 104 mg (68%). Found (%): C, 42.43; H, 5.14; I, 34.80. $C_{13}H_{19}IO_4$. Calculated (%): C, 42.62; H, 5.23; I, 34.66. R_f = 0.24 (hexane—ethyl acetate, 7 : 3), $[\alpha]_D^{20}$ +43 (*c* 9, $CHCl_3$). IR, ν/cm^{-1}: 1710, 1760, 3635. ^{1}H NMR, δ: 5.22 (dd, 1 H, C(2)H, *J* = 2.3 and 7.5 Hz); 4.60 (dd, 1 H, CH_2O, *J* = 2.5 and 12.2 Hz); 3.90 (dd, 1 H, CH_2O, *J* = 7.5 and 12.5 Hz); 3.48 (d, 1 H, C(5)H_a, *J* = 17.4 Hz); 2.80 (m, 2 H); 2.40—2.55 (m, 3 H); 2.33 (br.s, 1 H, OH); 1.60—1.90 (m, 2 H); 1.43 (s, 3 H, CH_3); 1.20 (m, 1 H); 1.00 (s, 3 H, CH_3). ^{13}C NMR, δ: 19.25 (CH_3); 27.29 (C(10)); 31.67 (C(9)); 41.05 (CH_3); 42.87 (C(8)); 43.15 (C(7)); 50.35 (C(5)); 51.03 (C(11)); 63.78 (C(1)); 65.12 (CH_2O); 81.18 (C(2)); 166.93 (CO_2); 202.71 (C(6)).

References

1. I. N. Gaisina, O. V. Tikhonov, N. K. Selezneva, A. V. Abutkov, A. A. Fatykhov, L. V. Spirikhin, and M. S. Miftakhov, *Zh. Org. Khim.*, 1999, **35**, 1020 [*Russ. J. Org. Chem.*, 1999, **35** (Engl. Transl.)].
2. I. N. Gaisina, N. G. Komissarova, N. K. Selezneva, A. V. Abutkov, R. R. Muslukhov, and M. S. Miftakhov, *Zh. Org. Khim.*, 1999, **35**, 1025 [*Russ. J. Org. Chem.*, 1999, **35** (Engl. Transl.)].
3. K. C. Nicolaou, W.-M. Dai, and R. K. Guy, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 15.
4. C. S. Swindell, *Org. Prep. Proc. Int.*, 1991, **23**, 465.
5. N. Fischer and G. Opitz, *Org. Synth.*, 1973, **5**, 877.
6. A. Fürstner, *Synthesis*, 1989, **8**, 571.
7. L. A. Paquette, N. A. Pegg, D. Toops, G. D. Maynard, and R. D. Rogers, *J. Am. Chem. Soc.*, 1990, **112**, 277.
8. L. A. Paquette and S. Bailey, *J. Org. Chem.*, 1995, **60**, 749.
9. P. Weyerstahl, C. Gansau, and T. Claßen, *Flavour and Fragrance J.*, 1991, **6**, 1.
10. A. H. Haines, *Methods for the Oxidation of Organic Compounds*, Academic Press, London, 1985.
11. T. Money, *Nat. Prod. Rep.*, 1985, 254.

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