Chemistry of Natural Compounds and Bioorganic Chemistry

New approach to the synthesis of lactones of the iridane series

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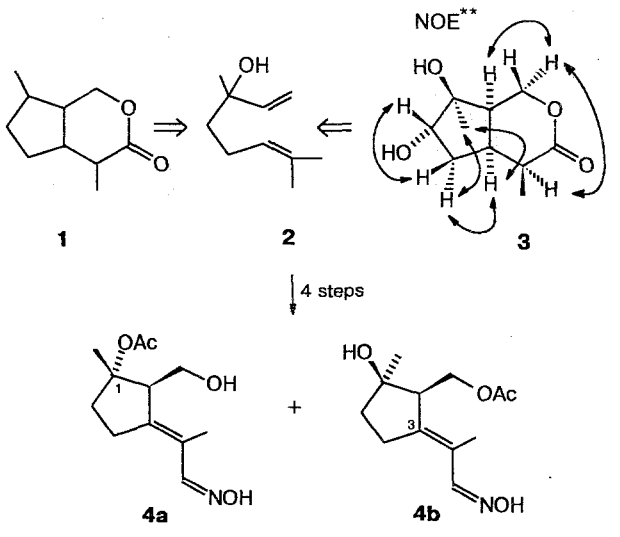
A new approach to the synthesis of lactones of the iridane series starting from (±)-linalool was developed. Synthesis of a bicyclic iridoid structurally related to the naturally occurring iridolactone villosol was performed.

Key words: (±)-linalool, iridolactone, α,β-unsaturated aldoxime, 6α,7β-dihydroxy-4β,7α-dimethyl-4α,4aα,5,6α,7,7aα-hexahydrocyclopenta[*c*]pyran-3(1*H*)-one, ^1H, ^{13}C, 2D-NOESY NMR spectra, molecular mechanics, conformational analysis.

Iridolactones with a carbon skeleton **1** have been found among metabolites of a number of insects and have also been isolated from some plants.[1] In the last few years synthesis of these compounds and related natural substances from simple linear precursors has become of interest.[1,2] Herein we deal with a strategy based on the transformation of linalool **2** to the mixture of oximes* **4a/4b** ≈ 4:1 (Scheme 1**), which was described previously.[3] Compound **4a** was converted to lactone **3,** structurally related to the natural iridolactone villosol.[4]

The selected synthetic route to **3** included the oxidative hydrolysis of the mixture **4** in the presence of $Tl(NO_3)_3$ (*cf.* with Ref. 5). The routine workup of the

Scheme 1



† Deceased.

* In Ref. 3 the mixture of regio- and stereoisomeric acetoxy derivatives **4** is erroneously referred to as the mixture of epimeric primary acetates at C(1).

** Here and below the arrows specify the nuclear Overhauser effects (NOE) observed in the experiments.

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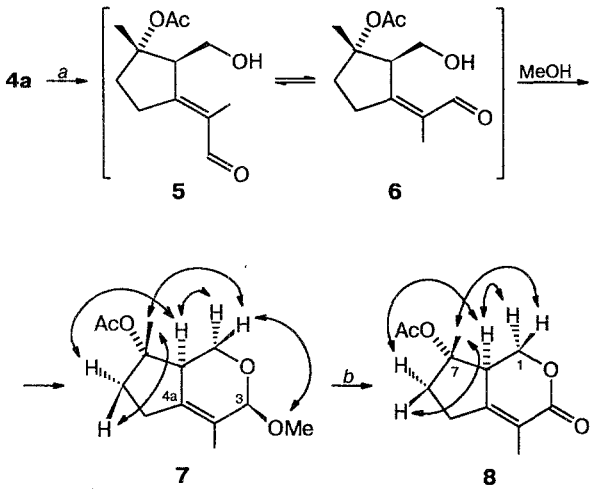
Scheme 2



Reagents and conditions: *a.* $Tl(NO_3)_3/HClO_4/MeOH$, 20 °C; *b.* $CrO_3/H_2SO_4/Me_2CO$, 20 °C.

reaction mixture including the chromatography on SiO_2 gave bicyclic acetal **7** in 50 % yield (Scheme 2).

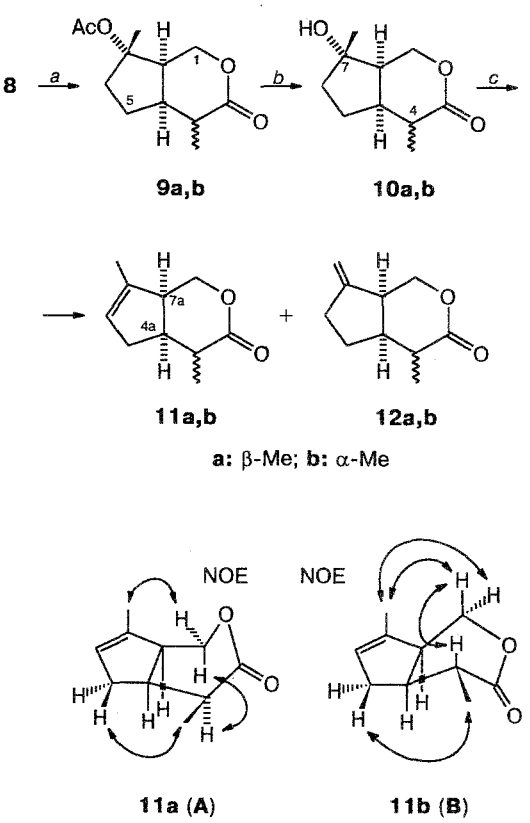
Obviously, the formation of **7** includes the isomerization of *E*-acroleine **5** yielded initially from the major component of **4** to *Z*-**6**. Acetal **7** was then treated with the Jones reagent to give the unsaturated lactone **8**.

The structures of **7** and **8,** unreported previously, were confirmed by spectroscopic and elemental analysis data. In particular, the relative configuration of the substituents in the molecule of acetal **7** was deduced by 2D-NOESY (see Scheme 2). NOEs correlating with the structure shown were also observed in the two-dimensional spectrum of lactone **8**.

Reduction of the double bond in **8** by nickel boride in methanol (Scheme 3) (*cf.* Ref. 6) was found to be nonselective and gave epimers **9** (≈1:1 by GLC and ^1H NMR) with the carbon skeleton **1**. The controlled hydrolysis of these acetates and the dehydration of the tertiary alcohols **10** according to the known procedure[7] yielded the mixture of stereoisomeric lactones **11a,b** and concomitant minor exomethylene components **12a,b** in a ratio of 4:4:1:1, respectively. We succeeded in isolating the pairs of regioisomers **11a/12a** and **11b/12b** with the same relative configuration of the C(4) center by flash chromatography on SiO_2. The composition of the mixture of **11/12** was deduced by GLC and ^1H NMR. In particular, the peaks of the $H_2C{=}C$ protons with $\delta \approx 4.9$ and 5.1 in ^1H NMR spectrum belong to regioisomers **12**. Their relative integral intensity correlated with the content of the mixture minor components established by GLC.

The structures of bicyclic iridoids **9—12,** unreported previously, were established on the basis of NMR spectrometry data in view of the spectral characteristics of related compounds known from literature. The lactones

Scheme 3



Reagents and conditions: *a.* $NiCl_2 \cdot 6H_2O/NaBH_4/MeOH$, 20 °C; then $H_2SO_4/MeOH$ to pH ≈ 3, 20 °C; *b.* 27 % $HClO_4/MeOH$, 20 °C; *c.* DMSO, reflux.

9a—12a and **9b—12b** were assigned to irido and isoirido type, respectively (*cf.* Ref. 8). The stereochemistry of the olefins **11a** and **11b** (and also of the corresponding initial acetates **9** and alcohols **10**) was deduced using the registered NOEs (see Scheme 3), vicinal coupling constants {H}—{H} (Table 1) and the data of the conformational analysis of molecular models of these substances by molecular mechanics.[9] In particular, **11a** is characterized with small (<4 Hz) coupling constant values for heminal protons at C(1) with HC(7a), whereas in the case of **11b** one of these constants (≈11 Hz) is significantly larger than the other one (≈6 Hz). These are the characteristic features of the lactones of irido and isoirido type, respectively (*cf.* Ref. 8). The accordance of the experimental coupling constants to those calculated by Karplus' equation[10] (see Table 1) using the geometrical parameters obtained by molecular mechanics is an additional corroboration for the structure of **11**. The calculations were performed for **11a** (**A**) and **11b** (**B**) conformations, which are similar to those found for the natural crystalline irido- and isoiridolactones, respectively, and are also considered to be the most thermodynamically preferable for these substances in solutions (see Refs. 1, 8). It should also be

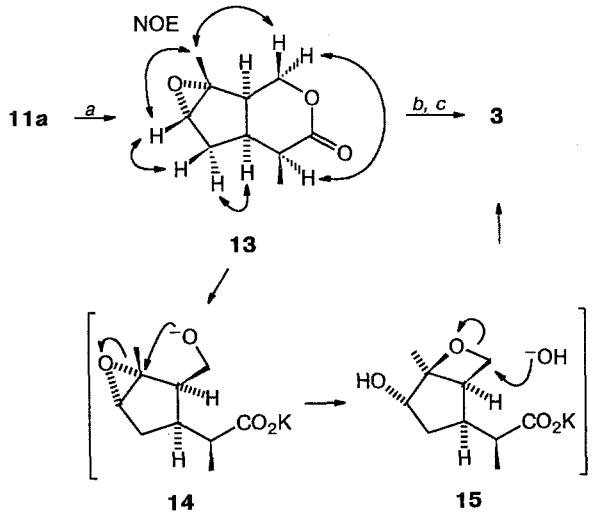
Table 1. Experimental and calculated {H}—{H} coupling constants (*J*/Hz) for **11a,b**

{H}—{H}	J_{exp}/J_{calc}	
	11a	**11b**
α-HC(1)—HC(7a)	3.9/4.14	11.4/11.65
β-HC(1)—HC(7a)	0.9/0.76	5.9/5.20
HC(4)—HC(4a)	5.6/3.19	11.33/11.66
HC(4a)—HC(7a)	10.20/10.78	9.90/10.00
HC(4a)—α-HC(5)	9.60/9.85	5.4/7.49
HC(4a)—β-HC(5)	5.40/7.63	9.36/9.87
α-HC(5)—HC(6)	2.40/4.04	1.90/3.23
β-HC(5)—HC(6)	2.22/3.24	2.37/4.03
HC(6)—HC(7a)	2.0/—	1.86/—
MeC(4)—HC(4)	6.5/—	6.4/—
α-HC(1)—β-HC(1)	−11.9/—	−11.3/—
α-HC(5)—β-HC(5)	−11.9/—	−11.3/—

noted that the boat geometry of the δ-lactone cycle with the Me group in the equatorial position suggests the spatial proximity of axial protons at C(1) and C(4), which has really been revealed for **11** by 2D-NOESY (see Scheme 3).

The final stage of the synthesis of the target substance **3** included treatment of the mixture of the unsaturated lactones with excess of *m*-chloroperbenzoic acid (MCPBA). The subsequent chromatographic separation of the reaction mixture on SiO_2 gave epoxide **13** in a moderate yield as a result of reagent attack of olefin **11a** from the less spatially hindered side (Scheme 4). Finally, **13** was stereospecifically converted to diol **3** by treating with KOH in aqueous DMSO. The stereochemical result of this procedure appears to be caused by the initial intramolecular attack of the oxirane cycle

Scheme 4



Reagents and conditions: *a.* MCPBA/Et_2O, 20 °C;
b. KOH/DMSO/H_2O, reflux;
c. Saturated $NaHSO_4/H_2O$ to pH ≈ 3, 20 °C.

with alkoxide ion **14**. The intermediate oxetane **15** (*cf.* Ref. 11) formed was then cleaved by action of hydroxide ions.

Lactones **3** and **13**, obtained for the first time, were characterized by spectral data. In particular, the spatial proximity of β-HC(5) and HC(6) protons and also of the Me group at C(7) to HC(4a) and α–HC(5) protons in the case of substance **3** and to β–HC(1) and HC(6) protons in the case of lactone **13** registered in the 2D-NOESY spectra is a reliable corroboration of the structure of these substances.

Experimental

IR spectra (ν/cm^{-1}) of $CHCl_3$ solutions were obtained on a Specord M-80 spectrometer. UV spectra were recorded on a Specord UV-VIS spectrophotometer. ^{1}H NMR spectra (δ, *J*/Hz) of $CDCl_3$ solutions were registered on Bruker WM-250 (250.13 MHz) and AMX-400 (400.13 MHz) instruments. ^{13}C NMR spectra (50.32 MHz) were obtained on a Bruker AC-200 instrument. Chemical shifts were determined relative to the solvent using the δ scale (7.27 for ^{1}H and 77.0 for ^{13}C). ^{13}C NMR spectra of substances **3**, **7**, **8**, **11a,b**, and **13** are given in Table 2. Mass spectra (EI, 70 eV) were taken on Varian MAT CH-6 and Varian MAT 311A mass spectrometers. R_f values are given for the fixed SiO_2 layer (Silufol) (hexane—ethyl acetate, 4:3).* GLC analysis was performed on an LKhM 8MD instrument (2 m × 3 mm columns with 15 % Carbowax 20M and SE-30 on Chromaton N-AW-HMDS).

7α-Acetoxy-3β-methoxy-4,7β-dimethyl-1,3,5,6,7,7aα-hexahydrocyclopenta[*c*]pyran (7). To a solution of 4.30 g (17.8 mmol) of a mixture of **4a/4b**, 4:1 (see Ref. 3), in 25 mL of MeOH a solution of 7.3 g (18.7 mmol) of $Tl(NO_3)_3$ and 0.4 mL of 27 % $HClO_4$ in 25 mL of MeOH was added over 5 min with vigorous stirring at 20 °C (Ar). After 2 h at 20 °C the reaction mixture was neutralized with NEt_3 and evaporated *in vacuo*. The residue was treated with 50 mL of $CHCl_3$, and the resulting solution was filtered. The filtrate was washed with

* Unless otherwise specified.

Table 2. ^{13}C NMR chemical shifts (δ) for **3**, **7**, **8**, **11a,b**, and **13**

C atom	**3**	**7**	**8**	**11a**	**11b**	**13**
1	65.41	59.11	67.84	66.35	68.74	65.90
3	177.17	97.91	165.37	179.73	175.76	—
4	37.45	134.90[a]	120.88	36.78	38.00[a]	38.04
4a	36.74	135.59[a]	156.83	38.86	38.91[a]	36.85
5	33.11	25.00[b]	26.50[a]	34.39	40.92[a]	31.34
6	77.89	37.22[b]	38.10[a]	126.42	126.17	64.52
7	80.97	87.02	85.92	136.90	136.72	66.31
7a	45.11	48.41	48.01	48.28	48.07	43.09
MeC(4)	12.40	14.17	12.52	12.80	14.02[b]	12.68
MeC(7)	21.64	18.21	18.46	14.10	14.65[b]	15.04
MeCO		21.84	21.69			
MeCO		170.17	170.08			
MeO		55.43				

Note. Chemical shift values marked with the same symbols[a,b] in columns may be interchanged.

water, and the water layer was separated and extracted with $CHCl_3$. The combined organic extract was dried over Na_2SO_4 and evaporated *in vacuo*. The residue (4.4 g) was chromatographed on 150 g of SiO_2. Gradient elution from hexane to Et_2O (up to 15 % of the latter) gave 2.27 g (53 %) of **7** as a colorless oil, R_f 0.62. IR: 940, 1020, 1050, 1065, 1080, 1095, 1150, 1245, 1270, 1375, 1740, 2950, and 3020. ^1H NMR: 1.23 (br.s, 3 H, MeC(7)); 1.58 (br.s, 3 H, MeC(4)); 1.88 (m, 1 H, α-HC(6), J = −13.0, 11.0, 10.4, and 0.9); 1.96 (s, 3 H, MeCO); 2.21 (m, 1 H, β-HC(5), J = −17.9, 11.0, 8.7, 2.0, and 1.4); 2.27 (m, 1 H, β-HC(6), J = −13.0, 8.7, and 2.21); 2.36 (m, 1 H, α-HC(5), J = −17.9, 10.4, 2.2, 2.2, and 1.9); 2.7 (m, 1 H, HC(7a)); 3.40 (s, 3 H, MeO); 3.62 (ddd, 1 H, β-HC(1), J = 11.1, −10.7, and 0.7); 3.88 (dd, 1 H, α-HC(1), J = −10.7 and 5.6); 4.55 (br.s, 1 H, HC(3)). MS, *m/z*: 210 $[M-30]^+$, 209, 194, 181, and 180. Found (%): C, 64.62; H, 8.57. $C_{13}H_{20}O_4$. Calculated (%): C, 64.98; H, 8.39.

7α-Acetoxy-4,7β-dimethyl-5,6,7,7aα-tetrahydrocyclopenta[*c*]pyran-3(1*H*)-one (8). To a solution of 2.27 g (9.45 mmol) of **7** in 20 mL of acetone the Jones reagent prepared from 1.32 g (15.7 mmol) of CrO_3, 1.15 mL of conc. H_2SO_4, 4 mL of H_2O, and 44 mL of acetone was added during 15 min with vigorous stirring at 20 °C. After 15 min at 20 °C, the mixture was quenched with 1 mL of Pr^iOH during 5 min, treated with 100 mL of $CHCl_3$, evaporated *in vacuo* for 3/4, and filtered. The filtrate was evaporated *in vacuo*, and the residue (2 g) was chromatographed on 100 g of SiO_2. Gradient elution from hexane to Et_2O (up to 60 % of the latter) gave 1.88 g (89 %) of **8** as a colorless oil, R_f 0.30. IR: 910, 1045, 1060, 1150, 1300, 1375, 1385, 1410, 1715, 3030. UV (EtOH, λ_{max}/nm): 232 (ε 8340). ^1H NMR: 1.32 (s, 3 H, MeC(7)); 1.79 (br.s, 3 H, MeC(4)); 1.98 (m, 1 H, α-HC(6), J = −13.0, 11.0, 10.0, and 0.8); 1.99 (s, 3 H, MeCO); 2.22 (m, 1 H, β-HC(6), J = −13.0, 8.6, and 2.3); 2.32 (m, 1 H, β-HC(5), J = −19.2, 11.0, 8.6, and 3.0); 2.47 (m, 1 H, α-HC(5), J = −19.2, 10.0, 2.3, and 1.3); 2.98 (m, 1 H, HC(7a), J = 13.1, 5.9, 3.0, and 1.3); 4.11 (dd, 1 H, β-HC(1), J = 13.1, and −10.5); 4.63 (dd, 1 H, α-HC(1), J = −10.5 and 5.9). MS, *m/z*: 224 $[M]^+$. Found (%): C, 64.29; H, 7.34. $C_{12}H_{16}O_4$. Calculated (%): C, 64.27; H, 7.19.

7α-Acetoxy-4β,7β-dimethyl-4α,4aα,5,6,7,7aα-hexahydrocyclopenta[*c*]pyran-3(1*H*)-one (9a) and 7α-acetoxy-4α,7β-dimethyl-4β,4aα,5,6,7,7aα-hexahydrocyclopenta[*c*]pyran-3(1*H*)-one (9b). To a solution of 0.5 g (2.23 mmol) of **8** and 0.26 g (1.14 mmol) of $NiCl_2 \cdot 6H_2O$ in 25 mL of MeOH 0.33 g (8.7 mmol) of $NaBH_4$ was added in portions during 5 min with vigorous stirring at 0 °C (Ar). After 1 h at 0 °C and 1 h at 20 °C the mixture was acidified with 50 % H_2SO_4 in MeOH to pH ≈ 3, kept for 30 min, and treated with the saturated $KHCO_3$ solution to pH ≈ 7 and then extracted with Et_2O. The organic layer was washed with water, dried over Na_2SO_4, and evaporated *in vacuo*. The residue (0.6 g) was chromatographed on 40 g of SiO_2. Gradient elution from hexane to Et_2O (up to 60 % of the latter) gave 0.44 g (87 %) of the mixture of **9a/9b**, ~1:1 (GLC and ^1H NMR data) as a colorless oil, R_f 0.30. IR: 1020, 1040, 1125, 1175, 1255, 1370, 1380, 1450, 1460, 1730, 2940, 2980, and 3010. MS, *m/z*: 184 $[M-42]^+$, 167 $[M-59]^+$, and 166 $[M-60]^+$. Found (%): C, 63.96; H, 7.92. $C_{12}H_{18}O_4$. Calculated (%): C, 63.70; H, 8.02.

^1H NMR for lactone **9a**: 1.15 (d, 3 H, MeC(4), J = 6.5); 1.53 (s, 3 H, MeC(7)); 1.7—2.9 (m, 7 H, CH, CH_2); 1.98 (s, 3 H, MeCO); 4.36 (dd, 1 H, α-HC(1), J = 12.5 and 3.5); 4.72 (d, 1 H, β-HC(1), J = 12.5).

^1H NMR for lactone **9b**: 1.18 (d, 3 H, MeC(4), J = 6.5); 1.45 (s, 3 H, MeC(7)); 1.7—2.9 (m, 7 H, CH, CH_2); 1.98 (s, 3 H, MeCO); 3.95 (dd, 1 H, α-HC(1), $J_1 = J_2$ = 11.5); 4.49 (dd, 1 H, β-HC(1), J = 11.5 and 6.0).

7α-Hydroxy-4β,7β-dimethyl-4α,4aα,5,6,7,7aα-hexahydrocyclopenta[*c*]pyran-3(1*H*)-one (10a) and 7α-hydroxy-4α,7β-dimethyl-4β,4aα,5,6,7,7aα-hexahydrocyclopenta[*c*]pyran-3(1*H*)-one (10b). To a solution of 0.17 g (0.75 mmol) of the mixture of **9a,b** in 3.2 mL of MeOH was added 2.3 mL of 27 % $HClO_4$ at 20 °C. After 72 h at 20 °C the reaction mixture was neutralized with saturated $KHCO_3$ solution and treated with Et_2O. The water layer was separated and extracted with Et_2O. The routine treatment of the combined organic extract gave 0.2 g of residue, which was chromatographed on 10 g of SiO_2. The gradient elution from hexane to Et_2O and then to MeOH (up to 5 % of the latter) yielded 95 mg (75 %) of the mixture of **10a/10b**, ~1:1 (by ^1H NMR) as a colorless amorphous mass without distinct melting point, R_f 0.28 (ethyl acetate). IR: 1035, 1115, 1170, 1360, 1380, 1460, 1710, 1740, 2940, 2970, 3010, and 3610. MS, *m/z*: 166 $[M-18]^+$. Found (%): C, 65.02; H, 8.79. $C_{10}H_{16}O_3$. Calculated (%): C, 65.19; H, 8.75.

^1H NMR for **10a**: 1.20 (d, 3 H, MeC(4), J = 6.5); 1.42 (s, 3 H, MeC(7)); 1.5—2.1 (m, 4 H, CH_2); 2.32 (dd, 1 H, HC(7a), J = 9.0 and 4.0); 2.6 (m, 1 H, HC(4)); 2.75 (m, 1 H, HC(4)); 4.27 (dd, 1 H, α-HC(1), J = 12.0 and 4.0); 4.43 (d, 1 H, β-HC(1), J = 12.0).

^1H NMR for **10b**: 1.22 (d, 3 H, MeC(4), J = 6.5); 1.29 (c, 3 H, MeC(7)); 1.5—2.5 (m, 7 H, CH, CH_2); 3.86 (dd, 1 H, α-HC(1), $J_1 = J_2$ = 12); 4.27 (dd, 1 H, β-HC(1), J = 12.0 and 6.0).

4β,7-Dimethyl-1,4aα,5,7aα-tetrahydrocyclopenta[*c*]pyran-3(4α*H*)-one (11a) and 4α,7-dimethyl-1,4aα,5,7aα-tetrahydrocyclopenta[*c*]pyran-3(4β*H*)-one (11b). A solution of 0.25 g (1.36 mmol) of the mixture **10** in 2.5 mL of DMSO was refluxed for 12 h (Ar), treated with Et_2O and the saturated NaCl solution. The water layer was separated and extracted with Et_2O. The routine treatment of the combined organic extract yielded 0.25 g of the residue, which was dissolved in Et_2O and filtered through the short SiO_2 layer. The filtrate was evaporated, and the residue (0.2 g) was distilled to give 0.12 g (44 %) of the mixture of **11a/11b/12a/12b**, ~4:4:1:1 (by GLC and ^1H NMR), m.p. 70 °C (1 Torr). MS, *m/z*: 166 $[M]^+$. Found (%): C, 72.29; H, 8.72. $C_{10}H_{14}O_2$. Calculated (%): C, 72.26; H, 8.49. The mixture was chromatographed on 10 g of SiO_2. The gradient elution from hexane to Et_2O (up to 50 % of the latter) yielded (in order of elution) 51 mg of the mixture of **11b/12b**, ~4:1 (GLC and ^1H NMR data), R_f 0.51, and 55 mg of the mixture of **11a/12a**, ~4:1 (by GLC and ^1H NMR), R_f 0.44.

11a/12a: colorless crystals, m.p. 40—45 °C (pentane). IR: 900, 930, 970, 1010, 1025, 1110, 1155, 1360, 1375, 1440, 1710, 1740, 2930, and 3010.

11b/12b: colorless crystals, m.p. 40—52 °C (pentane). IR: 900, 930, 970, 1040, 1070, 1120, 1170, 1325, 1350, 1375, 1450, 1740, 2930, 2980, and 3010.

^1H NMR for **11a***: 1.15 (d, 3 H, MeC(4)); 1.69 (s, 3 H, MeC(7)); 2.04 (m, 1 H, β-HC(5)); 2.41 (m, 1 H, α-HC(5)); 2.79 (m, 1 H, HC(4)); 2.9—3.0 (m, 2 H, HC(4a), HC(7a)); 4.25 (m, 1 H, α-HC(1)); 4.33 (m, 1 H, β-HC(1)); 5.35 (br.s, 1 H, HC(6)).

^1H NMR for **11b***: 1.20 (d, 3 H, MeC(4)); 1.63 (m, 3 H, MeC(7)); 2.17 (m, 1 H, β-HC(5)); 2.3—2.5 (m, 2 H, HC(4), HC(4a)); 2.74 (m, 1 H, α-HC(5)); 3.02 (m, 1 H, HC(7a)); 3.93 (dd, 1 H, β-HC(1)); 4.41 (dd, 1 H, α-HC(1)); 5.39 (m, 1 H, HC(6)).

* Coupling constants are given in Table 1.

4β,7β-Dimethyl-6α,7α-epoxy-4α,4aα,5,6β,7,7aα-hexahydrocyclopenta[*c*]pyran-3(1*H*)-one (13). A solution of 40 mg (0.24 mmol) of the mixture of **11a/12a** and 95 mg (0.30 mmol) of MCPBA in 0.5 mL of Et_2O was stirred for 2.5 h at 20 °C and evaporated *in vacuo*. The residue (140 mg) was chromatographed on 10 g of SiO_2. Gradient elution from hexane to Et_2O yielded 25 mg of **13** as colorless crystals, m.p. 115–120 °C (pentane). IR: 1010, 1045, 1070, 1090, 1110, 1135, 1150, 1240, 1250, 1380, 1450, 1750, 2930, 2980, and 3010. ^{1}H NMR: 0.82 (d, 3 H, MeC(4), J = 6.7); 1.05 (m, 1 H, β-HC(5)); 1.21 (s, 3 H, MeC(7)); 1.86 (m, 1 H, α-HC(5)); 2.2–2.32 (m, 2 H, HC(4a), HC(7a)); 2.56 (m, 1 H, HC(4)); 3.09 (br.s, 1 H, HC(6), $J_{HC(6),\beta\text{-}HC(5)}$ = 1.5); 4.05 (m, 1 H, α-HC(1), J = 12.7, 4.5); 4.13 (br.d, 1 H, β-HC(1), J = 12.7). MS (high resolution), *m/z*: 182 $[M]^+$. Found: molecular weight 182.09412; calculated for $C_{10}H_{14}O_3$: molecular weight 182.09421.

6α,7β-Dihydroxy-4β,7α-dimethyl-4α,4aα,5,6β,7,7aα-hexahydrocyclopenta[*c*]pyran-3(1*H*)-one (3). A solution of 23 mg (0.13 mmol) of **13** and 40 mg (0.71 mmol) of KOH in 2.1 mL of DMSO and 0.38 mL of water was refluxed for 6 h and treated with the saturated $NaHSO_4$ solution to pH ≈ 3. After 30 min at 20 °C, the reaction mixture was neutralized with the saturated $NaHCO_3$ solution and extracted repeatedly with ethyl acetate. The combined extract was dried over Na_2SO_4 and evaporated *in vacuo*. The residue (30 mg) was chromatographed on 10 g of SiO_2. Gradient elution from Et_2O to MeOH (up to 25 % of the latter) gave 10 mg (40 %) of **3** as a colorless oil, R_f 0.23 (ethyl acetate–MeOH, 9:1). IR: 880, 1030, 1050, 1080, 1115, 1385, 1450, 1740, 2940, 2980, 3020, 3460, and 3630. ^{1}H NMR: 1.03 (d, 3 H, MeC(4), J = 6.6); 1.17 (s, 3 H, MeC(7)); 1.51 (m, 1 H, β-HC(5), $J_{\beta\text{-}HC(5),\alpha\text{-}HC(5)}$ = −13.5, $J_{\beta\text{-}HC(5),HC(4a)}$ = 8.0, and $J_{\beta\text{-}HC(5),HC(6)}$ = 5.6); 1.59 (m, 1 H, α-HC(5), $J_{\alpha\text{-}HC(5),\beta\text{-}HC(5)}$ = −13.5, $J_{\alpha\text{-}HC(5),HC(4a)}$ = 8.8, and $J_{\alpha\text{-}HC(5),HC(6)}$ = 4.9); 2.20 (dd, 1 H, HC(7a), J = 10.6 and 5.2); 2.68 (quint, 1 H, HC(4), J = 6.5); 2.75 (m, 1 H, HC(4a), J = 10.6, 8.8, 8.0, and 6.5); 3.68 (t, 1 H, HC(6), J = 5.2); 4.17 (dd, 1 H, α-HC(1), J = 12.2 and 5.2); 4.51 (br.d, 1 H, β-HC(1), J = 12.2). MS (high resolution), *m/z*: 200 $[M]^+$. Found: molecular weight 200.10402; calculated for $C_{10}H_{16}O_4$: molecular weight 200.10476.

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