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Lactones. Part 16: Lactonization of γ,δ-epoxy esters with *p*-toluenesulfonic acid monohydrate☆

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Abstract—The reaction of cyclic γ,δ-epoxy esters with *p*-toluenesulfonic acid monohydrate is described. The reaction carried out in benzene or methylene chloride gave tosyloxy lactones as product. The ethoxy or methoxy lactones were obtained when ethanol or methanol were used as solvent. A mechanism of this lactonization is proposed.

1. Introduction

The acid induced ring-closing procedure is well known as an efficient method for the synthesis of lactones. Among the acids, *p*-toluenesulfonic acid is very often used for the synthesis of lactones from hydroxy esters,[2–6] hydroxy acids,[7,8] hydroxy amides[9] and epoxy esters.[10,11]

In the course of the lactonization of epoxy ester **2a** with an equimolar amount of *p*-toluenesulfonic acid monohydrate in non-aqueous solvents, the formation of δ-tosyloxy-γ-lactone and δ-ethoxy-γ-lactone was observed. Here, we present the results of our studies on this reaction. We have found it interesting for two reasons. The first reason is the different course of this lactonization in comparison with lactonization of epoxy esters carried out with this acid earlier.[10,11] The reaction of acyclic γ,δ-epoxy esters with equimolar amounts of *p*-toluenesulfonic acid monohydrate in benzene afforded δ-hydroxy-γ-lactones as the only products.[11] The lactonization of β,γ-epoxy ester obtained from methyl scalar-17(24)-en-25-oate with *p*-toluenesulfonic acid in chloroform afforded 16-unsaturated lactone (scalar-16-en-25,24-olide) as the only product.[10] The second reason is a possibility of application of this reaction to the synthesis of substituted derivatives of lactones via the nucleophilic substitution of a tosyloxy group.

2. Results and discussion

The substrates for lactonization, epoxy esters **2a**–**d**, were obtained by oxidation of corresponding, known δ,γ-unsaturated esters **1a**,[12] **1b**[13] and **1c**[14] with *m*-chloroperbenzoic acid (Scheme 1). Both, thin layer and gas chromatography indicated that only one epoxy ester was formed from **1a** and **1b**. In the case of epoxidation of ester **1c**, the mixture of epoxy esters: *cis* (**2c**, 80%) and *trans* (**2d**, 20%) was obtained. The pure epoxy esters were separated by column chromatography.

The small differences in chemical shifts of methyl groups at C-5 ($\Delta\delta$=0.04 for **2a** and 0.02 for **2b**) suggest that the oxirane ring is relatively far away from *trans* pseudoaxial methyl group at C-5. In the case of **2a**, it is possibly in twisted chair conformation of the cyclohexane ring with C-1, C-2, C-3 and C-4 in one plane. The oxirane ring is *cis* oriented in relation to the pseudoequatorial methylcarbethoxy group at C-1. For **2b**, it is possible rather in the boat conformation of this molecule with C-1 and C-4 as stem and stern atoms then in the half or twisted chair conformation. Coupling constants of H-1 with H-2 (3.8 Hz) and H-3 with protons of CH_2-4 (3.9 and 1.9 Hz) confirmed this conformation. The oxirane ring is *cis* oriented to the methylcarbethoxy group. In the case of epoxy ester **2c**, the half-chair conformation with C-1, C-2, C-3, C-4 and C-5 in one plane is suggested. Such conformation and *cis* orientation of epoxy ring toward the methylcarbethoxy group in **2c** could be proposed on the basis of the ^{1}H NMR spectral data. Lack of coupling constants of H-2 with H-1 and H-3 with one of H-4 in the multiplets of H-2 and H-3 indicates a conformation with dihedral angles between these protons close to 90°. Coupling constants of H-2 with H-1 (1.1 Hz) and H-3 with CH_2-4 protons (2.1 and 1.8 Hz) found in the spectrum of *trans* epoxy ester (**2d**) rather suggest a

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Table 1. Compositions (according to GC) of the product mixtures of lactonization of epoxy esters **2a**–**c**

Substrate	Solvent	**3a**,**b**,**c**	**4a**,**b**,**c**	**5a**,**b**,**c**	**6a**,**b**,**c**
2a	Benzene	95 (67)	1		4
2b		96 (63)	1		3
2c		92 (71)	3		5
2a	Methylene chloride	85 (67)	12 (8)		3
2b		86 (70)	12 (8)		2
2c		77 (75)	23 (20)		
2a	Ethanol	16	84 (60)		
2b		8	92 (64)		
2c		6	94 (78)		
2a	Methanol	7	1	92 (70)	
2b		16	1	83 (79)	
2c		5		95 (80)	

Isolated yields are given in brackets.

twisted chair conformation of cyclohexane ring with C-1, C-2, C-3 and C-4 in one plane. The X-ray structures of tosyloxy and hydroxy lactones formed from epoxy esters **2a**–**c** fully confirmed the assignations presented above.

Epoxy esters **2a**–**c** were subjected to the reaction with *p*-toluenesulfonic acid monohydrate at room temperature in different solvents: benzene, methylene chloride, ethanol and methanol (Scheme 1). The results of this reaction presented in Table 1 indicate that the mixtures of compounds were obtained.

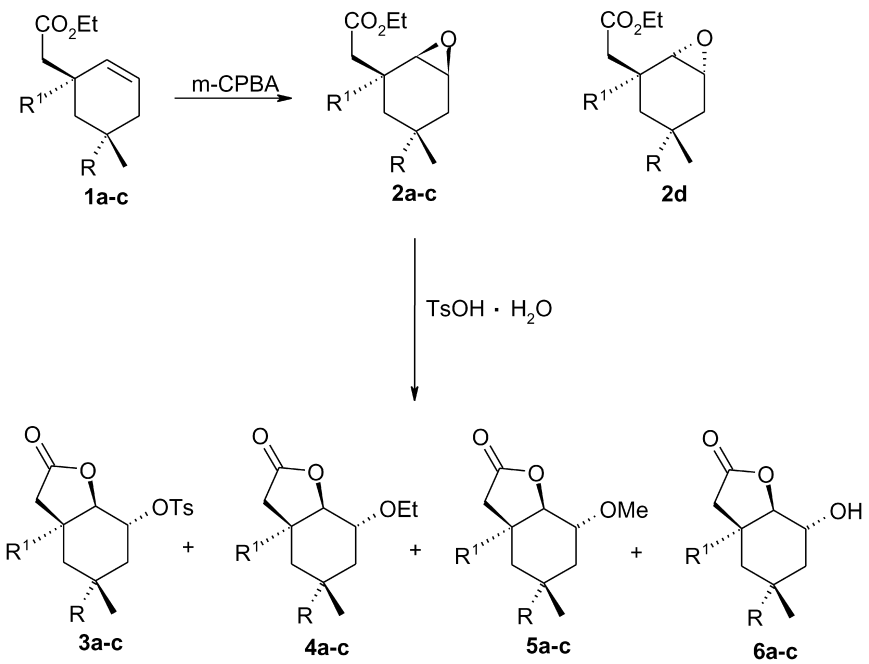
The composition of the product mixture depends on the solvent used in the reaction. The lactonization in benzene gave the δ-tosyloxy γ-lactones **3a** and **3b** in almost quantitative and **3c** in 92% yield. *trans* Epoxy ester (**2d**) in the same conditions afforded only a hydroxylactone product with different retention time on GC compared to **6c**. Tosyloxy lactones were also main products (77–86%) when the lactonization was carried out in methylene chloride. The ethoxy lactones **4a**–**c** were identified and isolated as the other products of the reaction in this solvent. In the reactions carried out in methyl or ethyl alcohol, the corresponding δ-methoxy- or δ-ethoxy-γ-lactones were formed as the main products. They decidedly predominated (84–95%) over δ-tosyloxy-γ-lactones (5–16%).

The ethoxy and methoxy lactones are not formed via the substitution of tosyloxy group by ethanol or methanol but directly from epoxides. We have verified this in a separate experiment in which the tosyloxy lactone **3a** was stirred in ethanol with a catalytic amount of *p*-toluenesulfonic acid at room temperature for 24 h. We did not observe any exchange of tosyloxy group by ethoxy. The hydroxy lactones **6a**–**c** identified in the product mixtures were the same (by GC) as those obtained by lactonization of epoxy esters **2a**–**c** with perchloric or tartaric acid[15,16] in aqueous solution.

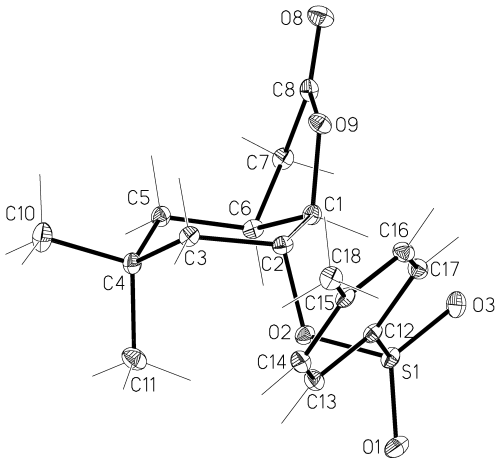
The structures of compounds obtained were determined on the basis of data from their ^{1}H NMR and IR spectra and X-ray analysis.

The X-ray structures of tosyloxy lactone (**3a**) and hydroxy lactone (**6a**) (Fig. 1) showed that the cyclohexane ring in the first molecule exists in a chair conformation, whereas in the hydroxy lactone it exists in a twisted boat conformation. In both molecules the lactone ring is *trans* orientated toward the axial or pseudoaxial methyl group at C-4. The C–O bonds of the tosyloxy or hydroxy group are *trans* with respect to the C–O bond of the lactone ring. The X-ray analysis of **6a** indicates the presence of two symmetrically independent molecules in the crystals.

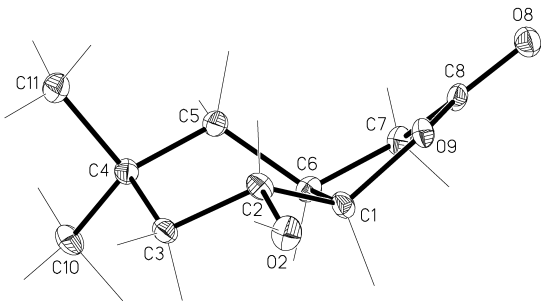
Such relative orientation of lactone ring and tosyloxy or hydroxy group is also seen in the coupling constants values between H-1 and H-2 and between them and neighbouring protons. The values of coupling constant values of H-1 with H-2 (5.7 Hz) and with H-6 (6.0 Hz) found in the ^{1}H NMR



Scheme 1. (a) R=CH_3, R^1=H; (b) R, R^1=CH_3; (c), (d) R, R^1=H.



3a



6a

Figure 1. Crystal structure of **3a** and **6a**.

spectrum of **6a** are consist with torsion angles between C–H bonds of these protons, −15 and −22° respectively, from X-ray structure. The coupling constants of this proton with the H-2 (4.5 Hz) and H-6 (4.0 Hz) found in the spectrum of **3a** indicate equatorial positions of H-1 and H-2.

The *trans* diaxial orientation of C–O bonds and *trans* equatorial positions of H-1 and H-2 can be ascribed also in the ethoxy (**4a**) and methoxy lactones (**5a**). The values of $J_{H\text{-}1,H\text{-}2}$=(4.8 Hz for **4a** and 5.0 Hz for **5a**) and $J_{H\text{-}1,H\text{-}6}$= (5.0 Hz for both compounds) indicate equatorial positions of coupled protons.

The X-ray analysis of compounds obtained from epoxy ester **2b**, the tosyloxy lactone (**3b**) and hydroxy lactone (**6b**), indicated that the cyclohexane ring in all of them exists in a slightly twisted chair conformation (Fig. 2). The additional methyl group at C-6 forces the *cis* orientation of the lactone ring to the axial methyl group at C-4. The C–O bonds of the lactone moiety and tosyloxy or hydroxy group are in a *trans* relation and occupy equatorial positions. The X-ray analysis of **6b** indicates the presence of two symmetrically independent molecules in the crystals.

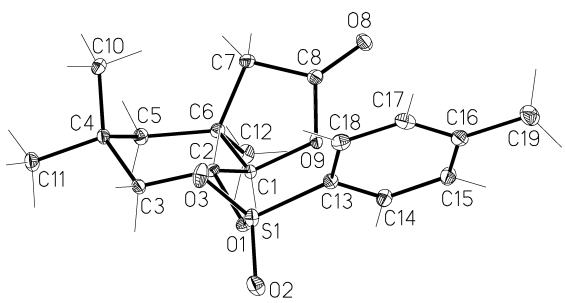
The coupling constants of H-1 and H-2 protons are consistent with the torsion angles determined by X-ray analysis. Similar values of coupling constants $J_{H\text{-}1,H\text{-}2}$=6.5 (**3b**), 6.5 (**4b**), 6.4 (**5b**) and 7.7 Hz (**6b**) found in the ^{1}H NMR spectra of these compounds indicate that the conformations of molecule and relative orientations of substituents of cyclohexane ring are almost the same.

X-Ray analysis of tosyloxy lactone (**3c**) (Fig. 3) obtained from epoxy ester **2c** showed that the cyclohexane ring exists in a chair conformation and the lactone ring is *cis* located towards the methyl group at C-4. The C–O bonds are situated in *trans* axial positions.

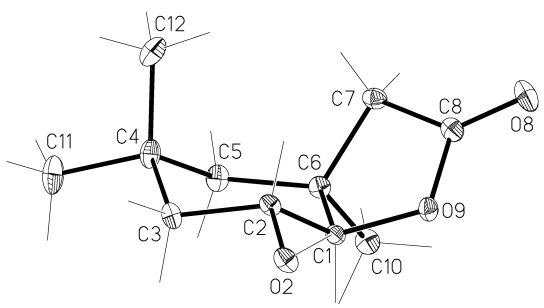
The multiplet of H-1 in the ^{1}H NMR spectrum of **3c**, **4c**, **5c** and **6c** looks like a broad singlet. This shape indicates equatorial orientations of H-2 and H-1.

Results obtained from the experiments reported above are not consistent with those presented earlier for lactonization of acyclic δ,γ-epoxy esters.[11] The lactonization of ethyl 3,7-dimethyl-3,4-epoxyoctanoate and its two 3- or 7-methyl homologues with *p*-toluenesulfonic acid monohydrate carried out in benzene afforded δ-hydroxy-γ-lactone as the only product.

These two different results indicate that the mechanisms of lactonization are probably different. This is perhaps due to



3b



6b

Figure 2. Crystal structures of **3b** and **6b**.

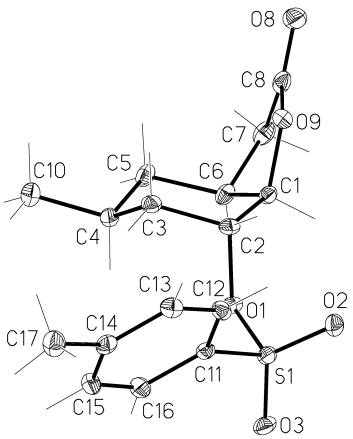


Figure 3. Crystal structure of **3c**.

the difference in distance between the oxirane ring and carboethoxy group in both types of epoxy esters.

Two possible mechanisms of the lactonization of **2a–c** could be taken into consideration. The relatively short distance between the epoxy oxygen atom and carbon atom of carbonyl group (3.4 Å for **2a**, according to AM1 method, HyperChem) in cyclic epoxy esters makes it possible that this oxygen can easily attack (as a nucleophile) the carbonyl carbon of the protonated carboethoxy group with synchronous attack of nucleophiles present in the reaction medium on C-3 (Scheme 2). The *cis* orientation of epoxy rings and the methylcarboethoxy groups makes such mechanism of lactonization possible.

The second mechanism assumes opening of the oxirane ring followed by lactonization of resulting 2-hydroxy-3-tosyloxy or 2-hydroxy-3-alkoxy esters (Scheme 3).

3. Conclusions

Although, studies on the mechanism of this lactonization are in progress, we incline towards mechanism 1 (Scheme 2). This choice is suggested by the following observations.

1. We did not identify the 2-hydroxy-3-tosyloxy or 2-hydroxy-3-alkoxy esters as intermediates in the course of lactonization of **2a–c**.
2. The stereospecificity of the lactonization process has been observed. The tosyloxy or alkoxy group is always situated in a *trans* position to the C–O bond of the lactone ring.

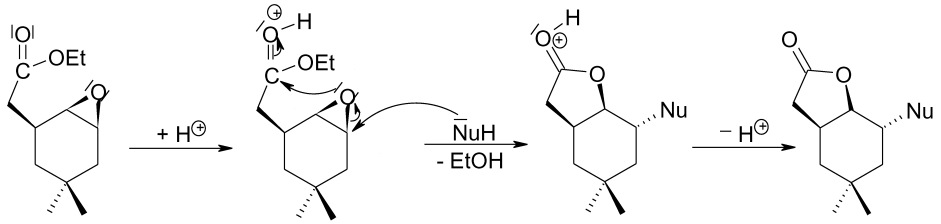
4. Experimental

The purity of intermediates and isolated products was checked by TLC: silica gel DC-Alufolien Kieselgel 60 F_{254} (Merck) with the application of hexane–acetone 9:1 (for epoxy esters), hexane–acetone 3:1 (for hydroxy, tosyloxy and alkoxy lactones) as the developing systems. The same eluents were applied in the course of preparative column chromatography (silica gel: Kieselgel 60, 230–400 mesh) for the separation of product mixtures. GC analysis were performed on Hewlett–Packard 5890 instrument using the following capillary columns HP-1 (Crosslinked Methyl Silicone Gum) 25 m×0.32 mm×0.52 μm and HP-5 (Crosslinked Phenyl Methyl Silicone) 30 m×0.52 mm×0.88 μm. ^{1}H NMR spectra were recorded for $CDCl_3$ solutions with TMS as internal standard on a Bruker Avance DRX 300 Spectrometer. IR spectra were determined with a Specord M-80 and Mattson IR 300 infrared spectrophotometers. Melting points (uncorrected) were determined on a Boetius apparatus.

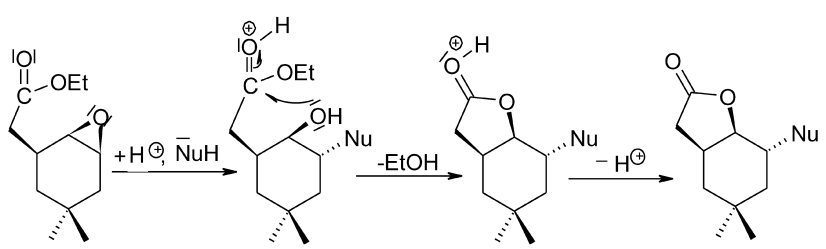
All reagents were purchased from Fluka. The starting materials: ethyl (5,5-dimethyl-2-cyclohexen-1-yl) acetate (**1a**), ethyl (1,5,5-trimethyl-2-cyclohexen-1-yl) acetate (**1b**) and ethyl 5-methyl-2-cyclohexen-1-yl)acetate (**1c**) were obtained from dimedone[12] isophorone[16] and 5-methyl-1,3-cyclohexanedione, respectively.

4.1. X-Ray crystallographic data

All measurements of crystals were performed at 100 K using an Oxford Cryosystem device on a Kuma KM4CCD κ-axis diffractometer with graphite-monochromated Mo Kα



Scheme 2. NuH=TsOH, EtOH, MeOH or H_2O.



Scheme 3. NuH=TsOH, EtOH, MeOH or H_2O.

radiation (λ=0.71073 Å). Crystals were positioned at 65 mm from the CCD camera. 612 frames were measured at 0.75° intervals with a counting time of 10–20 s. Accurate cell parameters were determined and refined by least-squares fit of 1800–3100 the strongest reflections. The data were corrected for Lorentz and polarization effects. No absorption correction was applied. Data reduction and analysis were carried out with the Oxford Diffraction (Poland) Sp. z o.o. (formerly Kuma Diffraction Wrocław, Poland) programs. Structures were solved by direct methods (program SHELXS97[17]) and refined by the full-matrix least-squares method on all F^2 data using the SHELXL97[18] programs. Non-hydrogen atoms were refined with anisotropic displacement parameters; hydrogen atoms were included from geometry of molecules and $\Delta\rho$ maps. They were refined with isotropic displacement parameters.

Crystallographic data (excluding structure factors) for crystals **3a**,**3b**,**3c**, **6a** and **6b** in this paper, have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 205102–205106, respectively. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

4.2. Epoxidation of esters 1a–c

A solution of *m*-chloroperbenzoic acid (0.03 mol) in 60 cm^3 of methylene chloride was added to a solution of ester (0.015 mol) in methylene chloride (100 cm^3). When the reaction was completed (TLC, 24 h) the mixture was diluted with ethyl ether and washed successively with aqueous solutions of Na_2CO_3 and Na_2SO_3 and water. The crude product was purified by column chromatography (silica gel, hexane–acetone 9:1). The yields, physical and spectral data of epoxy esters **2a**, **2b** and **2c** are given below.

4.2.1. Ethyl (5,5-dimethyl-2,3-epoxycyclohex-1-yl) acetate (2a). 2.6 g, 81%. Colourless liquid; n_D^{20}=1.4535; [found: C, 67.6; H, 9.6. $C_{12}H_{20}O_3$ requires C, 67.89; H, 9.50%]; ν_{max} (liquid film) 1748, 1188, 1152, 1032 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 4.17 (2H, q, *J*=7.0 Hz, OCH_2CH_3), 3.10–3.16 (2H, m, H-2, H-3), 2.71 (1H, m, H-1), 2.56 (1H, dd, *J*=14.9, 7.5 Hz, CH_aH_b-7), 2.29 (1H, dd, *J*=14.9, 5.7 Hz, CH_aH_b-7), 1.60 (1H, ddd, *J*=15.3, 5.0, 1.8 Hz, CH_aH_b-4), 1.54 (1H, d, *J*=15.3 Hz, CH_aH_b-4), 1.27 (3H, t, *J*=7.0 Hz, OCH_2CH_3), 1.04 (1H, ddd, *J*=3.0, 5.7, 1.9 Hz, CH_aH_b-6), 1.00 (1H, d, *J*=13.0 Hz, CH_aH_b-6), 0.90 (3H, s, $C(CH_3)_2$), 0.86 (3H, s, $C(CH_3)_2$).

4.2.2. Ethyl (1,5,5-trimethyl-2,3-epoxycyclohex-1-yl)acetate (2b). 2.65 g, 78%. Colourless liquid; n_D^{20}=1.4600; [found: C, 69.2; H, 9.4. $C_{13}H_{22}O_3$ requires C, 68.88; H, 9.80%]; ν_{max} (liquid film) 1748, 1372, 1364, 1240, 1156, 1036 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 4.12 (2H, q, *J*=7.1 Hz, OCH_2CH_3), 3.23 (1H, ddd, *J*=3.9, 3.8, 1.9 Hz, H-3), 2.97 (1H, d, *J*=3.8 Hz, H-2), 2.46 (1H, d, *J*=14.2 Hz, $CH_aH_bCO_2$), 2.32 (1H, d, *J*=14.2 Hz, $CH_aH_bCO_2$), 1.61–1.64 (2H, m, CH_2-4), 1.23 (1H d, *J*=14.1 Hz, CH_aH_b-6), 1.24 (3H, t, *J*=7.1 Hz, OCH_2CH_3), 1.22 (3H, s, CH_3-1), 1.10 (1H d, *J*=14.1 Hz, CH_aH_b-6), 0.91 (3H, s, $C(CH_3)_2$), 0.89 (3H, s, $C(CH_3)_2$).

4.2.3. *cis*-Ethyl (5-methyl-2,3-epoxycyclohex-1-yl)acetate (2c). 1.8 g, 60%. Colourless liquid; n_D^{20}=1.4540; [found: C, 66.7; H, 9.0. $C_{11}H_{18}O_3$ requires C, 66.64; H, 9.15%]; ν_{max} (liquid film) 1748, 1192, 1040 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 4.13 (2H, q, *J*=7.1 Hz, OCH_2CH_3), 3.16 (1H, dd, *J*=5.1, 4.0 Hz, H-3), 3.10 (1H, d, *J*=4.0 Hz, H-2), 2.49 (1H, dd, *J*=17.7, 9.7 Hz, CH_aH_b-7), 2.27–2.36 (2H, m, H-1, CH_aH_b-7), 1.99 (1H, m, CH_aH_b-4), 1.25 (3H, t, *J*=7.1 Hz, OCH_2CH_3), 0.83 (3H, d, *J*=6.2 Hz, CH_3-5).

4.2.4. *trans*-Ethyl (5-methyl-2,3-epoxycyclohex-1-yl)acetate (2d). 0.4 g, 15%. Colourless liquid; n_D^{20}=1.4573; [found: C, 66.5; H, 9.2. $C_{11}H_{18}O_3$ requires C, 66.64; H, 9.15%]; ν_{max} (liquid film) 1744, 1244, 1168, 1040 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 4.12 (2H, q, *J*=7.1 Hz, OCH_2CH_3), 3.15 (1H, ddd, *J*=3.8, 2.1, 1.8 Hz, H-3), 2.86 (1H, dd, *J*=3.8, 1.1 Hz, H-2), 2.06–2.47 (7H, m, CH_2-4, CH_2-6, CH_2-7, H-1), 1.25 (3H, t, *J*=7.1 Hz, OCH_2CH_3), 0.88 (3H, d, *J*=6.6 Hz, CH_3-5).

4.3. Lactonization of epoxy esters 2a–c with perchloric acid

Lactonization of epoxy esters **2a–c** (4.5 mmol) with perchloric acid in water–tetrahydrofurane solution (40 mL, THF–H_2O–$HClO_4$, 10:5:0.1) was carried out as described earlier.[11,15] The yield, physical and spectral data of hydroxy lactones **6a**,**6b**,**6c** are given below.

4.3.1. 2-Hydroxy-4,4-dimethyl-9-oxabicyclo[4.3.0]-nonan-8-one (6a). 0.5 g, 63%. White crystals, mp 53–54°C; [found: C, 65.0; H, 8.8. $C_{10}H_{16}O_3$ requires C, 65.19; H, 8.75%]; ν_{max} (KBr) 3464, 1784, 1183, 1028 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 4.40 (1H, t, *J*=5.9 Hz, H-1), 4.06 (1H, dddd, *J*=5.9, 5.5, 5.2, 4.2 Hz, H-2), 2.76 (1H, dd, *J*=13.8, 8.3 Hz, CH_aH_b-7), 2.35 (1H, s, OH), 2.26 (1H, d, *J*=13.8 Hz, CH_aH_b-7), 1.59 (1H, dd, *J*=14.0, 4.2 Hz, CH_aH_b-3), 1.24–1.42 (3H, m, CH_2-5, CH_aH_b-3), 1.04 (3H, s, $C(CH_3)_2$), 1.01 (3H, s, $C(CH_3)_2$).

Crystal data for **6a**. $C_{10}H_{16}O_3$, M_w=184.23, monoclinic, $P2_1/c$, *a*=21.939(4), *b*=13.311(3), *c*=6.929(2) Å, β=94.97(2)°, *V*=2015.7(8) $Å^3$, *Z*=8, D_c=1.214 mg m^{-3}, μ=0.088 mm^{-1}, *F*(000)=800, crystal size 0.30×0.25×0.20 mm^3, 13713 collected refl., 4680 indep. refl., R_{int}=0.0781, 363 parameters, *S*=1.152, R_1=0.1120, $R_w(F^2)$=0.2606.

4.3.2. 2-Hydroxy-4,4,6-trimethyl-9-oxabicyclo[4.3.0]-nonan-8-one (6b). 0.88 g, 99%. White crystals, mp 109–110°C; [found: C, 66.3; H, 9.2. $C_{11}H_{18}O_3$ requires C, 66.64; H, 9.15%]; ν_{max} (KBr) 3408, 1784, 1164, 1056 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 3.90 (1H, d, *J*=7.7 Hz, H-1), 3.86 (1H, ddd, *J*=7.7, 4.0, 2.1 Hz, H-2), 2.68 (1H, d, *J*=17.5 Hz, CH_aH_b-7), 2.15 (1H, d, *J*=17.5 Hz, CH_aH_b-7), 2.12 (1H, s, OH), 1.66 (1H, ddd, *J*=13.7, 4.0, 2.1 Hz, CH_aH_b-3), 1.62 (1H, dd, *J*=13.7, 2.1 Hz, CH_aH_b-3), 1.28–1.36 (2H, m, CH_2-5), 1.18 (3H, s, CH_3-6), 1.06 (3H, s, $C(CH_3)_2$), 1.01 (3H, s, $C(CH_3)_2$).

Crystal data for **6b**. $C_{22}H_{36}O_6$, M_w=396.51, monoclinic, $P2_1/c$, *a*=13.8460(15), *b*=12.8157(11), *c*=12.9695(13) Å, β=109.630(9)°, *V*=2167.6(4) $Å^3$, *Z*=4, D_c=

1.215 Mg m^{-3}, μ=0.087 mm^{-1}, F(000)=864, crystal size 0.27×0.25×0.20 mm^3, 14683 collected refl., 5009 indep. refl., R_{int}=0.0283, 397 parameters, S=1.122, R_1=0.0428, $R_w(F^2)$=0.0944.

4.3.3. 2-Hydroxy-4-methyl-9-oxabicyclo[4.3.0]nonan-9-one (6c). 0.75 g, 98%. Colourless liquid; n_D^{20}=1.4821; [found: C, 64.0; H, 8.0. $C_9H_{14}O_3$ requires C, 63.51; H, 8.29%]; ν_{max} (liquid film) 3448, 2964, 1796, 1216, 1172, 1060 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 4.25–4.29 (2H, m, H-2, H-1), 2.66 (1H, dd, J=16.3, 6.7 Hz, CH_aH$_b$-7), 2.61 (1H, m, H-6), 2.18 (1H, d, J=16.3 Hz, CH$_a$$H_b$-7), 1.66–1.74 (4H, m, C$H_aH_b$-3, C$H_aH_b$-5, H-4, OH), 1.34 (1-H, ddd, J=14.5, 12.1, 2.6 Hz, CH$_a$$H_b$-3), 0.88 (3H, d, J=6.6 Hz, CH$_3$-4), 0.83 (1H, m, CH$_a$$H_b$-5).

4.4. Lactonization epoxy esters with *p*-toluenesulfonic acid monohydrate

Mixture of epoxy ester (**1a**–**c**) (1 mmol) and *p*-toluenesulfonic acid monohydrate (1.1 mmol) in corresponding solvent (20 cm^3) was stirred at room temperature for 24 h. Then the reaction mixture in methylene chloride or benzene was washed with saturated $NaHCO_3$ aqueous solution, brine and dried ($MgSO_4$). In the case when the reaction was carried and in methanol or ethanol the reaction mixture was diluted with water and the product was extracted with methylene chloride. The extracts were washed with saturated $NaHCO_3$ solution, brine and dried ($MgSO_4$). After solvent evaporation the product mixture was analysed by GC and products were separated by column chromatography (silica gel, hexane–acetone 3:1). The compositions of product mixtures and yields are presented in Table 1. The physical and spectral data of compound obtained are given below.

4.4.1. 2-Tosyloxy-4,4-dimethyl-9-oxabicyclo[4.3.0]nonan-8-one (3a). 0.23 g, 67%. White crystals, mp 124–125°C; [found: C, 60.2; H, 6.6; S, 9.3. $C_{17}H_{22}O_5S$ requires C, 60.33; H, 6.55; S, 9.47%]; ν_{max} (KBr) 3016, 1800, 1472, 1352, 1180, 836 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.36–7.80 (4H, m, C_6H_4), 4.77 (1H, ddd, J=4.6, 4.5, 4.0 Hz, H-2), 4.39 (1H, dd, J=4.5, 4.0 Hz, H-1), 2.26–2.73 (2H, m, CH_aH$_b$-7, H-6), 2.46 (3H, s, C_6H_4–CH_3), 2.20 (1H, m, CH$_a$$H_b$-7), 1.56 (2H, m, CH$_2$-3), 1.26–1.43 (2H, m, CH$_2$-5), 1.02 (3H, s, C(CH_3)$_2$), 0.93 (3H, s, C(CH_3)$_2$).

Crystal data for **3a**. $C_{17}H_{22}O_5S$, M_w=338.41, monoclinic, $P2_1/c$, a=10.3028(9), b=14.8023(13), c=11.7590(14) Å, β=112.347(9)°, V=1658.6(3) Å^3, Z=4, D_c=1.355 Mg m^{-3}, μ=0.218 mm^{-1}, F(000)=720, crystal size 0.30×0.25×0.20 mm^3, 11260 collected refl., 3837 indep. refl., R_{int}=0.0302, 296 parameters, S=1.102, R_1=0.0423, $R_w(F^2)$=0.0911.

4.4.2. 2-Tosyloxy-4,4,6-trimethyl-9-oxabicyclo[4.3.0]-nonan-8-one (3b). 0.25 g, 70%. White crystals, mp 113–114°C; [found: C, 61.3; H, 6.8; S, 9.0. $C_{18}H_{24}O_5S$ requires C, 61.34; H, 6.84; S, 9.10%]; ν_{max} (KBr) 1796, 1472, 1372, 1180, 1036 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.36–7.80 (4H, m, C_6H_4), 4.65 (1H, ddd, J=9.1, 6.5, 4.2 Hz, H-2), 4.03 (1H, d, J=6.5 Hz, H-1), 2.52 (1H, d, J=17.3 Hz, CH_aH$_b$-7), 2.46 (3H, s, C_6H_4–CH_3), 2.18 (1H, d, J=17.3 Hz, CH$_a$$H_b$-7), 1.83 (1H, ddd, J=14.0, 4.2, 1.0 Hz, H$_e$-3), 1.56 (1H, dd, J=14.0, 9.1 Hz, H$_a$-3), 1.50 (1H, d, J=14.7 Hz, CH_aH$_b$-5), 1.25 (1H, d, J=14.7 Hz, CH$_a$$H_b$-5), 1.23 (3H, s, CH$_3$-6), 1.07 (3H, s, C(C$H_3$)$_2$), 1.03 (3H, s, C(C$H_3$)$_2$).

Crystal data for **3b**. $C_{18}H_{24}O_5S$, M_w=352.43, monoclinic, $P2_1/c$, a=8.020(2), b=19.520(4), c=11.365(2) Å, β=101.45(3)°, V=1743.8(6) Å^3, Z=4, D_c=1.342 Mg m^{-3}, μ=0.210 mm^{-1}, F(000)=752, crystal size 0.30×0.25×0.20 mm^3, 11620 collected refl., 4034 indep. refl., R_{int}=0.0269, 313 parameters, S=1.073, R_1=0.0392, $R_w(F^2)$=0.0885.

4.4.3. 2-Tosyloxy-4-methyl-9-oxabicyclo[4.3.0] nonan-8-one (3c). 0.24 g, 75%. White crystals, mp 105–106°C; [found: C, 59.3; H, 6.3; S, 9.8. $C_{16}H_{20}O_5S$ requires C, 59.23; H, 6.21; S, 9.88%]; ν_{max} (KBr) 2872, 1800, 1600, 1376, 1180, 840 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.30–7.73 (4H, m, C_6H_4), 4.78 (1H, m, H-2), 4.23 (1H, m, H-1), 2.56 (1H, dd, J=16.0, 6.5 Hz, CH_aH$_b$-7), 2.54 (1H, m, H-6), 2.39 (3H, s, C_6H_4–CH_3), 2.13 (1H, d, J=16.0 Hz, CH$_a$$H_b$-7), 0.83 (3H, d, J=6.5 Hz, CH$_3$-4).

Crystal data for **3c**. $C_{16}H_{20}O_5S$, M_w=324.38, monoclinic, $P2_1/c$, a=19.798(2), b=7.0236(8), c=11.7633(16) Å, β=105.355(11)°, V=1577.3(3) Å^3, Z=4, D_c=1.366 Mg m^{-3}, μ=0.226 mm^{-1}, F(000)=688, crystal size 0.30×0.25×0.20 mm^3, 10457 collected refl., 3701 indep. refl., R_{int}=0.0333, 279 parameters, S=1.069, R_1=0.0466, $R_w(F^2)$=0.0866.

4.4.4. 2-Hydroxy-4-methyl-9-oxabicyclo[4.3.0]nonan-9-one (6d). 0.16 g, 94%. Colourless liquid; n_D^{20}=1.4890; [found: C, 63.8; H, 8.1. $C_9H_{14}O_3$ requires C, 63.51; H, 8.29%]; ν_{max} (liquid film) 3464, 1792, 1172, 1016 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 4.25–4.29 (2H, m, H-1, H-2), 2.66 (1H, dd, J=16.2, 6.7 Hz, CH_aH$_b$-7), 2.60 (1H, m, H-6), 2.18 (1H, d, J=16.2 Hz, CH$_a$$H_b$-7), 1.67–1.84 (3H, m, C$H_aH_b$-3, CH$_a$$H_b$-5, H-4), 1.33 (1H, dt, J=13.5, 2.7 Hz, CH$_a$$H_b$-3), 0.85 (3H, d, J=6.2 Hz, CH$_3$-4), 0.77 (1H, m, CH_aH$_b$-5).

4.4.5. 2-Ethoxy-4,4-dimethyl-9-oxabicyclo[4.3.0]nonan-8-one (4a). 0.12 g, 60%. Colourless liquid; n_D^{20}=1.4665; [found: C, 68.1; H, 9.1. $C_{12}H_{20}O_3$ requires C, 67.89; H, 9.50%]; ν_{max} (liquid film) 1792, 1180, 1128, 1012 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 4.42 (1H, dd, J=5.0, 4.8 Hz, H-1), 3.65 (1H, dt, J=7.1, 4.8 Hz, H-2), 3.57 (2H, q, J=6.9 Hz, OCH_2CH$_3$), 2.72 (1H, dd, J=15.9, 7.9 Hz, CH_aH$_b$-7), 2.66 (1H, m, H-6), 2.19 (1H, d, J=15.9 Hz, CH$_a$$H_b$-7), 1.20–1.47 (4H, m, CH$_2$-3, CH$_2$-5), 1.19 (3H, t, J=6.9 Hz, OCH$_2$CH_3), 1.02 (3H, s, C(CH_3)$_2$), 0.98 (3H, s, C(CH_3)$_2$).

4.4.6. 2-Ethoxy-4,4,6-trimethyl-9-oxabicyclo[4.3.0]nonan-8-one (4b). 0.14 g, 64%. Colourless liquid; n_D^{20}=1.4638; [found: C, 70.0; H, 9.4. $C_{13}H_{22}O_3$ requires C, 68.99; H, 9.80%]; ν_{max} (liquid film) 1788, 1384, 1368, 1168, 1104, 1028 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 4.02 (1H, d, J=6.5 Hz, H-1), 3.58 (2H, q, J=7.0 Hz, OCH_2CH$_3$), 3.51 (1H, ddd, J=10.0, 6.5, 4.1 Hz, H-2), 2.57 (1H, d, J=17.3 Hz, CH_aH$_b$-7), 2.18 (1H, d, J=17.3 Hz, CH$_a$$H_b$-7), 1.60 (1H, ddd, J=13.7, 4.1, 1.0 Hz, H$_e$-3), 1.35 (1H, dd, J=13.7, 10.0 Hz, H$_a$-3), 1.50 (1H, d, J=14.7 Hz, CH_aH$_b$-5), 1.29

(1H, d, J=14.7 Hz, CH_aH_b-5), 1.22 (3H, s, CH_3-6), 1.18 (3H, t, J=7.0 Hz, OCH_2CH_3), 1.03 (3H, s, $C(CH_3)_2$), 1.01 (3H, s, $C(CH_3)_2$).

4.4.7. 2-Ethoxy-4-methyl-9-oxabicyclo[4.3.0]nonan-8-one (4c). 0.15 g, 78%. Colourless liquid; n_D^{20}=1.4640; [found: C, 66.7; H, 9.0. $C_{11}H_{18}O_3$ requires C, 66.64; H, 9.15%]; ν_{max} (liquid film) 1796, 1168, 1120, 1044 cm^{-1}; δ_H (300 MHz, $CDCl_3$), 4.30 (1H, m, H-1), 3.79 (1H, m, H-2), 3.52 (2H, m, OCH_2CH_3), 2.63 (1H, dd, J=16.5, 6.6 Hz, CH_aH_b-7), 2.54 (1H, m, H-6), 2.16 (1H, d, J=16.5 Hz, CH_aH_b-7), 1.51–1.76 (4H, m, CH_aH_b-3, CH_aH_b-5, H-4), 1.17 (3H, t, J=7.0 Hz, OCH_2CH_3), 0.86 (3H, d, J=6.4 Hz, CH_3-4), 0.75 (1H, m, CH_aH_b-5).

4.4.8. 2-Methoxy-4,4-dimethyl-9-oxabicyclo[4.3.0]-nonan-8-one (5a). 0.14 g, 70%. Colourless liquid; n_D^{20}= 1.4698; [found: C, 66.7; H, 8.9. $C_{11}H_{18}O_3$ requires C, 66.64; H, 9.15%]; ν_{max} (liquid film) 1796, 1168, 1100, 1044 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 4.39 (1H, t, J=5.0 Hz, H-1), 3.53 (1H, m, H-2), 3.38 (3H, s, OCH_3), 2.71 (1H, dd, J=16.6, 7.9 Hz, CH_aH_b-7), 2.62 (1H, m, H-6), 2.17 (1H, d, J= 16.6 Hz, CH_aH_b-7), 1.44 (2H, m, CH_2-3), 1.32 (1H, dd, J=13.8, 5.0 Hz, CH_aH_b-5), 1.17 (1H, d, J=13.8 Hz, CH_aH_b-5), 0.99 (3H, s, $C(CH_3)_2$), 0.96 (3H, s, $C(CH_3)_2$).

4.4.9. 2-Methoxy-4,4,6-trimethyl-9-oxabicyclo[4.3.0]-nonan-8-one (5b). 0.17 g, 79%. Colourless liquid; n_D^{20}= 1.4709; [found: C, 68.1; H, 9.1. $C_{12}H_{20}O_3$ requires C, 67.89; H, 9.50%]; ν_{max} (liquid film) 1788, 1389, 1368, 1164, 1104 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 4.02 (1H, d, J=6.4 Hz, H-1), 3.45 (1H, m, H-2), 3.40 (3H, s, OCH_3), 2.56 (1H, d, J=17.3 Hz, CH_aH_b-7), 2.19 (1H, d, J=17.3 Hz, CH_aH_b-7), 1.61 (1H, dd, J=13.7, 3.9 Hz, H_e-3), 1.32 (1H, dd, J=13.7, 10.0 Hz, H_a-3), 1.49 (1H,d, J=14.7 Hz, CH_aH_b-5), 1.30 (1H,d, J=14.7 Hz, CH_aH_b-5), 1.22 (3H, s, CH_3-6), 1.03 (3H, s, $C(CH_3)_2$), 1.01 (3H, s, $C(CH_3)_2$).

4.4.10. 2-Methoxy-4-methyl-9-oxabicyclo[4.3.0]nonan-8-one (5c). 0.15 g, 80%. Colourless liquid; n_D^{20}=1.4675; [found: C, 65.7; H, 8.3. $C_{10}H_{16}O_3$ requires C, 65.19; H, 8.75%]; ν_{max} (liquid film) 1800, 1216, 1168, 1088 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 4.32 (1H, m, H-1), 3.70 (1H, m, H-2), 3.36 (3H, s, OCH_3), 2.64 (1H, dd, J=16.6, 6.7 Hz, CH_aH_b-7), 2.57 (1H, m, H-6), 2.17 (1H, d, J=16.6 Hz, CH_aH_b-7), 1.52–1.85 (3H, m, CH_aH_b-3, CH_aH_b-5, H-4), 1.15 (1H, m, CH_aH_b-3), 0.87 (3H, d, J=6.4 Hz, CH_3-4), 0.75 (1H, m, CH_aH_b-5).

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References

1. Lochyński, S.; Frąckowiak, B.; Olejniczak, T.; Ciunik, Z.; Wawrzeńczyk, C. *Tetrahedron: Asymmetry* **2002**, *13*, 1761–1767.
2. Taylor, S. K.; Hopkins, J. A.; Spangenberg, K. A. *J. Org. Chem.* **1991**, *56*, 5951–5955.
3. Kato, M.; Watanabe, M.; Vagler, B.; Awen, B. Z.; Masuda, Y.; Tooyama, Y.; Yoshikoshi, A. *J. Org. Chem.* **1991**, *56*, 7071–7076.
4. Kawai, Y.; Hida, K.; Dao, D. H.; Ohno, A. *Tetrahedron Lett.* **1998**, *39*, 9219–9222.
5. Yamane, T.; Takahashi, M.; Ogasawara, K. *Synthesis* **1995**, 444–448.
6. Drioli, S.; Nitti, P.; Pitacco, G.; Tossut, L.; Valentin, E. *Tetrahedron: Asymmetry* **1999**, *10*, 2713–2728.
7. Snowden, R. L.; Linder, S. M. *Tetrahedron Lett.* **1991**, *32*, 4119–4120.
8. Rao, A. V. R.; Rao, S. M.; Sharma, G. V. M. *Tetrahedron Lett.* **1994**, *35*, 5735–5738.
9. Schultz, A. G.; Dai, M.; Thann, F. S.; Zhang, X. *Tetrahedron Lett.* **1998**, *39*, 6663–6666.
10. Ragoussis, V.; Liapis, M.; Ragoussis, N. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2545–2551.
11. Olejniczak, T.; Nawrot, J.; Ciunik, Z.; Wawrzeńczyk, C. *Pol. J. Chem.* **2000**, *74*, 673–680.
12. Wawrzeńczyk, C.; Lochyński, S. *Monatsh. Chem.* **1985**, *116*, 99–110.
13. Jones, G. B.; Huber, R. S.; Chau, S. *Tetrahedron* **1993**, *49*, 369–380.
14. Sayo, N.; Kimmura, Y.; Nakai, T. *Tetrahedron Lett.* **1982**, *23*, 3931–3934.
15. Olejniczak, T.; Grabarczyk, M.; Wawrzeńczyk, C. *J. Mol. Catal., B: Enzym.* **2001**, *11*, 243–247.
16. Grabarczyk, M.; Góra, J.; Wawrzeńczyk, C. Polish Patent Appl. P-342504, 2000.
17. Sheldrick, G. M. *Acta Crystallogr.* **1990**, *A46*, 467–473.
18. Sheldrick, G. M. *SHELXL97: Programm for the Refinement of Crystal Structures*; University of Göttingen: Germany, 1997.