SYNTHESIS OF CARBA ANALOGUES OF DEOXY-4-*C*-(HYDROXYMETHYL)-PENTOFURANOSES, INTERMEDIATES IN THE SYNTHESIS OF CARBOCYCLIC NUCLEOSIDES

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Racemic dimethyl 4-methoxy- (**11** and **12**), diallyl 4-allyloxy- (**13** and **14**) and dimethyl 4-(ethylsulfanyl)-2-hydroxycyclopentane-1,1-dicarboxylates (**15** and **16**) were prepared by base-catalyzed addition of methanol, allyl alcohol and ethylsulfane, respectively, to dimethyl (4-oxobut-2-en-1-yl)malonate (**6**). Deallylation of **13** and **14** afforded 4-hydroxycyclopentanes **27** and **28**. Reduction of **11**–**16** with lithium aluminium hydride gave the corresponding 4-substituted 2,2-bis(hydroxymethyl)cyclopentanols. Dimethyl (2*S*,3*S*,4*R*)-, (2*R*,3*S*,4*R*)-3-benzyloxy-4-formyloxy-2-hydroxycyclopentane-1,1-dicarboxylates (**35, 36**) and dimethyl (2*S*,3*S*,4*R*)-, (2*R*,3*S*,4*R*)-3-benzyloxy-2-benzoyloxy-4-methoxycyclopentane-1,1-dicarboxylates (**39, 40**) were synthesized starting from D-glucose. Reduction of dimethyl cyclopentane-1,1-dicarboxylates **39** and **40** with lithium aluminium hydride, benzoylation of the formed hydroxy derivatives, hydrogenolysis of benzyl groups, conversion of the liberated hydroxy groups into dithiocarbonates and their reduction with tributylstannane afforded, after removal of the protecting groups, (2*R*,4*R*)-1,1-bis(hydroxymethyl)-4-methoxycyclopentan-2-ol ((2*R*,4*R*)-**17**) and (3*R*,4*R*)-1,1-bis(hydroxymethyl)-4-methoxycyclopentan-3-ol (**51**). Reduction of a mixture of esters **35** and **36** gave (2*R*,3*R*)-2-benzyloxy-5-(hydroxymethyl)hexane-1,3,6-triol (**52**) as the major product and (2*R*,3*S*,4*R*)-3-benzyloxy-1,1-bis(hydroxymethyl)cyclopentane-2,4-diol (**53**) as the minor product. The latter was converted into (3*R*,4*R*)-1,1-bis(hydroxymethyl)cyclopentane-3,4-diol (**58**). 3-Deoxycarba analogues **51** and **58** arose by migration of benzoyl group in the preparation of the dithiocarbonates.

Key words: Carbasugars; Pseudosugars; Carbocyclic pentofuranoses; Substituted 1,1-bis(hydroxymethyl)cyclopentanes; Carbohydrates; Carbocyclic nucleosides; Cyclopentanes.

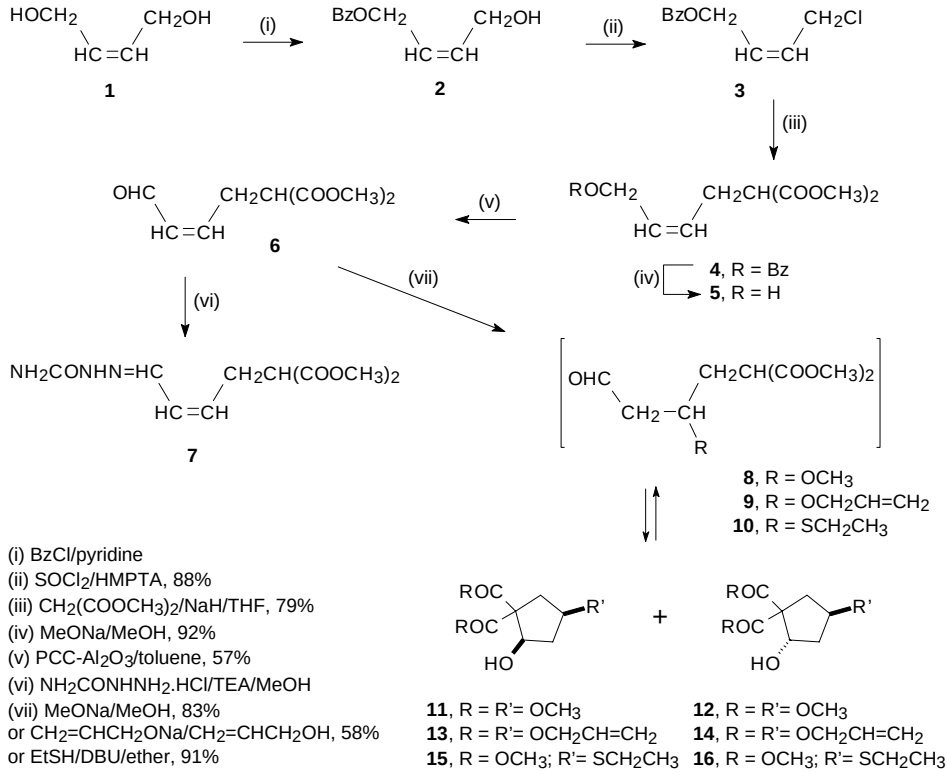
Polyhydroxycyclopentanes and cyclohexanes can be regarded as carbocyclic sugar analogues. The approach to five-membered carbocycles opens an alternative synthetic way to carbocyclic nucleoside analogues which have recently attracted much interest because of their significant antiviral[1a-1d], cancerostatic[1e] and purinergic[1f] activity.

This study is a part of our program aimed at the synthesis of 2′-deoxy-4′-*C*-substituted nucleosides and at structure–antiviral activity relationship studies[2] and deals with the synthesis of carba analogues of deoxy-4-*C*-(hydroxymethyl)pentofuranoses.

For the synthesis of the target carba analogues, we have chosen two synthetic approaches. The first, leading only to racemic products, starts from *cis*-but-2-ene-1,4-diol.

In the other approach, the starting compound is 3-*O*-benzyl-1,2:5,6-di-*O*-isopropylidene-D-glucofuranose.

Partial benzoylation of diol **1** (Scheme 1) afforded the monobenzoate **2** which on reaction with thionyl chloride in hexamethylphosphoramide gave chloro derivative **3** in the yield of 88%. Although the literature[3] reports an elegant preparation of 1-benzoyloxy-4-bromobut-2-ene using polymer-supported trityl chloride, the above-mentioned

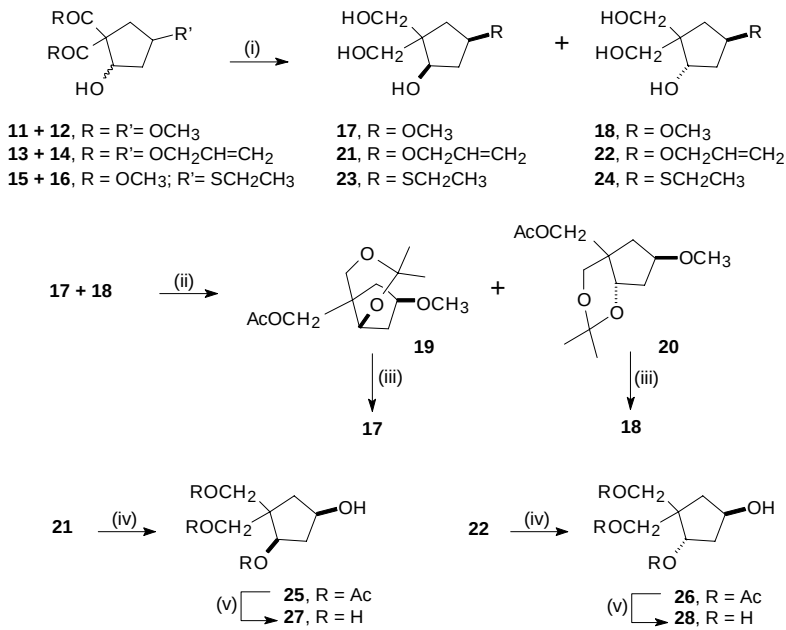


SCHEME 1

synthesis is more suitable for large-scale preparations. Alkylation of diethyl malonate with the chloro derivative **3** led to compound **4** (79% yield) which was debenzoylated with methanolic sodium methoxide. The obtained hydroxy derivative **5** was oxidized with pyridinium chlorochromate on alumina[4] to give aldehyde **6** (57% yield) which was characterized as semicarbazone **7**. In the next step, we made use of the facile nucleophilic addition of alcohols and mercaptans to α,β-unsaturated aldehydes[5]. Reaction of aldehyde **6** with 0.05 M methanolic sodium methoxide gave a mixture of the *cis*- (**11**) and *trans*- (**12**) substituted cyclopentane derivatives (83% yield) in the ratio 1 : 2. The reaction proceeds *via* the intermediate aldehyde **8** which immediately undergoes cyclization to a mixture of cyclopentane derivatives **11** and **12**. Similarly, the reaction of

aldehyde **6** with 0.05 M sodium allylalcoholate in allyl alcohol furnished a mixture of allyl derivatives **13** and **14** (58% yield), again in a 1 : 2 ratio. The dimethyl esters were transesterificated with allylalcohol in course of this reaction. The isomers **11** and **12**, and **13** and **14** were separated by chromatography on silica gel. The separated isomers were unstable: in methanolic solution, both the *cis*-isomer **11** and the *trans*-isomer **12** undergo interconversion and after 10 days at room temperature a 1 : 2 equilibrium mixture of both isomers was obtained. Apparently, the cyclization reaction of aldehyde **8** to the cyclopentane derivatives **11** and **12** is reversible. The cyclopentane ring is opened in a neutral methanolic solution at room temperature, the equilibration being significantly accelerated on addition of a base. The aldehyde **6** reacted with ethylsulfane in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene, affording a mixture of 4-ethylsulfanyl derivatives **15** and **16** in the yield of 98%. In this case, the isomer ratio in the reaction mixture was 5 : 8. Because of the identical chromatographic mobilities, compounds **15** and **16** could not be separated.

Reduction of the diesters to the corresponding bis(hydroxymethyl) derivatives was carried out with lithium aluminium hydride in boiling tetrahydrofuran. Because of instability of the individual isomers, we reduced mixtures of the *cis*- and *trans*-isomers.

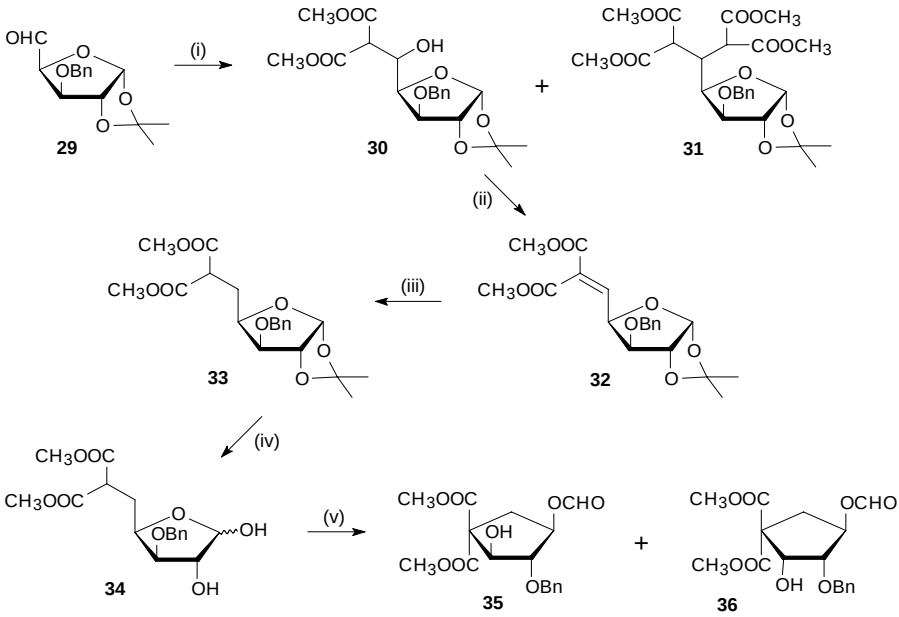


(i) $LiAlH_4$/THF, 29.5-37%; (ii) 1. 2,2-dimethoxypropane/acetone/DMF/H_2SO_4, 2. Ac_2O/DMAP/acetonitrile; (iii) 1. MeONa/MeOH, 2. Dowex 50 (H^+)/aqueous MeOH; (iv) 1. Ac_2O/DMAP/acetonitrile, 2. tris(triphenylphosphine)rhodium(I) chloride, 3. HCOOH, 60-66%; (v) MeONa/MeOH

SCHEME 2

Reduction of a mixture of dimethyl 2-hydroxy-4-methoxycyclopentane-1,1-dicarboxylates **11** and **12** (Scheme 2) afforded a mixture of bis(hydroxymethyl) derivatives **17** and **18** in 37% yield. Ketalization and acetylation of this mixture gave isopropylidene derivatives **19** and **20,** which were separated by chromatography on silica gel. After removal of the protecting groups we obtained the *cis*-derivative **17** and the *trans*-isomer **18**. The 4-allyloxy derivatives **21** and **22** and the 4-ethylsulfanyl derivatives **23** and **24** (obtained in 30 and 29.5% yield) were separated by chromatography on silica gel. Acetylation of the allyloxy derivatives **21** and **22** and removal of the allyl groups[6] afforded the tri-*O*-acetyl derivatives **25** and **26** which were methanolyzed with methanolic sodium methoxide to give free tetrahydroxy compounds **27** and **28**.

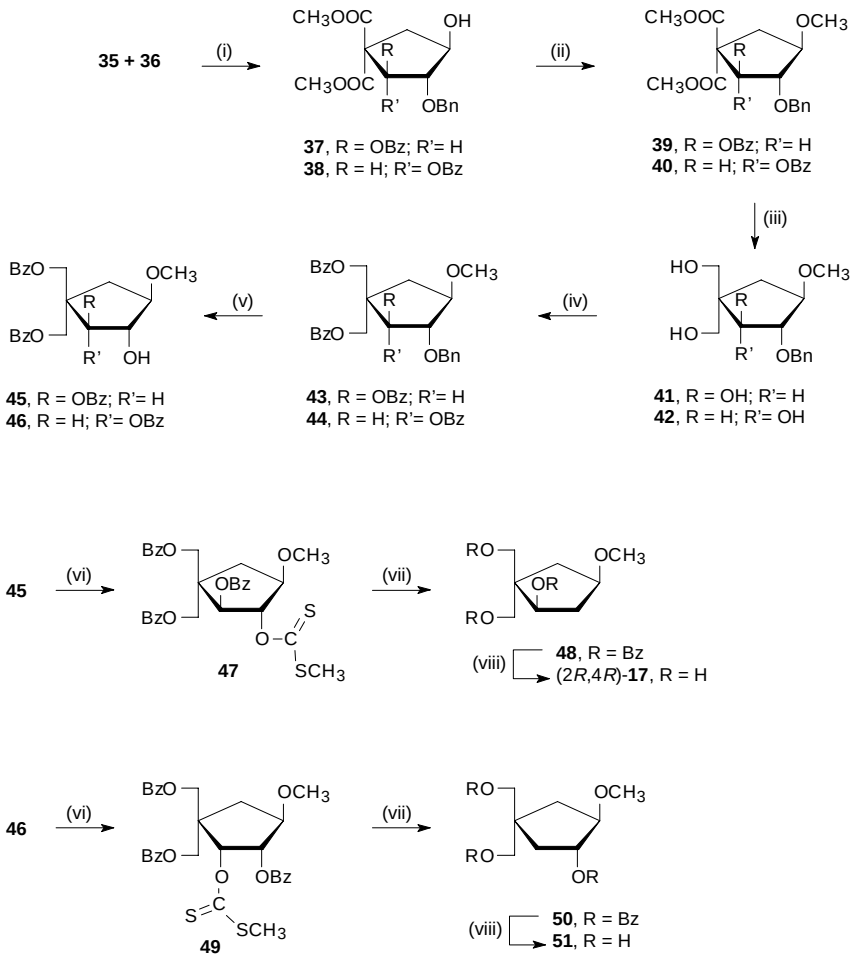
Carba analogues of deoxy-*C*-(hydroxymethyl)-D-pentofuranoses were also synthesized stereospecifically starting from D-glucose. Using a described[7] procedure, the aldehyde **29** was converted into cyclopentane derivatives **35** and **36** (Scheme 3). However, some of the described reaction steps had to be modified to be suitable for a large-scale synthesis. The described preparation of compound **32** by reaction of aldehyde **29** with dimethyl malonate in a mixture of pyridine and acetic anhydride led to a mixture that could be separated only with difficulties. Our modification of this reaction step



(i) $CH_2(COOCH_3)_2$/TEA, -10 °C, 69%; (ii) MsCl/pyridine, 99% or Ac_2O/pyridine, 80% or Ac_2O/DMAP/acetonitrile, 98%; (iii) $NaBH_4$/MeOH; (iv) Dowex 50 (H^+)/dioxane-water; (v) $NaIO_4$/dioxane-water, 64% based on reacted **33**

SCHEME 3

consisted in the reaction of aldehyde **29** with dimethyl malonate in the presence of triethylamine at –10 °C without any solvent. This procedure afforded crystalline hydroxy compound **30** in the yield of 69%. The configuration at the C-5 carbon atom was not studied. From the reaction mixture, we also isolated a small amount of the product of double addition of dimethyl malonate, **31,** whose amount increased with increasing



(i) 1. BzCl/pyridine, 2. $KHCO_3$/aqueous MeOH, 85%; (ii) $CH_2N_2/BF_3.Et_2O$, 82%; (iii) $LiAlH_4$/THF; (iv) BzCl/pyridine; (v) H_2/Pd-C, 25% of **45**, 12% of **46** (both based on the mixture of **39** and **40**); (vi) 1. NaH/DMF, 2. CS_2, 3. MeI, 92% of **47**; (vii) Bu_3SnH/AIBN, 92% of **48**, 63% of **50** (based on **46**); (viii) MeONa/MeOH, 89% of (2*R*,4*R*)-**17**, 93% of **51**

SCHEME 4

reaction temperature. The hydroxy compound **30** was converted into the unsaturated derivative **32** by treatment with methanesulfonyl chloride in pyridine (99% yield) or with acetic anhydride in pyridine (90% yield) or with acetic anhydride in acetonitrile in the presence of 4-(dimethylamino)pyridine (80% yield). Compound **32** was then converted into diester **33** using a described[7] procedure. Deketalization of compound **33** which, in contrast to the described procedure, was performed on Dowex 50(H^+) in aqueous dioxane, afforded diol **34**. This reaction is accompanied by partial hydrolysis of the methyl esters and therefore it was interrupted when TLC revealed their hydrolysis. Because of great difference in the chromatographic mobilities, the compounds **33** and **34** were easily separated by chromatography on silica gel. Reaction of dihydroxy derivative **34** with sodium periodate in aqueous 1,4-dioxane gave a 4 : 1 mixture of cyclopentane derivatives **35** and **36** in the overall yield of 64% based on the reacted ketal **33**. This mixture was used in the next step without separation and the isomers were separated in subsequent stages where it was easier.

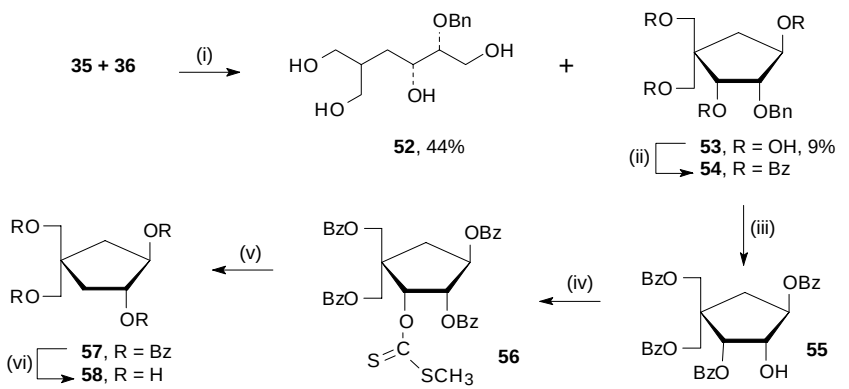
Benzoylation of the mixture of **35** and **36** (Scheme 4) by treatment with benzoyl chloride in pyridine and subsequent deformylation with potassium hydrogencarbonate in aqueous methanol[8] afforded a mixture of benzoates **37** and **38**. As determined by NMR spectroscopy, the ratio of both isomers was 3 : 2. Thus, also in this case isomerization takes place, similarly to the diesters **11**–**14**. The mixture of benzoates **37** and **38** was methylated with diazomethane under catalysis with boron trifluoride etherate[9] and the obtained methoxy derivatives **39** and **40** were reduced with lithium aluminium hydride in boiling tetrahydrofuran to give bis(hydroxymethyl) derivatives **41** and **42.** Their benzoylation with benzoyl chloride in pyridine afforded tribenzoates **43** and **44**. Hydrogenolysis of the benzyl groups furnished compounds **45** and **46** with free 3-hydroxy group (25% and 12% yields based on the esters **39** and **40**) which were separated by chromatography on silica gel. The hydroxy derivative **45** was converted into dithiocarbonate **47** using a described[10] procedure and the dithiocarbonate was treated with tributylstannane under catalysis with 2,2′-azobis(2-methylpropionitrile) to give the deoxy derivative **48**. Both reactions were facile and gave high yields. Methanolysis of the benzoyl groups with methanolic sodium methoxide afforded the free carba analogue (2*R*,4*R*)-**17**.

Dithiocarbonate **49** was prepared from the hydroxy derivative **46** in the same manner as the dithiocarbonate **47**. The first step in the preparation of dithiocarbonates is the conversion of the free hydroxy group into alkoxide by treatment with sodium hydride in dimethylformamide. In this case, the benzoyl group migrates and the 3-*O*-benzoyl derivative is apparently more stable. Reduction of the dithiocarbonate **49** with tributylstannane gave the deoxy derivative **50** and, after debenzoylation, the free carba analogue **51**. The reduction of the mixture of dimethyl esters **35** and **36** with lithium aluminium hydride (Scheme 5) was accompanied by cleavage of the cyclopentane ring and the reaction gave as the major product the acyclic compound **52**. Thus, this reaction

outcome confirms indirectly the mechanism of the isomerization of 1,1-bis(hydroxymethyl)cyclopentan-2-ols. In this case, the reduction of the aldehyde is faster than the reverse cyclization to the cyclopentane derivative. In addition to compound **52**, we obtained the compound **53** which was characterized as the benzoyl derivative **54** in the yield of 8% based on the mixture of isomers **35** and **36**. The isomer with (2*S*)-configuration could not be isolated. Hydrogenolysis afforded derivative with free 3-hydroxy group (**55**) which, similarly to the 4-methoxy derivative **45**, was converted into the dithiocarbonate **56**. Also in this case, the benzoyl group migrated during its preparation. Reduction of dithiocarbonate **56** with tributylstannane and subsequent methanolysis of the obtained benzoate **57** afforded the free carba analog **58**.

The structure of the studied cyclopentane derivatives was verified by ^{1}H NMR spectral analysis (decoupling experiments). The pairs of *cis*- and *trans*-isomers were assigned on the basis of the expected differences in chemical shifts of H-3a and H-3b protons due to shielding effects of groups in the position 2.

Racemic pseudo-2-deoxy-4-*C*-(hydroxymethyl)-D,L-pentofuranoses (**27** and **28**), their glycosides (**17**, **18**, **21** and **22**) and ethyl thioglycosides (**23** and **24**) were prepared by a cheap non-stereoselective synthesis which was realized in a few easy steps. The more complicated alternative approach, starting from D-glucose, led to pseudo-3-deoxy-4-*C*-(hydroxymethyl)-β-D-ribofuranose (**58**), methyl pseudo-2-deoxy-4-*C*-(hydroxymethyl)-β-D-xylofuranoside ((2*R*,4*R*)-**17**) and methyl pseudo-3-deoxy-4-*C*-(hydroxymethyl)-β-D-ribofuranoside (**58**). Within the scope of this project, some derivatives of the carba analogues of 2-deoxy-4-*C*-(hydroxymethyl)pentofuranoses will be synthesized as intermediates in nucleoside syntheses.



(i) $LiAlH_4$/THF, 44% of **52**, 9% of **53**; (ii) BzCl/pyridine; (iii) H_2/Pd-C, 91%; (iv) 1. NaH/DMF, 2. CS_2, 3. MeI, 83%; (v) Bu_3SnH/AIBN, 75% (based on **55**); (vi) MeONa/MeOH, 90%

SCHEME 5

EXPERIMENTAL

The melting points were determined on a Kofler block and are uncorrected. Optical rotations were obtained at 20 °C with a Perkin–Elmer 241 polarimeter. ^{1}H NMR spectra (δ, ppm; *J*, Hz) were recorded with Varian UNITY 200 and Varian UNITY 500 instruments in hexadeuteriodimethyl sulfoxide with tetramethylsilane as internal standard. Column chromatography was performed on 30-60 μm silica gel (Service Laboratories of the Institute) and thin-layer chromatography (TLC) on Silufol UV 254 foils (Kavalier, Votice). Solvents were evaporated at 2 kPa and bath temperature 30–60 °C; the compounds prepared were dried over phosphorus pentoxide at 13 Pa. Lithium aluminium hydride was used as a 1 M solution in tetrahydrofuran, supplied by Aldrich.

cis-1-Benzoyloxy-4-chlorobut-2-ene (**3**)

Benzoyl chloride (47 ml, 0.4 mol) was added dropwise during 4 h to a solution of *cis*-but-2-ene-1,4-diol (**1**) (49 ml, 0.6 mol) in a mixture of pyridine (200 ml) and dichloromethane (600 ml), cooled to 0 °C. The solvent was evaporated and the residue dissolved in ethyl acetate (1 l). The solution was washed with water (200 ml), 5% hydrochloric acid to acid reaction of the washings, again with water (200 ml), 10% aqueous sodium hydrogencarbonate, dried over sodium sulfate, and the solvent was evaporated. The residue was dissolved in toluene (100 ml) and the solution was shaken with anhydrous calcium chloride (400 g) for 30 min. The mixture was filtered and the solid on the filter washed with toluene (1.5 l). The solid complex of the product with calcium chloride was dissolved in water (600 ml) and the solution extracted with ethyl acetate (3 × 400 ml). The combined extracts were washed with 10% aqueous sodium hydrogencarbonate (200 ml), dried and taken down. Yield 47 g (61%, based on benzoyl chloride) of *cis*-4-benzoyloxybut-2-en-1-ol (**2**). To a solution of **2** in HMPTA (195 ml) thionyl chloride (19.5 ml) was added at 0 °C, the solution was set aside at room temperature overnight and then added dropwise to a stirred 10% solution of sodium hydrogencarbonate (700 ml). The mixture was extracted with ethyl acetate (2 × 500 ml), the combined extracts were washed with water (2 × 300 ml), dried over sodium sulfate and the solvent was evaporated. After standing for 4 h at 5 °C, the chloro derivative **3** (45.41 g; 88%) crystallized, m.p. 33.5–34 °C. For $C_{11}H_{11}ClO_2$ (210.7) calculated: 62.72% C, 5.26% H, 16.83% Cl; found: 62.94% C, 5.24% H, 16.75% Cl. ^{1}H NMR spectrum ($CDCl_3$): 4.22 d, 2 H, *J*(CH_2,CH) = 6.6 (CH_2Cl); 4.93 d, 2 H, *J*(CH_2,CH) = 5.8 (CH_2OBz); 5.80–5.98 m, 2 H (CH=CH); 7.39–7.61 m, 3 H and 8.02–8.06 m, 2 H (H-arom.).

Dimethyl *cis*-(4-Benzoyloxybut-2-en-1-yl)malonate (**4**)

A suspension of sodium hydride in oil (60%; 9.6 g, 0.24 mol) was slowly added under argon to a solution of chloro derivative **3** (42.1 g, 0.2 mol) and dimethyl malonate (29 ml, 0.25 mol) in tetrahydrofuran (400 ml), cooled to 0 °C. After stirring at room temperature overnight, the mixture was neutralized with acetic acid, diluted with ethyl acetate, washed with water (3 × 1 l), dried over sodium sulfate and the solvent was evaporated. Chromatography of the residue on a column of silica gel (3 kg) in toluene–ethyl acetate (9 : 1) afforded 48.2 g (79%) of oily product **4**. For $C_{16}H_{18}O_6$ (306.3) calculated: 62.74% C, 5.92% H; found: 62.58% C, 5.81% H. ^{1}H NMR spectrum: 2.66 t, 2 H, *J*(1,CH) = *J*(1,2) = 7.2 (2 × H-1); 3.65 s, 6 H (2 × OCH_3); 3.67 t, 1 H (CH); 4.85 d, 2 H, *J*(4,3) = 6.1 (2 × H-4); 5.54–5.80 m, 2 H (H-2, H-3), 7.48–8.00 m, 5 H (H-arom.).

Dimethyl *cis*-(4-Hydroxybut-2-en-1-yl)malonate (**5**)

A solution of benzoate **4** (30.63 g, 20 mmol) in 0.1 M methanolic sodium methoxide (350 ml) was allowed to stand at room temperature for 5 h and then neutralized with Dowex 50 (H^+). The ion

exchanger was filtered off, washed with methanol and the combined filtrates were taken down. The residue was chromatographed on a column of silica gel (1 kg). Elution with ethyl acetate–toluene (1 : 3) gave methyl benzoate and subsequent elution with ethyl acetate–toluene (3 : 1) afforded 18.6 g (92%) of oily product **5**. For $C_9H_{14}O_5$ (202.2) calculated: 53.46% C, 6.98% H; found: 53.24% C, 7.11% H. ^{1}H NMR spectrum: 2.47–2.55 m, 2 H (2 × H-1); 3.58 t, 1 H, *J*(CH,1) = 7.3 (CH); 3.65 s, 6 H (2 × OCH_3); 3.93–4.01 m, 2 H (2 × H-4); 4.60 t, 1 H, *J*(OH,4) = 5.2 (4-OH); 5.22–5.37 m, 1 H (H-3); 5.48–5.62 m, 1 H (H-2).

Dimethyl *cis*-(4-Oxobut-2-en-1-yl)malonate (**6**)

Pyridinium chlorochromate on alumina[4] (56 g) was added portionwise to a stirred and cooled (ice bath) solution of hydroxy derivative **5** (4.04 g, 20 mmol) in toluene (70 ml). After stirring at 0 °C for 1 h and at room temperature for 2 h, the alumina was removed by filtration and washed with toluene (150 ml). The combined filrates were taken down to give 2.3 g (57%) of oily product **6**. An analytical sample was obtained by chromatography on a column of silica gel in ethyl acetate–toluene (2 : 3). For $C_9H_{14}O_5$ (200.2) calculated: 53.99% C, 6.04% H; found: 53.71% C, 6.27% H. ^{1}H NMR spectrum: 2.80 ddd, 2 H, *J*(1,CH) = 7.1, *J*(1,2) = 6.7, *J*(1,3) = 1.5 (2 × H-1); 3.65 s, 6 H (2 × CH_3); 3.87 t, 1 H (CH); 6.11 ddt, 1 H, *J*(3,2) = 15.6, *J*(3,4) = 7.8 (H-3); 6.93 dt, 1 H (H-2); 9.45 d, 1 H (H-4).

Dimethyl *cis*-(4-Oxobut-2-en-1-yl)malonate Semicarbazone (**7**)

Semicarbazide hydrochloride (339 mg) and triethylamine (0.3 ml) were added to a solution of aldehyde **6** (400 mg, 2 mmol) in methanol (8 ml). The mixture was stirred at room temperature for 3 h and the solvent was evaporated. The residue was partitioned between ethyl acetate (10 ml) and water (5 ml). The aqueous layer was washed with ethyl acetate (10 ml) and both combined organic layers were dried over magnesium sulfate. Evaporation of the solvent and crystallization from water afforded 334 mg (65%) of semicarbazone **7**, m.p. 125–126 °C. For $C_{10}H_{15}N_3O_5$ (257.3) calculated: 46.69% C, 5.88% H, 16.34% N; found: 46.91% C, 5.94% H, 16.47% N. ^{1}H NMR spectrum: 2.63 dd, 2 H, *J*(1,CH) = 7.3, *J*(1,2) = 7.0 (2 × H-1); 3.65 s, 6 H (2 × CH_3); 3.71 t, 1 H (CH); 5.82–5.97 m, 1 H (H-3); 6.06–6.18 m, 1 H (H-2); 6.23 bs, 1 H (H-4); 7.42 s, 1 H and 7.47 s, 1 H (NH_2); 9.99 s, 1 H (NH).

Dimethyl (±)-*cis*- (**11**) and (±)-*trans*-2-Hydroxy-4-methoxycyclopentane-1,1-dicarboxylate (**12**)

A solution of aldehyde **6** (2.0 g, 10 mmol) in 0.05 M methanolic sodium methoxide (100 ml) was set aside at room temperature for 2.5 h. After neutralization with Dowex 50 (H^+) and evaporation, the residue was chromatographed on a silca gel column (200 g) in toluene–ethyl acetate (3 : 2) to give 1.92 g (83%) of oily mixture of **11** and **12**. Repeated flash chromatography of a small amount of the mixture separated both the racemates. The composition of fractions was monitored by TLC. On the plates used (Silufol) both the racemates were distinctly separated. Spots were detected by cautious heating of the plate over a flame and then by UV light. The ratio of the fast-eluting fraction (racemate **11**) to the slow-eluting one (racemate **12**) was 1 : 2.

Racemate **11**: For $C_{10}H_{16}O_6$ (232.2) calculated: 51.72% C, 6.94% H; found: 51.51% C, 7.07% H. ^{1}H NMR spectrum: 1.60 ddd, 1 H, *J*(3a,2) = 3.7, *J*(3a,4) = 5.6, *J*(3a,3b) = 13.9 (H-3a); 2.29 dd, 1 H, *J*(5a,4) = 6.8, *J*(5a,5b) = 13.4 (H-5a); 2.30 ddd, 1 H, *J*(3b,2) = 6.0, *J*(3b,4) = 7.4 (H-3b); 2.37 dd, 1 H, *J*(5b,4) = 8.1 (H-5b); 3.17 s, 3 H (OCH_3); 3.62 s , 3 H and 3.64 s, 3 H (2 × $COOCH_3$); 4.46 btd, 1 H, *J*(2,OH) = 5.6 (H-2); 5.19 d, 1 H (2-OH).

Racemate **12**: For $C_{10}H_{16}O_6$ (232.2) calculated: 51.72% C, 6.94% H; found: 51.40% C, 7.12% H. ^{1}H NMR spectrum: 1.88 ddd, *J*(3a,2) = 3.7, *J*(3a,4) = 6.2, *J*(3a,3b) = 14.0 (H-3a); 1.96 dddd, *J*(3b,2) = 5.8, *J*(3b,4) = 3.8, *J*(3b,5a) = 1.3 (H-3b); 2.08 ddt, 1 H, *J*(5a,2) = *J*(5a,3b) = 1.2, *J*(5a,4) = 2.3, *J*(5a,5b) = 14.3 (H-5a); 2.58 dd, 1 H, *J*(5b,4) = 6.2 (H-5b); 3.08 s, 3 H (OCH_3); 3.61 s, 6 H (2 × $COOCH_3$).

Isomerization of Dimethyl (±)-*cis*- (**11**) and (±)-*trans*-2-Hydroxy-4-methoxycyclopentane-1,1-dicarboxylates (**12**)

A. Methanolic 0.5 M solutions of compounds **11** and **12** (1 ml) were set aside at room temperature for 10 days. The course of the isomerization was followed by TLC. The solutions were evaporated and the ^{1}H NMR spectra of both residues were measured. The racemate ratio **11** : **12** in both samples was 1 : 2.

B. To 0.5 M methanolic solutions of compounds **11** and **12** (1 ml) was added one drop of triethylamine. After 5 min, TLC of both solutions showed that an equilibrium was established. After evaporation of the solvent, the ratio **11** : **12** in both samples was 1 : 2 (by ^{1}H NMR).

Diallyl (±)-*cis*- (**13**) and (±)-*trans*-4-Allyloxy-2-hydroxycyclopentane-1,1-dicarboxylate (**14**)

A solution of aldehyde **6** (2.0 g, 10 mmol) in 0.05 M solution of sodium allyl alcoholate in allyl alcohol (100 ml) was set aside under argon at room temperature for 4 h, then neutralized with acetic acid and the solvent was evaporated. The residue was dissolved in ethyl acetate (100 ml), the solution was washed with water (20 ml), 10% solution of sodium hydrogencarbonate (20 ml) and with water, dried over magnesium sulfate, and the solvent was evaporated. Column chromatography on silica gel (200 g) in toluene–ethyl acetate (3 : 1) afforded 1.8 g (58%) of a mixture of racemates **13** and **14**. Similarly to the methoxy derivatives, both isomers were separated by flash chromatography of a small amount of the mixture. The ratio of the fast-eluting fraction (racemate **13**) to the slow-eluting one (racemate **14**) was 1 : 2.

Racemate **13**: For $C_{16}H_{22}O_6$ (310.3) calculated: 61.92% C, 7.15% H; found: 61.69% C, 7.07% H. ^{1}H NMR spectrum: 1.63 ddd, 1 H, *J*(3a,2) = 3.7, *J*(3a,3b) = 13.9, *J*(3a,4) = 6.1 (H-3a); 2.33 dd, 1 H, *J*(5a,4) = 6.8, *J*(5a,5b) = 13.2; 2.34 ddd, 1 H, *J*(3b,2) = 5.9, *J*(3b,4) = 8.0 (H-3b); 2.43 dd, 1 H, *J*(5b,4) = 8.3 (H-5b); 3.83 m, 1 H (H-4); 3.85 m, 2 H (OCH_2); 4.49 m, 1 H (H-2); 4.60 m, 4 H (2 × CH_2); 5.05–5.32 m, 6 H (3 × CH_2=); 5.28 d, 1 H, *J*(OH,2) = 5.6 (2-OH); 5.80 m, 1 H (CH=); 5.85 m, 2 H (2 × CH=).

Racemate **14**: For $C_{16}H_{22}O_6$ (310.3) calculated: 61.92% C, 7.15% H; found: 61.98% C, 7.40% H. ^{1}H NMR spectrum: 1.92 ddd, 1 H, *J*(3a,2) = 3.4, *J*(3a,3b) = 14.2, *J*(3a,4) = 6.4 (H-3a); 2.00 ddd, 1 H, *J*(3b,2) = 5.9, *J*(3b,4) = 3.9 (H-3b); 2.13 brdd, 1 H, *J*(5a,4) = 2.2, *J*(5a,5b) = 14.2 (H-5a); 2.63 dd, 1 H, *J*(5b,4) = 6.1 (H-5b); 3.80 m, 2 H (OCH_2); 4.06 brtdd, 1 H (H-4); 4.50–4.66 m, 4 H (2 × OCH_2); 4.73 td, 1 H, *J*(2,OH) = 5.9 (H-2); 5.05–5.35 m, 6 H (3 × CH_2=); 5.31 d, 1 H (2-OH); 5.80 m, 1 H (CH=); 5.85 m, 2 H (2 × CH=).

Dimethyl (±)-*cis*- (**15**) and (±)-*trans*-4-Ethylsulfanyl-2-hydroxycyclopentane-1,1-dicarboxylate (**16**)

Ethylsulfane (1.5 ml) and 1,8-diazabicyclo[5.4.0]undec-7-ene (0.1 ml) were added to a solution of aldehyde **6** (2.50 g, 12.5 mmol) in ether (10 ml). After standing overnight at room temperature, the mixture was neutralized with acetic acid (0.1 ml) and the solvent was evaporated. The residue was dissolved in ethyl acetate (50 ml) and the solution was washed with water (2 × 15 ml), dried over magnesium sulfate and taken down. Chromatography on a column of silica gel (300 g) in toluene–ethyl acetate (3 : 2) afforded 2.99 g (91%) of oily mixture of racemates **15** and **16**. For $C_{11}H_{18}O_5S$

(262.3) calculated: 50.36% C, 6.92% H, 12.22% S; found: 50.05% C, 7.05% H, 11.98% S. ^{1}H NMR spectrum, racemate **15**: 1.15 t, 3 H, $J(CH_3,CH_2)$ = 7.3 (CH_3); 1.53 ddd, 1 H, J(3a,2) = 4.4, J(3a,3b) = 13.7, J(3a,4) = 8.8 (H-3a); 2.32 dd, 1 H, J(5a,4) = 7.8, J(5a,5b) = 13.2 (H-5a); 2.36 dd, 1 H, J(5b,4) = 9.0 (H-5b); 2.47 ddd, J(3b,2) = 6.1, J(3b,4) = 8.8 (H-3b); 2.53 q, 2 H (SCH_2); 2.92 brpent, 1 H (H-4); 3.61 s, 1 H (OCH_3); 3.64 s, 1 H (OCH_3); 4.55 ddd, 1 H, J(2,OH) = 5.3 (H-2); 5.40 d, 1 H (2-OH); racemate **16**: 1.16 t, 3 H, $J(CH_3,CH_2)$ = 7.3 (CH_3); 1.75 ddd, 1 H, J(3a,2) = 5.0, J(3a,3b) = 13.4, J(3a,4) = 9.0 (H-3a); 1.81 dd, 1 H, J(5a,4) = 6.4, J(5a,5b) = 14.2 (H-5a); 2.05 ddd, J(3b,2) = 2.2, J(3b,4) = 7.1 (H-3b); 2.50 q, 2 H (SCH_2); 2.94 dd, 1 H, J(5b,4) = 8.6 (H-5b); 3.42 btt, 1 H (H-4); 3.61 s, 3 H (OCH_3); 3.62 s, 3 H (OCH_3); 4.63 ddd, 1 H, J(2,OH) = 5.4 (H-2); 5.37 d, 1 H (2-OH).

(±)-*cis*- (**19**) and (±)-*trans*-6-Acetoxymethyl-8-methoxy-3,3-dimethyl-2,4-dioxabicyclo-[4.3.0]nonane (**20**)

A solution of the mixture of esters **11** and **12** (1.39 g, 6 mmol) in tetrahydrofuran (4 ml) was added dropwise at 60 °C (reflux condenser) under argon to a stirred 1 M solution of lithium aluminium hydride in tetrahydrofuran (10.5 ml). The mixture was then refluxed for 2 h. After cooling, ethyl acetate (1.5 ml) was added, followed after 15 min by water (6 ml). The mixture was taken down *in vacuo* and the dry residue was extracted with warm ethyl acetate (5 × 15 ml). The solid residue was air-dried and mixed with warm 90% aqueous methanol. The insoluble portion was filtered off and washed with methanol. Direct extraction of the reaction mixture with methanol led to a mixture that could be filtered only with great difficulties. The combined extracts and filtrates were taken down and the residue was chromatographed on a column of silica (140 g) in ethyl acetate–acetone–ethanol–water (36 : 6 : 5 : 3). Yield 392 mg (37%) of a mixture of trihydroxy derivatives **17** and **18**. To a stirred solution of the mixture of trihydroxy derivatives in dimethylformamide (1.3 ml), acetone (1.3 ml) and 2,2-dimethoxypropane (1.3 ml), sulfuric acid (3 drops) was added. The solution was allowed to stand at room temperature for 5 h and then neutralized with solid sodium hydrogencarbonate. The solid was filtered off, washed with acetone and the combined filtrates were evaporated. The residue was codistilled with xylene and dissolved in acetonitrile (3 ml). To this solution were added acetic anhydride (0.4 ml) and 4-dimethylaminopyridine (200 mg) and the mixture was set aside at room temperature for 3 h. Then methanol (1 ml) was added and the solvent was evaporated. A solution of the residue in ethyl acetate (15 ml) was washed with water (2 × 5 ml), 5% aqueous solution of sodium hydrogencarbonate, dried over magnesium sulfate and taken down. Chromatography on a column of silica gel (80 g) in ethyl acetate–toluene (1 : 3) afforded 260 mg (17% based on the starting mixture of **11** and **12**) of the isopropylidene derivative **20** as a thick oil. For $C_{13}H_{22}O_5$ (258.3) calculated: 60.45% C, 8.58% H; found: 60.19% C, 8.75% H. ^{1}H NMR spectrum: 1.22 s, 3 H and 1.31 s, 3 H ($C(CH_3)_2$); 1.46 bdd, 1 H, J(7a,8) = 4.4, J(7a,7b) = 13.7 (H-7a); 1.79 ddd, 1 H, J(9a,1) = 5.4, J(9a,9b) = 14.2, J(9a,8) = 6.8 (H-9a); 1.97 dd, 1 H, J(7b,8) = 7.1 (H-7b); 1.98 dd, 1 H, J(9b,8) = 6.8 (H-9b); 2.03 s, 3 H (CH_3CO); 3.16 s, 3 H (OCH_3); 3.41 d, 1 H and 3.67 d, 1 H, J(gem) = 11.5 (CH_2O); 3.85 d, 1 H and 4.05 d, 1 H, J(gem) = 11.0 (CH_2O); 3.98 qd, 1 H (H-8); 4.02 brd, 1 H (H-1). Evaporation of the second fraction gave 142 mg (9%) of isopropylidene derivative **19** as a thick oil. For $C_{13}H_{22}O_5$ (258.3) calculated: 60.45% C, 8.58% H; found: 60.14% C, 8.69% H. ^{1}H NMR spectrum: 1.23 s, 3 H and 1.32 s, 3 H ($C(CH_3)_2$); 1.61 ddd, 1 H, J(9a,1) = 1.2, J(9a,9b) = 14.9, J(9a,8) = 3.7 (H-9a); 1.77 dd, 1 H, J(7a,8) = 6.6, J(7a,7b) = 13.2 (H-7a); 1.80 dd, 1 H, J(7b,8) = 6.6 (H-7b); 2.03 s, 3 H (CH_3CO); 2.21 ddd, 1 H, J(9b,1) = 6.1, J(9b,8) = 7.8 (H-9b); 3.49 d, 1 H and 3.66 d, 1 H, J(gem) = 11.5 (CH_2O); 3.81 d, 1 H and 3.87 d, 1 H, J(gem) = 11.2 (CH_2O); 3.89 m, 1 H (H-8); 3.91 dd, 1 H (H-1).

(±)-*cis*-2,2-Bis(hydroxymethyl)-4-methoxycyclopentan-1-ol (**17**)

A solution of isopropylidene derivative **19** (129 mg, 0.5 mmol) in 0.1 M methanolic sodium methoxide (1.5 ml) was set aside at room temperature for 3 h and then neutralized with Dowex 50 (H^+). The ion exchanger was filtered off, washed with methanol and the combined filtrates were taken down. The residue was dissolved in 80% aqueous methanol, Dowex 50 (H^+) was added and the mixture was stirred under reflux for 30 min. The Dowex was filtered off, washed with methanol and the combined filtrates were evaporated. Chromatography of the residue on silica gel column (10 g) in ethyl acetate–acetone–ethanol–water (36 : 6 : 5 : 3) afforded 74 mg (84%) of trihydroxy derivative **17** as a thick oil. For $C_8H_{16}O_4$ (176.2) calculated: 54.53% C, 9.15% H; found: 54.92% C, 9.41% H. ^{1}H NMR spectrum: 1.46 dd, 1 H, *J*(3a,4) = 6.1, *J*(3a,3b) = 13.4 (H-3a); 1.52 dt, 1 H, *J*(5a,1) = *J*(5a,4) = 7.3, *J*(5a,5b) = 12.9 (H-5a); 1.74 dd, 1 H, *J*(3b,4) = 7.6 (H-3b); 2.19 dt, 1 H, *J*(5b,1) = *J*(5b,4) = 6.8 (H-5b); 3.14 s, 3 H (OCH_3); 3.21 dd, 1 H, *J*(CH,OH) = 5.4 and 3.29 dd, 1 H, *J*(CH,OH) = 5.1, *J*(gem) = 10.5 (CH_2O); 3.40 dd, 1 H, *J*(CH,OH) = 6.1 and 3.49 dd, 1 H, *J*(CH,OH) = 4.9, *J*(gem) = 10.7 (CH_2O); 3.83 ddd, 1 H, *J*(1,OH) = 5.1 (H-1); 4.14 t, 1 H, *J*(CH_2,OH) = 5.5 (CH_2O**H**); 4.46 t, 1 H, *J*(CH_2,OH) = 5.2 (CH_2O**H**); 4.52 d, 1 H (1-OH).

(±)-*trans*-2,2-Bis(hydroxymethyl)-4-methoxycyclopentan-1-ol (**18**)

Using the same procedure as in the preparation of the cyclopentane derivative **17,** isopropylidene derivative **20** (258 mg, 1 mmol) was converted into trihydroxy derivative **18** (151 mg; 85%) which was obtained as a thick oil. For $C_8H_{16}O_4$ (176.2) calculated: 54.53% C, 9.15% H; found: 54.21% C, 9.31% H. ^{1}H NMR spectrum: 1.36 dd, 1 H, *J*(3a,4) = 4.5, *J*(3a,3b) = 13.8 (H-3a); 1.78 dd, 1 H, *J*(3b,4) = 7.2 (H-3b); 1.80 m, 2 H (H-5a, H-5b); 3.13 s, 3 H (OCH_3); 3.26 dd, 1 H, *J*(CH,OH) = 5.5 and 3.34 dd, 1 H, *J*(CH,OH) = 5.2, *J*(gem) = 10.5 (CH_2O); 3.39 dd, 1 H, *J*(CH,OH) = 5.8 and 3.43 dd, 1 H, *J*(CH,OH) = 5.2, *J*(gem) = 10.7 (CH_2O); 3.81 m, 1 H (H-4); 3.95 td, *J*(1,5a) = *J*(1,5b) = 6.1, *J*(1,OH) = 4.8 (H-1); 4.16 bt, 1 H, *J*(OH,CH_2) = 5.5 (CH_2O**H**); 4.44 brt, 1 H, *J*(OH,CH_2) = 5.3 (CH_2O**H**); 4.52 d, 1 H (1-OH).

(±)-*cis*- (**21**) and (±)-*trans*-4-Allyloxy-2,2-bis(hydroxymethyl)cyclopentan-1-ol (**22**)

A mixture of esters **13** and **14** (3.72 g, 12 mmol) dissolved in tetrahydrofuran (12 ml) was slowly added dropwise to a stirred and boiling 1 M solution of lithium aluminium hydride in tetrahydrofuran (21 ml) in an argon atmosphere. After reflux for 2 h, the mixture was cooled and ethyl acetate (3 ml), followed after 15 min with water, was added. The mixture was taken down *in vacuo* and the residue was extracted with warm ethyl acetate (5 × 30 ml). The solid residue was air-dried and mixed with 90% aqueous methanol. The insoluble portion was filtered off and washed with methanol. The combined extracts and filtrates were taken down and the residue was chromatographed on a silica gel column (300 g) in ethyl acetate–acetone–ethanol–water (80 : 10 : 5 : 5) to give 725 mg (30%) of a mixture of **21** and **22**. Repeated column chromatography on silica gel (400 g) in the same solvent system afforded 435 mg of racemate **22** and 120 mg of racemate **21**.

Racemate **21**: For $C_{10}H_{18}O_4$ (202.2) calculated: 59.39% C, 8.97% H; found: 59.69% C, 9.11% H. ^{1}H NMR spectrum: 1.38 dd, 1 H, *J*(3a,4) = 4.9, *J*(3a,3b) = 13.7 (H-3a); 1.79 dd, 1 H, *J*(3b,4) = 6.1 (H-3b); 1.81 m, 2 H (H-5a, H-5b); 3.27 dd, 1 H, *J*(CH,OH) = 5.4 and 3.35 dd, 1 H, *J*(CH,OH) = 5.3, *J*(gem) = 10.5 (CH_2O); 3.38 dd, 1 H, *J*(CH,OH) = 5.6 and 3.43 dd, 1 H, *J*(CH,OH) = 5.4, *J*(gem) = 10.7 (CH_2O); 3.84 dq, 2 H, J = 1.5 and 5.4 (OCH_2); 3.96 ddd, 1 H, *J*(1,5a) = 2.2, *J*(1,5b) = 6.1, *J*(1,OH) = 5.0 (H-1); 3.97 qd, 1 H, *J*(4,5) = 6.1 (H-4); 4.15 t, 1 H, *J*(OH,CH_2) = 5.5 (CH_2O**H**); 4.45 t, 1 H, *J*(OH,CH_2) = 5.4 (CH_2O**H**); 4.52 d, 1 H (1-OH); 5.09 dq, 1 H, *J* = 1.5, 1.5, 2.2 and 10.5 and 5.20 dq, 1 H, *J* = 1.7, 1.7, 2.2 and 17.3 (CH_2=); 5.85 ddt, 1 H, *J* = 5.4, 5.4, 10.5 and 17.3 (CH=).

Racemate **22**: For $C_{10}H_{18}O_4$ (202.2) calculated: 59.39% C, 8.97% H; found: 59.70% C, 9.15% H. ^{1}H NMR spectrum: 1.48 dd, 1 H, *J*(3a,4) = 6.6, *J*(3a,3b) = 13.2 (H-3a); 1.54 dt, *J*(5a,1) = 7.6, *J*(5a,5b) = 12.7, *J*(5a,4) = 7.3 (H-5a); 1.75 dd, 1 H, *J*(3b,4) = 7.3 (H-3b); 2.19 dt, *J*(5b,1) = *J*(5b,4) = 6.6 (H-5b); 3.20 dd, 1 H, *J*(CH,OH) = 5.4 and 3.28 dd, 1 H, *J*(CH,OH) = 4.9, *J*(gem) = 10.5 (CH_2O); 3.41 dd, 1 H, *J*(CH,OH) = 5.8 and 3.50 dd, 1 H, *J*(CH,OH) = 4.9, *J*(gem) = 10.7 (CH_2O); 3.77 pent, 1 H (H-4); 3.82 ddd, 1 H, *J*(1,OH) = 4.9 (H-1); 3.85 dq, 2 H, *J* = 1.5, 1.5, 1.5 and 5.4 (OCH_2); 4.14 t, 1 H, *J*(OH,CH_2) = 5.5 (CH_2O**H**); 4.47 t, 1 H, *J*(OH,CH_2) = 5.4 (CH_2O**H**); 4.54 d, 1 H (1-OH); 5.09 dq, 1 H, *J* = 1.7, 1.7, 1.7 and 10.5 and 5.21 dq, 1 H, *J* = 1.7, 1.7, 1.7 and 17.3 (CH_2=); 5.86 ddt, 1 H, *J* = 5.4, 5.4, 10.5 and 17.3 (CH=).

(±)-*cis*- (**23**) and (±)-*trans*-4-Ethylsulfanyl-2,2-bis(hydroxymethyl)cyclopentan-1-ol (**24**)

A solution of esters **15** and **16** (2.62 g, 10 mmol) in tetrahydrofuran (8 ml) was slowly added dropwise under argon to a boiling 1 M solution of lithium aluminium hydride in tetrahydrofuran (16 ml). The mixture was then refluxed for 3 h. After cooling, ethyl acetate (10 ml) was added followed, after 20 min, by water (10 ml). The solvent was evaporated and the residue extracted with hot ethyl acetate (6 × 40 ml) and then with 90% aqueous methanol (2 × 30 ml). The solid material was washed with methanol and the combined extracts and filtrates were evaporated. Column chromatography of the residue on silica gel (300 g) in ethyl acetate–acetone–ethanol–water (105 : 15 : 3 : 2) afforded 365 mg (18%) of racemate **23** and 610 mg (29.5%) of racemate **24**.

Racemate **23**: For $C_9H_{18}O_3S$ (206.3) calculated: 52.40% C, 8.79% H, 15.54% S; found: 52.09% C, 8.87% H, 15.29% S. ^{1}H NMR spectrum: 1.17 t, 3 H, *J*(CH_3,CH_2) = 7.3 (CH_3); 1.44 dd, 1 H, *J*(3a,4) = 10.0, *J*(3a,3b) = 13.2 (H-3a); 1.46 ddd, 1 H, *J*(5a,1) = 8.2, *J*(5a,5b) = 12.3, *J*(5a,4) = 10.5 (H-5a); 1.88 dd, 1 H, *J*(3b,4) = 7.8 (H-3b); 2.26 ddd, 1 H, *J*(5b,1) = 6.5, *J*(5b,4) = 7.0 (H-5b); 2.50 q, 2 H (SCH_2); 2.94 tt, 1 H (H-4); 3.22 dd, 1 H, *J*(CH,OH) = 5.4 and 3.32 dd, 1 H, *J*(CH,OH) = 5.3, *J*(gem) = 10.5 (CH_2O); 3.38 dd, 1 H, *J*(CH,OH) = 5.9 and 3.44 dd, 1 H, *J*(CH,OH) = 5.0, *J*(gem) = 10.8 (CH_2O); 3.87 ddd, *J*(1,OH) = 5.0 (1-OH); 4.15 t, 1 H, *J*(OH,CH_2) = 5.3 (CH_2O**H**); 4.51 t, 1 H, *J*(OH,CH_2) = 5.5 (CH_2O**H**); 4.66 d, 1 H (1-OH).

Racemate **24**: For $C_9H_{18}O_3S$ (206.3) calculated: 52.40% C, 8.79% H, 15.54% S; found: 52.11% C, 8.90% H, 15.23% S. ^{1}H NMR spectrum: 1.17 t, 3 H, *J*(CH_3,CH_2) = 7.3 (CH_3); 1.24 dd, 1 H, *J*(3a,4) = 8.4, *J*(3a,3b) = 13.7 (H-3a); 1.69 ddd, 1 H, *J*(5a,1) = 6.0, *J*(5a,5b) = 13.2, *J*(5a,4) = 8.9 (H-5a); 1.93 dd, 1 H, *J*(3b,4) = 7.9 (H-3b); 1.94 ddd, 1 H, *J*(5b,1) = 4.5, *J*(5b,4) = 7.5 (H-5b); 2.49 q, 2 H (SCH_2); 3.29 pent, 1 H (H-4); 3.26 dd, 1 H, *J*(CH,OH) = 5.3 and 3.30 dd, 1 H, *J*(CH,OH) = 5.3, *J*(gem) = 10.6 (CH_2O); 3.41 dd, 1 H, *J*(CH,OH) = 5.6 and 3.45 dd, 1 H, *J*(CH,OH) = 5.4, *J*(gem) = 10.8 (CH_2O); 3.98 dt, 1 H, *J*(1,OH) = 4.5 (H-1); 4.18 t, 1 H, *J*(OH,CH_2) = 5.5 (CH_2O**H**); 4.51 t, 1 H, *J*(OH,CH_2) = 5.3 (CH_2O**H**); 4.56 d, 1 H (1-OH).

(±)-*cis*-4-Acetoxy-3,3-bis(acetoxymethyl)cyclopentan-1-ol (**25**)

4-Dimethylaminopyridine (16 mg) was added to a mixture of allyloxy derivative **21** (144 mg, 0.5 mmol), acetonitrile (1 ml) and acetic anhydride (0.3 ml). The mixture was stirred until the starting hydroxy derivative dissolved and then was set aside at room temperature for 1 h. The solvent was evaporated and the residue chromatographed on a column of silica gel (10 g) in toluene–ethyl acetate (2 : 1). The obtained triacetate (151 mg) was dissolved in a mixture of ethanol (7 ml), toluene (3 ml) and water (1 ml). Tris(triphenylphosphine)rhodium(I) chloride (50 mg) was added to the solution under stirring and the mixture was refluxed for 10 h. Formic acid (0.6 ml) was added and after another hour of reflux, the mixture was taken down. The residue was column-chromatographed on silica gel (20 g) in ethyl acetate–toluene (2 : 1); yield 95 mg (66%) of triacetyl derivative **25** as a thick oil. For $C_{13}H_{20}O_7$ (288.3) calculated: 54.16% C, 6.99% H; found: 53.83% C, 7.18% H. ^{1}H NMR spec-

trum: 1.56 dd, 1 H, *J*(2a,1) = 6.0, *J*(2a,2b) = 13.7; 1.60 dt, 1 H, *J*(5a,4) = *J*(5a,1) = 7.3, *J*(5a,5b) = 13.7 (H-5a); 1.81 dd, 1 H, *J*(2b,1) = 6.8 (H-2b); 1.98 s, 3 H, 1.99 s, 3 H and 2.00 s, 3 H (3 × $COCH_3$); 2.33 dt, 1 H, *J*(5b,4) = *J*(5b,1) = 6.8 (H-5b); 3.90 d, 1 H and 3.97 d, 1 H, *J*(gem) = 11.0 (CH_2O); 4.08 d, 1 H and 4.14 d, 1 H, *J*(gem) = 11.0 (CH_2O); 4.11 pent, 1 H, *J*(1,OH) = 4.2 (H-1); 4.83 d, 1 H (1-OH); 4.94 t, 1 H (H-4).

(±)-*trans*-4-Acetoxy-3,3-bis(acetoxymethyl)cyclopentan-1-ol (**26**)

Using the same procedure as described for the preparation of the triacetate **25**, allyloxy derivative **22** (309 mg, 1.5 mmol) was converted into triacetate **26** (261 mg; 60%). For $C_{13}H_{20}O_7$ (288.3) calculated: 54.16% C, 6.99% H; found: 53.90% C, 7.16% H. ^{1}H NMR spectrum: 1.49 dd, 1 H, *J*(2a,1) = 3.4, *J*(2a,2b) = 13.9 (H-2a); 1.86 ddd, 1 H, *J*(5a,4) = 7.3, *J*(5a,5b) = 13.9, *J*(5a,1) = 6.6 (H-5a); 1.90 dd, 1 H, *J*(2b,1) = 6.1 (H-2b); 1.98 ddd, 1 H, *J*(5b,4) = 6.8, *J*(5b,1) = 3.5 (H-5b); 1.98 s, 3 H, 1.99 s, 3 H and 2.00 s, 3 H (3 × $COCH_3$); 3.98 d, 1 H and 4.01 d, 1 H, *J*(gem) = 11.0 (CH_2O); 3.94 d, 1 H and 4.15 d, 1 H, *J*(gem) = 11.0 (CH_2O); 4.21 m, 1 H (H-1); 4.82 d, 1 H, *J*(OH,1) = 3.7 (1-OH); 5.17 dd, 1 H (H-4).

(±)-*cis*-4,4-Bis(hydroxymethyl)cyclopentane-1,3-diol (**27**)

A solution of triacetate **25** (72 mg, 0.25 mmol) in 0.1 M methanolic sodium methoxide (1 ml) was allowed to stand for 2 h at room temperature. Neutralization with Dowex 50 (H^+) and evaporation afforded 38 mg (94%) of alcohol **27** as a thick oil. For $C_7H_{14}O_4$ (162.2) calculated: 51.84% C, 8.70% H; found: 51.51% C, 8.89% H. ^{1}H NMR spectrum: 1.37 dd, 1 H, *J*(5a,1) = 6.3, *J*(5a,5b) = 13.2 (H-5a); 1.50 dt, 1 H, *J*(2a,3) = *J*(2a,1) = 7.6, *J*(2a,2b) = 12.7 (H-2a); 1.68 dd, 1 H, *J*(5b,1) = 7.3 (H-5b); 2.07 dt, 1 H, *J*(2b,3) = *J*(2b,1) = 6.3 (H-2b); 3.79 ddd, 1 H, *J*(3,OH) = 3.5 (H-3); 3.93 ttd, 1 H, *J*(1,OH) = 3.5 (H-1); 4.13 t, 1 H, *J*(OH,CH_2) = 3.5 (CH_2O**H**); 4.43 t, 1 H, *J*(OH,CH_2) = 4.5 (OH); 4.50 d, 1 H (OH); 4.51 d, 1 H (OH).

(±)-*trans*-4,4-Bis(hydroxymethyl)cyclopentane-1,3-diol (**28**)

Triacetate **26** (144 mg, 0.5 mmol) was methanolyzed in the same manner as described in the preceding experiment to give 75 mg (93%) of alcohol **28**. For $C_7H_{14}O_4$ (162.2) calculated: 51.84% C, 8.70% H; found: 51.57% C, 8.83% H. ^{1}H NMR spectrum: 1.26 dd, 1 H, *J*(5a,1) = 4.4, *J*(5a,5b) = 13.7 (H-5a); 1.72 dd, 2 H, *J*(2,3) = 6.4, *J*(2,1) = 5.6 (2 × H-2); 1.76 dd, 1 H, *J*(5b,1) = 6.8 (H-5b); 3.30 dd, 1 H, *J*(CH,OH) = 4.6 and 3.38 dd, 1 H, *J*(CH,OH) = 4.6, *J*(gem) = 10.5 (CH_2O); 3.37 dd, 1 H, *J*(CH,OH) = 4.4 and 3.42 dd, 1 H, *J*(CH,OH) = 4.4, *J*(gem) = 10.7 (CH_2O); 4.01 td, 1 H, *J*(3,OH) = 4.4 (H-3); 4.13 t, 1 H (CH_2O**H**); 4.14 m, 1 H (H-1); 4.43 d, 1 H (3-OH); 4.47 d, 1 H, *J*(OH,1) = 4.9 (1-OH); 4.50 t, 1 H (CH_2O**H**).

Methyl 3-*O*-Benzyl-6-deoxy-1,2-*O*-isopropylidene-6-*C*-(methoxycarbonyl)-α-D-*gluco*(or β-L-*ido*)-hepto-1,4-furanuronate (**30**)

Triethylamine (67 ml) was added dropwise to a stirred and cooled (–10 °C) solution of 1,5-dialdofuranose **29** (139 g, 0.5 mol) in dimethyl malonate (86 ml, 0.75 mol). The mixture was set aside at –5 °C overnight. The crystalline product was filtered off, washed with 60% aqueous methanol and dried. Yield 141 g (69%) of product **30,** m.p. 102–103 °C. For $C_{20}H_{26}O_9$ (410.4) calculated: 58.53% C, 6.39% H; found: 58.62% C, 6.52% H. $[\alpha]_D$ –15.7 (*c* 0.56, methanol). ^{1}H NMR spectrum: 1.24 s, 3 H and 1.39 s, 3 H ($C(CH_3)_2$); 3.60 d, 1 H, *J*(6,5) = 5.8 (H-6); 3.62 s, 3 H (CH_3O); 3.94 d, 1 H, *J*(3,4) = 2.8 (H-3); 4.10 dd, 1 H, *J*(4,5) = 9.4 (H-4); 4.41 ddd, 1 H, *J*(5,OH) = 7.3 (H-5); 4.58 d, 1 H and 4.66 d,

1 H, *J*(gem) = 11.6 (CH_2Ph); 4.68 d, 1 H, *J*(2,1) = 3.7 (H-2); 5.53 d, 1 H (5-OH); 5.78 d, 1 H (H-1); 7.36 s, 5 H (H-arom.).

The mother liquors were taken down and the residue was codistilled with ethanol and toluene. A part (0.9 g) of the residue (total amount 91 g) was dissolved in acetonitrile (12 ml). Acetic anhydride (0.5 ml), followed by 4-dimethyl-aminopyridine, was added. After standing at room temperature for 2 h, methanol (1 ml) was added and after another 10 min, the solvent was evaporated and the residue dissolved in ethyl acetate. This solution was washed with water (10 ml), 5% hydrochloric acid (10 ml), water (10 ml), 10% aqueous sodium hydrogencarbonate (2 × 10 ml), dried over magnesium sulfate and the solvent was evaporated. Column chromatography on silica gel (130 g) in toluene–ethyl acetate (3 : 1) afforded 48 mg of compound **32** and 220 mg of 3-*O*-benzyl-5-*C*-[bis(methoxycarbonyl)-methyl]-5,6-dideoxy-1,2-*O*-isopropylidene-6-*C*-(methoxycarbonyl)-α-D-*xylo*-hepto-1,4-furanuronate (**31**). For $C_{25}H_{32}O_{12}$ (524.5) calculated: 57.25% C, 6.15% H; found: 57.42% C, 6.21% H. $[\alpha]_D$ –47.0 (*c* 0.91, chloroform). ^{1}H NMR spectrum: 1.30 s, 3 H and 1.49 s, 3 H ($C(CH_3)_2$); 3.56 m, 1 H, Σ*J* = 17.3 (H-5); 3.56 s, 3 H, 3.70 s, 3 H, 3.71 s, 3 H and 3.72 s, 3 H (4 × $COOCH_3$); 3.76 d, 1 H, *J*(6,5) = 3.7 (H-6); 3.97 d, 1 H, *J*(3,4) = 3.1 (H-3); 4.17 d, 1 H, *J*(6′,5) = 4.3 (H-6′); 4.48 d, 1 H and 4.66 d, 1 H, *J*(gem) = 11.9 (CH_2Ph); 4.59 d, 1 H, *J*(2,1) = 4.0 (H-2); 4.66 dd, 1 H, *J*(4,5) = 9.2 (H-4); 5.86 d, 1 H (H-1); 7.33 s, 5 H (H-arom.).

Methyl 3-*O*-Benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-6-*C*-(methoxycarbonyl)-α-D-*xylo*-hept-5-eno-1,4-furanuronate (**32**)

A. Methanesulfonyl chloride (35 ml) was added to a stirred and cooled (ice bath) solution of ester **30** (82.1 g, 0.2 mmol) in pyridine (600 ml). The mixture was stirred at 0 °C for 1 h and then at room temperature for 3 h. After cooling in an ice bath, water (40 ml) was added and after 15 min, the solvent was evaporated. The residue was partitioned between ethyl acetate (1.5 l) and water (500 ml). The organic layer was separated and washed with water (500 ml), 5% hydrochloric acid (500 ml), water (500 ml), and 10% aqueous sodium hydrogencarbonate (300 ml), dried over sodium sulfate, and the solvent was evaporated. Yield 78.2 g (99%) of chromatographically pure product **32** which was used in the next reaction step without purification. An analytical sample was obtained by chromatography on a column of silica gel in toluene–ethyl acetate (3 : 1). For $C_{20}H_{24}O_8$ (392.4) calculated: 61.22% C, 6.16% H; found: 61.13% C, 6.21% H. ^{1}H NMR spectrum was identical with that of the compound prepared according to ref.[7].

B. Acetic anhydride (0.2 ml) and 4-dimethylaminopyridine (100 mg) were added to a solution of hydroxy derivative **30** (410 mg, 1 mmol) in acetonitrile (4 ml) and the mixture was set aside at room temperature for 1 h. Methanol (1 ml) was added and, after standing for 10 min, the mixture was taken down. The residue was dissolved in ethyl acetate (10 ml) and the solution washed with water (2 × 5 ml), 5% aqueous sodium hydrogencarbonate (2 × 5 ml), dried over sodium sulfate and the solvent was evaporated. Yield 385 mg (98%) of chromatographically pure compound **32**.

C. Acetic anhydride (0.4 ml) was added to a solution of ester **30** (410 mg, 1 mmol) in pyridine (4 ml) and the mixture was allowed to stand for 2 days at room temperature. Methanol (1 ml) was added and after standing for 15 min, the solvent was evaporated. The residue was dissolved in ethyl acetate (10 ml) and the solution washed with water (5 ml), 5% hydrochloric acid (5 ml), water (5 ml), 5% aqueous sodium hydrogencarbonate (5 ml), dried over magnesium sulfate, and the solvent was evaporated. Column chromatography on silica gel (40 g) in toluene–ethyl acetate (3 : 1) afforded 314 mg (80%) of **32**.

Dimethyl (2*S*,3*S*,4*R*)- (**35**) and (2*R*,3*S*,4*R*)-3-Benzyloxy-4-formyloxy-2-hydroxycyclopentane-1,1-dicarboxylate (**36**)

Dowex 50 (H^+, 103 ml) was added to a solution of ketal **33** (ref.[7]; 78.9 g, 0.2 mol) in a mixture of dioxane (470 ml) and water (280 ml) and the reaction mixture was stirred at 80 °C for 6 h. After cooling, the ion exchanger was filtered off, washed with dioxane and the combined filtrates were taken down. Column chromatography of the residue on silica gel (800 g) in toluene–ethyl acetate (2 : 1) afforded 28.2 g (36%) of the starting ketal **33** and 29.3 g (41%) of anomeric mixture of diols **34**. This mixture was dissolved in 1,4-dioxane (1.2 l) and a solution of sodium periodate (26 g) in water (160 ml) was added with stirring. After stirring at room temperature for 1 h, another portion of sodium periodate (17.6 g) in water (95 ml) was added. The mixture was stirred at room temperature for another hour, the insoluble material was filtered off and washed with dioxane. Evaporation of the combined filtrates afforded 27.8 g of a crude mixture of products **35** and **36** which, in some cases could be used in the following step without purification. Column chromatography of a part (2.78 g) of the crude mixture on silica gel (30 g) in toluene–ethyl acetate (2 : 1) gave 2.11 g of chromatographically pure mixture of isomers **35** and **36**. The crude product before the chromatography thus contained 76% of a mixture of pure isomers **35** and **36**. The overall yield of the mixture based on the reacted ketal **33** was 64%. For $C_{16}H_{20}O_8$ (340.3) calculated: 56.47% C, 5.92% H; found: 56.31% C, 6.01% H. ^{1}H NMR spectrum, isomer **35**: 2.31 dd, 1 H, *J*(5a,4) = 8.2, *J*(5a,5b) = 14.0 (H-5a); 2.61 dd, 1 H, *J*(5b,4) = 8.2 (H-5b); 3.65 s, 3 H and 3.66 s, 3 H (2 × $COCH_3$); 3.92 dd, 1 H, *J*(3,2) = 6.1, *J*(3,4) = 5.8 (H-3); 4.56 d, 1 H and 4.66 d, 1 H, *J*(gem) = 11.9 (CH_2Ph); 4.55 m, 1 H (H-2); 4.91 ddd, 1 H (H-4); 6.03 d, 1 H, *J*(OH,2) = 6.1 (2-OH); 7.31 m, 5 H (H-arom. benzyl); 8.22 s, 1 H (CH=O); isomer **36**: 1.76 dd, 1 H, *J*(5a,4) = 5.2, *J*(5a,5b) = 14.9 (H-5a); 3.11 dd, 1 H, *J*(5b,4) = 9.2 (H-5b); 3.64 s, 3 H and 3.65 s, 3 H (2 × $COCH_3$); 3.96 dd, 1 H, *J*(3,2) = 5.0 (H-3); 4.48 d, 1 H and 4.57 d, 1 H, *J*(gem) = 11.9 (CH_2Ph); 4.56 m, 1 H (H-2); 5.12 ddd, 1 H, *J*(4,3) = 7.9 (H-4); 5.68 d, 1 H, *J*(OH,2) = 5.8 (2-OH); 7.35 m, 5 H (H-arom. benzyl); 8.21 s, 1 H (CH=O). The ratio **35** : **36** was 4 : 1.

Dimethyl (2*S*,3*S*,4*R*)- (**37**) and (2*R*,3*S*,4*R*)-2-Benzoyloxy-3-benzyloxy-4-hydroxycyclopentane-1,1-dicarboxylate (**38**)

Benzoyl chloride (3 ml) was added to a stirred and cooled (ice bath) solution of 2-hydroxy derivatives **35** and **36** (7.05 g, 20 mmol) in pyridine (70 ml). After standing at room temperature for 4 h, the mixture was cooled to 0 °C. Methanol (5 ml) was added and after 10 min, the solvent was evaporated. The residue was dissolved in ethyl acetate (200 ml), the solution was washed with water (3 × 50 ml), dried over sodium sulfate and the solvent was evaporated. The residue was dissolved in methanol (100 ml) and to this solution, 10% aqueous solution of potassium hydrogencarbonate was added under stirring until it became turbid (≈20 ml). The mixture was stirred for 1 h at room temperature, the insoluble portion was removed by filtration and washed with methanol, and the combined filtrates were neutralized with acetic acid and taken down. Column chromatography of the residue on silica gel (700 g) in toluene–ethyl acetate (3 : 1) afforded 7.29 g (85%) of benzoates **37** and **38**. For $C_{23}H_{24}O_8$ (428.4) calculated: 64.48% C, 5.65% H; found: 64.35% C, 5.71% H. ^{1}H NMR spectrum, isomer **37**: 2.44–2.52 m, 2 H (2 × H-5); 3.48 s, 3 H and 3.68 s, 3 H (2 × $COCH_3$); 3.83–3.92 m, 2 H (H-3, H-4); 4.64 s, 2 H (CH_2Ph); 5.47 d, 1 H, *J*(OH,4) = 5.2 (4-OH); 6.03 d, 1 H, *J*(2,3) = 4.6 (H-2); 7.26 s, 5 H (H-arom. benzyl); 7.51–7.74 m, 3 H and 7.86–7.91 m, 2 H (H-benzoyl); isomer **38**: 1.84 dd, 1 H, *J*(5a,4) = 6.7, *J*(5a,5b) = 14.0 (H-5a); 3.02 dd, 1 H, *J*(5b,4) = 8.2 (H-5b); 3.50 s, 3 H and 3.71 s, 3 H (2 × $COCH_3$); 3.95–4.05 m, 1 H (H-3); 4.21 m, 1 H (H-4); 4.54 d, 1 H and 4.60 d, 1 H, *J*(gem) = 11.6 (CH_2Ph); 5.40 d, 1 H, *J*(OH,4) = 5.2 (4-OH); 6.10 d, 1 H, *J*(2,3) = 4.6 (H-2); 7.22 s, 5 H (H-arom. benzyl); 7.51–7.74 m, 3 H and 7.86–7.91 m, 2 H (H-benzoyl). The ratio **37** : **38** was 3 : 2.

Dimethyl (2*S*,3*S*,4*R*)- (**39**) and (2*R*,3*S*,4*R*)-2-Benzoyloxy-3-benzyloxy)-4-methoxycyclopentane-1,1-dicarboxylate (**40**)

Boron trifluoride etherate (50 ml) was added dropwise through a capillary at 0 °C to a stirred solution of alcohols **37** and **38** (4.28 g, 10 mmol) in 1 M ethereal solution of diazomethane. After the evolution of nitrogen ceased and the solution decolorized, the formed solid was removed by filtration and washed with ether (2 × 20 ml). The combined filtrates were washed with 5% aqueous sodium hydrogencarbonate (50 ml), dried over sodium sulfate, and the solvent was evaporated. The residue was chromatographed on a column of silica gel (400 g) in toluene containing 6% ethyl acetate, affording 3.62 g (82%) of methoxy derivatives **39** and **40**. For $C_{24}H_{26}O_8$ (442.5) calculated: 65.15% C, 5.92% H; found: 64.91% C, 5.90% H. ^{1}H NMR spectrum, isomer **39**: 2.44 dd, 1 H, *J*(5a,4) = 7.9, *J*(5a,5b) = 13.7 (H-5a); 2.71 dd, 1 H, *J*(5b,4) = 7.3 (H-5b); 3.27 s, 3 H (OCH_3); 3.52 s, 3 H and 3.68 s, 3 H (2 × $COCH_3$); 3.78 ddd, 1 H, *J*(4,3) = 4.9 (H-4); 4.00 m, 1 H (H-3); 4.60 d, 1 H and 4.65 d, 1 H, *J*(gem) = 11.9 (CH_2Ph); 6.02 d, 1 H, *J*(2.3) = 4.0 (H-2); 7.28 m, 5 H (H-arom. benzyl); 7.51–7.75 m, 3 H and 7.87–7.92 m, 2 H (H-benzoyl); isomer **40**: 2.00 dd, 1 H, *J*(5a,4) = 5.2, *J*(5a,5b) = 14.6 (H-5a); 3.11 dd, 1 H, *J*(5b,4) = 7.9 (H-5b); 3.27 s, 3 H (OCH_3); 3.52 s, 3 H and 3.72 s, 3 H (2 × $COCH_3$); 3.96–4.08 m, 2 H (H-3, H-4); 4.53 d, 1 H and 4.58 d, 1 H, *J*(gem) = 11.6 (CH_2Ph); 6.08 d, 1 H, *J*(2.3) = 4.3 (H-2); 7.23 m, 5 H (H-arom. benzyl); 7.51–7.75 m, 3 H and 7.87–7.92 m, 2 H (H-benzoyl). Ratio **37** : **38** was 3 : 2.

(2*S*,3*S*,4*R*)- (**45**) and (2*R*,3*S*,4*R*)-2-Benzoyloxy-1,1-bis(benzoyloxymethyl)-4-methoxycyclopentan-3-ol (**46**)

A solution of a mixture of esters **39** and **40** (4.42 g, 10 mmol) in tetrahydrofuran (10 ml) was slowly added dropwise under argon to a stirred boiling 1 M solution of lithium aluminium hydride in tetrahydrofuran (23 ml). After reflux for further 3 h, the mixture was cooled and ethyl acetate (5 ml) was slowly added, followed by water (10 ml). The mixture was taken down and the residue was extracted first with hot ethyl acetate (6 × 50 ml) and then with 90% aqueous methanol (2 × 40 ml). The combined extracts were neutralized with Dowex 50 (H^+), the ion exchanger was removed by filtration, washed with methanol and the combined fitrates were evaporated. Column chromatography on silica gel in ethyl acetate–acetone–ethanol–water (40 : 5 : 3 : 1) afforded 1.63 g of a mixture of alcohols **41** and **42** which was dried by codistillation with pyridine (2 × 20 ml). The residue was dissolved in pyridine (15 ml) and to this solution, benzoyl chloride (2.5 ml) was slowly added dropwise under stirring. After standing for 5 h at room temperature, water (2 ml) was added and after further 15 min the mixture was taken down. The residue was partitioned between ethyl acetate (60 ml) and water (30 ml). The organic layer was separated and washed with water (30 ml), 5% hydrochloric acid (30 ml), water (30 ml), 10% aqueous sodium hydrogencarbonate solution (3 × 20 ml), dried over sodium sulfate, and the solvent was evaporated. The residue was dissolved in a mixture of methanol (20 ml) and dimethylformamide (2 ml) and hydrogenated over Pd/C (10%, 300 mg) at room temperature for 40 h. The catalyst was removed by filtration through Celite, washed with methanol and the combined filtrates were taken down. Column chromatography of the residue on silica gel (350 g) in toluene–ethyl acetate (3 : 1) afforded 614 mg (12%) of the (2*R*,3*S*,4*R*)-isomer **46** and 1.28 g (25%) of the (2*S*,3*S*,4*R*)-isomer **45**.

Isomer **45**: For $C_{29}H_{28}O_8$ (504.5) calculated: 69.04% C, 5.59% H; found: 69.27% C, 5.77% H. $[\alpha]_D$ –51.9 (*c* 0.876, chloroform). ^{1}H NMR spectrum: 1.82 dd, 1 H, *J*(5a,4) = 7.3, *J*(5a,5b) = 14.0 (H-5a); 2.29 dd, 1 H, *J*(5b,4) = 7.8 (H-5b); 3.35 s, 3 H (OCH_3); 3.74 q, 1 H (H-4); 4.24 ddd, *J*(3,2) = 7.6, *J*(3,4) = 6.6, *J*(3,OH) = 5.7 (H-3); 4.43 d, 1 H and 4.47 d, 1 H, *J*(gem) = 11.2 (CH_2O); 4.45 d, 1 H and 4.51 d, 1 H, *J*(gem) = 11.2 (CH_2O); 5.38 d, 1 H (H-2); 5.63 d, 1 H (3-OH); 7.40 m, 6 H, 7.60 m, 3 H, 7.80 d, 2 H and 7.87 d, 4 H (H-arom.).

Isomer **46**: For $C_{29}H_{28}O_8$ (504.5) calculated: 69.04% C, 5.59% H; found: 69.05% C, 5.73% H. $[\alpha]_D$ +51.8 (*c* 0.678, chloroform). ^{1}H NMR spectrum: 1.79 dd, 1 H, *J*(5a,4) = 3.5, *J*(5a,5b) = 14.5 (H-5a); 2.28 dd, 1 H, *J*(5b,4) = 6.6 (H-5b); 3.33 s, 3 H (OCH_3); 3.81 dt, 1 H, *J*(4,3) = 3.5 (H-4); 4.31 td, 1 H (H-3); 4.42 d, 1 H and 4.50 d, 1 H, *J*(gem) = 11.2 (CH_2O); 4.59 d, 1 H and 4.62 d, 1 H, *J*(gem) = 11.2 (CH_2O); 5.42 d, 1 H, *J*(2,3) = 4.6 (H-2); 5.53 d, 1 H, *J*(OH,3) = 4.8 (3-OH); 7.35 t, 2 H, 7.43 t, 2 H, 7.45 t, 2 H, 7.60 m, 3 H, 7.86 m, 4 H and 7.96 d, 2 H (H-arom.).

(2*S*,3*S*,4*R*)-2-Benzoyloxy-1,1-bis[(benzoyloxy)methyl]-4-methoxy-3-{[(methylsulfanyl)-thiocarbonyl]oxy}cyclopentane (**47**)

Carbon disulfide (0.76 ml) was added to a solution of alcohol **45** (1.01 g, 2 mmol) in dimethylformamide (6 ml) and, after cooling to 0 °C, sodium hydride (60% dispersion in mineral oil, 265 mg) was added. After stirring for 30 min at 0 °C, methyl iodide (1.51 ml) was added and the mixture was stirred for 30 min at 0 °C and then warmed up to room temperature during another 30 min. Water (70 ml) was added and the mixture was extracted with ethyl acetate (80 ml). The organic layer was washed with water (3 × 80 ml), dried and the solvent was evaporated. Column chromatography on silica gel (120 g) in toluene with 8% of ethyl acetate afforded 1.09 g (92%) of dithiocarbonate **47**. For $C_{31}H_{30}O_8S_2$ (594.7) calculated: 62.61% C, 5.08% H, 10.78% S; found: 62.85% C, 4.99% H, 10.72% S. $[\alpha]_D$ +8.6 (*c* 0.640, chloroform). ^{1}H NMR spectrum: 2.09 dd, 1 H, *J*(5a,4) = 6.8, *J*(5a,5b) = 14.4 (H-5a); 2.44 d, 1 H, *J*(5b,4) = 8.3 (H-5b); 2.53 s, 3 H (SCH_3); 3.30 s, 3 H (OCH_3); 4.27 ddd, 1 H, *J*(4,3) = 6.3 (H-4); 4.49 d, 1 H and 4.56 d, 1 H, *J*(gem) = 11.2 (CH_2O); 4.56 d, 1 H and 4.60 d, 1 H, *J*(gem) = 11.2 (CH_2O); 5.83 d, 1 H, *J*(2,3) = 7.6 (H-2); 6.58 dd, 1 H (H-3); 7.32 t, 2 H, 7.42 t, 2 H, 7.46 t, 2 H, 7.60 m, 3 H, 7.82 d, 4 H and 7.98 d, 2 H (H-arom.).

(2*S*,4*R*)-2-Benzoyloxy-1,1-bis(benzoyloxymethyl)-4-methoxycyclopentane (**48**)

A 1 M tributylstannane (2.8 ml) solution in toluene and azobis(2-propionitrile) (100 mg) were added to a boiling solution of dithiocarbonate **47** (892 mg, 1.5 mmol) in toluene (7 ml). After reflux for 30 min, the mixture was taken down and the residue chromatographed on a column of silica gel (90 g) in toluene–ethyl acetate (22 : 3) to give 672 mg (92%) of deoxy derivative **48**. For $C_{29}H_{28}O_7$ (488.5) calculated: 71.30% C, 5.78% H; found: 71.41% C, 5.91% H. $[\alpha]_D$ –61.2 (*c* 0.85, chloroform). ^{1}H NMR spectrum: 1.98 ddd, *J*(3a,2) = 5.9, *J*(3a,3b) = 14.2, *J*(3a,4) = 4.6 (H-3a); 2.04 dd, 1 H, *J*(5a,4) = 4.4, *J*(5a,5b) = 14.2 (H-5a); 2.13 dd, 1 H, *J*(5b,4) = 6.6 (H-5b); 2.63 dt, 1 H, *J*(3b,2) = *J*(3b,4) = 6.0 (H-3b); 3.23 s, 3 H (OCH_3); 3.99 tt, 1 H (H-4); 4.42 d, 1 H and 4.45 d, 1 H, *J*(gem) = 11.2 (CH_2O); 4.57 d, 1 H and 4.67 d, 1 H, *J*(gem) = 11.2 (CH_2O); 5.51 dd, 1 H (H-2); 7.39 t, 2 H, 7.43 t, 2 H, 7.44 t, 2 H, 7.60 t, 3 H, 7.85 d, 2 H, 7.89 d, 2 H and 7.90 d, 2 H (H-arom.).

(2*S*,4*R*)-1,1-Bis(hydroxymethyl)-4-methoxycyclopentan-2-ol ((2*R*,4*R*)-**17**)

Tribenzoate **48** (489 mg, 1 mmol) was dissolved under stirring in 1 M methanolic sodium methoxide (5 ml) and the solution was set aside at room temperature overnight. Then it was neutralized with Dowex 50 (H^+), the ion exchanger was removed by filtration, washed with methanol and the combined filtrates were evaporated. Column chromatography on silica gel (20 g) in ethyl acetate–acetone–ethanol–water (36 : 6 : 5 : 3) afforded 157 mg (89%) of trihydroxy derivative (2*R*,4*R*)-**17**. For $C_8H_{16}O_4$ (176.2) calculated: 54.53% C, 9.15% H; found: 54.18% C, 9.13% H. $[\alpha]_D$ –33.1 (*c* 0.64, methanol). ^{1}H NMR spectrum was identical with that of the racemate **17**.

(3*R*,4*R*)-3-Benzoyloxy-1,1-bis(benzoyloxymethyl)-4-methoxycyclopentane (**50**)

The alcohol **46** (505 mg, 1 mmol) was converted into the dithiocarbonate **49** (491 mg) in the same manner as described for the dithiocarbonate **47**. To a boiling solution of **49** in toluene (5 ml) was added 1 M solution of tributylstannane (1.6 ml) in toluene, followed by azobis(2-propionitrile) (60 mg). The solution was refluxed for 30 min and then the solvent was evaporated. Column chromatography of the residue on silica gel (50 g) in toluene–ethyl acetate (9 : 1) afforded 306 mg (63%, based on **46**) of deoxy derivative **50**. For $C_{29}H_{28}O_7$ (488.5) calculated: 71.30% C, 5.78% H; found: 71.03% C, 6.00% H. $[\alpha]_D$ +11.6 (*c* 0.50, chloroform). ^{1}H NMR spectrum: 1.88 dd, 1 H, *J*(5a,4) = 4.4, *J*(5a,5b) = 14.4 (H-5a); 1.93 dd, 1 H, *J*(2a,2b) = 14.7, *J*(2a,3) = 3.6 (H-2a); 2.18 dd, 1 H, *J*(5b,4) = 6.4 (H-5b); 2.32 dd, 1 H, *J*(2b,3) = 6.6 H-2b); 3.35 s, 3 H (OCH_3); 4.06 ddd, 1 H, *J*(4,3) = 3.6 (H-4); 4.37 s, 2 H (CH_2O); 4.39 d, 1 H and 4.43 d, 1 H, *J*(gem) = 11.0 (CH_2O); 5.36 dt, 1 H (H-3); 7.48 m, 6 H, 7.52 m, 3 H and 7.97 m, 6 H (H-arom.).

(3*R*,4*R*)-1,1-Bis(benzoyloxymethyl)-4-methoxycyclopentan-3-ol (**51**)

Tribenzoate **50** (244 mg, 0.5 mmol) was methanolyzed in the same manner as the benzoate **48** and gave 82 mg (93%) of trihydroxy derivative **51**. For $C_8H_{16}O_4$ (176.2) calculated: 54.53% C, 9.15% H; found: 54.17% C, 9.27% H. $[\alpha]_D$ –43.0 (*c* 0.93, methanol). ^{1}H NMR spectrum: 1.24 dd, 1 H, *J*(2a,2b) = 13.4, *J*(2a,3) = 6.3 (H-2a); 1.25 dd, 1 H, *J*(5a,4) = 6.3, *J*(5a,5b) = 13.7 (H-5a); 1.63 dd, 1 H, *J*(2b,3) = 6.8 (H-2b); 1.71 dd, 1 H, *J*(5b,4) = 6.8 (H-5b); 3.19 d, 2 H, *J*(CH_2,OH) = 5.1 (CH_2O); 3.20 s, 3 H (OCH_3); 3.24 d, 2 H, *J*(CH_2,OH) = 5.0 (CH_2O); 3.42 ddd, 1 H, *J*(4,3) = 4.9 (H-4); 3.83 tt, 1 H (H-3); 4.47 t, 1 H, *J*(OH,CH_2) = 5.1 (CH_2O**H**); 4.60 t, 1 H, *J*(OH,CH_2) = 5.0 (CH_2O**H**); 4.73 d, 1 H, *J*(OH,3) = 5.1 (3-OH).

Reduction of Mixture of Isomers **35** and **36** with Lithium Aluminium Hydride

A solution of esters **35** and **36** (3.52 g, 10 mmol) in tetrahydrofuran (15 ml) was added dropwise under argon during 10 min to a boiling 1 M solution of lithium aluminium hydride (30 ml) in tetrahydrofuran and the mixture was refluxed for 2 h. After cooling, the mixture was decomposed by slow addition of ethyl acetate (5 ml) and water (10 ml). The solvent was evaporated to dryness and the residue was extracted with hot ethyl acetate (6 × 50 ml) and then with 90% aqueous methanol (2 × 40 ml). The combined extracts were neutralized with Dowex 50 (H^+), the ion exchanger was filtered off, washed with methanol, and the combined filtrates were taken down. Chromatography of the residue on a column of silica gel (150 g) in ethyl acetate–acetone–ethanol–water (80 : 12 : 5 : 3) gave 1.2 g (44%) of acyclic derivative **52** and 250 mg (9%) of the cyclopentane derivative **53**.

(2*R*,3*R*)-2-Benzyloxy-5-(hydroxymethyl)hexane-1,3,6-triol (**52**): For $C_{14}H_{22}O_5$ (270.3) calculated: 62.20% C, 8.20% H; found: 61.91% C, 8.37% H. $[\alpha]_D$ +9.7 (*c* 1.15, methanol). ^{1}H NMR spectrum: 1.30 ddd, *J*(4a,3) = 10.0, *J*(4a,4b) = 13.9, *J*(4a,5) = 5.6 (H-4a); 1.43 ddd, *J*(4b,3) = 3.4, *J*(4b,5) = 7.6 (H-4b); 1.68 m, 1 H (H-5); 3.28 ddd, 1 H, *J*(2,1a) = 6.1, *J*(2,1b) = 4.6, *J*(2,3) = 3.9 (H-2); 3.32–3.44 m, 4 H (2 × H-6, CH_2O); 3.49 ddd, 1 H, *J*(1a,1b) = 11.2, *J*(1a,2) = 6.1, *J*(1a,OH) = 5.3 (H-1a); 3.62 dt, 1 H, *J*(1b,2) = *J*(1b,OH) = 4.9 (H-1b); 3.70 ddt, 1 H, *J*(3,OH) = 5.9 (H-3); 4.32 t, 1 H, *J*(CH_2,OH) = 4.9 (CH_2O**H**); 4.41 t, 1 H, *J*(CH_2,OH) = 5.1 (CH_2O**H**); 4.44 d, 1 H (3-OH); 4.53 t, 1 H, *J*(CH_2,OH) = 5.3 (CH_2O**H**).

Benzoyl chloride (0.5 ml) was added dropwise to a solution of **53** in pyridine (3 ml). After standing for 4 h at room temperature, the mixture was taken down and the residue was partitioned between ethyl acetate (25 ml) and water (10 ml). The organic layer was separated and washed with water (10 ml), 5% hydrochloric acid (10 ml), water (10 ml), 10% aqueous sodium hydrogencarbonate solution (10 ml), dried over sodium sulfate, and the solvent was evaporated. Column chromatography on silica gel in

toluene containing 6% of ethyl acetate gave 530 mg (8%, based on the mixture of isomers **35** and **36**) of benzoyl derivative **54**. For $C_{42}H_{36}O_9$ (684.7) calculated: 73.67% C, 5.30% H; found: 73.95% C, 5.42% H. $[\alpha]_D$ +7.6 (*c* 0.632, chloroform). ^{1}H NMR spectrum: 1.96 dd, 1 H, *J*(5a,4) = 5.6, *J*(5a,5b) = 14.7 (H-5a); 2.66 dd, 1 H, *J*(5b,4) = 8.3 (H-5b); 4.57 dd, 1 H, *J*(3,2) = 4.9, *J*(3,4) = 5.6 (H-3); 4.58 s, 2 H (CH_2Ph); 4.61 d, 1 H and 4.66 d, 1 H, *J*(gem) = 12.4 (CH_2O); 4.62 d, 1 H and 4.65 d, 1 H, *J*(gem) = 11.4 (CH_2O); 5.52 dt, 1 H (H-4); 5.85 d, 1 H (H-2); 7.19 m, 3 H, 7.23 m, 2 H, 7.37 t, 2 H, 7.45 t, 2 H, 7.48 t, 2 H, 7.54 t, 2 H, 7.61 t, 2 H, 7.65 t, 1 H, 7.69 t, 1 H, 7.89 m, 4 H, 7.95 d, 2 H and 7.99 d, 2 H (H-arom.).

(2*R*,3*S*,4*R*)-2,4-Bis(benzoyloxy)-1,1-bis(benzoyloxymethyl)cyclopentan-3-ol (**55**)

Benzoyl derivative **54** (200 mg, 0.29 mmol) was hydrogenated in a mixture of methanol (2 ml) and dimethylformamide (0.4 ml) over Pd/C (10%, 25 mg) at atmospheric pressure for 25 h. The catalyst was removed by filtration through Celite, washed with methanol and the combined filtrates were taken down. The residue was dissolved in ethyl acetate (10 ml) and the solution was washed with water (5 ml), 5% aqueous sodium hydrogencarbonate solution (5 ml), dried, and the solvent was evaporated. Yield 157 mg (91%) of alcohol **55**. For $C_{35}H_{30}O_9$ (594.6) calculated: 70.70% C, 5.09% H; found: 70.97% C, 5.22% H. $[\alpha]_D$ +30.0 (*c* 0.751, chloroform). ^{1}H NMR spectrum: 1.96 dd, 1 H, *J*(5a,4) = 4.4, *J*(5a,5b) = 14.9 (H-5a); 2.61 dd, 1 H, *J*(5b,4) = 7.3 (H-5b); 4.57 d, 1 H and 4.59 d, 1 H, *J*(gem) = 11.4 (CH_2O); 4.58 q, 1 H (H-3); 4.66 s, 2 H (CH_2O); 5.35 dt, 1 H, *J*(4,3) = 4.4 (H-4); 5.60 d, 1 H, *J*(2,3) = 4.8 (H-2); 5.85 d, 1 H, *J*(OH,3) = 5.1 (3-OH); 7.32 t, 2 H, 7.44 m, 4 H, 7.56 m, 3 H, 7.62 t, 1 H, 7.63 t, 1 H, 7.69 t, 1 H, 7.88 d, 2 H, 7.90 d, 2 H, 7.99 d, 2 H and 8.20 d, 2 H (H-arom.).

(3*R*,4*R*)-3,4-Bis(benzoyloxy)-1,1-bis(benzoyloxymethyl)cyclopentane (**57**)

Alcohol **55** (130 mg, 0.22 mmol) was treated similarly as described for dithiocarbonate **47**. Chromatography on a column of silica gel (15 g) in toluene containing 8% of ethyl acetate afforded 125 mg (83%) of dithiocarbonate **56**. Compound **56** was converted into deoxy derivative **57** as described for the deoxy derivative **48.** Yield of **57** was 96 mg (75% based on **55**), m.p. 126.5–127.5 °C (ethanol). For $C_{25}H_{30}O_8$ (578.6) calculated: 72.65% C, 5.23% H; found: 72.41% C, 5.22% H. $[\alpha]_D$ –27.7 (*c* 0.575, chloroform). ^{1}H NMR spectrum: 2.08 m, 2 H (H-2a, H-5a); 2.53 dd, 2 H, *J*(2b,3) = *J*(5b,4) = 6.6, *J*(2b,2a) = *J*(5b,5a) = 14.5 (H-2b, H-5b); 4.46 d, 2 H and 4.49 d, 2 H, *J*(gem) = 11.0 (2 × CH_2O); 5.63 m, 2 H (H-3, H-4); 7.51 m, 8 H, 7.66 m, 4 H and 7.99 m, 8 H (H-arom.).

(3*R*,4*R*)-1,1-Bis(hydroxymethyl)cyclopentane-3,4-diol (**58**)

Methanolysis of benzoate **57** (63 mg, 0.11 mmol) was performed as described for the benzoate **48** and gave 16 mg (90%) of tetrahydroxy derivative **58**, m.p. 180–182.5 °C. For $C_7H_{14}O_4$ (162.2) calculated: 51.84% C, 8.70% H; found: 51.71% C, 8.75% H. $[\alpha]_D$ –31.1 (*c* 0.193, methanol). ^{1}H NMR spectrum: 1.21 dd, 2 H, *J*(2a,3) = *J*(5a,4) = 6.1, *J*(2a,2b) = *J*(5a,5b) = 13.4 (H-2a, H-5a); 1.67 dd, 2 H, *J*(2b,3) = *J*(5b,4) = 5.9 (H-2b, H-5b); 3.23 d, 4 H, *J*(CH_2,OH) = 5.1 (2 × CH_2O); 3.67 m, 2 H (H-3, H-4); 4.56 d, 2 H, *J*(OH,3) = *J*(OH,4) = 4.4 (3-OH, 4-OH); 4.58 t, 2 H (2 × CH_2O**H**).

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