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

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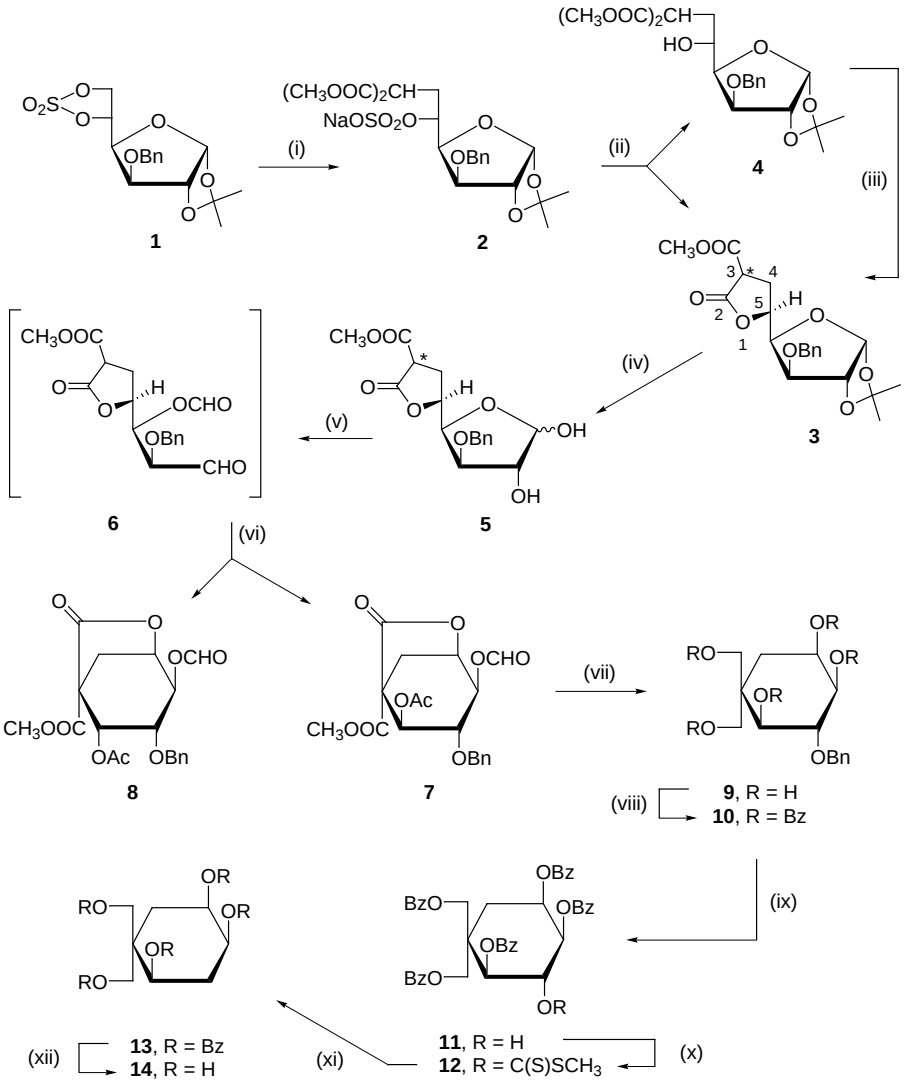
3-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose-5,6-*O*-sulfate (**1**) was treated with sodium salt of dimethyl malonate to obtain, after hydrolysis, methyl 5-(3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-erythrofuranos-4-yl)-2-oxotetrahydrofuran-3-carboxylate (**3**) which was converted to the mixture of methyl (2*S*,3*R*,4*R*)- (**7**) and (2*R*,3*R*,4*R*)-2-(acetyloxy)-3-(benzyloxy)-4-(formyloxy)-7-oxo-6-oxabicyclo[3.2.1]octane-1-carboxylate (**8**). The compound **7** was reduced with lithium aluminium hydride to give (1*R*,2*R*,3*R*,4*S*)-3-(benzyloxy)-5,5-bis(hydroxymethyl)cyclohexane-1,2,4-triol (**9**) which was transformed to (1*R*,2*S*,4*R*)-5,5-bis(hydroxymethyl)cyclohexane-1,2,4-triol (**14**). Treatment of sodium salt of diethyl malonate with 3-*O*-benzyl-5,6-dideoxy-6-iodo-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranose (**19**) gave diethyl (3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranos-6-yl)malonate (**20**) which was converted to (1*R*,3*R*)-4,4-bis(hydroxymethyl)cyclohexane-1,3-diol (**28**) by a similar procedure to that used for **14**.

Keywords: Carbasugars; Pseudosugars; Carbocyclic hexopyranoses; Substituted 1,1-bis-(hydroxymethyl)cyclohexanes; Carbohydrates; Cyclohexanes; Cyclitols; Glucose.

Polyhydroxycyclohexanes can be regarded as carbocyclic sugar analogues. An approach to six-membered carbocycles opens a synthetic way to carba analogues of nucleosides with pyranoses and/or hexitols as sugar moieties. Because the hexitol nucleosides exhibit antiviral activity[1], their carbocyclic congeners and cyclohexene analogues were prepared[2].

In continuation of our previous studies[3] aimed at the syntheses of carbocyclic 4′-substituted deoxynucleosides with potential antiviral activity, this study concerns syntheses of 4-*C*-(hydroxymethyl)pseudohexopyranoses. D-Glucose was chosen as a starting compound for synthesis of the target compounds.

Treatment of sulfate[4] **1** (Scheme 1) with sodium salt of dimethyl malonate in dimethylformamide afforded sodium salt of sulfate **2** which gave directly, on hydrolysis with 8% aqueous sulfuric acid, a mixture of

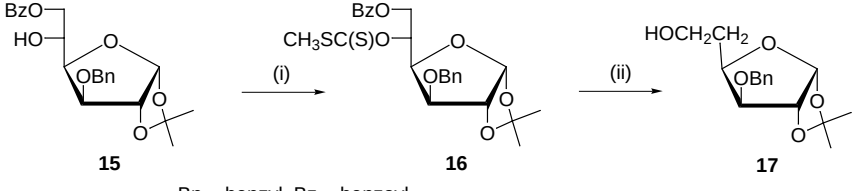


(i) $(MeOOC)_2CH_2$/NaH/DMF; (ii) 8% aqueous H_2SO_4/CH_2Cl_2, 67% of **3**, 11% of **4** based on reacted **1**; (iii) 0.1 M MeONa/MeOH; (iv) Dowex 50(H^+)/aqueous dioxane; (v) $NaIO_4$/aqueous dioxane; (vi) $(CH_3CO)_2O$/pyridine, 35% of **7**, 2.5% of **8** based on reacted **3**; (vii) $LiAlH_4$/THF, 79%; (viii) benzoyl chloride/pyridine, 93%; (ix) Pd/C/MeOH-DMF, 91%; (x) 1. NaH/CS_2/DMF, 2. MeI, 90%; (xi) Bu_3SnH/AIBN/toluene, 82%; (xii) 0.1 M MeONa/MeOH, 94%

SCHEME 1

lactone **3** and diester **4** (67 and 11% yields, respectively, based on sulfate **1**). The diester **4** was converted to the lactone by treatment with 0.1 M methanolic sodium methoxide. The lactone **3** is an equimolar mixture of (3*R*)- and (3*S*)-isomers. The isomers could not be separated by chromatography on silica gel. Deketalization of compound **3** which was performed on Dowex 50(H^+) in aqueous 1,4-dioxane, afforded an anomeric mixture of diols **5**. This reaction was accompanied by partial hydrolysis of the methyl ester and therefore it was interrupted when TLC revealed their hydrolysis. Reaction of diols **5** with sodium periodate followed by acetylation gave a mixture of cyclohexane derivatives **7** and **8**. Both isomers were separated and obtained in a crystalline form (35% of **7** and 2.5% of **8** based on ketal **3**). Because only the (3*S*)-isomer of aldehyde **6** was able to undergo a cyclization reaction, the yield of **7** and **8** was low. Reduction of the ester **7** to the corresponding bis(hydroxymethyl) derivative **9** was carried out with lithium aluminum hydride in boiling tetrahydrofuran. Benzoylation of **9** by treatment with benzoyl chloride in pyridine and subsequent hydrogenolysis of the obtained benzoate **10** afforded substituted cyclohexanol **11** (91% yield). It was converted into dithiocarbonate **12** which was subsequently treated with tributylstannane in the presence of 2,2′-azobis-(2-methylpropanonitrile), using a described[5] procedure to give the deoxy derivative **13**. Both reactions were facile and gave high yields (90 and 82%, respectively). Methanolysis of compound **13** afforded free carba analogue **14**.

For the synthesis of the target diol **28**, 3-*O*-benzyl-5-deoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranose (**17**) was used as a starting compound. Because syntheses of **17** reported in the literature[6] are not suitable for large-scale preparation, **17** was obtained by deoxygenation of 6-*O*-benzoyl-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose[7] (**15**) as follows: monobenzoate **15** was first converted into dithiocarbonate **16** (91% yield) which was then treated with tributylstannane in the peresence of 2,2′-azobis(2-methylpropanonitrile) to give, after methanolysis of the benzoyl group, 5-deoxyglucose **17** in the yield of 76% (Scheme 2).



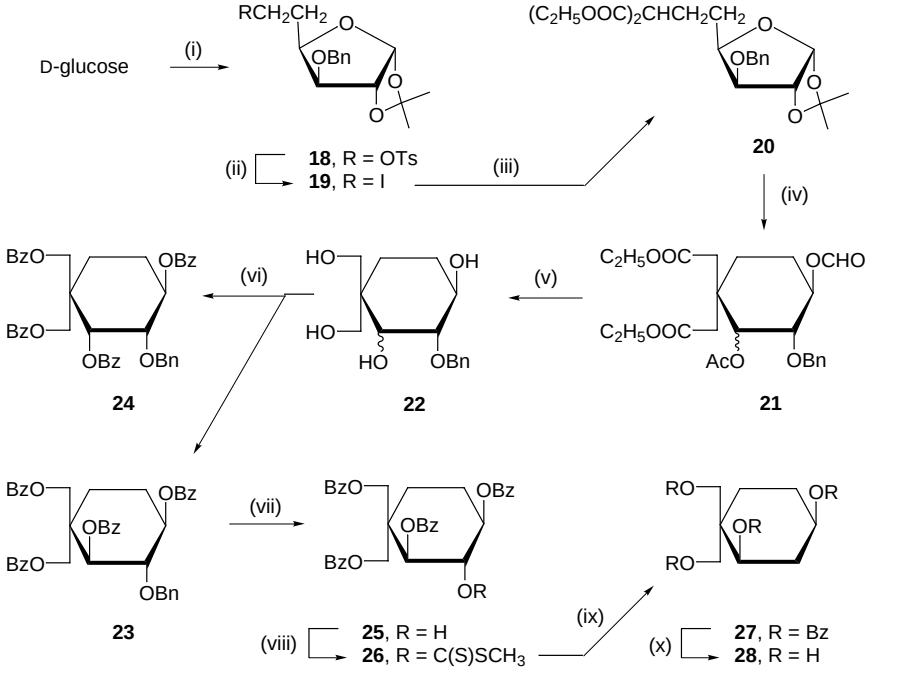
15 **16** **17**

Bn = benzyl, Bz = benzoyl

(i) 1. CS_2/NaH/DMF, 2. MeI, 91%; (ii) 1. Bu_3SnH/AIBN/toluene, 2. 0.1 M MeONa/MeOH, 76%

SCHEME 2

Treatment of 5-deoxyglucose **17** with tosyl chloride in pyridine afforded tosylate **18** (92% yield) and subsequent nucleophilic displacement of the tosyl group by iodine gave 5,6-dideoxy-6-iodoglucose **19** in the yield of 79% (Scheme 3). Reaction of the iodo derivative **19** with sodium salt of dimethyl malonate in dimethylformamide led to malonate **20** (87% yield). Its deketalization with Dowex 50(H^+) in aqueous 1,4-dioxane, oxidation with sodium periodate and acetylation afforded a mixture of (2*R*)- and (2*S*)-diesters **21** (41% yield). In this case, deketalization was not accompanied by ester hydrolysis. The diastereomeric mixture **21** was treated with lithium aluminum hydride in boiling tetrahydrofuran giving a mixture of (3*R*)- and (3*S*)-diols **22** in the yield of 41%. Attempts to separate of diesters **21** and diols **22** by chromatography failed. However, the benzoates **23** and **24** obtained from the mixture of diols by reaction with benzoyl chloride in



(i) TsCl/pyridine, 92%; (ii) NaI/MeCOEt, 89%; (iii) $(EtOOC)_2CH_2$/NaH/DMF, 87%; (iv) 1. Dowex 50(H^+)/aqueous dioxane, 2. $NaIO_4$/aqueous dioxane, 3. $(CH_3CO)_2O$/pyridine, 41%; (v) $LiAlH_4$/THF, 84%; (vi) benzoyl chloride/pyridine, 62% of **23**, 19% of **24**; (vii) Pd/C/MeOH-DMF, 95%; (viii) 1. NaH/CS_2/DMF, 2. MeI, 79%; (ix) Bu_3SnH/AIBN/toluene, 95%; (x) MeONa/MeOH, 85%

SCHEME 3

pyridine, were easily separated by chromatography on silica gel (62% yield of **23** and 19% yield of **24**). The benzyl group in compound **23** was removed by hydrogenolysis and the resulting cyclohexanol **25** was converted to dithiocarbonate **26** by the above procedure (see compound **12**). Treatment of **26** with tributylstannane in the presence of 2,2′-azobis(2-methylpropanonitrile) afforded benzoate **27** which was methanolyzed to give diol **28** in the yield of 85%.

The structure of the cyclohexane derivatives **7**, **8**, **10**, **23** and **24** was determined by ^{1}H NMR spectroscopy. Coupling constants of cyclohexanes **7** (J(2,3) = J(3,4) = 8.5 Hz), **10** (J(2,3) = J(3,4) = 8.5 Hz), **23** (J(2,3) = 8.8 Hz and J(3,4) = 8.5 Hz) and constants of the isomeric compounds **8** (J(2,3) = 4.6 Hz and J(3,4) = 8.8 Hz) and **24** (J(2,3) = 3.2 Hz and J(3,4) = 7.2 Hz) correspond with (2*S*)-configuration of the compounds **7**, **10**, **23** and (2*R*)-configuration of the isomers **8** and **24**.

In conclusion, new carba analogues of 2-deoxy-4-*C*-(hydroxymethyl)-hexopyranoses were synthesized as intermediates in nucleoside syntheses starting from inexpensive D-glucose.

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 and are given in 10^{-1} deg cm^2 g^{-1}. ^{1}H NMR spectra (δ, ppm; *J*, Hz) were recorded with Varian UNITY 200 instrument 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 tetrahydrofurane, supplied by Aldrich.

Methyl 5-(3-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-erythrofuranos-4-yl)-2-oxotetrahydrofuran-3-carboxylate (**3**)

Sodium hydride (60% dispersion in mineral oil, 4.8 g, 120 mmol) was added under argon at 0 °C to a stirred solution of dimethyl malonate (15 ml, 131 mmol) in dimethylformamide (400 ml) and, after stirring at 0 °C for 15 min, a solution of sulfate[4] **1** (37.2 g, 100 mmol) in dimethylformamide (150 ml) was added. The mixture was stirred at room temperature for 2 h and then the solvent was evaporated. The solution of the residue in water (400 ml) was washed with ethyl acetate (2 × 100 ml) and the aqueous solution was evaporated. The mixture of the residue, dichloromethane (300 ml) and 8% aqueous sulfuric acid (120 ml) was stirred at room temperature for 15 h; the organic layer was then separated, washed with water (2 × 100 ml), dried over anhydrous sodium sulfate, and the solvent was taken down. The residue was dissolved in 0.1 M methanolic sodium methoxide (400 ml) and the solution was set aside overnight at room temperature. Dowex 50(H$^+$) was added to neutralize the reaction

mixture, the resin was filtered off, washed with methanol, and the combined filtrates were evaporated to give 30.6 g (78%) of **3** as an equimolar mixture of (3*R*)- and (3*S*)-isomers. For $C_{20}H_{24}O_8$ (392.4) calculated: 61.22% C, 6.16% H; found: 61.23% C, 6.26% H. ^{1}H NMR ($CDCl_3$): 1.32 s, 6 H, 1.48 s, 3 H and 1.51 s, 3 H (2 × $C(CH_3)_2$); 2.60–2.84 m, 4 H (2 × H-4); 3.61–3.79 m, 2 H (2 × H-3); 3.80 s, 3 H and 3.81 s, 3 H (2 × CH_3O); 4.05 d, 1 H, *J*(3′,4′) = 3.4 and 4.10 d, 1 H, *J*(3′,4′) = 3.4 (2 × H-3′); 4.25–4.31 m, 2 H (2 × H-4′); 4.55 d, 2 H and 4.68 d, 2 H, J_{gem} = 11.6 (2 × CH_2Ph); 4.62 d, 1 H, *J*(2′,1′) = 3.4 and 4.63 d, 1 H, *J*(2′,1′) = 3.7 (2 × H-2′); 5.92 d, 1 H and 5.94 d, 1 H (2 × H-1′); 7.27–7.40 m, 10 H (H-arom.).

In a small-scale experiment, a mixture of **3** and diester **4** (150 mg) prior to methanolysis was separated by silica gel chromatography (ethyl acetate–toluene, 1 : 3) to afford **3** (120 mg) and dimethyl malonate **4** (19 mg).

Dimethyl (3-O-Benzyl-6-deoxy-1,2-O-isopropylidene-α-D-glucofuranos-6-yl)malonate (**4**). For $C_{21}H_{28}O_9$ (424.5) calculated: 59.42% C, 6.65% H; found: 59.19% C, 6.47% H. ^{1}H NMR (DMSO-d_6): 1.24 s, 3 H and 1.39 s, 3 H ($C(CH_3)_2$); 1.81 ddd, 1 H, *J*(6a′,CH) = 4.9, *J*(6a′,5′) = 9.2, *J*(6a′,6b′) = 14.0 (H-6a′); 2.14–2.30 m, 1 H (H-6b′); 3.64 s, 3 H and 3.65 s, 3 H (2 × CH_3O); 3.70 t, 1 H, *J*(CH,6b′) = 4.9 (CH); 3.68–3.84 m, 2 H (H-4′, H-5′); 3.91 d, 1 H, *J*(3′,4′) = 3.1 (H-3′); 4.56 d, 1 H and 4.65 d, 1 H, J_{gem} = 11.6 (CH_2Ph); 4.67 d, 1 H (H-2′); 4.98 d, 1 H, *J*(OH,5′) = 6.7 (5′-OH); 5.82 d, 1 H, *J*(1′,2′) = 3.7 (H-1′); 7.33 m, 5 H (H-arom.).

Methyl (2*S*,3*R*,4*R*)- (**7**) and (2*R*,3*R*,4*R*)-2-(Acetyloxy)-3-(benzyloxy)-4-(formyloxy)-7-oxo-6-oxabicyclo[3.2.1]octane-1-carboxylate (**8**)

A mixture of **3** (7.84 g, 20 mmol), dioxane (53 ml), water (32 ml), and Dowex 50 (H^+ form, 15 ml) was stirred at 80 °C for 6 h. Then the resin was filtered off, washed with dioxane, and the solvent was evaporated. A solution of the residue in ethyl acetate (300 ml) was washed with water (100 ml), 10% aqueous potassium hydrogencarbonate (100 ml), dried over anhydrous sodium sulfate, and the solvent was evaporated. To a stirred solution of the residue in dioxane (100 ml), a saturated solution of sodium periodate (85 ml) was added dropwise during 20 min. The insoluble portion was filtered off and washed with dioxane. The combined filtrates were evaporated to one third of the original volume and partitioned between ethyl acetate (300 ml) and water (100 ml). The organic phase was separated, washed with water (100 ml), dried over anhydrous sodium sulfate, and the solvent was evaporated. Acetic anhydride (6 ml, 64 mmol) was added to a solution of the residue in pyridine (75 ml) and the solution was set aside at room temperature for 2 days. Methanol (5 ml) was added and, after 15 min, the solvent was evaporated. A solution of the residue in ethyl acetate (200 ml) was washed with water (3 × 75 ml), dried over anhydrous sodium sulfate and taken down. Chromatography on a column of silica gel (800 g) in toluene–ethyl acetate (3 : 1) and crystallization from methanol afforded 200 mg (2.5%) of compound **8** and 2.75 g (35%) of compound **7**.

Compound **7**: M.p. 116.5–117.5 °C. For $C_{19}H_{20}O_9$ (392.4) calculated: 58.16% C, 5.14% H; found: 57.97% C, 5.19% H. $[\alpha]_D$ –50.3 (*c* 0.77, chloroform). ^{1}H NMR ($CDCl_3$): 2.03 s, 3 H (CH_3CO); 2.25 d, 1 H, *J*(8a,8b) = 13.1 (H-8a); 2.86 dd, 1 H, *J*(8b,5) = 6.7 (H-8b); 3.77 s, 3 H (CH_3O); 3:89 t, 1 H, *J*(3,2) = *J*(3,4) = 8.5 (H-3); 4.63 s, 2 H (CH_2-benzyl); 4.82 dd, 1 H, *J*(5,4) = 1.2 (H-5); 5.06 ddd, 1 H, *J* = 0.9 (H-4); 5.57 d, 1 H (H-2); 7.21–7.34 m, 5 H (H-arom.); 8.01 s, 1 H (CH=O).

Compound **8**: M.p. 120–121 °C. For $C_{19}H_{20}O_9$ (392.4) calculated: 58.16% C, 5.14% H; found: 58.13% C, 5.17% H. $[\alpha]_D$ –168.2 (*c* 0.786, chloroform). ^{1}H NMR ($CDCl_3$): 2.10 s, 3 H

(CH_3CO); 2.71 d, 1 H, *J*(8a,8b) = 12.6 (H-8a); 2.96 ddd, 1 H, *J*(8b,2) = 1.6, *J*(8b,5) = 6.4 (H-8b); 3.79 dd, 1 H, *J*(3,2) = 4.6, *J*(3,4) = 8.8 (H-3); 3.83 s, 3 H (CH_3O); 4.40 d and 4.74 d, J_{gem} = 10.9 (CH_2-benzyl); 4.90 dd, 1 H, *J* = 1.1 (H-5); 5.10 d, 1 H (H-4); 6.18 dd, 1 H (H-2); 7.22–7.38 m, 5 H (H-arom.); 8.05 s, 1 H (CH=O).

(1*R*,2*R*,3*R*,4*S*)-3-(Benzyloxy)-5,5-bis(hydroxymethyl)cyclohexane-1,2,4-triol (**9**)

A solution of ester **7** (5.89 g, 15.0 mmol) in tetrahydrofuran (45 ml) was slowly added dropwise to a stirred boiling 1 M solution of lithium aluminium hydride (45 ml) in an argon atmosphere. The mixture was refluxed for 2 h, cooled and ethyl acetate (6 ml) was added, after 15 min followed by water. The mixture was taken down 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 through a Celite pad and washed with methanol. The combined extract and filtrates were taken down and the residue was chromatographed on a silica gel column (400 g) in ethyl acetate–acetone–ethanol–water (36 : 6 : 5 : 3) to give 3.59 g (79%) of the hydroxy derivative **9**. For $C_{15}H_{22}O_6$ (298.3) calculated: 60.39% C, 7.43% H; found: 60.11% C, 7.62% H. $[\alpha]_D$ –32.8 (*c* 1.280, water). ^{1}H NMR (DMSO-d_6): 1.47 dd, 1 H, *J*(6a,1) = *J*(6b,1) = 3.7, J_{gem} = 15.0 (2 × H-6); 3.19–3.68 m, 7 H (2 × CH_2, H-1, H-3, H-4); 3.75–3.82 m, 1 H (H-2); 4.46 t, 1 H, *J* = 5.5 (CH_2O**H**); 4.50 t, 1 H, *J* = 5.5 (CH_2O**H**); 4.60 d, 1 H, *J* = 6.7 (OH); 4.65 d, 1 H, *J* = 5.5 (OH); 4.75 s, 2 H (CH_2Ph); 4.94 d, 1 H, *J* = 4.3 (OH); 7.23–7.44 m, 5 H (H-arom.).

(2*S*,3*R*,4*R*,5*R*)-2,3,5-Tris(benzoyloxy)-3-(benzyloxy)-1,1-bis[(benzoyloxy)-methyl]cyclohexane (**10**)

The hydroxy derivative **9** (3.43 g, 11.5 mmol) was dissolved in pyridine (70 ml) and taken down. To a solution of the residue in pyridine (70 ml), benzoyl chloride (8.1 ml, 69.8 mmol) was added under cooling. The mixture was set aside at room temperature for 50 h and cooled down to 0 °C. Water (4.5 ml) was then added and after 10 min the mixture was concentrated, and the residue was partitioned between ethyl acetate (300 ml) and water (100 ml). The organic phase was washed with water, 5% hydrochloric acid, water and 10% aqueous potassium hydrogencarbonate (100 ml each), then dried over anhydrous sodium sulfate, and the solvent was evaporated. Chromatography of the residue on a silica gel column (500 g) in toluene–ethyl acetate (91 : 9) gave 8.76 g (93%) of benzoate **10**. For $C_{50}H_{42}O_{11}$ (818.9) calculated: 73.34% C, 5.17% H; found: 73.15% C, 5.27% H. $[\alpha]_D$ –52.0 (*c* 0.636, chloroform). ^{1}H NMR ($CDCl_3$): 2.20 dd, 1 H, *J*(6a,5) = 3.1, *J*(6a,6b) = 15.3 (H-6a); 2.76 dd, 1 H, *J*(6b,5) = 5.2 (H-6b); 4.42 d, 1 H and 4.62 d, 1 H, J_{gem} =11.6 (CH_2); 4.53 t, 1 H, *J*(3,2) = *J*(3,4) = 8.5 (H-3); 4.68 d, 1 H and 4.74 d, 1 H, J_{gem} = 11.0 (CH_2); 4.82 s, 2 H (CH_2); 5.60 dd, 1 H, *J*(4,5) = 3.4 (H-4); 5.87 m, 1 H (H-5); 5.91 d, 1 H (H-2); 6.99–7.11 m, 5 H (H-arom. benzyl); 7.29–7.55 m, 15 H and 7.72–8.03 m, 10 H (H-arom. benzoyl).

(1*R*,2*S*,5*R*,6*S*)-2,5,6-Tris(benzoyloxy)-3,3-bis[(benzoyloxy)methyl]cyclohexan-1-ol (**11**)

Benzyl derivative **10** (8.19 g, 10.0 mmol) was hydrogenated in a mixture of methanol (60 ml) and dimethylformamide (15 ml) over Pd/C (10%, 1.5 g) at atmospheric pressure for 45 h. The catalyst was removed by filtration through a Celite pad, washed with methanol, and the combined filtrates were taken down. The residue was dissolved in ethyl acetate (200 ml) and the solution was washed with water (2 × 100 ml), 5% aqueous sodium

hydrogencarbonate solution (50 ml), dried over anhydrous sodium sulfate, and the solvent was evaporated. Yield 6.63 g (91%) of alcohol **11**. For $C_{43}H_{36}O_{11}$ (728.8) calculated: 70.87% C, 4.98% H; found: 70.87% C, 5.03% H. $[\alpha]_D$ –38.9 (*c* 1.426, chloroform). ^{1}H NMR (DMSO-d_6): 2.41 dd, 1 H, *J*(4a,5) = 2.0, *J*(4a,4b) = 15.4 (H-4a); 2.64 dd, 1 H, *J*(4b,5) = 4.1 (H-4b); 4.43 brs, 2 H (CH_2); 4.56 m, 1 H, *J*(1,2) = 8.9, *J*(1,6) = 9.2, *J*(1,OH) = 5.6 (H-1); 4.76 d, 1 H and 4.99 d, 1 H, J_{gem} = 11.8 (CH_2); 5.46 dd, 1 H, *J*(6,5) = 3.4 (H-6); 5.66 d, 1 H (H-2); 5.77 m, 1 H (H-5); 5.91 d, 1 H (1-OH); 7.28–8.01 m, 25 H (H-arom.).

(2*S*,3*R*,4*S*,5*R*)-2,4,5-Tris(benzoyloxy)-1,1-bis[(benzoyloxy)methyl]-3-{[(methylsulfanyl)thiocarbonyl]oxy}cyclohexane (**12**)

Carbon disulfide (3.1 ml, 51.5 mmol) was added to a solution of alcohol **11** (5.83 g, 8.0 mmol) in dimethylformamide (25 ml) and, after cooling to 0 °C, sodium hydride (60% dispersion in mineral oil, 1.06 g, 26.5 mmol) was added. After stirring at 0 °C for 30 min, methyl iodide (6.1 ml, 98 mmol) was added, the mixture was stirred at 0 °C for another 30 min and then warmed up to room temperature during another 30 min. Water (280 ml) was added and the mixture was extracted with ethyl acetate (280 ml). The organic layer was washed with water (3 × 200 ml), dried with anhydrous sodium sulfate, and the solvent was evaporated. Chromatography on a silica gel column (800 g) in toluene–ethyl acetate (93 : 7) gave 5.90 g (90%) of dithiocarbonate **12**. For $C_{45}H_{38}O_{11}S_2$ (818.9) calculated: 66.00% C, 4.68% H, 7.83% S; found: 66.22% C, 4.70% H, 7.66% S. $[\alpha]_D$ –99.1 (*c* 0.565, chloroform). ^{1}H NMR (DMSO-d_6): 2.29 s, 3 H (SCH_3); 2.54 dd, 1 H, *J*(6a,5) = 1.5 (H-6a); 2.76 dd, 1 H, *J*(6b,5) = 2.8, *J*(6b,6a) = 15.1 (H-6b); 4.43 d, 1 H and 4.49 d, 1 H, J_{gem} = 11.6 (CH_2O); 4.81 d, 1 H and 5.03 d, 1 H, J_{gem} = 11.8 (CH_2O); 5.87 m, 1 H (H-5); 6.06 dd, 1 H, *J*(4,3) = 10.2, *J*(4,5) = 3.5 (H-4); 6.25 d, 1 H, *J*(2,3) = 10.4 (H-2); 7.20 t, 1 H (H-3); 7.21–7.87 m, 25 H (H-arom.).

(2*R*,4*S*,5*R*)-2,4,5-Tris(benzoyloxy)-1,1-bis[(benzoyloxy)methyl]cyclohexane (**13**)

A 1 M tributylstannane solution in toluene (8 ml) and 2,2′-azobis(2-methylpropanonitrile) (300 mg, 1.8 mmol) were added to a boiling solution of dithiocarbonate **12** (4.09 g, 5.0 mmol) in toluene (40 ml). After 30 min reflux, the mixture was taken down and the residue was chromatographed on a column of silica gel (450 g) in toluene–ethyl acetate (93 : 7) to give 2.92 g (82%) of deoxy derivative **13**. For $C_{43}H_{36}O_{10}$ (712.8) calculated: 72.46% C, 5.09% H; found: 72.40% C, 5.12% H. $[\alpha]_D$ –14.6 (*c* 0.884, chloroform). ^{1}H NMR ($CDCl_3$): 2.11 dd, 1 H, *J*(6a,5) = 3.2, *J*(6a,6b) = 15.1 (H-6a); 2.49–2.78 m, 2 H (2 × H-3); 2.82 dd, 1 H, *J*(6b,5) = 6.0 (H-6b); 4.45 d, 1 H and 4.61 d, 1 H, J_{gem} = 11.6 (CH_2O); 4.83 d, 1 H and 4.88 d, 1 H, J_{gem} = 11.9 (CH_2O); 5.52–5.60 m, 1 H (H-4); 5.69 dd, 1 H, *J*(2,3a) = 4.6, *J*(2,3b) = 9.2 (H-2); 5.73 m, 1 H (H-5); 7.2–7.59 m, 15 H and 7.71–8.01 m, 10 H (H-arom.).

(1*R*,2*S*,4*R*)-5,5-Bis(hydroxymethyl)cyclohexane-1,2,4-triol (**14**)

Benzoate **13** (713 mg, 1.0 mmol) was dissolved under stirring in 0.1 M methanolic sodium methoxide (9 ml) and the solution was set aside at room temperature overnight. The mixture was then neutralized with Dowex 50(H^+), the resin was filtered off, washed with methanol, and the combined filtrates were evaporated. Column chromatography on silica gel (25 g) in ethyl acetate–acetone–ethanol–water (15 : 3 : 4 : 3) afforded 180 mg (94%) of hydroxy derivative **14**. For $C_8H_{16}O_5$ (192.2) calculated: 49.99% C, 8.39% H; found:

49.68% C, 8.68% H. $[\alpha]_D$ –17.0 (*c* 0.672, water). ^{1}H NMR (DMSO-d_6): 1.30 dd, 1 H, *J*(6a,1) = 3.9, *J*(6a,6b) = 14.1 (H-6a); 1.50 dd, 1 H, *J*(6b,1) = 6.7 (H-6b); 1.61 dt, 1 H, *J*(3a,2) = *J*(3a,4) = 3.8, *J*(3a,3b) = 12.8 (H-3b); 1.83 dt, 1 H, *J*(3b,2) = *J*(3b,4) = 8.1 (H-3b); 3.25–366 m, 7 H (2 × CH_2O, H-2, H-4, H-5); 4.23 t, 1 H, *J*(OH,CH_2) = 5.5 (CH_2O**H**); 4.41 t, 1 H, *J*(OH,CH_2) = 5.3 (CH_2O**H**); 4.46 d, 1 H, *J* = 4.6 (OH); 4.58 d, 2 H, *J* = 6.1 (2 × OH).

6-*O*-Benzoyl-3-*O*-benzyl-1,2-*O*-isopropylidene-5-*O*-[(methylsulfanyl)-thiocarbonyl]-α-D-glucofuranose (**16**)

Carbon disulfide (17.5 ml, 0.29 mol) was added to a solution of glucose derivative[7] **15** (18.65 g, 45 mmol) in dimethylformamide (135 ml) and, after cooling to 0 °C, sodium hydride (60% dispersion in mineral oil, 6.0 g, 0.15 mol) was added. After stirring at 0 °C for 30 min, methyl iodide (35 ml, 0.56 mol) was added and the mixture was stirred at 0 °C for 30 min and then warmed up to room temperature during another 30 min. Water (1.5 l) was added and the mixture was extracted with ethyl acetate (1.7 l). The organic layer was washed with water (3 × 1.5 l), dried with anhydrous sodium sulfate, and the solvent was evaporated. Chromatography of the residue on a silica gel column (1.2 kg) in toluene–ethyl acetate (93 : 7) gave 22.7 g (91%) of dithiocarbonate **16**. For $C_{25}H_{28}O_7S_2$ (504.6) calculated: 59.50% C, 5.59% H, 12.71% S; found: 59.32% C, 5.70% H, 12.63% S. $[\alpha]_D$ –54.8 (*c* 1.521, chloroform). ^{1}H NMR ($CDCl_3$): 1.33 s, 3 H and 1.49 s, 3 H ($C(CH_3)_2$); 2.15 s, 3 H (SCH_3); 4.06 d, 1 H, *J*(3,4) = 3.1 (H-3); 4.52 d, 1 H and 4.60 d, 1 H, J_{gem} = 11.9 (CH_2Ph); 4.56 dd, 1 H, *J*(6a,5) = 4.3, *J*(6a,6b) = 12.8 (H-6a); 4.62 d, 1 H, *J*(2.1) = 3.7 (H-2); 4.70 dd, 1 H, *J*(4,5) = 7.9 (H-4); 5.05 dd, 1 H, *J*(6b,5) = 1.8 (H-6b); 5.96 d, 1 H (H-1); 6.23 m, 1 H (H-5); 7.30 s, 5 H (H-arom. benzyl); 7.38–7.59 m, 3 H and 8.01–8.05 m, 2 H (H-arom. benzoyl).

3-*O*-Benzyl-5-deoxy-1,2-isopropylidene-α-D-*xylo*-hexofuranose (**17**)

2,2′-Azobis(2-methylpropanonitrile) (1.5 g, 9.1 mmol) was added to a boiling solution of dithiocarbonate **16** (22.2 g, 44 mmol) and tributylstannane (90 mmol) in toluene (300 ml). The mixture was refluxed for additional 30 min, cooled, and the solvent was evaporated. A solution of the residue in 0.1 M methanolic sodium methoxide (200 ml) was set aside overnight, neutralized with 10% hydrochloric acid and taken down. The residue was partitioned between ethyl acetate (1 l) and water (0.5 l). The organic layer was washed with water (500 ml), dried over anhydrous sodium sulfate, and the solvent was evaporated. Chromatography of the residue on a silica gel column (1 kg) in toluene–ethyl acetate (9 : 1) gave 9.85 g (76%) of compound **17**. For $C_{16}H_{22}O_5$ (294.4) calculated: 65.29% C, 7.53% H; found: 65.11% C, 7.58% H. ^{1}H NMR spectrum was identical with that of the compound prepared according to ref.[6b].

3-*O*-Benzyl-5-deoxy-1,2-*O*-isopropylidene-6-*O*-tosyl-α-D-*xylo*-hexofuranose (**18**)

A solution of compound **17** (9.71 g, 33 mmol) in pyridine (150 ml) was evaporated, redisolved in pyridine (100 ml) and tosyl chloride (7.63 g, 40 mmol), and 4-(dimethylamino)pyridine (250 mg, 2.0 mmol) were added. The mixture was set aside at room temperature overnight. Water (5 ml) was added at 0 °C and, after 10 min, the solvent was evaporated. The residue was partitioned between ethyl acetate (500 ml) and water (100 ml). The organic layer was separated and washed with 5% hydrochloric acid, water and 5% aqueous sodium hydrogencarbonate (100 ml each), dried over anhydrous sodium sulfate and

taken down to give 13.7 g (92%) of tosylate **18**. An analytical sample was prepared by chromatography on a silica gel column in toluene–ethyl acetate (9 : 1). For $C_{23}H_{28}O_7S$ (448.5) calculated: 61.59% C, 6.29% H, 7.15% S; found: 61.30% C, 6.36% H, 7.36% S. ^{1}H NMR (DMSO-d_6): 1.24 s, 3 H and 1.36 s, 3 H ($C(CH_3)_2$); 1.92 q, 2 H, J(5,4) = J(5.6) = 6.7 (2 × H-5); 2.40 s, 3 H (CH_3); 3.68 d, 1 H, J(3,4) = 3.1 (H-3); 4.01–4.13 m, 3 H (H-4, 2 × H-6); 4.40 d, 1 H and 4.63 d, 1 H, J_{gem} = 11.6 (CH_2Ph); 4.69 d, 1 H, J(2,1) = 3.7 (H-2); 5.78 d, 1 H (H-1); 7.25–7.34 m, 5 H (H-arom. benzyl); 7.45 d, 2 H and 7.75 d, 2 H, J = 7.9 (H-arom. tosyl).

3-*O*-Benzyl-5-deoxy-1,2-*O*-isopropylidene-6-iodo-α-D-*xylo*-hexofuranose (**19**)

A solution of tosylate **18** (13.5 g, 30 mmol) and sodium iodide (15 g, 100 mmol) in butan-2-one (170 ml) was refluxed for 1 h. After cooling, the insoluble portion was filtered off and the solvent was evaporated. The residue was dissolved in ethyl acetate (500 ml) and the solution was washed with water, aqueous sodium thiosulfate, water, dried over anhydrous sodium sulfate and taken down. Chromatography on a silica gel column (700 g) in toluene–ethyl acetate (87 : 13) afforded 10.84 g (89%) of iodo derivative **19**. For $C_{16}H_{21}IO_4$ (404.3) calculated: 47.54% C, 5.24% H, 31.39% I; found: 47.80% C, 5.27% H, 31.49% I. $[\alpha]_D$ –38.4 (*c* 1.800, chloroform). ^{1}H NMR ($CDCl_3$): 1.33 s, 3 H and 1.51 s, 3 H ($C(CH_3)_2$); 1.99–2.16 m, 1 H (H-5a); 2.22–2.40 m, 1 H (H-5b); 3.11–3.30 m, 2 H (2 × H-6); 3.83 d, 1 H, J(3,4) = 3.1 (H-3); 4.26 m, 1 H, J(4,5a) = 4.9, J(4,5b) = 8.5 (H-4); 4.48 d, 1 H and 4.71 d, 1 H, J_{gem} = 11.9 (CH_2PH); 4.63 d, 1 H, J(2,1) = 4.3 (H-2); 5.91 d, 1 H (H-1); 7.30–7.41 m, 5 H (H-arom.).

Diethyl (3-*O*-Benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranos-6-yl)malonate (**20**)

Sodium hydride (60% dispersion in mineral oil, 1.2 g, 30 mmol) was added under argon at 0 °C to a stirred solution of diethyl malonate (5.0 ml, 33 mmol) in dimethylformamide (100 ml) and, after stirring at 0 °C for 15 min, a solution of iodide **19** (10.11 g, 25 mmol) in dimethylformamide (30 ml) was added. The mixture was stirred at room temperature for 6 h and then the solvent was evaporated. The residue was partitioned between ethyl acetate (500 ml) and water (100 ml). The organic phase was washed with water (100 ml), dried over anhydrous sodium sulfate, and the solvent was evaporated. Chromatography on a column of silica gel (400 g) in toluene–ethyl acetate (87 : 13) afforded malonate **20** (9.50 g, 87%). For $C_{23}H_{32}O_8$ (436.5) calculated: 63.29% C, 7.39% H; found: 63.01% C, 7.42% H. $[\alpha]_D$ –35.6 (*c* 0.772, chloroform). ^{1}H NMR ($CDCl_3$): 1.25 t, 6 H, J = 7.3 (2 × CH_3); 1.31 s, 3 H and 1.48 s, 3 H ($C(CH_3)_2$); 1.66–2.05 m, 4 H (2 × H-5′, 2 × H-6′); 3.35 t, 1 H, J(2,6′a) = J(2,6′b) = 7.3 (H-2); 3.79 d, 1 H, J(3′,4′) = 3.1 (H-3′); 4.18 q, 4 H, J = 7.3 (2 × CH_2Me); 4.10–4.18 m, 1 H (H-4′); 4.49 d, 1 H and 4.69 d, 1 H, J_{gem} = 11.9 (CH_2PH); 4.61 d, 1 H, J(2′,1′) = 3.7 (H-2′); 5.90 d, 1 H (H-1′); 7.23–7.36 m, 5 H (H-arom.).

Diethyl (2*R*,S,3*S*,4*R*)-2-(Acetyloxy)-3-(benzyloxy)-4-(formyloxy)cyclohexane-1,1-dicarboxylate (**21**)

A mixture of **20** (8.73g, 20 mmol), dioxane (53 ml), water (32 ml) and Dowex 50 (H^+ form, 15 ml) was stirred at 80 °C for 20 h. Then the resin was filtered off, washed with dioxane, and the solvent was evaporated. A solution of the residue in ethyl acetate (300 ml) was washed with water (100 ml) and 10% aqueous potassium hydrogencarbonate (100 ml), dried

over anhydrous sodium sulfate, and the solvent was evaporated. To a stirred solution of the residue in dioxane (100 ml), a saturated solution of sodium periodate (85 ml) was added dropwise during 20 min. The insoluble portion was filtered off and washed with dioxane. The combined filtrates were concentrated to about 40 ml and partitioned between ethyl acetate (300 ml) and water (100 ml). The organic phase was separated, washed with water (100 ml), dried over anhydrous sodium sulfate, and the solvent was evaporated. A mixture of the residue, pyridine (60 ml) and acetic anhydride (6 ml) was set aside at room temperature overnight. Methanol (5 ml) was added and, after 15 min, the solvent was evaporated. A solution of the residue in ethyl acetate (200 ml) was washed with water (3 × 100 ml), dried over anhydrous sodium sulfate and taken down. Chromatography on a column of silica gel (450 g) in toluene–ethyl acetate (92 : 8) afforded 3.60 g (41%) of **21**. For $C_{22}H_{28}O_9$ (436.5) calculated: 60.54% C, 6.47% H; found: 60.31% C, 6.61% H. ^{1}H NMR ($CDCl_3$): 1.17–1.31 m (2 × CH_3 2*R* + 2*S*); 1.48–1.59 m (H-6a 2*R* + 2*S*); 1.99 s ($COCH_3$ 2*S*); 2.05 s ($COCH_3$ 2*R*); 2.09–2.31 m (2 × H-5, H-6b 2*R* + 2*S*); 3.89 dd, *J*(3,2) = 3.1, *J*(3,4) = 9.8 (H-3 2*R*); 4.04–4.33 m (2 × $MeCH_2$ 2*R* + 2*S*, H-3 2*S*); 4.49 d and 4.78 d, J_{gem} = 11.6 (CH_2Ph 2*R*); 4.68 d and 4.71 d, J_{gem} = 11.6 (CH_2Ph 2*S*); 4.88–5.09 m (H-4 2*R* + 2*S*); 5.37 d (H-2 2*S*); 6.21 d (H-2 2*R*); 7.24–7.36 m (H-arom. 2*R* + 2*S*); 7.97 s (CHO 2*S*); 8.03 s (CHO 2*R*); (2*R*)-isomer and (2*S*)-isomer in the 1 : 3 ratio.

(1*R*,2*S*,3*R*,S)-2-(Benzyloxy)-4,4-bis(hydroxymethyl)cyclohexane-1,3-diol (**22**)

Ester **21** (2.18 g, 5 mmol) dissolved in tetrahydrofuran (20 ml) was slowly added dropwise to a stirred refluxing 1 M solution of lithium aluminium hydride (25 ml) in argon atmosfere. After additional 2 h reflux, the mixture was cooled and ethyl acetate (4 ml) was added, followed after 15 min by water (15 ml). The mixture was taken down and the residue was extracted with warm ethyl acetate (5 × 30 ml). The solid residue was air-dried and mixed with 90% aqueous methanol (60 ml). The insoluble portion was filtered off through a Celite pad and washed with hot methanol. The combined extracts and filtrates were taken down and the residue was chromatographed on a silica gel column (350 g) in ethyl acetate–acetone–ethanol–water (100 : 15 : 6 : 4) giving 1.18 g (84%) of compound **22**. For $C_{15}H_{22}O_5$ (282.3) calculated: 63.81% C, 7.85% H; found: 63.50% H, 8.01% H. ^{1}H NMR (DMSO-d_6): 1.11–1.64 m (2 × H-5, 2 × H-6 3*R* + 3*S*); 3.16–3.60 m (2 × CH_2O, H-2 3*R* + 3*S*, H-1, H-3 3*S*); 3.68–3.82 m (H-1 3*R*); 3.89 dd, *J*(3,2) = 3.05, *J*(3,OH) = 4.3 (H-3 3*R*); 4.19 t, *J*(CH_2,OH) = 5.2 (CH_2O**H** 3*R*); 4.28–4.84 m (CH_2O**H** 3*S*, 2 × CH_2O**H**, 1-OH, 3-OH, 2 × CH_2Ph 3*R* + 3*S*); 7.22–7.44 m (H-arom); after exchange with D_2O: 4.50 d and 4.59 d, J_{gem} = 12.2 (CH_2Ph 3*R*); 4.69 d and 4.74 d, J_{gem} = 11.3 (CH_2Ph 3*S*); (2*R*)-isomer and (2*S*)-isomer in the 1 : 3 ratio.

(2*S*,3*S*,4*R*)- (**23**) and (2*R*,3*S*,4*R*)-2,4-Bis(benzoyloxy)-1,1-bis[(benzoyloxy)methyl]-3-(benzyloxy)cyclohexane (**24**)

A mixture of isomeric tetrahydroxy derivatives **22** (1.13 g, 4.0 mmol) was codistilled with pyridine (15 ml), redissolved in pyridine (12 ml), and benzoyl chloride (2.4 ml, 20.7 mmol) was added under cooling. The mixture was set aside at room temperature for 2 days, water (1 ml) was added at 0 °C and, after 10 min, concentrated *in vacuo*. The residue was partitioned between ethyl acetate (100 ml) and water (50 ml). The organic phase was washed with water (100 ml), 5% hydrochloric acid (100 ml), water (50 ml) and 10% aqueous potassium hydrogencarbonate (50 ml), then dried over anhydrous sodium sulfate, and the solvent was evaporated. Chromatography of the residue on a silica gel column (300 g) in toluene–

ethyl acetate (96 : 4) gave benzoate **24** (527 mg, 19%) and, after crystallization from methanol, 1.74 g (62%) of benzoate **23**.

Compound **23**: M.p. 141–142 °C. For $C_{43}H_{38}O_9$ (698.8) calculated: 73.91% C, 5.48% H; found: 74.13% C, 5.36% H. $[\alpha]_D$ –38.8 (*c* 0.752, chloroform). ^{1}H NMR ($CDCl_3$): 1.74–2.34 m, 4 H (2 × H-5, 2 × H-6); 4.18 dd, 1 H, *J*(3,2) = 8.8, *J*(3,4) = 8.5 (H-3); 4.45 d, 1 H and 4.57 d, 1 H, J_{gem} = 11.6 (CH_2); 4.61 d, 1 H and 4.69 d, 1 H, J_{gem} = 11.1 (CH_2); 4.67 d, 1 H and 4.92 d, 1 H, J_{gem} = 11.6 (CH_2); 5.29 ddd, 1 H, *J*(4,5a) = 4.9, *J*(4,5b) = 9.2 (H-4); 5.79 d, 1 H (H-2); 6.94–7.07 m, 5 H (H-arom. benzyl); 7.28–7.60 m, 12 H and 7.92–8.03 m, 8 H (H-arom.).

Compound **24**: Colourless foam. For $C_{43}H_{38}O_9$ (698.8) calculated: 73.91% C, 5.48% H; found: 73.64% C, 5.59% H. $[\alpha]_D$ –25.9 (*c* 0.804, chloroform). ^{1}H NMR ($CDCl_3$): 1.79–2.44 m, 4 H (2 × H-5, 2 × H-6); 4.07 dd, 1 H, *J*(3,2) = 3.2, *J*(3,4) = 7.2 (H-3); 4.47–4.73 m, 6 H (3 × CH_2); 5.52 m, 1 H, Σ*J* = 18.3 (H-4); 6.04 d, 1 H (H-2); 7.08–7.61 m, 17 H and 7.98–8.06 m, 8 H (H-arom.).

(1*S*,2*S*,6*R*)-2,6-Bis(benzoyloxy)-3,3-bis[(benzoyloxy)methyl]cyclohexan-1-ol (**25**)

Benzyl derivative **23** (1.40 g, 2.0 mmol) was hydrogenated in a mixture of methanol (12 ml) and dimethylformamide (6 ml) over Pd/C (10%, 250 mg) at atmospheric pressure for 50 h. The catalyst was removed by filtration through a Celite pad, washed with methanol, and the combined filtrates were taken down. The residue was dissolved in ethyl acetate (40 ml), the solution was washed with water (3 × 20 ml), dried over anhydrous sodium sulfate, and the solvent was evaporated. Yield 1.16 g (95%) of alcohol **25**. For $C_{36}H_{32}O_9$ (608.7) calculated: 71.04% C, 5.30% H; found: 70.89% C, 5.27% H. $[\alpha]_D$ –39.9 (*c* 0.903, chloroform). ^{1}H NMR ($CDCl_3$): 1.74–2.27 m, 4 H (2 × H-4, 2 × H-5); 4.29 m, 1 H, *J*(1,2) = 9.7, *J*(1,6) = 9.5, *J*(1,OH) = 5.5 (H-1); 4.40 d, 1 H and 4.57 d, 1 H, J_{gem} = 11.4 (CH_2); 4.71 d, 1 H and 4.96 d, 1 H, J_{gem} = 11.9 (CH_2); 5.17 m, 1 H, Σ*J* = 24.7 (H-6); 5.65 d, 1 H (H-2); 7.28–7.61 m, 12 H and 7.92–8.06 m, 8 H (H-arom.).

(2*S*,3*S*,4*R*)-2,4-Bis(benzoyloxy)-1,1-bis[(benzoyloxy)methyl]-3-{[(methylsulfanyl)-thiocarbonyl]oxy}cyclohexane (**26**)

Carbon disulfide (0.68 ml, 11.3 mmol) was added to a solution of alcohol **25** (1.10 g, 1.8 mmol) in dimethylformamide (5 ml) and, after cooling to 0 °C, sodium hydride (60% dispersion in mineral oil, 239 mg, 6.0 mmol) was added. After stirring at 0 °C for 30 min, methyl iodide (1.36 ml, 21.8 mmol) was added and the mixture was stirred at 0 °C for 30 min and then warmed up to room temperature during another 30 min. Water (60 ml) was added and the mixture was extracted with ethyl acetate (70 ml). The organic layer was washed with water (3 × 60 ml), dried with anhydrous sodium sulfate, and the solvent was evaporated. Column chromatography on silica gel (110 g) in toluene–ethyl acetate (96 : 4) afforded 994 mg (79%) of dithiocarbonate **26**. For $C_{38}H_{34}O_9S_2$ (698.8) calculated: 65.31% C, 4.90% H, 9.18% S; found: 65.44% C, 4.86% H, 9.10% S. $[\alpha]_D$ –36.0 (*c* 0.916, chloroform). ^{1}H NMR ($CDCl_3$): 1.80–2.43 m, 4 H (2 × H-5, 2 × H-6); 2.73 s, 3 H (SCH_3); 4.40 d, 1 H and 4.52 d, 1 H, J_{gem} = 11.5 (CH_2); 4.73 d, 1 H and 5.05 d, 1 H, J_{gem} = 11.9 (CH_2); 5.41 m, 1 H, *J*(4,5a) = 9.6, *J*(4,5b) = 4.9 (H-4); 5.90 d, 1 H, *J*(2,3) = 10.1 (H-2); 6.87 dd, 1 H, *J*(3,4) = 9.8 (H-3); 7.26–7.61 m, 12 H and 7.90–8.08 m, 8 H (H-arom.).

(2*R*,4*R*)-2,4-Bis(benzoyloxy)-1,1-bis[(benzoyloxy)methyl]cyclohexane (**27**)

A 1 M tributylstannane solution in toluene (2.1 ml) and 2,2′-azobis(2-methylpropanonitrile) (100 mg, 0.6 mmol) were added to a boiling solution of dithiocarbonate **26** (908 mg, 1.3 mmol) in toluene (10 ml). After 30 min reflux, the mixture was evaporated and the residue was chromatographed on a silica gel column (110 g) in toluene–ethyl acetate (93 : 7) giving 735 mg (95%) of deoxy derivative **27**. For $C_{36}H_{32}O_8$ (592.7) calculated: 72.96% C, 5.44% H; found: 72.69% C, 5.45% H. $[\alpha]_D$ –45.0 (*c* 1.084, chloroform). ^{1}H NMR ($CDCl_3$): 1.66–2.56 m, 6 H (2 × H-3, 2 × H-5, 2 × H-6); 4.49 d, 1 H and 4.59 d, 1 H, J_{gem} = 11.3 (CH_2); 4.70 d, 1 H and 4.95 d, 1 H, J_{gem} = 11.6 (CH_2); 5.25 m, 1 H, *J*(4,3a) ≈ *J*(4,3b) ≈ *J*(4,5a) ≈ *J*(4,5b) ≈ 4.5 (H-4); 5.59 dd, 1 H, *J*(2,3a) = 4.6, *J*(2,3b) = 9.8 (H-2); 7.30–7.58 m, 12 H and 7.95–8.03 m, 8 H (H-arom.).

(1*R*,3*R*)-4,4-Bis(hydroxymethyl)cyclohexane-1,3-diol (**28**)

Benzoate **27** (593 mg, 1.0 mmol) was dissolved under stirring in 0.1 M methanolic sodium methoxide (7 ml) and the solution was set aside at room temperature overnight. The mixture was neutralized with Dowex 50(H^+), the resin was removed by filtration and washed with methanol, and the combined filtrates were evaporated. Column chromatography on silica gel (20 g) in ethyl acetate–acetone–ethanol–water (16 : 3 : 4 : 2) and crystallization from acetone afforded 150 mg (85%) of hydroxy derivative **28**, m.p. 95.0–95.5 °C. For $C_8H_{16}O_4$ (176.2) calculated: 54.53% C, 9.15% H; found: 54.54% C, 9.10% H. $[\alpha]_D$ –8.1 (*c* 0.767, water). ^{1}H NMR (DMSO-d_6): 0.89–1.56 m, 5 H and 1.76–1.86 m, 1 H (2 × H-2, 2 × H-5, 2 × H-6); 3.30–3.61 m, 6 H (2 × CH_2, H-1, H-3); 4.23 t, 1 H, *J*(OH,CH_2) = 4.9 (CH_2O**H**); 4.42 t, 1 H, *J*(OH,CH_2) = 5.0 (CH_2O**H**); 4.51 d, 1 H, *J*(OH,CH) = 5.2 (OH); 4.53 d, 1 H, *J*(OH,CH) = 5.5 (OH).

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REFERENCES

1. a) Verheggen I., Van Aerschot A., Toppet S., Snoeck R., Janssen G., Balzarini J., De Clercq E., Herdewijn P.: *J. Med. Chem.* **1993**, *36*, 2033; b) Verheggen I., Van Aerschot A., Van Meervelt L., Rozenski J., Wiebe L., Snoeck R., Andrei G., Balzarini J., Claes P., De Clercq E., Herdewijn P.: *J. Med. Chem.* **1995**, *38*, 826.
2. a) Konkel M. J., Vince R.: *Tetrahedron* **1996**, *52*, 799; b) Rosenquist A., Kvarnström I., Classon B., Samuelsson B.: *J. Org. Chem.* **1996**, *61*, 6282; c) Wang J., Herdewijn P.: *J. Org. Chem.* **1999**, *64*, 7820.
3. a) Hřebabecký H., Masojídková M., Holý A.: *Collect. Czech. Chem. Commun.* **1998**, *63*, 2044; b) Hřebabecký H., Holý A.: *Collect. Czech. Chem. Commun.* **1999**, *64*, 1485; c) Hřebabecký H., Holý A.: *Collect. Czech. Chem. Commun.* **2000**, *65*, 395.
4. Calvo-Flores F. G., García-Mendoza P., Hernández-Mateo F., Isac-García J., Santoyo-Gonzáles F.: *J. Org. Chem.* **1997**, *62*, 3944.

5. Wysocki R. J., Jr., Siddiqui M. A., Barchi J. J., Jr., Driscoll J. S., Marquez V. E.: *Synthesis* **1991**, 1005.
6. a) Czernecki S., Georgoulis C., Provelenghiou C.: *Tetrahedron Lett.* **1975**, 2623; b) Bonini C., Di Fabio R., Sotgiu G., Cavegnero S.: *Tetrahedron* **1989**, *45*, 2895.
7. Whistler R. L., Lake W. C.: *Methods Carbohydr. Chem.* **1972**, *6*, 286.