PREPARATION OF 1,6:3,4-DIANHYDRO-β-D-ALTROPYRANOSE AS STARTING SUBSTANCE FOR THE SYNTHESIS OF 3-SUBSTITUTED D-MANNOSE DERIVATIVES*

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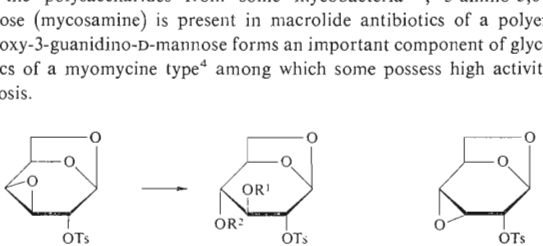
Acetolysis of 1,6 : 3,4-dianhydro-2-O-*p*-toluenesulfonyl-β-D-galactopyranose (*I*) gave 3,4-di--O-acetyl-1,6-anhydro-2-O-*p*-toluenesulfonyl-β-D-glucopyranose (*II*) which was converted with sodium methoxide to 1,6 : 3,4-dianhydro-β-D-altropyranose (*X*). The 1,6-anhydride bond in diacetate *II* was cleaved with acetic anhydride or hydrogen bromide in acetic acid under formation of a mixture of anomeric tetraacetates of 2-O-*p*-toluenesulfonyl-D-glucopyranose or the corresponding acetates of α-D-glucopyranosyl bromide *XIII* and its 6-bromo-6-deoxy derivative *XIV*.

In addition to D-mannose which is one of the components of some biologically interesting oligo- and polysaccharides in natural substances its 3-substituted derivatives also occur. Thus, for example, 3-O-methyl-D-mannose is the main building unit of the polysaccharides from some mycobacteria[1,2], 3-amino-3,6-dideoxy--D-mannose (mycosamine) is present in macrolide antibiotics of a polyene type[3], and 3-deoxy-3-guanidino-D-mannose forms an important component of glycopeptidic antibiotics of a myomycine type[4] among which some possess high activity against tuberculosis.



I *II*, R^1; R^2 = Ac *VIII*
III, R^1; R^2 = H
IV, R^1 = H; R^2 = Ac
V, R^1 = Ts; R^2 = Ac
VI, R^1 = H; R^2 = $CH_2CH_2OCH_2CH_2OH$
VII, R^1 = Ac; R^2 = $CH_2CH_2OCH_2CH_2OAc$

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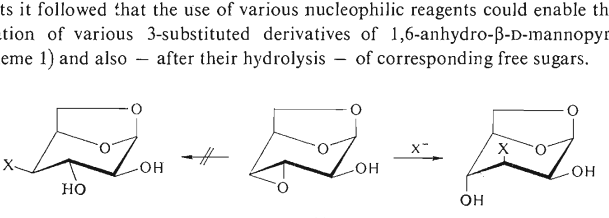
Notwithstanding the fact that the synthesis of 3-substituted derivatives of D-mannose has been described in literature (for example 3-amino-3-deoxy-D-mannose[5-7] and 3-O-methyl-D-mannose[8,9]) a generally utilizable method for the preparation of these compounds is still lacking. From this point of view 1,6:3,4-dianhydro-β-D-altropyranose (*X*) seems to be a suitable starting compound, since its oxirane ring has the tendency to open with a high regioselectivity in the position $C_{(3)}$ so that 4-substituted derivatives are practically not formed[10,11]. From preliminary experiments it followed that the use of various nucleophilic reagents could enable the preparation of various 3-substituted derivatives of 1,6-anhydro-β-D-mannopyranose (Scheme 1) and also – after their hydrolysis – of corresponding free sugars.



X

SCHEME 1

The aim of this study is the elaboration of a suitable synthesis of 1,6:3,4-dianhydro-β-D-altropyranose (*X*). The earlier preparation of dianhydride *X* consisted[12] in acid hydrolysis of the oxirane ring in 1,6:3,4-dianhydro-2-O-*p*-toluenesulfonyl-β-D-galactopyranose (*I*), subsequent cyclization of the 1,6-anhydro-2-O-*p*-toluenesulfonyl-β-D-glucopyranose (*III*) formed, which gave 1,6:2,3-dianhydro-β-D-mannopyranose (*IX*), and its isomerization to *X* under base catalysis. This procedure is disadvantageous in that the hydrolysis of epoxide *I* with 10% sulfuric acid in aqueous dioxane gives tosyl derivative *III* in a yield of about 50%. As we have observed when reproducing the procedure, 1,6-anhydro-4-O-(5-hydroxy-3-oxapentyl)-2-O-*p*-toluenesulfonyl-β-D-glucopyranose (*VI*) is formed simultaneously by participation of dioxane in the reaction. Compound *VI* was obtained as the main product by the action of concentrated sulfuric acid on tosyl epoxide *I* in a mixture of dioxane and diethylene glycol. Its structure was demonstrated by conversion to diacetyl derivative *VII* and by means of ^{1}H NMR spectrometry.

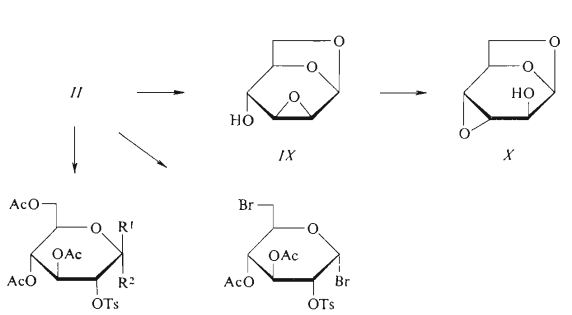
Since the effort to improve the yield of dianhydride *X* by modifying the conditions of hydrolysis was unsuccessful we tried to acetolyse the oxirane ring in compound *I* under various conditions. While acetolysis with acetic anhydride in the presence of sulfuric acid or boron trifluoride etherate at room temperature led to the formation of a mixture of several substances, in boiling anhydrous acetic acid, under catalysis with boron trifluoride etherate, 3,4-di-O-acetyl-1,6-anhydro-2-O-*p*-toluenesulfonyl-β-D-glucopyranose (*II*) was formed as the sole product. Even a small amount of water in acetic acid suppressed the formation of diacetate *II* and monoacetyl

derivative *IV* became the main product. The D-*gluco* configuration and the $^1C_4$(D) conformation of diacetate *II* was demonstrated by ^{1}H NMR spectrum on the basis of the observed coupling constants $J_{1,2} = 1{\cdot}5$, $J_{2,3} = 2{\cdot}3$, $J_{3,4} \approx 2{\cdot}4$ and $J_{1,3} \approx 1{\cdot}2$ Hz, and its structure was further confirmed by comparison with an authentic sample of diacetate *II* which was obtained[13,14] by partial tosylation of 1,6-anhydro-β-D-glucopyranose and subsequent acetylation.

The structure of monoacetyl derivative *IV* was demonstrated by means of ^{1}H NMR spectroscopy: the presence of a free hydroxy group on $C_{(3)}$ followed from the comparison with the spectrum of diacetate *II*. In agreement with the assumed structure of acetate *IV* its tosylation took place under formation of 2,3-di-O-*p*-toluenesulfonyl derivative *V* which was then reacted with sodium methoxide to give the expected 1,6:3,4-dianhydro-2-O-*p*-toluenesulfonyl-β-D-allopyranose (*VIII*). According to physical constants and the IR spectra it was identical with an authentic sample[15] which was prepared by tosylation of 1,6:3,4-dianhydro-β-D-allopyranose.

Mild deacetylation of diacetate *II* with barium methoxide gave the known[12] tosyl derivative *III*. On reaction of diacetate *II*, or of substance *IV* or *III* with sodium methoxide in methanol, 1,6:3,4-dianhydro-β-D-altropyranose (*X*) was formed. The reaction sequence *I*→*II*→*X* permitted the preparation of dianhydride *X* in a total yield of 75%. If the ion exchanger IRA 400 in OH^- cycle (ref.[16]) is used in the reaction of diacetate *II* or compound *III* instead of sodium methoxide, only 1,6:2,3-dianhydro-β-D-mannopyranose (*IX*) is formed, without its isomerization to compound *X*.

The synthetic utilization of tosyl derivative *III* also depends on the possibility to cleave its 1,6-anhydride bond under formation of a reducing hexose. Since the hydrolysis of this compound in aqueous medium took place with much greater



XI, $R^1 = H$; $R^2 = OAc$
XII, $R^1 = OAc$; $R^2 = H$
XIII, $R^1 = H$; $R^2 = Br$

XIV

Ac = CH_3CO
Ts = p-$CH_3C_6H_4SO_2$

difficulty than in the case of common glycosides, we investigated the relatively easy acetolysis. Under the effect of acetic anhydride and the catalysis with perchloric acid a mixture of α- and β-anomers of 1,3,4,6-tetra-O-acetyl-2-O-*p*-toluenesulfonyl--D-glucose (*XI*) and (*XII*) was formed from diacetate *II*; similar behaviour is observed for methyl 2-O-*p*-toluenesulfonyl-α-D-glucopyranoside[17]. Reaction of diacetate *II* with hydrobromic acid in acetic anhydride at room temperature gave the known[17-20] 3,4,6-tri-O-acetyl-2-O-*p*-toluenesulfonyl-α-D-glucopyranosyl bromide (*XIII*), while at an elevated temperature and prolonged reaction time corresponding 6-bromo--6-deoxy derivative *XIV* is formed in addition to monobromo derivative *XIII*.

EXPERIMENTAL

The melting points were determined on a Boetius micromelting point apparatus. Optical rotation was measured on Bendix-Ericsson ETL 143A polarimeter. The IR spectra were measured on a UR 20 spectrophotometer and the ^{1}H NMR spectra on a Varian HA-200 instrument at 200 MHz, in deuteriochloroform, δ-scale, coupling constants in Hz, using tetramethylsilane as internal reference. For thin-layer chromatography silica gel G according to Stahl was used (layer thickness 0·2—0·3 mm) with: A benzene–acetone 10 : 1, B chloroform–methanol 10 : 1, C chloroform–methanol 20 : 1, as developing solvents. Detection was carried out with 50% sulfuric acid and carbonization. The solvents were evaporated on a vacuum rotatory evaporator at about 50°C. Samples for analysis were dried over phosphorus pentoxide at 10 Pa.

3,4-Di-O-acetyl-1,6-anhydro-2-O-*p*-toluenesulfonyl-β-D-glucopyranose (*II*)

A) A mixture of epoxide *I* (10 g), acetic acid (120 ml), acetic anhydride (3 ml) and boron trifluoride etherate (1 ml) was refluxed for 15 min and then evaporated. The residue contained only diacetate *II* with R_F 0·51 (in system A, thin-layer chromatography). It was crystallized from ethanol affording 11·6 g (87%) of compound *II*, m.p. 116—117°C, $[\alpha]_D$ −44° (*c* 1·5 chloroform). For $C_{17}H_{20}O_9S$ (400·4) calculated: 50·99% C, 5·03% H, 8·00% S; found: 50·70% C, 4·96% H, 7·85% S. ^{1}H NMR spectrum: 2·02 s (3 H, $OCOCH_3$ on $C_{(3)}$), 2·11 s (3 H, $OCOCH_3$ on $C_{(4)}$), 2·46 s (3 H, $CH_3C_6H_4$), 3·76 dd (1 H, H-6_{exo}; $J_{6,6}$ = 7·7, $J_{6,5}$ = 5·7), 4·04 dd (1 H, H-6_{endo}; $J_{6,6}$ = 7·7, $J_{6,5}$ = 0·8), 4·26 m (1 H, H-2; $J_{2,3}$ = 2·3, $J_{2,1}$ = 1·5, $J_{2,4} \approx 0{\cdot}7$, $J_{2,5} \approx 0{\cdot}5$), ≈ 4·58 m (2 H, H-5 and H-4), 4·86 m (1 H, H-3; $J_{3,1}$ = 1·2, $J_{3,2}$ = 2·3, $J_{3,4} \approx 2{\cdot}4$, $J_{3,5} \approx 1{\cdot}6$), 5·44 t (1 H, H-1; $J_{1,3} \approx 1{\cdot}2$, $J_{1,2}$ = 1·5, $J_{1,6endo} \neq 0$, $J_{1,6exo} \neq 0$), 7·36, 7·84 (4 H, arom. ring).

B) Acetic anhydride (0·4 ml) was added to a solution of tosyl derivative[14] *III* (200 mg) in pyridine (2 ml) and the mixture was set aside overnight. After pouring onto ice a crystalline product precipitated which was recrystallized from ethanol. Yield of compound *II* was 240 mg (94%), m.p. 114—116°C, $[\alpha]_D$ −43° (*c* 0·9, chloroform).

1,6-Anhydro-2-O-*p*-toluenesulfonyl-β-D-glucopyranose (*III*)

Five drops of a barium methoxide solution (0·5 g of barium in 10 ml of methanol) were added to a solution of diacetate *II* (1 g) in 10 ml of methanol and the mixture was allowed to stand for 20 min. After neutralization with solid carbon dioxide methanol was evaporated and the residue crystallized from toluene. Yield, 750 mg (95%) of tosyl ester *III* the properties of which, its m.p. 117—119°C and $[\alpha]_D$ −48° (*c* 1·3, chloroform), agree with the properties mentioned in literature[12,14].

4-O-Acetyl-1,6-anhydro-2-O-*p*-toluenesulfonyl-β-D-glucopyranose (*IV*)

Boron trifluoride etherate (0·1 ml) and water (0·2 ml) were added to a solution of epoxide *I* (1 g) in 10 ml of acetic acid and the mixture was refluxed for 20 min. According to thin-layer chromatography in system A the reaction mixture contained in addition to the main product *IV* (R_F 0·25) a small amount of diacetate *II* (R_F 0·51). After distilling off acetic acid the residue was dissolved in 15 ml of water and the solution extracted with three 10 ml portions of chloroform. The combined extracts were dried over magnesium sulfate and chloroform was evaporated. The residue was crystallized from an ethanol–ether mixture, affording 780 mg (65%) of compound *IV*, m.p. 121–123°C, $[\alpha]_D$ −59° (*c* 0·9, chloroform). For $C_{15}H_{18}O_8S$ (358·4) calculated: 50·27% C, 5·06% H, 8·95% S; found: 49·99% C, 4·89% H, 8·65% S. ^{1}H NMR spectrum: 2·13 s (3 H, OCO.CH_3), 2·46 s (3 H, $CH_3C_6H_4$), 3·12 d (1 H, OH, $J_{OH,3}$ = 5·4), 3·71 ddd (1 H, H-6_{exo}, $J_{6,6}$ = 7·6, $J_{5,6}$ = 5·5, $J_{6,1}$ = 0·4), 3·91 m (1 H, H-3, $J_{3,OH}$ = 5·4, $J_{3,2}$ = 2·9, $J_{3,4}$ = 3·2, $J_{3,1}$ = 1·2, $J_{3,5}$ = 1·4), 4·12 dd (1 H, H-6_{endo}, $J_{6,6}$ = 7·6, $J_{6,5}$ = 0·9, $J_{6,1}$ = 0·3), 4·23 m (1 H, H-2, $J_{2,1}$ = 1·4, $J_{2,3}$ = 2·9, $J_{2,4}$ = 0·7, $J_{2,5}$ = 0·5), 4·56 m (1 H, H-5, $J_{5,4}$ = 1·6, $J_{5,3}$ = 1·4, $J_{5,2}$ = 0·5, $J_{5,6}$ = 5·5 + 0·9), 4·59 m (1 H, H-4, $J_{4,3}$ = 3·2, $J_{4,2}$ = 0·7, $J_{4,5}$ = 1·6, $J_{4,1}$ = 0·5), 5·32 m (1 H, H-1, $J_{1,2}$ = 1·4, $J_{1,3}$ = 1·2, $J_{1,5}$ = 0·5, $J_{1,6endo}$ = 0·3, $J_{1,6exo}$ = 0·4).

1,6-Anhydro-4-O-(5-hydroxy-3-oxapentyl)-2-O-*p*-toluenesulfonyl-β-D-glucopyranose (*VI*)

Diethylene glycol (10 ml) and 1 ml of boron trifluoride etherate were added to a solution of epoxide *I* (10 g) in dioxane (100 ml) and the mixture was heated at 100°C for 4 h, when the mixture no longer contained the starting compound (thin-layer chromatography in system A). The solution was concentrated under reduced pressure (50 Pa, 80°C bath temperature) to minimal volume and the residue was dissolved in a mixture of ethanol and ether. Standing in an ice-box produced 8 g (59%) of compound *VI*, m.p. 110–112°C, $[\alpha]_D$ −42° (*c* 1·4, chloroform), R_F 0·49 (in system B). For $C_{17}H_{24}O_9S$ (404·4) calculated: 50·49% C, 5·98% H, 7·93% S; found: 50·68% C, 5·86% H, 8·00% S. ^{1}H NMR spectrum: 2·47% s (3 H, $CH_3C_6H_4$), 3·07 (1 H, OH), 3·38 dd (1 H, H-4, $J_{4,3}$ = 3·5, $J_{4,5}$ = 1·4), 3·50–3·85 m (9 H, CH_2-groups on $C_{(4)}$ and H-6_{exo}), 3·96 dd (1 H, H-6_{endo}, $J_{6,6}$ = 7·65, $J_{6,5}$ ≈ 1·00). 3·98 dt (1 H, H-3, $J_{3,2}$ = 3·5, $J_{3,4}$ = 3·5, $J_{3,1}$ = 1·1, $J_{3,5}$ = 1·1), 4·21 bd (1 H, H-2, $J_{2,3}$ = 3·5), 4·59 dq (1 H, H-5, $J_{5,6exo}$ = 5·5, $J_{5,6endo}$ ≈ 1, $J_{5,4}$ = 1·4, $J_{5,3}$ = 1·1), 5·27 bs (1 H, H-1), 7·40 d and 7·88 d (4 H, arom. ring). Calculated molecular mass: 404·4; found: 399 (vapour pressure osmometer Knauer, acetonitrile, compound *III* as standard, 45°C).

4-O-(5-Acetoxy-3-oxapentyl)-3-O-acetyl-1,6-anhydro-2-O-*p*-toluenesulfonyl-β-D-glucopyranose (*VII*)

Compound *VI* (0·5 g) was acetylated with acetic anhydride (3 ml) in pyridine (3 ml) at room temperature overnight. Water was added dropwise and the mixture put into an ice box. The precipitated crystals were recrystallized from ethanol and washed with ether. Yield of compound *VII*, 492 mg (81%), m.p. 81–83°C, $[\alpha]_D$ −28° (*c* 1·6, chloroform), R_F 0·35 (in system A). For $C_{21}H_{28}O_{11}S$ (488·5) calculated: 51·63% C, 5·78% H, 6·56% S; found: 51·91% C, 5·78% H, 6·71% S.

1,6:3,4-Dianhydro-2-O-*p*-toluenesulfonyl-β-D-allopyranose (*VIII*)

p-Toluenesulfonyl chloride (1 g) was added to a solution of monoacetate *IV* (1 g) in pyridine (15 ml) and the mixture was allowed to react at room temperature for 50 h. Another portion

(1 g) of *p*-toluenesulfonyl chloride was added and after standing for 100 h at room temperature the mixture was poured into water, extracted with chloroform and the extract was dried over magnesium sulfate and evaporated. The ditosyl derivative *V* (1,3 g) obtained in this manner was dissolved in a mixture of 5 ml chloroform and 10 ml methanol, and 15 ml of methanol containing 0·7 g of sodium were added dropwise to it. After 14 h standing at room temperature the mixture was neutralized with 5% hydrochloric acid, evaporated and the residue extracted with three 20 ml portions of chloroform. The extract was dried over calcium chloride and evaporated and the residue was crystallized from ethanol. Yield, 0·4 g (48%) of compound *VIII*, m.p. 116–118°C and $[\alpha]_D$ −98° (*c* 1·0, chloroform), R_F 0·46 (system A). Literature[15] gives m.p. 116–117°C and $[\alpha]_D$ −95° (*c* 0·4, chloroform). The infrared spectrum of compound *VIII* was identical with the spectrum of an authentic sample[15].

1,6:2,3-Dianhydro-β-D-mannopyranose (*IX*)

Ion exchanger IRA 400 in OH^- form (7 g, washed with 50 ml methanol before use) was added to a solution of diacetate *II* (1 g) in methanol (25 ml) and the mixture was stirred for 30 min until the starting substance *II* disappeared (R_F 0·51 in system A on thin layer). The ion exchanger was filtered off, methanol was evaporated and the residue crystallized from a mixture of ethanol and ether. Yield, 283 mg (80%) of dianhydride *IX*, m.p. 68–70°C, $[\alpha]_D$ −35° (*c* 0·5, water), R_F 0·35 (in system C), the properties of which were identical with those of an authentic sample[12].

1,6:3,4-Dianhydro-β-D-altropyranose (*X*)

A solution of sodium (12 g) in methanol (350 ml) was added to a solution of diacetate *II* (30 g) in methanol (250 ml) and the mixture was allowed to stand until compound *II* had disappeared (2 h). At that point the mixture contained two substances, one with R_F 0·38 and the other with R_F 0·34 (in system C). After 12 h of standing at room temperature the substance with R_F 0·34 (1,6:2,3-dianhydro-β-D-mannopyranose (*IX*)) disappeared. Then the mixture was neutralized with 5% hydrochloric acid and evaporated. The residue was extracted with five 50 ml portions of hot acetone, the extract was filtered and the solvent evaporated. The residue (9 g; 85%) was product *X* which was crystallized from ethanol, m.p. 160–162°C, $[\alpha]_D$ −120° (*c* 0·6, water), in agreement with the literature data[12].

1,3,4,6-Tetra-O-acetyl-2-O-*p*-toluenesulfonyl-α- and -β-D-glucopyranose (*XI*) and (*XII*)

Diacetyl derivative *II* (1 g) was dissolved in 15 ml of acetic anhydride and 0·3 ml of conc. perchloric acid were added dropwise to the solution. The mixture was allowed to stand at room temperature for 24 h, poured into 100 ml of icy water. The precipitated crystals were filtered off and crystallized from ethanol. Yield, 1·2 g (96%) of a mixture of anomers *XI* and *XII*, m.p. 115–126°C. Repeated fractional crystallization of this mixture gave 700 mg of α-anomer *XI*, m.p. 126–127°C and $[\alpha]_D$ +80° (*c* 0·9, chloroform); literature[17] gives m.p. 115–116°C, $[\alpha]_D$ +73° (*c* 2·0, chloroform), lit.[18] gives m.p. 127°C, $[\alpha]_D$ +75° (*c* 1·4, chloroform). For $C_{21}H_{26}O_{12}S$ (502·5) calculated: 50·19% C, 5·22% H, 6·38% S; found: 50·36% C, 5·27% H, 6·32% S.

The second fraction, β-anomer *XII* (150 mg), had m.p. 152–154°C and $[\alpha]_D$ +21° (*c* 0·9, chloroform); lit.[19] gives m.p. 148–150°C, $[\alpha]_D$ +17° (*c* 1·7, chloroform), lit.[20] gives m.p. 159–160°C, $[\alpha]_D$ +21° (*c* 0·82, chloroform). For $C_{21}H_{26}O_{12}S$ (502·5) calculated: 50·19% C, 5·22% H, 6·38% S; found: 50·08% C, 5·19% H, 6·34% S.

3,4,6-Tri-O-acetyl-2-O-*p*-toluenesulfonyl-α-D-glucopyranosyl Bromide (*XIII*)

A solution of hydrogen bromide in acetic acid (39%, 25 ml) was added to a solution of diacetate *II* (2·5 g) in acetic anhydride (12·5 ml) and the mixture was allowed to stand at room temperature for 100 h, when the solution contained the substance with R_F 0·41 (in system A, thin-layer chromatography) only. The mixture was poured into icy water, extracted with chloroform and the extract was washed with 5% sodium hydrogen carbonate and water, then dried over anhydrous calcium chloride and evaporated. Crystallization of the residual syrup from ether gave 2·6 g (79%) of bromo derivative *XIII*, m.p. 112–114°C, $[\alpha]_D$ +165° (*c* 0·5, chloroform); lit.[19] gives m.p. 113–116°C $[\alpha]_D$ +176° (*c* 1·19, chloroform). For $C_{19}H_{23}BrO_{10}S$ (523·4) calculated: 43·60% C, 4·43% H, 15·27% Br, 6·13% S; found: 43·77% C, 4·51% H, 15·14% Br, 6·00% S.

3,4-Di-O-acetyl-6-bromo-6-deoxy-2-O-*p*-toluenesulfonyl-α-D-glucopyranosyl Bromide (*XIV*)

A 34% solution of hydrogen bromide in acetic acid (10 ml) was added to a solution of diacetate *II* (1 g) in 5 ml of acetic anhydride and the mixture was allowed to stand at room temperature for 24 h. It was then heated at 70°C for 6 h, when thin-layer chromatography in system A showed in it two main products, with R_F values 0·41 and 0·60. The reaction mixture was concentrated, the syrup obtained was dissolved in chloroform and the solution washed with sodium hydrogen carbonate solution. After drying over anhydrous calcium chloride and filtration the solvent was evaporated, leaving a residue which was crystallized from ether, affording 0·65 g (48%) of dibromo derivative *XIV* (R_F 0·60). After further crystallization from ether it had m.p. 155 to 157°C and $[\alpha]_D$ +161° (0·56, chloroform). For $C_{17}H_{20}Br_2O_8S$ (544·2) calculated: 37·52% C, 3·70% H, 29·37% Br, 5·89% S; found: 37·69% C, 3·83% H, 29·24% Br, 5·70% S. ^{1}H NMR spectrum: 1·80 s (3 H, $OCOCH_3$), 2·05 s (3 H, $OCOCH_3$), 2·47 s (3 H, $CH_3C_6H_4$), 3·42 dd (1 H, H-6; $J_{6,6} = 11·9$, $J_{6,5} = 4·7$), 3·54 dd (1 H, H-6; $J_{6,6} = 11·9$, $J_{6,5} = 2·8$), 4·31 ddd (1 H, H-5; $J_{5,4} = 10·0$, $J_{5,6} = 4·7$ and 2·8), 4·51 dd (1 H, H-2; $J_{2,1} = 4·2$, $J_{2,3} = 9·8$), 5·12 t (1 H, H-4; $J_{4,3} = 9·2$, $J_{4,5} = 10·0$), 5·47 t (1 H, H-3; $J_{3·2} = 9·8$, $J_{3,4} = 9·2$), 6·45 d (1 H, H-1; $J_{1,2} = 4·2$), 7·38 d (2 H, arom. ring), 7·60 d (2 H, arom. ring).

The mother liquor was concentrated to give 0·65 g of a syrup which was separated by column chromatography on silica gel (16g), using benzene–ether (9 : 1) for elution. Thus further 0·11 g (8%) of dibromo derivative *XIV* and 0·28 g (21%) of monobromo derivative *XIII* were obtained.

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