PREPARATION OF BRANCHED-CHAIN HEXOSES BY REACTION OF 1,6-ANHYDRO-2,4-DI-O-p-TOLUENESULFONYL--β-D-HEXOPYRANOS-3-ULOSES WITH GRIGNARD REAGENTS*

M. Černý[a], M. Kollmann[a], J. Pacák[a] and M. Buděšínský[b]

[a] *Department of Organic Chemistry, Charles University, 128 40 Prague 2,*
[b] *Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, 166 10 Prague 6*

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Reaction of 1,6-anhydro-2,3-di-O-*p*-toluenesulfonyl-β-D-*ribo*-hexopyranos-3-ulose (*I*) and the corresponding D-*lyxo*-derivative *II* with methylmagnesium iodide gives 2,4-di-O-tosyl derivatives of 3-C-methylated hexoses *IV* and *V* which on detosylation with sodium amalgam and acetylation afforded 2,4-di-O-acetyl derivatives *X* and *XI*. On deacetylation they gave 1,6-anhydro--3-C-methyl-β-D-allopyranose (*XII*) and 1,6-anhydro-3-C-methyl-β-D-talopyranose (*XIII*) that were converted to isopropylidene derivatives *XVI* and *XVII*, or, by acid hydrolysis, to 3-C-methylhexoses *XIV* and *XV*. The steric course of the Grignard reagent addition to the carbonyl group of anhydrides *I*—*III* and the effect of the 3-C-methyl group in 1,6-anhydrohexoses on their behaviour in acid medium and on complex formation with boric acid or manganese ions in alkaline medium are also discussed. The structures of diacetyl derivatives *X* and *XI* and of isopropylidene derivatives *XVI* and *XVII* were confirmed by PMR spectra.

The interest in branched-chain sugars was elicited by their occurrence in nature, primarily in micro-organisms and higher plants[1]. There is only scant information in literature[1] on their biological properties, but as far as they are nucleoside components they might possess cyto- or virostatic effects[2,3]. They also could be interesting as models for the study of glycolytic enzymes.

In this paper we describe the synthesis of methyl- or phenyl-3-C-substituted 1,6-anhydro-β-D-hexopyranoses or corresponding hexoses, in which we make use of the reaction of Grignard reagents[4–6] with 1,6-anhydro-2,4-di-O-*p*-toluenesulfonyl--β-D-hexopyranos-3-uloses. Free 3-C-methyl aldohexoses have not yet been listed in literature, but their substituted derivatives were described recently, as for example, 1,2 : 5,6-di-O-isopropylidene-3-C-methyl-α-D-allofuranose[7] (and an analogous dicyclohexylidene derivative[8]). In antibiotics 3-C-methyl derivatives of 6-deoxy- and 2,6-dideoxyhexoses and their methyl ethers were found, such as L-mycarose[9], L-olivomycose[10], D-evermicose[11], L-cladinose[12], L-nogalose[13], L-arcanose[14] and L-vinelose[15].

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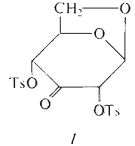
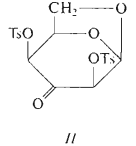
The starting 1,6-anhydro-2,4-di-O-*p*-toluenesulfonyl-β-D-*ribo*-hexopyranos-3--ulose (*I*) was prepared from 1,6-anhydro-2,4-di-O-*p*-toluenesulfonyl-β-D-glucopyranose on oxidation with chromium trioxide in acetic acid[16], and it was then converted by total or partial isomerisation with pyridine to D-*lyxo*- (*II*) and D-*arabino*--ketone (*III*). The reaction of keto derivatives *I*–*III* with methylmagnesium iodide took place best when the chloroform solution of ketone was addded to excess Grignard reagent in ether. Keto derivatives *I* and *II* afforded single products, 1,6-anhydro--3-C-methyl-2,4-di-O-*p*-toluenesulfonyl-β-D-allopyranose (*IV*) in the first case and in the second case 1,6-anhydro-3-C-methyl-2,4-di-O-*p*-toluenesulfonyl-β-D-talopyranose (*V*). From keto derivative *III* a mixture of approximately equal amounts of 3-C-methyl derivatives of D-*altro*- and D-*manno*-configuration, *VI* and *VII*, was formed. Ketones *I* and *II* also react with phenylmagnesium bromide (as with methylmagnesium iodide), probably under formation of ditosyl derivatives for which we propose the structures *VIII* and *IX*. So far we did not confirm the structures of these compounds and did not further study their properties.

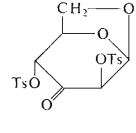
Tosyl derivatives *IV* and *V* were converted to 2,4-di-O-acetyl-1,6-anhydro-3-C--methyl-β-D-*allo*- (*X*) or D-*talo*-hexopyranose (*XI*) on reaction with sodium amalgam in ethanol and subsequent acetylation with acetic anhydride and sodium acetate. The tertiary hydroxyl group of these diacetates is unreactive and thus, even when reacted with acetic anhydride and sodium acetate under reflux, or acetyl chloride and pyridine at elevated temperature, triacetyl derivatives were not formed in a pre-preparative scale, but decomposition of the reaction mixtures already took place.



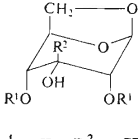
I

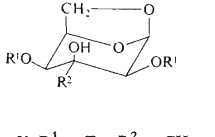


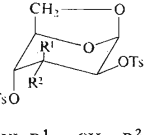
II



III







IV, $R^1 = Ts$, $R^2 = CH_3$ *V*, $R^1 = Ts$, $R^2 = CH_3$ *VI*, $R^1 = CH_3$, $R^2 = OH$
VIII, $R^1 = Ts$, $R^2 = Ph$ *IX*, $R^1 = Ts$, $R^2 = Ph$ *VII*, $R^1 = OH$, $R^2 = CH_3$
X, $R^1 = Ac$, $R^2 = CH_3$ *XI*, $R^1 = Ac$, $R^2 = CH_3$
XII, $R^1 = H$, $R^2 = CH_3$ *XIII*, $R^1 = H$, $R^2 = CH_3$

$Ts = p\text{-}CH_3C_6H_4SO_2$ $Ac = CH_3CO$ $Ph = C_6H_5$

Transesterification of diacetyl derivatives *X* and *XI* with methanol gave 1,6-anhydro--3-C-methyl-β-D-allopyranose (*XII*) and 1,6-anhydro-3-C-methyl-β-D-talopyranose (*XIII*), the first of which sublimates at reduced pressure. Acid hydrolysis of anhydrides *XII* and *XIII* with Amberlite IR 120 gave equilibrium mixtures of the starting compounds and 3-C-methyl-D-allose (*XIV*) or 3-C-methyl-D-talose (*XV*) which were analysed quantitatively by gas chromatography.

We endeavoured to determine the configuration of anhydrides *XII* and *XIII* by measuring the conductivity of their aqueous solutions eventually containing boric acid (Table I), but no conclusive results were obtained. Anhydro derivative of D-*allo* configuration, *XII*, displayed – as expected – appreciably increased conductivity in boric acid solution, in contrast to aqueous solution. However, D-*talo*--isomer *XIII* formed under the same conditions a relatively weakly conducting complex; this did not exclude convincingly the possibility that in reality it could be 1,6--anhydro-3-C-methyl-β-D-idopyranose. Therefore we consider their reaction with acetone in which 1,6-anhydro-3,4-O-isopropylidene-3-C-methyl-β-D-allopyranose (*XVI*) and 1,6-anhydro-2,3-O-isopropylidene-3-C-methyl-β-D-talopyranose (*XVII*) were formed a more reliable proof of the structure of both anhydrides *XII* and *XIII*. From the presence of an O-isopropylidene group in the molecule it follows that at least two vicinal hydroxyl groups have *cis*-configuration. As in reductive detosylations no change in the configuration of liberated hydroxyl groups normally takes place, the configuration of the tertiary hydroxyl group on $C_{(3)}$ in anhydrides *XVI* and *XVII* is also proved. The position of the O-isopropylidene group in compounds *XVI* and *XVII* was demonstrated by PMR spectra (Table II). The methyl group signals at 1·42 and 1·54 p.p.m. in the spectrum of compound *XVI*, and at 1·49 and 1·59 p.p.m. in the spectrum of compound *XVII* prove the presence of the O-isopropylidene group in both derivatives. The hydroxyl proton of compound *XVI* gives a doublet at 2·90 p.p.m. Double resonance experiments and deuteration with CD_3. .COOD demonstrated unambiguously that the observed splitting by 3·0 Hz is the result of the interaction of the hydroxyl proton with the $C_{(2)}$-hydrogen (broad triplet at 3·24 p.p.m.). Hence, the substance must possess the structure of 3,4-O-isopropylidene derivative *XVI*. The hydroxyl proton of the isopropylidene derivative *XVII* also gives in the spectrum a sharp doublet at 2·81 p.p.m. the splitting of which (9·6 Hz) is, however, the consequence of the coupling with the $C_{(4)}$-hydrogen (demonstrated by double resonance and deuteriation experiments) to which a broadened quartet at 3·82 p.p.m. belongs. Hence the substance possesses the structure of 2,3--O-isopropylidene derivative *XVII*. The fact that the hydroxyl protons of both derivatives, *XVI* and *XVII*, give sharp doublets in deuteriochloroform, indicates that the exchange of hydroxyl groups protons is distinctly suppressed by hydrogen bonding. From models it follows that in both cases the hydrogen bond may be formed only by intereraction with free electron pairs of the acetal oxygen at $C_{(3)}$. The values of the observed $^3J_{CH,OH}$ values (3·0 Hz and 9·6 Hz for *XVI* and *XVII*, resp.) are in

agreement with the torsion angles of the interacting hydrogens in corresponding intramolecularly H-bonded conformations.

Those results are in agreement with the rules of optical rotation of 1,6-anhydro-β-D-hexopyranoses and their isopropylidene derivatives according to which the formation of a dioxolane ring in the endo position, comprising $C_{(2)}$ and $C_{(3)}$ atoms (for example in D-*talo* configuration), is linked with a shift of $[\alpha]_D$ to positive values, and in a dioxolane ring with $C_{(3)}$ and $C_{(4)}$ atoms involved, to negative values in relation to unsubstituted 1,6-anhydro-β-D-hexopyranose. In contrast to this, the formation of *exo*-cyclic dioxolane ring (for example in D-*allo* configuration) containing $C_{(2)}$ and $C_{(3)}$ atoms causes a shift of $[\alpha]_D$ in the negative direction, while in the case of a dioxolane ring with $C_{(3)}$ and $C_{(4)}$ atoms it is in the positive direction[17]. The reaction of anhydride *XII* and *XIII* with acetone took place with a higher regioselectivity than in the case of 1,6-anhydro-β-D-allopyranose[18] and 1,6-anhydro-β-D-talopyranose[19]. D-*allo*-Configuration of anhydride *XII* was also checked by the fact that its ditosyl derivative *IV* did not react with sodium methoxide (under conditions when 1,6-anhydro-2,4-di-O-*p*-toluenesulfonyl-β-D-glucopyranose afforded 1,6 : 3,4-dianhydro-2-O-*p*-toluenesulfonyl-β-D-galactopyranose[20]), while the second possible isomer, *i.e.* 1,6-anhydro-3-C-methyl-2,4-di-O-*p*-toluenesulfonyl-β-D-glucopyranose, should have reacted.

The structure of diacetyl derivatives *X* and *XI* was proved by PMR spectroscopy (Table II). As already said above the configuration of the $C_{(3)}$-methyl in both substances was determined by the preparation of isopropylidene derivatives *XVI* and *XVII*. For a direct proof of the methyl group configuration in *X* and *XI* by PMR spectra we tried to make use of the nuclear Overhauser effect (NOE). From the model

TABLE I

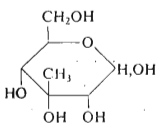
Electric Conductivity $\varkappa$ of Aqueous Solutions of 1,6-Anhydro-β-D-hexopyranoses and Their Complexes with Boric Acid

1,6-Anhydro-β-D--hexopyranose (0·5M)	$\varkappa_1$[a] (H_2O)	$\varkappa_2$[a] (in 0·5M H_3BO_3)	Δ[b] $\varkappa_2 - \varkappa_1$
3-C-methyl-*allo XII*	50	4 000	+3 900
allo-	20	100	+ 40
3-C-methyl-*talo XIII*	56	220	+ 120
talo-	35	420	+ 340
gluco-	15	36	− 19

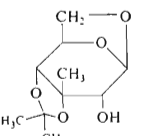
[a] The measurement was carried out in a non-temperated microcell at room temperature (about 23−25°C). $\varkappa$-Values are given in S . 10^{-6} units; [b] difference in conductivities is corrected to the conductivity of 0·5M-H_3BO_3.

it follows that the $C_{(3)}$-methyl group and the $C_{(6)}$-*endo*-hydrogen should be close enough in substance *X* for the observation of a NOE enhancement at the $C_{(6)}$-*endo*--hydrogen on methyl group irradiation; in substance *XI* the effect should not be observed. NOE experiments in various solvents and concentrations gave, however, negative results with both substances. In the case of compound *X* this could be explained by the change of the $^1C_4$ chair conformation of the pyranose ring in the boat conformation $B_{3,0}$, caused by steric interactions of the methyl group on $C_{(3)}$ and the methylene group of the 1,6-anhydro ring, or also by the interactions of 1,3-diaxial acetoxy groups. However, an analysis of models indicates that in the $B_{3,0}$ conformation the coupling constants $J_{1,2}$ and $J_{4,5}$ should be practically non-existent which is in contradiction with the observed values, $J_{1,2}$ = 1,8 Hz and $J_{4,5}$ = 1·8 Hz (ref.[21]). The pyranose ring of diacetyl derivative *X* evidently assumes a not too distorted $^1C_4$ conformation and the reason for the absence of a NOE between the $C_{(3)}$--methyl group and the $C_{(6)}$-*endo* hydrogen consists probably in a little effective relaxation mechanism in consequence of the competition of close anisotropic oxygen atoms.

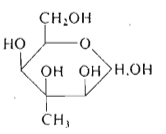
The reaction of tosyl ketone *I* and *II* with methylmagnesium iodide takes place highly selectively and, as expected, similarly as during their reduction with sodium borohydride[16]. The methyl anion approaches to the carbonyl group of compounds *I* and *II* from the sterically less hindered side. In compound *I* the steric hindrance of the carbonyl group due to the 1,6-anhydro bridge has no decisive effect. The latter is produced by the axial *p*-toluenesulfonyloxy groups which hinder the access to the



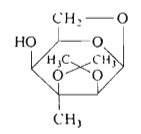
XIV



XVI



XV



XVII

TABLE II

Characteristic Parameters of the PMR Spectra of Acetylated and Isopropylidene Derivatives of 1,6-Anhydro-3-C-methyl-β-D-hexopyranoses

Compound[a]	H-1	H-2	H-4	H-5
X	5·48 $J_{1,2} = 1{\cdot}8$ $J_{1,4} \neq 0 < 0{\cdot}5$ $J_{1,6'} \neq 0 < 0{\cdot}5$	4·56 $J_{2,1} = 1{\cdot}8$ $J_{2,4} = 0{\cdot}7$	4·67 $J_{4,5} = 1{\cdot}8$ $J_{4,2} = 0{\cdot}7$ $J_{4,1} \neq 0 < 0{\cdot}5$	4·60 $J_{5,4} = 1{\cdot}8$ $J_{5,6} = 0{\cdot}8$ $J_{5,6'} = 5{\cdot}2$
XI	5·43 $J_{1,2} = 1{\cdot}7$ $J_{1,5} \neq 0 < 0{\cdot}3$ $J_{1,6} \neq 0 < 0{\cdot}3$ $J_{1,6'} \neq 0 < 0{\cdot}3$	4·72 $J_{2,1} = 1{\cdot}7$	4·94 $J_{4,5} = 4{\cdot}1$ $J_{4,6'} = 1{\cdot}0$	4·50 $J_{5,4} = 4{\cdot}1$ $J_{5,6} = 0{\cdot}5$ $J_{5,6'} = 5{\cdot}1$
XVI	5·50 $J_{1,2} = 1{\cdot}8$	3·24 $J_{2,1} = 1{\cdot}8$ $J_{2,OH} = 3{\cdot}0$ $J_{2,4} = 0{\cdot}6$ $J_{2,5} \neq 0 < 0{\cdot}4$	≈3·75	4·71 $J_{5,4} = 1{\cdot}4$ $J_{5,6} = 1{\cdot}4$ $J_{5,6'} = 4{\cdot}6$
XVII	5·29 $J_{1,2} = 3{\cdot}2$ $J_{1,5} \neq 0 < 0{\cdot}3$ $J_{1,6} \neq 0 < 0{\cdot}2$ $J_{1,6'} \neq 0 < 0{\cdot}3$	3·92 $J_{2,1} = 3{\cdot}2$	3·82 $J_{4,5} = 5{\cdot}4$ $J_{4,OH} = 9{\cdot}6$ $J_{4,6} \neq 0 < 0{\cdot}3$ $J_{4,6'} \neq 0 < 0{\cdot}3$	4·38 $J_{5,4} = 5{\cdot}4$ $J_{5,6} = 1{\cdot}0$ $J_{5,6'} = 5{\cdot}8$

carbonyl group from the equatorial (*exo*) side. This is in agreement with literature[22] and also with the behaviour of the tosyl ketone *III* in which the simultaneous occurrence of one axial and the other equatorial *p*-toluenesulfonyloxy group is the cause of the double course of the reaction, giving rise to epimers *VI* and *VII*.

All aldohexoses form equilibrium mixtures with their 1,6-anhydro derivatives in acid medium. Their composition depends mainly on the energy differences of hexoses in conformations $^1C_4$ and $^4C_1$, while the conformation of the hydroxyl group on carbon $C_{(3)}$ plays a predominant role: If it is in 1,6-anhydrohexose axial, steric interactions with the 1,6-anhydro bridge occur which decrease the stability of the 1,6-anhydrohexose[23,24]. From the experimentally determined difference between conformation energies of the methyl and the hydroxyl group in position 1,1 on the cyclohexane ring ($-\Delta G^0_{343K} \approx 0{\cdot}24$ kcal mol^{-1}) it follows that the methyl group prefers the equatorial and the hydroxyl group the axial position[25,26]. Therefore,

TABLE II
(*Continued*)

H-6 (*endo*)	H-6′ (*exo*)	—OH	—OAc	$C_{(3)}$–CH_3	$C(CH_3)_2$
3·93 $J_{6,5} = 0·8$ $J_{6,6'} = 8·3$	3·71 $J_{6',6} = 8·3$ $J_{6',1} \neq 0 < 0·5$ $J_{6',5} = 5·2$	2·79	2·14 2·16	1·49	—
4·55 $J_{6,5} = 0·5$ $J_{6,6'} = 7·4$ $J_{6,1} \neq 0 < 0·3$	3·69 $J_{6',6} = 7·4$ $J_{6',5} = 5·1$ $J_{6',4} = 1·0$ $J_{6',1} \neq 0 < 0·3$	2·79	2·15	1·15	—
≈3·75	≈3·75	2·90 $J_{OH,2} = 3·0$	—	1·44	1·42 1·54 $J_{CH_3,CH_3} = 0·6$
4·13 $J_{6,5} = 1·0$ $J_{6,6'} = 7·4$ $J_{6,1} \neq 0 < 0·2$ $J_{6,4} \neq 0 < 0·3$	3·63 $J_{6',6} = 7·4$ $J_{6',5} = 5·8$ $J_{6',4} \neq 0 < 0·3$ $J_{6',1} \neq 0 < 0·3$	2·81 $J_{OH,4} = 9·6$	—	1·53	1·49 1·59 $J_{CH_3,CH_3} = 0·7$

[a] The spectra were measured on a Varian HA-100 instrument at 100 MHz frequency, in deuteriochloroform with tetramethylsilane as internal reference. Chemical shifts are given in p.p.m. (δ-scale), coupling constants J in Hz. The assignment of signals and the proofs of the interaction mentioned were carried out by double resonance experiments.

the axial methyl group on $C_{(3)}$ manifests itself in 1,6-anhydroaldohexopyranoses by larger destabilisation effects than the axial hydroxyl group. In consequence of this, the equilibrium hexose–1,6-anhydrohexose is in 3-C-methyl-D-allose (*XIV*) shifted completely to free hexose (only traces of anhydro derivative *XII* were determined) in contrast to D-allose (14% of 1,6-anhydro derivative[24]); in the case of 3-C-methyl-D-talose (*XV*) the equilibrium mixture contains approximately 30% of anhydro derivative *XIII*, *i.e.* much more than in D-talose (2·8% of anhydride[24]).

When carrying out conductivity measurements (Table I) we observed that 1,6-anhydro-β-D-allopyranose, which we considered as a suitable model for conductivity

studies of the 1,2,3-triol system, formed in boric acid solution only a weakly conductive complex in comparison with its 3-C-methyl derivative *XII* which under the same conditions displayed an appreciable increase of conductivity in comparison with an aqueous solution. In comparison with this, 1,6-anhydro-β-D-talopyranose and its 3-C-methyl derivative *XIII* behaved in a similar manner, but gave with boric acid only weakly conductive complexes. According to expectation, 1,6-anhydro-β-D-glucopyranose did not give a conductive complex with boric acid, which is in agreement with literature[27–29] according to which vicinal diols form conductive complexes only if geometrical conditions for the formation of the five-membered boradioxolane ring are fulfilled. The difference in behaviour of 1,6-anhydro-β-D-allopyranose and their 3-C-methyl derivative *XII* is probably due to the fact that 3-C-methyl group is deviated from the 1,6-anhydro bridge under the effect of steric interactions. This slightly changes the relative position of the hydroxyl groups in anhydro derivative *XII* and even this small change in geometry increases appreciably the stability of the complex with boric acid. In support of this view it may be stated that both mentioned anhydro derivatives also differ distinctly in the stability of complexes with Mn^{2+}, Mn^{3+} and Mn^{4+} in alkaline medium, as shown by the polarisation curves[30].

The measured values of optical rotation of anhydride *XII* in aqueous solution ($[\alpha]_D$ −73·5°, $[M]_D$ −129°) and anhydride *XIII* ($[\alpha]_D$ −72°, $[M]_D$ −127°) when compared with the corresponding values for 1,6-anhydro-β-D-allopyranose[31] ($[\alpha]_D$ −75·8°, $[M]_D$ −123°) and for 1,6-anhydro-β-D-talopyranose[16,32] ($[\alpha]_D$ −82°, $[M]_D$ −132°) are in agreement with the supposition[33] that the substituents on atom $C_{(3)}$ of 1,6-anhydroaldohexopyranoses affect the optical rotation of the system only very little unless its pseudosymmetry according to the plane passing through the $C_{(3)}$ carbon, $O_{(5)}$ oxygen of the pyranoid ring, and the center of the $C_{(6)}$—$O_{(6)}$ bond is disturbed.

EXPERIMENTAL

The melting points were determined on a micromelting point apparatus Boëtius. Optical rotation was measured at 25°C on an automatic polarimeter Bendix Ericsson, type 143 A. The infrared spectra were measured in chloroform on an instrument from the Development Department, Tesla, Brno, and the PMR spectra in deuteriochloroform on a Varian HA-100 instrument. For gas chromatography of trimethylsilyl derivatives a Chrom 3 apparatus was used, column dimensions 182 cm × 0·5 cm with Chromosorb W—AW HMDS, impregnated with 4% of OV-101 phase, column temperature 171°C (T_i 210°C), carrier gas flow 40 ml N_2/min. Conductivity measurements were carried out with a Radiometer CDM 3 conductometer. Reaction course and purity of the products were followed chromatographically on silica gel thin layers, 20—40 mesh particle size (Lachema), containing 7% of gypsum. Solvent systems: S_1 benzene–acetone 9 : 1, S_2 benzene–acetone–methanol 90 : 10 : 3 S_3 chloroform–2-propanol–conc. ammonia–water 10 : 10 : 1 : 1, detection was carried out with 5% sulfuric acid and heat (charring). The solvents were evaporated under reduced pressure at 20—50°C; samples for analysis were dried over phosphorus pentoxide at 20—80°C and 0·01 Torr.

1,6-Anhydro-2,4-di-O-*p*-toluenesulfonyl-β-D-glucopyranose

p-Toluenesulfonyl chloride (250 g) was added in portions to a solution of 100 g of 1,6-anhydro-β-D-glucopyranose in 300 ml of acetone and 300 ml of pyridine, under vigorous stirring at 20 to 25°C. The mixture was allowed to stand at room temperature for 96 hours, diluted with 3 l of water, and the separated product was filtered off after several hours' standing, and washed with a small amount of water[20]. The crude product (300 g) was dissolved in 2 l of hot ethanol and the solution was refluxed for 15 minutes with 30 g of charcoal. After filtration the solution was concentrated and the remaining syrup dissolved in 800 ml of benzene. A part (250 ml) of the benzene was distilled off and 30 ml of pyridine were added to the remaining solution and the mixture was allowed to stand in a refrigerator for crystallisation. After filtration under suction and washing with a small amount of cold ethanol 150 g of ditosyl derivative were obtained (containing 8% of crystal pyridine). The mother liquor was concentrated and used for the preparation of 1,6 : 3,4-dianhydro-2-O-*p*-toluenesulfonyl-β-D-galactopyranose[20].

1,6-Anhydro-3-C-methyl-2,4-di-O-*p*-toluenesulfonyl-β-D-allopyranose (*IV*)

A solution of 7 g of ditosyl ketone[16] *I* in 70 ml of chloroform was added slowly under stirring and cooling with ice to a solution of methylmagnesium iodide prepared from 12 ml of methyl iodide and 6 g of magnesium in 140 ml of diethyl ether. The mixture was then stirred for 1 hour under cooling and 2 hours at room temperature (control by thin layer chromatography in S_1). After pouring the mixture into 200 ml of 10% hydrochloric acid the organic solution was separated, decolorised with sodium thiosulfate solution and, after drying over calcium chloride, filtered through a small column of charcoal. After concentration the residue was crystallised from ethanol; yield 4·9 g (69%), m.p. 136–137°C, $[\alpha]_D$ −41° (*c* 0·49; chloroform). IR spectrum: ν(OH) 3599 cm^{-1}, ν(C=O) absent. For $C_{21}H_{24}O_9S_2$ (484·5) calculated: 52·08% C, 4·98% H, 13·22% S; found: 52·24% C, 5·25% H, 13·34% S.

1,6-Anhydro-3-C-methyl-2,4-di-O-*p*-toluenesulfonyl-β-D-talopyranose (*V*)

This compound was prepared from 7 g of ditosyl ketone[16] *II* and methylmagnesium iodide in the same manner as in the case of ditosyl derivative *IV*. Yield 5·7 g (81%), m.p. 171°C, $[\alpha]_D$ −33° (*c* 0·43; chloroform). IR spectrum: ν(OH) 3577 cm^{-1}. For $C_{21}H_{24}O_9S_2$ (484·5) calculated: 52·08% C, 4·98% H, 13·22% S; found: 52·35% C, 5·04% H, 13·10% S.

1,6-Anhydro-3-C-methyl-2,4-di-O-*p*-toluenesulfonyl-β-D-altropyranose (*VI*)
and 1,6-Anhydro-3-C-methyl-2,4-di-O-*p*-toluenesulfonyl-β-D-mannopyranose (*VII*)

Reaction of 7 g of ditosyl ketone[16] *III* with methylmagnesium iodide, carried out as in the case of the preparation of ditosyl derivative *IV*, gave after crystallisation from ethanol a mixture of ditosyl esters *VI* and *VII* of m.p. 77–86°C, which according to thin-layer chromatography in S_1 contained approximately the equal amount of both components. Yield 4·5 g (62%), IR spectrum: ν(OH) 3575 cm^{-1}, ν(C=O) absent. For $C_{21}H_{24}O_9S_2$ (484·5) calculated: 52·08% C, 4·98% H, 13·22% S; found: 51·85% C, 5·22% H, 13·27% S.

1,6-Anhydro-3-C-phenyl-2,4-di-O-*p*-toluenesulfonyl-β-D-allopyranose (*VIII*)

A solution of 5 g of ditosyl ketone[16] *I* in 50 ml of chloroform was added dropwise and under cooling with ice to a solution of phenylmagnesium bromide prepared from 8 ml of bromobenzene and 6 g of magnesium in 100 ml of diethyl ether. The mixture was stirred at room temperature

until the reaction was over (approximately 4 hours, control by thin layer chromatography in S_1), then poured into 200 ml of 10% hydrochloric acid, stirred and the solid product was stored. From the filtrate the organic layer was separated, washed several times with water, dried over calcium chloride, filtered through a column of charcoal, and evaporated. The residue was combined with the previously obtained product and crystallised from ethanol. Yield 4·6 g (66%), m.p. 227°C, with decomposition, $[\alpha]_D$ −32·5° (*c* 0·51; chloroform). For $C_{26}H_{26}O_9S_2$ (546·6) calculated: 57·10% C, 4·80% H; found: 57·30% C, 4·82% H.

1,6-Anhydro-3-C-phenyl-2,4-di-O-*p*-toluenesulfonyl-β-D-talopyranose (*IX*)

This compound was prepared from 5 g of ditosyl ketone[16] *II* and phenylmagnesium bromide by the same procedure as in the case of phenyl derivative *VIII*. Yield 4·7 g (69%), m.p. 245°C, $[\alpha]_D$ −42·5° (*c* 0·49; chloroform). For $C_{26}H_{26}O_9S_2$ (546·6) calculated: 57·10% C, 4·80% H; found: 56·96% C, 4·92% H.

2,4-Di-O-acetyl-1,6-anhydro-3-C-methyl-β-D-allopyranose (*X*)

Ditosyl ester *IV* (7 g) was added in portions to a stirred mixture of sodium amalgam (prepared from 6 g of sodium and 70 g of mercury) and 150 ml of 90% ethanol. The reaction course was followed by thin-layer chromatography in S_1. The temperature rose to about 50°C during the reaction which was over after 50—60 minutes, when a sample of the reaction mixture became completely soluble in water. Mercury was then separated and the reaction mixture neutralised with acetic acid and evaporated. The residue was dissolved in approximately 80 ml of water and the solution extracted several times with a saturated solution of chlorine in chloroform. The aqueous solution was acidified with hydrochloric acid to pH 4—4·5 and evaporated, and the remaining water was eliminated by azeotropic distillation with benzene. The residue was acetylated with 20 ml of acetic anhydride and 3 g anhydrous sodium acetate by 3 hour's heating on a boiling water bath. The reaction course was followed chromatographically on thin layers in system S_2. The reaction mixture was cooled, additioned with 100 ml of water, and extracted several times with chloroform. The combined chloroform extracts were washed with sodium hydrogen carbonate and water, and were dried over calcium chloride. After evaporation of the chloroform the residue was crystallised from a mixture of ether and light petroleum. Yield 2·9 g (78%), m.p. 155°C (sinters about 110°C), $[\alpha]_D$ −65° (*c* 0·99; chloroform). IR spectrum: ν(C=O) 1745 cm^{-1}, ν(OH) 3595 cm^{-1}. For $C_{11}H_{16}O_7$ (260·2) calculated: 50·75% C, 6·19% H; found: 50·76% C, 6·30% H.

2,4-Di-O-acetyl-1,6-anhydro-3-C-methyl-β-D-talopyranose (*XI*)

This compound was prepared from 7 g ditosyl ester *V* using the same procedure as for the preparation of compound *X*. Yield 3 g (80%), m.p. 144°C (sinters about 100°C), $[\alpha]_D$ −68° (*c* 1·0; chloroform). IR spectrum: ν(C=O) 1755 cm^{-1}, ν(OH) 3590 cm^{-1}. For $C_{11}H_{16}O_7$ (260·2) calculated: 50·75% C, 6·19% H; found: 50·97% C, 6·26% H.

1,6-Anhydro-3-C-methyl-β-D-allopyranose (*XII*)

Diacetate *X* (3 g) was dissolved in 20 ml of methanol and deacetylated with sodium methoxide according to Zemplén. After 60 minutes reaction, the course of which was followed by thin-layer chromatography in S_2, the solution was neutralised with acetic acid and evaporated. The residue was dissolved in 50 ml of water, the solution was deionised with Dowex 50 W and filtered through

a layer of charcoal. The filtrate was evaporated and the residue sublimed at 100°C and 0·01 Torr. The yield was 1·5 g (73%), m.p. 190°C (unsharp, the substance sublimates distinctly above 100°C), $[\alpha]_D$ −73·5° (*c* 0·97; water). For $C_7H_{12}O_5$ (176·1) calculated: 47·70% C, 6·86% H; found: 47·77% C, 6·64% H.

1,6-Anhydro-3-C-methyl-β-D-talopyranose (*XIII*)

Deacetylation of 3 g of diacetate *XI* was carried out in the same manner as with anhydro derivative *XII*. The crude product, obtained by neutralisation of the reaction mixture and evaporation, was dissolved in 50 ml of boiling acetone. After cooling, the solution was filtered and evaporated again. The residue was dissolved in 20 ml of water, and the solution deionised using Dowex 50W and evaporated. The residue was dissolved in 30 ml of boiling acetone, light petroleum was added until incipient turbidity and the solution was allowed to stand for crystallisation in a refrigerator. After filtration the mother liquors were diluted with additional light petroleum for further crystallisation. Total yield 1·6 g (76%) of a substance with m.p. 49—50°C $[\alpha]_D$ −71·5 (*c* 0·7; water). For $C_7H_{12}O_5$ (176·1) calculated: 47·70% C, 6·86% H; found: 47·90% C, 6·80% H.

3-C-Methyl-D-allose (*XIV*)

A solution of 200 mg of anhydro derivative *XII* in 5 ml of water was heated with 1 g of Amberlite IR-120 in a sealed tube on a water bath. After 4 hours, when the hydrolysis was over (as indicated by thin-layer chromatography in S_3), the solution was filtered, the cation exchanger washed with water and the combined solutions concentrated to a syrup. The yield was quantitative. The syrup crystallised out partly, but it was not analytically pure. Chromatography on paper Whatman No 1 in 1-butanol–pyridine–water (6 : 4 : 3) (descending arrangement, detection with Bonner reagent[34]) demonstrated a spot of the reducing sugar *XIV* of R_F 0·45 in the reaction product in addition to traces of other substances. As standards anhydro derivative *XII* of R_F 0·59 and D-glucose, R_F 0·32, were employed. Optical rotation of the product was determined by dissolving 14·90 mg of anhydro derivative *XII* in 1·2 ml of 0·1N-H_2SO_4 and heating in a sealed tube at 100°C for 4 hours: $[\alpha]_D$ +17° (*c* 1·35). Further heating did not change the optical rotation value. A small sample of the syrup was converted according to Sweeley[35] to trimethylsilyl derivative. Its pyridine solution was concentrated at 40°C/1 Torr and the residue dissolved in chloroform and injected into a gas chromatography column: the silyl derivative of hexose *XIV* was identified, while the silyl derivative of anhydride *XII* was present only in traces.

3-C-Methyl-D-talose (*XV*)

Anhydro derivative *XIII* (200 mg) was hydrolysed and worked up in the same manner as in the preparation of methylallose *XIV*. The yield was practically quantitative, but the syrup would not crystallise even after prolonged standing. By chromatography on paper Whatman No 1 in 1-butanol–pyridine–water (6 : 4 : 3) the starting anhydro derivative *XIII*, R_F 0·67, was detected in the mixture in addition to the reducing methyltalose *XV*, R_F 0·50. Gas chromatography indicated 30% of the starting anhydro derivative *XIII* in the reaction mixture.

1,6-Anhydro-3,4-O-isopropylidene-3-C-methyl-β-D-allopyranose (*XVI*)

Anhydrous copper-II sulfate (0·5 g) and 250 mg of anhydro derivative *XII* were added to 20 ml of acetone containing two drops of concentrated sulfuric acid and the mixture was shaken

at room temperature. The reaction course was followed chromatographically on a thin-layer plate, using S_1 for development. When the reaction was complete (approximately after 8 hours) the mixture was filtered, the residue on the filter washed with a small amount of acetone and the combined filtrates were neutralised with a 5% aqueous sodium hydroxide solution. The solution was then filtered, acetone distilled off, and the residue crystallised from an ether–light petroleum mixture after standing in a refrigerator. Yield 260 mg (85%), m.p. 105–106°C, $[\alpha]_D$ −61° (*c* 0·7; chloroform). For $C_{10}H_{16}O_5$ (216·2) calculated: 56·25% C, 7·45% H; found: 56·07% C, 7·45% H.

1,6-Anhydro-2,3-O-isopropylidene-3-C-methyl-β-D-talopyranose (*XVII*)

This compound was prepared from 250 mg of anhydro derivative *XIII* using the same procedure as in the preparation of isopropylidene derivative *XVI*. In order to complete the reaction the reaction time had to be prolonged to 34 hours. Yield 230 mg (75%), m.p. 81°C, $[\alpha]_D$ −33° (*c* 0·8; chloroform). For $C_{10}H_{16}O_5$ (216·2) calculated: 56·25% C, 7·45% H; found: 56·42% C, 7·41% H.

Electric Conductivity of 1,6-Anhydro-β-D-hexopyranoses and Their Derivatives (Table I)

The measurements were carried out on a Radiometer CDM 3 conductometer according to ref.[27], using redistilled water and an aqueous 0·5M-H_3BO_3 solution. The conductivity of 0·5M aqueous solutions of anhydro derivatives of hexoses was measured first, then a corresponding amount of boric acid was added to the solution in order to obtain a 0·5M solution, and when equilibrium was attained electric conductivity was measured again.

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