PREPARATION AND THE PROPERTIES OF 2,3-, 2,4-, AND 3,4-DIDEOXY DERIVATIVES OF 1,6-ANHYDRO-β-D-*glycero*-HEXOPYRANOSULOSES AND CORRESPONDING ALCOHOLS*

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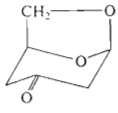
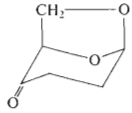
This paper describes the preparation of 1,6-anhydro-dideoxy-β-D-*glycero*-hexopyranosuloses *I*—*III*, their IR, UV, PMR and CD spectra, optical rotation and reduction with sodium borohydride to corresponding 1,6-anhydro-dideoxy-β-D-hexopyranoses. As yet the undescribed 2,4-dideoxy derivatives *X* and *XIII* were prepared from 1,6-anhydro-4-deoxy-2-O-*p*-toluenesulfonyl-β-D-*xylo*-hexopyranose (*IV*). The elimination and the substitution of the tosyloxy group in 1,6-anhydro-2,4-dideoxy-3-O-*p*-toluenesulfonyl-β-D-*threo*-hexopyranose (*XII*) was investigated and compared with the reactivity of other tosyl esters or mesyl esters of this series. In a complete series of dideoxy derivatives of 1,6-anhydro-β-D-hexopyranoses hydrogen bonds and optical rotation were discussed and the $[M]_D$ value of the 1,3-diolic O/O interaction was determined, on the basis of which the absolute configuration of (±) *trans*-1,3-cyclohexanediols was proposed.

During the study of optical rotation of derivatives of 1,6-anhydro-β-D-hexopyranoses we found that 1,6-anhydro-2,4-dideoxy-β-D-*glycero*-hexopyranos-3-ulose (*I*) contrary to expectation has a high negative Cotton effect[1]. Similar "anomalies" were also observed in some of its 2,4-di-*p*-toluenesulfonyloxy, dibenzoyloxy and dibenzyloxy derivatives. We were interested in knowing which properties would have ketones isomeric with the 3-keto derivative *I*, *i.e.* 1,6-anhydro-2,3-dideoxy-β-D-*glycero*-hexopyranos-4-ulose (*II*) and 1,6-anhydro-3,4-dideoxy-β-D-*glycero*-hexopyranos-2-ulose (*III*). In this paper we describe their preparation and IR, UV, CD and PMR



I



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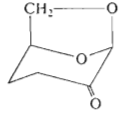
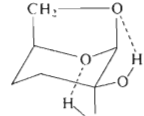


III



IIIa

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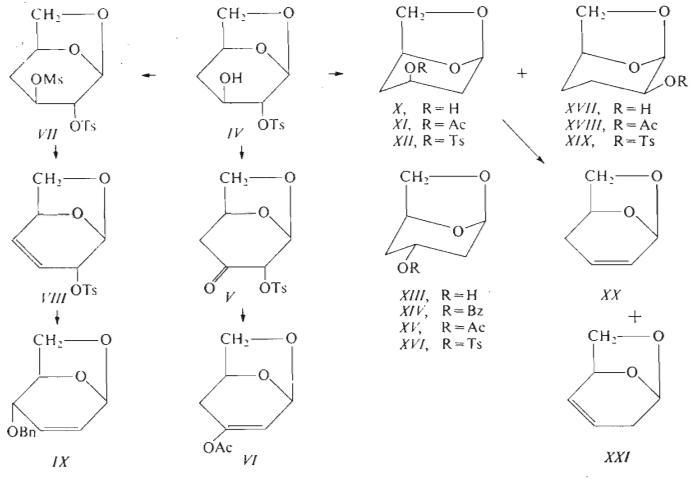
spectra, as well as the products of their reduction with sodium borohydride, *i.e.* six isomeric 1,6-anhydro-dideoxy-β-D-hexopyranoses.

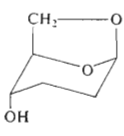
Anhydrohexopyranos-3-ulose *I* prepared according to ref.[1] by reductive detosylation of 1,6-anhydro-2,4-di-O-*p*-toluenesulfonyl-β-D-*ribo*-hexopyranos-3-ulose with Raney nickel in acetone contained according to gas chromatography a small amount of 1,6-anhydro-2,4-dideoxy-β-D-hexopyranoses. It was freed of them by oxidizing them with ruthenium tetroxide in dichloromethane to the original ketone *I*. The attempted preparation of ketone *I* by another route was not very successful: 1,6-anhydro-4-deoxy-2-O-*p*-toluenesulfonyl-β-D-*xylo*-hexopyranose[2] (*IV*) was oxidized with chromium trioxide in acetic acid to α-tosyl ketone *V* (ref.[3]) which was then converted with zinc dust in acetic anhydride to 3-O-acetyl-1,6-anhydro-2,4-dideoxy-β-D-*glycero*--hex-2-enopyranose (*VI*) the acid hydrolysis of which afforded ketone *I*. However, the yield of the enol acetate *VI* is relatively low (30%), and ketone *I* formed by its acid hydrolysis together with other unidentified products can be isolated only with difficulty. The structure of the unstable enol acetate *VI*, 50% of which decomposes, for example, on 24 hours' standing in commercial chloroform, was proved by the IR and PMR spectra. In the IR spectrum a very strong band was present at 1600



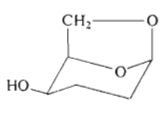
Ts = *p*-$CH_3C_6H_4SO_2$ Bz = C_6H_5CO
Ms = CH_3SO_2 Bn = $C_6H_5CH_2$
Ac = CH_3CO

cm^{-1} due to $\nu_{(C=C)}$ of the enol ester double bond and two equally intensive bands at 1685 and 1750 cm^{-1} corresponding to $\nu_{(C=O)}$. In the PMR spectrum the chemical shift of proton H_2 (7·44 δ) and $J_{1,2}$ (6·1 Hz) confirm the existence of the double bond in position 2, 3, which is also in agreement with the high positive value of $[\alpha]_D$ (*cf.*[4]).

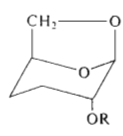
Another oxo compound, 1,6-anhydro-2,3-dideoxy-β-D-*glycero*-hexopyranos-4--ulose (*II*), was prepared by oxidation of 1,6-anhydro-2,3-dideoxy-β-D-*erythro*-hexopyranose (*XXII*) with ruthenium tetroxide[5]. The starting dideoxy derivative *XXII* was prepared by the following sequence of reactions: 1,6-anhydro-2-deoxy-4-O-benzyl-3-O-*p*-toluenesulfonyl-β-D-*arabino*-hexopyranose was converted to 1,6-anhydro--4-O-benzyl-2,3-dideoxy-β-D-*erythro*-hex-2-enopyranose (*IX*) with potassium tert--butoxide and the product was reduced catalytically and simultaneously debenzylated on palladium on charcoal[4]. Benzyl ether *IX* was also prepared from 1,6-anhydro--4-deoxy-3-O-methanesulfonyl-2-O-*p*-toluenesulfonyl-β-D-*xylo*-hexopyranose[4] (*VII*). The latter when treated with potassium tert-butoxide afforded 1,6-anhydro-3,4-dideoxy-2-O-*p*-toluenesulfonyl-β-D-*erythro*-hex-3-enopyranose (*VIII*) the reaction of which with sodium benzyl alcoholate led to benzyl ether *IX* in 56% yield. This means that the substitution of the tosyloxy group took place with allylic rearrangement and suprafacially. The sterical course of this reaction corresponds to the behaviour of substituted 1-cyclohexenyl esters[6–8], but it is not in agreement with the observations made with some hex-2-enopyranosides[9–12]; for example, in the case of ethyl 2,3-dideoxy-4,6-di-O-methanesulfonyl-α-D-*erythro*-hex-2-enopyranoside[11] the substitution of the 4-mesyloxy group by the azide, iodide or benzoate ions takes place with Walden inversion and without an allylic rearrangement. As it was already shown earlier[13,14] allyl halogenides are substituted with a rearrangement (by a S_N2' mechanism) mainly if a direct S_N2 substitution is hindered by sterical or polar effects. On the same basis the differing reactivity of allyl derivatives of hex-2-enopyranoside type[9–12] and of the allyl tosylate *VIII* prepared by us may also be explained. In the latter case the direct substitution (S_N2) of the quasiaxial 2-tosyloxy group is hindered by the 1,6-anhydro bridge, or by the oxygen atoms of the acetal group, similarly as in the described case of the axial 2-tosyloxy group in 1,6-anhydro-β-D-hexopyranoses[15,16]. In agreement with this it was observed that in 1,6-anhydro-3-O-ben-



XXII



XXIII



XXIV, R = H
XXV, R = Ts

zoyl-2,4-di-O-*p*-toluenesulfonyl-β-D-glucopyranose only the 4-tosyloxy group is substituted under the effect of sodium benzoate in dimethylformamide at 130°C, thus giving rise to 1,6-anhydro-3,4-di-O-benzoyl-2-O-*p*-toluenesulfonyl-β-D-galactopyranose[17]. The structure of allyl tosylate *VIII* was confirmed by PMR and IR spectroscopy and also by catalytic reduction on platinum, giving rise to the known 1,6-anhydro-3,4-dideoxy-2-O-*p*-toluenesulfonyl-β-D-*erythro*-hexopyranose (*XXV*). Allyl tosylate *VIII* is a poorly stable compound at room temperature and it decomposes spontaneously. It reacts with various nucleophilic reagents even under mild conditions, as was shown by preliminary experiments.

1,6-Anhydro-3,4-dideoxy-β-D-*glycero*-hexopyranos-2-ulose (*III*) was prepared on oxidation of 1,6-anhydro-3,4-dideoxy-β-D-*erythro*-hexopyranose (*XXIV*) with ruthenium tetroxide[5]. The starting alcohol *XXIV* was obtained by catalytic reduction of 1,6 : 2,3-dianhydro-4-deoxy-β-D-*ribo*-hexopyranose on Raney nickel[18].

In contrast to keto derivatives *I* and *II* the ketone *III* gives in an aqueous or ethanolic solution hydrates or hemiacetals, which was followed by measuring optical rotation changes (in dependence on time) in the given solvents, and also by the measurement of the drop in the intensity of the carbonyl band in the IR region. In 96% ethanol, at 25°C, approximately 50% of the free carbonyl form of ketone *III* is present in the equilibrium mixture. An increased addition ability of the carbonyl group in ketone *III* may be explained by the −I effect of the acetal group $O_{(5)}—C_{(1)}—O_{(6)}$ (*cf.*[19,20]) and by the possibility of the stabilization of the hydrate or the hemiacetal by means of hydrogen bonds[21] to $O_{(5)}$ and $O_{(6)}$ (see *IIIa*). IR and UV spectra of ketones *I*–*III* express the dependence of the frequency of the carbonyl group absorption on its distance from the oxygen atoms of the acetal group and may be

TABLE I

Spectral Properties of 1,6-Anhydro-β-D-hexopyranosuloses

Compound	IR $\nu_{(CO)}$, cm^{-1} [a]		UV λ_{max} nm [b]	CD ($\Delta\varepsilon$), (λ_{max}, nm)[c,d]	
	cyclohexane	CCl_4	cyclohexane	cyclohexane	dioxan
2-ulose *III*	1 755[e]	1 749[f]	308 ($\varepsilon \approx 7$)	−1·358 (314)	−1·125 (313)
3-ulose *I*[g]	1 739	1 732	291 ($\varepsilon \approx 14$)	−0·156 (298)	−0·273 (295)
4-ulose *II*	1 744[e]	1 740[e]	300 ($\varepsilon \approx 17$)	−0·583 (300)	−0·793 (300)

[a] Concentration 4%, cell width 0·1 mm; [b] concentration 10^{-2}M, cell width 4 cm; [c] concentration 10^{-2}M, cell width 0·1 and 0·2 cm; [d] the curves show a clear vibrational structure of the carbonyl group in excited state, which is more distinct in cyclohexane than in dioxan (splitting to several maxima); the highest maximum was recorded; [e] the band has a weak inflexion on the side (arm) of lower frequency; [f] the band has an inflexion on the side of lower frequency; [g] lit.[1] gives $\nu_{(CO)}$ in $CHCl_3$ 1 730 cm^{-1} and CD ($\Delta\varepsilon$, dioxan) −0·27.

a measure of the −I effect of the acetal group. In agreement with this the frequency of the $\nu_{(C=O)}$ vibration in the IR spectra of ketones[22] is increased in the order *I*, *II* and *III*, and the absorption of the $n \rightarrow \pi^*$ transition in the UV spectra shows a bathochromic shift[23] in the same order (Table I). Although the differences in energies are not large, they may be considered as significant, with respect to the rigidity of the system. On withdrawal of the electrons from the carbonyl group ($\overset{\delta+}{\leftarrow}C=O$) the order of the double bond is increased and the $n \rightarrow \pi^*$ transition ($\overset{\delta+}{\leftarrow}C=\overset{\curvearrowleft}{O}:$) is facilitated by the decrease of the excited state energy ($\overset{\delta-}{\leftarrow}\dot{C}=O\bullet$). This qualitative statement may be also reached on the basis of the application of the HMO method on the π-system of the carbonyl under the supposition that the inductive effect causes only a change in the coulombic integral of the p_z orbital on the carbon atom of the carbonyl group[24]. However, the possibility that the frequency $\nu_{(C=O)}$ can be affected by a change of the valence angle of the sp^2 hybridized carbonyl carbon atom[25] cannot be excluded, but it is not likely that this effect could be decisive: bicyclo[3.2.1]octan-3-one[26,27] and bicyclo[3.2.1]octan-2-one[28] differ only very little in their frequency of absorption $\nu_{(C=O)}$ from cyclohexanone.

The PMR spectra of ketones *I*–*III* correspond to their structures (for discussion of the PMR spectrum of ketone *I* see ref.[1]). The carbonyl group of ketone *III* causes – in comparison with ketone *I* – a shift of the anomeric hydrogen H_1 by 0·71 p.p.m. upfield. A similar shift (0·37 p.p.m.) is also observed in the case of the hydrogen atom H_5 of ketone *II*; both facts are in agreement with the anisotropy of the carbonyl group[29,30].

The values of $[\alpha]_D$ of ketones *I* and *II* in various solvents do not differ substantially from the optical rotation of 1,6-anhydro-2,3,4-trideoxy-β-D-*glycero*-hexopyranose ($[\alpha]_D$ −105° in water)[4], the basic skeleton of this group of compounds. In contrast to this, in aprotic solvents we observed unexpectedly high negative values $[\alpha]_D$ for ketone *III* (see also Table II).*

In an aqueous solution where ketone *III* exists practically completely in hydrated form this "anomalous" optical rotation is decreased to such a degree that it is close to the $[\alpha]_D$ values of ketones *I* and *II*.

Under the supposition that ketones *I*–*III* exist in chair conformation** and that the magnitude of the Cotton effect is mainly determined by the mutual positions of the oxygen atoms and the carbonyl groups in the molecule (the effect of the methylene group, when compared with the effect of oxygen, is much less in the same spacial

* The recently described 1,6-anhydro-3,4-dideoxy-β-D-*glycero*-hex-3-enopyranos-2-ulose has $[\alpha]_D$ −460° (1·0, chloroform)[31].

** For ketone *I* the chair conformation is in agreement with the measurements of the PMR data[1]. In the case of ketones *II* and *III* the complexity of the PMR spectra prevented an unambiguous prediction, but for sterical reasons the chair conformation may be presumed.

situation; *cf.* the discussion in ref.[1]), the Cotton effects of ketones *I* and *II* follow the octant rule. An exception is ketone *III* in which a very high negative Cotton effect value was observed (−1·358 in cyclohexane and −1·125 in dioxan). Although the explanation of this "anomaly" is far from being easy, it is possible that it is caused by the interaction of non-bonding electron pairs of oxygen atoms of the neighbouring $O_{(5)}$—$C_{(1)}$—$O_{(6)}$ group with antibonding π^*-orbital of the carbonyl group. From the results of other investigators[1,32,33] concerning the Cotton effect of the carbonyl group of keto derivatives of 1,6-anhydro hexoses, and observing the antioctant rule[34,35], demonstrated in ketones substituted in the α-position by oxygen containing groups, the conclusion should be drawn that the use of the CD measurements for structural proofs – and especially for conformation proofs of sugar keto derivatives – is possible only with greatest caution.

In the subsequent part of our study we investigated the reduction of ketones *I*–*III* with sodium borohydride in methanol. From particular ketones a mixture of isomeric alcohols was formed in all cases. Its composition was determined by gas chromatography by comparison with authentic samples (see Table III). In the case of ketones *II* and *III*, where the sterical hindrance to the approach of the reducing agent by the 1,6-anhydro bridge and the energetically disadvantageous formation of the axial hydroxy group act in the same direction, the reduction takes place, as expected, highly selectively under formation of predominantly equatorial alcohols, *i.e.* 84% of 1,6-anhydro-2,3-dideoxy-β-D-*threo*-hexopyranose (*XXIII*) or 89% of 1,6-anhydro-3,4-dideoxy-β-D-*threo*-hexopyranose (*XVII*) respectively. The reduction

TABLE II

Optical Rotation of 1,6-Anhydro-β-D-hexopyranosuloses

The measurement was carried out in a 1 cm cell at 0·8 to 1·0% concentration for substances *I* and *II*, and 0·3 to 0·4% concentration for substance *III*.

Compound	$[\alpha]_D^{25}$				$[M]_D$
	cyclohexane	dioxan	chloroform	water[a]	water
2-ulose *III*	−258°	−274°	−246°	−114°	−146°
3-ulose *I*[b]	− 79°	− 94°	−103°	− 88°	−113°
4-ulose *II*	− 72°	− 78°	− 83°	− 74°	− 95°

[a] Optical rotation was measured 5 minutes after the dissolution of the ketones in water and it corresponds to the equilibrium value. In ethanol $[\alpha]_D$ of substance *III* decreases after its fresh dissolution, *i.e.* (2 minutes after mixing) from −244° to −183° (after about one hour), in methanol the decrease is much faster (several minutes) and the rotation is stabilised at −138°. In water the value was −114° after 1 minutes after dissolution; [b] lit.[1] gives $[\alpha]_D$ −98° (*c* 0·8, chloroform).

of bicyclo[3,2,1]octan-2-one with sodium borohydride in methanol takes place in a similar manner under formation of 89% of the *exo*-isomer and 11% of the *endo*-isomer[28].* In the case of ketone *I* where both effects controlling the reaction act against one another 56% of 1,6-anhydro-2,4-dideoxy-β-D-*threo*-hexopyranose (*X*) and 44% of the isomeric 1,6-anhydro-2,4-dideoxy-β-D-*erythro*-hexopyranose (*XIII*) with the equatorial hydroxyl group are formed. For the preparation of 2,3-dideoxy-*threo*-derivative (*XXIII*) on a preparative scale the above mentioned reduction was employed, with the difference that it was carried out at −60°C in the presence of an appreciable excess of hydride (the rate of decomposition of hydride in methanol is appreciable even at low temperature, while the rate of its reaction with the ketone is decreased, *cf.* ref[24,37]). A small admixture of *erythro*-derivative *XXII*, formed simultaneously, was eliminated by chromatography on a column of alumina.

The as yet undescribed 2,4-dideoxy derivatives *X* and *XIII* could be prepared by reduction of ketone *I* with sodium borohydride, but the unfavourable ratio in which both alcohols were formed by this reduction and the difficulty of their chromatographic separation prompted us to look for a better method of their synthesis. One of the possibilities consisted in the reductive splitting off of the tosyloxy group, neighbouring on the *trans*-hydroxyl group, with lithium aluminum hydride, as was described for 4,6-O-benzylidene derivatives of aldohexopyranosides[38–40]. On application of this procedure to 1,6-anhydro-4-deoxy-2-O-*p*-toluenesulfonyl-β-D-*xylo*-hexopyranose (*IV*) a mixture was obtained containing 2,4-dideoxy-*threo*-alcohol *X* and 3,4-dideoxy-*threo*-alcohol *XVII* in a 4 : 1 ratio, while on reduction of 1,6 : 2,3-dianhydro-4-deoxy-β-D-*lyxo*-hexopyranose a mixture of both alcohols *X* and *XVII* is formed under similar conditions in a 1·7 : 1 ratio[18]. This confirms, in agreement with the literature, that the reduction of monotosyl derivative *IV* does not take place *via* the corresponding epoxy derivative exclusively. A mixture of dideoxy derivatives *X* and *XVII* could be separated in the form of their acetates *XI* and *XVIII* by chromatography on silica gel, and after their deacetylation pure substances *X* and *XVII* were obtained.

For the preparation of dideoxy-*erythro*-alcohol *XIII* which cannot be obtained by reduction of either 1,6 : 2,3-dianhydro-4-deoxy- or 1,6 : 3,4-dianhydro-2-deoxy-β-D-*ribo*-hexopyranose[18] we took advantage of rather great reactivity of the axial tosyloxy group in 1,6-anhydro-2,4-dideoxy-3-O-*p*-toluenesulfonyl-β-D-*threo*-hexopyranose (*XII*) with sodium benzoate in boiling dimethylformamide. The benzoyl derivative *XIV* prepared in this manner was converted to 1,6-anhydro-2,4-dideoxy-β-D-*erythro*-hexopyranose (*XIII*) by transesterification. The product was purified by chromatography and distillation and characterised as *p*-toluenesulfonyl derivative *XVI*. From the preparative point of view the following procedure was more suitable

* While this paper was going to press the reduction of bicyclo[3,2,1]octane-2- and 3-one with sodium borohydride in 2-propanol was described[36], with similar results.

for the preparation of dideoxy derivative *XIII*: A mixture of dideoxy derivatives *X* and *XVII* (obtained on reaction of tosyl derivative *IV* with lithium aluminum hydride) was converted to a mixture of tosyl derivatives *XII* and *XIX*. During their heating with sodium benzoate in dimethylformamide only the 3-tosyl derivative *XII* reacted, as expected, under formation of benzoate *XIV*, while 2-tosyl derivative *XIX* did not react at all (*cf.* ref.[3]). In the mixture of benzoyl derivative *XIV* and unreacted tosyl derivative *XIX* benzoate *XIV* was hydrolysed selectively and the mixture formed of dideoxy derivative *XIII* and tosyl derivative *XIX* was separated on a silica gel column.

The great reactivity of the tosyloxy group in tosyl ester *XII* during substitution is analogous to the reaction in which *p*-toluenesulfonic acid was split off under the effect of potassium tert-butoxide giving rise to unsaturated compounds. A mixture of 1,6-anhydro-2,3,4-trideoxy-β-D-*glycero*-hex-2- (*XX*) and hex-3-enopyranose (*XXI*) was formed in 2 : 1 ratio. This indicates the greater reactivity of hydrogen on $C_{(2)}$ than on $C_{(4)}$ on one hand, and on the other hand it means that the reaction was controlled predominantly kinetically and not thermodynamically; the equilibrium which takes place between both unsaturated compounds in alkaline medium has the composition 15·5% of compound *XX* and 84·5% of compound *XXI* (ref.[4]).

On catalytic reduction of enol acetate *VI* on platinum in methanol and subsequent deacetylation the expected dideoxy derivatives *X* and *XIII* are not formed, but probably both isomeric 1,5-anhydro-2,4-dideoxy-D-*erythro*- or *threo*-hexitols as could be judged from the mass spectrum of the product of reduction, obtained by a gas chromatography-mass spectroscopy combination. During the reduction of enol

TABLE III

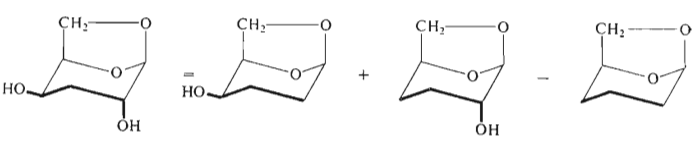
Dideoxy Derivatives of 1,6-Anhydro-β-D-hexopyranoses[a]

Compound (configuration)	$[\alpha]_D^{25}$ water	$\nu_{(OH)}$ assoc. cm^{-1}	$\nu_{(OH)}$[b] free cm^{-1}	$\Delta\nu_{(OH)}$ cm^{-1}	$[M]_D^{25}$ water	Reduction of ketone *I*—*III* with $NaBH_4$, % of dideoxy derivatives
2,3-*erythro*- (*XXII*)	−119°	3 585	3 626	41	−155°	16 (*II*)
2,3-*threo*- (*XXIII*)	− 57·5°	—	3 626	—	− 75°	84 (*II*)
2,4-*erythro*- (*XIII*)	− 91°	—	3 624	—	−118°	44 (*I*)
2,4-*threo*- (*X*)	− 81°	3 576	3 624	48	−105°	56 (*I*)
3,4-*erythro*- (*XXIV*)	− 58°	3 586	3 626	40	− 75°	11 (*III*)
3,4-*threo*- (*XVII*)	−133°	3 589	3 624	35	−173°	89 (*III*)

[a] The measurement of hydrogen bonds was carried out in cells of 2 and 4 cm width at a concentration of about $3 \cdot 10^{-3}$ M, in tetrachloromethane on Unical SP 700 apparatus; [b] the intensity of the bands was very low and therefore their position could not be read accurately.

acetate *VI* on palladium on charcoal in methanol the reaction mixture contained only a very low amount of dideoxy derivatives *X* and *XIII* in addition to the main products, probably methyl 3-O-acetyl-2,4-dideoxy-α,β-D-*erythro*- or- *threo*-hexopyranosides. We supposed that in both mentioned reductions the $C_{(1)}—O_{(6)}$ bond could be hydrogenolysed under formation of a common intermediate — 3-O-acetyl--1,2,4-trideoxy-β-D-hex-1-enopyranose. The reduction of enol acetate *VI* with sodium borohydride has also no preparative value for the preparation of dideoxy derivatives *X* and *XIII* either, because these compounds represent only a minor component of the complex reaction mixture.

In all dideoxy derivatives of 1,6-anhydro-β-D-hexopyranoses the $\nu_{(OH)}$ frequency was measured in order to determine the existence of hydrogen bonding (Table III). The results of these measurements which are generally in good agreement with the results obtained for partially substituted derivatives of 1,6-anhydro-β-D-glucopyranoses[41] have demonstrated that dideoxy derivatives *X*, *XXII* and *XXIV* assume in tetrachloromethane the $^1C_4$ chair conformation and not the second possible $B_{3,0}$ conformation. According to expectation only two dideoxy derivatives did not display an intramolecular hydrogen bond, *i.e.* 2,4-dideoxy-*erythro*- *XIII* and 2,3-dideoxy--*threo* derivative *XXIII*. For compound *XIII* the hydrogen bond $C_{(3)}OH\ldots O_{(5)}$ could be envisaged only in the case of the boat conformation, but its formation evidently cannot be forced, the same as in the case of 4-hydroxytetrahydropyran, which does not form an intramolecular hydrogen bond either[42,43]. Substance *XVII* can form a hydrogen bond both in the $^1C_4$ and in the $B_{3,0}$ conformations, while *XXIII* cannot form a hydrogen bond in the $^1C_4$ conformation; if conformation $B_{3,0}$ were to be forced and the hydrogen bond formed, then it would be very weak. The strongest hydrogen bond is formed by the axial hydroxyl group on $C_{(3)}$ with the $O_{(6)}$ atom, although it is less strong than the analogous hydrogen bond in *cis*-1,3-cyclohexanediol[44] or in methyl 2,4-O-phenylboronyl-β-D-*xylo*-pyranoside[45]. The reason for this may be seen in the mild flattening of the tetrahydropyrane ring in consequence of the so-called antireflex effect[46] which increases the distance of $C_{(3)}OH$ from $O_{(6)}$, and mainly in the fact that the non-bonding electron pair is not oriented colinearly



$[M]_{D,exp} = -12°$ $[M]_{D,exp.} = -75°$ $[M]_{D,exp.} = -75°$ $[M]_{D,exp.} = -120°$

$[M]_{D,calc.} = (-75) + (-75) - (-120) = -30°$

$[M]_{D,exp.} - [M]_{D,calc.} = (-12) - (-30) = +18°$

with the σ bond $O_{(3)}$—H because the rigid system does not enable a more suitable orientation[47]. Some authors when discussing the formation and stability of the hydrogen bond still do not attribute the proper importance to this fact. The first supposition is in agreement with the finding that in 1,6-anhydro-2,4-di-O-methyl--β-D-glucopyranose a still weaker hydrogen bond exists than in compound *X*, because the repulsion of the diaxial methoxyl groups on carbon atoms $C_{(2)}$ and $C_{(4)}$ still more flattens the tetrahydropyran ring. In dideoxy derivatives *XXII* and *XXIV* the hydrogen bond($\nu_{(OH)}$ 3585−6 cm^{-1}) is stronger than in 2-hydroxytetrahydropyran ($\nu_{(OH)}$ 3604 cm^{-1}, ref.[42], 3590 cm^{-1}, ref.[43]) which is probably caused by the sterical deformation of the bicyclic system of dideoxy derivatives. The same shift of the $\nu_{(OH)}$ frequency in substances *XXII* and *XXIV* shows that the inductive effect of oxygen has no practical influence on the strength of the hydrogen bond, as also follows from other measurements[48]. In compound *XVII* the shift of the frequency $\nu_{(OH)}$ is very close to the value for the ideal five-membered hydrogen bond[49] and it is identical with the value found in monomethyl ether of *cis*-1,2-cyclohexanediol.[50].

Empirical methods for the calculation of the optical rotation of polyhydroxy compounds are generally based on the summation of pairwise interactions of the vicinal diol system in which for the gauche interaction of the hydroxy groups ($\psi_{O/O}$ = = 60°) the value $[M]_D$ ±45° was determined experimentally. In these methods[51–54] it is supposed — not quite in agreement with some theories[55] — that the value $[M_D]$ of the pairwise interaction of the 1,3-diol system is small, and therefore it is not taken into account. If this supposition were correct, then the value $[M]_D$ of 1,6-anhydro-3-deoxy-β-D-*xylo*-hexopyranose[56,57] (experimental value is −12°) should be equal to the sum of $[M]_D$ of substances *XXIII* (−75°) and *XXIV* (−75°) diminished

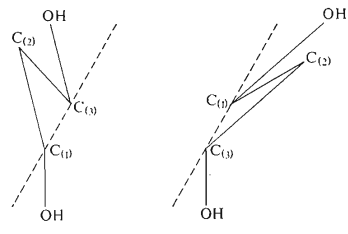


FIG. 1

Enantiomeric Pair of the *trans*-1,3-Diol System on a Cyclohexane or Tetrahydropyran Ring

by $[M]_D$ of 1,6-anhydro-2,3,4-trideoxy-β-D-*glycero*-hexopyranose[4] (−120°), *i.e.* $[M]_D = (-75) + (-75) - (-120) = -30°$. The difference between the measured and the calculated value is $(-12) - (-30) = +18°$. A similar calculation of $[M]_D$ of 1,6-anhydro-3-deoxy-β-D-*arabino*-hexopyranose[58] ($[M]_D$ experimentally determined was −228°) from the values $[M]_D$ of dideoxy derivatives *XXII* (refs[4,18]) (−155°) and *XVII* (ref.)[18] (−173°) gave the value $[M]_D = -208°$, *i.e.* $[M]_{D,found} - [M]_{D,calc.} = -20°$. From the differences of the calculated and the measured values (+18 and −20°) it follows that the value $[M]_D = \pm 19°$ should be attributed to the pairwise interaction of the 1,3-*trans*-diol system ($\psi_{O/O} = 120°$), the sign of which is determined by the relative position of the hydroxyl groups (Fig. 1), similarly as in the case of the vicinal diol O/O interaction. The calculated values are in excellent agreement with the experimentally determined $[\alpha]_D$ values of *trans*-1,3-cyclohexanediols, ±16·2°, which corresponds to $[M]_D$ ±18·8°, ref.[59]. On the basis of the considerations mentioned the absolute configuration of (1*S*,3*S*)-*trans*-1,3-cyclohexanediol may be attributed to the *trans*-1,3-cyclohexanediol with the value $[\alpha]_D$ +16·2°, and the configuration 1*R*, 3*R* to its antipode.

EXPERIMENTAL

The melting points were determined on a Boëtius micromelting point apparatus. Optical rotation was measured at 23—25° on an automatic Bendix-Ericsson polarimeter, type 143A. The PMR spectra were measured in deuteriochloroform on Varian HA-100 and Varian EMS 300 with tetramethylsilane as internal reference; the chemical shift values are in δ-scale (p.p.m.), *J* is in Hz. The infrared spectra were obtained both with an experimental prototype of the Research Institute for Apparatus Technique (Brno) and with a Zeiss UR 20 apparatus (Jena, GDR). The CD spectra were measured on a Dichrographe Rousell-Jouan spectropolarimeter, and the UV spectra on a Unicam SP 700 apparatus. The purity of the substances was controlled by thin-layer or gas chromatography. Thin-layer chromatography was carried out on silica gel in benzene–acetone 10 : 1 (unless stated otherwise), detection by spraying with concentrated sulfuric acid and heating. Gas chromatography was carried out on a Chrom III apparatus, column 183 cm/0·6 cm, Chromosorb W with 15% of Carbowax 20 M. Dichloromethane for the oxidation with ruthenium tetroxide was purified by shaking with sulfuric acid, 24 hours standing with a small amount of bromine, washing with a sodium thiosulfate solution and water, and drying over calcium chloride and distillation through a column (about 15 TP). Sodium borohydride was purified by crystallisation from diglyme and drying *in vacuo*[60]. All solutions were concentrated under reduced pressure, samples for analysis were dried over phosphorus pentoxide.

1,6-Anhydro-3,4-dideoxy-2-O-*p*-toluenesulfonyl-β-D-*erythro*-hex-3-enopyranose (*VIII*)

Mesyl tosyl ester[4] *VII* (10 g) was dissolved in 75 ml boiling benzene and after cooling to 50°C 50 ml of a 1M solution of potassium tert-butoxide in tert-butyl alcohol was added. The temperature was kept at 50°C for 30 minutes, the mixture cooled and diluted with water. The benzene layer was separated and the aqueous one extracted twice with dichloromethane. The combined dichloromethane extracts and the benzene layer were dried over anhydrous magnesium sulfate, filtered and evaporated. The residue was crystallised from a mixture of ether and light petroleum

to afford 3·5 g (47%) of substance which when crystallised from aqueous methanol had m.p. 85—86°C (decomposes after melting), $[\alpha]_D$ −161° (*c* 0·50, chloroform). PMR spectrum, Varian HA-100, double resonance: 7·83 (2 H aromatic, doublet, J = 8·2); 7·35 (2 H aromatic, doublet, J = 8·2); 6·31 (H-4, quadruplet, $J_{3,4}$ = 9·8, $J_{4,5}$ = 4·5, $J_{4,2}$ = 0·8); 5·61 (H-3, multiplet, $J_{3,4}$ = 9·8, $J_{2,3}$ = 3·8, $J_{1,3}$ = 1·5, $J_{3,5}$ = 0·3); 5·51 (H-1), multiplet, $J_{1,2}$ = 1·2, $J_{1,3}$ = 1·5); 4·73 (H-5, multiplet, $J_{4,5}$ = 4·5, $J_{3,5}$ = 0·3); 4·39 (H-2, multiplet, $J_{2,3}$ = 3·8, $J_{1,2}$ = 1·2, $J_{2,4}$ = = 0·8); 3·72—3·52 (H-6, H-6′, multiplet); 2·46 (CH_3, singlet). For $C_{13}H_{14}O_5S$ (282·3) calculated: 55·30% C, 5·00% H; found: 55·36% C, 5·01% H.

1,6-Anhydro-3-O-benzyl-2,3-dideoxy-β-D-*erythro*-hex-2-enopyranose (*IX*)

Sodium (100 mg) solution in 2 ml of benzyl alcohol was evaporated to dryness *in vacuo* (0·05 Torr) and the residue dissolved in 10 ml of dry tetrahydrofuran. Tosyl derivative *VIII* (300 mg) was added to the solution and the mixture allowed to stand at room temperature for 24 hours, tetrahydrofuran was distilled off under reduced pressure, the residue diluted with water and extracted with benzene. The benzene solution was dried over anhydrous magnesium sulfate, concentrated to a small volume and chromatographed with benzene on a column of 15 g of alumina (with 5% of water). After evaporation of benzene 130 mg (56%) of substance *IX* were obtained which after crystallisation from aqueous methanol had m.p. 56—57°C, $[\alpha]_D$ +158° (*c* 0·60; chloroform), lit.[4] gives m.p. 56—57°C, $[\alpha]_D$ +155° (*c* 0·50, chloroform), IR spectrum was identical with that of the authentic sample.

1,6-Anhydro-2,3-dideoxy-β-D-*glycero*-hexopyranos-4-ulose (*II*)

To a solution of dideoxy derivative *XXII* (0·5 g), prepared by hydrogenation of the substance *IX* in the manner described[4], in 10 ml of dichloromethane a solution of ruthenium tetroxide in dichloromethane (prepared by shaking 0·8 g of ruthenium dioxide with an aqueous solution of sodium periodate and extraction with dichloromethane[5]) was added dropwise under stirring and cooling and the mixture was allowed to stand for about 10 minutes. Excess ruthenium tetroxide was decomposed with a few drops of isopropyl alcohol. The separated ruthenium dioxide was filtered off, the filtrate dried over anhydrous magnesium sulfate, and after evaporation of the solvent the residue was distilled *in vacuo*. Yield 0·35 g (71%), b.p. 89°C/16 Torr, $[\alpha]_D$ −83° (*c* 0·8, chloroform). For spectral data and the $[\alpha]_D$ values in other solvents see Table I and II. PMR spectrum, Varian HA-100: 5·72 (H-1, triplet, $J_{1,2ax} \approx J_{1,2eq}$ = 1·7, ΣJ = 3·5); 4·49 (H-5, doublet of doublets, $J_{5,6exo}$ = 5·0, $J_{5,6endo}$ = 1·4); 3·96 (H-6exo, doublet of doublets, $J_{6exo,6endo}$ = 8·3, $J_{exo,5}$ = 5·2, $J_{exo,1} \neq 0 < 0{\cdot}5$); 3·84 (H-6endo, doublet of doublets, $J_{6endo,6exo}$ = 8·3, $J_{6endo,5}$ = 1·4, $J_{6endo,1}$ = 0·5); 2·0—2·6 (CH_2—CH_2, multiplet). For $C_6H_8O_3$ (128·1) calculated: 56·24% C, 6·29% H; found: 56·29% C, 6·17% H.

1,6-Anhydro-3,4-dideoxy-β-D-*glycero*-hexopyranos-2-ulose (*III*)

This was prepared from 1,6-anhydro-3,4-dideoxy-β-D-*erythro*-hexopyranose[18] (*XXIV*) in an analogous manner as ketone *II*. From 0·5 g of alcohol *XXIV* 0·26 g (53%) of ketone *III* were obtained, b.p. 104°C/16 Torr, $[\alpha]_D$ −246° (*c* 0·4, chloroform). For spectral data and $[\alpha]_D$ values in other solvents see Tables I and II. PMR spectrum, Varian HA-100: 5·09 (H-1, singlet, $J_{1,3}$ = 0·8, $J_{1,6} \neq 0 < 1$); 4·70 (H-5, multiplet), 4·04 (H-6endo, doublet of doublets, $J_{6endo,6exo}$ = 7·7, $J_{endo,5}$ = 1·4); 3·94 (H-6exo, doublet of doublets with fine splitting, $J_{6exo,6endo}$ = 7·7, $J_{exo,5}$ =

$= 4{\cdot}8$, $J_{6exo,1} \neq 0 < 1$); 2·8—1·9 (CH_2—CH_2, multiplet). For $C_6H_8O_3$ (128·1) calculated: 56·24% C, 6·29% H; found: 56·04% C, 6·08% H.

1,6-Anhydro-2,4-dideoxy-β-D-*glycero*-hexopyranos-3-ulose (*I*)

This compound was prepared from 12 g of 1,6-anhydro-2,4-di-O-*p*-toluenesulfonyl-β-D-*ribo*-hexopyranos-3-ulose by reductive detosylation with Raney nickel[1]; the product contained a small amount of dideoxy derivatives *X* and *XIII* of which it was freed by oxidation to completion (with ruthenium tetroxide in dichloromethane) as in the preparation of ketone *II*. The yields of ketone *I* were about 1·5 g (46%), b.p. 103°C/16 Torr, $[\alpha]_D$ —103° (*c* 0·8; chloroform). For spectral data and $[\alpha]_D$ values in further solvents see Tables I and II. PMR spectrum, Varian HA-100: 5·80 (H-1, triplet, $J_{1,2ax} \approx J_{1,2eq} = 1{\cdot}7$; $\Sigma J = 3{\cdot}4$); 4·86 (H-5, multiplet, $\Sigma J = 12{\cdot}1$); 3·87 (H-6endo, H-6exo, unresolved multiplet;); 2·85 (H-4ax, doublet of doublets with fine splitting, $J_{4ax,4eq} = 17{\cdot}0$, $J_{4ax,5} = 4{\cdot}8$, $J_{4ax,6} \neq 0$, $J_{4ax,2} \neq 0$); 2·56 (H-2eq, H-2ax, doublet, $J_{1,2eq} \approx \approx J_{1,2ax} = 1{\cdot}7$, $\Sigma J = 3{\cdot}4$); 2·45 (H-4eq, doublet with fine splitting, $J_{4eq,4ax} = 17{\cdot}0$, $J_{4eq,5} = = 1{\cdot}4$, $J_{4eq,1} \neq 0 < 1$).

1,6-Anhydro-2,3-dideoxy-β-D-*threo*-hexopyranose (*XXIII*)

Sodium borohydride (100 mg) was dissolved in 3 ml of methanol at —30°C, the solution cooled down to —60°C and additioned with 180 mg of ketone *II* and the mixture allowed to stand at —60°C for 30 hours. After the temperature had been raised to room temperature the mixture was evaporated to dryness. The residue was mixed with 0·5 ml of a 20% sodium hydroxide solution and the mixture extracted eight times with 2 ml portions of dichloromethane. The extract was dried over magnesium sulfate and the solvent evaporated. The residue was chromatographed on 12 g of alumina (activity II) with ether–dichloromethane 9 : 1. A fraction containing *threo*-derivative *XXIII* was eluted first. After evaporation of the solvents the residue was sublimated at 110—130°C (bath temperature) and 20 Torr. Yield 130 mg (71%) of substance *XXIII*, m.p. 95—100°C. The product was crystallised from an ether–cyclohexane mixture; m.p. 100—103°C, $[\alpha]_D$ —57·5° (*c* 1·09, water). For $C_6H_{10}O_3$ (130·1) calculated: 55·37% C, 7·75% H; found: 55·27% C, 7·87% H.

Reduction of Ketones *I*—*III* with Sodium Borohydride in Methanol (Table III)

To a 1% solution of ketone *I*—*III* in methanol (2 ml) 4 mg of sodium borohydride were added and the mixture allowed to stand at room temperature for 20 minutes. The solvent was distilled off *in vacuo*, 0·2 ml of a 10% sodium hydroxide solution added, and the mixture extracted six times with 0·3 ml portions of dichloromethane. The extract was analysed by gas chromatography at 167—168°C, nitrogen flow 40 ml/min, overpressure in the injection port 0·93 atm. The retention times in minutes for 1,6-anhydro-dideoxy-hexopyranoses were the following: 2,4-dideoxy-*threo* (*X*) 6·35; 2,3-dideoxy-*erythro* (*XXII*) 7·2; 3,4-dideoxy-*erythro* (*XXIV*) 7·4; 3,4-dideoxy-*threo* (*XVII*) 9·3; 2,3-dideoxy-*threo* (*XXIII*) 13·2; 2,4-dideoxy-*erythro* (*XIII*) 13·9. The identification was carried out by comparison with authentic samples.

Elimination of *p*-Toluenesulfonic Acid from 1,6-Anhydro-2,4-dideoxy-3-O-*p*-toluenesulfonyl-β-D-*threo*-hexopyranose (*XII*)

A mixture of substance *XII* (10 mg) in 0·3 ml of benzene and 0·3 ml of a 1M solution of potassium tert-butoxide in tert-butyl alcohol was allowed to stand at 20°C for 2 hours, then diluted with

0·6 ml of water and extracted three times with 1·5 ml of dichloromethane. The extract was dried over magnesium sulfate and the ratio of unsaturated derivatives determined by gas chromatography. The mixture contained 66·5% of 1,6-anhydro-2,3,4-trideoxy-β-D-*glycero*-hex-2-enopyranose (*XX*) and 33·5% of 1,6-anhydro-2,3,4-trideoxy-β-D-*glycero*-hex-3-enopyranose (*XXI*). It was shown that the extraction procedure does not affect the concentration ratio of both olefins. The conditions for chromatography were those from the preceding paper[4].

Reduction of 1,6-Anhydro-4-deoxy-2-O-*p*-toluenesulfonyl-β-D-*xylo*-hexopyranose (*IV*) with Lithium Aluminum Hydride

A suspension of 1·09 g of lithium aluminum hydride in 11·3 ml of dry tetrahydrofuran was refluxed for 2 hours, then additioned with 2 g of deoxy tosyl derivative *IV* (ref.[2]) and the mixture stirred under refluxing for 16 hours. After decomposition with an equivalent amount of water (2·1 ml) under cooling and stirring 70 ml of ether were added and the mixture dried over anhydrous magnesium sulfate. After evaporation of ether the residue was extracted ten times with 70 ml portions of boiling ether. The combined ethereal extracts were evaporated to give 1·0 g of a syrup which was purified by filtration through a layer of silica gel using benzene and acetone (8%) as eluent. Yield, 0·7 g (80%) of a syrup, $[\alpha]_D$ −87° (water), which after distillation at 60°C/0·01 Torr has $[\alpha]_D$ −89° (*c* 0·6, water). For $C_6H_{10}O_3$ (130·1) calculated: 55·37% C, 7·75% H; found: 55·22% C, 7·85% H. The product behaves as if it was pure on thin layers, but gas chromatographic analysis demonstrated that it was a mixture of dideoxy derivatives *X* (80%) and *XVII* (20%); a similar composition was calculated from optical rotation.

3-O-Acetyl-1,6-anhydro-2,4-dideoxy-β-D-*threo*-hexopyranose (*XI*) and 2-O-Acetyl-1,6-anhydro-3,4-dideoxy-β-D-*threo*-hexopyranose (*XVIII*)

A mixture of 600 mg of dideoxy derivatives *X* and *XVII* obtained by the reaction of deoxy tosyl derivative *IV* with $LiAlH_4$ was acetylated with 2·5 ml of acetic anhydride in 5 ml of pyridine. After 24 hours standing the reaction mixture was decomposed with water and worked up in the conventional manner by extraction with chloroform. After separation and evaporation of chloroform the syrupy residue (775 mg, 98%) was chromatographed on a column of silica gel (50 g). Elution with benzene gave first acetate *XVIII*, and a mixture of benzene and acetone (6%) eluted acetate *XI*. Concentration of the benzene fractions gave 117 mg of acetate *XVIII* which was distilled at 75°C (bath temperature) and 0·01 Torr in a Hickmann flask in the presence of a molecular sieve (Potasit 3, type 3A); m.p. 30—35°C, $[\alpha]_D$ −120° (*c* 0·5, chloroform). For $C_8H_{12}O_4$ (172·2) calculated: 55·80% C, 6·96% H; found: 55·75% C, 6·80% H. Concentration of the benzene–acetone fractions yielded 645 mg of acetate *XI* which was also distilled at 75°C of the bath temperature and 0·01 Torr, m.p. 18—22°C, $[\alpha]_D$ −93° (*c* 0·7, chloroform). For $C_6H_{12}O_4$ (172·2) calculated: 55·80% C, 6·96% H; found: 55·62% C, 7·28% H.

1,6-Anhydro-2,4-dideoxy-β-D-*threo*-hexopyranose (*X*)

Acetyl derivative *XI* (305 mg) was deacetylated in methanol in the presence of catalytic amount of 1M sodium methoxide; sodium ions were eliminated by addition of Amberlite IR 120 H^+. After filtration with charcoal and evaporation of the solvent 206 mg (89%) of a syrup were obtained which after the addition of ether and evaporation crystallised. Its distillation at 50°C/0·01 Torr gave a product of m.p. 37—50°C, $[\alpha]_D$ −81° (*c* 0·7, water) which would not crystallize from a solvent. For $C_6H_{10}O_3$ (130·1) calculated: 55·36% C, 7·75% H; found: 55·25% C, 8·03% H.

1,6-Anhydro-3,4-dideoxy-β-D-*threo*-hexopyranose (*XVII*)

Deacetylation of acetate *XVIII* in the conventional manner gave the syrupy deoxy derivative *XVII*, b.p. 70°C/0·01 Torr, $[\alpha]_D$ −133° (*c* 0·5, water). The product was identical with an authentic sample of *XVIII*, prepared according to literature[18] which gives m.p. 28°C (unsharp), $[\alpha]_D$ −133° (*c* 0·6, water). For $C_6H_{10}O_3$ (130·1) calculated: 55·36% C, 7·75% H; found: 55·42% C, 7·99% H.

1,6-Anhydro-2,4-dideoxy-3-O-*p*-toluenesulfonyl-β-D-*threo*-hexopyranose (*XII*) and 1,6-Anhydro-3,4-dideoxy-2-O-p-toluenesulfonyl-β-D-*threo*-hexopyranose (*XIX*)

Tosylation of 440 mg of a mixture of dideoxyderivatives *X* and *XVII* (prepared from deoxytosyl derivative *IV*) in 7 ml of pyridine with 1·5 g of *p*-toluenesulfonyl chloride, carried out at room temperature for 48 hours and decomposition of the reaction mixture with water, gave 800 mg of a material (95%) which after repeated crystallisation from ether yielded 550 mg (65%) of tosyl derivative *XII*. The substance had m.p. 68—70°C, $[\alpha]_D$ −37° (*c* 0·5, chloroform). For $C_{13}H_{16}O_5S$ (284·3) calculated: 54·91% C, 5·67% H; found: 55·08% C, 5·66% H. The mother liquors after crystallisation of *XII* (combined from several tosylations) were chromatographed on silica gel with a mixture of benzene and 6% acetone yielding in addition to further fractions of substance *XII* with a lower R_F value also the tosyl derivative *XIX* with a higher R_F value; after repeated crystallisation from a mixture of acetone, ether and light petroleum the analytical sample had m.p. 83—85°C, $[\alpha]_D$ −80° (*c* 0·4, chloroform). Literature[18] gives m.p. 83—85°C, $[\alpha]_D$ −82° (*c* 0·66, chloroform).

1,6-Anhydro-3-O-benzoyl-2,4-dideoxy-β-D-*erythro*-hexopyranose (*XIV*)

A mixture of 155 mg of tosyl derivative *XII*, 0·25 mg of sodium benzoate and 4 ml of dimethylformamide was refluxed for 40 minutes. After evaporation of dimethylformamide the residue was extracted with acetone, the acetone solution evaporated to dryness and the syrup obtained freed from the residual dimethylformamide by filtration of its solution in benzene with 6% of acetone through 7 g of silica gel. After concentration 90 mg (70%) of a chromatographically pure syrupy benzoyl derivative *XIV* were obtained, $[\alpha]_D$ −80° (*c* 0·6, chloroform).

1,6-Anhydro-2,4-dideoxy-β-D-*erythro*-hexopyranose (*XIII*)

a) A mixture of tosyl derivatives *XII* and *XIX* (550 mg) was dissolved in 15 ml of dimethylformamide, 0·8 g of sodium benzoate were added to it and the suspension boiled for 40 minutes. According to thin-layer chromatography in benzene–acetone (94 : 6) derivative *XII* has reacted quantitatively. The mixture was evaporated, the residue extracted three times with 25 ml of acetone and the syrupy benzoyl derivative *XIV*, obtained together with *XIX* after evaporation of acetone and the residues of dimethylformamide, was debenzoylated with a catalytic amount of sodium methoxide in methanol. After 48 hours the solution was neutralised with Amberlite IR 120 H^+, the filtrate after filtration off of the cation exchanger was decolorized with charcoal and evaporated to a syrupy material (470 mg) containing traces of methyl benzoate. Chromatography on a silica gel column in benzene–acetone (6%) eluted methyl benzoate and the unreacted tosyl derivative *XIX*. Then using benzene with 15% of acetone 153 mg (54%) of a syrup were eluted. After its distillation from a Hickmann flask at 85°C (bath temp.) and 0·01 Torr analytically pure dideoxy derivative *XIII* was obtained, $[\alpha]_D$ −91° (*c* 0·9, water). For $C_6H_{10}O_3$ (130·1) calculated: 55·36% C, 7·75% H; found: 55·14% C, 7·93% H.

b) On catalytic debenzoylation of the benzoyl derivative *XIV* carried out under the usual conditions with sodium methoxide derivative *XIII* was obtained having the same physical properties as the product obtained under *a*).

1,6-Anhydro-2,4-dideoxy-3-O-*p*-toluenesulfonyl-β-D-*erythro*-hexopyranose (*XVI*)

Tosylation of 6 mg of syrupy dideoxy derivative *XIII* with *p*-toluenesulfonyl chloride in pyridine for 16 hours gave, after decomposition of the reaction mixture with water, 12 mg (91%) of tosyl derivative *XVI*, m.p. 105–107°C; after crystallisation from ether–light petroleum or ethanol–water the melting point was 90–92°C (decomp.), $[\alpha]_D$ −79° (*c* 0·5, chloroform). For $C_{13}H_{16}O_5S$ (284·3) calculated: 54·91% C, 5·67% H; found: 55·10% C, 5·82% H.

3-O-Acetyl-1,6-anhydro-2,4-dideoxy-β-D-*erythro*-hexopyranose (*XV*)

Dideoxy derivative *XIII* (40 mg) was acetylated with boiling acetic anhydride in the presence of sodium acetate and the reaction mixture was worked up in the usual manner, *i.e.* extracted with chloroform. Yield 35 mg of a syrup (66%) which was chromatographically pure and had on a thin layer of silica gel (with a mixture of benzene and 15% of ether) a substantially higher R_F value than the acetyl derivative *XI*. Distillation of the syrup at 75°C (bath temp.)/0·01 Torr gave analytically pure acetyl derivative *XV*, $[\alpha]_D$ −98° (*c* 0·6, chloroform). For $C_8H_{12}O_4$ (172·2) calculated: 55·80% C, 6·96% H; found: 55·98% C, 7·15% H.

3-O-Acetyl-1,6-anhydro-2,4-dideoxy-β-D-*glycero*-hex-2-enopyranose (*VI*)

A mixture of 1 g of tosylketone *V* (ref.[3]), 10 g of zinc dust, and 15 ml of acetic anhydride was refluxed under stirring for 10 minutes. After cooling zinc was filtered off, washed four times with 20 ml of benzene, and the combined filtrates evaporated to dryness, finally in a vacuum of an oil pump. The syrup obtained, 600 mg, contained the unreacted ketone *V*, enolacetate *VI*, and a larger amount of decomposition products, but no ketone *I*. It was chromatographed on a column of 50 g of silica gel with benzene and 15% of ether. In addition to 115 mg of starting compound *V*, 170 mg (30%) of syrupy enolacetate *VI* were obtained, which was distilled at 100°C/0·05 Torr; $[\alpha]_D$ +170° (*c* 1·0, chloroform). Enolacetate is poorly stable, it already decomposes in commercial chloroform (a 50% decomposition after 24 hours' standing). PMR spectrum, Varian EMS 300: 7·44 (H-2, doublet, $J_{1,2} = 6·1$), 5·45 (H-1, doublet, $J_{1,2} = 6·1$), 5·1–4·0 (H-5, H-6endo, H-6exo, multiplet), 2·9–2·2 (H-4ax, H-4eq, multiplet), 2·09 (CH_3CO, singlet). For $C_8H_{10}O_4$ (170·2) calculated: 56·47% C, 5·92% H; found: 56·38% C, 5·81% H.

After a deacetylation of the enolacetate *VI* with methanolic hydrogen chloride carried out in the usual manner the reaction mixture contained according to thin-layer chromatography and gas chromatography a small amount of ketone *I* in addition to several other products.

Reduction of 3-O-Acetyl-1,6-anhydro-2,4-dideoxy-β-D-*glycero*-hex-2-eno-pyranose (*VI*)

a) A mixture of enolacetate *VI* (20 mg), sodium borohydride (20 mg), and methanol (2 ml) was stirred at 0°C for 5 minutes. Gas chromatography of the reaction mixture showed that it contained dideoxy derivatives *X* and *XIII* as minor components in an approximate 1 : 1 ratio. Their preparative separation on silica gel can be carried out with benzene containing 7% of acetone, or, after their transformation to acetyl derivatives *XI* and *XV*, with benzene with 10% of ether.

b) A solution of 30 mg of enolacetate *VI* in 5 ml of methanol was hydrogenated on platinum at normal pressure. The reaction mixture was then deacetylated with sodium methoxide and

concentrated. The product in which no dideoxy derivatives *X* and *XIII* were detected, but a single spot with a lower R_F value (thin-layer chromatography in benzene with 20% of ether), was analysed with a gas chromatograph and mass spectrometer LKB 9000. Mass spectrum (only most important peaks are given): *m/e* 114 (M—18), 101 (M—31), 83.

c) Enolacetate *VI* (30 mg) was hydrogenated in methanol on palladium on charcoal at normal pressure for 2 hours. The reaction mixture was evaporated (syrup). Thin-layer chromatography (benzene with 20% of ether) detected in it the presence of two compounds which were not identical with either of the dideoxy derivatives *X* and *XIII* or the products formed by reduction on platinum, see *b*). Combination of gas chromatography and mass spectrometry (LKB 9000) gave the following important peaks: *m/e* 187 (M—17), 145 (M—59), 117 (M-59—18).

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