DERIVATIVES OF 6-DEOXY-D-GULOSE (ANTIAROSE)

K.Čapek[a], I.Tíkal[a], J.Jarý[a] and M.Masojídková[b]

[a]*Laboratory of Monosaccharides, Institute of Chemical Technology, Prague 6 and*
[b]*Department of Nuclear Magnetic Resonance, Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, Prague 6*

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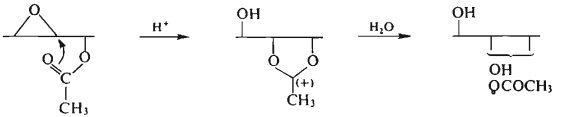
Reaction of methyl 3,4-anhydro-6-deoxy-α-D-galactopyranoside (*I*) with aqueous sulfuric acid in acetone affords 6-deoxy-2,3-O-isopropylidene-β-D-gulofuranose (*II*) as the main product along with methyl 6-deoxy-α-D-gulopyranoside (*III*) and a small amount of its *gluco*-isomer. Methyl 2-O-acetyl-3,4-anhydro-6-deoxy-α-D-galactopyranoside (*XI*) affords a mixture of the 2-O-acetyl derivative *XV* and the 3-O-acetyl derivative *XIV* as the principal product and the isopropylidene derivative *II* as the by-product. In brief reaction periods, the isopropylidene derivative *II* is not formed at all. The structure of compound *II* is confirmed by hydrolysis to 6-deoxy-D-gulose (*IV*), conversion to 2,3-O-isopropylidene-β-L-erythrofuranose (*VII*), and by NMR spectra. The considerable difference in composition of reaction mixtures after hydrolysis of the anhydro derivatives *I* and *XI* is probably due to the different hydrolysis rate of glycosides *III*, *XIV*, and *XV* to 6-deoxy-D-gulose (*IV*) which affords by the action of acetone the isopropylidene derivative *II*. Optimum conditions for the preparation and isolation of methyl 6-deoxy-α-D-gulopyranoside (*III*) are described along with preparations of its derivatives.

The reaction of methyl 6-deoxy-2,3-O-isopropylidene-4-O-methanesulfonyl-α-L-mannopyranoside and its *talo*-isomer with sodium azide[1-3] and hydrazine[4,5] has been recently found to obey a complex mechanism which might be elucidated with the use of analogous reactions of the correcponding α-D-*gulo*-isomer. 6-Deoxy-D-gulose (antiarose) was discovered[6] in natural material in the last decade of the previous century and its first synthesis effected[7] in 1935. Notwithstanding, a very few of its derivatives can be found in the literature. In the present paper, we wish to report the preparation of methyl 6-deoxy-α-D-gulopyranoside (*III*) and the corresponding isopropylidene mesyl derivative *XVIII*.

In our investigations, methyl 3,4-anhydro-6-deoxy-α-D-galactopyranoside[8] (*I*) was used as the starting material. The cleavage of this compound with various agents (azide[9], hydrogen bromide[10], lithium aluminum hydride[10]) is known to afford predominantly the derivatives of the *gulo* configuration. In view of the isomerisation



SCHEME 1

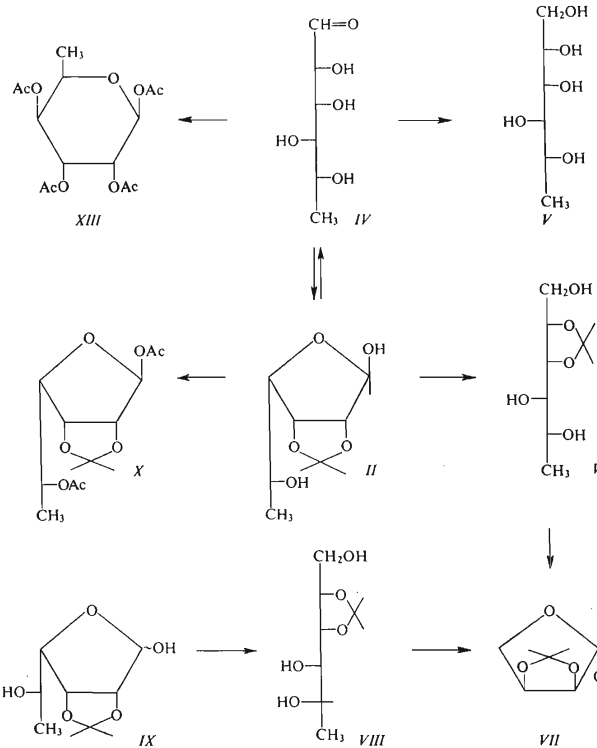


TABLE I

Composition of Reaction Mixtures (%) after Treatment of the Anhydro Galactoside *I* with Sulfuric Acid in Acetone

M	Time, h	*I*	*II*	*III* + *gluco*-isomer
0·05	27	85·0	0	10·6
0·25	27	18·5	34·2	15·5
0·5	10	28	28·5	17·2
0·5	27	21·4	37·8	14·6

to methyl 2,3-anhydro-6-deoxy-α-D-gulopyranoside[8] in alkaline media, we paid attention only to the acid hydrolysis of the anhydro galactoside *I*. Such hydrolytical conditions were required which would cause opening of the epoxide ring, the glycoside bond remaining untouched. As shown by thin-layer chromatography on silica gel, the action of sulfuric acid in most solvents examined (water, aqueous acetone, aqueous methanol, dioxane) results in a complete hydrolysis to the reducing sugars. Similar results were obtained with the use of acetic acid. The highest proportion of glycosides is formed by the action of aqueous sulfuric acid in acetone or tetrahydrofuran. Moreover, in contrast to tetrahydrofuran as solvent, an additional compound was found in acetone. For this reason, the hydrolysis of the anhydro galactoside *I* in acetone was studied in detail. The reaction mixture was separated on a column of silica gel to afford in all experiments the unreacted anhydro galactoside *I*, the isopropylidene derivative *II* (identified as 6-deoxy-2,3-O-isopropylidene-β-D-gulofuranose), and the glycosidic material. As shown by thin-layer chromatography on silica gel impregnated with a borate buffer solution,* the latter material represents a mixture of methyl 6-deoxy-α-D-gulopyranoside (*III*) and methyl 6-deoxy-α-D-glucopyranoside, wherein the derivative *III* predominates. The reducing sugars have not been isolated from the column. Results of hydrolysis of the anhydro galactoside *I* with aqueous sulfuric acid in acetone are summarised in Table I.

It may be seen from Table I that the highest proportion of the glycosidic material is obtained by the action of very dilute sulfuric acid. From the preparative standpoint, however, this procedure is not suitable because of a considerable amount of the unreacted starting compound. Increasing concentrations of sulfuric acid and increasing reaction periods of time lead to the predominant formation of the isopropylidene derivative *II* as the hydrolysis product of the anhydro galactoside *I*.

* By other techniques, *e.g.*, thin-layer chromatography on silica gel with gypsum, silica gel and aluminium oxide, or paper chromatography in various solvent systems, the separation of compound *III* from the *gluco* isomer failed.

TABLE II

Chemical Shifts (p.p.m.) and J Constants (c.p.s.)

Varian HA-100 apparatus; deuteriochloroform as solvent; tetramethylsilane as internal standard; chemical shifts and interaction constants from 1st order analysis.

Compound	H(1)	H(2)	H(3)	H(4)	H(5)	H(6)	OCH_3	OAc
II	5·41	4·61	4·73	3·98	4·13	1·28	—	—
X	6·14	4·67	4·76	4·05	5·21	1·33	—	2·07 2·06
XII	4·77	5·07	5·16	4·83	4·335	1·13	3·42	2·15 2·105 2·05
XIII	5·99	5·10	5·41	4·88	4·27	1·19	—	2·16 2·13 2·10 1·99
XIV	4·61	4·0[c]	5·01	3·42	4·04	1·16	3·48	2·06
XV	4·77	5·03	3·95	3·58	4·15	1·18	3·43	2·04[d]
XVII	4·77	4·28	4·15	5·04	4·30	1·16	3·44	2·13
XVIII	4·80[e]	4·40[e] (2H)	4·40[e] (2H)	4·70[e]	4·33	1·28	3·46	—

Configuration of the isopropylidene derivative *II* was determined by the acid hydrolysis to 6-deoxy-D-gulose (*IV*). Since our specimen of compound *IV* possessed a lower melting point that reported[7,11], we performed a sodium borohydride reduction to 6-deoxy-D-gulitol (*V*). The infrared spectrum of the latter product was identical with that of the enantiomeric 6-deoxy-L-gulitol, obtained in turn by desulfurisation[12] of 2,3,4,5,6-penta-O-acetyl-D-glucose diethyldithioacetal.

The sodium borohydride reduction of the isopropylidene derivative *II* followed by oxidation of the resulting alcoholic sugar *VI* with sodium periodate afforded 2,3-O-isopropylidene-β-L-erythrofuranose (*VII*), the infrared spectrum (containing all the remarkable bands reported[13]) and the mass spectrum of which was identical with those of an authentic specimen obtained by the same reaction sequence[14] from 6-deoxy-2,3-O-isopropylidene-L-mannofuranose (*IX*) *via* the derivative *VIII*. It was confirmed in this manner that the dioxolane ring of the isopropylidene derivative *II* is attached to carbon atoms 2 and 3. The size of the oxygen ring, position of the anomeric hydroxylic function as well as the confirmation of the chemical evidence follows for the isopropylidene derivative *II* from its NMR spectrum and the NMR spectrum

TABLE II
(*Continued*)

Ip[a]	OH	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	Note
1·44	4·26	≠ 0[b]	6·0	3·0	7·5	5·9	
1·30	3·29						
1·48	—	≠ 0[b]	6·0	3·1	8·6	6·2	$J_{1,4} = 0$[b]
1·31							
—	—	4·0	4·0	4·0	1·5	6·7	$J_{1,3} = 1{,}0$
—	—	8·7	3·5	3·8	1·5	6·5	$J_{1,5} \neq 0$[b]
—	5·0[c]	4·2	3·8	3·5	1·0	6·7	$J_{1,3} = 0{\cdot}4$[c]
	4·0						
—	4·36	3·5	3·4	3·4	1·0	6·7	$J_{1,3} = 1{,}0$
	3·80						$J_{1,5} \neq 0$[b]
1·54	—	4·0	6·3	2·2	1·9	6·7	
1·34							
1·54	—	—	—	—	2·7	6·7	$\delta_{OSO_2CH_3} = 3{\cdot}11$
1·36							

[a] The abbreviation Ip designates the O-isopropylidene group; [b] unresolved splitting, $J \neq 0$ confirmed by double resonance experiments; [c] an approximate value; [d] an additional signal of the O-acyl group at 2·07 p.p.m. was present; [e] a complex multiplet, an approximate medium value, confirmed by double resonance experiments.

of its di-O-acetyl derivative *X*, obtained by acetylation of compound *II* with acetic anhydride in pyridine. NMR spectrum of compound *II* (in deuteriochloroform) exhibits characteristic singlets of methyl protons of the O-isopropylidene group at 1·44 p.p.m. and 1·30 p.p.m. and a doublet of the secondary methyl group at 1·28 p.p.m. (J = 5·9). Protons of two hydroxylic functions (formation of broad signals at 4·26 p.p.m. and 3·29 p.p.m.) were identified by an exchange experiment (by the addition of CD_3COOD). Addition of deuterated acetic acid caused also contraction of two proton signals resulting in the formation of a singlet at 5·41 p.p.m. and a complex multiplet in the 3·95–4·25 p.p.m. region. On the basis of chemical shift, the singlet at 5·41 p.p.m. is attributable to the anomeric $H_{(1)}$ proton and the multiplet centered at 4·13 p.p.m. is indicative of the proton in interaction with the secondary methyl group (confirmed by double resonance experiments), *i.e.*, the

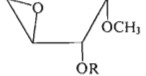
proton at $C_{(5)}$. Consequently, both hydroxylic functions should be secondary and attached at positions 1 and 5. For this reason, the isopropylidene derivative *II* possesses obviously the furanoid structure. The complete assignment of protons in spectrum of compound *II* was performed by the double resosnance method (for all characteristic parameters see Table II). The observed continuity of vicinal interaction constants and distribution of chemical shift indicates the structure of 6-deoxy-2,3-O-isopropylidene-β-D-gulofuranose for compound *II*, in accordance with reported NMR spectra of analogous compounds, *e.g.*, methyl 2,3-O-isopropylidene-β-D-gulofuranoside[15]. The same conclusions were arrived by a detailed NMR analysis of the diacetyl derivative *X*. In accordance with position of hydroxylic functions in spectrum of compound *II*, the signals of $H_{(1)}$ and $H_{(5)}$ protons of compound *X* exhibited a characteristic shift towards a lower field (roughly 1 p.p.m.).

As shown in the preceding paragraphs, hydrolysis of the anhydro derivative *I* affords the guloside *III* only in a low yield and in admixture with methyl 6-deoxy-α-D-glucopyranoside which may be separated only with difficulty. For this reason we drew our attention to the hydrolysis of methyl 2-O-acetyl-3,4-anhydro-6-deoxy-α-D-galactopyranoside (*XI*) with aqueous sulfuric acid in acetone. As shown by Buchanan[16,17] on some anhydro derivatives, the neighbouring *trans*-O-acetyl group exerts a directive influence on the scission of the adjacent epoxide ring by acidic reagents (see Scheme 1). Consequently, such a scission proceeds stereospecifically. It has been determined by thin-layer chromatography on silica gel that after heating for $5^1/_2$ hours the reaction mixture is free of the acetyl derivative (in contrast to the unsubstituted derivative *I*). The dominant reaction products are represented by two compounds possessing very close R_F values one of which is identical with that of the isopropylidene derivative *II*. Alkaline deacetylation of this reaction mixture led to disappearance of both compounds mentioned in favour of the guloside *III*. As shown by thin-layer chromatography on silica gel impregnated with a borate buffer solution, the guloside *III* did not contain any methyl 6-deoxy-α-D-glucopyranoside. After a longer heating of the derivative *XI* with aqueous sulfuric acid in acetone and the subsequent alkaline deacetylation, the reaction mixture contained the isopropylidene derivative *II*.

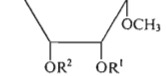
After the hydrolysis of the acetyl derivative *XI*, three different procedures were used to isolate the reaction products. Procedure (*A*) was applied to the reaction mixture which did not contain any isopropylidene derivative *II* (after the hydrolysis period of $5^1/_2$ hours). The reaction mixture was acetylated with acetic anhydride in pyridine, the product purified by crystallisation, and the mother liquors processed on a column of silica gel to afford about 80% of the methyl 2,3,4-tri-O-acetyl-6-deoxy-α-D-gulopyranoside (*XII*) and 2% of 1,2,3,4-tetra-O-acetyl-6-deoxy-β-D-gulopyranose (*XIII*) as the by-product. Procedure (*B*) was applied to the same reaction mixture which, however, was not subjected to the additional acetylation. As shown by thin-layer chromatography, the reaction mixture contains predominantly the mono-O

acetyl derivatives as products of the hydrolytical cleavage of the anhydro derivative *XI*. The crystalline methyl 3-O-acetyl-6-deoxy-α-D-gulopyranoside (*XIV*) was isolated in a pure state while the 2-O-acetyl derivative *XV* contained always a small amount of another mono-O-acetyl derivative, as shown by NMR spectrum. When the hydrolysis of the acetyl derivative *XI* was performed for longer periods of time, *i.e.*, when the resulting mixture contained also the isopropylidene derivative *II*, the isolation procedure (*C*) was used. In this case, the reaction mixture was deacetylated* with methanolic sodium methoxide and then chromatographed on a column of silica gel. After a 16 hours' hydrolysis of the anhydro derivative *XI*, the reaction mixture contained 5·3% of the isopropylidene derivative *II* and 70% of the guloside *III*, while 14% of *II* and 55% of *III* was isolated after 27 hours.

Acetylation of compound *III* with acetic anhydride in pyridine afforded the crystalline peracetyl derivative *XII*, identical with the specimen isolated from the reaction mixture by procedure (*A*). The NMR spectrum of compound *XII* exhibits three singlets of acetyl groups (2·05, 2·105, and 2·15 p.p.m.), a singlet characteristic of the methoxyl group at 3·42 p.p.m., and a doublet of the secondary methyl group at 1·13 p.p.m. indicative of the methyl group attached to carbon atom $C_{(5)}$. The assignment of protons was performed by means of double resonance experiment. Thus, the $H_{(5)}$ proton formed an octet at 4·335 p.p.m. ($J_{5,6} = 6·7$, $J_{5,4} = 1·5$) and exhibited interaction with a further $H_{(4)}$ proton, forming a quartet at 4·83 p.p.m. ($J_{4,5} = 1·5$ and $J_{4,3} = 4·0$). In the 5·10–5·30 p.p.m. region, there was present a complex multiplet (relative intensity 2 H), formed by a triplet of $H_{(3)}$ proton at 5·16 p.p.m. ($J_{3,4} = 4·0$, $J_{3,2} = 4·0$, and $J_{3,1} = 1·0$) and a triplet of $H_{(2)}$ proton at 5·07 p.p.m. ($J_{2,3} = 4·0$, $J_{2,1} = 4·0$). The anomeric $H_{(1)}$ proton formed a broad doublet at 4·77 p.p.m. ($J_{1,2} = 4·0$ and $J_{1,3} = 1·0$). Position of the $H_{(5)}$ proton in spectrum indicates the pyranoid structure of compound *XII* and, consequently,



I, R = H
XI, R = CH_3CO



III, $R^1 = R^2 = R^3 = H$
XII, $R^1 = R^2 = R^3 = CH_3CO$
XIV, $R^1 = R^3 = H$, $R^2 = CH_3CO$
XV, $R^1 = CH_3CO$, $R^2 = R^3 = H$

XVI, R = H
XVII, R = CH_3CO
XVIII, R = CH_3SO_2

SCHEME 2

* Since the R_F values of the acetyl derivatives *X* and *XIII* in procedure (*A*) are almost identical, procedure (*C*) is more advantageous.

the parent derivative *III* (*cf.* ref.[18]). Furthermore, the magnitudes of all observed vicinal interactions of $H_{(1)}-H_{(5)}$ protons in the derivative *XII* indicate that their relative arrangement is axial-equatorial or equatorial-equatorial which corresponds to the Cl conformation of the derivative *XII* and the α-configuration at the anomeric center.

The tetra-O-acetyl derivative *XIII*, isolated as the minor product by the $5^1/_2$ hours' hydrolysis of the anhydro derivative *XI*, was obtained in a high yield also by acetylation of 6-deoxy-D-gulose (*IV*) with acetic anhydride in pyridine. NMR spectrum of compound *XIII* exhibits singlets of four O-acetyl groups at 1·99, 2·10, 2·13, and 2·16 p.p.m. and a doublet of the secondary methyl group on $C_{(5)}$ at 1·19 p.p.m. There was present also an octet of the $H_{(5)}$ proton at 4·27 p.p.m. ($J_{5,6} = 6·5$ and $J_{5,4} = 1·5$), a quartet of the $H_{(4)}$ proton at 4·88 p.p.m. ($J_{4,5} = 1·5$ and $J_{4,3} = 3·8$), a triplet of the $H_{(3)}$ proton at 5·41 p.p.m. ($J_{3,4} = 3·8$ and $J_{3,2} = 3·5$), and a quartet of the $H_{(2)}$ proton at 5·10 p.p.m. ($J_{2,3} = 3·5$ and $J_{2,1} = 8·7$). The anomeric $H_{(1)}$ proton formed a doublet at 5·99 p.p.m. ($J_{1,2} = 8·7$). Comparison of NMR spectral data of the derivative *XIII* with those of the derivative *XII* shows that compound *XIII* also possesses the pyranoid structure with a Cl conformation and β-D-configuration of the O-acetyl group at carbon atom $C_{(1)}$. The β-D-configuration of compound *XIII* is also favoured by the low value of optical rotation of the derivative *XIII*.

The NMR spectral data (Table II) are also in accordance with the structure of derivatives *XIV* and *XV* (isolated by procedure *B*) and position of their O-acyl group.

Reaction of glycoside *III* with acetone in the presence of anhydrous copper sulfate afforded sirupous methyl 6-deoxy-2,3-O-isopropylidene-α-D-gulopyranoside (*XVI*). On acetylation with acetic anhydride or mesylation with methanesulfonyl chloride in pyridine, the isopropylidene derivative *XVI* was converted to the crystalline acetyl derivative *XVII* and the mesyl derivative *XVIII*, respectively. Structures *XVII* and *XVIII* were confirmed by analysis of the NMR spectral data (see Table II) with the use of double resonance experiment.

As it may be seen from the above hydrolytical experiments with the anhydro derivative *I* and its 2-O-acetyl derivative *XI* under otherwise identical conditions, the composition of the reaction mixture after hydrolysis is quite different. The isopropylidene derivative *II* obtained as the predominant product in hydrolysis of the anhydro derivative *I*, is obviously formed by condensation of 6-deoxy-D-gulose (*IV*) with acetone. This idea is favoured by the formation of more than 80% of the isopropylidene derivative *II* on heating compound *IV* in an analogous reaction medium and for the same period of time as in the case of the hydrolysis of derivatives *I* and *XI*. Hydrolysis of the unsubstituted anhydro derivative *I* occurs stereospecifically under the predominant formation of the glycoside *III* which is then fastly hydrolysed to the reducing sugar *IV*. Condensation of compound *IV* with acetone affords the isopropylidene derivative *II*. In the case of the acetylated anhydro derivative *XI*, the hydrolysis proceeds stereoselectively under the formation of the mono-O-acetyl derivatives *XIV*

and *XV* both of which (or at least one of them) are hydrolysed to compound *Ie* but this hydrolysis is much slower (compound *IV* has been isolated in the form of th*V* derivative *XIII* in the case of the $5^1/_2$ hours' hydrolysis). This retardation might be due to suppression of protonisation (necessary for acidic hydrolysis of glycosidic bond) of acetal oxygens in the obviously predominant intermediate given in Scheme 1. Moreover, the epoxide ring cleavage occurs more readily with the derivative *XI* than in the case of the unsubstituted compound *I*. Consequently, the hydrolysis of compound *XI* affords, in contrast to compound *I*, a high yield of the glycoside *III*.

EXPERIMENTAL

Melting points were taken on a heated microscope stage (Kofler block) and are uncorrected. Mixed melting points were determined in a capillary. Optical rotation was measured on an Opton apparatus at 21°C. Analytical specimens were dried for 8–10 hours at 0·1 Torr and room temperature. Solvents were taken down on a rotatory evaporator at max. 45°C/15 Torr. Crystallisations were performed with the light petroleum fraction, b.p. 45–60°C. Dowex 50 W cation exchange resin and Amberlite IRA 400 anion exchange resin were used for deionisations. Thin-layer chromatography was performed on silica gel G Merck (with gypsum). Chromatography "C" was performed on 25 × 75 mm plates; chromatograms were detected by a spray with a 5% solution of ceric sulfate in 10% aqueous sulfuric acid and heating. Chromatography "CB" was performed on 105 × 240 mm plates coated with a suspension of silica gel G (3 g) in 6 ml of s solution prepared from 100 ml of 0·02M boric acid and 3 ml of 0·02M sodium tetraborate[19], dried on air and then at 100°C for 30 minutes. Spots were detected by a spray with the α-naphthol reagent and heating at 100°C for 3–6 minutes. Preparative chromatography was performed on silica gel produced by Lachema, Brno, Czechoslovakia.

Hydrolysis of the Anhydro Galactoside *I*

Preliminary experiments. A solution of the anhydro galactoside *I* (50 mg) in 2 ml of the corresponding solvent or solvent mixture (water; 1 : 1 methanol–water; 1 : 1 acetone–water; dioxane; tetrahydrofuran; acetone; acetic acid) was treated (except for the acetic acid experiment) with 0·5M-H_2SO_4 (0·1 ml) and the whole heated at 80°C. Samples were withdrawn at certain intervals and subjected to chromatography "C" in 5 : 1 chloroform–ethanol with the use of an aqueous solution of the anhydro galactoside *I*, methyl 6-deoxy-α-D-glucopyranoside[20], and 6-deoxy-D-glucose[21] as the reference mixture (1 : 1 : 1).

Hydrolysis in acetone. A solution containing the anhydro galactoside *I* (1·00 g), acetone (50 ml), and sulfuric acid of the corresponding concentration (1 ml) was boiled for the period of time given in Table I. The reaction mixture was then neutralised with solid barium carbonate, filtered, the filtrate evaporated to dryness, and the residue chromatographed on a column of silica gel (50 g). The purity of eluates was checked by chromatography "C" in 5 : 1 chloroform–ethanol. Compounds *I* and *II* were eluted with 100 : 3 benzene–ethanol, the glycosidic material (compound *III* and the *gluco*-isomer) was eluted with 10 : 1 benzene–ethanol. The isopropylidene derivative *II* was recrystallised from a mixture of ethyl acetate and light petroleum, m.p. 104–106°C. Optical rotation: $[\alpha]_D$ −34·6 ± 1° (*c* 1·1, chloroform; after 2 hours, the rotation value was the same). Infrared spectra: characteristic absorptions at 3600, 3420 (broad band), 2990, 1240, 1170, and 1110 cm^{-1}. For $C_9H_{16}O_5$ (204·2) calculated: 52·93% C, 7·90% H; found: 53·04% C, 7·97% H. As shown by chromatography "CB" in 5 : 4 : 1 n-butyl alcohol–acetic acid–water, the glycosidic material represents a mixture of compound *III* and methyl 6-deoxy-α-D-glucopyranoside (com-

pound *III* predominates). When this mixture was heated for one hour with 0·5M-H_2SO_4, the hydrolysate contained mainly the compound *IV* along with 6-deoxy-D-glucose[21], as shown by chromatography "CB".

Hydrolysis of the Isopropylidene Derivative *II*

A solution of compound *II* (196 mg) in 0·005M-H_2SO_4 (40 ml) was heated at 80°C for one hour and neutralised by shaking with an anion exchange resin. The resin was filtered off, the filtrate evaporated to dryness, the residue dried, and triturated with a small amount of ethyl acetate–ethanol to solidify. The solid (157 mg) was crystallised three times from the same mixture of solvents: m.p. of compound *IV*, 125–129°C, reported[7], m.p. 130–131°C and[11] 130–134°C. Optical rotation: $[\alpha]_D$ −45·6° → 41·6° (*c* 0·8, water; constant after 3 hours); reported[7], $[\alpha]_D$ −42·3° → → −38° (water) and [11] $[\alpha]_D$ −39·3° (water).

Reduction of Compound *IV*

A solution of compound *IV* (105 mg) in water (10 ml) was treated with sodium borohydride (25 mg), the whole stirred at room temperature for 8 hours, shaken with a cation exchange resin, and filtered. The filtrate was evaporated to dryness, the residue coevaporated with methanol, and crystallised twice from ethanol–light petroleum to afford 56 mg of compound *V*, m.p. 130 to 131·5°C, $[\alpha]_D$ −3·0° (*c* 1·4, water); reported[12], m.p. 130–132°C, $[\alpha]_D$ −2·3° (water). For the L-enantiomer reported[12], m.p. 133–134°C, $[\alpha]_D$ +4·5° (water), and[22] m.p. 131–132°C, $[\alpha]_D$ +3·97 ± 0·5° (water). Infrared spectra of compound *V* and its L-enantiomer[12] were identical.

2,3-O-Isopropylidene-β-L-erythrofuranose (*VII*)

a) *From the isopropylidene derivative* II. A solution of compound *II* (148 mg) in water (5 ml) was treated under stirring with sodium borohydride (76 mg) and the whole stirred at room temperature for 30 minutes. Cation exchange resin was then added, the reaction mixture filtered, the filtrate evaporated to dryness and the residue coevaporated with two 25 ml portions of methanol. The residual sirup *VI* (146 mg) was chromatographically homogeneous as shown by chromatography "C" in 5 : 1 chloroform–ethanol. Compound *VI* was dissolved in water (5 ml) and this solution treated portionwise under stirring at 10°C with sodium periodate (160 mg). The reaction mixture was stirred at room temperature for one hour, extracted with five 15 ml portions of ethyl acetate, the combined extracts washed with water (10 ml), dried over sodium sulfate, and evaporated to dryness. The residue was briefly dried at 0·1 Torr and cooled in a mixture of dry ice and acetone to deposit crystals which were purified by sublimation at 0·05 Torr and room temperature. Yield, 95 mg of compound *VII*, m.p. 29–31°C, $[\alpha]_D$ +76·6° (*c* 0·8, methanol). Infrared and mass spectra of compound *VII* were identical with those of the specimen obtained from the derivative *IX*.

b) *From the derivative* IX. A slightly modified reported[14] procedure was used to convert compound *IX* (500 mg) into the derivative *VII* (282 mg) which was purified under the above mentioned conditions. Optical rotation: $[\alpha]_D$ +76·1° (*c* 0·9, methanol); reported[14], $[\alpha]_D$ +72° (*c* 2·4, methanol).

Hydrolysis of the Acetyl Anhydro Derivative *XI*

Procedure A. A solution containing compound *XI* (2·00 g; 9·9 mmol), acetone (100 ml), and 0·25M-H_2SO_4 (2 ml) was refluxed for $5^1/_2$ hours, neutralised with solid barium carbonate, filtered, and the filtrate evaporated to dryness under diminished pressure. The semicrystalline

residue was dissolved in pyridine (30 ml), the solution treated with acetic anhydride (4 ml), the resulting mixture allowed to stand at room temperature for 48 hours, decomposed with water, and extracted with chloroform (100 ml). The extract was washed successively with 15% aqueous sulfuric acid, water, 5% aqueous sodium hydrogen carbonate, and water again, dried over magnesium sulfate, and evaporated to dryness. The residue (2·67 g) was recrystallised from light petroleum to afford 2·16 g (72%) of the peracetyl glycoside *XII*, m.p. 80–82°C. The mother liquor was evaporated to dryness and the residue chromatographed on a column of silica gel (30 g) to afford (benzene or 200 : 1 benzene–ethanol as eluants) 63 mg (2%) of the chromatographically homogeneous compound *XIII*, 128 mg of a mixture of compounds *XII* and *XIII*, and 207 mg (6·9%) of compound *XII*. Overall yield of compound *XII*, 79%. The analytical sample of the peracetyl glycoside *XII* was recrystallised twice from light petroleum; m.p. 81–83°C; $[\alpha]_D$ +107·0 ± 1·0° (*c* 1, chloroform). For $C_{13}H_{20}O_8$ (304·3) calculated: 51·31% C, 6·63% H; found: 51·63% C, 6·67% H. The derivative *XIII* was recrystallised from a mixture of ethanol and light petroleum; m.p. 138–139°C, undepressed on admixture with a specimen obtained by acetylation of compound *IV* (the infrared spectra of both specimen of compound *XIII* were identical).

Procedure B. Reaction mixture obtained by hydrolysis of the acetyl anhydro derivative *XI* was processed as above up to the neutralisation step with barium carbonate. The acetonic solution was evaporated and the residue applied to a column of silica gel (100 g) which was eluted with 50 ml portions of 100 : 3 benzene–ethanol. Fractions 1–20 afforded a sirupous residue consisting mainly of the 2-O-acetyl derivative *XV*, as shown by chromatography "C" in 10 : 1 benzene–ethanol. Fractions 21–30 afforded the crystalline 3-O-acetyl derivative *XIV*. Fractions 1–20 were rechromatographed on silica gel, but the residue was s'rupous again and consisted mainly of the 2-O-acetyl derivative *XV*, as shown by NMR spectra. After a twofold crystallisation of collected crystalline fractions from a mixture of ethyl acetate and light petroleum, compound *XIV* melted at 143·5–145·5°C; $[\alpha]_D$ +112·0 ± 1° (*c* 0·8, chloroform). For $C_9H_{16}O_6$ (220·2) calculated: 49·09% C, 7·32% H; found: 48·98% C, 7·22% H.

Procedure C. A solution containing the acetyl anhydro derivative *XI* (1·00 g), acetone (50 ml), and 0·25M-H_2SO_4 (1 ml) was refluxed for 16 hours, neutralised with barium carbonate, filtered, and the filtrate evaporated to dryness. The residue was dissolved in methanol (20 ml), the solution treated with 1M-$NaOCH_3$ in methanol (1 ml), the whole kept at room temperature overnight, neutralised with gaseous carbon dioxide, and evaporated to dryness. The residue was chromatographed on a column of silica gel (50 g). Elution with 100 : 3 benzene–ethanol afforded 53 mg (5·3%) of the isopropylidene derivative *II*; elution with 10 : 1 benzene–ethanol furnished 618 mg (70%) of the sirupous derivative *III*. The 27 hours' hydrolysis was performed similarly. After recrystallisation from a mixture of ethyl acetate and light petroleum, the isopropylidene derivative *II* melted at 104–105·5°C, $[\alpha]_D$ −35·6° (*c* 0·8, chloroform). The sirupous derivative *III* was redistilled for analysis at 150°C (bath temperature)/0·05 Torr; $[\alpha]_D$ +111·0° (*c* 1·0, water). For $C_7H_{14}O_5$ (178·2) calculated: 47·19% C, 7·92% H; found: 47·45% C, 7·91% H.

Methyl 6-Deoxy-2,3-O-isopropylidene-α-D-gulopyranoside (*XVI*)

A solution of compound *III* (1080 mg) in acetone (100 ml) was treated with freshly calcinated copper sulfate (15 g) and the whole shaken for 27 hours. The inorganic salt was filtered off and the filtrate evaporated to dryness. The sirupous residue was diluted with water (50 ml) and extracted with three 50 ml portions of chloroform. The extracts were combined, dried over magnesium sulfate, and evaporated to dryness to afford 1096 mg (83%) of the sirupous derivative *XVI* which was redistilled for analysis at 115°C (bath)/0·05 Torr. Optical rotation: $[\alpha]_D$ +64·5° (*c* 0·8, chloroform). For $C_{10}H_{18}O_5$ (218·2) calculated: 55·03% C, 8·34% H; found: 55·03% C, 8·29% H. Evaporation of the aqueous layer afforded the unreacted starting compound *III*.

Methyl 6-Deoxy-2,3-O-isopropylidene-4-O-methanesulfonyl-α-D-gulopyranoside (*XVIII*)

Methanesulfonyl chloride (0·4 ml) was added at −70°C to a mixture of the isopropylidene derivative *XVI* (603 mg) and pyridine (10 ml). The reaction mixture was allowed to stand at −15°C for 48 hours, decomposed with water, and diluted with chloroform (50 ml). This mixture was washed successively with 15% aqueous sulfuric acid, water, 5% aqueous sodium hydrogen carbonate, and water again. The chloroform solution was then dried over sodium sulfate and the solvent evaporated. Recrystallisation of the residue from a mixture of ethyl acetate and light petroleum afforded 675 mg (82·5%) of compound *XVIII*, m.p. 110−113°C (m.p. of the analytical sample, 112−114°C). Optical rotation: $[\alpha]_D$ +71·7° (*c* 0·8, chloroform). For $C_{11}H_{20}O_7S$ (296·3) calculated: 44·59% C, 6·80% H, 10·82% S; found: 44·80% C, 6·85% H, 10·70% S.

Preparation of the Acetyl Derivatives

The compound to be acetylated was dissolved in pyridine, the solution treated with a 3−5 fold excess of acetic anhydride, the whole mixture allowed to stand at room temperature for 24−48 hours, decomposed with water, diluted with chloroform, and the chloroform layer washed successively with 15% aqueous sulfuric acid, water, 5% aqueous sodium hydrogen carbonate, and water again. After drying over sodium sulfate, the chloroform solution was evaporated to dryness under diminished pressure.

1,5-*Di*-O-*acetyl*-6-*deoxy*-2,3-O-*isopropylidene*-β-D-*gulofuranose* (X). From 150 mg of compound *II*, there was obtained (after recrystallisation from light petroleum) 181 mg (86%) of compound *X*, m.p. 104·5−105·5°C. After several recrystallisations from the same solvent, the melting point was 106−106·5°C. Optical rotation: $[\alpha]_D$ −55·2° (*c* 0·6, chloroform). For $C_{13}H_{20}O_7$ (288·3) calculated: 54·16% C, 6·99% H; found: 54·40% C, 6·97% H.

Methyl 2,3,4-*tri*-O-*acetyl*-6-*deoxy*-α-D-*gulopyranoside* (XII). From 58 mg of compound *III*, there was obtained 96 mg (97%) of compound *XII*, m.p. 78−80°C. After recrystallisation from light petroleum, the melting point was 82−83°C. Optical rotation: $[\alpha]_D$ +107·5° (*c* 1, chloroform), The derivative *XII* was identical (infrared spectra, mixed melting point) with a specimen obtained from compound *XI* by procedure *A*.

1,2,3,4-*Tetra*-O-*acetyl*-6-*deoxy*-β-D-*gulopyranose* (XIII). From 105 mg of compound *IV*, there was obtained 210 mg of a solid the recrystallisation of which from a mixture of ethanol and light petroleum afforded 136 mg of the derivative *XIII*, m.p. 137−139°C, $[\alpha]_D$ +5·2° (*c* 2·2, chloroform). Evaporation of mother liquours and crystallisation of the residue from the same solvent mixture afforded another crop of compound *XIII* (34 mg) of the same melting point. Overall yield, 80%. For $C_{14}H_{20}O_9$ (332·2) calculated: 50·60% C, 6·07% H; found: 50·71% C, 6·00% H.

Methyl 4-O-*acetyl*-6-*deoxy*-2,3-O-*isopropylidene*-α-D-*gulopyranoside* (XVII). From 63 mg of the isopropylidene derivative *XVI*, there was obtained (after recrystallisation from light petroleum) 50 mg of the derivative *XVII*, m.p. 66−67·5°C (m.p. of the analytical sample, 68 to 69·5°C). Optical rotation: $[\alpha]_D$ +64·1° (*c* 0·6, chloroform). For $C_{12}H_{20}O_6$ (260·3) calculated: 55·37% C, 7·75% H; found: 55·24% C, 7·78% H.

Preparation of the Isopropylidene Derivative *II* from Compound *IV*.

A mixture of compound *IV* (189 mg), acetone (50 ml), and 0·25M-H_2SO_4 (1 ml) was refluxed for 27 hours, neutralised with solid barium carbonate, and filtered. The filtrate was evaporated to dryness, the residue diluted with water (25 ml), and the aqueous solution extracted with six 25 ml portions of ethyl acetate. The extracts were combined and evaporated to dryness under

diminished pressure to afford 190 mg (81%) of the chromatographically homogeneous (as shown by chromatography "C" in 10 : 1 benzene–ethanol) compound *II*, m.p. 103·5–105·5°C, undepressed on admixture with specimens obtained from compounds *I* or *XI* (infrared spectra of all these specimens were also identical). Optical rotation: $[\alpha]_D$ −35·1° (*c* 0·9, chloroform). The aqueous layer represented a mixture of compounds *II* and *IV*, as shown by chromatography "C".

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REFERENCES

1. Stevens C. L., Glinski R. P., Taylor K. G., Blumbergs P., Sirokman F.: J. Am. Chem. Soc. *88*, 2073 (1966).
2. Hanessian S.: Chem. Commun. *1966*, 796.
3. Brimacombe J. S., Ching O. A., Stacey M.: J. Chem. Soc. (C) *1969*, 1270.
4. Jarý J., Novák P., Samek Z.: Chem. Ind. (London) *1967*, 1490.
5. Jarý J., Novák P., Samek Z.: This Journal *33*, 1744 (1968).
6. Kiliani H.: Arch. Pharm. *234*, 438 (1896).
7. Levene P. A., Compton J.: J. Biol. Chem. *111*, 335 (1935).
8. Jarý J., Čapek K.: This Journal *31*, 315 (1966).
9. Čapek K., Jarý J.: This Journal *31*, 2558 (1966).
10. Čapek K., Němec J., Jarý J.: This Journal *33*, 1758 (1968).
11. Kaufmann H.: Helv. Chim. Acta *48*, 769 (1965).
12. Bollenback G. N., Unerkofler L. A.: J. Am. Chem. Soc. *72*, 741 (1950).
13. Lerner L. M.: Carb. Res. *9*, 1 (1969).
14. Baxter J. N., Perlin A. S.: Can. J. Chem. *38*, 2217 (1960).
15. Arzoumanian H., Acton E. M., Goodman L.: J. Am. Chem. Soc. *86*, 74 (1964).
16. Buchanan J. G.: J. Chem. Soc. *1958*, 2511.
17. Buchanan J. G., Fletcher R.: J. Chem. Soc. *1965*, 6316.
18. Lemieux R. U., Stevens J. D.: Can. J. Chem. *43*, 2059 (1965).
19. Jacin H., Mishkin A. R.: J. Chromatog. *18*, 170 (1965).
20. Evans M. E., Long L. J., Parrish F. W.: J. Org. Chem. *33*, 1074 (1968).
21. Votoček E.: Ber. *44*, 819 (1911).
22. Müller H., Reichstein K.: Helv. Chem. Acta *21*, 251 (1938).

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