PREPARATION OF 6-AMINO-6-DEOXY-D-ALLONIC AND 6-AMINO-6-DEOXY-D-GLUCONIC ACID

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Partial tosylation of monoisopropylidene glucose *I* and monoisopropylidene allose *II* gave their 6-O-tosyl derivatives *III* and *IV* which were further converted to 6-azido-6-deoxy-D-glucose (*XV*) and 6-azido-6-deoxy-D-allose (*XVI*) *via* 5,6-anhydrocompounds *XII* and *X* as intermediates. Oxidation of the products gave corresponding lactones *XVIII* and *XVII*. On their catalytic hydrogenation in methanol lactams *XXII* and *XXI* were prepared, while hydrogenation in water gave 6-amino-6-deoxy-D-allonic (*XXIII*) and 6-amino-6-deoxy-D-gluconic (*XXIV*) acids.

The knowledge of a biological activity of ε-aminocaproic acid[1] led us to the idea of preparing some of their hydroxylated analogues from the sugar series – 6-amino--6-deoxyhexonic acids. With the exception of the isomer of D-*galacto* configuration[2] these compounds have not yet been described so far, but some derivatives of them are already known. Weidmann and Fauland[3] prepared the lactam of 6-amino-6-deoxy-D-gulonic acid by catalytic hydrogenation of the oxime of D-glucuronic acid, while Hanessian[4] prepared the lactams of 6-amino-6-deoxy-D-gluconic acid and 6-amino--6-deoxy-D-galactonic acid on catalytic hydrogenation of lactones of corresponding 6-azido-6-deoxyaldonic acids in methanolic solution.

In this paper we describe the preparation of 6-amino-6-deoxy-D-gluconic and 6-amino-6-deoxy-D-allonic acids. The starting 1,2-O-isopropylidene-α-D-glucofuranose (*I*) or 1,2-O-isopropylidene-α-D-allofuranose (*II*) was submitted to partial tosylation with 1·2 equivalents of *p*-toluenesulfonyl chloride at low temperature. The mixture obtained was separated by preparative column chromatography on silica gel. Pure 6-O-tosyl derivative of *allo* configuration *IV* was thus obtained in a better yield than when purification was carried out by crystallization, as described earlier[5]. As evident from the data in Table I the composition of the reaction mixture after tosylation of monoisopropylidene hexose *I* and *II* is quite different. While the *gluco* isomer *I* mostly affords the 6-O-tosyl derivative *III*, the *allo* isomer *II* affords a more complex mixture in which 3-O-tosyl derivative *V*, 5-O-tosyl derivative *VI* and 3,6-di-O-tosyl derivative *VII* are present in addition to 6-O-tosyl derivative *IV*. The change in the molar ratio hexose/*p*-toluenesulfonyl chloride in both directions or the change of the reaction time did not lead to an increase in the yield of 6-O-tosyl derivative *IV*.

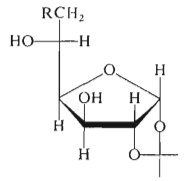
When the tosylation of *allo* isomer was followed with thin-layer chromatography, it was observed that the 3-O-tosyl derivative *V* is already formed at the initial stage of the reaction, in contrast to the *gluco* isomer; the formation of the compound *V* and its subsequent conversion to 3,6-di-O-tosyl derivative *VII* are evidently the reason for the lower yield of 6-O-tosyl derivative *IV*. It may be judged from a comparison of the steric models that the higher reactivity of the hydroxyl group in the position 3 of the *allo* isomer *II* – as compared with *gluco* isomer *I* – is evidently not due to its steric accessibility. In the *allo* isomer *II* this hydroxyl group is namely in the less advantageous *endo* position, with respect to the two *cis*-condensed five-membered rings. More probably the dominant effect is exerted by the intramolecular hydrogen bond $C_{(3)}$—O···H → O—$C_{(2)}$ which can be formed in the *allo* isomer but not in the *gluco* isomer[6]. The structure of 3-O-tosyl derivative *V* was proved both by comparison of the physical constants with the literature data[7,8], and by comparison with an authentic sample prepared by partial hydrolysis of 1,2 : 5,6-di-O-isopropylidene-3-O--*p*-toluenesulfonyl-α-D-allofuranose (*VIII*). The structure of di-O-tosyl derivative *VII* in addition to comparison with the described[7,8] data was also checked by conversion to 5,6-anhydro-1,2-O-isopropylidene-3-O-*p*-toluenesulfonyl-α-D-allofuranose (*IX*) the physical data of which coincided with the properties of the preparation obtained by tosylation of 5,6-anhydro-1,2-O-isopropylidene-α-D-allofuranose (*X*). The structure of anhydro derivative *X* and of its 3-O-tosyl derivative *IX* was also confirmed by ^{1}H-NMR spectra. When anhydro derivative *X* was tosylated 6-chloro-6-deoxy--1,2-O-isopropylidene-α-D-allofuranose (*XI*) was isolated as a by-product in addition to the 3-O-tosyl derivative *IX*. This compound is evidently formed by the cleavage of the oxirane ring of the anhydro derivative *IX* with pyridinium chloride, as shown by the result of the mutual reaction of the two compounds.

TABLE I

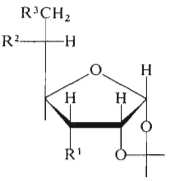
Composition of the Product of Partial Tosylation of Monoisopropylidene Hexoses *I* and *II* with *p*-Toluenesulfonyl Chloride in Pyridine (mol %)

Hexose	Molar ratio sugar : chloride	Ditosyl derivative	6-O-Tosyl derivative	3-O-Tosyl derivative	Starting hexose
gluco (*I*)	1 : 1·2[a]	11·4[c]	80·1	—	1
allo (*II*)	1 : 1·1[b]	10·1[d]	37·0	5·3	36·0
	1 : 1·2[a]	24·4[d]	48·6	4·0[e]	12·5
	1 : 1·3[a]	24·4[d]	49·6	4·7	13·9

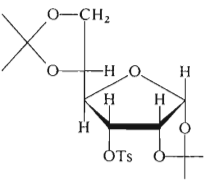
[a] Reaction time 24 h; [b] reaction time 13 h; [c] the structure is not determined; [d] 3,6-di-O-tosyl derivative predominates, other isomers are present in trace amounts; [e] a small amount of a compound of m.p. 173—175°C was also isolated, probably 1,2-O-isopropylidene-5-O-*p*-toluenesulfonyl-α-D-allofuranose[5].



I, R = OH
III, R = OTs
XIII, R = N_3
Ts = *p*-toluenesulfonyl



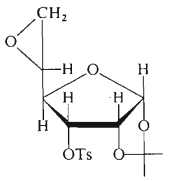
II, $R^1 = R^2 = R^3 = OH$
IV, $R^1 = R^2 = OH$, $R^3 = OTs$
V, $R^2 = R^3 = OH$, $R^1 = OTs$
VI, $R^1 = R^3 = OH$, $R^2 = OTs$
VII, $R^2 = OH$, $R^1 = R^3 = OTs$
XIV, $R^1 = R^2 = OH$, $R^3 = N_3$



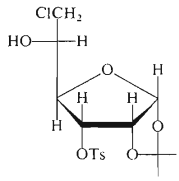
VIII

Tosyl derivatives *III* and *IV* were exposed to the effect of a strong anion exchanger[9] and the 5,6-anhydro-1,2-O-isopropylidene-α-D-glucofuranose (*XII*) and 5,6-anhydro-1,2-O-isopropylidene-α-D-allofuranose (*X*) obtained were converted to 6-azido-6-deoxy-1,2-O-isopropylidene hexose of D-*gluco*- (*XIII*) or D-*allo*- (*XIV*) configuration, respectively, on reaction with sodium azide in 2-methoxyethanol. The preparation of the azido derivatives *via* anhydro derivative seems to be more advantageous in view of the better yields and a considerable saving of time, than the direct substitution of tosyl derivatives *III* and *IV* with sodium azide in boiling acetone, described earlier[5]. 6-Azido-6-deoxy-D-glucose (*XV*) and 6-azido-6-deoxy-D-allose (*XVI*) were prepared on splitting off of the protecting ketal group with a strong cation exchanger in water. When oxidized with bromine water at room temperature aldose *XVI* gave a product to which the structure of the γ-lactone of 6-azido-6-deoxy-D-allonic acid (*XVII*) was assigned on the basis of its elemental analysis and the wave-number of the carbonyl groups, ν(C=O) 1765 cm^{-1}. Oxidation of aldose *XV*, carried out under the same conditions or in water in the presence of barium carbonate afforded a substance after repeated crystallization from 2-propanol, the elemental analysis of which corresponded to a lactone; the wave-number value of the carbonyl group, ν(C=O) 1716 cm^{-1}, confirmed the closing of a six-membered ring and the optical rotation agreed with the described value[4], but the m.p. 114–116°C differed from the value 132°C given for the δ-lactone of 6-azido-6-deoxy-D-gluconic acid (*XVIII*). If the semisolid oxidation product was purified by washing with cold 2-propanol only, crystals of m.p. 131–132°C were obtained the IR spectrum of which was identified with the substance obtained by multiple crystallization. Hence, the assumption seems to be probable that the higher melting and the lower melting crystals are two crystalline modifications of the δ-lactone *XVIII*. An attempt at the isolation of 6-azido-6-deoxy-D-gluconic (*XIX*) and 6-azido-6-deoxy-D-allonic (*XX*) acid from

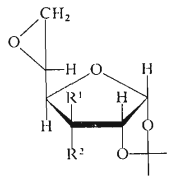
the oxidation product by their retention on a strong anion exchanger and back-elution with dilute acetic acid[10] was unsuccessful. Both acids clearly present in acetic acid eluates very rapidly gave an equilibrium mixture with the corresponding lactones in the course of the working-up procedure. When azido lactones *XVII* and *XVIII* were



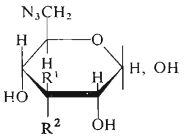
IX



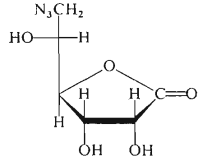
XI



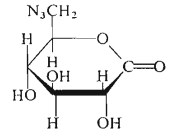
X, $R^1 = H$, $R^2 = OH$
XII, $R^1 = OH$, $R^2 = H$



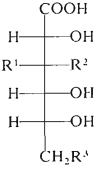
XV, $R^1 = OH$, $R^2 = H$
XVI, $R^1 = H$, $R^2 = OH$



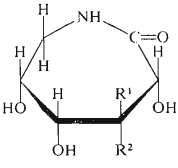
XVII



XVIII



XIX, $R^1 = OH$, $R^2 = H$, $R^3 = N_3$
XX, $R^1 = H$, $R^2 = OH$, $R^3 = N_3$
XXIII, $R^1 = H$, $R^2 = OH$, $R^3 = NH_2$
XXIV, $R^1 = OH$, $R^2 = H$, $R^3 = NH_2$



XXI, $R^1 = H$, $R^2 = OH$
XXII, $R^1 = OH$, $R^2 = H$

reduced with hydrogen on Adams catalyst in methanol lactams *XXI* and *XXII* were obtained of which the *gluco*-isomer *XXII* was on the basis of its constants identical with a described[4] substance. Reduction of azido lactones *XVII* and *XVIII* with hydrogen on Adams catalyst in aqueous medium afforded the required 6-amino-6-deoxy-

-D-allonic (*XXIII*) and 6-amino-6-deoxy-D-gluconic (*XXIV*) acids. For the preparation of these substances by reduction with hydrogen in aqueous solution the equilibrium mixture of the azido acids and their lactones, obtained by oxidation of azido hexoses, could also be used. By their relatively high melting points, zero R_F values in TLC on silica gel in a number of solvents, and the position of the wave-numbers of the carbonyl group in the region of ν(C=O) 1610, 1640 cm^{-1} both 6-amino-aldonic acids confirm the existence of internal salts which stabilize their open chain and prevent lactonization.

EXPERIMENTAL

The melting points were determined on a Kofler block and they are not corrected. Optical rotation values were measured on an Opton instrument at 20°C and 0·5 — 1 g/100 ml concentration. The IR spectra were measured on a Perkin–Elmer 325 instrument, in potassium bromide pellets. The ^{1}H-NMR spectra were measured on a Varian-XL-15 apparatus in deuteriochloroform, using tetramethylsilane as internal reference. The chemical shifts are given in δ-scale (ppm), the coupling constants in Hz. Samples for elemental analysis were dried at room temperature and a 7—15 Pa pressure. Thin-layer chromatography was carried out on silica gel according to Stahl (Merck, Darmstadt) on 25 × 75 mm plates, layer thickness 0·2—0·3 mm, using the following systems for development: S_1 chloroform–methanol 10%, S_2 chloroform–methanol 20%. Detection was carried out with 1% cerium(IV) sulfate in 10% sulfuric acid. Column chromatographies were carried out on silica gel CH (Lachema, Brno), 100—160 μm particle size, using the mixture S_3 (benzene–ethanol 0—5%), S_4 (benzene–ethanol 5%) and S_5 (benzene–ethanol 0 to 10%) for elution. The solvents were evaporated on a rotatory evaporator and under reduced pressure (water pump) at a bath temperature not exceeding 50°C. For crystallization light petroleum boiling at 45—60°C was used.

Partial Tosylation of 1,2-O-Isopropylidene-α-D-glucofuranose (*I*) and 1,2-O-Isopropylidene-α-D-allofuranose (*II*)

A cooled solution of *p*-toluenesulfonyl chloride (the amount corresponded to the selected molar ratio of the reaction components) in 15 ml of chloroform was added dropwise at —30°C and over 5 minutes to a solution of 2·2 g (10 mmol) of monoisopropylidenealdose[11,12] in 15 ml of pyridine. The mixture was allowed to stand at —20°C for 4 h and then at 5°C for 20 h. The tosylation course was monitored by thin-layer chromatography in system S_1. After 24 h reaction time the mixture was decomposed with 1 ml of water and after half-an-hour's standing it was neutralized with a saturated solution of 1·3 g of sodium hydrogen carbonate, then evaporated and the residue was transferred onto a column of 100 g of silica gel. Elution was carried out with system S_5 and the fraction analysed on thin layers in system S_1. The composition of the product determined according to the ratio of the starting substances is given in Table I. The structure of the compounds isolated was checked by comparison with authentic samples and the data from literature: 1,2--O-Isopropylidene-6-O-*p*-toluenesulfonyl-α-D-glucofuranose (*III*), m.p. 106—107°C, lit.[13] gives m.p. 108°C. 1,2-O-Isopropylidene-3,6-di-O-*p*-toluenesulfonyl-α-D-allofuranose (*VII*), m.p. 117 to 118°C, lit.[7] gives m.p. 117—118°C or[8] 120—121°C. 1,2-O-Isopropylidene-6-O-*p*-toluenesulfonyl--α-D-allofuranose (*IV*), m.p. 117—119°C, lit.[5] gives 117—119°C. 1,2-O-Isopropylidene-3-O--*p*-toluenesulfonyl-α-D-allofuranose (*V*), m.p. 153°C, $[\alpha]_D$ +101·2° (pyridine), for $C_{16}H_{22}O_8S$ (374·4) calculated: 51·33% C, 5·92% H, 8·56% S; found: 51·19% C, 6·36% H, 8·32% S, lit.[7]

gives m.p. 130°C, $[\alpha]_D$ +50° (acetone), or[8] m.p. 150—151°C, $[\alpha]_D$ +95° (dimethylformamide), +94° (acetone).

1,2-O-Isopropylidene-6-O-*p*-toluenesulfonyl-α-D-glucofuranose (*III*)

A cooled solution of 16·5 g (87 mmol) of *p*-toluenesulfonyl chloride in 50 ml of chloroform (free of ethanol) was added dropwise at —10 to —15°C under stirring to a cooled solution of 17 g (77 mmol) of monoisopropylidene glucose *I* (ref.[11]) in 70 ml of pyridine and the mixture was allowed to stand at 0°C for 15 h and then one hour at room temperature. During the reaction the mixture was analysed by thin-layer chromatography in system S_1. After 16 h the mixture was decomposed with 20 ml of icy water and extracted with 250 ml of cold diluted hydrochloric acid (1 : 1). The chloroform layer was washed with water, saturated sodium hydrogen carbonate solution and again with water, then dried over magnesium sulfate and evaporated. The residue (28 g) was recrystallized from 200 ml of ether. Yield 19 g (65%) of chromatographically pure monotosyl derivative *III*, m.p. 105—106°C.

5,6-Anhydro-1,2-O-isopropylidene-α-D-allofuranose (*X*)

A solution of 2·8 g (7·5 mmol) of 6-O-tosyl derivative *IV* in 30 ml of methanol was stirred with 30 ml of Dowex-2 (OH^-) at room temperature and the reaction course was followed by thin-layer chromatography in system S_1. After 30 minutes the anion exchanger was filtered off and washed with four 20 ml portions of methanol. The product, obtained by evaporation of the combined filtrates was crystallized from benzene. Yield, 1.42 g (94%) of compound *X*, m.p. 65—68°C, $[\alpha]_D$ +63·5 ± 1·5° (chloroform). For $C_9H_{14}O_5$ (202·2) calculated: 53·46% C, 6·98% H; found: 53·42% C, 7·02% H. ^{1}H-NMR spectrum: 5·78 (1 H, d, $J_{1,2}$ ~3·5, H—1); 4·53(1 H, q, $J_{2,1}$ ~3·5, $J_{2,3}$ ~5, H—2); 3·94 (1 H, q, $J_{4,3}$ ~8·5, $J_{4,5}$ ~2, H—4); 3·25 (1 H, m, $J_{5,4}$ ~2, $J_{5,6} = J_{5,6'}$ ~3·5, H—5); 2·81 (2 H, m, H—6, H—6'); 1·54, 1·35 (2× 3 H, s, $C(CH_3)_2$).

5,6-Anhydro-1,2-O-isopropylidene-α-D-glucofuranose (*XII*)

Using an analogous procedure anhydro derivative *XII* (1·29 g; 59%), m.p. 130—131°C (lit.[14] gives m.p. 133°C) was prepared from 3·74 g (10 mmol) of 6-O-tosyl derivative *III*.

5,6-Anhydro-1,2-O-isopropylidene-3-O-*p*-toluenesulfonyl-α-D-allofuranose (*IX*)

A. A 1M solution of sodium methoxide (1 ml) in methanol was added to a solution of 217 mg of compound *VII* in 10 ml of methanol. The mixture was allowed to stand at room temperature for 90 min, until thin-layer analysis (in S_1) showed that the starting compound had disappeared. After neutralization with carbon dioxide the solvent was evaporated and the residue purified by rapid column chromatography on 10 g of silica gel (elution with S_4). After crystallization from ethanol 128 mg (88%) of compound *IX* were obtained, m.p. 151—152°C, $[\alpha]_D$ +90·3° (chloroform). For $C_{16}H_{20}O_7S$ (356·4) calculated: 53·92% C, 5·66% H, 9·00% S; found: 54·14% C, 5·77% H, 9·47% S. ^{1}H-NMR spectrum: 7·84, 7·34 (2 × 2 H, arom.); 5·71 (1 H, d, $J_{1,2}$ ~3·5, H—1); 4·51 (1 H, q, $J_{2,1}$ ~3·5, $J_{2,3}$ ~5, H—2); 4·44 (1 H, q, $J_{3,2}$ ~5, $J_{3,4}$ ~8, H—3); 4·21 (1 H, q, $J_{4,3}$ ~8, $J_{4,5}$ ~3, H—4); 3·08 (1 H, m, H—5); 2·61 (2 H, m, H—6, H—6'); 2·42 (3 H, s, CH_3); 1·49, 1·26 (2 × 3 H, s, $C(CH_3)_2$).

B. *p*-Toluenesulfonyl chloride (300 mg; 1·58 mmol) in 3 ml of chloroform was added to a solution of compound *X* (146 mg, 0·72 mml) in 5 ml of pyridine at 0°C and the mixture was allowed

to stand at 5°C for 40 h. After working up 234 mg of a material was obtained which was chromatographed on a column of 15 g of silica (elution with S_3). This gave 94 mg of anhydrotosyl derivative *IX*, m.p. 152—153°C, the IR spectrum of which was identical with the spectrum of the substance obtained under *A*. As a by-product 88 mg of crystals of m.p. 138°C (from ethyl acetate) and $[\alpha]_D + 78{\cdot}9°$ (chloroform) were obtained from the chromatography, to which the structure of 6-chloro derivative *XI* was assigned on the basis of the agreement of physical properties and the IR spectra.

6-Chloro-6-deoxy-1,2-O-isopropylidene-3-*p*-O-toluenesulfonyl-α-D-allofuranose (*XI*)

Anhydrotosyl derivative *IX* (50 mg) was dissolved in 3 ml of pyridine containing 1 mmol of pyridinium chloride. The mixture was allowed to stand at room temperature for 17 h, then evaporated and the residue partitioned between water and chloroform. From the chloroform extract 51 mg of a substance were obtained melting at 138—139°C (from ethyl acetate), $[\alpha]_D + 84°$ (chloroform), which was identical with the by-product obtained in the tosylation of anhydro derivative *X* on the basis of IR spectra. For $C_{16}H_{21}ClO_7S$ (392·9) calculated: 48·92% C, 5·39% H, 9·02% Cl, 8·16% S; found: 49·04% C, 5·47% H, 9·57% Cl, 8·14% S.

1,2-O-Isopropylidene-3-O-*p*-toluenesulfonyl-α-D-allofuranose (*V*)

A solution of 1,2:5,6-di-O-isopropylidene-3-O-*p*-toluenesulfonyl-α-D-allofuranose (*VIII*) (414 mg, 1 mmol, ref.[15]) in 20 ml of 50% acetic acid was stirred at 40°C for 4 h. After subsequent 24 h standing at room temperature it was neutralized with potassium carbonate and extracted with chloroform. From the evaporated chloroform extract 248 mg (64%) of compound *V*, melting at 151—153°C and with $[\alpha]_D + 102{\cdot}2°$ (in pyridine), were obtained by crystallization from benzene. The IR spectrum of this compound was identical with the spectrum of tosyl derivative *V* isolated from the product of partial tosylation of monoisopropylidene allose *II*.

6-Azido-6-deoxy-1,2-O-isopropylidene-α-D-glucofuranose (*XIII*)
and 6-Azido-6-deoxy-1,2-O-isopropylidene-α-D-allofuranose (*XIV*)

A mixture of 500 mg (2·48 mmol) of anhydro derivative *XII*, 500 mg of sodium azide and 300 mg of ammonium chloride was heated at 130°C in a solution of 6 ml of ethylene glycol monomethyl ether containing 0·5 ml of water. The reaction course was followed by thin-layer chromatography in system S_1. After 30 min the mixture was evaporated, the residue decolorized with active charcoal in aqueous solution and filtered. The filtrate was extracted with chloroform and the extract evaporated. The residue (650 mg) was crystallized repeatedly from ethyl acetate and light petroleum, affording 280 mg (41%) of azido derivative *XIII*, m.p. 105—106°C; IR spectrum, 2100 cm^{-1}. Literature[16] gives m.p. 104°C for it.

Using the same procedure 636 mg (88%) of azido derivative *XIV* were obtained from 620 mg of anhydro derivative *X*. M.p. of the product was 115—116°C (benzene) and other physical data were in agreement with the data of the described preparation[5].

6-Azido-6-deoxy-D-glucose (*XV*) and 6-Azido-6-deoxy-D-allose (*XVI*)

A solution of 5·9 g (21·6 mmol) of isopropylidene derivative *XIII* in 50 ml of water was stirred with 50 ml of cation exchanger Dowex-50 W (H^+) at 60°C for 30 min. The reaction course was monitored with thin-layer chromatography in system S_1. The cation exchanger was filtered and washed with water and the combined filtrates evaporated. Yield, 4·43 g of azidoaldose *XV*,

which had m.p. 130—132°C after crystallization from 2-propanol. IR spectrum, 2120 cm^{-1}. Literature[4] gives m.p. 128—130°C.

Using an analogous procedure 980 mg (84%) of azidoaldose *XVI* of m.p. 95—97°C (from 2-propanol and ether), $[\alpha]_D$ +16·7° (3 min) → +12·3° (24 h, water) ware obtained from 1·4 g (5·74 mmol) of isopropylidene derivative *XIV*. For $C_6H_{11}N_3O_5$ (205·2) calculated: 35·13% C, 5·40% H, 20·48% N; found: 35·38% C, 5·50% H, 20·57% N. Acetylation of azidoallose *XVI* with acetic anhydride in pyridine gave peracetyl derivative of m.p. 178—179°C (methanol), $[\alpha]_D$ −15·4 ± 1° (chloroform). Literature[17] gives for 1,2,3,4-tetra-O-acetyl-6-azido-6-deoxy-β-D-allopyranose m.p. 178—179°C, $[\alpha]_D$ −15·5° (chloroform).

Oxidation of 6-Azido-6-deoxy-D-glucose

A. *In neutral medium*: A solution of azidoglucose *XV* (560 mg, 2·7 mmol) in 15 ml of water was stirred with 120 µl of bromine in the presence of 1·2 g of barium carbonate at room temperature for 2 h. After addition of another 120 µl of bromine the mixture was stirred for 5 h and then allowed to stand overnight. After checking by thin-layer chromatography (in S_2) the excess of bromine was eliminated with a stream of air, barium carbonate was filtered off, and the filtrate stirred with 5 g of silver carbonate for 1 h. After filtration the solution was passed through a column of 25 ml of Dowex-50 W (H^+). The aqueous eluate was evaporated *in vacuo* affording 522 mg (94·5%) of crystals melting from 124°C (dewing) to 132°C. Double crystallization from 2-propanol and ether gave 120 mg of a compound with m.p. 114—116°C, $[\alpha]_D$ +80 ± 1·5° (acetone), IR spectrum 2084, 1716 cm^{-1}. For $C_6H_9N_3O_5$ (203·2) calculated: 35·47% C, 4·47% H, 20·69% N; found: 35·61% C, 4·53% H, 20·41% N. In another experiment the crystalline material from the evaporated aqueous eluate from the cation exchanger was only washed with cooled 2-propanol. The obtained crystals of m.p. 130—132°C had the same IR spectra as the compound melting at 114—116°C. Literature[4] gives for lactone *XVIII* m.p. 129—130°C, $[\alpha]_D$ +82° (acetone).

B. *In acid medium*: A solution of azidoglucose *XV* (1·18 g, 5·8 mmol) in 50 ml of water, containing 0·5 ml of bromine was stirred at room temperature. After 36 and 48 h 0·5 ml of bromine was added each time. After 90 g the reaction mixture no longer contained the starting aldose (check by thin-layer chromatography, in S_2). The excess bromine was eliminated by bubbling air through the solution which was then evaporated in a vacuum. The residue was dissolved in water and filtered through a column of 50 ml of anion exchanger Dowex-2 (OH). The column was eluted with 100 ml of water, and then with 15% of acetic acid. In acetate fractions totally 1·18 g of a material was eluted, which after triple crystallization from 2-propanol and ether gave 215 mg of crystals of m.p. 114—116°C the physical constants and the IR spectrum of which were identical with those of the substance described under *A*.

Lactone of 6-Azido-6-deoxy-D-allonic Acid (*XVII*)

A solution of azidoallose *XVI* (706 mg, 3·4 mmol) in 20 ml of water was stirred with 1·5 ml of bromine at room temperature for 48 h. After elimination of excess bromine and evaporation of the solution the residue was crystallized from 2-propanol. Yield, 378 mg (54%) of lactone *XVII*, m.p. 149—150°C, $[\alpha]_D$ +15·2 ± 1° (acetone); IR spectrum: 2125, 1765 cm^{-1}. For $C_6H_9N_3O_5$ (203·2) calculated: 35·47% C, 4·47% H, 20·69% N; found: 35·63% C, 4·54% H, 20·82% N.

Lactam of 6-Amino-6-deoxy-D-allonic Acid (*XXI*)
and Lactam of 6-Amino-6-deoxy-D-gluconic Acid (*XXII*)

Lactone *XVII* (203 mg, 1 mmol) was reduced with hydrogen in methanol (40 ml) on 200 mg of PtO_2 at room temperature and normal pressure. The reaction was followed using thin-layer chromatography in system S_2. After 4 h the catalyst was filtered off, the filtrate evaporated and the residue crystallized from methanol. Yield 151 mg (85·5%) of lactam *XXI*, m.p. 167—170°C, $[\alpha]_D$ −91·4 ± 1° (water); IR spectrum: 1665 cm^{-1}. For $C_6H_{11}NO_5$ (177·2) calculated: 40·68% C, 6·26% H, 7·91% N; found: 40·59% C, 6·45% H, 7·97% N.

Lactone *XVIII* (104 mg, 0·51 mmol) was reduced in an analogous manner. Yield, 81 mg (90%) of lactam *XXII*, m.p. 212°C, IR spectrum: 1660 cm^{-1}. Literature[4] gives m.p. 212—214°C, IR spectrum: 1650, 1665 cm^{-1}.

6-Amino-6-deoxy-D-allonic Acid (*XXIII*)

Lactone *XVII* (458 mg, 2·25 mmol) was reduced with hydrogen at room temperature and pressure in 50 ml of water in the presence of 400 mg of Pt O_2 for 48 h. After this the reaction mixture on a thin layer of silica gel in system S_2, showed only the presence of one spot of $R_F = 0$. After filtration and evaporation the residue was crystallized from water to yield 116 mg (39%) of acid *XXIII*, m.p. 194—196°C, $[\alpha]_D$ +10·7° (water); IR spectrum: 1640, 1610 cm^{-1}. For $C_6H_{13}NO_6$ (195·2) calculated: 36·92% C, 6·71% H, 7·18% N; found: 36·93% C, 6·91% H, 7·08% N.

6-Amino-6-deoxy-D-gluconic Acid (*XXIV*)

A solution of 3·1 g of oxidation product of aldose *XV* (according to thin-layer chromatography a mixture of azidolactone *XVIII* and azido acid *XIX*) in 90 ml of water was stirred with 250 mg of PtO_2 under hydrogen at room temperature and atmospheric pressure. After 24 h reaction 100 mg of fresh catalyst were added and hydrogenation was continued for another 24 h. The solution was filtered, decolorized with charcoal and evaporated. The residue was crystallized from water. After filtering off the crystals the mother liquors were diluted with ethanol to afford another crop of crystals of the same quality. Total yield of acid *XXIV* was 1·88 g (69%), m.p. 202°C (decomp.), $[\alpha]_D$ +21·5 ± 1·5 (water); IR spectrum: 1640, 1610 cm^{-1}. For $C_6H_{13}NO_6$ (195·2) calculated: 36·92% C, 6·71% H, 7·18% N; found: 36·88% C, 6·66% H, 7·02% N. The same product was obtained by catalytic hydrogenation of chromatographically pure lactone *XVII* in water.

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REFERENCES

1. Melichar B., Čeladník M., Palát K., Kňažko L., Nováček L., Sova J.: *Chemická léčiva*, p. 343. Avicenum, Zdravotnické nakladatelství, Prague 1972.
2. Freudenberg K., Doser A.: Ber. Deut. Chem. Ges. *58*, 294 (1925).
3. Weidmann H., Fauland E.: Justus Liebig's Ann. Chem. *679*, 192 (1964).
4. Hanessian S.: J. Org. Chem. *34*, 675 (1969).

5. Jarý J., Kefurtová Z., Kovář J.: This Journal *34*, 1452 (1969).
6. Bartsch J., Prey V.: Justus Liebig's Ann. Chem. *717*, 198 (1968).
7. Heap J. M., Owen L. N.: J. Chem. Soc. (C) *1970*, 707.
8. Brimacombe J. S., Mofti A. M.: Carbohyd. Res. *18*, 157 (1971).
9. Staněk J., Černý M.: Synthesis *1972*, 698.
10. Čapek K.: Unpublished results.
11. Schmidt O. T. in the book: *Methods in Carbohydrate Chemistry* (R. L. Whistler, M. L. Wolfrom, Eds), Vol. II, p. 332. Academic Press, New York 1963.
12. Theander O.: Acta Chem. Scand. *17*, 1751 (1963).
13. Ohle H., Dickhäuser E.: Ber. Deut. Chem. Ges. *58*, 2593 (1925).
14. Ohle H., Vargha L.: Ber. Deut. Chem. Ges. *62*, 2435 (1929).
15. Richardson A. C. in the book: *Methods in Carbohydrate Chemistry* (R. L. Whistler, J. N. BeMiller, Eds), Vol. VI, p. 220. Academic Press, New York 1972.
16. Cramer F., Otterbach H., Springmann H.: Chem. Ber. *92*, 384 (1959).
17. Brimacombe J. S., Hunedy F., Husian A.: J. Chem. Soc. (C) *1970*, 1273.

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