6-AMINO-6-DEOXYHEXONOLACTAMS

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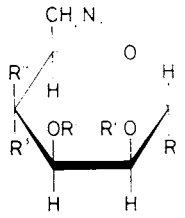
6-Azido-6-deoxy-D-mannose (*III*), prepared from methyl 4,6-O-benzylidene-α-D-mannopyranoside, 6-azido-6-deoxy-D-talose (*XI*), prepared from methyl 6-azido-2,3-O-isopropylidene-α-D--mannopyranoside (*VII*) via 4-keto derivative *VIII*, and 6-azido-6-deoxy-L-idose (*XVIII*), obtained from 5,6-anhydro-1,2-O-isopropylidene-β-L-idofuranose, on oxidation with bromine and subsequent reduction of the azido group afforded the corresponding 6-amino-6-deoxyhexonolactams *V*, *XV*, and *XXI*. 6-Amino-6-deoxyhexonic acids *IV* and *XIV* were also prepared.

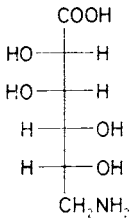
Some time ago Weidmann and Fauland[1] prepared a sugar analogue of ε-caprolactam, 6-amino-6-deoxyhexonolactam of the L-*gulo* configuration, by a simple transformation of D-glucurono-6,3-lactone. Later, Hanessian[2] described the synthesis of the D-*gluco* and D-*galacto* isomers and we prepared[3,4] isomers of D-*allo* and D-*altro* configuration. Our present communication concerns the synthesis of three hitherto undescribed configurational isomers of 6-amino-6-deoxyhexonolactam and their tetra-O-acetyl derivatives.

6-Amino-6-deoxyhexonolactams of the D-*manno*, D-*talo*, and L-*ido* configuration were prepared via the 6-azido-6-deoxy derivatives of the corresponding hexoses as the key intermediates. As the starting compound for preparation of 6-azido-6-deoxy-D--mannose (*III*) and 6-azido-6-deoxy-D-talose (*XI*) we employed methyl 2,3-di-O-acetyl-6-azido-4-O-benzoyl-6-deoxy-α-D-mannopyranoside (*I*), obtained from D-mannose or methyl 4,6-O-benzylidene-α-D-mannopyranoside according to Horton[5]. Acetolysis of *I* afforded 1,2,3-tri-O-acetyl-6-azido-4-O-benzoyl-6-deoxy-α-D-mannopyranose (*II*). The structure and the anomeric α-configuration of *II* were confirmed by ^{1}H NMR spectrum and the positive value of optical rotation. Deacylation of *II* with sodium methoxide in methanol gave syrupy 6-azido-6-deoxy-D-mannose (*III*) which on oxidation with bromine in neutral medium furnished a mixture of three compounds behaving on thin-layer chromatography (TLC) as the corresponding azido acid and its two lactones. Catalytic hydrogenation of this mixture afforded crystalline 6-amino--6-deoxy-D-mannonic acid (*IV*) whose properties resembled those of the previously described configurational isomers[3,4]. Amino acid *IV* was converted into methyl ester hydrochloride which on treatment with an equivalent amount of sodium

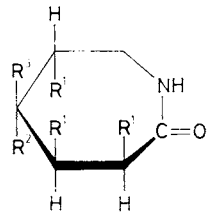
methoxide in methanol gave crude 6-amino-6-deoxy-D-mannonolactam (*V*). Since this material contained, in addition to inorganic salts, still other ballast compounds, the crude product *V* was acetylated and the obtained 2,3,4,5-tetra-O-acetyl derivative *VI* was purified by chromatography on silica gel. Deacetylation of the crystalline *VI* afforded the lactam *V* in the pure state and crystalline form*.



I, $R^1 = OCH_3$; $R^2 = COCH_3$; $R^3 = OCOCH_3$; $R^4 = H$
II, $R^1 = OCOCH_3$; $R^2 = COCH_3$; $R^3 = OCOCH_3$; $R^4 = H$
III, $R^1 = R^3 = OH$; $R^2 = R^4 = H$
VII, $R^1 = OCH_3$; $R^2 = >C(CH_3)_2$; $R^3 = OH$; $R^4 = H$
VIII, $R^1 = OCH_3$; $R^2 = >C(CH_3)_2$; $R^3 + R^4 = O$
IX, $R^1 = OCH_3$; $R^2 = >C(CH_3)_2$; $R^3 = H$; $R^4 = OH$
X, $R^1 = OCH_3$; $R^2 = R^3 = H$; $R^4 = OH$
XI, $R^1 = R^4 = OH$; $R^2 = R^3 = H$
XII, $R^1 = R^4 = OCOCH_3$; $R^2 = COCH_3$; $R^3 = H$



IV



V, $R^1 = R^2 = OH$; $R^3 = H$
VI, $R^1 = R^2 = OCOCH_3$; $R^3 = H$
XV, $R^1 = R^3 = OH$; $R^2 = H$
XVI, $R^1 = R^3 = OCOCH_3$; $R^2 = H$

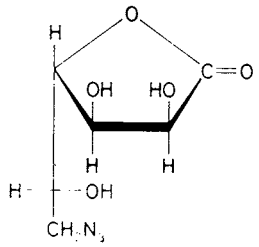
For the preparation of the D-*talo* isomer, the glycoside *I* was deacylated and the obtained methyl 6-azido-6-deoxy-α-D-mannopyranoside was converted into methyl 6-azido-6-deoxy-2,3-O-isopropylidene-α-D-mannopyranoside (*VII*). The isopropyli-

* Using this method of purification of a non-crystalline lactam via its acetyl derivative, we also obtained crystalline 6-amino-6-deoxy-D-altronolactam, previously described[4] as a syrup. Its physical constants are given in Table I.

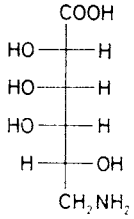
dene group was introduced into the positions 2 and 3 either by reaction with 2,2-dimethoxypropane in the presence of catalytic amount of *p*-toluenesulfonic acid[6,7] or by reflux with acetone and anhydrous copper sulfate and a strong cation exchanger. The former method gave purer product in better yields, required shorter reaction time and was less laborious. The structure of the syrupy isopropylidene derivative *VII* was confirmed by analysis of its ^{1}H NMR spectrum. The relatively low value of $J(3, 4)$ (6·4 Hz), as compared with the value for the glycoside *I* ($J(3, 4) = 8{\cdot}9$ Hz), indicates a deformation of the $^4C_1$-(D)-pyranose ring due to attachment of the dioxolane ring. The hydroxyl in compound *VII* was oxidized again in two ways: with pyridinium dichromate[7,8] in dichloromethane in the presence of a molecular sieve, or with ruthenium dioxide and sodium periodate in tetrachloromethane[9]. Both procedures afforded practically the same yields, the former being longer but requiring simpler processing. The oxidation product – syrupy methyl 6-azido-6-deoxy-2,3-O-isopropylidene-α-D-*lyxo*-4-hexosuloside (*VIII*) – absorbed at 1 745 cm^{-1} in the IR spectrum and its ^{13}C NMR spectrum exhibited a signal at δ 201·84 ppm, corresponding to a non-hydrated keto group. Its structure was confirmed by the ^{1}H NMR spectrum. The hexosuloside *VIII* was reduced with sodium borohydride to give methyl 6-azido-6-deoxy-2,3-O-isopropylidene-α-D-talopyranoside (*IX*). In the ^{1}H NMR spectrum of *IX* the coupling constant $J(4, 5)$ is much smaller than that for the mannopyranoside *VII* (1·5 Hz versus 9·5 Hz), indicating thus the opposite configuration at the C-4 carbon atom in these two compounds. Acid hydrolysis under mild conditions converted the derivative *IX* into methyl 6-azido-6-deoxy-α-D-talopyranoside (*X*) whereas treatment with boiling dilute mineral acid led to 6-azido-6-deoxy-D-talose (*XI*). The syrupy azidohexose *XI* was characterized as the tetra-O-acetyl derivative *XII* which, according to ^{1}H NMR spectrum, was a 1·5 : 1 mixture of α- and β-anomer. In an unbuffered aqueous medium compound *XI* was oxidized with bromine to afford syrupy 6-azido-6-deoxy-D-talono-1,4-lactone (*XIII*). This structure with a five-membered lactone ring is supported by the negative optical rotation and the considerable stability of the lactone in aqueous solution. Catalytic hydrogenation of lactone *XIII* on palladium in water afforded amorphous 6-amino-6-deoxy-D-talonic acid (*XIV*). Crystalline 6-amino-6-deoxy-D-talonolactam (*XV*) and its tetra-O-acetyl derivative were prepared from the acid *XIV* analogously as described for the *manno*-isomer. The lactam *XV* was also obtained directly from lactone *XIII* by hydrogenation on palladium in methanol.

The isomer of the *ido* configuration was prepared starting from 5,6-anhydro-1,2-O-isopropylidene-β-L-idofuranose, obtained in turn from 1,2-O-isopropylidene-α-D-glucofuranurono-6,3-lactone by the published procedure[10,11]. Azidolysis of the oxirane ring in the mentioned anhydro compound under conditions used for analogous *gluco* and *allo* derivatives[3] gave 6-azido-6-deoxy-1,2-O-isopropylidene-β-L-idofuranose (*XVII*). Its hydrolysis in water in the presence of a strong cation ex

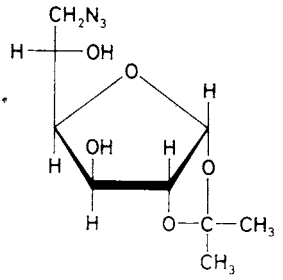
changer liberated 6-azido-6-deoxy-L-idose (*XVIII*) which was characterized as the crystalline tetra-O-acetyl derivative *XIX*. Oxidation of the azidohexose *XVIII* with bromine in neutral medium furnished 6-azido-6-deoxy-L-idono-1,4-lactone (*XX*) whose structure was confirmed by an IR absorption band at 1 765 cm^{-1} and positive optical rotation. The lactone *XX* was hydrogenated over palladium in methanol to give 6-amino-6-deoxy-L-idonolactam (*XXI*) from which the 2,3,4,5-tetra-O-acetyl derivative *XXII* was obtained by acetylation.



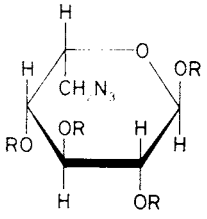
XIII



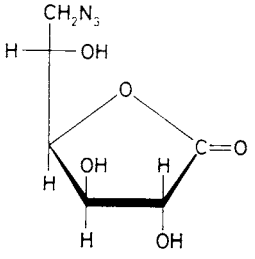
XIV



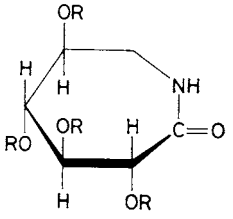
XVII



XVIII, R = H
XIX, R = $COCH_3$



XX



XXI, R = H
XXII, R = $COCH_3$

Our present work has thus completed the set of all eight configuration isomers of 6-amino-6-deoxyhexonolactam some of which had been already prepared previously[1-4]. We also prepared the corresponding tetra-O-acetyl derivatives by acetylation procedure described in Experimental. The physical constants of all the eight stereoisomeric lactams and their 2,3,4,5-tetra-O-acetyl derivatives are listed in Table I.

EXPERIMENTAL

Melting points were determined on a Kofler block and are uncorrected. Optical rotations were measured on an Opton instrument, accuracy 1—2°. IR spectra were recorded on a Perkin–Elmer 325 spectrometer in KBr pellets or in chloroform. NMR spectra were taken on a Bruker AM 400

TABLE I

Physical properties of 6-amino-6-deoxyhexonolactams and their 2,3,4,5-tetra-O-acetyl derivatives

Configuration	Free lactam		2,3,4,5-Tetra-O-acetyl derivative	
	m.p., °C[a] (solvent)	$[\alpha]_D^{20}$ (*c*, in water)	m.p., °C[a] (solvent)	$[\alpha]_D^{20}$ (*c*, in chloroform)
D-*allo* (ref.[3])	177 (methanol)	−91·4° (1·1)	210 (acetone)	−101·1° (0·8)
D-*altro* (ref.[4])	187[b] (methanol)	−22·9° (0·8)	204 (ethyl acetate–light petroleum)	+36·8° (1·0)
D-*galacto* (ref.[2])	184[c] (methanol–ethanol)	−21·5°[c] (1·5)	172 (acetone–ether)	−98·4° (1·0)
D-*gluco* (refs.[2,3])	212[d] (methanol)	−70·0°[d] (0·9)	153 (benzene–ethanol)	−113·0° (0·9)
L-*gulo* (ref.[1])	205[e] (water)	+52·0°[e] (0·9)	215[f] (water)	+93·4°[f] (1·2)
L-*ido* (this work)	180 (water–methanol)	+2·3°[g] (3·6)	190·5 (acetone–ether)	−21·8° (1·1)
D-*manno* (this work)	179 (methanol–ethanol)	+24·0° (1·1)	196 (acetone–ether)	+18·1° (1·8)
D-*talo* (this work)	235 (water–ethanol)	0°[h] (1·1)	207 (acetone–ether)	+9·4° (1·1)

[a] The melting points are usually accompanied wtih thermal decomposition and depend on the rate and time of heating. This can explain some differences between our and reported values. In our study the sample was inserted at a temperature about 15°C below the value, determined in a preliminary measurement, and then heated at a rate of about 4°C/min. [b] In ref.[4] the syrupy lactam was not characterized. [c] Ref.[2] reports m.p. 175–177°C, $[\alpha]_D$ −22°. [d] Reported[2] m.p. 212–214°C, $[\alpha]_D$ −71°. [e] Reported[1] m.p. 195°C, $[\alpha]_D$ +49°. [f] Reported[1] m.p. 214–215°C, $[\alpha]_D$ +75° (water). [g] $[\alpha]_{365}^{20}$ −4·0°. [h] $[\alpha]_{20}^{365}$ −17·4°.

(400 MHz for ^1H and 100 MHz for ^{13}C resonance) instrument in deuterochloroform or deuterium oxide using tetramethylsilane and sodium 4,4-dimethyl-4-silapentanesulfonate as the respective internal standards. The reactions were monitored by thin-layer chromatography (TLC) on 25 × 75 mm plates of silica gel G (Merck) (thickness 0·2—0·3 mm) in the following systems: chloroform–methanol 100 : 5 (S1), 100 : 10 (S2), 100 : 20 (S3), dichloromethane–ether 3 : 1 (S4), ether–light petroleum 1 : 2 (S5), and benzene–ethyl acetate 9 : 1 (S6). Spots were detected by spraying with 1% cerium (*IV*) sulfate in 10% sulfuric acid, followed by heating. Preparative column chromatography was carried out on silica gel CH 100—200 μm (Lachema). HPLC analyses were performed on a 350 × 4 mm glass column, packed with Ostion LGKS 0 802 ion exchanger (Na^+ form), eluent deionized water, flow rate 6 ml/h at 50°C, detection with an Optilab 5 902 (Tecator) refractometer.

O-Acetylation of Sugar Lactams and Their Deacetylation (General Procedure)

Acetic anhydride (8—24 mmol) was added to a cold solution of the lactam (1—3 mmol) in pyridine (10—30 ml). The reaction mixture was set aside at room temperature for 60 h, decomposed with crushed ice and extracted with chloroform (3 × 30—50 ml). The chloroform extract was washed, dried and the solvent was evaporated. The residue was purified either by crystallization from acetone–ether or by preparative chromatography in S1, followed by crystallization of the chromatographically homogeneous fraction. A solution of the tetra-O-acetyllactam (0·3 to 1·0 mmol) in methanol (5—20 ml) was treated with methanolic sodium methoxide (0·3—1·0 mmol) at room temperature, the transesterification course being monitored by thin-layer chromatography in S3. After 24 h the reaction mixture was concentrated to a half, decomposed with the same amount of water under cooling, and the solution was filtered through a layer (1—2 ml) of Dowex 50W (H^+ form) and Amberlite IR-4 (OH^- form). After evaporation of the filtrate and the washing water, the lactam was crystallized from an appropriate solvent (see Table I).

1,2,3-Tri-O-acetyl-6-azido-4-O-benzoyl-6-deoxy-α-D-mannopyranose (*II*)

A solution of glycoside *I* (ref.[5]; 223 mg; 0·5 mmol) in acetic anhydride (3 ml) containing sulfuric acid (0·1 ml) was allowed to stand at room temperature. The reaction was monitored by thin-layer chromatography in S6 (starting *I*: R_F 0·5, product: R_F 0·28). After 60 h the mixture was decomposed with ice-cold water (15 ml) and extracted with toluene. The extract was washed with saturated aqueous solution of sodium hydrogen carbonate, the solvent was evaporated and the residue was purified by chromatography on silica gel (15 g) in S6 affording, along with some starting compound (12 mg), 190 mg (80%) of the tetra-O-acyl derivative *II*, m.p. 101—102°C (ether–light petroleum), $[\alpha]_D^{20}$ +62·8° (*c* 1·05, chloroform). ^1H NMR (C^2HCl_3): 1·91 s, 3 H (OAc); 2·21 s, 6 H (2 × OAc); 3·38 dd, 1 H (H-6, $J(6, 5)$ = 5·65; $J(6, 6')$ = 13·55); 3·44 dd, 1 H (H-6′, $J(6', 5)$ = 3·0; $J(6', 6)$ = 13·5); 4·15 m, 1 H (H-5, $J(5, 4)$ = 9·2; $J(5, 6)$ = 5·6; $J(5, 6')$ = 3·0); 5·32 dd, 1 H (H-2, $J(2, 1)$ = 1·8; $J(2, 3)$ = 3·1); 5·57 dd, 1 H (H-3, $J(3, 2)$ = 3·1; $J(3, 4)$ = 10·1); 5·62 dd, 1 H (H-4, $J(4, 3)$ = 10·1; $J(4·5)$ = 9·2); 6·15 d, 1 H (H-1, $J(1, 2)$ = = 1·8); 7·45 t, 7·60 t and 8·0 d, 5 H (H-arom.). For $C_{19}H_{21}N_3O_9$ (435·4) calculated: 52·42% C, 4·86% H, 9·65% N; found: 52·22% C, 4·82% H, 9·52% N.

6-Azido-6-deoxy-D-mannose (*III*)

A solution of the derivative *II* (5·24 g; 11 mmol) in methanol (50 ml) was mixed with 1·4M sodium methoxide in methanol (5 ml). After standing for 30 min the reaction was complete (one spot, R_F 0·19 in S3). The solvent was evaporated and the residue partitioned between water and chloro-

form. The aqueous portion was filtered through a column (15 ml) of Dowex 50W (H^+ form), the filtrate was decolorized with charcoal and taken down. The obtained syrupy azidomannose *III* (2·47 g; 100%) had $[\alpha]_D^{20}$ +31° (*c* 4·3, water) and was uniform on HPLC. For $C_6H_{11}N_3O_5$ (205·2) calculated: 35·12% C, 5·40% H, 20·48% N; found: 35·37% C, 5·52% H, 20·27% N.

6-Amino-6-deoxy-D-mannonic Acid (*IV*)

Oxidation of azidomannose *III* (2·1 g; 10·2 mmol) with bromine under conditions described for isomeric azidohexose[4] afforded a syrupy product (1·66 g) consisting (TLC in S3) of the azido acid (R_F 0) and two compounds of R_F 0·50 and 0·57, detected by the hydroxamate test[12]. This mixture was without purification reduced in water (85 ml) on 5% Pd/C. After 5 h the catalyst was filtered off, the filtrate was taken down and the residue crystallized from water and ethanol to give 462 mg (23%) of the acid *IV*, m.p. 209°C (decomp.), $[\alpha]_D^{20}$ −2·4°, $[\alpha]_{365}^{20}$ −4·5° (*c* 0·96, water). For $C_6H_{13}NO_6$ (195·2) calculated: 36·92% C, 6·71% H, 7·18% N; found: 36·76% C, 6·74% H, 7·42% N.

6-Amino-6-deoxy-D-mannonolactam (*V*) and 2,3,4,5-Tetra-O-acetyl-6-amino-6-deoxy-D-mannonolactam (*VI*)

Amino acid *IV* (360 mg; 1·84 mmol) was gently refluxed for 5 h with methanol (25 ml), containing about 2% HCl. After evaporation and drying, the residue was dissolved in methanol (25 ml) and made alkaline with methanolic sodium methoxide (1·8 mmol). The solvent was evaporated and the residue was acetylated using the above-described procedure. Crystallization of the chromatographically uniform product from acetone–ether afforded 575 mg (90%) of the tetra-O-acetyl derivative *VI*, m.p. 195·5—196·5°C, $[\alpha]_D^{20}$ +18·1° (*c* 1·8, chloroform). For $C_{14}H_{19}\cdot NO_9$ (345·3) calculated: 48·70% C, 5·55% H, 4·06% N; found: 48·72% C, 5·58% H, 3·86% N. Compound *VI* (315 mg; 0·91 mmol) was deacetylated according to the general procedure (vide supra). Crystallization from methanol and ethanol gave lactam *V* (149 mg;92 %), m.p. 179 to 180°C, $[\alpha]_D^{22}$ +24·0° (*c* 1·06, water). For $C_6H_{11}NO_5$ (177·2) calculated: 40·68% C, 6·26% H, 7·91% N; found: 40·52% C, 6·22% H, 7·88% N.

Methyl 6-Azido-6-deoxy-2,3-O-isopropylidene-α-D-mannopyranoside (*VII*)

Glycoside *I* was deacylated in methanol with catalytic amount of sodium methoxide. After the end of the reaction, the solvent was evaporated and the residue was partitioned between water and chloroform. Sodium ions were removed from the aqueous phase by shaking with a small amount of Dowex 50W (H^+ form). The syrupy methyl 6-azido-6-deoxy-α-D-mannopyranoside, obtained by evaporation of water and drying in vacuo, was converted into *VII* by the two following alternative procedures.

A) Methyl 6-azido-6-deoxy-α-D-mannopyranoside (4·97 g; 22·7 mmol) was stirred at room temperature with 2,2-dimethoxypropane (15 ml) and *p*-toluenesulfonic acid monohydrate (100 mg) until the mixture became homogeneous (about 90 min). The reaction mixture, containing only one compound (R_F 0·46 in S4; R_F 0 for the starting compound), was neutralized with saturated solution of sodium carbonate (5 ml), the volatile material was evaporated and the residue was partitioned between dichloromethane and water. Evaporation of the dried organic phase furnished the syrupy isopropylidene derivative *VII* (5·7 g; 97%), $[\alpha]_D^{20}$ +8·1° (*c* 0·96, chloroform). ^{1}H NMR (C^2HCl_3): 1·35 s and 1·53 s, 2 × 3 H ($(CH_3)_2C$); 3·41 s, 3 H (OCH_3); 3·44 dd, 1 H (H-6, *J*(6, 6′) = 13·2, *J*(6, 5) = 2·6); 3·51 dd, 1 H (H-6′, *J*(6′, 6) = 13·2, *J*(6′, 5) = 6·7); 3·55 m, 1 H (H-4, *J*(4, 3) = 6·4; *J*(4, 5) = 9·5, *J*(4, OH) = 3·3); 3·70 m, 1 H

(H-5, $J(5, 4) = 9{\cdot}5$, $J(5, 6) = 2{\cdot}6$), $J(5, 6') = 6{\cdot}7$); 3·90 d, 1 H (O—H, $J(OH, 4) = 3{\cdot}3$); 4·095 dd, 1 H (H-3, $J(3,2) = 5{\cdot}7$, $J(3, 4) = 6{\cdot}4$); 4·12 d, 1 H (H-2, $J(2, 3) = 5{\cdot}8$); 4·95 s, 1 H (H-1, $J(1, 2) = 0$). For $C_{10}H_{17}N_3O_5$ (259·3) calculated: 46·33% C, 6·61% H, 16·21% N; found: 46·43% C, 6·52% H, 16·41% N.

B) A mixture of methyl 6-azido-6-deoxy-α-D-mannopyranoside (2·0 g; 9·1 mmol), anhydrous copper sulfate (4 g), Dowex 50W (H^+ form, 1 g) and acetone (100 ml) was refluxed for 16 h. The reaction was followed by TLC in S1. After removal of the solids by filtration, the acetone was evaporated and the unreacted starting compound was removed by partitioning between water and benzene. The residue (2·3 g) after evaporation of the benzene fraction was purified by chromatography on silica gel in S1 to give 1·96 g (83%) of syrupy *VII*, identical with the product obtained by procedure *A*).

Methyl 6-Azido-6-deoxy-2,3-O-isopropylidene-α-D-*lyxo*-4-hexosuloside (*VIII*)

A) Nalsit 4A molecular sieve (12 g) and pyridinium dichromate[8] (6 g) were added to a stirred solution of isopropylidene derivative *VII* (1·99 g; 7·7 mmol) in dichloromethane (40 ml). The reaction was followed by TLC in S6. After 72 h the reaction mixture was diluted with ether (120 ml) and filtered through a layer of silica gel G (50 g). The silica gel was washed and the combined filtrates were taken down. For analysis, the syrupy residue (1·76 g; 89%) was purified by chromatography on silica gel in chloroform, containing 1—10% of methanol. IR spectrum ($CHCl_3$): 3 010, 2 995, 2 940, 2 100, 1 745, 1 450, 1 390, 1 380 cm^{-1}. ^1H NMR (C^2HCl_3): 1·35 s and 1·47 s, 2 × 3 H, ($(CH_3)_2C$); 3·50 s, 3 H (OCH_3); 3·53 dd, 1 H (H-6, $J(6, 6') = 13{\cdot}3$, $J(6, 5) = 3{\cdot}5$); 3·62 dd, 1 H (H-6′, $J(6', 6) = 13{\cdot}3$, $J(6', 5) = 7{\cdot}6$); 4·28 dd, 1 H (H-5, $J(5, 6) = 3{\cdot}5$, $J(5, 6') = 7{\cdot}6$); 4·40 d and 4·43 d, 2 × 1 H (H-2 and H-3, $J(2, 3) = 5{\cdot}8$); 4·92 s, 1 H (H-1, $J(1, 2) = 0$). ^{13}C NMR (C^2HCl_3): 25·51, 26·74 (2 × CH_3—C); 111·83 ($(CH_3)_2C$; 56·10 (CH_3—O); 50·80 (C-6); 73·14 (C-5); 201·84 (C-4); 75·51 and 78·36 (C-2 and C-3); 98·28 (C-1). $[\alpha]_D^{20}$ +83·1° (*c* 1·2, chloroform). For $C_{10}H_{15}N_3O_5$ (257·2) calculated: 46·69% C, 5·88% H, 16·33% N; found: 46·98% C, 5·87% H, 16·02% N.

B) Ruthenium dioxide (45 mg), followed by 5% solution of sodium periodate in water (30 ml; added in three portions), was added to a stirred solution of isopropylidene derivative *VII* (600 mg; 2·3 mmol) in tetrachloromethane (15 ml). The reaction course was monitored by TLC in S6. After 8 h the reaction mixture was decomposed with 2-propanol (2·5 ml), taken down and the residue was partitioned between water and chloroform. The organic extract afforded 490 mg (82%) of the syrupy product *VIII*, identical with the compound obtained under *A*.

Methyl 6-Azido-6-deoxy-2,3-O-isopropylidene-α-D-talopyranoside (*IX*)

Sodium borohydride (850 mg; 22·3 mmol) was added at 5°C to a solution of keto derivative *VIII* (2·10 g; 8·2 mmol) in aqueous methanol (1 : 1; 100 ml). The reaction was monitored by TLC in S6 (*VIII*, R_F 0·8; *IX*, R_F 0·23). After standing for 60 min, the reaction mixture was decomposed with acetic acid (1·5 ml) and taken down. The residue was three times coevaporated with methanol (100 ml), dissolved in water (15 ml) and extracted with chloroform. The solvent was evaporated and the residue was purified by chromatography on silica gel in benzene–ethyl acetate (5 : 1), affording 1·59 g (75%) of chromatographically pure hexoside *IX*, $[\alpha]_D^{20}$ −17·6° (*c* 0·82, chloroform.) IR spectrum (tetrachloromethane): 3 546, 2 985, 2 920, 2 900, 2 850, 2 820, 2 090, 1 440, 1 375, 1 360 cm^{-1}. ^1H NMR (C^2HCl_3): 1·39 and 1·59 s, 2 × 3 H ($(CH_3)_2C$); 2·39 d, 1 H (O—H, $J(OH, 4) = 4{\cdot}9$; 3·30 dd, 1 H (H-6, $J(6, 5) = 3{\cdot}9$, $J(6, 6') = 12{\cdot}8$); 3·48 s, 3 H (OCH_3); 3·70 m, 1 H (H-4, $J(4, OH) = 4{\cdot}9$, $J(4, 5) = 1{\cdot}5$, $J(4, 3) = 5{\cdot}0$); 3·76 dd, 1 H (H-6′, $J(6', 5) = 8{\cdot}8$, $J(6', 6) = 12{\cdot}8$); 3·86 m, 1 H (H-5, $J(5, 4) = 1{\cdot}5$, $J(5, 6) = 3{\cdot}9$, $J(5, 6') = 8{\cdot}8$); 4·09 dd,

1 H (H-2, $J(2, 3) = 6{\cdot}45$, $J(2, 1) = 0{\cdot}8$); 5·01 d, 1 H (H-1, $J((1, 2) = 0{\cdot}8$). For $C_{10}H_{17}N_3O_5$ (259·3) calculated: 46·33% C, 6·61% H, 16·21% N; found: 46·30% C, 6·93% H, 16·33% N.

Methyl 6-Azido-6-deoxy-α-D-talopyranoside (*X*)

A mixture of isopropylidene derivative *IX* (1·42 g; 5·48 mmol), water (25 ml) and Dowex 50W (H^+ form; 2 ml) was stirred at 75°C for 1 h. After this time the reaction mixture did not contain any starting compound (TLC in S2; *IX*, R_F 0·87, *X*, R_F 0·41). Separation of the Dowex and evaporation gave 1·20 g (100%) of syrupy glycoside *X*. An analytical sample was purified by chromatography on silica gel in system S1; $[\alpha]_D^{22}$ +43·1° (*c* 1·1, ethanol). For $C_7H_{13}N_3O_5$ (219·2) calculated: 38·36% C, 5·98% H, 19·17% N; found: 38·48% C, 6·20% H, 19·42% N.

6-Azido-6-deoxy-D-talose (*XI*)

Isopropylidene derivative *IX* (1·09 g; 4·19 mmol) was stirred with 1M-HCl (25 ml) for 1 h at 90°C and then at 110°C; the volatile products were continuously distilled off, the volume being kept constant by addition of water. The hydrolysis was followed by TLC in S2 (*XI*, R_F 0·16). After 2·5 h the reaction mixture was cooled and neutralized by filtration through a column of Amberlite IR-4B (OH^- form) which was then washed with water (250 ml). Concentration of the filtrate, decolorization with charcoal and evaporation to dryness afforded the syrupy azidotalose *XI* (760 mg; 88·5%), $[\alpha]_D^{20}$ +6·5° (*c* 1, water). Tetra-O-acetyl derivative *XII*, prepared by acetylation of *XI* with acetic anhydride in pyridine, melted at 101–102°C; according to ^{1}H NMR spectrum it was a 1·5 : 1 mixture of the α- and β-anomers. For $C_{14}H_{19}N_3O_9$ (373·3) calculated: 45·04% C, 5·13% H, 11·26% N; found: 45·27% C, 5·13% H, 11·02% N.

6-Amino-6-deoxy-D-talonic Acid (*XIV*)

A solution of *XI* (643 mg; 3·13 mmol) in water (45 ml) was stirred with bromine (1 ml) at room temperature. The oxidation was followed by TLC in S2. After 52 h *XI* (R_F 0·19) was completely converted into the lactone *XIII* (R_F 0·33). The excess bromine was removed by a stream of air, the colourless solution was taken down and the residue was freed from remaining water and hydrogen bromide by repeated evaporation with toluene. The syrupy lactone *XIII* (628 mg; 98·6%), $[\alpha]_D^{20}$ −21·9° and −20·3° (*c* 2·9, water, after 50 min and 27 h, respectively), in water (60 ml) was hydrogenated by stirring with 5% Pd/C (350 mg), with renewal of hydrogen. According to TLC in S3 the reduction was complete after 90 min. The usual work-up of the reaction mixture afforded the amino acid *XIV* as a dry foam (585 mg; 97·3%), $[\alpha]_D^{20}$ +3·4°, $[\alpha]_{365}^{20}$ +15·9° (*c* 1·3, water). For $C_6H_{13}NO_6$ (195·2) calculated: 36·92% C, 6·71% H, 7·18% N; found: 36·68% C, 6·56% H, 7·40% N.

6-Amino-6-deoxy-D-talonolactam (*XV*) and 2,3,4,5-Tetra-O-acetyl-6-amino-6-deoxy-D-talonolactam (*XVI*)

A) Methanolic hydrogen chloride (10%, 10 ml) was added to a solution of amino acid *XIV* (578 mg; 2·96 mmol) in methanol (40 ml). The mixture was refluxed for 3 h, cooled and the solvent was evaporated. The syrupy methyl ester hydrochloride was dried in vacuo to constant weight, dissolved in methanol and made alkaline with 1M methanolic sodium methoxide (3·3 ml). After evaporation of the solvent, the unseparated mixture of the formed lactam and inorganic salt was acetylated in pyridine (30 ml) as described above. Crystallization of the product from acetone–ether afforded 475 mg (47%) of the tetra-O-acetyl derivative *XVI*, m.p. 207°C, $[\alpha]_D^{22}$

+9·4° (*c* 1·1, chloroform). For $C_{14}H_{19}NO_9$ (345·3) calculated: 48·70% C, 5·55% H, 4·06% N; found: 48·70% C, 5·52% H, 3·87% N. Deacetylation of *XVI* (183 mg; 0·53 mmol) using the above-described procedure gave lactam *XV* (87 mg; 92%), m.p. 235°C (decomp.) (water–ethanol); $[\alpha]_D^{20}$ 0°, $[\alpha]_{365}^{20}$ −17·4° (*c* 1·1, water). IR spectrum (KBr): 3 500–3 100, 2 920, 1 660, 1 470, 1 410, 1 340, 1 325, 1 285, 1 240, 1 200 cm^{-1}. For $C_6H_{11}NO_5$ (177·2) calculated: 40·68% C, 6·26% H, 7·92% N; found: 40·57% C, 6·23% H, 7·74% N.

B) Azido lactone *XIII* (320 mg; 1·57 mmol) was hydrogenated in methanol (50 ml) by stirring with 5% Pd/C (250 mg) at room temperature and atmospheric pressure with renewal of hydrogen. The reaction was complete after 130 min (according to TLC in S3). The obtained lactam *XV* (276 mg; 99%) and its tetra-O-acetyl derivative *XVI* were identical with the products described under *A*).

6-Azido-6-deoxy-1,2-O-isopropylidene-β-L-idofuranose (*XVII*)

A mixture of 5,6-anhydro-1,2-O-isopropylidene-β-L-idofuranose[10,11] (2·3 g; 11·4 mmol), sodium azide (2·3 g), ammonium chloride (1·5 g), 2-methoxyethanol (36 ml) and water (3 ml) was heated to 140°C for 20 min. The solution was taken down, the residue was repeatedly codistilled with water (20 ml) and the product was separated from inorganic salts by partition between chloroform and water. The crystalline azido derivative *XVII*, obtained from the chloroform extract, was purified by chromatography on silica gel in benzene–ethanol (95 : 5) followed by crystallization from ethyl acetate; yield 2·1 g (75%), m.p. 102°C; $[\alpha]_D^{20}$ −26·0° (*c* 1·0, chloroform). IR; spectrum (KBr): 2 100 cm^{-1}. For $C_9H_{15}N_3O_5$ (245·2) calculated: 44·08% C, 6·17% H, 17·13% N, found: 44·10% C, 6·17% H, 17·27% N.

6-Azido-6-deoxy-L-idose (*XVIII*)

A solution of isopropylidene derivative *XVII* (1·9 g; 7·8 mmol) in water (25 ml) was stirred with Dowex 50W (H^+ form; 5 ml) at 60°C. The hydrolysis was monitored by TLC (S1; *XVII*, R_F 0·38, *XVIII*, R_F 0·1). After 100 min no starting compound was detected and the Dowex was removed by filtration and washed with water (2 × 25 ml). The combined filtrates were taken down to give 1·6 g (100%) of syrupy *XVIII*, $[\alpha]_D^{20}$ −9·1° (*c* 1·5; water; 36 h). The tetra-O-acetyl derivative *XIX*, prepared by acetylation of *XVIII* (100 mg) with acetic anhydride in pyridine in 74% yield, melted at 124°C; $[\alpha]_D^{20}$ +46·8° (*c* 1·2, chloroform). ^1H NMR (C^2HCl_3): 2·131 s, 2·139 s, 2·141 s and 2·150 s, 4 × 3 H (4 × OAc); 3·32 dd, 1 H (H-6, $J(6, 5)$ = 5·1; $J(6, 6')$ = = 13·0); 3·65 dd, 1 H (H-6′, $J(6', 5)$ = 8·05, $J(6', 6)$ = 13·0); 4·27 m, 1 H (H-5, $J(5, 4)$ = 2·8, $J(5, 6)$ = 5·1, $J(5, 6')$ = 8·0); 4·88 dd, 1 H (H-4, $J(4, 5)$ = 2·8, $J(4, 3)$ = 4·4); 5·03 dd, 1 H (H-2, $J(2, 3)$ = 4·4, $J(2, 1)$ = 2·2); 5·24 t, 1 H (H-3, $J(3, 2)$ = 4·4, $J(3, 4)$ = 4·4); 6·106 d, 1 H (H-1, $J(1, 2)$ = 2·2). For $C_{14}H_{19}N_3O_9$ (373·3) calculated: 45·04% C, 5·13% H, 11·26% N; found: 44·82% C, 5·11% H, 11·02% N.

6-Azido-6-deoxy-L-idono-1,4-lactone (*XX*)

To a solution of *XVIII* (1·47 g; 7·1 mmol) in water (40 ml) were added barium carbonate (3 g; 15 mmol) and two 0·25 ml portions of bromine during 1 h. After stirring for 4 h, TLC in S3 showed only one spot (R_F 0·64) identical with that of the starting *XVIII*; however, double detection with diphenylamine–aniline–phosphoric acid[12] and hydroxylamine–ferric chloride proved that the oxidation was complete. After filtration of insoluble salts and removal of the excess bromine with a stream of air, the colourless solution was stirred for 1 h with silver carbonate and desalted on a column of Dowex 50W (H^+ form; 6 ml). The combined filtrates on evaporation

gave 1·34 g (92%) of chromatographically homogeneous syrupy lactone *XX*. IR spectrum (Nujol): 2 100, 1 765 cm^{-1}, $[\alpha]_D^{20}$ +74·1° (*c* 1·7, water, 20 min to 22 h unchanged). For $C_6H_9N_3O_5$ (203·2) calculted: 35·47% C, 4·47% H, 20·68% N; found: 35·69% C, 4·61% H, 20·36% N.

6-Amino-6-deoxy-L-idonolactam (*XXI*) and 2,3,4,5-Tetra-O-acetyl-6-amino-6-deoxy-L-idonolactam (*XXII*)

A solution of lactone *XX* (1·3 g; 6·4 mmol) in methanol (50 ml) was stirred at room temperature with 5% Pd/C (0·5 g) in a renewed hydrogen atmosphere. Thin-layer chromatography in system S3 showed that during 6 h the original spot of R_F 0·65 gradually disappeared whereas an elongate, not well detectable spot of R_F 0·05—0·15 grew stronger. Removal of the catalyst and evaporation of the solvent afforded 1·06 g (92%) of crystalline residue which was crystallized from water–ethanol to give *XXI*, m.p. 179—180°C; $[\alpha]_D^{20}$ +2·3°, $[\alpha]_{436}^{20}$ −4·0° (*c* 3·55, water). For $C_6H_{11}NO_5$ (177·2) calculated: 40·68% C, 6·26% H, 7·91% N; found: 40·44% C, 6·14% H, 7·86% N. Mother liquors from the crystallization of *XXI* were taken down and the residue (550 mg) was acetylated in pyridine (20 ml) as described above. Work-up of the reaction mixture followed by crystallization of the product (936 mg) from ether–acetone (3 : 1) afforded 850 mg (79%) of tetra-O-acetyllactam *XXII*, m.p. 181°C (modification change) and 190·5°C (decomp.); $[\alpha]_D^{25}$ −21·8° (*c* 1·1, chloroform). For $C_{14}H_{19}NO_9$ (345·3) calculated: 48·70% C, 5·55% H, 4·06% N; found: 48·88% C, 5·54% H, 3·85% N.

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