Aminosugars. XXII. Syntheses and Properties of 6-Deoxy-6- and 3-Deoxy-3-guanidino-D-hexoses[1]

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Methyl 6-deoxy-6-guanidino-α-D-glucopyranoside, 6-deoxy-6-guanidino-D-galactose, 3-deoxy-3-guanidino-D-allose (**7**), and 3-deoxy-3-guanidino-D-glucose were synthesized by guanidination of the corresponding aminosugars. The acetate of **7** was proved to exist in a bicyclic structure; 2′,4′,6′-tri-*O*-acetyl-D-allopyrano[1′,2′,3′;4,5,6]-2-acetylimino-1,3-diacetyl-perhydropyrimidine, whereas others exist as the usual pyranoses. Properties of the new compounds and the synthetic methods were examined.

During the last decade, the syntheses and properties of aldoses having an amino or a mercapto group at *C*-4, *C*-5, or *C*-6 position have been extensively studied. It was clarified that the former two exist in various tautomeric mixtures involving five- and six-membered hemiacetal formation with functional groups at *C*-4 and *C*-5 positions, while the latter involve the corresponding septanose and bicyclic 1,6-anhydrosugar, in addition to the usual pyranose.[2] In a previous paper of this series,[3] we disclosed that 2-deoxy-2-guanidino-D-glucose exists mainly in a new bicyclic structure, α-D-glucofurano[1′,2′;4,5]-2-imino-imidazolidine, under acidic conditions, which isomerizes into 2-amino-4-(D-*arabino*-tetrahydroxybutyl)imidazole *via* the corresponding 2-imino-imidazoline-4 structure in an alkaline solution. The results stimulated us to examine the structure of 6-deoxy-6- and 3-deoxy-3-guanidino-hexoses.

Syntheses of guanidino-sugars have not been studied extensively. However, 6-deoxy-guanidino-1,2-*O*-isopropylidene-α-D-glucofuranose[4] and methyl 3-deoxy-4,6-*O*-benzylidene-3-nitroguanidino-α-D-allopyranoside[5] were synthesized by the cyanamide method. Formation of 2-deoxy-2-guanidino-D-glucopyranosyl thiol and -D-galactopyranosyl thiol through the S→N migration of amidino group in the corresponding 1-thiopseudourea derivatives was indicated by Wolfrom *et al.*[6] Glycosylguanidines could not be obtained in a pure state by direct condensation of aldoses with free guanidine,[7] but they were synthesized through glycosylisothioureas.[8] 2-Deoxy-2-guanidino-α-D-altropyranoside was obtained by the reaction of the corresponding 2,3-epoxide with guanidine, but substitution of 3-*O*- or 6-*O*-tosyl-hexoside with guanidine was unsuccessful.[9]

In this paper the syntheses and properties of several 6-deoxy-6- and 3-deoxy-3-guanidino-D-hexoses are reported.

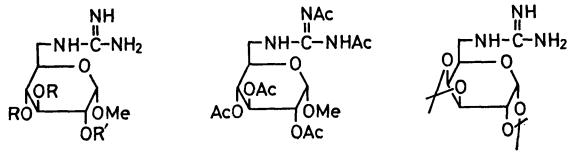
Results and Discussion

6-Deoxy-6-guanidino-D-hexoses. Reaction of methyl 6-amino-6-deoxy-α-D-glucopyranoside[10] with 1.5 equivalent of cyanamide in water at 60 °C with an adjusted pH of 8.2—8.6 gave the corresponding 6-guanidino derivative (**1**) as crystalline flavianate, in 26 and 50% yield for 9 hr and 1 day, respectively. When the pH of the reaction mixture was not adjusted, it increased beyond 10 with the progress of guanidination, a di-*O*-carbamoyl-mono-*O*-amidino derivative (**2**) of **1** being obtained in 73% yield based on cyanamide. The compound showed characteristic absorptions of carbamoyl (1742 and 1588 cm^{-1}) and guanidino groups (1680 and 1615 cm^{-1}) in the IR spectrum, and ring proton signals of α-D-glucopyranose in the NMR spectrum. The position of three *O*-substituents was not determined definitely. However, the *C*-2 position was considered to be the most reasonable for the *O*-amidino group, since 3- and 4-*O*-amidino groups once formed seem to be hydrolyzed to *O*-carbamoyl groups by the intramolecular catalytic action of 6-guanidino group. Acetylation of **1** with acetic anhydride in pyridine gave methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-diacetylguanidino-α-D-glucopyranoside (**3**) in 31% yield, together with 6-monoacetylguanidino derivative. The former showed characteristic absorptions of diacetylguanidino group [λ_{max}^{EtOH} (nm), 221 (ε 8.35×10^3), 255 (ε 1.58×10^4); ν_{max} 1698, 1620, and 1555 cm^{-1}]. It is worth noting that *N*-acetyl groups in diacetylguanidino moiety of **3** are very labile,[11] whereas *O*-glycosidic linkage in **1** strongly resisted acid hydrolysis. De-*O*-acetylation of **3** in methanol with a small amount of sodium methoxide at room temperature caused the shift of λ_{max}^{EtOH} to 234 nm, indicating the elimination of one *N*-acetyl group. **3** was easily converted into **1** only by refluxing in methanol for 14 hr. This means that the alkalinity of 6-guanidino group arose from diacetylguanidino group[12] catalyzed de-*O*-acetylation by the ester-exchange reaction. Treatment of **1** with 6 M hydrochloric acid at 80 °C for 1 day gave no hydrolyzed product, indicating that the protonation of 6-guanidino group prevents the approach of other protons to *C*-1 position, as was observed in the case of 2-amino-2-deoxy-hexosides.[13]

For comparison of synthetic methods, synthesis of **1** by the *S*-methylisothiourea method in ammonia solution[14] was examined. This method gave nearly the same yield as the former (Table 1), but the use of hydrochloride of the aminosugar and diluted ammonia within 10% gave a better yield. This indicates that a suitable buffer action is desirable in this reaction, and that highly concentrated ammonia may consume *S*-methylisothiourea by its conversion into free guanidine.

In order to obtain a 6-guanidino derivative having no protecting group at *C*-1, 6-amino-6-deoxy-1,2;3,4-di-*O*-isopropylidene-α-D-galactose[15] was treated with *S*-methylisothiourea under the best conditions (Table 1), to give 6-guanidino derivative (**4**) as flavianate in

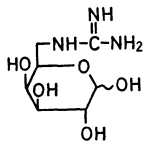
35% yield. Hydrolysis of **4** with flavianic acid gave de-*O*-isopropylidenated product (**5**) as flavianate in 65% yield, which was also obtained in 59% yield by successive guanidination and hydrolysis without isolation of **4**. An attempted substitution of 1,2;3,4-di-*O*-isopropylidene-6-*O*-tosyl-α-D-galactose[16] with guanidine in butanol or in dimethylformamide gave unsuccessful results, similarly to those reported by Danilov and Lishanskii.[9] Acetylation of **5** with acetic anhydride in pyridine gave a sirupy hexaacetate (**6**) in 28% yield, which showed characteristic absorptions of diacetylguanidines. Ring-proton signals of the NMR spectrum of **6** (Fig. 1) confirmed by simulation proved completely its structure to be 1,2,3,4-tetra-*O*-acetyl-6-deoxy-6-diacetylguanidino-β-D-galactopyranose.



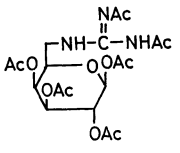
(**1**) R=R′=H
(**2**) R=CONH$_2$, R′=C(NH)NH$_2$

(**3**)

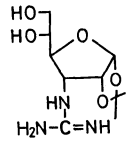
(**4**)



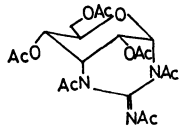
(**5**)



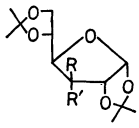
(**6**)



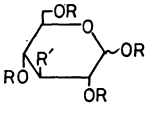
(**7**)



(**8**)



(**9**) R=H, R′=NHCN
(**10**) R=H, R′=NHCONH$_2$
(**11**) R=H, R′=NHCSNH$_2$
(**12**) R=NHC(NH)-NH$_2$, R′=H



(**13**) R=H, R′=NHC(NH)NH$_2$
(**14**) R=Ac, R′=NHC(NAc)-NHAc

Table 1. Guanidination of methyl 6-amino-6-deoxy-α-D-glucopyranoside with *S*-methylisothiourea sulfate in aqueous ammonia[a]

Molar ratio[b]	Concentration of ammonia (%)	Reaction time (days)	Yield (%)
1.5	0	4	40
1.5	9	1	35
1.5	5	4	48
1.5	9	4	48
1.5	10	4	51[c]
1.5	28	4	28
1.5	28	4	40[c]
1.2	0	1/3[d]	18
1.5	0	1[d]	31

a) 5 mmol of aminosugar in a 20 ml solution, at room temperature unless otherwise stated. b) *S*-methylisothiourea to the aminosugar. c) aminosugar used as the hydrochloride. d) reaction temperature 80 °C.

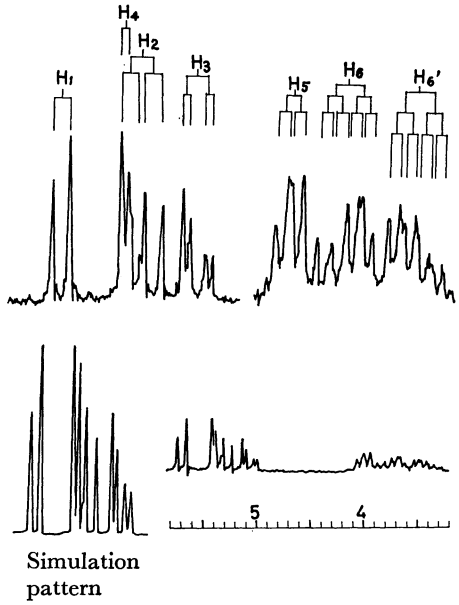


Fig. 1. Ring-proton signals in the NMR spectrum of **6**.

Although the 6-guanidino group in **1** clearly showed the electrostatic effect on the *C*-1 position, the fact that **5** showed positive Sakaguchi reaction after removal of flavianic acid, and that it was converted into **6** suggests that the nucleophilicity of guanidino group is not so strong as to make the septanose or an additional seven-membered aminal ring by surmounting new non-bonded interactions, which will arise by change of the conformation.

*3-Deoxy-3-guanidino-*D*-hexoses.* Guanidination of 3-amino-3-deoxy-1,2;5,6-di-*O*-isopropylidene-α-D-allofuranose[17] by *S*-methylisothiourea method was unsuccessful, and that with cyanamide in water gave a Sakaguchi-reaction positive product. However, it could not be isolated in a pure state. The fusion method[18] of the aminosugar hydrochloride with 1.5 equivalent of cyanamide at 130 °C for 40 min gave the de-5,6-*O*-isopropylidenated 3-guanidino derivative (**7**) as crystalline picrate in 57% yield. When the free aminosugar was used cyanamide dimerized rapidly to biguanide, no product being obtained. Hydrolysis of **7** with 2 M hydrochloric acid gave 3-deoxy-3-guanidino-D-allose as a hygroscopic sirup which is negative to both the Sakaguchi and Fehling reactions. Acetylation of this sirup with acetic anhydride in pyridine gave a sirupy hexaacetate (**8**), UV absorption of which (λ_{max}^{EtOH} 217 nm) differs from that of **3** and **6**. NMR spectrum of **8** (Fig. 2) showed the presence of α-D-allopyranose ring from the long-range coupling between H_1 and H_3 (J=1.9 Hz) and a *trans*-diaxial coupling ($J_{4,5}$=10.6 Hz). Although 1,2,4,6-tetra-*O*-acetyl-3-deoxy-3-diacetylguanidino-α-D-allopyranose structure is possible, **8** was determined to be 2′,4′,6′-tri-*O*-acetyl-α-D-allopyrano[1′,2′,3′;4,5,6]-2-acetylimino-1,3-diacetyl-perhydropyrimidine from the absence of diacetylguanidino moiety in UV spectrum, negative Sakaguchi and Fehling reaction of 3-deoxy-3-guanidino-D-allose, and the presence of lower-shifted acetylimino proton signal (δ 2.52) in the NMR spectrum, as observed in that of 3′,5′,6′-tri-*O*-acetyl-α-D-glucofurano[1′,2′;4,5]-2-acetyl-

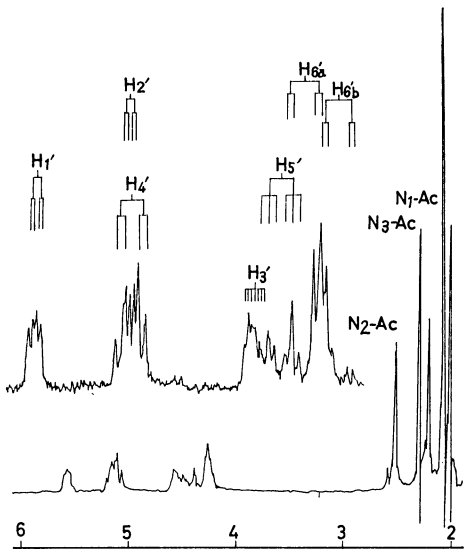


Fig. 2. The NMR spectrum of **8**.

imino-1,3-diacetylimidazolidine.[3]

For the sake of comparison, synthesis of **7** by indirect guanidination was attempted. Reaction of 3-amino-3-deoxy-1,2;5,6-di-*O*-isopropylidene-α-D-allofuranose with cyanogen bromide or with potassium cyanate gave the corresponding 3-cyanamido (**9**) and 3-ureido derivative (**10**) in 89 and 73% yields, respectively. Dehydration of **10** with methanesulfonyl chloride gave **9** in 50% yield. Reaction of **9** with methanolic ammonia at 90 °C in a sealed tube or with hydrogen sulfide in pyridine gave **8** or the corresponding 3-thioureido derivative (**11**) in 26 and 20% yields, respectively. Direct conversion of the aminosugar into **11** by the reaction with potassium thiocyanate gave only the de-5,6-*O*-isopropylidenated product, which was confirmed as the corresponding 5,6-di-*O*-acetyl derivative.[19] These results indicate that the fusion method is the best for synthesis of **7**.

In order to examine whether 3-deoxy-3-guanidino-D-glucose can make an additional aminal-ring, synthesis was carried out as follows. Though the reason is not clear, guanidination of 3-amino-3-deoxy-1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose[20] with cyanamide by the fusion method was unsuccessful. Thus an indirect method was adopted. Reaction of the aminosugar with cyanogen bromide in ether gave the corresponding 3-cyanamide as a sirup, which was then treated with methanolic ammonia in a sealed tube at 80—90 °C for 20 hr to give the corresponding 3-guanidino derivative (**12**) as the crystalline flavianate. Hydrolysis of **12** with flavianic acid gave 3-deoxy-3-guanidino-D-glucose (**13**) also as crystalline flavianate, which is positive to the Sakaguchi and Fehling tests. Base-catalyzed acetylation of **13** gave a sirup containing three products, from which a hexaacetate (**14**) was isolated with a preparative tlc.

The NMR spectrum of **14** indicated that it is composed of α- (H_1: δ 6.31, $J_{1,2}$=3.5 Hz) and β-anomers (H_1: δ 5.71, $J_{1,2}$=8.0 Hz) in the ratio 3:1. The relative amount of the α-anomer increased with reaction time, but both anomers could not be separated. Chemical shifts of ring-protons were different only in that of H_1 and H_2, and irradiation of amino-proton (δ 8.11, $J_{N,3}$=9.0 Hz) caused H_3 proton signal from quartet to triplet (δ 4.79, $J_{2,3}=J_{3,4}$=9.7 Hz). Consequently, **14** was determined to be 1,2,4,6-tetra-*O*-acetyl-3-deoxy-3-diacetylguanidino-α,β-D-gluco-pyranose.

The result suggests again that **13** could not make additional intramolecular aminal-ring, probably due to strong nonbonded interactions for the inversion of the conformation from *C*1 to 1*C*, as observed in the case of **6**.

Experimental

All melting points are uncorrected. The solutions were evaporated under reduced pressure at a bath temperature not exceeding 45 °C. Specific rotations were measured in a 0.5 dm tube, with a Carl Zeiss LEP-Al Polarimeter. The IR spectra were recorded in KBr discs with a Hitachi Model EPI-GS grating IR spectrophotomeser. The NMR spectra were taken with a JMN-4H-100 MHz Spectrometer in deuteriochloroform unless otherwise stated, using tetramethylsilane as an internal standard. Chemical shifts and coupling constants were recorded in δ and Hz units, and IR frequencies in cm^{-1}.

Methyl 6-Deoxy-6-guanidino-α-D-glucopyranoside (1) Dihydrochloride. i) Cyanamide Method: a) A solution of methyl 6-amino-6-deoxy-α-D-glucopyranoside hydrochloride[10] (1.15 g, 5 mmol), cyanamide (0.32 g, 7.5 mmol) and 1 M sodium hydroxide (1 ml, 1 mmol) in water (10 ml) was kept at 80 °C for 17 hr. The pH of the solution which changed to 10.0 was adjusted with 2 M hydrogen chloride to 5.0, and the solution was evaporated to give a sirup. The sirup was dissolved in ethanol (20 ml), filtered, and the filtrate was left to stand overnight in a refrigerator after addition of acetone, to give white crystals (**2**) (0.6 g, 73% based on cyanamide). Mp 183 °C, $[\alpha]_D^{23}$ +69.8° (*c* 1.0, H_2O); IR: 1742 and 1588 (urethane), 1680 and 1665 (guanidino group), 1615 (guanyl).

Found: C, 30.73; H, 6.27; N, 23.71; Cl, 17.42%. Calcd. for $C_{11}H_{23}N_7O_7Cl_2$: C, 30.28; H, 5.81; N, 23.48; Cl, 17.25%.

b) In a reaction similar to the above experiment, the pH of the solution was adjusted to 8.2 at the beginning and maintained at 8.0—8.6 during the course of reaction at 60 °C. The reaction mixture was treated with Amberlite IRA-410 (3 ml), and filtered. The solute was absorbed on a column of Amberlite CG-50 (15 ml), and the column was washed successively with deionized water (200 ml), 5% aqueous ammonia (200 ml), and water (200 ml), and then eluted with 0.5 M hydrogen chloride. The neutral effluent was evaporated, and the residue was extracted with ethanol. The extract was evaporated, and the residual sirup was dissolved in water (20 ml), deionized with Amberlite IRA-410 (3 ml), and the solution was evaporated to give a sirup. From a mixed solution of the sirup in water (0.5 ml) and flavianic acid (1.5 g) in ethanol (10 ml), yellow flavianate (**1**, 1.045 g) was obtained as crystals. The second crop (0.245 g) was obtained from the mother liquor. Yield, 1.29 g (50%); mp 155 °C (dec.); $[\alpha]_D^{23}$ +43.5° (*c* 2.0, H_2O); IR: 1673 and 1655 (sh) (mono substituted guanidine).

Found: C, 38.62; H, 4.38; N, 12.58; S, 6.02%. Calcd for $C_{18}H_{23}N_5O_{13}S$: C, 38.60; H, 4.14; N, 12.52; S, 5.73%.

ii) S-Methylisothiourea Method: A solution of methyl 6-amino-6-deoxy-α-D-glucopyranoside[10] (0.69 g, 3 mmol) and *S*-methylisothiourea sulfate (0.62 g, 4.5 mmol) in ammonia (10%, 10 ml) was left to stand at room temperature for 4 days, treated with Amberlite IRA-410 (3 ml) to remove sulfate ion, and then filtered. The filtrate was passed through an Amber-

lite CG-50-I column, and treated as above to give **1** in 51% (0.86 g) yield.

Methyl 2,3,4-Tri-O-acetyl-6-deoxy-6-diacetylguanidino-α-D-glucopyranoside (3). To a cold solution of **1** (8.34 g, 15 mmol) in pyridine (5 ml) was added dropwise acetic anhydride (15 ml, 150 mmol) for 30 min with stirring. The resulting solution was kept at room temperature for 2 day, poured into ice-water (200 ml), and then extracted with chloroform (50 ml ×4). The extract was successively washed with 2 M hydrochloric acid (40 ml×4), saturated sodium bicarbonate (40 ml ×4) and water, dried, and evaporated. The residue was fractionated on a silica-gel column (Kiesel Gel 60) with methanol–benzene (0.5—1.0% methanol), into **3** (2.04 g, 31%) and a mixture of methyl 6-monoacetylguanidino-6-deoxy-2,3,4-tri-*O*-acetyl-α-D-glucopyranoside and another unknown compound (0.62 g). $[\alpha]_D^{23}$ +71.5° (*c* 1.98, $CHCl_3$), +86.9° (*c* 0.84, EtOH); IR: 1750 (OAc), 1705, 1616, and 1555 (diacetylguanidine); λ_{max}^{EtOH} (nm) 221 (ε 8.35×10³) and 254.7 (1.58×10⁴); NMR: 4.97 (H_1: d, $J_{1,2}$=3.2), 4.87 (H_2; q, $J_{2,3}$=9.5), 5.49 (H_3; t, $J_{3,4}$=9.5), 3.95 (H_5; m, $J_{5,6}$=7.0, $J_{5,6'}$=3.4), 3.55—3.80 (H_6 and H_6'), 3.44 (OMe), 2.21, 2.12, 2.09 and 2.02 (5×Ac).

Found: C, 48.13; H, 5.90; N, 9.53%. Calcd for $C_{18}H_{27}N_3O_{10}$: C, 48.54; H, 6.11; N, 9.44%.

When a solution of **3** (305 mg, 0.69 mmol) in ethanol (20 ml) was refluxed for 14 hr, it became positive to the Sakaguchi reaction, and showed one spot on paper chromatography (Toyoroshi No. 50), using ethyl acetate–pyridine–acetic acid–water (5: 5: 1: 3) as developing solvent, of which R_f value (0.36) consists with that of **1**. Addition of flavianic acid (288 mg) in ethanol (5 ml) to the product gave the flavianate of **1**. Yield, 260 mg (69%).

6-Deoxy-6-guanidino-1,2; 3,4-di-O-isopropylidene-α-D-galactopyranose (4) Flavianate. A solution of 6-amino-6-deoxy-1,2; 3,4-di-*O*-isopropylidene-α-D-galactopyranose[15] (1.56 g, 6 mmol) and *S*-methylisothiourea sulfate (1.25 g, 9 mmol) in 10% ammonia (15 ml) was left to stand at room temperature for 4 day and then evaporated. The residue was dissolved in water (8 ml). The solution was treated with Amberlite IRA-410, and the solute was absorbed on an Amberlite CG-50-I (15 ml) column. The column was eluted with deionized water, aqueous ammonia (5%, 200 ml), and then 0.5 M hydrochloric acid. The last effluent was evaporated, and the residue was extracted with ethanol (20 ml). The ethanol solution was diluted with water (20 ml), treated with Amberlite IRA-410 (4 ml), and then evaporated to give a sirup (0.8 g). A solution of the sirup and flavianic acid (1.05 g) in ethanol (20 ml) was left to stand in a refrigerator for one day to give yellow crystals. Yield, 1.29 g (35%); mp 135 °C; $[\alpha]_D^{23}$ −20.6° (*c* 1.0, EtOH): IR: 1668 and 1650 (monosubstituted guanidine).

Found: C, 44.51; H, 4.85; N, 10.89; S, 5.38%. Calcd for $C_{23}H_{29}N_5O_{13}S$: C, 44.87; H, 4.75; N, 11.38; S, 5.21%.

6-Deoxy-6-guanidino-D-galactose (5) Flavianate. a) A solution of the flavianate of **4** (123 mg, 0.2 mmol) and flavianic acid (35 mg, 0.1 mmol) in water (5 ml) was kept at 65 °C for 2 hr, and then evaporated. From the residue, excess flavianic acid was removed with ethanol to give yellow crystals. Yield, 70 mg (65%); mp 200 °C (dec.); $[\alpha]_D^{23}$ +14.3°⟶+18.5° (*c* 0.7, H_2O); IR: 1675 and 1645 (monosubstituted guanidine).

Found: C, 38.61; H, 4.30; N, 12.79; S, 5.97%. Calcd for $C_{17}H_{21}N_5O_{13}S$: C, 38.13; H, 3.95; N, 13.08; S, 5.99%.

This compound was positive to the Fehling test, and to the Sakaguchi reaction after removal of flavianic acid with IRA-410.

b) A solution of 6-amino-6-deoxy-1,2; 3,4-di-*O*-isopropylidene-α-D-galactopyranose (1.30 g, 5 mmol) and *S*-methylisothiourea sulfate (1.04 g, 7.5 mmol) in aqueous ammonia (10%, 8 ml) was treated as above, without isolation of **4**. Yellow crystals (**5**). identical with those described above, were obtained in 59% (1.58 g) yield.

1,2,3,4-Tetra-O-acetyl-6-deoxy-6-diacetylguanidino-β-D-galactopyranose (6). To a cold solution of the flavianate of **5** (5.36 g, 0.01 mmol) in pyridine (30 ml) was added dropwise acetic anhydride (10 ml, 100 mmol), and the resulting solution was left to stand at room temperature for 2 day, and then poured into ice–water (500 ml). The aqueous solution was extracted with chloroform (100 ml×5), and the extract was washed 2 M hydrochloric acid, saturated bicarbonate and water. with Evaporation of the extract gave a sirup (3.4 g) which was fractionated on a silica-gel column (Kiesel Gel 60), using benzene–acetone (5: 1) as effluent. The first fraction gave a pure sirupy hexaacetate (1.2 g, 27.3%). $[\alpha]_D^{23}$ +16.5° (*c* 1.17, EtOH); IR: 1745 (OAc), 1694, 1600, and 1555 (diacetylguanidine); λ_{max}^{EtOH} (nm) 254 (ε 1.73×10⁴), 221 (8.94×10³); NMR: 13.04 and 9.15 (2×NH), 5.69 (H_1; d, $J_{1,2}$=7.9), 5.33 (H_2; q, $J_{2,3}$=10.0), 5.07 (H_3; q, $J_{3,4}$=3.7), 5.40 (H_4; q, $J_{4,5}$=0.5), 4.00 (H_5; q, $J_{5,6}$=8.0, $J_{5,6'}$=5.0), 3.74 (H_6; dq, $J_{6,6'}$=14.0, $J_{6,\ NH}$=8.0), 3.41 ($H_{6'}$; dq, $J_{6',\ NH}$=5.0), 1.95, 2.00, 2.09, 2.13, and 2.15 (6×Ac).

Found: C, 47.82; H, 5.66; N, 8.75%. Calcd for $C_{19}H_{27}N_3O_{11}$: C, 48.18; H, 5.75; N, 8.88%.

3-Deoxy-3-guanidino-1,2-O-isopropylidene-α-D-allofuranose (7) picrate. a) A homogeneous solution of 3-amino-3-deoxy-1,2; 5,6-di-*O*-isopropylidene-α-D-allofuranose hydrochloride[17] (296 mg, 1 mmol) and cyanamide (64 mg, 1.5 mmol) in water (10 ml) was evaporated and the residue was heated at 130—133 °C for 40 min on a silicone-oil bath. The cooled reaction mixture was dissolved in water (6 ml), treated with Amberlite IRA-410 (3 ml), and evaporated to one-third volume. Addition of picric acid (276 mg) in methanol (4 ml) to the remaining solution gave yellow crystals (295 mg, 56.6%) which were recrystallized from water. Mp 193—193.5 °C, $[\alpha]_D^{23}$ +47.9° (*c* 1.09, MeOH), IR: 1645 (monosubstituted guanidine), the Sakaguchi reaction; positive.

Found: C, 37.41; H, 4.51; N, 17.02%. Calcd for $C_{16}H_{22}N_6O_{12}$–H_2O: C, 37.21; H, 4.76; N, 16.52%.

b) A solution of **9** (100 mg, 0.35 mmol) in saturated methanolic ammonia (15 ml) was heated in a sealed tube at 80 °C for 15 hr, and then evaporated to give a sirup. From the sirup and picric acid (100 mg) in methanol–water (4 ml, 50%), yellow crystals, identical with **7**, were obtained (46 mg, 26%).

2',4',6'-Tri-O-acetyl-α-D-allopyrano[1',2',3'; 4,5,6]-2-acetylimino-1,3-diacetyl-perhydropyrimidine (8). A solution of **7** (254 mg, 0.5 mmol) in 2 M hydrochloric acid was heated at 70 °C for 6 hr, and picric acid deposited was filtered off. The water layer was extracted with ether (10 ml×5) and then evaporated to give a sirup (135 mg). The sirup was acetylated with acetic anhydride (0.5 ml) in pyridine (2 ml), and the reaction mixture was poured into ice–water and extracted with chloroform (20 ml×5). The extract was successively washed with 2 M hydrochloric acid, saturated sodium bicarbonate and water, and then evaporated to give a sirup (165 mg). This sirup showed three spots on tlc (MeOH: pyridine=9: 1), and was fractionated into a mixture (122 mg) of spot I and spot II (main), and spot III (46 mg). From the mixture, sirupy spot II (35 mg, 15%) was obtained in a pure state by fractionation on a silica-gel column (Wakogel C-200) using benzene–ethyl acetate (4: 1) as effluent, which was crystallized from ether. Mp 134 °C, $[\alpha]_D^{23}$ +188° (*c* 0.235, EtOH), IR: 1725 (OAc), 1700 (=NAc), 1635 (NAc). λ_{max}^{EtOH} 216 nm, NMR: 5.57 ($H_{1'}$; q, $J_{1',2'}$=3.4, $J_{1',3'}$=1.9), 5.17 ($H_{2'}$; q, $J_{2',3'}$=2.5), 5.12 ($H_{4'}$; q, $J_{4',5'}$=10.6), 4.59

($H_{3'}$; m, $J_{3',4'}=3.9$), 4.46 ($H_{5'}$; sex, $J_{5',6'_a}=3.5$, $J_{5',6'_b}=3.0$), 4.34 ($H_{6'_a}$; q, $J_{6'_a,6'_b}=12.0$), 4.24 ($H_{6'_b}$; q), 2.52 (=NAc), 2.30 and 2.22 (NAc), 2.09 and 2.02 (3×OAc).

Found: C, 49.51; H, 5.51; N, 9.21%. Calcd for $C_{19}H_{25}N_3O_{10}$: C, 50.11; H, 5.53; N, 9.23%.

3-Cyanamido-3-deoxy-1,2; 5,6-di-O-isopropylidene-α-D-allofuranose (9). a) To a solution of 3-amino-3-deoxy-1,2; 5,6-di-*O*-isopropylidene-α-D-allofuranose[17] (130 mg, 0.5 mmol) in ether (5 ml) was added portionwise cyanogen bromide (27 mg, 0.25 mmol) in ether (3 ml) with stirring, and the resulting solution was left to stand at room temperature for 4 hr. A white precipitate (67 mg) deposited was filtered off, and the filtrate was evaporated. The residue was extracted with benzene, and the extract was again evaporated to give colorless sirup (62.3 mg, 89%) which was purified on a silica-gel column. This sirup crystallized on standing. Mp 83—84 °C, $[\alpha]_D^{23}$ +76.1° (*c* 1.80, EtOH), IR: 2220 (CN).

Found: C, 54.89; H, 7.07; N, 9.56%. Calcd for $C_{13}H_{20}N_2O_5$: C, 54.92; H, 7.09; N, 9.85%.

b) A solution of **10** (151 mg, 0.5 mmol) and methanesulfonyl chloride (58 ml, 0.75 mmol) in pyridine (4 ml) was left to stand at room temperature for one day, poured into ice-water (30 ml), and then extracted to give a sirup (112 mg, 79%) which was purified on a silica-gel column as above. Yield, 96 mg (68%).

3-Deoxy-1,2; 5,6-di-O-isopropylidene-3-ureido-α-D-allofuranose (10). A solution of 3-amino-3-deoxy-1,2; 5,6-di-*O*-isopropylidene-α-D-allofuranose (259 mg, 1 mmol), potassium cyanate (122 mg, 1.5 mmol), and acetic acid (0.06 ml, 1 mmol) in water (5 ml) was heated at 100 °C for 90 min, and treated with Amberlite IRA-410 (2 ml) for one day and then with Amberlite CG-50-I to remove potassium ion and unreacted starting material. The effluent was evaporated to give a sirup (258 mg, 85.5%) which crystallized from ether. Yield, 220 mg (73%), mp 164 °C, $[\alpha]_D^{23}$ +87.4° (*c* 1.0, EtOH), IR: 1675 (ureido).

Found: C, 51.18; H, 7.27; N, 9.52%. Calcd for $C_{13}H_{22}N_2O_6$: C, 51.64; H, 7.34; N, 9.27%.

3-Deoxy-1,2; 5,6-di-O-isopropylidene-3-thioureido-α-D-allofuranose (11). To a solution of **9** (177 mg, 0.62 mmol) in pyridine (5 ml) was passed hydrogen sulfide at room temperature for 5 hr. The solution was then evaporated to give a sirup which crystallized from ethanol (40 mg, 20%). Recrystallization from methanol gave fine needles. Mp 219—220 °C, $[\alpha]_D^{23}$ +108.4° (*c* 0.5, EtOH), IR: 3430, 3360, and 3330 (NH), 1532 (thioureido).

Found: C, 48.64; H, 7.00, N, 9.00; S, 9.83%. Calcd for $C_{13}H_{22}N_2O_5S$: C, 49.04; H, 6.97; N, 8.79; S, 10.07%.

3-Deoxy-3-guanidino-1,2; 5,6-di-O-isopropylidene-α-D-glucofuranose (12) Flavianate. To a cold solution of 3-amino-3-deoxy-1,2; 5,6-di-*O*-isopropylidene-α-D-glucofuranose[20] (2.5 g, 9.7 mmol) in ether (60 ml) was added with stirring 0.5 equivalent of cyanogen bromide in ether (40 ml), and the resulting solution was left to stand at room temperature for 6 hr, the hydrobromide of the aminosugar then being filtered. The sirupy product obtained by evaporation of the filtrate was purified on a silica-gel column with benzene–ethyl acetate (8: 1) as effluent. The cyanamido derivative (1.11 g, 81.5% based on cyanogen bromide) showed the characteristic absorption of nitrile (2200 cm^{-1}) in IR spectrum. A solution of the cyanamide in methanol (50 ml) saturated with ammonia was heated in a sealed tube at 80—90 °C for 20 hr, and then evaporated. Addition of flavianic acid (1.4 g, 3.8 mmol) in ethanol to a suspension of the resulting sirup in a small amount of water gave the flavianate of **12** as yellow crystals, which were recrystallized from aqueous acetone. Mp 185—190 °C (decomp.), yield, 39% based on the cyanamide; $[\alpha]_D^{23}$ −22.4° (*c* 1.0, pyridine).

Found: C, 44.77; H, 4.73; N, 11.47; S, 5.58%. Calcd for $C_{23}H_{29}N_5O_{13}S$: C, 44.87; H, 4.74; N, 11.37; S, 5.21%.

3-Deoxy-3-guanidino-D-glucose (13) Flavianate. A suspension of the flavianate of **12** (500 mg, 0.81 mmol) and flavianic acid (200 mg, 0.51 mmol) in water (60 ml) was heated at 80 °C for 4 hr to give a homogeneous solution, and the solution was then evaporated. The residue was washed with ethanol to give **13** quantitatively as flavianate. For elemental analyses. a portion of it was recrystallized from methanol. Mp 210 °C (decomp.); $[\alpha]_D^{23}$ +17.2→+23.8° (in H_2O, after 48 hr).

Found: C, 38.65; H, 4.01; N, 13.41%. Calcd for $C_{17}H_{21}N_5O_{13}S$: C, 38.13; H, 3.95; N, 13.08%.

This compound was positive in the Sakaguchi and Fehling reactions.

1,2,3,4-Tetra-O-acetyl-3-deoxy-3-diacetylguanidino-α,β-D-glucopyranose (14). Acetylation of **13** (300 mg, 0.56 mmol) with acetic anhydride (620 mg, 6.08 mmol) in pyridine gave sirupy product which showed three spots (R_f=0.66, 0.52 and 0.12) on a preparative tlc with benzene–ethyl acetate (1: 1) as developing solvent. The portion R_f=0.52 was extracted with acetone to give **14** (50 mg, 19%) as a sirup. $[\alpha]_D^{23}$ +35.8° (*c* 1.21, $CHCl_3$); λ_{max}^{EtOH} 256 and 220 nm.

Found: C, 48.52; H, 5.82; N, 8.32%. Calcd for $C_{19}H_{27}N_3O_{11}$: C, 48.19; H, 5.74; N, 8.87%.

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