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On the Configuration of Branched-Chain Derivatives of 1,2 : 5,6-Di-*O*-isopropylidene-*α*-D-*ribo*-hexofuranos-3-ulose

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In order to obtain a 3-*C*-hydroxymethyl-D-glucose derivative some nucleophilic reactions of 1,2 : 5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranos-3-ulose (**1**) and the configurations of products have been examined. *Gluco*- and *allo*-configurations of known 3-*C*-nitromethyl derivatives of **1** were confirmed by the fact that 3-*C*-acetaminomethyl-1,2-*O*-isopropylidene-α-D-*xylo*- and *ribo*-pentodialdofuranoses, derived by four successive transformations, showed the absence and presence of the aminal-ring formation between the aldehyde and acetamino groups, respectively. A 3-*C*-carbethoxymethyl derivative obtained by the Reformatsky reaction of **1** with ethyl bromoacetate was proved to be of *allo*-configuration by the lactone-formation between C_5-hydroxyl and carboxyl groups. The configuration of 3-*C*-hydroxymethyl derivative (**15**) obtained by treatment of known 3-*C*-methylene derivative of **1** with permanganate was proved to be of *gluco*-type by comparison of the corresponding 3-*C*-aminomethyl derivative (**5**), derived by three-step conversions, with that obtained from 3-*C*-nitromethyl derivatives. **15** was also obtained by epoxidation of **1** with diazomethane followed by ring-opening with alkali. Treatment of **5** and its *allo*-epimer with nitrous acid gave, respectively, a ring-expanded product and the 3′,5-anhydride, the former being also recognized in the epoxidation products. Structures of new compounds were examined by NMR spectra and stereoselectivity of reactions discussed.

Studies are increasingly being made on branched-sugars rarely found in nature[1], and on osuloses as important intermediates for synthesis of deoxy-, amino-, and branched-sugars[2].

In order to obtain a 3-*C*-hydroxymethyl derivative of D-glucose as an intermediate for a total synthesis of tetrodotoxin[3], we examined nitromethane-condensation, the Reformatsky reaction and diazomethane-condensation of 1,2 : 5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranos-3-ulose (**1**)[4] and the configurations of the products. The compound was obtained by treatment of 3-*C*-methylene derivative of **1** with permanganate or by diazomethane-condensation of **1**, followed by ring-opening of the resulting epoxide.

Results and Discussion

Nitromethane Condensation and the Reformatsky Reaction. It is known that the nitromethane condensation of **1** afforded 1,2 : 5,6-di-*O*-isopropylidene-3-*C*-nitromethyl-α-D-allofuranose (**2**) or a mixture of **2** and the corresponding 3-epimer (**3**), depending on the conditions[5—7]. The structure of **2** and **3** was confirmed from the fact that 1,2-*O*-isopropylidene-3-*C*-nitromethyl-α-D-pentofuranose derived from **3** by oxidative elimination of atom at position 6 gave the corresponding 3,5-*O*-isopropylidene ring[7] and that a part of **3** was converted into **2** through 3-dehydro-3-deoxy-1,2 : 5,6-di-*O*-isopropylidene-3-*C*-nitromethylene-α-D-*ribo*-hexofuranose[6]. Their structures were confirmed by examining whether the corresponding 3-*C*-acetaminomethyl-1,2-*O*-isopropylidene-α-D-*ribo*-hexofuranose[6]. Their structures were confirmed by examining whether the corresponding 3-*C*-acetaminomethyl-1,2-*O*-isorpopylidene-α-D-pentodialdofuranoses can form an aminal-ring between the aldehyde and

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1) F. Shafizadeh, "Advances in Carbohydrate Chemistry," Vol. 11, Academic Press, New York, N. Y. (1956), p. 263.

2) J. S. Brimacombe, *Angew. Chem.*, **81**, 415 (1969).

3) K. Tsuda, C. Tamura, R. Tachikawa, K. Sakai, O. Amakasu M. Kawamura, and S. Ikuma, *Chem. Pharm. Bull.* (Tokyo), **12**, 634, 642 (1964); T. Goto, Y. Kishi, S. Takahashi and Y. Hirata, *Tetrahedron Lett.*, **1964**, 779, 1831; R. B. Woodward, *Pure. Appl. Chem.*, **9**, 49 (1964).

4) P. J. Beynon, P. M. Collins and W. G. Overend, *Proc. Chem. Soc.*, **1964**, 342; K. Onodera, S. Hirano and N. Kashimura, *J. Amer. Chem. Soc.*, **87**, 4651 (1965); K. Onodera, H. Hirano and N. Kashimura, *Carbohyd. Res.*, **6**, 276 (1968); B. T. Lowton, W. A. Szarek and J. K. N. Jones, *ibid.*, **10**, 456 (1969).

5) G. J. Lourens, *Tetrahedron Lett.*, **1969**, 3733.

6) H. P. Albrecht and J. G. Moffat, *ibid.*, **1970**, 1063.

7) A. Rosenthal, K. -S. Ong, and D. Baker, *Carbohyd. Res.*, **13**, 113 (1970).

acetamino groups. Hydrogenation of **2** and **3** in the presence of palladium-charcoal gave the corresponding 3-*C*-aminomethyl derivatives (**4**) and (**5**), respectively. They were then converted into 3-*C*-acetaminomethyl derivatives (**6**) and (**7**) by acetylation in ethanol. The compounds were obtained in crystalline state, and characterized by NMR. The results for **6** and **7** are given in Figs. 1—3.

The first-order analysis of the original spectrum of **6** was hindered by overlapping of proton signals. However, deuteration of the amido and hydroxyl protons and addition of a few drops of benzene to cause a shift in several peaks (Fig. 1) made it easy to assingn $H_{3'a}$ and H_{6b} protons. Other protons were assigned from the intensities and coupling constants. The coupling constant between H_4 and H_5 was also determined by the examination of pseudo-contact shift (Fig. 2) with tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedionato)-europium (III)[8] [Eu(fod)$_3$]. Tickling of H_6 protons caused H_5 proton signal to disclose a large coupling corresponding to that of H_4, and irradiation of H_5 changes H_{6a} and H_{6b} signals to a broadened AB quartet from AB part of an ABX system. From a comparison of the magnitude of contact shifts of several kinds of protons, it is concluded that nitrogen atom in **6** is the more predominant ligand than oxygen of *tert*-hydroxyl group.

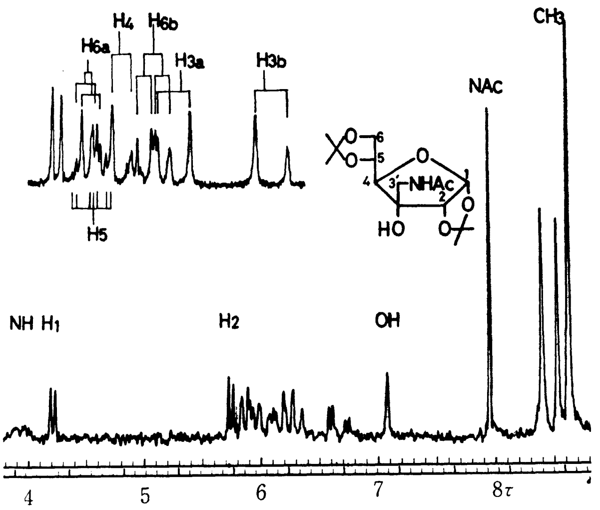

Fig. 1. NMR spectrum of **6** in CDCl$_3$.

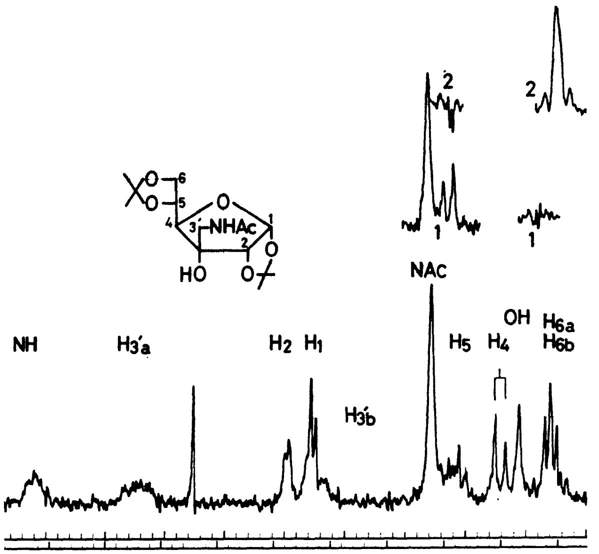

Fig. 2. NMR spectrum of **6** (16 mg) in the presence of Eu(fod)$_3$ (10 mg).

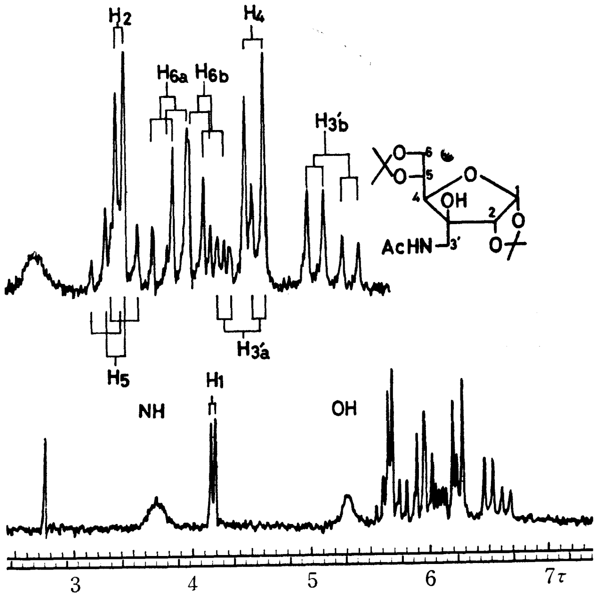

Fig. 3. NMR spectrum of **7** in CDCl$_3$.

Signals in the NMR spectrum of **7** (Fig. 3) were assigned only by means of double-resonance technique. Such a difference in D-*allo* and D-*gluco* derivatives was generally observed.

Hydrolyses of 5,6-*O*-isopropylidene groups of **6** and **7** were performed by treatment with 0.01 N sulfuric acid for 2 hr, and the products were directly oxidized with periodate to give 1,2-*O*-isopropylidene-3-*C*-acetaminomethyl-α-D-*xylo*- and and D-*ribo*-pentodialdofuranose (**8**) and (**9**), respectively. **8** showed charac-

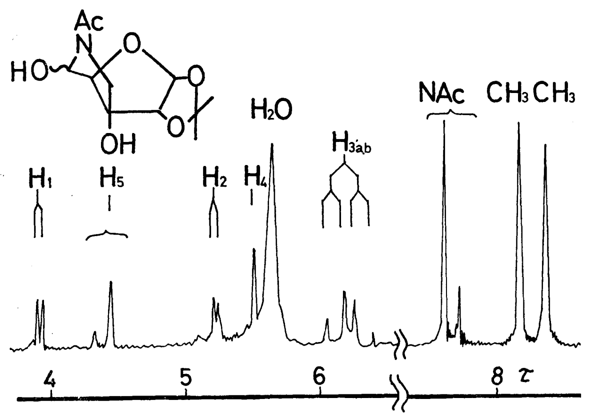

Fig. 4. NMR spectrum of **8** in CDCl$_3$.

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[8] R. E. Rondeau and R. E. Sievers, *J. Amer. Chem. Soc.*, **93**, 1522 (1971).

teristic absorptions of tertiary amide (1605 and 1615 cm^{-1}) in IR spectrum, and showed no aldehyde proton signal in NMR spectrum (Fig. 4). The existence of two singlets for both *N*-acetyl and H_5 protons which could not collapse at 60°C indicates that **8** exists in aminal structures (**8′**) in which two configurations are possible at C_5. **9** also showed a secondary amide absorption (1640 and 1540 cm^{-1}) and an aldehyde proton signal at τ 0.37 (Fig. 5). The configurations of **2** and **3** were confirmed.

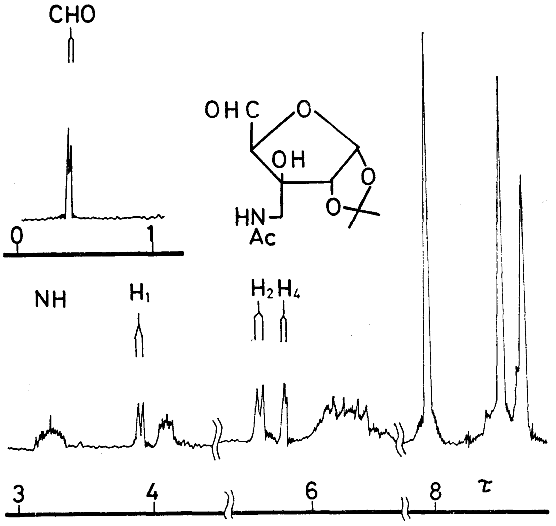


Fig. 5. NMR spectrum of **9** in $CDCl_3$.

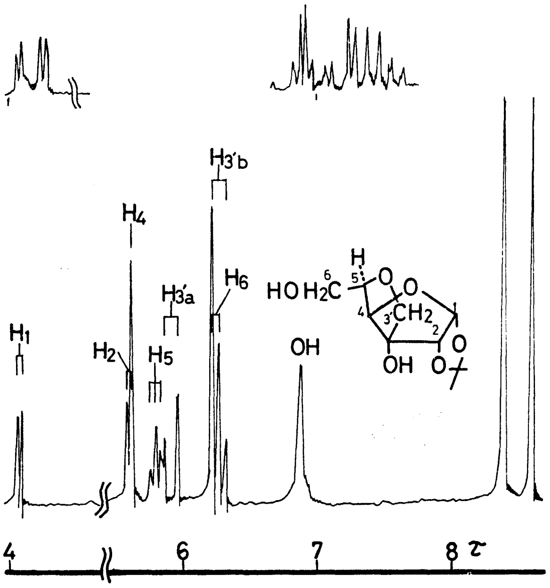
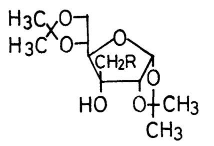
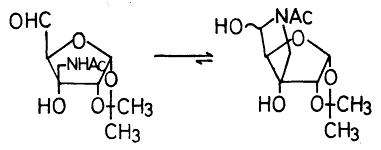


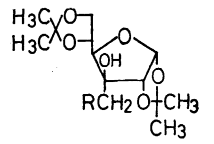
Fig. 6. NMR spectrum of the sirup from the mother liquor.



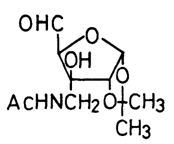
(**2**) R=NO_2
(**4**) R=NH_2
(**6**) R=NHAc
(**12**) R=$CO_2C_2H_5$
(**14**) R=COOH



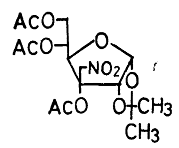
(**8**) (**8′**)



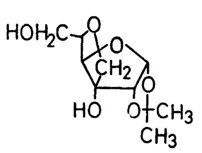
(**3**) R=NO_2
(**5**) R=NH_2
(**7**) R=NHAc
(**15**) R=OH
(**16**) R=OTs



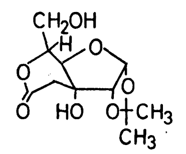
(**9**)



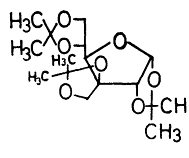
(**10**)



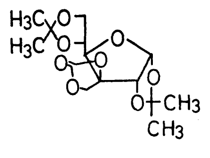
(**11**)



(**13**)



(**17**)



(**18**)

Acetylation of **2** with acetic anhydride in the presence of *p*-toluenesulfonic acid gave 3,5,6-tri-*O*-acetyl-1,2-*O*-isopropylidene-3-*C*-nitromethyl-α-D-allofuranose (**10**). However, conversion of **10** into the corresponding 3-*C*-nitromethylene derivative[7] was unsuccessful. Deamination of **4** and **5** was attempted. Treatment of **4** with barium nitrite in acetic acid at 0°C for 12 hr gave 1,2-*O*-isopropylidene-3′,5-anhydro-3-*C*-hydroxymethyl-α-D-allofuranose (**11**) in 20% yield. Disappearance of the characteristic absorption of an amino (1580 cm^{-1}) and appearance of that of hydroxyl (3250 and 3410 cm^{-1}) group in IR spectrum, and the presence of H_4 signal as singlet and H_5 as triplet supports the structure (Fig. 6). A similar treatment of **5** gave a sirup. The presence of a six-membered ketone was deduced by IR spectrum (1730 cm^{-1}) and NMR spectrum (two kinds of H_1 signals at τ 4.08 and 4.25, and two quartet at τ 7.1—7.7). The spectral information was also confirmed on a sirup obtained from the mother liquor of **11**. Thus it is concluded that deamination of **4** and **5** induced ring-expansion C_3′-carbonium ion, and a part of carbonium ion cyclized with sterically close C_5-oxygen in the case of **4**.

Treatment of **1** with ethyl bromoacetate in the presence of zinc metal and catalytic amount of iodine, followed by chromatographic separation of the product on a silica gel column gave the corresponding 3-*C*-

carbethoxymethyl derivative (**12**) as a sirup and a small amount of 1,2-*O*-isopropylidene-3-*C*-carboxymethyl-α-D-allofuranose-3′,5-lactone (**13**) as crystals. Treatment of **12** with alkali gave the corresponding 3-*C*-carboxymethyl derivative (**14**). However, application of dehydrative decarboxylation of β-hydroxy-carboxylic acid in quinoline with copper powder[9] to **14** gave unchanged product and again a small amount of **13**. This proves that **12** and **14** have the *allo*-configuration. IR spectrum of **12**, **13** and **14** showed, respectively, characteristic absorption bands of ester (1725 cm^{-1}), lactone (1735 cm^{-1}), and carboxylic acid (1695 cm^{-1}). The presence of much less hindered C_6-methylene signals in the NMR spectrum of **13** also supports the structure (Fig. 7).

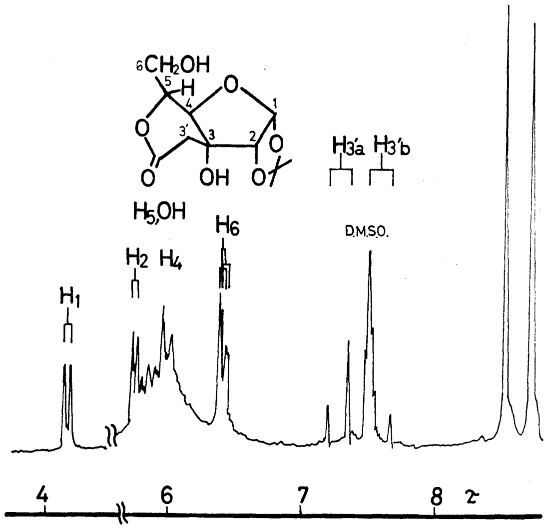
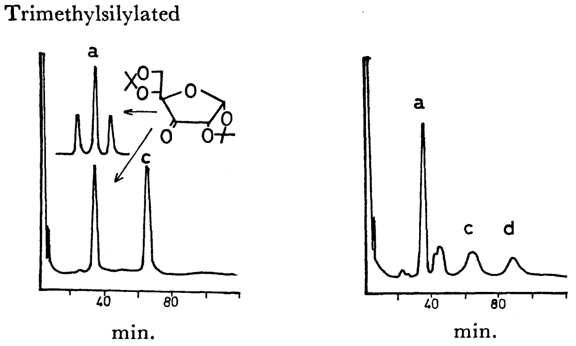


Fig. 7. NMR spectrum of **13** in DMSO.

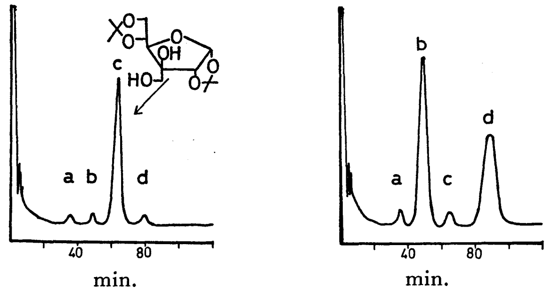
*Synthesis of 3-C-Hydroxymethyl-1,2: 5,6-di-O-isopropylidene-α-*D*-glucofuranose by means of the Wittig or Diazomethane Reaction.* It has been reported that the reaction of **1** with methylenetriphenylphosphorane in dimethyl sulfoxide or in ether gave the corresponding 3-*C*-methylene derivative[10,11]. Treatment of this compound with potassium permanganate gave 3-*C*-hydroxymethyl-1,2 : 5,6-di-*O*-isopropylidene-α-D-glucofuranose (**15**) in 70% yield. The NMR spectrum of **15** gave a pattern close to that of **7**, except for the $C_{3'}$-methylene protons which appeared as a singlet at τ 6.15. The configuration at C_3 was proved chemically as follows. Partial tosylation of **15** gave a monotosylate (**16**) whose tosylated position was deduced to be $C_{3'}$ from the lower shift of $C_{3'}$-methylene signals (at τ 5.05 and 5.80 as AB quartet) in the NMR spectrum. The compound was converted into the corresponding azide, and then hydrogenated to give the corresponding 3-*C*-aminomethyl derivative which was identical with **5** in melting point and spectral data.

As another synthetic method of **15**, direct epoxidation of **1** with diazomethane was tried, followed by ring-opening with alkali and the product was examined by gas liquid chromatography (Fig. 8). When epoxidation was carried out in ether or methanol, the product contained many species, but the products obtained by the reaction in benzene contained the desired compound (peak c) as the main product. In fact, **15** was separated in 25% yield which was identical with the authentic specimen in melting point and spectral data. Three trimethylsilylated species of **1** indicated the occurrence of two kinds of enolization[12] to some extent. The glpc of the sirup obtained from the mother liquor showed nearly complete separation of **15** (peak c) by simple crystallization. Peaks d and b were respectively deduced to be 3-epimer of **15** and a ring expanded product mentioned in the case of the deamination of **4**. However, it could not be isolated.



i) Standard samples.

ii) Reaction products in methanol.



iii) Reaction products in benzene.

iv) Sirups obtained by separation of **11** from iii.

Fig. 8. Gas chromatograms of the reaction products of **1** with diazomethane.
(1.5% OV-17 on Shimalite; 115°C: N_2 flow rate, 60 m*l*/min.)

The configurations of reaction products obtained can be understood by the attacking of nucleophiles from the outside of the V-shaped fused five-membered ring in **1**, except in the reaction of diazomethane in benzene. Such stereoselectivities have also been recognized in the Grignard reaction of 5-deoxy-1,2-*O*-isopropylidene-β-L-*threo*-pentofuranos-3-ulose[13] and in hydrogenation of **1**[14] or the corresponding

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[9] M. Vichel and N. A. Abraham, *Bull. Soc. Chim. France*, **1960**, 1196.

[10] W. A. Szark, J. S. Jewell, I. Szczerek, and J. K. N. Jones, *Can. J. Chem.*, **47**, 4473 (1969).

[11] A. Rosenthal and M. Sprinzl, *ibid.*, **47**, 3951 (1969).

[12] W. Meyer zu Reckendorf, *Angew. Chem.*, **79**, 151 (1967).

[13] J. R. Dyer, W. E. McGonigal and K. C. Eice, *J. Amer. Chem. Soc.*, **87**, 654 (1965).

[14] P. M. Collins, *Tetrahedron*, **21**, 1809 (1965).

cyclohexylidene dreivative[15].

The abnormal stereoselectivity of the reaction of diazomethane in benzene can be explained only by assuming an interaction between oxygen atoms in 1,2-*O*-isopropylidene group of **1** and the polarized structure of diazomethane[16].

Experimenal

All boiling and melting points are uncorrected. The solutions were evaporated under diminished 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 with a Hitachi Model EPI-GS grating IR spectrophotometer. The NMR spectra were taken in deuteriochloroform unless otherwise stated with a JMN-4H-100 MHz and partly with Varian XL-100 Spectrometer using tetramethylsilane as an internal standard. Chemical shifts and coupling constants were recorded in τ and Hz units, and frequencies in cm^{-1}.

*3-*C*-Aminomethyl-1,2: 5,6-di-*O*-isopropylidene-α-*D*-allofuranose (**4**) and -glucofuranose (**5**).* A solution of 1,2 : 5,6-di-*O*-isopropylidene-3-*C*-nitromethyl-α-D-allofuranose (**2**) or -glucofuranose (**3**) (5 g, 15.6 mmol) in methanol-water (100 ml) was hydrogenated in the presence of palladium-charcoal (5%, 2.5 g). After hydrogenation, the solution was filtered and methanol was evaportaed. The water layer was then extracted with chroloform. The extract was washed with water, dried, and concentrated to give crystals which was recrystallized from methanol-ether. The yield was 4.26 g (94%) in both cases.

Compound **4**: mp 122—123°C; $[a]_D^{23}$ +25.4° (*c* 0.06, ethanol). IR: 3360 and 3290 (NH_2), 1583 (C–N); NMR: 4.26 (H_1; d, $J_{1,2}$=3.81), 5.38 (H_2; d), 5.77—6.20 (H_4, H_5, H_{6a}, H_{6b}), 6.83 and 7.38 ($H_{3'a}$ and $H_{3'b}$; ABq, $J_{a,b}$=13.0), 8.12 (OH and NH_2, s), 8.39, 8.54, and 8.62 (4 C–CH_3).

Found: C, 54.36; H, 8.04; N, 5.18%. Calcd for $C_{13}H_{23}NO_6$: C, 53.96; H, 8.01; N, 4.84%.

Compound **5**: mp 114—115°C; $[\alpha]_D^{23}$ +28.8° (*c* 1.0, ethanol). IR: 3330 and 3280 (NH_2), 1615 (C–N); NMR: 4.13 (H_1; d, $J_{1,2}$=3.5), 5.69 (H_2; d), 6.23 (H_4; d, $J_{4,5}$=7.9), 5.66 (H_5; sex, $J_{5,6a}$=5.6), 5.84 (H_{6a}; q, $J_{5,6b}$=5.7), 5.96 (H_{6b}; q, $J_{6a,6b}$=8.3), 6.90 ($H_{3'a}$; d, $J_{3'a,b}$=13.2), 7.03 ($H_{3'b}$; d), 7.88 (OH and NH, s), 8.49 8.58, 8.65 and 8.68 (4 C–CH_3).

Found: C, 52.58; H, 8.30; N, 4.62%. Calcd for $C_{13}H_{23}NO_6 \cdot 1/2H_2O$; C, 52.40; H, 8.06; N, 4.70%.

*3-*C*-Acetaminomethyl-1,2 : 5,6-di-*O*-isopropylidene-α-*D*-allofuranose (**6**) and -glucofuranose (**7**).* Acetic anhydride (0.5 g, 4.9 mmol) was added to a solution of **4** or **5** (0.3 g, 1.04 mmol) in methanol (3 m*l*) and then kept at room temperature for one day. The solution was treated by the usual procedure to give crystals which were recrystallized from ether-*n*-hexane. Yields were nearly quantitative in both cases.

Compound **6**: mp 156—156.5°C; $[\alpha]_D^{23}$ +56.3° (*c* 1.0, ethanol). IR: 3450 (OH), 3375 (NH), 1645 and 1515 (NHAc); NMR: 4.22 (H_1; d, $J_{1,2}$=4.0), 5.75 (H_2; d), 3.92 (NH), *ca.* 5.88 (H_{6a}; q, $J_{5,6a}$=2.0), *ca.* 5.89 (H_5; sex), 6.01 (H_4; *d*, $J_{4,5}$=8.4), 6.16 (H_{6b}; q, $J_{6a,b}$=8.0, $J_{6b,5}$=6.3), 6.27 ($H_{3'b}$), 6.64 ($H_{3'b}$; q, $J_{a,b}$=13.6, $J_{3'b,NH}$=3.8), 7.08 (OH, s), 7.97 (NAc; s), 8.41, 8.54 and 8.64 (4 C–CH_3).

Found: C, 54.21; H, 7.70; N, 4.08%. Calcd for $C_{15}H_{25}NO_7$: C, 54.37; H, 7.61; N, 4.23%.

The pseudocontact shift was measured in the presence of 5 or 10 mg of $Eu(fod)_3$ to 16 mg of **6**. The extent and order of shift (ppm) of protons in the latter case were as follows; NAc (4.24) > $H_{3'b}$ (3.67) > $H_{3'a}$ (2.84) > NH (2.54) > H_2 (2.23) > OH (1.64) > H_5 (0.09) > H_4 (0.73) > H_1 and H_{6b} (0.47), C–CH_3 (0.30, 0.28, 0.23 and 0.14), H_{6a} (0.18).

Compound **7**: mp 120—121°C, $[\alpha]_D^{23}$ +63.8° (*c* 1.44, ethanol). IR: 1650 and 1542 (NHAc); NMR: 3.55 (NH; broad s), 4.16 (H_1; d, $J_{1,2}$=4.5), 5.29 (OH; s), 5.66 (H_2; d), 5.65 (H_5; q, $J_{5,6b}$=5.8), 5.88 (H_{6a}; q, $J_{5,6a}$=5.9), 6.04 (H_{6b}; q, J_{ab}=8.6), 6.24 (H_4; d, $J_{4,5}$=7.8), 6.22 and 6.55 ($H_{3'ab}$; each q, J_{ab}=14.7, $J_{3'b,NH}$=5 5, $J_{3'b,NH}$=6.8), 7.96 (NAc; s), 8.50, 8.59, 8.64 and 8.69 (4 C–CH_3).

Found: C, 54.51; H, 7.59; N, 4.20%. Calcd for $C_{15}H_{25}NO_7$: C, 54.37; H, 7.61; N, 4.23%.

*3-*C*-Acetaminomethyl-1,2-*O*-isopropylidene-α-*D*-*ribo*-pentodialdofuranose-5,*N*-aminal (**8'**).* A solution of **6** (1.5 g, 4.5 mmol) in 0.1 N-sulfuric acid (50 m*l*) was kept at room temperature for 2 hr, neutralized with barium hydroxide and then filtered. The filtrate was extracted with chloroform, and the extract was evaporated to give a sirup (1.10 g). Oxidation of the sirup in water with sodium periodate (0.81 g, 3.78 mmol) gave crystals (0.4 g, 34%) soluble in dimethyl sulfoxide, but insoluble in usual organic solvents. Mp 219.5—220.7°C; $[\alpha]_D^{23}$ +25.4°→+29.7° (after 24 hr, c 1.0, water). IR: 3480 (OH), 1607 and 1625 (=NAc); NMR (DMSO-d_6): 3.92 (H_1; d, $J_{1,2}$=3.1), 4.32 and 4.44 H_5; two kinds of s), 5.23 (H_2; d), 5.52 (H_4; s), 6.12 and 6.33 ($H_{3'ab}$; ABq, $J_{a,b}$=14.0), 7.62 and 7.72 (NAc; two kinds of s), 8.17 and 8.36 (2 C–CH_3).

Found: C, 50.61; H, 6.60; N, 5.37%. Calcd for $C_{11}H_{17}NO_6$: C, 50.96; H, 6.61; N, 5.40%.

*3-*C*-Acetaminomethyl-1,2-*O*-isopropylidene-α-*D*-*xylo*-pentodialdofuranose (**9**).* A solution of 3-*C*-acetaminomethyl-1,2-*O*-isopropylidene-α-D-glucofuranose (0.5 g, 1.73 mmol) and sodium periodate (0.4 g 1.87 mmol) in water (50 m*l*) was allowed to stand for 5 hr, and the sodium iodate separated by addition of ethanol was filtered off. After evaporation of ethanol from the filtrate, the water layer was extracted with chloroform to give a sirup which could not be crystallized. The amount of sirup was too small for its physical constants to be determined. However, satisfactory spectral information was obtained to deduce the structure without any further purification.

IR: 1725 (CHO), 1640 and 1540 (NHAc); NMR: 0.41 (CHO; d, $J_{4,CHO}$=2.0), 3.81 (H_1; d, $J_{1,2}$=4.0), 5.62 (H_2; d), 5.81 (H_4; d), *ca.* 6.00—6.65 (OH, $H_{3'a}$, $H_{3'b}$), 7.97 (NAc; s), 8.51 and 8.67 (2 C–CH_3).

*3,5,6-Tri-*O*-acetyl-1,2-*O*-isopropylidene-3-*C*-nitromethyl-α-*D*-allofuranose (**10**).* A solution of **2** (6.0 g, 18.8 mmol) and a catalytic amount of *p*-toluenesulfonic acid in acetic anhydride (9.6 g, 95 mmol) was allowed to stand for one day, and poured into excess sodium bicarbonate in water. Extraction of the aqueous solution with chloroform gave crystals which were recrystallized from ethanol. Yield, 3.0 g (39.4%) mp 165—166°C, $[\alpha]_D^{23}$ +77.0° (*c* 1.0, ethanol). IR: 1750, 1730 (OAc), 1560, 1540 (NO_2); NMR: 4.28 (H_1; d, $J_{1,2}$=4.0), 4.67 (H_2; d), 4.45—4.65 (H_5; m), 4.94 and 5.15 ($H_{3'ab}$; ABq, $J_{a,b}$=11.7), 5.76 (H_4; d, $J_{4,5}$=8.0), 5.05 and 5.83 H_{6ab}; q and q, $J_{5,6a}$=3.0, $J_{5,6b}$=5.5, $J_{a,b}$=12.0), 7.92 and 7.94 (3 OAc), 8.45 and 8.65 (2 C–CH_3).

Found: C, 47.17; H, 5.88; N, 3.30%. Calcd for $C_{16}H_{23}NO_{11}$: C, 47.41; H, 5.72; N, 3.46%.

Treatment of this compound in benzene with sodium bicarbonate at 80°C gave only an intractable sirup.

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*3′,5-Anhydro-3-C-hydroxymethyl-1,2-O-isopropylidene-α-D-allofuranose (**11**).* To an ice-cooled solution of **4** (0.6 g, 2.08 mmol) and acetic acid (0.763 m*l*) in water (5 m*l*) was added dropwise barium nitrite monohydrate (0.95 g, 3.84 mmol) in water (5 m*l*) with stirring for 20 min, and the resulting solution was allowed to stand for 12 hr at 10°C. Extraction of the reaction mixture with chloroform gave crystals which were recrystallized from ethanol-*n*-hexane. Yield, 0.1 g (20.6%); mp 115.8—116°C; $[\alpha]_D^{23}$ +73.8° (*c* 1.0, chloroform). IR: 3410 and 3250 (OH); NMR: 4.06 (H_1; d, $J_{1,2}=4.5$), 5.61 (H_2; d), 5.62 (H_4; s), 5.80 (H_5; t, $J_{5,6}=5.0$), 5.92 and 6.27 ($H_{3'ab}$; ABq, $J_{a,b}=10.5$), 6.24 (H_6; d), 6.88 (OH; s), 8.40 and 8.61 (s C–CH_3).

Found: C, 51.63; H, 7.00%. Calcd for $C_{10}H_{16}O_6$: C, 51.72; H, 6.94%.

*Reformatsky Reaction of **1** with Ethyl Bromoacetate.* A suspension of **1** (1.2 g 4.65 mmol), ethyl bromoacetate (3.7 g, 22.2 mmol) and zinc metal (2.1 g, 31.9 mmol) in tetrahydrofuran (11 m*l*) was refluxed for 1.5 hr in the presence of a catalytic amount of iodine and then filtered. The filtrate was poured into ice water containing acetic acid (1.2 m*l*), and extracted with chloroform. The pale yellow sirup 1.2 g) obtained by evaporation of the extracts was fractionated on a silica gel C-100 (20 g) column. The column was succesively eluted with ligroin, ligroin-benzene (1 : 1), benzene, benzene-acetone (5 : 1) and acetone. Concentration of ligroin-benzene and benzene solution gave 3-*C*-carbethoxymethyl-1,2 : 5,6-di-*O*-isopropylidene-α-D-allofuranose (**12**) as a sirup (0.5 g, 29.5%), and 3-*C*-carboxymethyl-1,2-*O*-isopropylidene-α-D-allofuranose 3′,5-lactone (**13**) as crystals (0.3 g, 22.4%).

Compound **12**: IR: 1735 (ester); NMR: 4.26 (H_1; d, $J_{1,2}=3.75$), 5.21 (H_2; d), 5.65—6.20 (CH_2, H_4, H_5, H_{6a}, H_{6b}), 7.10 and 7.53 ($H_{3'ab}$; ABq, $J_{a,b}=15.0$), 7.83 (OH; s), 8.41, 8.54 and 8.63 (4 C–CH_3), 8.72 (CH_3 in ethyl; t, $J=5.0$).

Found: C, 54.95; H, 7.23%. Calcd for $C_{16}H_{26}O_8$: C, 55.48; H, 7.57%.

Compound **13**: mp 195—195.5°C; $[\alpha]_D^{23}$ +136.6° (*c* 1.0, acetone). IR: 1735 (lactone); NMR (DMSO): 4.16 (H_1; d, $J_{1,2}=4.2$), 5.76 (H_2; d), 5.98 (H_4; d, $J_{4,5}=5.0$), 5.78–6.20 (H_4, H_5, OH), 6.40 and 6.42 (H_{6ab}; two d, $J_{5,6}=5.0$), 7.30 and 7.52 ($H_{3'ab}$; ABq, $J_{a,b}=15.5$), 8.51 and 8.20 (2 C–CH_3).

Found: C, 50.62; H, 6.30%. Calcd for $C_{11}H_{16}O_7$: C, 50.77; H, 6.20%.

*3-C-Carboxymethyl-1,2 : 5,6-di-O-isopropylidene-α-D-allofuranose (**14**).* 0.1 N Sodium hydroxide (5 m*l*) was added to a solution of **12** (4.0 g, 10.9 mmol) in water (50 m*l*) which was then allowed to stand for 2 hr. The solution was acidified with acetic acid and extracted with chloroform. Evaporation of the extracts gave crystals which were recrystallized from petroleum ether. Yield, 2.8 g (80%), mp 111.5—112.5°C; $[\alpha]_D^{23}$ +22.7° (*c* 0.54, chloroform). IR: 1695 (COOH); NMR: 4.26 (H_1; d, $J_{1,2}=4.0$), 5.30 (H_2: d), 5.80—6.25 (H_4, H_5, H_{6a}, H_{6b}, OH), 7.04 and 7.52 ($H_{3'ab}$; ABq, $J_{a,b}=15.0$), 8.42, 8.56 and 8.64 (4 C–CH_3).

Found: C, 52.64; H, 6.85%. Calcd for $C_{14}H_{22}O_8$: C, 52.82; H, 6.97%.

An attempted dehydrative decarboxylation of **14** by refluxing in quinoline in the presence of copper powder for 10 hr gave unchanged **14** and a small amount of **13**.

*3-C-Hydroxymethyl-1,2 : 5,6-di-O-isopropylidene-α-D-glucofuranose **15**.* A) To a suspension of 1,2 : 5,6-di-*O*-isopropylidene-3-*C*-methylene-α-D-ribo-hexofuranose (3.4 g, 13.25 mmol) in water (30 m*l*) was added dropwise potassium permanganate (2.6 g, 15.4 mmol) in water (130 m*l*) for 30 min with stirring. After 1 hr, the solution was filtered and the filtrate was extracted with chloroform. The sirup obtained by evaporation of the extracts was crystallized from hexane. Yield, 2.71 g (70.3%); mp 84—86°C; $[\alpha]_D^{23}$ +21.8° (*c* 1.0, chloroform). NMR: 4.12 (H_1; d, $J_{1,2}=4.0$), 5.58 (H_2; d), 5.68 (H_5; m), 5.84 ($H_6{}^a$; q, $J_{5,6a}=4.8$, $J_{6a,6b}=8.0$), 5.96 (H_{6b}; q, $J_{5,6b}=5.0$), 6.15 ($H_{3'ab}$; s), 6.18 (H_4; d, $J_{4,5}=7.0$), 6.45 (OH; s), 8.48, 8.56, 8.63, 8.68 (4 C–CH_3).

Found: C, 54.59; H, 8.22%. Calcd for $C_{13}H_{22}O_7$: C, 53.78; H, 7.64%.

B) Dried diazomethane (0.726 g, 1.2 equivalent calculated from nitrosomethylurea) was added to a solution of **1** (3.42 g, 14.4 mmol) in benzene (40 m*l*), which was then evaporated. A solution of the resulting sirup in acetone-water (100 ml, 1 : 1 v/v) containing potassium hydroxide (0.5 g) was refluxed for 3 hr, and acetone was evaporated. Extraction of the water layer with chloroform gave a sirup which was extracted with hot *n*-hexane to give crystals. Yield, 0.95 g (25%); mp 86.0—86.5°C. It showed no depression of melting point by admixture with an authentic sample. The IR spectral data were found to be identical.

*3-C-Hydroxymethyl-1,2 : 5,6-di-O-isopropylidene-3′-O-(p-toluenesulfonyl)-α-D-glucofuranose (**16**).* To a solution of **15** (0.5 g, 1.72 mmol) was added *p*-toluenesulfonyl chloride (0.36 g, 2.27 mmol) with stirring. After standing overnight, the solution was poured into ice-water and extracted with chloroform. The extract was washed with cold N hydrochloric acid, saturated sodium bicarbonate solution and water. Evaporation of the extracts gave a sirup which was crystallized from ether-*n*-hexane. Yield, 0.66 g (86.4%); mp 116.5—117.5°C; $[\alpha]_D^{23}$ +98.4° (*c* 1.01, chloroform). NMR: 4.18 (H_1; d, $J_{1,2}=3.5$), 5.05 and 5.80 ($H_{3'ab}$; ABq, $J_{a,b}=10.0$), 5.66 (H_2; d), 5.92 (H_{6a}; q, $J_{5,6a}=6.0$, $J_{6a,6b}=8.0$), 6.36 (H_4; d, $J_{4,5}=8.0$), 6.60 (H_{6b}; q, $J_{5,6b}=6.0$), 7.25 (OH; broad s), 8.63, 8.67, 8.70 and 8.77 (4 C–CH_3).

Found: C, 54.52; H, 6.39; S, 7.47%. Calcd for $C_{20}H_{28}O_9S$: C, 54.05; H, 6.35; S, 7.21%.

*Preparation of **5** from **16**.* A solution of **16** (0.5 g, 1.13 mmol) and sodium azide (0.15 g, 2.26 mmol) in dimethylformamide (20 ml) was refluxed for 4 hr at 173°C, then poured into ice-water. The resulting solution was extracted with chloroform. Evaporation of the extracts gave a sirup which could not be completely separated from dimethylformamide. However, it gave a characteristic absorption of azide (2100 cm^{-1}) in IR spectrum. NMR: 4.13 (H_1; d, $J_{1,2}=3.4$), 5.58 (H_2; d), *ca.* 5.71 (H_5; m), 5.88 (H_{6a}; q, $J_{5,6a}=5.5$, $J_{6a,7b}=7.9$), 6.00 (H_{6b}; q, $J_{5,6b}=4.6$), 6.29 and 6.32 ($H_{3'ab}$; ABq, $J_{a,b}=10.2$), *ca.* 6.26 (H_4; d), 8.48, 8.85 and 8.65 (4 C–CH_3).

Hydrogenation of the sirup in ethanol (20 m*l*) in the presence of Raney nickel (0.5 g) at 40°C and 30 atm. gave the corresponding 3-*C*-aminomethyl derivative as crystals. Yield, 0.25 g (61%); mp 113—115°C. The spectral data of the crystals were identical with those of **5**.

*3-C-Hydroxymethyl-1,2 : 3,3′ : 5,6-tri-O-isopropylidene-α-D-glucofuranose (**17**).* A suspension of **15** (1 g, 3.45 mmol) and anhydrous copper sulfate (3 g) in acetone (50 m*l*) was refluxed for 72 hr, filtered through active carbon, and the filtrate was evaporated. The sirup crystallized gradually, but it could not be recrystallized because of its small solubility in organic solvents. Yield, 0.8 g (70%); mp 54—56°C; $[\alpha]_D^{23}$ +23.1° (*c* 0.6, ethanol); NMR: 4.18 (H_1; d, $J_{1,2}=3.5$), 5.66 (H_2; d), 6.08 (H_4; d, $J_{4,5}=13.0$), 5.56—6.06 (H_5, H_{6ab} and $H_{3'ab}$), 8.52, 8.58, 8.60, 7.66 and 8.68 (6 C–CH_3).

Found: C, 58.05; H, 7.99%. Calcd for $C_{16}H_{26}O_7$:

C, 58.17; H, 7.93%.

3-C-Hydroxymethyl-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose 3,3'-carbonate (**18**). To a solution of 15 (1 g, 3.45 mmol) in pyridine (10 m*l*) was bubbled excess phosgene under cooling. After standing for 1 hr the solution was poured into ice-water and extracted with chloroform. Evaporation of the extracts gave a sirup in 90% (0.98 g) yield. $[\alpha]_D^{23}$ +25.8° (*c* 0.1, chloroform); IR: 1820 (carbonate) NMR: 4.05 (H_1; d, $J_{1,2}$=4.4), 5.41 (H_2; d), 5.32 and 5.45 ($H_{3'ab}$; ABq, $J_{a,b}$=9.0), 5.72 (H_5: m), 5.87 (H_{6a}; q, $J_{5,6a}$=2.9), 5.99 (H_{6b}; q, $J_{6a,6b}$=8.4, $J_{5,6b}$=4.5), 6.10 (H_4; d, $J_{4,5}$=8.4), 8.49, 8.56, 8.65 and 8.66 (4 C–CH_3).

Found: C, 52.55; H, 6.35%. Calcd for $C_{14}H_{20}O_8$: C, 53.16; H, 6.37%.

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