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Branched-Chain Sugars. II. On the Configuration of Branched-Chain Sugars from Methyl 2-*O*-Benzoyl-4,6-*O*-benzylidene-α-D-ribo-hexopyranosid-3-ulose

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Stereoselectivities in diazomethane and nitromethane reaction of methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-α-D-ribo-hexopyranosid-3-ulose were examined. Reduction of the epoxidation product (**2**) gave an epimeric 3-*C*-methyl derivative in contrast with that obtained by the Grignard reaction. Comparison of NMR spectra of the corresponding di-*O*-acetate of the both epimers proved that **2** has the gluco-configuration. Ring-opening of the epoxide with alkali, methanolic ammonia, and acid gave the corresponding 3-*C*-hydroxymethyl, 3-*C*-aminomethyl (**17**), and de-*O*-benzylidenated product, respectively. Hydrogenation of the 3-*C*-nitromethyl derivative (**21**) obtained by nitromethane condensation, in the presence of Raney nickel, accompanied with benzoyl-migration to give 3-*C*-benzamidomethyl derivative (**22**). De-benzoylation of **22** with methanolic potassium hydroxide gave 3-*C*-aminomethyl derivative (**26**) and an orthoester-type compound. Comparison of **26** with **17** and their derivatives indicated that **21** has the allo-configuration. The both configurations were also supported by the optical rotation of 3-*C*-benzamidomethyl derivatives in cuprammonium solution.

In the previous paper,[1] we reported that the nitromethane and the Reformatsky reaction of 1,2 : 5,6-di-*O*-isopropylidene-α-D-ribo-hexofuranos-3-ulose gave D-allo-type branched-chain sugars, while the diazomethane reaction afforded D-gluco-type product, indicating that the reagent attacked the carbonyl group from the more hindered site. The stereoselectivity of the latter stimulated us to examine with a pyranosid-3-ulose, and nitromethane and diazomethane reaction of methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-α-D-ribo-hexopyranosid-3-ulose (**1**)[2] were examined in this report.

Results

Diazomethane Condensation. Diazomethane condensation of **1** in benzene–ethanol gave a sirupy spiro-epoxide (**2**) in 77% yield. In order to determine the configuration, **2** was hydrogenated with lithium aluminium hydride to the 3-*C*-methyl derivative (**3**), which was successively converted into the corresponding 2-*O*-acetate (**4**) and 2,3-di-*O*-acetate (**5**) by base- and acid-catalyzed acetylation, respectively. On the other hand, a 3-*C*-methyl derivative (**6**) obtained by the Grignard reaction, of which the configuration was assigned to be of allo-type,[2,3] was also converted into 2-*O*-acetate (**7**) and 2,3-di-*O*-acetate (**8**). Comparison of **3** with **6** and their derivatives showed that they are 3-epimers to each other, and the chemical shifts of *tert*-acetoxy protons in **5** (δ 1.95) and **8** (δ 2.05) indicated an equatorial and axial one, respectively.[4] Thus, the configuration of **2** was confirmed to be of D-gluco-type.

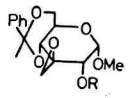
The epoxide-ring of **2** resisted, to some extent, to alkaline opening than the corresponding furanose derivative,[1] and alkali treatment of **2** at room temperature gave de-*O*-benzoylated epoxide (**9**), which was further converted to the 2-*O*-acetate (**10**). Treatment of **9** with refluxing aqueous potassium hydroxide for 10 hr gave a water-soluble 3-*C*-hydroxymethyl derivative (**11**), which was then acetylated to 2,3-di-*O*-acetate (**12**). Acetonation of **11** gave 3,3′-*O*-isopropylidene derivative (**13**), of which the position of the isopropylidene group was determined from the fact that **13** gave the mono-*O*-acetate (**14**) by base-catalyzed acetylation. The epoxide-ring opening was also performed by refluxing **2** with 80% acetic acid, accompanying with hydrolysis of the benzylidene group, to give methyl 2-*O*-benzoyl-3-*C*-hydroxymethyl-α-D-glucopyranoside (**15**), which was confirmed by conversion into the corresponding tetra-*O*-acetate (**16**). Moreover, treatment of **9** with ethanolic ammonia in a sealed tube at 90 °C for 3 hr gave 3-*C*-aminomethyl derivative (**17**), which was then converted into the corresponding *N*-benzoyl derivative (**18**), its di-*O*-acetate (**19**), and *N*,*O*-triacetate (**20**), respectively.

1) J. Yoshimura, K. Kobayashi, K. Sato, and M. Funabashi, This Bulletin, **45**, 1806 (1972).

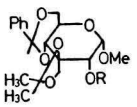
2) F. A. Carey and K. O. Hodgson, *Carbohyd. Res.*, **12**, 463 (1970).

3) G. B. Howarth, W. A. Szarek, and J. K. N. Jones, *Canad. J. Chem.*, **46**, 3691 (1968).

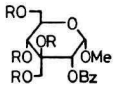
4) F. W. Lichtenthaler and P. Emig, *Tetrahedron Lett.*, **1967**, 577.



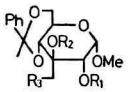
(**2**) R=Bz (**3**) $R_1=R_2=H$ (**6**) $R_1=R_2=H$
(**9**) R=H (**4**) R_1=Ac, R_2=H (**7**) R_1=Ac, R_2=H
(**10**) R=Ac (**5**) $R_1=R_2$=Ac (**8**) $R_1=R_2$=Ac



(**13**) R=H
(**14**) R=Ac



(**15**) R=H
(**16**) R=Ac

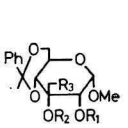


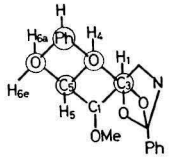
(**11**) $R_1=R_2=H$, R_3=OH
(**12**) R_1=Ac, R_2=H, R_3=OAc
(**17**) $R_1=R_2=H$, $R_3=NH_2$
(**18**) $R_1=R_2=H$, R_3=NHBz
(**19**) $R_1=R_2$=Ac, R_3=NHBz
(**20**) $R_1=R_2$=Ac, R_3=NHAc

Nitromethane Condensation. Reaction of **1** with nitromethane in tetrahydrofuran in the presence of sodium methoxide gave a 3-*C*-nitromethyl derivative (**21**) in 80% yield. Hydrogenation of **21** in the presence of Raney nickel accompanied with the migration of 2-*O*-benzoyl group to give 3-*C*-benzamidomethyl derivative (**22**). Base- and acid-catalyzed acetylation of **22** gave the corresponding 2-*O*-acetate (**23**) and 2,3-di-*O*-acetate (**24**), respectively. Debenzoylation of **22** with methanolic potassium hydroxide gave 3-*C*-aminomethyl derivative (**26**), an orthoester-type product (**25**), and **22**. Comparison of **22** with **18**, **24** with **19**, and **26** with **17** indicated them to be 3-epimers to each other. Furthermore, the positive rotational change ($[M]_{436}^{\text{Cupra A}}$ +1670°) of **22** in cuprammonium solution[5] and negative change ($[M]_{436}^{\text{Cupra A}}$ −635°) of **18** indicated D-allo and D-gluco-configuration, respectively. Thus, the configuration of **21** was proved to be of D-allo-type.

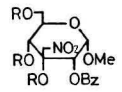
Compound **25**, having still two phenyl groups in the NMR and analytical data, showed no absorptions of amino and oxazolidine groups in IR spectrum, and changes to **22** by standing in a moist state. Attempted acetylation of **25** in dry pyridine gave quantitatively 3-*C*-acetamidomethyl-2-*O*-acetyl derivative (**27**) which was also obtained by acetylation of **26**. From these facts, **25** was deduced to be methyl 3-*C*-aminomethyl-4,6-*O*-benzylidene-2,3,*N*-benzylidine-α-D-allopyranoside. Formation of **25** will be explained by the nucleophillic attack of hydroxyl anions at C_2- and C_3-positions on the sterically favorable carbonyl function of benzamido group to give the thermodynamically controlled product. Conversion of **25** into **27** might occur through hydrolysis of acyloxonium ion formed by cleavage of the orthoamide bond by *N*-acetylation.[6]

5) R. E. Reeves, *Adv. Carbohyd. Chem.*, **6**, 131 (1951).

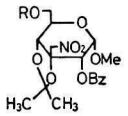




(**21**) R_1=Bz, R_2=H, $R_3=NO_2$ (**25**)
(**22**) $R_1=R_2$=H, R_3=NHBz
(**23**) R_1=Ac, R_2=H, R_3=NHBz
(**24**) $R_1=R_2$=Ac, R_3=NHBz
(**26**) $R_1=R_2$=H, $R_3=NH_2$
(**27**) R_1=Ac, R_2=H, R_3=NHAc



(**28**) R=H
(**29**) R=Ac



(**30**) R=H
(**31**) R=Ac

On the other hand, partial hydrogenation of **21** in the presence of palladium-charcoal or hydrolysis with 0.1 N-sulfuric acid gave methyl 2-*O*-benzoyl-3-*C*-nitromethyl-α-D-allo-pyranoside (**28**), which was then converted into the tri-*O*-acetate (**29**) by acid-catalyzed acetylation. Acetonation of **28** gave an isopropylidene derivative (**30**), which was converted to mono-*O*-acetate (**31**). The structure of **30** was deduced to be 3,4-*O*-isopropylidene derivative from the chemical shift of C–CH_3 protons (δ 1.47 and 1.49).[7]

Discussion

On the stereoselectivities in nucleophilic addition to methyl 4,6-*O*-benzylidene-α-D-ribo-hexopyranosid-3-uloses, following facts are known. Reduction[8] of 2-*O*-tosyl derivative; reduction,[8] the Grignard[9] and dimethyloxosulfonium methylide[10] reaction of the corresponding 2-acetamido-2-deoxy derivative; and the Grignard[11] and the oxosulfonium ylide[12] reaction of 2-deoxy derivative gave D-allo-type products, while the reaction of acetonitrile with the 2-deoxy derivative in liquid ammonia gave D-gluco-type product.[13] These results indicate that nucleophiles in the former reactions attacked the carbonyl group from the less hindered site, and in the latter from the hindered site (Fig. 1). Thus, nitromethane condensation mentioned here is classified into the former type, though it generally gives various mixture of diastereomers,

6) H. Bredereck, G. Simchen, and S. Rebsdat, *Chem. Ber.*, **101**, 1872 (1968).
7) N. Bagget, K. W. Buch, A. B. Foster, R. Jefferis, B. H. Rees, and J. M. Webber, *J. Chem. Soc.*, **1965**, 3382.
8) B. R. Baker and D. H. Buss, *J. Org. Chem.*, **30**, 2304, 2308 (1965).
9) B. R. Baker and D. H. Buss, *ibid.*, **31**, 217 (1966).
10) J. H. Jordaan and S. Smedley, *Carbohyd. Res.*, **16**, 177 (1971).
11) B. Flaharty, W. G. Overend, and N. R. Williams, *J. Chem. Soc. C*, **1966**, 398.
12) R. D. King, W. G. Overend, J. Wells, and N. R. Williams, *Chem. Commum.*, **1967**, 726.
13) A. Rosenthal and G. Schöllnhammer, *Carbohyd. Res.*, **15**, 421 (1970).

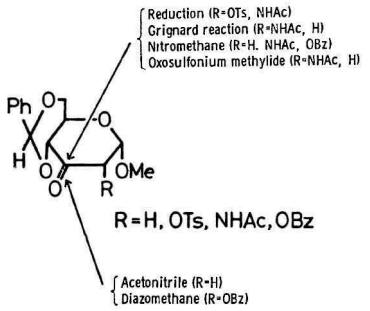


Fig. 1.

depending on the condition used.[14]

On the other hand, stereoselectivity of diazomethane addition is usually complicated by the formation of ring-expanded product depending on the solvent used. For an example, Flaherty *et al.*[15] obtained 30% of the ring-expanded product and a small amount of normal epoxide of D-gluco-type by the reaction with methyl 4,6-*O*-benzylidene-2-deoxy-α-D-erythro-hexopyranosid-3-ulose in methanol. However, 1,2-*O*-isopropylidene-α-D-furanos-3-uloses gave the normal spiro-epoxides which are resulted by attacking the reagent from the inside of the V-shaped *cis*-fused five-membered ring.[1,16] Reaction of methyl α-D-pyranosid-2-uloses in ether–alcohol, having two oxygens at the both vicinal carbon, gave a mixture of diastereomers,[17] however, one which has the epoxide carbon in the site of C_1-methoxy group was predominant. Inch *et al.*[18] examined the steric influence of *C*-alkyl group vicinal to the carbonyl group by the reaction with 4,6-*O*-benzylidene-3-deoxy-3-*C*-ethyl-α-D-arabino- and -ribo-hexo-pyranosid-2-ulose, and showed that *C*-ethyl group in reverse side to C_1-methoxy group enhanced the formation of the predominant product mentioned above, and that in the same side hindered it to afford another epimer predominantly. They discussed on the conformation of zwitterionic intermediates for explanation of the configuration of ring-expanded products.

However, accumulated data mentioned here indicate that the stereoselectivity might be controlled at first by attractive interactions between vicinal or neighboring hydroxyl oxygens and diazomethylene cation of zwitterionic intermediates, and therefore, the polarity of solvents play an important role. The complemental stereoselectivities of the Grignard and diazomethane reaction mentioned by us and by Horwitz *et al.*[16] support this deduction. Thus, the steric position of C_1-methoxy oxygen for the carbonyl group might control the configuration of the product in this experiment.

14) G. J. Lourens, *Tetrahedron Lett.*, **1969**, 3733; A. Rosenthal and K. S. Ong, *ibid.*, **1969** 3981; S. W. Gunner, R. D. King, W. G. Overend, and N. R. Williams, *J. Chem. Soc., C*, **1970**, 1954; A. Rosenthal, K. S. Ong, and D. Baker, *Carbohyd. Res.*, **13**, 113 (1970).

15) B. Flaherty, W. G. Overend, and N. R. Williams, *Chem. Comm.*, **1966** 434.

16) S. Naher, W. G. Overend, and N. R. Williams, *Chem. Ind.* (London), **1967**, 2114; J. P. Horwitz, N. Mody, and R. Gasser, *J. Org. Chem.*, **35**, 2335 (1970).

17) W. G. Overend and N. R. Williams, *J. Chem. Soc., C*, **1968**, 3446; R. J. Ferrier, W. G. Overend, G. A. Rafferty, H. M. Wall, and N. R. Williams, *ibid.*, **1968**, 1091.

18) T. D. Inch, G. J. Lewis, R. P. Pell, and N. R. Williams, *Chem. Commun.*, **1970**, 1549.

Experimental

All 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-G2 grating IR spectrophotometer. The NMR spectra were taken in deuteriochloroform, with a JNM-4H-100 MHz Spectrometer using tetramethylsilane as an internal standard. Chemical shifts and coupling constants were recorded in δ and Hz units, and frequencies in cm^{-1}.

Methyl 3,3'-Anhydro-2-O-benzoyl-4,6-O-benzylidene-3-C-(hydroxymethyl)-α-D-glucopyranoside (2). To a suspended solution of **1** (4 g, 10.4 mmol) in benzene (150 ml)–ethanol (50 ml) was added dropwise a solution of diazomethane (20 mmol) in ether (50 ml) at 0 °C. With proceeding the reaction, the mixture turned to homogeneous. After standing at 0 °C for 3 hr and at room temperature for 28 hr, the solution was evaporated, and the resulted sirup was fractionated through Kiesel-gel (70—325 mesh, Merck Co.), by eluating with benzene–methanol (15 : 1). From the first fraction, the spiro-epoxide was obtain as a sirup in 77.3% (3.2 g) yield. $[\alpha]_D^{23}$ +113° (*c* 1.06, $CHCl_3$); IR: 1720 (ester), 1590 and 710 (Ph); NMR: *ca.* 7.30 and 7.95 (2× Ph, m), 5.51 (PhCH=), 5.41 (H_1; d, $J_{1,2}$=3.7), 5.10 (H_2; d), 4.35 (H_5; sex, $J_{4,5}$=13.5), 3.97 (H_{6e}; t, $J_{6a,6e}$ =10, $J_{5,6e}$= 10), *ca.* 3.91 (H_4; d), *ca.* 3.90 (H_{6a}; t, $J_{5,6a}$=10), 3.40 (OMe), 3.20 (epoxy-CH_2; s).

Found: C, 65.77; H, 6.10%. Calcd for $C_{22}H_{22}O_7$; C, 66.32; H, 5.57%.

Methyl 4,6-O-Benzylidene-3-C-methyl-α-D-glucopyranoside (3). To a solution of **9** (800 mg, 2.64 mmol) in ether (30 ml) was added lithium aluminium hydride (0.2 g, 53 mmol), and the mixture was refluxed for 7 hr. The excess $LiAlH_4$ was carefully decomposed with water, and the water layer was extracted with ether. The combined ether extract was washed with water, dried with anhydrous magnesium sulfate, and evaporated to give a colorless sirup. The sirup was crystallized and recrystallized from chloroform–*n*-hexane. Yield, 86% (690 mg). A similar treatment of **2** gave the same compound in 79% yield. Mp 80—82 °C; $[\alpha]_D^{23}$ +91.0° (*c* 1.25, $CHCl_3$); IR: 3523 and 3250 (OH); NMR; 1.40 (C–CH_3; s).

Found: C, 60.84; H, 7.16%. Calcd for $C_{15}H_{20}O_6$: C, 60.80; H, 6.80%.

2-*O*-Acetyl and 2,3-di-*O*-acetyl derivatives of **3** was prepared as follows.

a) 2-O-Acetate (4): Acetylation of **3** with acetic anhydride in pyridine gave sirupy acetate in a quantitative yield. $[\alpha]_D^{23}$ +72.5° (*c* 1.44, $CHCl_3$); IR: 3450 (OH), 1740 (ester); NMR: 2.50 (OH; s), 2.10 (OAc), 1.45 (C–CH_3).

Found: C, 59.94; H, 6.60%. Calcd for $C_{17}H_{22}O_7$: C, 60.34; H, 6.55%.

b) 2,3-Di-O-acetate (5): A solution of **3** (100 mg) and *p*-toluenesulfonic acid (20 mg) in acetic anhydride (3 ml) was stirred at room temperature for 1.5 hr, poured into ice-water, and the resulted solution was extracted with chloroform. The extracts were washed with sodium bicarbonate

and then water, dried, and evaporated to give a crystals which was recrystallized from ethanol–*n*-hexane. Yield, 91% (105 mg); mp 156—157°C; $[\alpha]_D^{23}$ +15.4° (*c* 0.95; $CHCl_3$); IR: 1740 (ester); NMR: *ca.* 7.37 (Ph; m), 5.89 (H_2; d, $J_{1,2}$= 4.2), 5.55 (PhCH=), 4.87 (H_1; d), 4.85 (H_4; d, $J_{4,5}$=7.5), 4.30 (H_5; sex, $J_{5,6a}=J_{5,6e}$=7.5), 3.97—3.65 (H_{6a} and H_{6e}; m), 3.40 (OMe), 2.14 (*sec*-OAc), 1.95 (*tert*-OAc), 1.62 (C–CH_3).

Found: C, 60.18; H, 6.45%. Calcd for $C_{19}H_{24}O_8$: C, 59.99; H, 6.36%.

*2-O-Acetyl and 2,3-Di-O-acetyl Derivatives of Methyl 4,6-O-benzylidene-3-C-methyl-α-D-allopyranoside (**6**).* *a) 2-O-Acetate (**7**)*: This compound was obtained from **6**[2,3] by the usual method in a quantitative yield. Mp 95—96 °C; $[\alpha]_D^{23}$ +69.8° (*c* 1.2, $CHCl_3$). IR: 3475 (OH), 1730 (OAc); NMR: 2.16 (OAc), 1.28 (C–CH_3).

Found: C, 60.66; H, 6.72%. Calcd for $C_{17}H_{22}O_7$: C, 60.34; H, 6.55%.

*b) 2,3-Di-O-acetate (**8**)*: Acid-catalyzed acetylation of **6** gave **8** in a quantitative yield, which was recrystallized from ether–*n*-hexane. Mp 97—98°C; $[\alpha]_D^{23}$ +53.5° (*c* 1.03, $CHCl_3$); IR: 1740 (OAc); NMR: *ca.* 7.35 (Ph; m), 5.51 (PhCH=), 4.90 (H_1; d, $J_{1,2}$=4.2), 4.71 (H_2; d), 4.40—3.55 (H_4, H_5, H_{6a} and H_{6e}; m), 3.40 (OMe), 2.16 (*sec*-OAc), 2.05 (*tert*-OAc), 1.78 (C–CH_3).

Found: C, 60.41; H, 6.52%. Calcd for $C_{19}H_{24}O_8$: C, 59.99; H, 6.36%.

*Methyl 3,3′-Anhydro-4,6-O-benzylidene-3-C-(hydroxymethyl)-α-D-glucopyranoside (**9**).* A solution of **2** (1.0 g, 2.51 mmol) and potassium hydroxide (0.5 g) in acetone (20 ml)–water (10 ml) was stirred for 1.5 hr, until **2** has disappeared on tlc. Evaporation of acetone caused deposition of needles, which was gathered after further addition of water (15 ml). These crystals (0.67 g) contain crystalline water detectable in IR (3200, 3450, 3530 cm^{-1}) and NMR spectra. Recrystallization from ethanol–acetone gave needles in 81.5% (0.62 g) yield. Mp 179—180 °C; $[\alpha]_D^{23}$ +111 ° (*c* 1.06, $CHCl_3$); IR: 3320 (OH).

Found: C, 60.01; H, 5.83%. Calcd for $C_{15}H_{18}O_6 \cdot 1/3H_2O$: C, 59.98; H, 5.60%.

Usual acetylation of **9** gave the sirupy *2-O-acetate* (**10**) in a quantitative yield. $[\alpha]_D^{23}$ +96.0° (*c* 1.04, $CHCl_3$); IR; 1750 (OAc); NMR: 7.26 (Ph; m), 5.45 (PhCH=), 5.15 (H_1; d, $J_{1,2}$=3.7), 4.92 (H_2; d), 4.40—3.65 (H_4, H_5, H_{6a} and H_{6e}; m), 3.35 (OMe), 3.07 and 2.98 (epoxy-CH_2; ABq, $J_{a,b}$=5), 2.05 (OAc).

Found: C, 60.75; H, 6.09%. Calcd for $C_{17}H_{20}O_7$: C, 60.71; H, 5.99%.

*Methyl 3-Acetoxymethyl-2-O-acetyl-4,6-O-benzylidene-α-D-glucopyranoside (**12**).* A suspended solution of **9** (2.0 g) and potassium hydroxide (1.5 g) in water (75 ml) was refluxed for 10 hr to make the solution homogeneous, and then extracted with *n*-butanol, after neutralization of the cooled solution with 2N-hydrochloric acid. The extracts was washed with a small amount of water, evaporated to give a sirup (**11**) (1.7 g, 80%); $[\alpha]_D^{23}$ +77.8° (*c* 1.44, $CHCl_3$).

Found: C, 57.67; H, 6.81%. Calcd for $C_{15}H_{20}O_7$: C, 57.68; H, 6.46%.

Acetylation of **11** by the usual method give the sirupy *di-O-acetate* (**12**) in a quantitative yield. $[\alpha]_D^{23}$ +53.6° (*c* 1.14, $CHCl_3$); IR: 3450 (OH), 1735 (OAc); NMR: 7.32 (Ph; m), 5.41 (PhCH=), 5.10 and 4.27 (C_3-H_2; ABq, J= 12.5), 4.96 (H_1; d, $J_{1,2}$=3.7), 4.83 (H_2; d), 4.27 (H_5; m), 4.05—3.55 (H_4, H_{6a} and H_{6e}; m), 3.37 (OMe), 2.12 (*sec*-OAc), 1.78 (OAc).

Found: C, 57.46; H, 6.35%. Calcd for $C_{19}H_{24}O_9$: C, 57.57; H, 6.10%.

*Methyl 4,6-O-Benzylidene-3,3′-O-isopropylidene-α-D-glucopyranoside (**13**).* A suspended solution of **11** (200 mg, 0.64 mmol), anhydrous cupric sulfate (0.5 g) in acetone (20 ml) containing one drop of conc. sulfuric acid was stirred for 24 hr at room temperature, neutralized with barium carbonate, filtered through active carbon, and the filtrate was evaporated to give a sirup (210 mg). Crystallization of the sirup from ethanol–water gave needles in 53% (120 mg) mg) yield. Mp 133—134 °C; $[\alpha]_D^{23}$ +55.0° (*c* 1.18, $CHCl_3$); IR: 3500 (OH).

Found: C, 61.35; H, 7.00%. Calcd for $C_{18}H_{24}O_7$: C, 61.35; H, 6.86%.

Acetylation of **13** by the usual method gave the sirupy 2-O-*acetate* (**14**) in a good yield. $[\alpha]_D^{23}$+49.8° (*c* 1.31, $CHCl_3$); IR: 1750 (OAc), 1370 and 1380 (C–CH_3); NMR: *ca.* 7.40 (Ph; m), 5.60 (PhCH=), 5.03 (H_1; d, $J_{1,2}$=3.7), 4.89 (H_2; d), 4.40 and 4.25 (C_3-H_2; ABq, J=9.7), 4.45—4.20 (H_5; m), 3.90—3.60 (H_4, H_{6a} and H_{6e}; m), 3.38 (OMe), 2.16 (OAc), 1.49 and 1.36 (2×C–CH_3).

Found: C, 60.85; H, 7.09%. Calcd for $C_{20}H_{26}O_8$: C, 60.90; H, 6.64%.

*Methyl 3-C-Acetoxymethyl-3,4,6-tri-O-acetyl-2-O-benzoyl-α-D-glucopyranoside (**16**).* A solution of **2** (300 mg, 0.753 mmol) in acetic acid (80%, 60 ml) was refluxed for 18 hr, and evaporated to give a sirup. *n*-Butanol solution (150 ml) of the sirup was washed with saturated sodium bicarbonate and then a small amount of water, decolorized, and evaporated to give a sirup (**15**) in 73% (180 mg) yield. $[\alpha]_D^{23}$ +112° (c 1.10, $CHCl_3$).

Found: C, 54.34; H, 6.11%. Calcd for $C_{15}H_{20}O_8$: C, 54.87; H, 6.14%.

Acid-catalyzed acetylation of **15** (120 mg) gave **16** in a quantitative yield, which was recrystallized from ether–*n*-hexane. Mp 84—86°C; $[\alpha]_D^{23}$ +109° (*c* 1.01, $CHCl_3$); NMR: *ca.* 8.13 and 7.55 (Ph; m), 6.24 (H_1; d, $J_{1,2}$=3.75), 5.92 (H_4; d, $J_{4,5}$=10.0), 5.03 (H_2; d), 5.02 and 4.85 (C_3-H_2: ABq, J=10.5), 4.48—4.02 (H_5, H_{6a} and H_{6e}; m), 3.42 (OMe), 2.10, 2.08, 2.00, and 1.92 (4×OAc).

Found: C, 55.63; H, 5.72%. Calcd for $C_{23}H_{28}O_{12}$: C, 55.62; H, 5.69%.

*Methyl 4,6-O-Benzylidene-3-C-aminomethyl-α-D-glucopyranoside (**17**).* A solution of **9** (1.0 g, 3.3 mmol) in saturated ethanolic ammonia (25 ml) was heated for 3 hr in a sealed tube at 80—90°C, and evaporated to give needles, which was recrystallized from ethanol. Yield, 78% (0.8 g); mp 158—159 °C; $[\alpha]_D^{23}$ +92.0° (*c* 1.07, $CHCl_3$). IR: 3390 and 3350 (OH), 3300 (NH_2).

Found: C, 57.87; H, 6.87; N, 4.45%. Calcd for $C_{15}H_{21}NO_6$: C, 57.86; H, 6.80; N, 4.50%.

Acyl derivatives (**18**, **19**, and **20**) of **17** was obtained as follows.

*a) N-Benzoyl Derivatives (**18**)*: To a solution of **17** (300 mg, 0.965 mmol) in methanol (20 ml) was added benzoic anhydride (225 mg, 1.0 mmol) and the resulted solution was refluxed for 5 hr, evaporated to give a sirup which was crystallized from ether. Yield, 67.5% (260 mg); mp 154—155°C; $[\alpha]_D^{23}$+12.0° (*c* 1.05, $CHCl_3$). IR: *ca.* 3400 (NH and OH), 1640 (amide).

Found: C, 63.60; H, 6.20; N, 3.67%. Calcd for $C_{22}H_{25} \cdot NO_7$: C, 63.60; H, 6.07; N, 3.37%.

*b) 2,3-Di-O-acetyl-N-benzoyl Derivative (**19**)*: Acid-catalyzed acetylation of **18** gave the corresponding sirupy di-*O*-acetate in a quantitative yield. $[\alpha]_D^{23}$ −40.8° (*c* 1.48, $CHCl_3$).

Found: C, 62.44; H, 5.96; N, 2.77%. Calcd for C_{26}-

$H_{29}NO_9$: C, 62.51; H, 5.85; N, 2.80%.

c) N,O-*Triacetate (**20**)*: Acid-catalyzed acetylation of **17** (100 mg, 0.329 mmol) gave the *N,O*-triacetate in 97% (136 mg) yield. Mp 180—181°C; $[\alpha]_D^{23}$ −19.6° (*c* 1.36, $CHCl_3$). IR: 3300 (NH), 1750 and 1730 (OAc), 1640 and 1555 (amide); NMR: 7.42 (Ph; s), 6.45 (NH), 5.94 (H_1; d, $J_{1,2}$=4.7), 5.50 (PhCH=), 5.10 (H_4; d, $J_{4,5}$=10.0), 4.84 (H_2; d), 4.42—3.80 (H_5, $H_6{}^a$ and H_6 ; m), 3.87 and 3.68 ($C_3{}'H_2$; ABq, J=9.5), 3.39 (OMe), 2.13 (*sec*-OAc), 1.97 (NAc), 1.77 (*tert*-OAc).

Found: C, 57.62; H, 6.24; N, 3.30%. Calcd for $C_{21}H_{27}NO_9$: C, 57.66; H, 6.22; N, 3.20%.

*Methyl 2-O-Benzoyl-4,6-O-benzylidene-3-C-nitromethyl-α-D-allopyranoside (**21**)*. To a solution of nitromethane (30 ml) in tetrahydrofuran (30 ml) were added successively sodium methoxide (Na; 0.4 g, 174 mmol) and **1** (6 g, 156 mmol) with stirring, the resulted solution was stirred for 3 hr at room temperature, neutralized with acetic acid (60%), extracted with chloroform. The extract was washed with water, and evaporated to give needles which was recrystallized from acetone–ethanol. Yield, 80.5% (5.6 g); mp 169—170°C; $[\alpha]_D^{23}$ +73.8° (*c* 1.0, acetone). IR: 3440 (OH), 1720 (OBz), 1543 (NO_2); NMR: *ca.* 8.08 and 7.46 (Ph; m), 5.58 (PhCH=), 5.22 (H_1; d, $J_{1,2}$=4.3), 5.20 (H_2; d), 4.75 and 4.70 ($C_3{}'H_2$; ABq, J=12.0), 4.41 (H_{6e}; q), 4.25 (OH), 4.22 (H_5; sex, $J_{5,6a}$=9.0, $J_{5,6e}$=4.5), 3.81 (H_{6a}; t, $J_{6a,6e}$=9.0), 3.74 (H_4; d, $J_{4,5}$=9.5), 3.43 (OMe).

Found: C, 59.60; H, 5.40; N, 2.91%. Calcd for $C_{22}H_{23}NO_9$: C, 59.32; H, 5.21; N, 3.14%.

*Methyl 4,6-O-Benzylidene-3-C-benzamidomethyl-α-D-allo-pyranoside (**22**)*. A solution of **21** (4 g, 9 mmol) in methanol (100 ml) was hydrogenated in an autoclave in the presence of Raney nickel at 30 atm, 70 °C for 6 hr, filtered in hot state, and evaporated to give prisms which were recrystallized from ethanol. Yield, 2.4 g (65%); mp 234—235°C; $[\alpha]_D^{23}$ −19.3° (*c* 1.0, acetone).

Found: C, 64.04; H, 5.84; N, 3.40%. Calcd for $C_{22}H_{25}NO_7$: C, 63.60; H, 6.07; N, 3.37%.

Acetyl derivatives of **22** was synthesized as follows;

*a) 2-O-Acetate (**23**)*: Acetylation of **22** by the usual method and recrystallization of the product from ethanol–*n*-hexane gave 23 in 77% yield. Mp 214—215°C; $[\alpha]_D^{23}$ +44.4° (*c* 0.96, $CHCl_3$). IR: 3490 (OH), 3430 (NH), 1720 (OAc), 1642 and 1515 (amide); NMR: 7.70—7.30 (2×Ph; m), 7.00 (NH), 4.90 (H_1; d, $J_{1,2}$=4.0), 4.86 (H_2; d), 4.35 (H_{6e}; q, $J_{5,6e}$=9.5), 4.10 and 3.35 ($C_3{}'H_2$; ABq. J=13.5), *ca.* 4.02 (H_5; m), 3.58 (H_4; d, $J_{4,5}$=9.5), 3.24 (H_{6a}; q, $J_{6a,6e}$=9.3), 2.13 (OAc).

Found: C, 62.96; H, 5.87; N, 3.09%. Calcd for $C_{24}H_{27}NO_8$: C, 63.01; H, 5.95; N, 3.06%.

*b) 2,3-Di-O-acetate (**24**)*: Acid-catalyzed acetylation of **22**, and recrystallization of the product from ethanol–*n*-hexane gave **25** in 83% yield. Mp 175—176°C; $[\alpha]_D^{23}$+23.1° (*c* 1.05, $CHCl_3$).

Found: C, 62.43; H, 5.84; N, 2.83%. Calcd for $C_{28}H_{29}NO_9$: C, 62.51; H, 5.85; N, 2.80%.

*De-N-benzoylation of **22***. A suspended solution of **22** (3.0 g) in methanolic potassium hydroxide (6 g in 15 ml) was refluxed for 5 hr, the precipitate (sodium benzoate) was filtered off, and the filtrate was poured into water. The resulted solution was extracted with chloroform, and the extract was washed with water, and evaporated to give crystals which were recrystallized from acetone. Yield, 0.9 g (36%). The structure of this crystal was determined to be methyl 4,6-*O*-benzylidene-2,3,*N*-benzylidine-3-*C*-(hydroxymethyl)-α-D-allopyranoside (**25**). Mp 194—197°C (dec.); $[\alpha]_D^{23}$ +64.2° (*c* 1.0, EtOH); IR: 1600 (Ph), 1525 (C–N), and 1380.

Found: C, 61.03; H, 6.35; N, 3.20%. Calcd for $C_{22}H_{23}NO_6 \cdot 2H_2O$: C, 60.96; H, 6.28; N, 3.23%.

On the other hand, the water layer was extracted with *n*-butanol, after neutralization with 4N hydrochloric acid. Evaporation of *n*-butanol extracts gave de-*O*-benzoylated free amine **26** (24.0%, 0.6 g) and **22** (23.3%, 0.7 g) by fractional crystallization from methanol. Mp 205—210°C (dec.); $[\alpha]_D^{23}$ +79.4° (*c* 1.0, H_2O); IR: 3350 (OH), 3120 and 3050 (NH_2).

Found: C, 51.85; H, 6.27; N, 3.80%. Calcd for $C_{15}H_{21}NO_6 \cdot 2H_2O$: C, 51.86; H, 7.25; N, 4.03%.

Base-catalyzed acetylation of **25** and **26** gave the corresponding 3-C-*acetamidomethyl*-2-O-*acetyl derivative* (**27**) in a quantitative yield. Mp 168°C; $[\alpha]_D^{23}$+39.7° (*c* 0.92, $CHCl_3$); IR: 3430 (OH), 3360 (NH), 1720 (ester), 1650 and 1530 (amide).

Found: C, 57.65; H, 6.11; N, 3.43%. Calcd for $C_{19}H_{25}NO_8$: C, 57.71; H, 6.37; N, 3.54%.

*Methyl 2-O-Benzoyl-3-C-nitromethyl-α-D-allopyranoside (**28**)*. To a solution of **21** (3.0 g) in acetone (20 ml) was added portionwise 0.2 N sulfuric acid (15 ml) at 40 °C, maintained at the temperature for 3 hr, neutralized with sodium bicarbonate, and concentrated. The residue was extracted with ethanol, and the ethanol solution was evaporated to give a sirup which was recrystallized from methanol–water. Yield, 87% (2.1 g); mp 152—154°C; $[\alpha]_D^{23}$ +92.5° (*c* 1.0, ethanol). IR: 3410 and 3510 (OH), 1720 (OBz), 1540 (NO_2).

Found: C, 50.83; H, 5.03; N, 4.04%. Calcd for $C_{15}H_{19}NO_9$: C, 50.42; H, 5.36; N, 3.92%.

This compound was also prepared by partial hydrogenation of **22** in the presence of palladium-charcoal in 53% yield, and it was converted into sirupy tri-*O*-acetate (**29**) by acid-catalyzed acetylation in 90% yield. $[\alpha]_D^{23}$ +91.5° (*c* 1.25, $CHCl_3$); IR: 1720 and 1760 (ester), 1550 (NO_2).

Found: C, 52.97; H, 5.55; N, 2.87%. Calcd for $C_{21}H_{25}NO_{12}$: C, 52.17; H, 5.21; N, 2.90%.

*Methyl 2-O-Benzoyl-3,4-O-isopropylidene-3-C-nitromethyl-α-D-allopyranoside (**30**)*. A suspended solution of **28** (1 g), and anhydrous cupric sulfate (2 g) in acetone (50 ml) containing one drop of sulfuric acid was stirred for 3 days at room temperature, neutralized with barium carbonate, filtered, and the filtrate was evaporated to give a sirupy product. The sirup was fractionated through a Kiesel gel 60 (Merck) column with benzene–methanol effluent (15 : 1) to give **28** (0.25 g) and **30** (0.67 g, 58%) which was crystallized from ethanol–*n*-hexane. Mp 138—139°C.

Found: C, 54.18; G, 5.57; N, 3.83%. Calcd for $C_{18}H_{23}NO_9$: C, 54.40; H, 5.83; N, 3.53%.

Acid-catalyzed acetylation of **30** gave *6-O-acetate* (**31**) in a quantitative yield, which was recrystallized from ethanol–*n*-hexane. Mp 143—143.5°C; IR: 1720 (ester), 1560 (NO_2), 1370 (CCH_3); NMR: 8.07—4.51 (Ph; m), 5.87 (H_1; d, $J_{1,2}$=5.1), 4.99 (H_2; d), 4.64 ($C_3{}'H_2$; s), 4.58—5.10 (H_4, H_5, and $H_{6a,b}$; m), 3.40 (OMe), 2.10 (OAc), 1.40 and 1.29 (2×CCH_3).

Found: C, 54.44; H, 5.77; N, 3.11%. Calcd for $C_{20}H_{25}NO_{10}$: C, 54.66; H, 5.74; N, 3.19%.

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