Aminosugars. XXVIII. A Facile Synthesis of Benzyl *α*- and *β*-Kasugaminides *via* the Corresponding Abequosides[1]

Juji Yoshimura, Ken-ichi Sato, Hironobu Hashimoto, and Kuniaki Shimizu
Laboratory of Chemistry for Natural Products, Faculty of Science, Tokyo Institute of Technology, Meguro-ku, Tokyo 152

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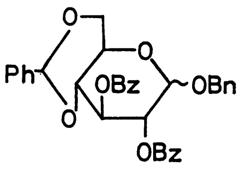
Synthesis of benzyl α- and β-kasugaminides (benzyl 2,4-diamino-2,3,4,6-tetradeoxy-α- and β-D-*arabino*-hexopyranosides) was carried out by the simultaneous substitution at 2,4-positions of 2,4-di-*O*-mesyl-abequosides (3,6-dideoxy-2,4-di-*O*-mesyl-α- and β-D-*xylo*-hexopyranosides) with sodium azide followed by hydrogenation. The substitution in *N*,*N*-dimethylformamide at higher temperature gave the elimination products (4-azido-2,3-unsaturated derivatives) and the subsequently rearranged products (3,4-unsaturated 2-azido derivatives), but, that in hexamethylphosphoric triamide at lower temperature gave the desired compounds in fairly good yields.

In connection with synthetic studies on kasugamycin[2,3] a few reports on the synthesis of racemic[4,5] and optically active[6] methyl α-kasugaminide (methyl 2,4-diamino-2,3,4,6-tetradeoxy-α-D-*arabino*-hexopyranoside) have been published. The necessity of the resolution of a racemate is a shortcoming in the former synthesis, whereas the stepwise conversion in the latter takes longer steps, and consequently gives a lower overall yield.

In order to study the relationship between the configuration of aminosugar moiety in kasugamycin and the biological activity, we intended to develope a better pathway for synthesis of optically active kasugaminide and its diastereomers. In this paper, a facile synthesis of benzyl α- and β-kasugaminides *via* the simultaneous S_N2-substitution at 2,4-positions of the corresponding abequosides (benzyl 3,6-dideoxy-α- and β-D-*xylo*-hexopyranosides) is descrided. As methyl α-abequoside[7-9] is known to be synthesized by the simultaneous deoxygenation of 3,6-positions of methyl 3,4-anhydro-6-*O*-*p*-tolylsulfonyl-α-D-galactopyranoside obtainable from D-glucose, the pathway offered here is advantageous.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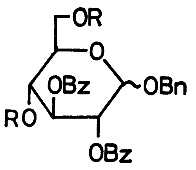
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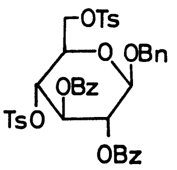
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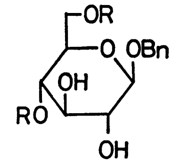
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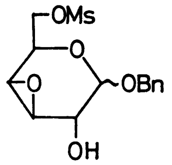
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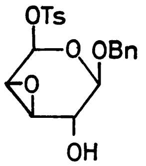
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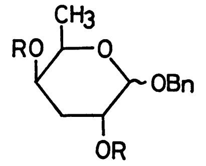
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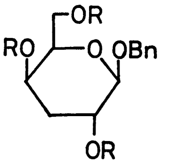
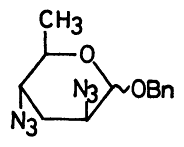

(10) R=H
(12) R=SO_2CH_3

Results and Discussion

According to the method of Siewert and Westphal,[7] benzyl α- and β-abequosides were newly prepared. Benzoylation of benzyl 4,6-*O*-benzylidene-α-[10] and β-D-glucopyranosides[11] in the usual manner gave the 2,3-di-*O*-benzoates (**1**α and **1**β) in good yields, respectively. Partial hydrolysis of the 4,6-*O*-benzylidene group in **1**α and **1**β proceeded quantitatively in 70% acetic acid at 90—95 °C to give **2**α and **2**β, respectively. Mesylation of **2**α and **2**β in the usual manner gave the corresponding 4,6-di-*O*-mesylates (**3**α and **3**β) in good yields, respectively. Benzyl 2,3-di-*O*-benzoyl-4,6-di-*O*-*p*-tolylsulfonyl-β-D-glucopyranoside (**4**) was also prepared from **2**β in a similar manner.

Examination of the conversion of **3**β in dichloromethane or chloroform into the corresponding epoxide (**7**β) by treatment with sodium methoxide in methanol indicated that **3**β was once changed into an intermediate (**5**) within 6 h and then gradually converted into **7**β.

In fact, **5** deposited from the reaction mixture, when the amount of solvents (especially methanol) was not enough. This conversion proceeded slower than that of the corresponding methyl glucoside,[7] and the use of a little excess (1.3—1.4 mol) sodium methoxide gave a better result. Thus, **7**α and **7**β were obtained in 64 and 75% yields, respectively. In a similar way, tosylated intermediate (**6**) and tosylated epoxide (**8**) were obtained from **4**. It was characteristic that NMR spectra of these epoxides showed a coupling between OH and H_2 and a AB-quartet of H_3 and H_4. Reduction of **7**α, **7**β, and **8** in tetrahydrofuran (THF) with 3 mol of lithium aluminium hydride (LAH) gave sirupy benzyl abequosides (**9**α and **9**β), respectively. When 1.5 mol of LAH were used in one instance, crystalline benzyl 3-deoxy-β-D-*xylo*-hexopyranoside (**10**) was separated on a silica gel column in 22% yield, indicating that the epoxide ring was more reducible than the 6-*O*-sulfonate group. Excepting the last step in the synthesis of **9**α and **9**β, the purification of the product in each reaction was not always necessary, and both α- and β-abequosides could be actually obtained in *ca.* 20% overall yield from D-glucose. Mesylation of **9**α or **9**β and **10** gave the corresponding 2,4-di-*O*-mesylates (**11**α or **11**β) and 2,4,6-tri-*O*-mesylate (**12**) in good yields, respectively.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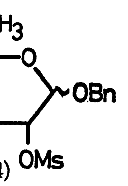
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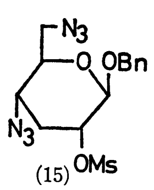
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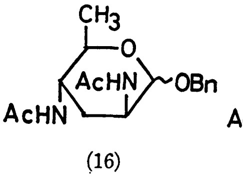
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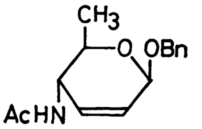
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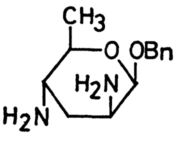
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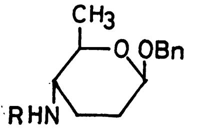
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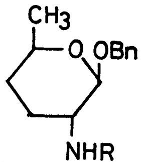
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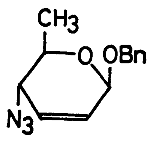
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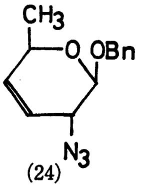
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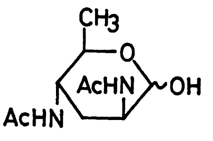
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The simultaneous substitution at 2,4-positions of mesylates mentioned above with sodium azide was unexpectedly accompanied with the formation of unsaturated products. Reaction of **11**β in *N*,*N*-dimethylformamide (DMF) with 3 mol of sodium azide at 120 °C overnight was incomplete, and two spots other than a small amount of the starting material were detected on TLC. Separation of the products on a silica gel column gave one monoazide (**14**β) in pure state, but the NMR spectrum of another fraction indicated the presence of unsaturated compounds. Reaction of **12** under the same condition gave also the corresponding 4,6-diazide (**15**) in a low yield. Even after the reaction of **11**β was continued at 160—165 °C[6] until **14**β disappeared, the mixture of products could not be separated by repeating column chromatography. Therefore, the separation was tried after hydrogenation of the products with LAH in THF followed by *N*-acetylation. Thus, benzyl *N*,*N*′-diacetyl-β-kasugaminide (**16**β) and benzyl 4-acetamido-2,3,4,6-tetradeoxy-β-D-*erythro*-hex-2-enopyranoside (**17**) could be isolated in 12 and 19% yields, respectively. When the hydrogenation was carried out in the presence of Raney nickel, the corresponding saturated amino derivatives could be separated by column chromatography into three sirupy products (**19**, **20**, and **18**) in 8, 19, and 42% yields, respectively. These compounds were characteriszed after quantitative conversion into *N*-acetyl derivatives (**21**, **22**, and **16**β). The first-order analysis of the NMR spectrum of **16**β (*cf.* Experimental) completely proved the allocated structure, and $J_{1,2}$ values of **21** ($J_{1,2e}$=2.4, $J_{1,2a}$=8.0) and **22** ($J_{1,2}$=8.2) supported them. It will be noteworthy that **19** is a glycoside of the enantiomer of natural L-tolyposamine.[12,13]

The results mentioned above suggest that the second substitution at *C*-2 of the initial product (**14**β) gives 2,4-diazide (**13**β), but the substitution is followed by the elimination of axial C_2-azido group to give benzyl 4-azido-2,3,4,6-tetradeoxy-β-D-*erythro*-hex-2-enopyranoside (**23**), which subsequently rearranges to the corresponding 2-azido-3-enopyranoside (**24**). Recently, several papers have been published on the thermal rearrangement of 2,3-unsaturated 4-azido- and 4-thiocyanatoglycopyranosides to 3,4-unsaturated sugars having nitrogen function at *C*-2.[14–16] These conversions were explained as a [3,3]-sigmatropic rearrangement of cyclic allylic systems in which the asymmetry at the initial allylic centre is transmitted to the new centre by the suprafacial migration.[14] Although the formation of a small amount of unsaturated product in the substitution of equatorial C_4-sulfonyloxy group attached to 3-deoxy-hexopyranoside-ring with sodium azide in DMF has been reported,[10] the question whether the formation of **23** is initiated from the equatorial C_2-sulfonyloxy group of **14**β or from axial C_2-azido group of **13**β was remained ambiguous.

Table 1. Substitution of **11**α and **11**β with sodium azide in HMPA

	Conditions		Products (%)		
	Temp (°C)	Time (h)	**14**	**13**	Unsaturated products
11α	80	20	86	—	—
11α	120	42	—	69	12[a]
11β	80	20	81	—	—
11β	100	5	78	—	—
11β	120	18	—	55	31[a]

a) Yields were estimated from the weight of crude products and the intensity ratio of olefinic proton and others in NMR spectra.

In order to prevent the formation of unsaturated compounds, the same substitution of **11**α and **11**β was examined at a lower temperature, using hexamethylphosphoric triamide (HMPA) as a solvent. As shown in Table 1, the reaction at 80 °C gave exclusively monosubstituted **14** in good yields. The continuation of the reaction at 120 °C until **14** disappeared also resulted in the formation of unsaturated compounds, but the yields of the desired diazides (**13**) were improved. Actually, **16**α and **16**β were obtained from the crude products in 60 and 46% yields, respectively, by subsequent hydrogenation and *N*-acetylation. The structure of **16**α and **16**β was further confirmed by respective hydrogenation into known *N*,*N*′-diacetyl-kasugamine (**25**).[17] It has been reported that the substitution of methyl 4,6-*O*-isopropylidene-3-*O*-methyl-2-*O*-methylsulfonyl-β-D-gluco- and D-mannopyranoside with potassium benzoate in DMF proceeded smoothly, whereas that of α-anomers did not occur.[18] Slower but steady substitution of the α-anomer in this experiment will be attributed to the absence of substituent at *C*-3 and to the flexibility of **11**α.

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 spectrometer. The NMR spectra were taken with a JEOL-4H-100 MHz spectrometer using tetramethylsilane as an internal standard, in deuteriochloroform unless otherwise stated. Chemical shifts and coupling constants were recorded in δ and Hz units, and IR frequencies in cm^{-1}.

*Benzyl 2,3-Di-O-benzoyl-4,6-O-benzylidene-α- and β-*D*-glucopyranosides (**1α** and **1β**).* Benzyl 4,6-*O*-benzylidene-β-D-glucopyranoside[11] was benzoylated with benzoyl chloride in benzene. A usual work up and recrystallization of the product from ethanol gave pure **1β** in 90.5% yield. Mp 167—168.5 °C; $[\alpha]^{22}_{\mathrm{D}}$ −19.9 ° (c 0.5, CHCl$_3$). IR: 1728 (ester), 1600 and 1490 (Ph); NMR: 7.90 and 7.60—7.00 (Ph; m), 5.73 (H$_3$: t, $J_{3,4}=9.2$), 5.52 (H$_2$: q, $J_{2,3}=8.8$), 5.51 (CH: s), 4.79 (H$_1$: d, $J_{1,2}=7.4$), 4.87 and 4.62 (CH$_2$: ABq, $J_{\mathrm{AB}}=12.5$), 4.41 (H$_{6e}$: q, $J_{6e,6a}=10.0$), 3.93 (H$_4$: t, $J_{4,5}=8.8$), 3.87 (H$_{6a}$: t, $J_{5,6a}=9.8$), 3.72 (H$_5$: m, $J_{5,6e}=5.0$). Found: C, 72.02; H, 5.34%. Calcd for C$_{34}$H$_{30}$O$_8$: C, 72.07; H, 5.34%.

Similarly, benzoylation of benzyl 4,6-*O*-benzylidene-α-D-glucopyranoside[10] gave **1α** in 93% yield. Mp 134—136 °C; $[\alpha]^{22}_{\mathrm{D}}$ +123.2 ° (c 0.35, CHCl$_3$). IR: 1700 (ester), 1600 (Ph); NMR: 7.95 and 7.50—7.10 (Ph; m), 6.10 (H$_3$: t, $J_{2,3}=J_{3,4}=9.3$), 5.51 (CH: s), 5.28 (H$_1$: broad s), 5.23 (H$_2$: q, $J_{1,2}=3.3$), 4.72 and 4.53 (CH$_2$: ABq, $J_{\mathrm{AB}}=13.0$), 4.33—3.75 (H$_4$, H$_5$, H$_6$, and H$_{6'}$: m). Found: C, 72.34; H, 5.77%. Calcd for C$_{34}$H$_{30}$O$_8$: C, 72.07; H, 5.34%.

*Benzyl 2,3-Di-O-benzoyl-α- and β-*D*-glucopyranosides (**2α** and **2β**).* A suspension of **2β** (30 g) in 70% acetic acid–ethanol–acetone (300 ml, 150 ml, and 90 ml) was heated for 2 h at 90—95 °C until **2β** disappeared on TLC, and then evaporated to give a sirup which was crystallized from benzene. Yield, 24 g (94%); mp 157—158 °C; $[\alpha]^{22}_{\mathrm{D}}$ +65.1 ° (c 1.2, CHCl$_3$); IR: 3460 (OH), 1725 and 1710 (ester), 1603 and 1495 (Ph). Found: C, 67.93; H, 5.56%. Calcd for C$_{27}$H$_{26}$O$_8$: C, 67.77; H, 5.48%.

In a similar manner, 4,6-*O*-benzylidene group of **1α** was hydrolyzed to give **2α** quantitatively. Mp 125—126 °C; $[\alpha]^{22}_{\mathrm{D}}$ +175.2 ° (c 0.5, CHCl$_3$). IR: 3500 and 3380 (OH), 1730 and 1705 (ester), 1600 and 1490 (Ph). Found: C, 67.53; H, 5.57%. Calcd for C$_{27}$H$_{26}$O$_8$: C, 67.77; H, 5.48%.

*Benzyl 2,3-Di-O-benzoyl-4,6-di-O-methylsulfonyl-α- and β-*D*-glucopyranosides (**3α** and **3β**).* Mesylation of **2β** with methanesulfonyl chloride in the usual manner, and crystallization of the product from chloroform–ethanol (1: 1) gave pure **3β** in 90% yield. Mp 165—166 °C; $[\alpha]^{22}_{\mathrm{D}}$ +43.7 ° (c 1.0, MeOH). IR: 1710 and 1733 (ester), 1595 and 1490 (Ph), 1345 and 1175 (sulfate); NMR: 8.02—7.08 (Ph: m), 5.70 (H$_3$: t, $J_{2,3}=J_{3,4}=9.0$), 5.46 (H$_2$: q), 4.98 (H$_4$: t, $J_{4,5}=9.0$), 4.83 and 4.69 (CH$_2$: ABq, $J_{\mathrm{AB}}=12.0$), 4.70 (H$_1$: d, $J_{1,2}=8.1$), 4.63 (H$_6$: q, $J_{5,6}=2.0$), 4.44 (H$_{6'}$: q, $J_{5,6'}=4.7$, $J_{6,6'}=10.8$), 3.93 (H$_5$: m), 2.86 and 3.08 (OSO$_2$CH$_3$). Found: C, 55.10; H, 4.84; S, 9.72%. Calcd for C$_{29}$H$_{30}$O$_{12}$S$_2$: C, 54.88; H, 4.76; S, 10.10%.

Similarly, **2α** was mesylated to give the 4,6-di-*O*-mesylate in 93% yield. Mp 182—183 °C, $[\alpha]^{22}_{\mathrm{D}}$ +137 ° (c 0.6, CHCl$_3$). IR: 1720 (ester), 1595 and 1490 (Ph), 1350 and 1180 (sulfate); NMR: 7.93 and 7.58—7.12 (Ph: m), 6.08 (H$_3$: t, $J_{2,3}=J_{3,4}=10.0$), 5.32 (H$_1$: d, $J_{1,2}=3.8$), 5.15 (H$_2$: q), 4.98 (H$_4$: t, $J_{4,5}=9.5$), 4.71 and 4.58 (CH$_2$: ABq, $J_{\mathrm{AB}}=11.5$), 4.50—4.10 (H$_5$, H$_6$, and H$_{6'}$: m), 3.05 and 2.86 (OSO$_2$CH$_3$). Found: C, 54.62; H, 4.68; S, 10.00%. Calcd for C$_{29}$H$_{30}$O$_{12}$S$_2$: C, 54.88; H, 4.76; S, 10.10%.

*Benzyl 2,3-Di-O-benzoyl-4,6-O-*p*-tolylsulfonyl-β-*D*-glucopyranoside (**4**).* Reaction of **2β** and *p*-toluenesulfonyl chloride in pyridine in the usual manner gave **4** in 67% yield. Mp 125—126 °C; $[\alpha]^{22}_{\mathrm{D}}$ +13.9 ° (c 1.0, CHCl$_3$). Found: C, 62.55; H, 4.81; S, 8.02%. Calcd for C$_{41}$H$_{38}$O$_{12}$S$_2$: C, 62.58; H, 4.87; S, 8.15%.

*Benzyl 3,4-Anhydro-6-O-methylsulfonyl-α- and β-*D*-glucopyranosides (**7α** and **7β**).* To a solution of **3β** (14.8 g, 124 mmol) in chloroform (150 ml) was added a methanol solution (100 ml) of sodium methoxide (0.56 g, 1.2 equivalent of sodium) and then kept in a refrigerator overnight. The reaction mixture was diluted with chloroform (100 ml), and then washed three times with water. The chloroform layer was dried and evaporated to give a sirup which was crystallized from benzene–petroleum ether. Yield 5.8 g (75%); mp 77—78 °C; $[\alpha]^{22}_{\mathrm{D}}$ −108.3 ° (c 1.0, CHCl$_3$). IR: 3400 (OH), 1490 (Ph), 1350 and 1190 (sulfate), 930 (epoxide); NMR: 7.30 (Ph: s), 4.80 and 4.53 (CH$_2$: ABq, $J_{\mathrm{AB}}=11.5$), 4.42—4.30 (H$_6$ and H$_{6'}$: m), 4.22 (H$_1$: d, $J_{1,2}=7.0$), 4.19 (H$_5$: t, $J_{5,6}=J_{5,6'}=5.7$), 3.68 (H$_2$: q, $J_{2,\mathrm{OH}}=3.8$), 3.21 and 3.12 (H$_3$ and H$_4$: each d, $J_{3,4}=3.8$), 2.99 (OSO$_2$CH$_3$), 2.66 (OH: d). Found: C, 51.38; H, 5.42; S, 9.41%. Calcd for C$_{14}$H$_{18}$O$_7$S: C, 50.90; H, 5.49; S, 9.71%.

When the amount of solvents or the reaction time in the above reaction was not enough, the intermediate, benzyl 4,6-di-*O*-methylsulfonyl-β-D-glucopyranoside (**5**) deposited from the reaction mixture or from the chloroform layer during the washing with water. It was characterized as follows; mp 101—103 °C; $[\alpha]^{22}_{\mathrm{D}}$ −41.8 ° (c 0.86, MeOH); IR: 3400 (OH), 1490 (Ph), 1350 and 1190 (sulfate). Found: C, 42.12; H, 5.39; S, 14.74%. Calcd for C$_{15}$H$_{22}$O$_{10}$S$_2$: C, 42.24; H, 5.20; S, 15.04%.

Similarly, **3α** was converted into **7α** in 64% yield. Mp 73—74 °C (from ethanol–hexane); $[\alpha]^{24}_{\mathrm{D}}$ +42.4 ° (c 0.5, CHCl$_3$), IR: 3350 (OH), 1495 (Ph), 1350 and 1190 (sulfate); NMR: 7.40 (Ph, s), 4.94 (H$_1$: d, $J_{1,2}=4.8$), 4.84 and 4.60 (CH$_2$: ABq, $J_{\mathrm{AB}}=11.5$), 4.45—4.30 (H$_6$ and H$_{6'}$: m), 3.85 (H$_2$: q, $J_{2,\mathrm{OH}}=10.5$), 3.30 and 3.24 (H$_3$ and H$_4$: ABq, $J_{3,4}=2.6$), 3.07 (OSO$_2$CH$_3$), 2.50 (OH: d). Found: C, 50.62; H, 5.56; S, 9.53%. Calcd for C$_{14}$H$_{18}$O$_7$S: C, 50.90; H, 5.49; S, 9.71%.

*Benzyl 3,4-Anhydro-6-O-*p*-tolylsulfonyl-β-*D*-glucopyranoside (**8**) and Benzyl 4,6-Di-O-*p*-tolylsulfonyl-β-*D*-glucopyranoside (**6**).* Epoxidation of **4** in the same manner as above, and separation of the product on a silica gel column gave **8** (sirup) and **6** (mp 110—112 °C) in 48.4% and 25% yields, respectively.

8: $[\alpha]^{22}_{\mathrm{D}}$ −93.4 ° (c 0.9, CHCl$_3$); NMR: 7.85—7.15 (Ph: m), 4.71 and 4.45 (CH$_2$: ABq, $J_{\mathrm{AB}}=14.0$), 4.25—4.02 (H$_5$, H$_6$, and H$_{6'}$: m), 3.61 (H$_2$: broad d), 3.13 and 3.02 (H$_3$ and H$_4$: ABq, $J_{\mathrm{AB}}=4.4$), 2.88 (OH: broad s), 2.37 (CH$_3$: s). Found: C, 59.26; H, 5.59; S, 7.76%. Calcd for C$_{20}$H$_{22}$O$_7$S: C, 59.10; H, 5.46; S, 7.89%.

6: $[\alpha]^{22}_{\mathrm{D}}$ −37.7 ° (c 1.0, MeOH). Found: C, 57.21; H, 5.35; S, 10.51%. Calcd for C$_{28}$H$_{30}$O$_{10}$S$_2$: C, 56.93; H, 5.12; S, 10.86%.

*Benzyl 3,6-Dideoxy-α- and β-*D*-*xylo*-hexopyranosides (**9α** and **9β**).* To a suspension of lithium aluminium hydride (LAH, 2.4 g, 63 mmol) in tetrahydrofuran (THF, 100 ml) was added dropwise a solution of **7β** (8 g, 18 mmol) in THF (70 ml) with stirring. The reaction mixture was refluxed for 5 h, and a mixed solution of water and ethyl acetate was added to decompose excess LAH. After bubbling carbon dioxide into the reaction mixture, it was filtered, and the filtered mass was washed with methanol–water (1: 1). The filtrate and washings were evaporated, and the residue was dissolved in water. Sodium periodate (2 g, 7.5 mmol) was added to the aqueous solution and kept in a refrigerator overnight. After addition of hydrogen peroxide (30%, 3 ml), the mixture was reduced with excess sodium thiosulfate, evaporated, and an aqueous solution of the residue was extracted with chloroform. Evaporation of the extracts gave a sirup (3.8 g) which was fractionated on a silica gel column (ethanol: benzene=1: 9) to give pure **9**β (3.0 g, 52%) as a sirup, $[\alpha]^{22}_{D}$ −107 ° (*c* 0.5, $CHCl_3$). Found: C, 65.81; H, 7.72%. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61%.

The same compound was also obtained from **8** in 48.5% yield. In a similar manner mentioned above, **9**α was obtained from **7**α in 53% yield as a sirup. $[\alpha]^{22}_{D}$ +119 ° (*c* 0.8, $CHCl_3$). Found: C, 64.98; H, 7.38%. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61%.

In case of 1.5 mol of LAH were used for hydrogenation of **7**β, fractionation of the product gave benzyl 3-deoxy-β-D-*xylo*-hexopyranoside (**10**) in 22% yield. Mp 95—95.5 °C; $[\alpha]^{22}_{D}$ −50.9 ° (*c* 1.1, MeOH). Found: C, 61.17; H, 7.08%. Calcd for $C_{13}H_{18}O_5$: C, 61.40; H, 7.14%.

*Benzyl 3,6-Dideoxy-2,4-di-*O*-methylsulfonyl-*α*- and *β-D-xylo-*hexopyranosides (11*α *and 11*β*).* Mesylation of **9**β in the usual manner, and crystallization of the product from ethanol gave **11**β in 77% yield. Mp 104—105 °C; $[\alpha]^{D}_{22}$ −64 ° (*c* 1.0, $CHCl_3$). IR: 1360 and 1170 (sulfate); NMR: 7.32 (Ph, s), 4.92 and 4.58 (CH_2: ABq, J_{AB}=12.0), 4.23 (H_4: m), 4.68—4.50 (H_1 and H_2: m), 3.80 (H_5: octet, $J_{4,5}$=1.5), 2.91 and 3.08 (2×OSO_2CH_3), 2.71 (H_{3e}: m, J_{gem}=12.7), 2.04 (H_{3a}: m), 1.35 (CH_3: d, $J_{CH_3,5}$=6.3). Found: C, 45.91; H, 5.68; S, 16.28%. Calcd for $C_{15}H_{22}O_8S_2$: C, 45.67; H, 5.62; S, 16.26%.

Similarly, **9**α was mesylated to give **11**α quantitatively. Mp 92—93 °C (from ethanol–hexane); $[\alpha]^{22}_{D}$ +95.2 ° (*c* 0.6, $CHCl_3$); IR: 1340 and 1175 (sulfate). Found: C, 45.86; H, 5.69; S, 16.31%. Calcd for $C_{15}H_{22}O_8S_2$: C, 45.67; H, 5.62; S, 16.26%.

*Benzyl 3-Deoxy-2,3,6-tri-*O*-methylsulfonyl-*β*-*O-xylo*-hexopyranoside (12).* Mesylation of **10** in pyridine with methanesulfonyl chloride gave the tri-*O*-mesylate in 76% yield. Mp 123—126 °C; $[\alpha]^{22}_{D}$ −59.6 ° (*c* 1.0, $CHCl_3$); IR: 1350 and 1180 (sulfate); NMR: 7.32 (Ph: s), 4.97 (H_4: m), 4.90 and 4.65 (CH_2: ABq, J_{AB}=12.0), 4.67—4.56 (H_1 and H_2: m), 4.40—4.25 (H_6 and H_6': m), 4.00 (H_5: sex, $J_{4,5}$=1.0, $J_{CH_3,5}$=7.9), 3.11, 3.04 and 2.93 (3×OSO_2CH_3), 2.81 (H_{3e}: sex, J_{gem}=14.3, $J_{2,3e}$, $J_{3e,4}$=3.5), 2.04 (H_{3a}: m, $J_{2,3a}$=9.0, $J_{3a,4}$=4.0). Found: C, 39.61: H, 4.91; S, 19.63%. Calcd for $C_{16}H_{24}O_{11}S_3$: C, 39.33; H, 4.95; S, 19.69%.

*Benzyl 4-Azido-3,4,6-trideoxy-2-*O*-methylsulfonyl-*α*- and *β-D-ribo-*hexopyranosides (14*α *and 14*β*).* i) Reaction in *N,N*-dimethylformamide (DMF). A suspension of **11**β (600 mg, 1.52 mmol) and sodium azide (500 mg, 7.69 mmol) in DMF (10 ml) was stirred at 120 °C overnight, filtered, and the filtrate was evaporated to give a sirup (450 mg) which showed two spots other than **11**β. The sirup was fractionated on a silica gel column (benzene: ethanol=10: 1). The first fraction (140 mg, 31.9%) was a mixture of **11**β and other products, and the second fraction was **14**β. Yield, 50 mg (9.6%); $[\alpha]^{22}_{D}$ −44.4 ° (*c* 0.4, $CHCl_3$); mp 76—78 °C (from ethanol). IR: 2120 (N_3), 1365 and 1180 (sulfate); NMR: 7.30 (Ph; s), 4.84 and 4.55 (CH_2: ABq, J_{AB}=11.5), 4.46 (H_1: d, $J_{1,2}$=7.0), 4.33 (H_2: dt, $J_{2,3a}$=8.0, $J_{2,3e}$=5.2), 3.27 (H_5: dq, $J_{4,5}$=9.6), 3.14 (H_4: sex, $J_{4,3a}$=9.6, $J_{4,3e}$=4.5), 2.87 (OSO_2CH_3), 2.58 (H_{3e}: dt, J_{gem}=12.0), 1.76 (H_{3a}: broad q), 1.31 (CH_3: d, J_{5,CH_3}=7,0). Found: C, 49.50; H, 5.61; N, 12.46; S, 9.21%. Calcd for $C_{14}H_{19}N_3O_5S$: C, 49.25; H, 5.61; N, 12.31; S, 9.39%. ii) Reaction in hexamethylphosphoric triamide (HMPA). A suspension of **11**β (1.2 g) and sodium azide (1 g) in HMPA (5 ml) was stirred at 80 °C for 20 h, and then poured into water (30 ml). The resulting solution was extracted with ether. The ether solution was washed with water, dried, and then evaporated to give a hard sirup (**14**β) which was crystallized from ethanol–hexane. Yield, 0.84 g (81%). The physical constants of this product were identical with those mentioned above.

The reaction of **11**α with sodium azide in the same manner gave sirupy **14**α in 86% yield. $[\alpha]^{22}_{D}$ +114.2 ° (*c* 0.76, $CHCl_3$); IR: 2100 (N_3), 1360 and 1180 (sulfate); NMR: 7.38 (Ph, s), 5.00 (H_1: d, $J_{1,2}$=3.4), 4.76 and 4.62 (CH_2: ABq, J_{AB}=12.0), 4.80—4.60 (H_2: m), 3.68 (H_5: dq, $J_{4,5}$=10.0, J_{5,CH_3}=6.3), 3.14 (H_4: sextet, $J_{3a,4}$=10.0, $J_{3e,4}$=5.3), 2.95 (OSO_2CH_3), 2.35 (H_{3e}: $J_{2,3e}$=5.6, J_{gem}=11.6), 2.18 (H_{3a}: q, $J_{2,3a}$=11.0), 1.22 (CH_3: d). Found: C, 49.45; H, 5.51; N, 12.18; S, 9.45%. Calcd for $C_{14}H_{19}N_3O_5S$: C, 49.25; H, 5.61; N, 12.31; S, 9.39%.

*Benzyl 4,6-Diazido-3,4,6-trideoxy-2-*O*-methylsulfonyl-*β-D-ribo-*hexopyranoside (15).* A suspension of **12** (980 mg, 2 mmol) and sodium azide (780 mg, 12 mmol) in DMF (13 ml) was stirred at 120 °C overnight, filtered, and the filtrate was evaporated. A usual extraction gave a sirup which showed two spots other than **12** on TLC. Separation of the sirup on a silica gel column (benzene: ethanol=10: 1) gave two main fractions of which the first fraction (230 mg, 35%) showed no absorption of a sulfonyloxy group, but the second fraction (110 mg, 14.3%) showed the mesyl signal in the NMR spectrum. The former was rechromatographed, but it could not be purified. The latter fraction crystallized on standing, and recrystallized from benzene–petroleum ether. Mp 78—80 °C; $[\alpha]^{22}_{D}$ −25.2 ° (*c* 0.6, $CHCl_3$); IR: 2100 (N_3), 1365 and 1180 (sulfate); NMR: 7.30 (Ph, s), 4.88 and 4.58 (CH_2: ABq, J_{AB}=11.5), 4.51 (H_1: d, $J_{1,2}$=7.0), 4.37 (H_2: dt, $J_{2,3e}$=5.3), 3.41 (H_4, H_5, H_6, and $H_{6'}$: broad s), 2.90 (OSO_2CH_3), 2.67 (H_{3e}: dt, $J_{3e,4}$=4.2), 1.81 (H_{3a}: broad q, J_{gem}=$J_{3a,4}$=$J_{3a,2}$=11.0). Found: C, 44.26; H, 4.65; N, 22.33; S, 7.99%. Calcd for $C_{14}H_{18}N_6O_5S$: C, 43.97; H, 4.74; N, 21.98; S, 8.39%.

Benzyl 2,4-Diacetamido-2,3,4,6-tetradeoxy-β-D-arabino-*hexopyranoside (16*β*) and Benzyl 4-Acetamido-2,3,4,6-tetradeoxy-*β-D-erythro-*hex-2-enopyranoside (17).* A suspension of **11**β (800 mg, 2 mmol) and sodium azide (700 mg, 10.8 mmol) in DMF (15 ml) and water (1.5 ml) was stirred at 120 °C for one day, and then at 160—165 °C until the initial product **14**β disappeared (8 h). Treatment of the reaction mixture in the usual way and purified on a silica gel column gave a sirup (450 mg). A suspension of this sirup (350 mg) and LAH (380 mg, 10 mmol) in THF was refluxed on a oil-bath for 3 h, and a small amount of water containing ethyl acetate was added to decompose excess LAH, and then filtered. After neutralization of the filtrate, it was evaporated. The residue was dried, and then acetylated in the usual manner to give a sirup which contained two main components. The two products were isolated in pure state by column chromatography repeated twice. Thus, the first fraction **16**β and the second **17** were obtained in 50 mg (12%) and 80 mg (19.4%) yields, respectively.

16β: Mp 146—147.5 °C; $[\alpha]^{22}_{D}$ −45.2 ° (*c* 1.0, $CHCl_3$); IR: 3270 (NH); 1650 and 1550 (amide); NMR: 7.29 (Ph: s), 4.80 and 4.55 (CH_2: ABq, J_{AB}=12.0), 4.54 (H_1: d, $J_{1,2}$=2.5), 4.14 (H_2: broad s), 3.83 (H_4: m), 3.43 (H_5: dq, $J_{4,5}$=8.2), 2.18 (H_{3e}: dt, $J_{3e,4}$=$J_{3e,2}$=4.7, J_{gem}=13.5), 1.93 and 1.96 (2×NAc), 1.53 (H_{3a}: octet, $J_{3a,4}$=10.0, $J_{3a,2}$=4.0), 1.29 (CH_3: d, $J_{CH_3,5}$=7.0). Found: C, 64.03; H, 7.62; N, 8.73%.

Calcd for $C_{17}H_{24}N_2O_4$: C, 63.73; H, 7.55; N, 8.74%.

17: Mp 162—164 °C; $[\alpha]_D^{22}$ −249 ° (*c* 0.2, $CHCl_3$); IR: 3270 (NH), 1640 and 1550 (amide); NMR: 7.30 (Ph, s), *ca.* 5.7 (olefinic H, m), 4.83 and 4.57 (CH_2: ABq, J_{AB}=12.0), 4.63 (H_1: d, $J_{1,2}$=4.5), 4.5—4.2 (H_4 and H_5: m), 1.91 (NAc), 1.33 (CH_3: d, $J_{CH_3,5}$=7.0). Found: C, 69.23; H, 7.29; N, 5.52%. Calcd for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36%.

*Preparation of Benzyl β-Kasugaminide (**18**), Benzyl 4-Amino-2,3,4,6-tetradeoxy-β-*D-erythro-*hexopyranoside (**19**), Benzyl 2-Amino-2,3,4,6-tetradeoxy-β-*D-erythro-*hexopyranoside (**20**), and Their Conversion into the Corresponding* N-*Acetates (**16β**, **21**, and **22**).*

In the same manner mentioned above, the reaction of **11β** (7.5 g) with sodium azide was carried out, and the crude product was hydrogenated in the presence of Raney nickel at 50 °C for 5 h under 50 atm hydrogen gas to give a sirup which showed three spots on TLC. The sirup on a silica gel (80 g Wakogel C-200) column was eluted with benzene–ethanol [in turn 7: 1 (500 ml), 5: 1 (500 ml), and 1: 1 (300 ml)] to give **20** (0.8 g, 19.0%), **19** (0.34 g, 8.1%), and **18** (1.82 g, 41.9%) as a sirup, respectively. Each sirup was acetylated with acetic anhydride and pyridine. The reaction mixture was directly evaporated to dryness, and the product was purified by column chromatography if necessary. Each acetate obtained in almost quantitative yield was characterized with NMR spectrum, respectively.

Compound **20** was not characterized.

22: mp 161.5—162 °C; $[\alpha]_D^{22}$ −90.4 ° (*c* 0.6, $CHCl_3$); IR: 3280 (NH), 1635 and 1550 (amide); NMR: 7.35 (Ph, s), 4.88 and 4.58 (CH_2: ABq, J_{AB}=12.0), 4.36 (H_1: d, $J_{1,2}$=8.2), 3.82—3.40 (H_2 and H_5: m), 2.3—1.3 (H_{3a}, H_{3e}, H_{4a}, and H_{4e}: m), 1.90 (NAc), 1.26 (CH_3: d, $J_{CH_3,5}$=6.5). Found: C, 68.72; H, 8.30; N, 5.60%. Calcd for $C_{15}H_{21}NO_3$: C, 68.41; H, 8.04; N, 5.32%.

19: $[\alpha]_D^{22}$ −70.8 ° (*c* 1.1, $CHCl_3$). Found: C, 69.95; H, 8.88; N, 6.32%. Calcd for $C_{13}H_{20}NO_2$: C, 70.55; H, 8.65; N, 6.33%.

21: mp 165—167 ° (admixture with **22** showed mp of 137—146 °C); $[\alpha]_D^{22}$ −89.8 ° (*c* 0.5, $CHCl_3$); IR: 3270 (NH), 1635 and 1545 (amide); NMR: 7.35 (Ph, s), 4.90 and 4.58 (CH_2: ABq, J_{AB}=12.0), 4.51 (H_1: q, $J_{1,2e}$=2.4, $J_{1,2a}$=8.0), 3.70 (H_4: dt, $J_{4,5}$=$J_{3a,4}$=10.0, $J_{3e,4}$=4.4), 3.36 (H_5: dq, J_{5,CH_3}=6.0), 1.98 (NAc), 2.22—1.38 (H_{2a}, H_{2e}, H_{3a}, and H_{3e}: m), 1.28 (CH_3). Found: C, 68.82; H, 8.20; N, 5.37%. Calcd for $C_{15}H_{21}NO_3$: C, 68.41; H, 8.04; N, 5.32%.

18: $[\alpha]_D^{22}$ −92.4 ° (*c* 0.4, $CHCl_3$). Found: C, 65.76; H, 8.95; N, 11.58%. Calcd for $C_{13}H_{20}N_2O_2$: C, 66.07; H, 8.53; N, 11.86%.

Physical properties of *N,N′*-diacetate of **18** were identical with **16β**.

*Benzyl 2,4-Diacetamido-2,3,4,6-tetradeoxy-α-*D-arabino-*hexopyranoside (**16α**).* A suspension of **11α** (2.4 g, 6.08 mmol) and sodium azide (2 g, 28.8 mmol) in HMPA (10 ml) was stirred at 120 °C for 42 h until the initial product (**14α**) disappeared on TLC, and the subsequent hydrogenation with LAH and *N*-acetylation of the product were carried out as mentioned before to give a sirup which showed three spots on TLC. The main spot was separated by a silica gel column chromatography to give crystals which were recrystallized from ethanol–hexane. Yield, 1.17 g (60%); mp 95—98 °C; $[\alpha]_D^{22}$ +77.9 ° (*c* 0.6, $CHCl_3$). IR: 3260 (NH), 1645 and 1545 (amide); NMR (D_2O exchanged): 7.32 (Ph, s), 4.68 (H_1: broad s, $J_{1,2}$=<1.5), 4.66 and 4.52 (CH_2: ABq, J_{AB}=11.5), 4.18 (H_2: broad t), 3.95 (H_4: q, $J_{4,3a}$=8.0, $J_{4,5}$=10.0), 3.64 (H_5: dq, J_{5,CH_3}=6.0), 1.98 and 1.95 (2×NAc), 2.05—1.72 (H_{3e} and H_{3a}: m), 1.20 (CH_3: d). Found: C, 63.25; H, 7.31; N, 8.29%. Calcd for $C_{17}H_{24}N_2O_4$: C, 63.73; H, 7.55; N, 8.74%.

N,N′-*Diacetylkasugamine (**25**).* A solution of **16β** (0.84 g, 2.62 mmol) in methanol–50% acetic acid (1: 1, 10 ml) was hydrogenolyzed in the presence of palladium–charcoal (5%, 0.5 g), filtered, and then the filtrate was evaporated to give a sirup which was crystallized from ethanol–hexane. Yield, 0.46 g (76%); mp 124—126 °C; $[\alpha]_D^{22}$ +65 ° (*c* 0.8, H_2O), [lit,[17] mp 123—125 °C; $[\alpha]_D^{20}$ +67 ° (*c* 1.0, H_2O)]. Found: C, 52.52; H, 8.02; N, 11.95%. Calcd for $C_{10}H_{18}N_2O_4$: C, 52.16; H, 7.88; N, 12.17%.

The same compound was also obtained from **16α** by hydrogenolysis in 80% yield.

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