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THE SYNTHESIS OF METHYL N,N'-DIACETYL-α-d-KASUGAMINIDE

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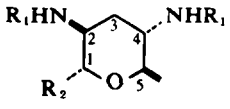
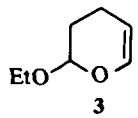
Abstract—The synthesis of methyl N,N'-diacetyl-α-d-kasugaminide (**24**) has been described. **3** was converted through hydroboration-amination to ethyl 4-acetamido-2, 3, 4, 6-tetradeoxy-α, β-dl-glucopyranosides (ethyl N-acetyl-αβ-dl-tolyposaminide) (**7** and **8**). Bromination of **7** and **8** gave the 2-bromo compounds (**17**, **18** and **19**). Displacement of Br of **17** with N_3 and subsequent hydrogenation and resolution furnished d-kasugaminide. Synthesis of ethyl α-dl-forosaminide has also been described.

Kasugamine (**1**) is the diamino sugar moiety of kasugamycin,[1] an antibiotic produced by *streptomyces kasugaensis* and a strong antagonist against *piricularia oryzae.* In this paper we describe in detail the synthesis, which has been reported in preliminary forms[2,3] of methyl N,N'-diacetyl-α-d-kasugaminide (**24**).

The preparation of methyl N,N'diacetyl-α-d-kasugaminide (**24**), with due consideration for the possibility to extend as the general synthetic method of hexoses from antibiotics, started from 2-ethoxy-6-methyl-3,4-dihydro-2H-pyran (**3**).[4]



1: R_1=H, R_2=OH
2: R_1=Ac, R_2=OMe



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In order to introduce at C-4 position the equatorial NH_2 group which is in *trans* disposition to Me group, the compound (**3**) was at first hydroborated[5] in dry THF to give an adduct (**4**). Subsequent treatment of the adduct with chloramine[6] in ether afforded an amine (**5**) and an alkyl boric acid (**6**). The amine was isolated as epimeric acetyl derivatives (**7**, m.p. 104–105° and **8**, m.p. 160–161°) in 12% yield from **3**, while the major product boric acid (**6**) was oxidized with H_2O_2 in alkaline soln to produce in good yield an alcohol (**9**), which afforded a low melting crystalline acetate (**10**), m.p. 52–53°, by acetylation with acetic anhydride in dry pyridine.

The Me/NH_2 trans stereochemistry of the amine (**5**) was ascertained by the half band width (21 Hz) of the NMR signal due to the C-4 proton of the acetyl derivatives.‡ The formation of **5** means the synthesis of ethyl α,β-dl-tolyposaminide,[7] a hydrolysis product of antibiotic tolypomycin, in three steps. Dimethylation of the amine (**5**) by Eschweilar-Clarke modification[8] gave ethyl α-dl-forosaminide (**11**),[9] obtainable from antibiotic spiramycin. The route through the compound (**3**) presents a simple and useful method for the stereospecific synthesis of rare deoxyamino sugars from readily available chemicals.

However, since the maximum theoretical yield of **5** from **3** is 100/3%, we next studied practical route from **3** to **5**. Of the various schemes considered two approaches below by equations (1, 2) were examined. The first plan involved iodination of the mesylate (**12**) from the alcohol (**9**), with inversion of configuration, and subsequent azidation, again with inversion. Reaction of the alcohol (**9**) with mesyl chloride in dry pyridine at room temp gave smoothly the mesylate (**12**). However, the compound (**12**) was revealed unexpectedly to be unreactive toward sodium iodide in dry DMF, and the starting material was recovered unchanged. By contrast, treatment of the mesylate (**12**) with sodium azide in dry DMF yielded an azide (**13**), and with sodium acetate in DMSO afforded an acetate (**14**).[9] The iodide ion may not approach so easily to the reaction center owing to the repulsion between the lone pair of iodide ion and that of O atom on the ring as shown **i**, while acetate and azide anions with delocalized negative charge may approach easily, since the repulsion would be small in these cases. Since in the azide (**13**) the configuration at C-4 was opposite (W_H of C-4 proton 9 Hz) for our purpose, the route through the mesylate (**12**) was abandoned.

The second route involved stereospecific reduction of an oxime group to equatorial NH_2 group. Oxidation of the alcohol (**9**) with chromium trioxide in dry pyridine at 85–90° afforded a ketone (**15**). Subsequently the ketone (**15**) was transformed by treatment with hydroxylamine hydrochloride in alkaline soln into an oxime (**16**) (89·0%). The oxime

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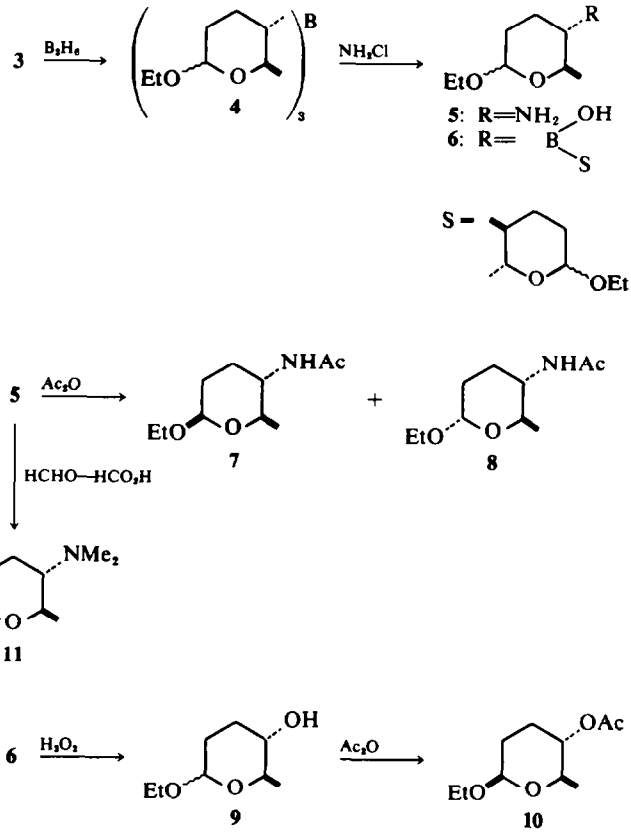
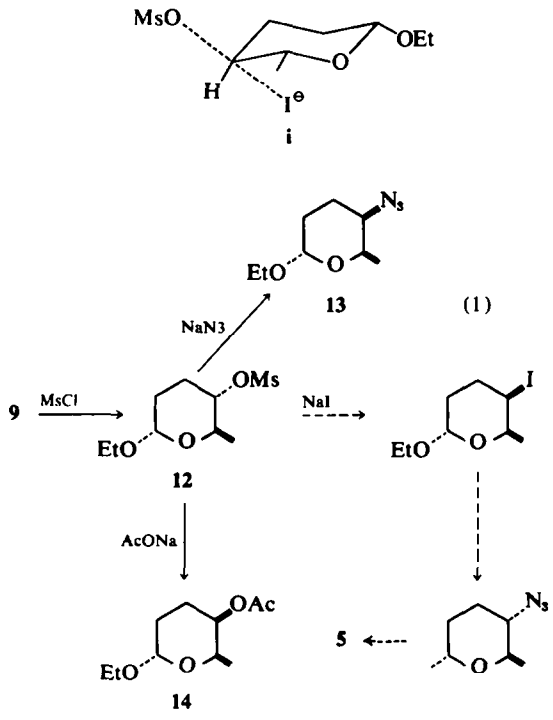
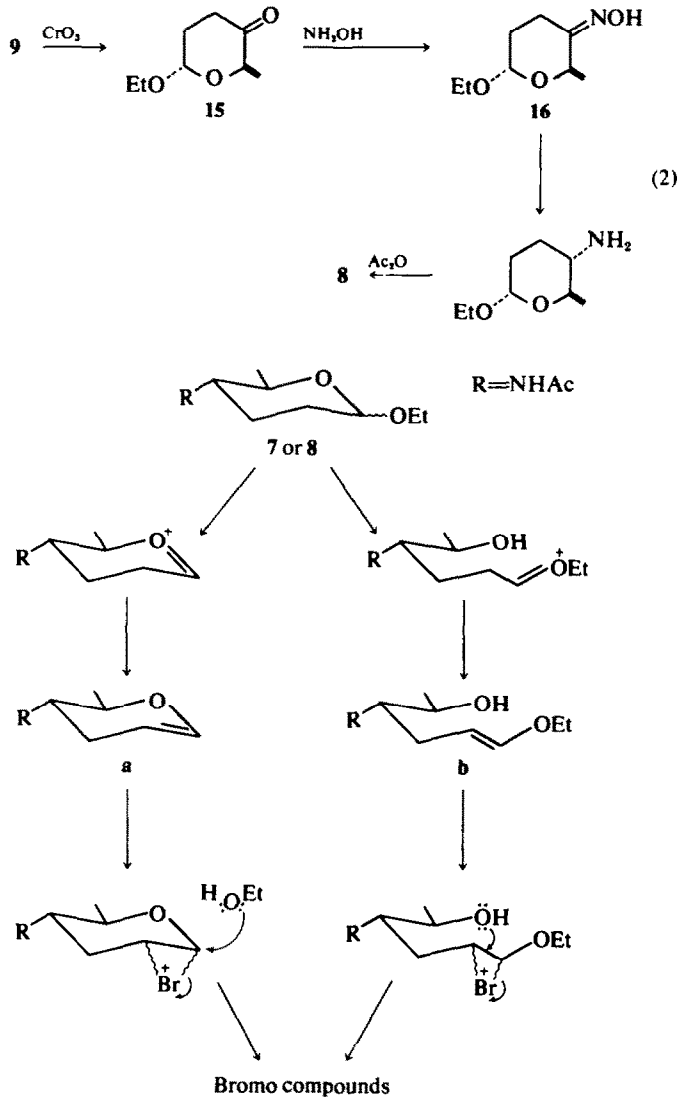
‡The configuration was confirmed at later stage by leading **5** to the kasugaminide (**23**).





(16) was then reduced with methallic sodium[10] in dry ethanol and subsequent treatment with acetic anhydride in pyridine afforded the acetyl compound, completely identical with **8** in m.p., TLC, IR and NMR spectra. Our next effort was to introduce Br atom at C-2 position. On treatment[11] with bromine in dry ethanol containing hydrogen chloride at 65-70° for 3 days, the acetamide (**7** or **8**) gave three bromo compounds (**17**), (**18**) and (**19**) in 19·8, 17·3 and 29·8% respectively, which were separated by column chromatography on silica gel using 20% hexane-chloroform as eluent. The reaction would probably proceed via vinyl ether **a** or **b**. The stereochemistry of these bromo compounds were made clear by chemical methods and NMR spectra. The doublet, which appeared at τ 5·62 with J = 9·0 Hz in the NMR spectrum of **17**, is attributed to the signal of the anomeric proton coupled with C-2 proton and indicates diequatorial disposition of Br and OEt. Treatment of either **17** or **18** with a saturated ethanolic soln of hydrogen chloride afforded an equilibrated mixture of **17** and **18** in a ratio of about 4:3. Therefore, **18** is the anomer (ax OEt and eq Br) of **17**. On the other hand, the diaxial configuration of Br and OEt in **19** is suggested by the J value of 1·5 Hz[12] of the doublet due to the anomeric proton at τ 5·15. As expected, reaction of **19** with

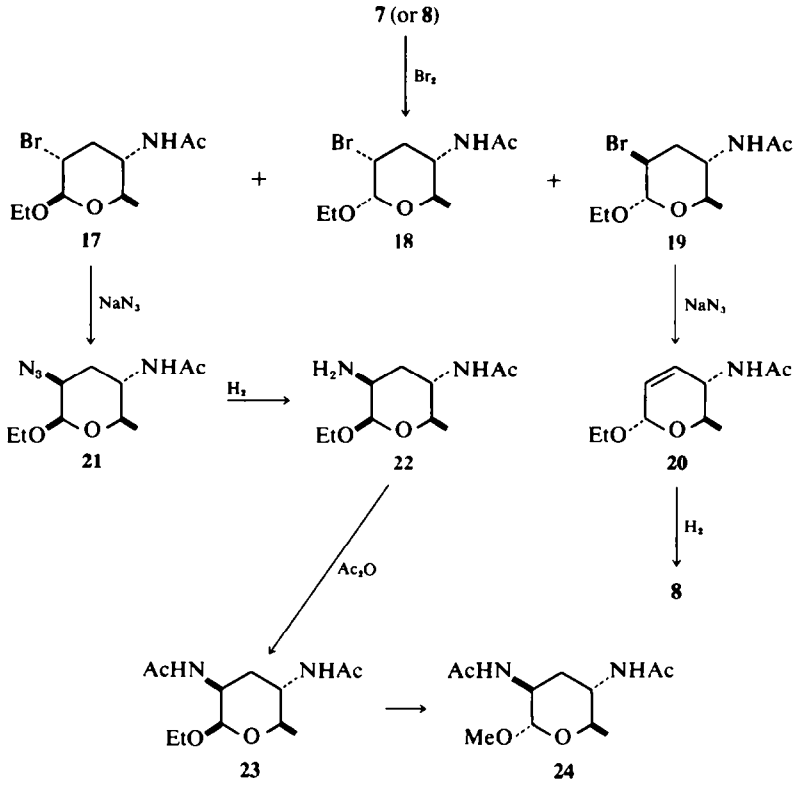


sodium bromide in dry HMPA at 95–100° for several days gave an equilibrium mixture of **18** (eq Br) and **19** (ax Br) in a ratio of 2:3. Thus both the isomer (**18** and **19**) can be converted to **17** (eq Br).

Treatment of **19** with sodium azide in DMF at 120° gave unexpectedly an unsaturated compound (**20**), although azide ion is known as a good nucleophile. The compound (**20**) could be reconverted into the original acetamide (**8**) by hydrogenation with hydrogen over platinum dioxide in EtOH at room temp in good yield. Ready elimination of HBr from **19** is in good agreement with the axial disposition of Br of **19**, deduced from the NMR spectrum.

On the other hand, on treatment with sodium azide in DMSO, equatorial bromo compound (**17**) yielded the azide (**21**, m.p. 180–180·5°, 67·6% yield) (W_H of C-2 proton 8 Hz), with the inversion of configuration at the reaction center, in 67% yield in contrast to the axial bromo epimer. Catalytic hydrogenation of **21** by hydrogen over platinum dioxide in EtOH produced an amine (**22**), which was transformed readily into a diacetyl derivative (**23**) by treatment with acetic anhydride in dry pyridine in 72% yield from **21**. In TLC, IR and NMR spectra, the diacetyl derivative (**23**) was completely identical with the authentic optical active sample, derived from kasugamycin.

Optical resolution[13] of the amine (**22**) was carried out through the salt of **22** with D-(−)-tartaric acid. The sparingly soluble salt was repeatedly recrystallized from a mixed solvent of MeOH and acetone and regenerated to the amine (**22**) with 2N NaOH soln at 50° for 2 hr. Treatment of the resolved amine with acetic anhydride in dry pyridine gave the optical active ethyl N,N'-diacetyl-β-d-kasugaminide (**23**), which was identical in α_D with the one derived



from antibiotic kasugamycin, in 32% yield from **21**. The optical active (**23**) was then converted into methyl α-d-glycoside (**24**, m.p. 193·5–195°, 57% yield) in MeOH containing hydrogen chloride.

The synthesis of d-**24** means the total synthesis of kasugamycin, since d-**24** had been already condensed with a d-inositol derivative to give kasuganobiosamine,[3] which in turn had been converted to kasugamycin.[1d]

Since the intermediate (**7** or **8**) can be readily obtained by hydroboration-amination as described above, the synthesis provides a simple route to synthetic kasugamycin.

EXPERIMENTAL

M.ps and b.ps were uncorrected. Specific rotations were determined in MeOH at room temp. IR spectra were recorded on a JASCO IR-S spectrophotometer. NMR spectra were obtained on a Jeol 3H-60 instrument. $CDCl_3$ was employed as the solvent with TMS as the internal reference unless otherwise indicated. The homogeneity of each compound was always checked by TLC on silica gel (Wako gel B-5) and the spots were developed with sulfuric acid indicator.

Hydroboration of 2-ethoxy-6-methyl-3,4-dihydro-2H-pyran (**3**).

To a soln of 0·811 mole diborane in 25 ml dry THF was added dropwise 15·0 g (0·106 mole) of **3**[4] in 5 ml dry THF at 0°. The soln was allowed to stand at room temp for 1 hr and then water was added dropwise to destroy excess diborane. The resulting **4** (15·5 g) was used in subsequent experiment without further purification.

Ethyl 4-amino-2,3,4,6-tetradeoxy-α,β-dl-glucopyranoside (**5**) *and ethyl 2,3,6-trideoxy-α,β-dl-glucopyranoside* (**9**). The hydroboration product (15·5 g) was dissolved in 54 ml 4N NaOH and mixed with chloramine,[14] which was prepared by treating 10% NaOCl (244 ml) with dil aqueous ammonia (21 ml) at 30°, and taken up in 100 ml of ether at 0°. The mixture was stirred at room temp for 1 hr and then acidified with 120 ml 4N HCl. The non-basic products were extracted with ether and evaporation of the solvent yielded 14·8 g of crude alkyl boric acid (**6**). To a soln of 14·8 g of **6** in 20 ml THF at 0° was added dropwise 36 ml 3N NaOH and 30 ml of 28% H_2O_2. After stirring at room temp for 1 hr, the soln was neutralized with dil HClaq and the product was extracted with AcOEt. The organic layer was washed with water, dried over Na_2SO_4 and evaporated *in vacuo*. The residue was purified by chromatography on silica gel. Elution with $CHCl_3$ containing 5% hexane gave 9·2 g (54·4%, from **3**) of **9**, ν_{max}^{neat} 3345, 1060 cm^{-1}; τ 8·81 (3H, d, J = 6·0 Hz), 8·76 (3H, d, J = 7·0 Hz), 7·26 (1H, s), 5·35 (1H, t, J = 1·5 Hz).

The above acidic aqueous soln containing basic products was added 20 g NaOH. The resulting alkaline soln was extracted with AcOEt. The AcOEt extract was dried over Na_2SO_4 and evaporation under reduced pressure left 6·5 g of the crude amine (**5**), ν_{max}^{neat} 3320, 1665 cm^{-1}.

Acetylation of ethyl 2,3,6-trideoxy-α,β-dl-glucopyranoside (**9**). A 681 mg sample of the alcohol (**9**) was dissolved in 1·1 ml of dry pyridine, and 1·1 g of Ac_2O was added. The soln was allowed to stand overnight at room temp. The mixture was then poured into water and the

product was extracted with AcOEt. The organic layer was washed successively with 1N HCl and 1N NaOH to remove pyridine and Ac_2O respectively, dried over Na_2SO_4 and evaporated *in vacuo*. The solid residue was recrystallized from AcOEt–hexane to afford 749 mg (87·1%) of an acetate (**10**), ν_{max}^{nujol} 1740, 1240 cm^{-1}; τ 8·75 (3H, d, J = 6·0 Hz), 8·73 (3H, t, J = 7·0 Hz), 7·90 (3H, s), 5·50 (1H, q, J = 9·0 + 3·0 Hz).

An analytical sample, m.p. 52-53°, was secured after an additional recrystallization. (Found: C, 59·32; H, 8·72. $C_8H_{16}O_3$ requires; C, 59·38; H, 8·97).

Ethyl 4-acetamido-2,3,4,6-tetradeoxy-α,β-dl-glucopyranosides (**7** *and* **8**). A 6·5 g sample of **5** was mixed with Ac_2O and pyridine in usual manner, and the soln was kept overnight at room temp. Evaporation *in vacuo* of Ac_2O and pyridine yielded a residue, which was chromatographed on silica gel. Elution was carried out with hexane containing 30% AcOEt to give **7** (minor product, less than 1%) at first and 2·5 g (11·8% from **3**) of its anomer (**8**) in the second place. Recrystallization of **7** from hexane–AcOEt gave white crystals, m.p. 104–105°, ν_{max}^{nujol} 3220, 1640, 1560 cm^{-1}; τ 8·80 (3H, d, J = 6·0 Hz), 8·77 (3H, t, J = 7·0 Hz), 7·98 (3H, s), 5·21 (1H, t, J = 1·5 Hz), 4·51 (1H, br s). (Found: C, 59·61; H, 9·57; N, 6·77. $C_{10}H_{19}O_3N$ requires: C, 59·67; H, 9·52; N, 6·96%).

A sample of **8** was purified for analysis by recrystallization from hexane–AcOEt. It had m.p. 160–161°, ν_{max}^{nujol} 3270, 1640, 1565 cm^{-1}; τ 8·73 (3H, t, J = 6·8 Hz), 8·70 (3H, d, J = 6·0 Hz), 7·93 (3H, s), 5·52 (1H, q, J = 9·0 + 3·5 Hz), 4·25 (1H, br s). (Found: C, 59·68; H, 9·62; N, 6·81. $C_{10}H_{19}O_3N$ requires: C, 59·67; H, 9·52; N, 6·96%).

Ethyl α-dl-forosaminide (**11**). A soln of 500 mg of the crude **5** in 15 ml formic acid and 12 ml of 30% formaline was refluxed for 17 hr. The cooled mixture was neutralized with dil HClaq and then product was extracted with AcOEt. The AcOEt phase was washed with water and dried over Na_2SO_4. The residue after evaporation of the solvent was chromatographed on silica gel. Elution with AcOEt–$CHCl_3$ (20:80) gave 52 mg (3·4% from **3**) of **11**; τ 8·77 (3H, t, J = 7·5 Hz), 8·65 (3H, d, J = 6·0 Hz), 7·71 (3H, s), 7·69 (3H, s), 5·29 (1H, t, J = 3·0 Hz).

An analytical sample was obtained after additional chromatography on silica gel. (Found: C, 64·01; H, 11·21; N, 7·36. $C_{10}H_{21}O_2N$ requires: C, 64·13; H, 11·30; N, 7·48%).

Mesylation of ethyl 2,3,6-trideoxy-α,β-dl-glucopyranoside (**9**). A soln of 1·02 g of **9** and 1·6 g methanesulfonyl chloride in 20 ml dry pyridine was stirred for 20 hr at room temp. Most of pyridine was removed *in vacuo*, the brown residue was dissolved in ether and the soln was washed successively with dil HClaq and with water, and dried over Na_2SO_4. Evaporation of the solvent gave a yellow oil, which was separated by chromatography on silica gel. Elution of the column with a mixed solvent of $CHCl_3$ and benzene gave 1·32 g (87·0%) of **12**, ν_{max}^{neat} 1165 cm^{-1}; τ 8·70 (3H, t, J = 7·5 Hz), 8·69 (3H, d, J = 6·0 Hz), 6·94 (3H, s), 5·27 (1H, t, J = 1·3 Hz).

Reaction of ethyl 4-O-methanesulfonyl-2,3,6-trideoxy-α-dl-glucopyranoside (**12**) *with sodium iodide.* To a soln of 101 mg of **12** in 3 ml dry DMF (or dry acetone) was added 200 mg NaI. The mixture was allowed to reflux for 22 hr. It was then diluted with water, extracted with AcOEt. The extract was washed with water and dried over Na_2SO_4. Removal of the solvent afforded the starting material unchanged quantitatively.

Ethyl 4-azido-2,3,4,6-tetradeoxy-α-dl-glucopyranoside (**13**). A 141 mg sample of **12** in 2 ml dry DMF was refluxed for 14 hr with 142 mg sodium azide. After cooling, the soln was diluted with water and extracted with AcOEt. The extract was washed successively with water and a saturated NaCl soln, and evaporated to leave a residue, which was distilled to give a colorless oil, ν_{max}^{neat} 2110, 1270 cm^{-1}; τ 8·84 (3H, t, J = 7·5 Hz), 8·82 (3H, d, J = 6·0 Hz), 5·21 (1H, t, J = 1·6 Hz).

An analytical sample, b.p. 74–75°/1·0 mm, was prepared by further distillation. (Found: C, 51·78; H, 8·13; N, 22·46. $C_8N_{15}O_3N_3$ requires: C, 51·87; H, 8·16; N, 22·69%).

Oxidation of ethyl 2,3,6-trideoxy-α,β-dl-glucopyranoside (**9**). A soln of 5·14 g of **9** in 15 ml dry pyridine was added with stirring into CrO_3-pyridine complex prepared by the portionwise addition of 7·4 g CrO_3 to 120 ml dry pyridine at 0°. The stirred soln was allowed to attain room temp during 1 hr and subsequently maintained at 80–85° for further 5 hr. The black soln was filtered. The filtrate was diluted with water and then extracted with AcOEt. The extract was washed with dil HClaq and NaClaq. Concentration of the soln dried over Na_2SO_4 gave an oil, which was chromatographed on silica gel with $CHCl_3$ to give 2·82 g (55·6%) of **15**, ν_{max}^{neat} 1730, 1415 cm^{-1}; τ 8·76 (3H, d, J = 6·0 Hz), 8·73 (3H, t, J = 7·0 Hz), 5·83 (1H, q, 6·0 Hz), 5·11 (1H, t, J = 3·5 Hz).

The semicarbazone of **15** was prepared by treating 112 mg of **15** in 2 ml EtOH with 200 mg semicarbazide hydrochloride in 2 ml 2N NaOH at 70–75° for 30 min. After cooling, the product was collected on a filter. Recrystallization from water containing a small amount of MeOH gave 126 mg (75·0%) of semicarbazone. One more recrystallization gave an analytical sample, m.p. 173·5–175°, ν_{max}^{neat} 3430, 2980, 1703 cm^{-1}. (Found: C, 50·45; H, 8·08; N, 19·51. $C_9H_{17}O_3N_3$ requires: C, 50·22; H, 7·96; N, 19·53%).

Ethyl 4-oximino-2,3,4,6-tetradeoxy-α-dl-glucopyranoside (**16**). A mixture of 0·864 g of **15** in 36 ml EtOH and 1·20 g hydroxylamine hydrochloride in 7 ml of 14·7% NaOH was refluxed for 4 hr. Most of EtOH was removed *in vacuo*, the residue was extracted with benzene and the organic layer was washed successively with dil HClaq and with water, and dried over Na_2SO_4. Evaporation of the solvent yielded a colorless oil, which still contained the starting material. Chromatography of the oil on silica gel with AcOEt–hexane (1:5) gave 0·842 g (89·0%) of **16** as an oil, ν_{max}^{neat} 3420, 1660 cm^{-1}.

Reduction of ethyl 4-oximino-2,3,4,6-tetradeoxy-α-dl-glucopyranoside (**16**). To a soln of 0·842 g of **16** in 15 ml dry EtOH, which was heated at 60–65°, was added dropwise 0·700 g metallic Na within 5 min. Heating was continued until Na disappeared. After cooling, the soln was neutralized with 4N HCl and extracted with AcOEt. Concentration of the extract dried over Na_2SO_4 *in vacuo* gave 0·240 g of a crude amine.

Treatment of 0·240 g of the amine with Ac_2O in pyridine in usual manner gave 0·224 g (48·5%, three step yield from **15**) of N-acetyl compound, which was identical with **8** as judged by m.p., TLC, IR and NMR spectra.

Bromination of ethyl 4-acetamido-2,3,4,6-tetradeoxy-β-dl-glucopyranoside (**7**) *and its anomer* (**8**). A soln of 8·65 g of **7** in 25 ml dry EtOH saturated with HCl and a soln of 13·0 g of Br_2 in 50 ml dry EtOH was mixed and the mixture was heated for 3 days at 65–70°. The mixture was neutralized with 4N NaOH and most of EtOH was removed *in vacuo*. The aqueous phase was extracted with AcOEt. The AcOEt extract was washed with sat NaClaq and dried over Na_2SO_4. Evaporation of the solvent afforded a yellow oil, which was chromatographed on silica gel. Elution with AcOEt–$CHCl_3$ (20:80) gave three

bromo compounds as white crystals. The first fraction was recrystallized from a mixed solvent of hexane and AcOEt to give 2·388 g (19·8%) of **17**, m.p. 152·5–154°, ν_{max}^{nujol} 3240, 1645, 1545 cm^{-1}; τ 8·76 (3H, d, J = 6·0 Hz), 8·74 (3H, t, J = 7·5 Hz), 8·02 (3H, s), 5·62 (1H, d, J = 9·0 Hz), 3·9 (1H, br s). (Found: C, 42·87; H, 6·77; N, 5·24; Br, 28·37. $C_{10}H_{18}O_3NBr$ requires: C, 42·87; H, 6·48; N, 5·00; Br, 28·57%). The second fraction was recrystallized from hexane–AcOEt to yield 2·084 g (17·3%) of **18**, m.p. 139–139·5°, ν_{max}^{nujol} 3180, 1645 cm^{-1}; τ 8·85 (3H, d, J = 6·0 Hz), 8·76 (3H, t, J = 7·0 Hz), 8·02 (3H, s), 5·27 (1H, d, J = 3·0 Hz), 4·30 (1H, br s). (Found: C, 42·97; H, 6·45; N, 4·74; Br, 28·76. $C_{10}H_{18}O_3NBr$ requires: C, 42·87; H, 6·48; N, 5·00; Br, 28·57%). The third fraction was also recrystallized from a mixed solvent of hexane and AcOEt to furnish 3·545 g (29·5%) of **19**, m.p. 138·5–139°, ν_{max}^{nujol} 3240, 1640, 1550 cm^{-1}; τ 8·75 (3H, t, J = 7·5 Hz), 8·72 (3H, d, J = 6·0 Hz), 7·95 (3H, s), 5·15 (1H, d, J = 1·5 Hz), 3·80 (1H, br s). (Found: C, 42·87; H, 6·45; N, 5·20; Br, 28·79. $C_{10}H_{18}O_3NBr$ requires: C, 42·87; H, 6·48; N, 5·00; Br, 28·57%).

Treatment of **8** with Br_2 in EtOH containing HCl as the above method described afforded a similar result.

Anomerization of ethyl 2-*bromo*-4-*acetamido*-2,3,4,6-*tetradeoxy*-β-dl-*glucopyranoside* (**17**) *and its anomer* (**18**). A soln of 32 mg of **17** in 5 ml dry EtOH saturated with HCl was heated at 65–70° for 3 days. The mixture was neutralized with 4N NaOH and most of EtOH was removed at reduced press. The aqueous layer was extracted with AcOEt and the extract was washed with water. Removal of the solvent dried over Na_2SO_4 *in vacuo* gave an oil, which was subsequently treated with Ac_2O in pyridine in the usual method. The resulting mixture was separated by chromatography on silica gel using a mixed solvent of hexane and AcOEt as eluent to give 14 mg (43·8%) of the starting material (**17**) and 11 mg (34·3%) of its anomer (**18**) which was identified by m.p., TLC, IR and NMR spectra.

According to the above procedure, treatment of 94 mg of **18** with ethanolic HCl followed by reaction with Ac_2O in pyridine gave 34 mg (36·2%) of the starting material (**18**) and 44 mg (45·7%) of **17**.

Reaction of ethyl 2-*bromo*-4-*acetamido*-2,3,4,6-*tetradeoxy*-α-dl-*mannopyranoside* (**19**) *with sodium bromide.* A mixture of 61 mg of **19** in 5 ml dry HMPA and 70 mg NaBr, which was dried by heating at 150° for 5 hr, was heated at 95–100° for 6 days. After cooling, the soln was diluted with water and extracted with AcOEt. The extract was washed with water. The soln was dried over Na_2SO_4 and the solvent was removed *in vacuo* yielding white crystals, which were chromatographed on silica gel. Elution with hexane–AcOEt (30:70) gave 31 mg (50·8%) of the starting material (**19**) and 23 mg (37·7%) of **18**, which was identical with an authentic sample as judged by m.p., IR and NMR spectra.

Ethyl 4-*acetamido*-2,3-*dehydro*-2,3,4,6-*tetradeoxy*-α-dl-*glucopyranoside* (**20**). To a soln of 2·11 g of **19** in 60 ml dry DMF, 5 g sodium azide was added. After being kept at 120–130° for 12 hr the soln was diluted with water and the products were extracted with AcOEt. The AcOEt layer was washed successively with water and sat NaClaq and dried. Removal of the solvent *in vacuo* gave white crystals. Recrystallization from hexane-AcOEt afforded 1·103 g (73·4%) of **20**, m.p. 136·5–137·5°, ν_{max}^{nujol} 3190, 1645, 1540 cm^{-1}; τ 8·78 (3H, t, J = 7·0 Hz), 8·75 (3H, d, J = 6·0 Hz), 8·00 (3H, s), 5·06 (1H, s), 4·26 (2H, s), 4·25 (1H, br s). (Found: C, 60·35; H, 8·60; N, 7·01. $C_{10}H_{17}O_3N$ requires: C, 60·28; H, 8·60; N, 7·03%).

Reduction of ethyl 4-*acetamido*-2,3-*dehydro*-2,3,4,6-*tetradeoxy*-α-dl-*glucopyranoside* (**20**). A 22 mg sample of the unsaturated **20** in 20 ml EtOH was hydrogenated over Adams platinum dioxide (5 mg) under atmospheric press for 4 hr at room temp. The catalyst was filtrated and the solvent was removed to give white crystals, which were recrystallized from hexane-AcOEt to afford 19 mg (86·4%) of **8**. The identity was proved by m.p., TLC, IR and NMR spectra.

Ethyl 2-*azido*-4-*acetamido*-2,3,4,6-*tetradeoxy*-β-dl-*mannopyranoside* (**21**). To a soln of 1·53 g of **17** in 200 ml DMSO, 4·1 g sodium azide was added and the mixture was heated for 24 hr at 100–105°. The soln was diluted with water and extracted with AcOEt. The extract was washed with water, a sat NaClaq and dried over Na_2SO_4. Concentration of the soln gave 0·893 g (67·6%) of **21**, ν_{max}^{nujol} 3300, 2140, 1640, 1560 cm^{-1}; τ 8·74 (3H, t, J = 6·5 Hz), 8·68 (3H, d, J = 6·0 Hz), 8·02 (3H, s), 5·40 (1H, d, J = 2·0 Hz), 3·75 (1H, br s).

An analytical sample, m.p. 180–180·5°, was obtained after two recrystallization from hexane-AcOEt. (Found: C, 49·48; H, 7·45; N, 23·03. $C_{10}H_{18}O_3N_4$ requires: C, 49·57; H, 7·49; N, 23·13%).

Recuction of ethyl 2-*azido*-4-*acetamido*-2,3,4,6-*tetradeoxy*-β-dl-*mannopyranoside* (**22**). A 47 mg sample of **21** in 20 ml EtOH was hydrogenated over 25 mg of Adams platinum dioxide under atmospheric press for 3 hr at room temp. The catalyst and the solvent were removed to give an oil, which was treated with Ac_2O in pyridine in usual manner to afford white crystals. Recrystallization from hexane-$CHCl_3$ gave 36 mg (71·9% from **21**) of **23**, ν_{max}^{neat} 3260, 1650, 1550 ccm^{-1}; τ 8·79 (3H, t, J = 6·5 Hz), 8·71 (3H, d, J = 6·0 Hz), 8·02 (3H, s), 7·98 (3H, s), 5·45 (1H, d, J = 2·0 Hz), 3·80 (2H, br s).

An analytical sample, m.p. 171–172·5°, was secured by recrystallixation. (Found: C, 55·67; H, 8·43; N, 10·81. $C_{12}H_{22}O_4N_2$ requires: C, 55·79; H, 8·58; N, 10·85%).

The IR and NMR spectra of dl-**23** was completely identical with those of d-**23**, which was prepared from kasugamycin as described below.

Ethyl N,N′-*diacetyl*-α-d-*kasugaminide* (**23**). A 10 g sample of N,N′-diacetyl-α-d-kasuganobiosamine[24] was dissolved in 30 ml of dry EtOH saturated with HCl. The soln was heated under reflux for 16 hr. After cooling, the soln was neutralized with 3N NaOH and extracted with AcOEt. The extract was washed with water, dried over $MgSO_4$ and concentrated *in vacuo* to give an oil, which was employed for the next step without further purification.

The resulting oil was treated with Ac_2O in pyridine at room temp in usual manner to give crude ethyl N,N′-diacetyl-β-d-kasugaminide, which was purified by chromatography on silica gel using AcOEt containing 5% EtOH as eluent to yield 43 mg of an oil (**23**), ν_{max}^{neat} 3260, 1650, 1550 cm^{-1}; τ 8·79 (3H, t, J = 6·5 Hz), 8·71 (3H, d, J = 6·0 Hz), 8·02 (3H, s), 7·98 (3H, s), 5·45 (1H, d, J = 2·0 Hz), 3·80 (2H, br s). After 3 days, the oil became white crystals. Recrystallization from AcOEt gave an analytical sample, m.p. 227·5–229°, $[\alpha]_D^{21}$ +171° (c, 1·0 in MeOH).

Resolution of the amine (**22**). To a soln of **22**, which was prepared from 314 mg of **21** as described above, in 5 ml dry MeOH was added 196 mg of D-(−)-tartaric acid in 4 ml dry MeOH. The soln was allowed to stand for 18 hr at room temp and MeOH was then removed *in vacuo* at room temp. The resulting salt was washed with acetone and eight recrystallization from a mixed solvent of MeOH and acetone gave 197 mg of a salt. The salt was dissolved

in 100 ml 2N NaOH and the free base was extracted with AcOEt. The organic layer was washed with sat NaClaq, dried over Na_2SO_4 and concentrated *in vacuo* to give 64 mg of crude optically active **22**. Subsequent treatment of 64 mg of **22** with Ac_2O in pyridine afforded 54 mg (32·3% from **21**) of d-**23** as white crystals. Recrystallization from AcOEt gave an analytical sample, $[\alpha]_D^{20}$ +168° (*c*, 1·0 in MeOH). (Found: C, 55·62; H, 8·41; N, 10·72. $C_{12}H_{22}O_4N_2$ requires: C, 55·79; H, 8·58; N, 10·85%).

The resolved material was confirmed to be identical with d-**23**, prepared from kasugamycin, in all respects including NMR, IR and mixed m.p.

Methyl N,N'-*diacetyl*-α-d-*kasugaminide* (**24**). A soln of 22 mg of d-**23** in 5 ml dry MeOH saturated with HCl was refluxed for 19 hr. After cooling, the mixture was neutralized with 2N NaOH and extracted with AcOEt. The AcOEt layer was washed with water, dried over $MgSO_4$ and concentrated *in vacuo* to afford an oil, which was also treated with Ac_2O in pyridine yielding a solid. Chromatography on silica gel and eluting with AcOEt containing 10% EtOH gave 12 mg (57·0%) of d-**24**, ν_{max}^{nujol} 3280, 1645, 1540 cm^{-1}; τ 8·78 (3H, d, $J = 6·0$ Hz), 8·02 (3H, s), 7·98 (3H, s), 6·63 (3H, s), 5·55 (1H, d, $J = 1·0$ Hz), 4·30 (1H, br s), 3·80 (1H, br s).

An analytical sample, m.p. 193·5–195°, $[\alpha]_D^{22}$ +107° (*c*, 1·0 in MeOH), was prepared after recrystallization from AcOEt. (Found: C, 53·80; H, 8·21; N, 11·40. $C_{11}H_{22}O_4N_2$ requires: C, 54·08; H, 8·25; N, 11·47%).

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