crystallized spontaneously. Recrystallization from methanol–ether at −10° afforded an analytical sample (mp 85–86.5°): ir (CS_2) 3080, 1740, 1240, and 885 cm^{-1}; nmr ($CDCl_3$) δ 0.55, 0.95, and 1.77 (singlets, C_{18}, C_{19}, and C_{21} protons), 2.05 (singlet, acetoxy protons), 4.62 and 4.75 (two adjacent singlets, exocyclic methylene and 3β protons); $[\alpha]_D$ ($CHCl_3$) +41°.

Anal. Calcd for $C_{24}H_{38}O_2$: C, 80.39; H, 10.68; O, 8.92. Found: C, 80.56; H, 10.52; O, 8.75.

The above irradiation was repeated many times. The yields in *tert*-butyl alcohol ranged from 35 to 38% and in benzene from 33 to 35%.

Final confirmation was obtained by lithium aluminum hydride reduction of the acetoxy compound **17** followed by standard ozonolysis of the resulting alcohol **18**. Thus a sample of 3α-hydroxy-5β-pregnan-20-one (**19**) was obtained whose physical constants and spectra were identical with those of an authentic sample.[8]

Acknowledgment.—The participation of Dr. F. J. Kakis in this project was made possible through a grant by the Research Corporation. We are grateful for this assistance.

Registry No.—**1**, 2204-14-0; **2**, 42151-39-3; **3**, 42151-40-6; **4a**, 42151-41-7; **4b**, 42151-42-8; **5**, 42151-43-9; **7**, 145-13-1; **8**, 2415-36-3; **9**, 978-98-3; **10**, 18000-86-7; **11**, 42151-47-3; **12**, 4729-67-3; **13**, 1249-75-8; **14**, 42151-48-4; **15**, 4144-29-0; **16a**, 42151-50-8; **16b**, 42151-51-9; **17**, 42151-52-0.

Synthesis of 4-Amino-4,6-dideoxy-D-allose Derivatives[1,2]

CALVIN L. STEVENS,* K. K. BALASUBRAMANIAN, CHARLES P. BRYANT,[3] JEAN B. FILIPPI, AND P. MADHAVAN PILLAI

Department of Chemistry, Wayne State University, Detroit, Michigan 48202

Received June 1, 1973

Base-catalyzed isomerization of methyl 6-deoxy-2,3-*O*-isopropylidene-α-L-*lyxo*-hexopyranosid-4-ulose (**2**) gave methyl 6-deoxy-2,3-*O*-isopropylidene-β-D-*ribo*-hexopyranosid-4-ulose (**3**) by inversion at C-5. Conversion of **3** to its oxime **6** followed by reduction with lithium aluminum hydride yielded methyl 4-amino-4,6-dideoxy-2,3-*O*-isopropylidene-β-D-allopyranoside (**7**). Acetylation of **7** with acetic anhydride in pyridine followed by hydrolysis of the isopropylidene group gave methyl 4-acetamido-4,6-dideoxy-β-D-allopyranoside (**8**), which was then deacetylated to give methyl 4-amino-4,6-dideoxy-β-D-allopyranoside (**9**). Conversion of **7** to several derivatives including the free sugar, 4-*N*,*N*-dimethylamino-4,6-dideoxy-D-allose (**12**), is discussed. Also, synthesis of methyl 6-deoxy-2,3-*O*-isopropylidene-α-D-*ribo*-hexopyranosid-4-ulose (**18**) and its conversion into methyl 4-amino-4,6-dideoxy-α-D-allopyranoside (**32**) and the *N*-acetate **33** are reported. Compound **33** was also obtained from 4-acetamido-4,6-dideoxy-2,3-di-*O*-methanesulfonyl-α-D-glucopyranoside (**35**) by internal displacement of the sulfonate ester at C-3 by the neighboring *N*-acetate followed by desulfonylation with sodium naphthalene reagent. The D-erythro stereochemistry at C-4 and C-5 of both **8** and **33** was confirmed by their degradation to D-allothreoninol.

The occurrence of several 4-amino-4,6-dideoxy sugar derivatives in biologically important natural sources[4] prompted us to undertake a comprehensive investigation on the synthesis and chemistry of this new class of carbohydrates. So far, the syntheses of the derivatives of seven of a possible total of eight of these hexoses (D series) have been recorded.[1,5] We now report the isomerization of an L-hexos-4-ulose into a D-keto sugar by base-catalyzed inversion at C-5 and the conversion of the new ketone into 4-amino-4,6-dideoxy-D-allose derivatives. A derivative of this amino sugar was also obtained from a 4-amino-4,6-dideoxy-D-glucose derivative by the internal displacement of a sulfonate ester at C-3 by the neighboring *N*-acetyl group.

Methyl 6-deoxy-2,3-*O*-isopropylidene-α-L-*lyxo*-hexopyranosid-4-ulose[6,7] (**2**) was prepared from methyl 6-deoxy-2,3-*O*-isopropylidene-α-L-mannopyranoside[8] (**1**) by oxidation with either a mixture of dimethyl sulfoxide and phosphorus pentoxide in pyridine[1a] or with a catalytic amount of ruthenium tetroxide in the presence of sodium hypochlorite.[9,10] When a solution of **2** in 80% aqueous pyridine was heated at 100°, a small proportion of a new product was formed as shown by

(1) Synthesis and Chemistry of 4-Amino-4,6-dideoxy Sugars. V. (a) Part III: C. L. Stevens, R. P. Glinski, and K. G. Taylor, *J. Org. Chem.*, **33**, 1586 (1968). (b) Part IV: C. L. Stevens, R. P. Glinski, K. G. Taylor, P. Blumbergs, and S. K. Gupta, *J. Amer. Chem. Soc.*, **92**, 3160 (1970).

(2) Preliminary accounts of parts of this work have appeared. See (a) C. L. Stevens and K. K. Balasubramanian, *Carbohyd. Res.*, **21**, 166 (1972); (b) C. L. Stevens and K. K. Balasubramanian, Abstracts, 156th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 1968, CARB 20; (c) C. L. Stevens and C. P. Bryant in "Methods in Carbohydrate Chemistry," Vol. 6, R. N. Whistler and J. N. BeMiller, Ed., Academic Press, New York, N. Y., 1972, p 235; (d) C. L. Stevens and C. P. Bryant, *ibid.*, p 337; (e) C. L. Stevens, C. P. Bryant, J. B. Filippi, and B. Gross, Abstracts, 157th National Meeting of the American Chemical Society, Minneapolis, Minn., April 1969, CARB 7.

(3) Taken in part from the Ph.D. Dissertation of C. P. Bryant, Wayne State University, 1969.

(4) (a) C. L. Stevens, R. J. Gasser, T. K. Mukherjee, and T. H. Haskell, *J. Amer. Chem. Soc.*, **78**, 6212 (1956); (b) C. L. Stevens, K. Nagarajan, and T. H. Haskell, *J. Org. Chem.*, **27**, 2991 (1962); (c) C. L. Stevens, P. Blumbergs, and F. A. Daniher, *J. Amer. Chem. Soc.*, **85**, 1552 (1963); (d) R. W. Wheat, E. L. Rollins, and J. M. Leatherwood, *Biochem. Biophys. Res. Commun.*, **9**, 120 (1962); (e) C. L. Stevens, P. Blumbergs, F. A. Daniher, R. W. Wheat, A. Kiyomoto, and E. L. Rollins, *J. Amer. Chem. Soc.*, **85**, 3061 (1963); (f) C. L. Stevens, P. Blumbergs, D. H. Otterbach, J. L. Strominger, M. Matsuhashi, and D. N. Dietzler, *ibid.*, **86**, 2937 (1964); (g) C. L. Stevens, P. Blumbergs, F. A. Daniher, J. L. Strominger, M. Matsuhashi, and D. N. Dietzler, *ibid.*, **86**, 2939 (1964); (h) B. Jann and K. Jann, *Eur. J. Biochem.*, **2**, 26 (1967); (i) C. H. Lee and C. P. Schaffner, *Tetrahedron Lett.*, 5837 (1966); (j) C. L. Stevens, S. K. Gupta, R. P. Glinski, K. G. Taylor, P. Blumbergs, C. P. Schaffner, and C. H. Lee, *Carbohyd. Res.*, **7**, 502 (1968).

(5) (a) C. L. Stevens, P. Blumbergs, and D. H. Otterbach, *J. Org. Chem.*, **31**, 2817 (1966); (b) C. L. Stevens, P. Blumbergs, F. A. Daniher, D. H. Otterbach, and K. G. Taylor, *ibid.*, **31**, 2822 (1966); (c) C. L. Stevens, P. Blumbergs, J. P. Dickerson, and D. Chitharanjam, Abstracts, 149th National Meeting of the American Chemical Society, Detroit, Mich., April 1965, p 5C; (d) C. L. Stevens, J. P. Dickerson, and K. G. Taylor, Abstracts, 152nd National Meeting of the American Chemical Society, New York, N. Y., Sept 1966, p 17C; (e) J. S. Brimacombe, O. A. Ching, and M. Stacey, *Carbohyd. Res.*, **8**, 498 (1968); (f) J. Jary, P. Novak, Z. Ksandr, and Z. Samek, *Chem. Ind. (London)*, 1490 (1967); (g) J. Jary and P. Novak, *Collect. Czech. Chem. Commun.*, **33**, 1744 (1968); (h) S. W. Gunner, W. G. Overend, and N. R. Williams, *Carbohyd. Res.*, **4**, 498 (1967).

(6) P. M. Collins and W. G. Overend, *Chem. Ind. (London)*, 374 (1963); *J. Chem. Soc.*, 1912 (1965); P. M. Collins, *J. Chem. Soc. C*, 1960 (1971).

(7) U. M. Parikh and J. K. N. Jones, *Can. J. Chem.*, **43**, 3452 (1965).

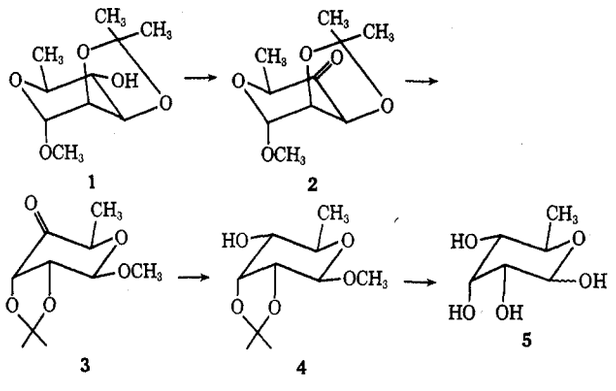
(8) P. A. Irvine and I. E. Muskat, *J. Biol. Chem.*, **105**, 431 (1934).

(9) M. B. Perry, National Research Council, Ottawa, Canada, personal communication, 1968.

(10) This method is similar to oxidation with ruthenium tetraoxide in the presence of sodium periodate. See, for example, (a) B. T. Lawton, W. A. Szarek, and J. K. N. Jones, *Carbohyd. Res.*, **10**, 456 (1969); (b) D. C. Baker, D. Horton, and C. G. Tindall, Jr., *ibid.*, **24**, 192 (1972).

gas chromatography. A detailed examination of this reaction indicated that equilibrium was reached after 2.5 hr and the mixture contained 82% of **2** and 18% of the new compound, subsequently shown to be methyl 6-deoxy-2,3-*O*-isopropylidene-β-D-*ribo*-hexopyranosid-4-ulose (**3**). Bases like triethylamine[11] and potassium hydroxide can also be used to effect this isomerization. When potassium hydroxide was used as the catalyst, ketone **3** was formed in higher proportions, but the recovery of the mixture of ketones was lower owing to the formation of undesirable side products.

Compound **3** was separated from **2** by preparative gas chromatography and was crystallized from pentane. An elemental analysis indicated **3** to be isomeric with **2**. The infrared spectrum had absorptions at 1730 (C=O) and 1375 cm^{-1} (*gem*-dimethyl) and nmr spectrum was consistent with structure **3**. The ORD curve of **3** exhibited a positive Cotton effect with a peak at 325 nm and a trough at 290 nm, whereas the starting ketone **2** had a negative Cotton effect with a trough at 330 nm and a peak at 290 nm. An investigation of the optical rotation of **3** showed that the rotation changed rapidly when **3** was dissolved in aqueous pyridine or methanol while the rotation remained constant in anhydrous pyridine and chloroform solutions. The change in rotation, however, was not due to isomerization but resulted from the addition of water or methanol to the carbonyl group, as ketone **3** was shown to remain unchanged by gas chromatography.[12]



Chemical proof for the structure of **3** was obtained as follows. Reduction of **3** with sodium borohydride in methanol gave methyl 6-deoxy-2,3-*O*-isopropylidene-β-D-allopyranoside[13] (**4**) as a colorless liquid in 90% yield. The crude reduction product consisted of at least 95% of one material as shown by gas chromatography. The stereoselectivity of this reaction is due to the attack by the hydride ion from the less hindered side of the carbonyl group and is in accordance with previous findings.[1a,10b] Hydrolysis of **4** with 1.0 *N* hot sulfuric acid gave 60% of 6-deoxy-D-allose[14] (**5**) identical with an authentic sample. The fact that an allose derivative was obtained by base-catalyzed isomerization indicates that inversion took place only at C-5. Although enolization at C-3 is also possible under the reaction conditions, the configuration at C-3 remained unchanged because a 2,3-cis stereochemistry is favored for the isopropylidene group as observed in similar isomerizations.[15]

As 4-keto sugars have been used for the synthesis of 4-amino hexoses,[1a,16] a valuable intermediate for the preparation of 4-amino-4,6-dideoxy-D-allose derivatives was found in compound **3**. Accordingly, treatment of **3** with hydroxylamine hydrochloride in a mixture of pyridine and ethanol at room temperature gave the oxime **6** as a mixture of isomers. The mixture was separated by preparative thin layer chromatography on silica gel to yield 62% of the major isomer as a crystalline material and 16% of the minor isomer as a gum. Reduction of **6** either as a pure isomer or as a mixture with lithium aluminum hydride in tetrahydrofuran at room temperature gave methyl 4-amino-4,6-dideoxy-β-D-allopyranoside (**7**) in 86% yield as a colorless liquid, isolated and characterized as the crystalline hydrogen *p*-toluenesulfonate. That it was possible to reduce each isomer separately to the same amine showed that the two oximes were in fact syn and anti isomers and not oximes of the isomeric ketones, **2** and **3**. The reduction product in each case, before any purification, was at least 95% of one material as shown by gas chromatography, indicating that the reduction of the oxime, as in the case of its ketone analog, **3**, proceeded by attack of the hydride ion almost exclusively from the less hindered side.[1a,10b]

Acetylation of **7** with acetic anhydride in pyridine followed by hydrolysis with 0.05 *N* hydrochloric acid gave methyl 4-acetamido-4,6-dideoxy-β-D-allopyranoside (**8**) in 52% yield. Degradation of this *N*-acetate **8** to D-allothreoninol by a previously described method[1b,17] confirmed the D-erythro stereochemistry at C-4 and C-5 as required for a D-allose derivative. Methyl 4-amino-4,6-dideoxy-β-D-allopyranoside (**9**) was obtained in 56% yield by the hydrolysis of **8** with a 9% solution of barium hydroxide in water under refluxing conditions. Hydrogenation of the amine **7** with formaldehyde in methanol in the presence of palladium on carbon as a catalyst gave methyl 4-*N*,*N*-dimethylamino-4,6-dideoxy-2,3-*O*-isopropylidene-β-D-allopyranoside (**10**), characterized as its hydrochloride. Removal of the isopropylidene group was accomplished by heating **10** with 0.1 *N* hydrochloric acid at 95° for 6 hr. Methyl 4-*N*,*N*-dimethylamino-4,6-dideoxy-β-D-allopyranoside (**11**) thus obtained was characterized as its hydrogen *p*-toluenesulfonate. Hydrolysis of **11** with 1.0 *N* hydrochloric acid under refluxing conditions for 24 hr provided the free sugar, 4-*N*,*N*-dimethylamino-4,6-dideoxy-D-allose (**12**), isolated and characterized as its crystalline hydrochloride salt.

The *N*-methyl derivative of **7** was prepared by two methods. Treatment of **7** with ethyl chloroformate in a mixture of pyridine and chloroform gave the *N*-carbethoxy derivative as an oil, which on reduction with lithium aluminum hydride in tetrahydrofuran yielded methyl 4-*N*-methylamino-4,6-dideoxy-2,3-*O*-

(11) P. M. Collins and P. Gupta, *J. Chem. Soc. C*, 1695 (1971), obtained a 3:1 mixture of **2** and **3** by treatment of **2** with triethylamine in aqueous ethanol.

(12) Certain keto sugar derivatives are known to form stable hydrates. See, for example, K. Antanakis and F. Leclercq, *Bull. Soc. Chim. Fr.*, 2142 (1971), and ref 10b.

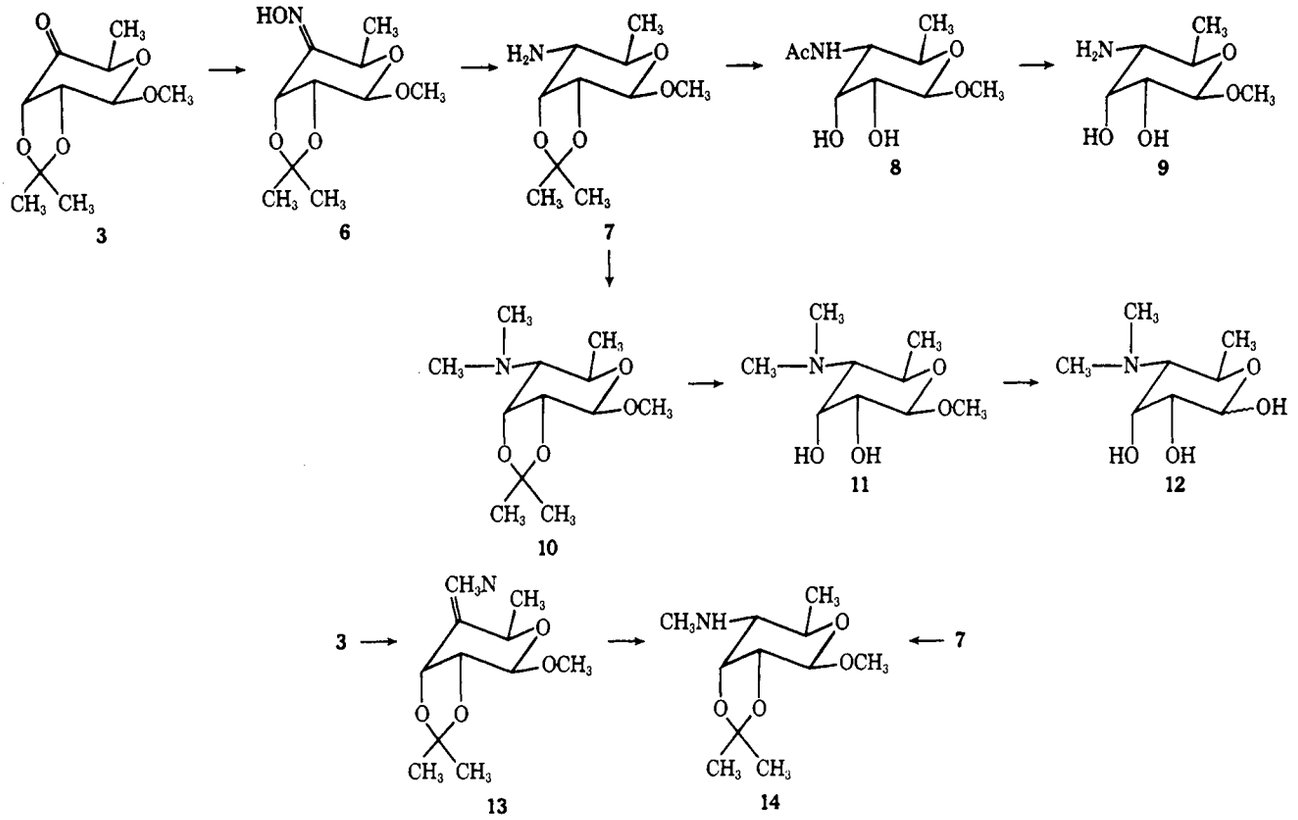
(13) St. Hofmann, Ek. Weiss, and T. Reichstein, *Helv. Chim. Acta*, **49**, 2209 (1966).

(14) P. A. Levene and J. Compton, *J. Biol. Chem.*, **116**, 169 (1936); H. Kaufmann, P. Muhlradt, and T. Reichstein, *Helv. Chim. Acta*, **50**, 2287 (1967).

(15) D. Horton, J. S. Jewell, E. K. Just, and J. D. Wander, *Carbohyd. Res.*, **18**, 49 (1971).

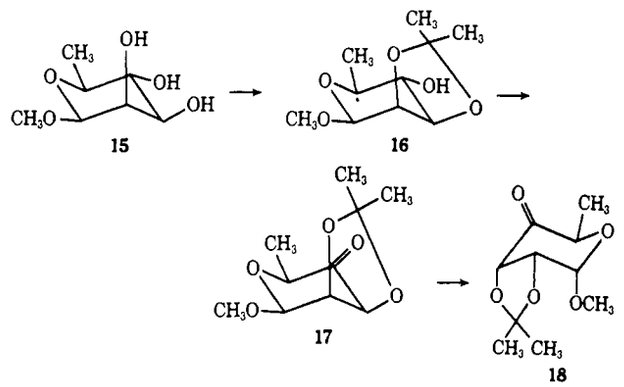
(16) E. L. Albano and D. Horton, *Carbohyd. Res.*, **11**, 485 (1969).

(17) C. L. Stevens, S. K. Gupta, R. P. Glinski, G. E. Gutowski, and C. P. Bryant, *Tetrahedron Lett.*, 1817 (1968).



isopropylidene-β-D-allopyranoside (14) characterized as its hydrochloride. Compound 14 was also obtained from ketone 3 by converting it to the imine 13 by treatment with methylamine in the presence of anhydrous sodium bisulfate followed by reduction with sodium borohydride in methanol. The identity of the two samples was established by superimposable ir spectra and a mixture melting point determination of the crystalline hydrochlorides.

As only the α-methyl glycosides of the other 4-amino-4,6-dideoxy hexoses were known in most cases,[1,5] the synthesis of methyl 4-amino-4,6-dideoxy-α-D-allopyranoside was necessary for comparative studies. This was accomplished by two methods as given below. Conversion of methyl 6-deoxy-β-L-mannopyranoside[18] (15) into the 2,3-*O*-isopropylidene derivative (16)



followed by oxidation with a mixture of phosphorous pentoxide and dimethyl sulfoxide in pyridine gave methyl 6-deoxy-2,3-*O*-isopropylidene-β-L-*lyxo*-hexopyranosid-4-ulose (17) as an oil. Isomerization of 17 to methyl 6-deoxy-2,3-*O*-isopropylidene-α-D-*ribo*-hexopyranosid-4-ulose (18) was achieved by base-catalyzed inversion at C-5 as in the conversion of 2 to 3. Thus, when a solution of 17 in 80% aqueous pyridine was heated on a steam bath for 2.5 hr, a mixture consisting of 64% of 18 and 36% of 17 was formed which was separated by preparative thin layer chromatography.

Ketone 18 was also obtained by an entirely different series of reactions as described here. Reductive debenzylation of methyl 6-deoxy-2,3-di-*O*-benzyl-4-*O*-methylsulfonyl-α-D-glucopyranoside[5a] (19) by hydrogenation in the presence of palladium on carbon and hydrochloric acid as catalysts gave methyl 6-deoxy-4-*O*-methylsulfonyl-α-D-glucopyranoside (20) as a gum which was characterized as its diacetyl derivative 21 and di-*p*-nitrobenzoyl derivative, 22. Treatment of 20 with sodium methoxide in a mixture of chloroform and methanol as solvent gave a 60% yield of the epoxide 23.[19] Although an acid opening of this epoxide (23) is expected to give a gulose derivative, its 6-hydroxy analog has been reported to yield a mixture of products on treatment with dilute acid.[20] However, methyl 2-*O*-acetyl-3,4-anhydro-α-D-galactopyranoside or its 6-triphenylmethyl derivative gave mostly methyl 3-*O*-acetyl-α-D-gulopyranoside under mild acid hydrolysis.[20,21] Compound 23 was therefore converted to methyl 6-deoxy-2-*O*-acetyl-3,4-anhydro-α-D-galactopyranoside[19] (24) by treatment with acetic anhydride and pyridine. Hydrolysis of 24 in acetone–water with a trace of sulfuric acid gave a single crystalline mono-

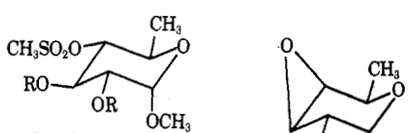
(18) E. Fischer, M. Bergmann, and R. Babe, *Ber. Deut. Chem. Ges. B*, **53**, 2362 (1920); L. Hough, J. K. N. Jones, and W. H. Wadman, *J. Chem. Soc.*, 1702 (1950).

(19) J. Jary and K. Capek, *Collect. Czech. Chem. Commun.*, **31**, 315 (1966).

(20) J. G. Buchanan, *J. Chem. Soc.*, 2511 (1958).

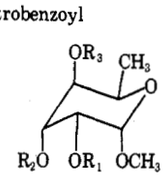
(21) J. G. Buchanan and R. Fletcher, *J. Chem. Soc.*, 6316 (1965); J. G. Buchanan in "Methods in Carbohydrate Chemistry," Vol. 6, R. L. Whistler and J. N. BeMiller, Ed., Academic Press, New York, N. Y., 1972, p 135.

acetate, **25**, in excellent yield. An examination of the nmr spectrum of **25** in acetone-d_6–D_2O showed that the proton on the acetate bearing carbon (the most deshielded hydrogen in the molecule) appeared as an unsymmetrical triplet at 306 Hz and the anomeric proton as a doublet (J = 4 Hz) at 270 Hz. As decoupling of either of these protons did not affect the appearance of the other, it was shown that the acetate group was not attached to C-2. As acyloxy groups are known to participate in the epoxide opening,[22] the acetate group could migrate to C-3 as found in a similar reaction.[21] That compound **25** was indeed the 3-*O*-acetate was shown by a spin-decoupling irradiation of the C-2 proton (which appeared as part of a multiplet at 240 Hz together with the C-5 hydrogen) when the anomeric proton collapsed into a singlet and the C-3 proton into a doublet (J = 4 Hz). Deacetylation of **25** with catalytic amounts of sodium methoxide in methanol yielded methyl 6-deoxy-α-D-gulopyranoside (**26**) as a clear, colorless gum, which was characterized as its crystalline triacetyl derivative, **27**. Compound **27** was also obtained by the acetylation of **25** with acetic anhydride in pyridine. Treatment of **26** with diethoxy-



19, R = $CH_2C_6H_5$
20, R = H
21, R = Ac
22, R = *p*-nitrobenzoyl

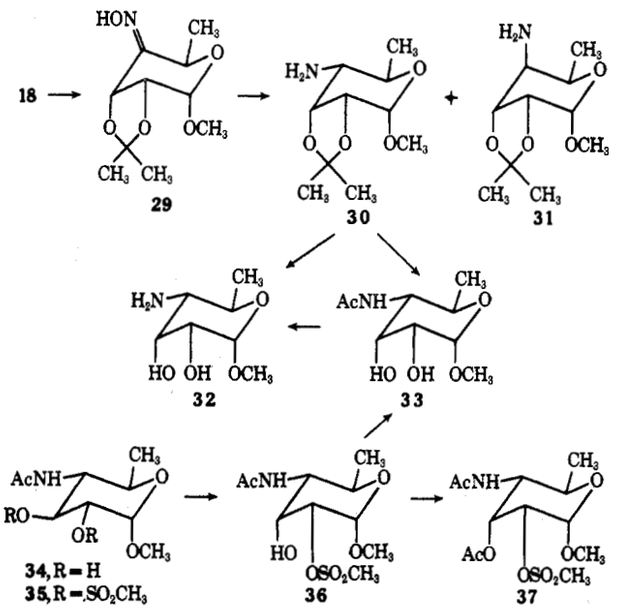
23, R = H
24, R = Ac



25, R_1 = R_3 = H; R_2 = Ac
26, R_1 = R_2 = R_3 = H
27, R_1 = R_2 = R_3 = Ac
28, R_1, R_2 = isopropylidene; R_3 = H

propane in acetone in the presence of *p*-toluenesulfonic acid as a catalyst gave methyl 6-deoxy-2,3-*O*-isopropylidene-α-D-gulopyranoside (**28**) in 80% yield. Compound **28** was oxidized to ketone **18** with catalytic amounts of ruthenium tetroxide in the presence of sodium hypochlorite.[9,10] The two samples of **18** obtained by the different methods were identical in all respects. Also, when either **17** or **18** was subjected to the isomerization conditions, the same mixture of the two compounds was formed as shown by gas chromatography.

Treatment of **18** with hydroxylamine hydrochloride in a mixture of pyridine and ethanol gave 80% of the oxime **29** as a mixture of syn and anti isomers. The mixture was separated by preparative thin layer chromatography to give the major component as a crystalline material and the minor isomer as a gum. Reduction of either the crystalline oxime or the mixture with lithium aluminum hydride in tetrahydrofuran at room temperature gave methyl 4-amino-4,6-dideoxy-2,3-*O*-isopropylidene-α-D-allopyranoside (**30**). Although **30** was isolated as its crystalline hydrogen *p*-toluenesulfonate in only 56% yield, a gas chromatographic analysis of the reduction mixture before any purification showed that over 95% of **30** was formed in the reaction. The minor component (less than 5%) was identified as methyl 4-amino-4,6-dideoxy-2,3-*O*-isopropylidene-α-D-gulopyranoside (**31**) by gas chromatography. Reduction of **29** with lithium aluminum hydride in refluxing tetrahydrofuran produced **30** and **31** in a ratio of 85:15. The higher temperature has apparently decreased the stereoselectivity of this reaction, as was found previously in the reduction of certain ketones with lithium aluminum hydride.[23] Hydrolysis of **30** as its hydrogen *p*-toluenesulfonate in



water on a steam bath for 30 min gave 89% of methyl 4-amino-4,6-dideoxy-α-D-allopyranoside (**32**) isolated and characterized as its hydrogen *p*-toluenesulfonate. The *N*-acetyl derivative **33** was obtained from **30** by acetylation with acetic anhydride in pyridine followed by hydrolysis of the isopropylidene group with an acid resin in methanol.

Methyl 4-acetamido-4,6-dideoxy-α-D-allopyranoside (**33**) was alternately synthesized by inversion of the hydroxyl group at C-3 of a glucose derivative.[24] Treatment of methyl 4-acetamido-4,6-dideoxy-α-D-glucopyranoside[5b] (**34**) with methanesulfonyl chloride in pyridine gave the 2,3-di-*O*-methylsulfonate **35** in 90% yield. When a solution of **35** in ethylene glycol monomethyl ether containing 2 equiv of sodium acetate was refluxed for 28 hr, 95% of methyl 4-acetamido-4,6-dideoxy-2-*O*-methylsulfonyl-α-D-allopyranoside (**36**) was obtained as a crystalline material. Compound **36** was further characterized as its *O*-acetyl derivative, **37**. Cleavage of the methylsulfonate group from compound **36** by sodium naphthalene reagent[25] yielded 57% of **33** identical in all respects with the previously prepared sample. Further, hydrolysis of **33** with a solution of barium hydroxide in water under refluxing conditions gave methyl 4-amino-4,6-dideoxy-α-D-allopyranoside (**32**) in 70% yield.

(22) For reviews, see (a) B. Capon, *Chem. Rev.*, **69**, 407 (1969); (b) L. Goodman, *Advan. Carbohyd. Chem.*, **22**, 109 (1967).

(23) O. R. Vail and D. M. S. Wheeler, *J. Org. Chem.*, **27**, 3803 (1962).

(24) For reviews on internal displacements of sulfonyloxy groups by neighboring *N*-acetates, see ref 22a and b.

(25) W. D. Closson, P. Wriede, and S. Bank, *J. Amer. Chem. Soc.*, **88**, 158 (1966); J. R. Ganson, S. Schulenberg, and W. D. Closson, *Tetrahedron Lett.*, 4397 (1970).

The D-erythro stereochemistry at C-4 and C-5 of **33** was confirmed as in the case of **8** by degradation to allothreoninol.[1b,17] Also, the structures of **8** and **33** were correlated by the following method. Methanolysis of **8** in the presence of hydrogen chloride gave a mixture of **8** and **33** by equilibration at the anomeric center. Treatment of this mixture with hexamethyldisilazane and trimethylchlorosilane in pyridine followed by gas chromatographic analysis of the trimethylsilyl derivatives showed the presence of two compounds corresponding to **8** and **33**. The identities of the peaks in the chromatogram were established by mixed injections with authentic samples.

Experimental Section[26]

Methyl 6-Deoxy-2,3-*O*-isopropylidene-α-L-*lyxo*-hexopyranosid-4-ulose[6,7] (**2**).—A 5.5% solution of NaOCl in water[27] was added dropwise to a rapidly stirred mixture of a solution of 1.0 g (4.6 mmol) of methyl 6-deoxy-2,3-*O*-isopropylidene-α-L-mannopyranoside[8] (**1**) in 10 ml of $CHCl_3$ (freed from EtOH by passing over a column of Woelm grade I alumina), 20 mg of active[2d] RuO_2, and 2 ml of water. Addition was continued until a permanent pale yellow color was obtained for the $CHCl_3$ layer, marking the presence of an excess of RuO_4 in solution. A gc analysis at this point showed that the oxidation was complete. The $CHCl_3$ layer was separated and the aqueous layer was extracted twice with $CHCl_3$. The combined organic solution was washed with $Na_2S_2O_3$ solution followed by water, dried (Na_2SO_4), and evaporated to dryness to yield 0.68 g (68%) of **2** as an oil, $[\alpha]^{26}D$ −105.83° (*c* 1.0 $CHCl_3$), ORD ($CHCl_3$) peak at 290 nm, trough at 330 nm (negative Cotton effect). This material was identical (ir, gc, tlc) with a sample of **2** obtained by the oxidation of **1** by DMSO–P_2O_5 in pyridine by a previously described procedure.[1a]

Methyl 6-Deoxy-2,3-*O*-isopropylidene-β-D-*ribo*-hexopyranosid-4-ulose (**3**).—A solution of 10 g (46.3 mmol) of **2** in 50 ml of 80% aqueous pyridine was heated at 100° for 3 hr. An analysis of the mixture by gc showed that it consisted of 82% of **2** and 18% of **3**. The solvents were removed *in vacuo*, and the residue was dissolved in ether, washed with a saturated solution of NaCl, dried (Na_2SO_4), and evaporated to dryness. The residual oil was distilled under reduced pressure to give 9.01 g (90.1%) of the mixture of ketones. Separation by preparative gc using a 8 ft × 2.5 in. 3% ethylene glycol succinate on Chromosorb W column at 120° gave 5.54 g of **2** (90% pure by gc), 593 mg of **3** (92% pure), and 1.3 g of a mixture of **2** and **3** for a total recovery of 8.43 g (93%). Compound **3** solidified and was recrystallized from cold pentane: mp 42–43°; ir ($CHCl_3$) 1730 (C=O), 1375 cm^{-1} (*gem*-dimethyl); nmr ($CDCl_3$) τ 8.55 (d, J = 8 Hz, 3, C-6 H), 6.4 (s, 3, OCH_3), 5.55 (q, J = 8 Hz, 1, C-5 H); ORD ($CHCl_3$) peak at 325 nm, trough at 290 nm (positive Cotton effect).

Anal. Calcd for $C_{10}H_{16}O_5$: C, 55.56; H, 7.44. Found: C, 55.48; H, 7.44.

For specific rotation of **3** in different solvents, see Table I.

In subsequent experiments for the preparation of **3**, ketone **2** was isomerized using KOH as described below.

Isomerization Studies of 2 Using KOH as a Catalyst.—A solution of 6.0 g (27.8 mmol) of **2** in 60 ml of CH_3OH was stirred with 30 ml of 0.5 *M* KOH in CH_3OH for 15 min at room temperature. The solution was neutralized with Dowex-50 (H^+), filtered, and evaporated to dryness. The residue on extraction with pentane followed by removal of the solvent gave 4.9 g (81.7%) of an oil containing 45% of **2** and 55% of **3** as shown by gc. The pentane-insoluble material was identified as 2-methyl-3-hydroxy-4-pyrone[28] (maltol), mp 160–162°.

Further studies showed that the proportion of **3** increased when the reaction was conducted for a longer time. However, the recovery of the mixture of ketones was poor as increasing amounts of maltol were formed.

TABLE I

SPECIFIC ROTATION OF **3** IN DIFFERENT SOLVENT SYSTEMS AT 26°

Solvent system	Concn, g/100 ml	Initial value,[a] deg	Equilibrium value,[b] deg
Chloroform	0.4	+36.18	+36.18
Pyridine	0.3	+33.2	+33.2
Pyridine–water (99:1)	0.3	+33.7	−15.1
Pyridine–water (96:4)[c]	0.3	+30.0	−16.0
Pyridine–water (94:6)[c]	0.3	+21.6	−33.3
Pyridine–water (80:20)	0.3	−62.2	−62.2
2-Propanol	0.3	+27.18	+26.1
Ethanol	0.3	+25.9	+8.0
Methanol[c]	0.3	+26.8	−25.0
Methanol–water (80:20)[c]	0.3	−4.0	−39.0
Water	0.3	−60.6	−60.6

[a] Specific rotation immediately after preparing the solution. [b] All the solutions on analysis by gc after reaching equilibrium showed the presence of only one ketone, **3**. [c] An ORD curve of this solution after reaching equilibrium did not exhibit any peaks. Only a plane curve was obtained.

Methyl 6-Deoxy-2,3-*O*-isopropylidene-β-D-allopyranoside (**4**).—A solution of 84 mg (0.4 mmol) of **3** in 5 ml of CH_3OH was treated with 37 mg of $NaBH_4$ at 0°. Analysis by gc and tlc after 30 min indicated that the reduction was complete. The solvent was removed *in vacuo* and the residue was heated on a steam bath with 1 ml of water for 5 min. The mixture was extracted with ether, dried (Na_2SO_4), and evaporated to dryness to give 80 mg (95%) of **4** as a liquid. Gc analysis of this material on three different columns indicated that it consisted of only one compound. A small portion of this material was evaporatively distilled for analysis, $[\alpha]^{26}D$ −50.0° (*c* 0.45, $CHCl_3$) [lit.[13] $[\alpha]D$ −47.4 ± 2° (*c* 2.22, acetone)].

Anal.[29] Calcd for $C_{10}H_{18}O_5$: C, 55.03; H, 8.31. Found: C, 55.23; H, 8.46.

6-Deoxy-D-allose (**5**).—A mixture of 80 mg of **4** and 3 ml of 1 *N* H_2SO_4 was heated on a steam bath for 1 hr. The solution was neutralized with solid $BaCO_3$ and filtered. The $BaSO_4$ was washed with water and the combined aqueous solution was evaporated to dryness. The residue was extracted with anhydrous EtOH and concentrated, ether was added, and the residue was cooled to give 45 mg (75%) of **5**, mp 143–145°, $[\alpha]^{26}D$ −4.2° (*c* 1.0, H_2O). A mixture melting point of this material with an authentic sample of 6-deoxy-D-allose[14] was undepressed.

Methyl 6-Deoxy-2,3-*O*-isopropylidene-β-D-*ribo*-hexopyranosid-4-ulose Oxime (**6**).—A mixture of 2.0 g (9.26 mmol) of **3** and 2.0 g of hydroxylamine hydrochloride in 20 ml of 1:1 pyridine–ethanol was heated on a steam bath for 45 min. The solvents were removed *in vacuo*, and the residue was mixed with water and extracted several times with ether. The ether solution was dried (Na_2SO_4) and evaporated to dryness to give 2.0 g (93%) of **6** as a gum which showed two spots on tlc. Trituration of this material with 25 ml of pentane yielded 1.2 g (57%) of a crystalline oxime (one spot on tlc) which was recrystallized from ether–pentane, mp 133–134.5°, $[\alpha]^{26}D$ + 42.5° (*c* 0.63, $CHCl_3$).

Anal. Calcd for $C_{10}H_{17}NO_5$: C, 51.94; H, 7.36; N, 6.06. Found: C, 52.14; H, 7.40; N, 6.21.

The pentane-soluble portion, which showed two spots on tlc, was separated by preparative tlc to give 126 mg more of the

(26) Melting points were taken on a Thomas-Hoover melting point apparatus and are uncorrected. Thin layer chromatography, both analytical and preparative, was carried out using silica gel G from Brinkmann Instruments. An ether–pentane (1:1) solvent system was used unless otherwise stated. Compounds were detected by spraying with 6 *N* H_2SO_4 followed by baking at 110°. Gas chromatographic analyses were performed on an F & M Model 810 instrument equipped with dual flame ionization detectors. A 3 ft × 0.25 in. 6% ethylene glycol succinate on Chromosorb W column was used unless mentioned otherwise. For separation of compounds by gc, an F & M Model 775 preparative gas chromatograph was used. The nmr spectra were taken on a Varian A-60 or T-60 spectrometer using tetramethylsilane as an internal standard. The infrared spectra were recorded on a Perkin-Elmer 237 B grating spectrophotometer. Specific rotations were measured on a Perkin-Elmer Model 141 polarimeter at 1-dm path lengths. Optical rotatory dispersion curves were obtained using a Cary 60 instrument. The pK_a's were determined in 50% aqueous methanol. Elemental analyses were performed by Midwest Microlab, Inc., Indianapolis, Ind.

(27) A solution of Roman Cleanser Bleach can be used instead of the sodium hypochlorite solution.

(28) J. R. Schenck and M. A. Spielman, *J. Amer. Chem. Soc.*, **67**, 2276 (1945).

(29) The authors thank Mr. Harold Hauser for preparing this analytical sample.

crystalline oxime, mp 133–134°, for a total yield of 1.326 g (62%). The slower moving band on extraction gave 342 mg (16.2%) of a gum (one spot on tlc), $[\alpha]^{26}D$ +9.14° (*c* 0.72, $CHCl_3$), ir ($CHCl_3$) and nmr ($CDCl_3$) similar to but not identical with those of the crystalline material.

Anal. Calcd for $C_{10}H_{17}NO_5$: C, 51.94; H, 7.36; N, 6.06. Found: C, 52.09; H, 7.55; N, 5.92.

When $CHCl_3$ solutions of the two pure isomers were left overnight at room temperature, mixtures of the two oximes were formed as shown by tlc and nmr.

Methyl 4-Amino-4,6-dideoxy-2,3-*O*-isopropylidene-β-D-allopyranoside (7).—A solution of 700 mg (2.1 mmol) of the crystalline oxime in 20 ml of dry tetrahydrofuran was stirred with 300 mg of $LiAlH_4$ at room temperature for 12 hr. The excess $LiAlH_4$ was destroyed by the careful addition of wet ether followed by water and the white, gelatinous precipitate was filtered off and washed with ether. The ether solution was dried (K_2CO_3) and evaporated to dryness to give 572 mg (86%) of **7** as an oil, more than 95% pure by gc. This material was dissolved in ether and treated with *p*-toluenesulfonic acid to give 557 mg (68%) of methyl 4-amino-4,6-dideoxy-2,3-*O*-isopropylidene-β-D-allopyranoside (**7**) hydrogen *p*-toluenesulfonate, mp 184–189°. Recrystallization from $CHCl_3$–ether gave an analytical sample, mp 191–193°, $[\alpha]^{26}D$ −28.5° (*c* 0.67, $CHCl_3$).

Anal. Calcd for $C_{17}H_{27}NO_7S$: C, 52.42; H, 7.03; N, 3.59. Found: C, 52.48; H, 7.16; N, 3.66.

Reduction of the minor isomer and the mixture of oximes separately under the above conditions gave essentially the same results.

Methyl 4-Acetamido-4,6-dideoxy-β-D-allopyranoside (8).—A solution of 365 mg (1.68 mmol) of **7** (free base) in 1 ml of pyridine was treated with 1 ml of acetic anhydride at room temperature for 12 hr. The solvents were removed *in vacuo*, and the residue was dissolved in $CHCl_3$, washed with water, dried (K_2CO_3), and evaporated to dryness to give 300 mg (68.5%) of methyl 4-acetamido-4,6-dideoxy-2,3-*O*-isopropylidene-β-D-allopyranoside as a gum, ir ($CHCl_3$) 1650 cm^{-1} (amide). This material was hydrolyzed with 0.05 *N* hydrochloric acid at 100° for 40 min. The solution was evaporated to dryness under reduced pressure followed by azeotroping with ethanol and benzene. The residue was triturated with ether to give 192 mg (75.6%) of **8** which was recrystallized from ethanol–ether, mp 224–225°, $[\alpha]^{26}D$ + 3.9° (*c* 0.4, CH_3OH).

Anal. Calcd for $C_9H_{17}NO_5$: C, 49.30; H, 7.82; N, 6.39. Found: C, 49.41; H, 7.75; N, 6.53.

Degradation of 80 mg (0.36 mmol) of **8** according to a previously reported procedure[1b,17] gave 18 mg (25.7% for four steps) of D-allothreoninol hydrogen oxalate, mp 172–173° dec. A mixture melting point with an authentic sample was unchanged.

Methyl 4-Amino-4,6-dideoxy-β-D-allopyranoside (9).—A mixture of 190 mg (0.868 mmol) of **8** and 3.0 ml of 9% $Ba(OH)_2$ in water was heated on a steam bath for 12 hr. The solution, after cooling, was carefully neutralized with 1 *N* H_2SO_4 and the $BaSO_4$ was removed by filtration. The filtrate was evaporated to dryness under vacuum followed by azeotroping with ethanol. The residue was extracted with hot $CHCl_3$. Removal of $CHCl_3$ yielded 86 mg (56%) of **9**, mp 168–172°. An analytical sample was prepared by recrystallization from ethanol–ether, mp 174–176°, $[\alpha]^{26}D$ −50.6° (*c* 0.75, CH_3OH), pK_a 7.20.

Anal. Calcd for $C_7H_{15}NO_4$: C, 47.45; H, 8.5; N, 7.82. Found: C, 47.77; H, 8.66; N, 8.06.

Methyl 4-*N*,*N*-Dimethylamino-4,6-dideoxy-2,3-*O*-isopropylidene-β-D-allopyranoside (10).—A solution of 600 mg (2.76 mmol) of **7** (free base) and 1.5 ml of 40% aqueous formaldehyde in 10 ml of CH_3OH was hydrogenated at atmospheric pressure in the presence of 100 mg of 5% Pd/C. After removal of the catalyst, the solution was evaporated to dryness to give 572 mg (88%) of **10** as a gum which was converted to the hydrochloride salt, 467 mg (70%), mp 199–201° dec. Recrystallization from ethanol–ether gave an analytical sample, mp 203–204° dec, $[\alpha]^{26}D$ −16.8° (*c* 0.5, CH_3OH), pK_a 6.32.

Anal. Calcd for $C_{12}H_{24}ClNO_4$: C, 51.14; H, 8.58; Cl, 12.60; N, 4.97. Found: C, 50.98; H, 8.63; Cl, 12.86; N, 5.07.

Methyl 4-*N*,*N*-Dimethylamino-4,6-dideoxy-β-D-allopyranoside (11).—A solution of 75 mg (0.3 mmol) of **10** in 2 ml of 0.1 *N* hydrochloric acid was heated at 95° under a nitrogen atmosphere for 6 hr. The solution was evaporated to dryness under vacuum and the residue was redissolved in ethanol and neutralized with solid K_2CO_3. The inorganic materials were filtered and the filtrate was evaporated to dryness. The residue was extracted with methanol and the methanol was removed *in vacuo* to give **11** as a gum. It was converted to the hydrogen *p*-toluenesulfonate salt, 70 mg (62%), mp 168–169° after recrystallization from ethanol–ether, $[\alpha]^{26}D$ −12.8° (*c* 0.5, CH_3OH), pK_a 6.80.

Anal. Calcd for $C_{16}H_{27}NO_7S \cdot {}^1/_2\ H_2O$: C, 49.73; H, 7.30; N, 3.62. Found: C, 49.37; H, 7.05; N, 3.63.

4-*N*,*N*-Dimethylamino-4,6-dideoxy-D-allose (12).—A solution of 95 mg (0.46 mmol) of **11** (free base) in 2 ml of 1.0 *N* hydrochloric acid was heated at 100° under a nitrogen atmosphere for 24 hr. The solution was evaporated to dryness under vacuum and repeatedly azeotroped with ethanol. The white, foamy solid was recrystallized from ethanol–ether to give 19 mg (17.1%) of 4-*N*,*N*-dimethylamino-4,6-dideoxy-D-allose (**12**) hydrochloride, mp 166–168°, $[\alpha]^{26}D$ +38.09° (initial) and +33.2° (equilibrium) (*c* 1.52, CH_3OH).

Anal. Calcd for $C_8H_{18}ClNO_4$: C, 42.20; H, 7.97; N, 6.15. Found: C, 42.16; H, 7.83; N, 5.90.

Methyl 4-*N*-Methylamino-4,6-dideoxy-2,3-*O*-isopropylidene-β-D-allopyranoside (14). A. From Amine 7.—A solution of 384 mg (1.77 mmol) of **7** in 1 ml of pyridine and 2 ml of $CHCl_3$ was stirred with 300 mg of ethyl chloroformate at 0° for 2 hr. The mixture was diluted with $CHCl_3$ and washed with $NaHCO_3$ solution followed by water. The $CHCl_3$ solution was dried and evaporated to dryness to give 480 mg (100%) of the *N*-carbethoxy derivative as an oil. This material without further purification was dissolved in 15 ml of tetrahydrofuran, treated with 250 mg of $LiAlH_4$ overnight at room temperature, and then heated under reflux for 3 hr. The mixture was cooled and the excess $LiAlH_4$ was decomposed with wet ether. Filtration and evaporation of the solvents gave 380 mg (92.5%) of **14** as a pale brown liquid which was converted to the hydrochloride salt, mp 216–217° dec after recrystallization from ethanol–ether, $[\alpha]^{26}D$ −12.63° (*c* 0.5, CH_3OH), pK_a 7.05.

Anal. Calcd for $C_{11}H_{22}ClNO_4$: C, 49.33; H, 8.28; N, 5.23. Found: C, 49.20; H, 8.42; N, 5.21.

B. From Ketone 3.—A mixture of 240 mg (1.1 mmol) of **3** in 20 ml of $CHCl_3$, 3 g of freshly fused $NaHSO_4$, and 2 ml of methylamine was stirred at room temperature for 12 hr. The solvents were removed under vacuum and the residue was extracted with ether. Removal of ether gave 200 mg (74.5%) of the imine **13** as a brown liquid, ir 1670 cm^{-1} (C=N). A solution of this material in 2 ml of CH_3OH at 0° was stirred with 180 mg of $NaBH_4$ for 30 min and then at room temperature for 30 min. The solvent was evaporated *in vacuo* and the residue was treated with water. The mixture was extracted with ether and dried (K_2CO_3), and the solvent was removed to give 148 mg (73.5%) of **14** as an oil which contained a small amount of another basic compound as shown by tlc. This material was converted to its HCl salt (52 mg) and recrystallized from ethanol–ether, mp 212–214° dec. A mixture melting point of the two samples prepared by methods A and B was 212–215° dec and they had superimposable ir spectra.

Methyl 6-Deoxy-2,3-*O*-isopropylidene-β-L-mannopyranoside (16).—A mixture of 356 mg (2.0 mmol) of methyl 6-deoxy-β-L-mannopyranoside[18,30] (**15**), 3 ml of 2,2-diethoxypropane, and 10 mg of *p*-toluenesulfonic acid was stirred at room temperature for 20 min. The solution was diluted with ether, washed with $NaHCO_3$ solution, dried (Na_2SO_4), and evaporated to dryness to give 385 mg (88%) of **16** as a viscous liquid, more than 90% pure by gc: nmr ($CDCl_3$) τ 8.64 (d, $J_{5,6}$ = 8 Hz, 3, CCH_3), 8.6 and 8.43 (both s, 3, *gem*-dimethyl), 5.3 (d, $J_{1,2}$ = 2.5 Hz, 1, C-1 H), 6.4 (s, 3, OCH_3); ir ($CHCl_3$) 1375 cm^{-1} (*gem*-dimethyl).

Methyl 6-Deoxy-2,3-*O*-isopropylidene-β-L-*lyxo*-hexopyranosid-4-ulose (17).—Phosphorus pentoxide (1 g) was added in small portions to a solution of 750 mg (3.44 mmol) of **16** in 10 ml of DMSO and 0.6 ml of pyridine at room temperature. The solution was heated at 65° for 14 hr and cooled, and the excess P_2O_5 was decomposed by the addition of ice. The mixture was extracted with ether washed with NaCl solution, dried (Na_2SO_4), and evaporated *in vacuo* to dryness and then azeotroped with toluene to remove the last traces of DMSO and pyridine. The liquid residue (510 mg, 74%) was purified by preparative tlc: ir ($CHCl_3$) 1730 (C=O) and 1375 cm^{-1} (*gem*-dimethyl); nmr ($CDCl_3$) τ 8.52 (d, $J_{5,6}$ = 7 Hz, 3, CCH_3), 5.2 (d, $J_{1,2}$ = 3 Hz, 1, C-1 H), 5.9 (q, $J_{6,5}$ = 7 Hz, 1, C-5 H); $[\alpha]^{26}D$ +45.09° (*c* 0.51, $CHCl_3$).

(30) Compound **15**, mp 137–138°, $[\alpha]^{26}D$ +93.2° (*c* 0.53, H_2O), was obtained in 3% yield from the mother liquors of the preparation of methyl 6-deoxy-α-L-mannopyranoside from L-rhamnose.

Anal. Calcd for $C_{10}H_{16}O_5$: C, 55.56; H, 7.40. Found: C, 55.99; H, 7.71.

Methyl 6-Deoxy-2,3-di-*O*-acetyl-4-*O*-methylsulfonyl-α-D-glucopyranoside (21).—A solution of 40 g (92 mmol) of methyl 6-deoxy-2,3-di-*O*-benzyl-4-*O*-methylsulfonyl-α-D-glucopyranoside[6a] (19) in 160 ml of tetrahydrofuran and 640 ml of CH_3OH was hydrogenated in the presence of 2.5 g of 10% Pd/C and 3 ml of concentrated HCl at atmospheric pressure. When the hydrogen uptake was complete (4.13 l.), the mixture was neutralized with Dowex-1 X_2 (OH^-), Pd/C was removed by filtration, and the filtrate was evaporated to dryness to give 23 g (98%) of methyl 6-deoxy-4-*O*-methylsulfonyl-α-D-glucopyranoside (20) as a gum. This material (11.26 g, 44 mmol) was treated with 20 ml of pyridine and 20 ml of acetic anhydride at room temperature for 16 hr. The solution was poured into ice water, filtered, and dried to give 13.6 g (91%) of 21, mp 93–95°. An analytical sample was prepared by recrystallization from benzene–ether–pentane, mp 94–95°, $[\alpha]^{26}D$ +120.9° (*c* 1.0, CH_3OH).

Anal. Calcd for $C_{12}H_{20}O_9S$: C, 42.34; H, 5.92; S, 9.42. Found: C, 42.51; H, 5.93; S, 9.20.

Methyl 6-Deoxy-2,3-di-*O*-(*p*-nitrobenzoyl)-4-*O*-methylsulfonyl-α-D-glucopyranoside (22).—A solution of 5.12 g (20 mmol) of 20 in 30 ml of pyridine was treated with 14.8 g (80 mmol) of *p*-nitrobenzoyl chloride at room temperature for 48 hr. The mixture was poured into ice water, filtered, dried, and recrystallized from $CHCl_3$–pentane to give 10.5 g (95%) of 22, mp 178–179°, $[\alpha]^{26}D$ +194.6° (*c* 1.0, $CHCl_3$).

Anal. Calcd for $C_{22}H_{22}N_2O_{18}S$: C, 47.65; H, 4.00; N, 5.05; S, 5.78. Found: C, 47.50; H, 3.89; N, 4.88; S, 5.56.

Methyl 6-Deoxy-3,4-anhydro-α-D-galactopyranoside (23).—A solution of 23 g (90 mmol) of 20 in 200 ml of CH_3OH and 200 ml of $CHCl_3$ was treated with sodium methoxide (130 mmol, obtained by dissolving 3.0 g of sodium in methanol) at 0° for 48 hr. The solution was neutralized with solid CO_2, the inorganics were filtered off, and the filtrate was evaporated to dryness. Extraction of the residue with ethyl acetate followed by removal of the solvent gave 11.75 g (80%) of 23 as a solid which was recrystallized from ether–pentane, mp 69.5–70°, $[\alpha]^{26}D$ +100° (*c* 0.92, $CHCl_3$) [lit.[19] mp 65.5–66.5°, $[\alpha]^{26}D$ +70.0° (*c* 0.5, H_2O)].

Anal. Calcd for $C_7H_{12}O_4$: C, 52.49; H, 7.55. Found: C, 52.73; H, 7.59.

Methyl 6-Deoxy-2-*O*-acetyl-3,4-anhydro-α-D-galactopyranoside (24).—A solution of 33.0 g (20.6 mmol) of 23 in 300 ml of pyridine was stirred with 41 ml of acetic anhydride at 0° for 8 hr. The solvents were removed *in vacuo*, and the residue was dissolved in $CHCl_3$, washed with water, dried (Na_2SO_4), and evaporated to dryness. The resulting solid was recrystallized from ether to give 38 g (94%) of 24, mp 113.5–114.5°, $[\alpha]^{23}D$ +128° (*c* 0.9, $CHCl_3$) [lit.[19] mp 112.5–114°, $[\alpha]^{23}D$ +131.5° (*c* 0.54, $CHCl_3$)].

Anal. Calcd for $C_9H_{14}O_5$: C, 53.46; H, 6.98. Found: C, 53.68; H, 6.96.

Methyl 6-Deoxy-3-*O*-acetyl-α-D-gulopyranoside (25).—A solution of 468 mg (2.32 mmol) of 24 in 20 ml of acetone was mixed with 0.6 ml of 2 *N* H_2SO_4 and heated under reflux for 2 hr. The cooled solution was neutralized with $BaCO_3$ and the barium salts were removed by filtration. The filtrate on evaporation under vacuum gave a solid which was recrystallized from ether to give 410 mg (80%) of 25: mp 144–145°; $[\alpha]^{26}D$ +133.9° (*c* 1.32, CH_3OH); nmr (acetone-d_6–D_2O) τ 8.8 (d, $J_{5,6}$ = 7 Hz, 3, CCH_3), 7.9 (s, 3, $COCH_3$), 6.6 (s, 3, OCH_3), 6.4 (broad d, 1, C-4 H), 6.0 (m, 2, C-2 and C-5 H), 5.3 (d, $J_{1,2}$ = 4 Hz, 1, C-1 H), 4.9 (t, 1, C-3 H).

Anal. Calcd for $C_9H_{16}O_6$: C, 49.09; H, 7.32. Found: C, 49.21; H, 7.16.

Methyl 6-Deoxy-2,3,4-tri-*O*-acetyl-α-D-gulopyranoside (27).—A solution of 354 mg (1.6 mmol) of 25 in 3 ml of pyridine and 600 mg of acetic anhydride was stirred at room temperature for 18 hr. The mixture was poured into ice water and extracted with $CHCl_3$. The $CHCl_3$ solution was successively washed with 2 *N* HCl, Na_2CO_3 solution, and water, dried ($MgSO_4$), and evaporated to dryness. The residue was recrystallized from ether–hexane to give 332 mg (67.6%) of 27, mp 81–82°, $[\alpha]^{26}D$ +112° (*c* 1.24, $CHCl_3$).

Anal. Calcd for $C_{13}H_{20}O_8$: C, 51.30; H, 6.62. Found: C, 51.57; H, 6.63.

Methyl 6-Deoxy-2,3-*O*-isopropylidene-α-D-gulopyranoside (28).—A solution of 16.3 g (74 mmol) of 25 in 225 ml of CH_3OH was treated with a catalytic amount of sodium methoxide at room temperature. When the deacetylation was complete as shown by tlc, the solution was neutralized with solid CO_2 and then evaporated to dryness. The residue was extracted with boiling ethyl acetate. Removal of the solvent *in vacuo* gave methyl 6-deoxy-α-D-gulopyranoside (26) as a gum. This material was dissolved in 225 ml of acetone and the solution was stirred with 37.5 ml of 2,2-diethoxypropane and 225 mg of *p*-toluenesulfonic acid at room temperature for 1 hr, at which point tlc indicated completion of the reaction. The solution was neutralized with $BaCO_3$, the barium salts were filtered, and the filtrate was evaporated to dryness. The residue was recrystallized from ethyl ether to give 13.25 g (82%) of 28, mp 48–50°, $[\alpha]^{26}D$ +67.7° (*c* 0.77, $CHCl_3$).

Anal. Calcd for $C_{10}H_{18}O_5$: C, 55.08; H, 8.31. Found: C, 55.29; H, 8.38.

Acetylation of 890 mg (5 mmol) of 26 with acetic anhydride in pyridine gave 1.2 g (80%) of the triacetate, 27, mp 81–82°; a mixture melting point with an analyzed sample was undepressed.

Methyl 6-Deoxy-2,3-*O*-isopropylidene-α-D-*ribo*-hexopyranosid-4-ulose (18). A. By the Oxidation of 28.—Treatment of 10 g (46 mmol) of 28 in 100 ml of ethanol-free $CHCl_3$ with catalytic amounts of RuO_2 and bleach solution as described for the preparation of 2 from 1 gave 7.1 g (71%) of 18 as a gum which crystallized on standing, mp 48°, $[\alpha]^{26}D$ +176.2° (*c* 1.07, $CHCl_3$).[31]

Anal. Calcd for $C_{10}H_{16}O_5$: C, 55.56; H, 7.46. Found: C, 55.70; H, 7.37.

B. By the Isomerization of 17.—A solution of 180 mg (0.83 mmol) of 17 in 2 ml of 80% aqueous pyridine was left overnight at room temperature. A gc analysis indicated that partial isomerization had taken place and the solution consisted of 76% 17 and 24% 18. The mixture was then heated on a steam bath and the reaction was monitored by gc. Equilibrium consisting of 34% 17 and 66% 18 was reached after 2.5 hr. The solvents were removed *in vacuo* and the residue was separated by preparative tlc to give 48 mg of 17 and 56 mg (31%) of 18 as a gum, $[\alpha]^{26}D$ +173.4° (*c* 0.5, $CHCl_3$). This material was identical (ir, gc, tlc) with an analyzed sample of 18 before it crystallized. Also, a solution of 18 (crystalline material) in 80% aqueous pyridine when heated on a steam bath produced an equilibrium mixture consisting of 66% of 18 and 34% of 17 as shown by gc.

Methyl 6-Deoxy-2,3-*O*-isopropylidene-α-D-*ribo*-hexopyranosid-4-ulose Oxime (29).—Ketone 18 (7 g, 32.4 mmol) was converted to 6.1 g (82%) of 29 as described for the conversion of 3 to 6. This gummy material was shown to be a mixture of two oximes by tlc. A portion of the mixture was separated by preparative tlc to give the major isomer as a crystalline material which was recrystallized from ether, mp 117–118°, $[\alpha]^{25}D$ +260° (*c* 1.12, $CHCl_3$).

Anal. Calcd for $C_{10}H_{17}NO_5$: C, 51.95; H, 7.35; N, 6.06. Found: C, 52.03; H, 7.41; N, 6.18.

Methyl 4-Amino-4,6-dideoxy-2,3-*O*-isopropylidene-α-D-allopyranoside (30).—A solution of 6.0 g (26 mmol) of 29 (gum, mixture of isomers) in 100 ml of tetrahydrofuran was reduced with 3.0 g of $LiAlH_4$, taking special care to keep the temperature below 30°. After 2 hr, a tlc indicated that the reaction was complete. The excess $LiAlH_4$ was decomposed by adding 3 ml of water, 3 ml of 15% NaOH, and 9 ml of water in that order. The inorganic materials were removed by filtration and the filtrate was evaporated to dryness and azeotroped with benzene under reduced pressure to give a gum. A gc analysis of this material using a 6 ft × 0.125 in., 3% SE-52 on a dichlorodimethylsilane-treated, acid-washed Chromosorb W column at 100° showed that it consisted of over 95% of 30 and less than 5% of 31.[32] A solution of this mixture in ether was treated with an ethereal solution of *p*-toluenesulfonic acid and the salt was recrystallized from $CHCl_3$–ether to give 30 as its hydrogen *p*-toluenesulfonate (5.6 g, 56%), mp 198–200°, $[\alpha]^{25}D$ +56.8° (*c* 0.89, CH_3OH), pK_a 6.35.

Anal. Calcd for $C_{17}H_{27}NO_7S$: C, 52.42; H, 7.00; N, 3.59; S, 8.23. Found: C, 52.47; H, 6.95; N, 3.60; S, 7.98.

(31) The specific rotation previously reported[2d] for compound 18 was that of a hydrated sample and therefore should be corrected.

(32) The two peaks on the gas chromatogram were identified as follows. A small portion of the gum when treated with acetic anhydride in pyridine followed by hydrolysis with Dowex-50 X_2 (H^+) in CH_3OH gave a mixture of *N*-acetates which was then treated with pyridine, hexamethyldisilazane, and trimethylchlorosilane according to C. C. Sweeley, R. Bentley, M. Makita, and W. W. Wells, *J. Amer. Chem. Soc.*, **85**, 2497 (1963). Analysis of this mixture by gc using the SE-52 column at 160° gave two peaks which corresponded to the di-*O*-trimethylsilyl ethers of authentic 33 and methyl 4-acetamido-4,6-dideoxy-α-D-gulopyranoside.[5d]

Reduction of the crystalline oxime (mp 117–118°) under the above conditions gave the same results. However, when **29** was reduced with $LiAlH_4$ in refluxing tetrahydrofuran, a mixture of **30** and **31** in the ratio 85:15 was obtained as shown by gc.[32]

Methyl 4-Amino-4,6-dideoxy-α-D-allopyranoside (32).—A solution of 1.0 g (2.57 mmol) of the hydrogen *p*-toluenesulfonate salt of **30** in 15 ml of water was heated on a steam bath for 30 min. The water was removed *in vacuo* to yield a gummy solid which was recrystallized from methanol–ether to give 0.8 g (89%) of **32** as its hydrogen *p*-toluenesulfonate, mp 183–185°, $[\alpha]^{25}D$ +83.5° (*c* 0.99, CH_3OH), pK_a 7.20.

Anal. Calcd for $C_{14}H_{23}NO_7S$: C, 48.14; H, 6.59; N, 4.01; S, 9.17. Found: C, 48.21; H, 6.75; N, 4.10; S, 9.19.

Methyl 4-Acetamido-4,6-dideoxy-2,3-di-*O*-methylsulfonyl-α-D-glucopyranoside (35).—Methanesulfonyl chloride (1.1 g, 9.7 mmol) was added dropwise to a stirred solution of 1.0 g (4.57 mmol) of methyl 4-acetamido-4,6-dideoxy-α-D-glucopyranoside[5b] in 16 ml of pyridine. After 4 hr, the solution was evaporated to dryness, the residue was dissolved in 25 ml of $CHCl_3$, and the $CHCl_3$ solution was washed two times with 20 ml of water. The aqueous solution was saturated with NaCl and extracted three times with 25 ml of $CHCl_3$. The $CHCl_3$ solution was dried (Na_2SO_4) and evaporated to dryness to yield 1.7 g (90%) of **35** as a clear, colorless gum which crystallized on standing. A sample was recrystallized from MeOH for analysis, mp 160–163°, $[\alpha]^{25}D$ +125° (*c* 0.95, CH_3OH).

Anal. Calcd for $C_{11}H_{21}NO_9S_2$: C, 35.19; H, 5.62; N, 3.73; S, 17.07. Found: C, 35.48; H, 5.81; N, 3.72; S, 17.34.

Methyl 4-Acetamido-4,6-dideoxy-2-*O*-methylsulfonyl-3-*O*-acetyl-α-D-allopyranoside (37).—A solution of 1.25 g (3.34 mmol) of **35** and 550 mg (6.68 mmol) of NaOAc in 95% aqueous ethylene glycol monomethyl ether was heated under reflux and the progress of the reaction was monitored by tlc ($CHCl_3$:acetone, 3:2 system). As all the starting material had disappeared in 28 hr, the solvent was removed at reduced pressure and the residue was taken up in 100 ml of $CHCl_3$ and washed three times with 10 ml of water. The $CHCl_3$ solution was dried (Na_2SO_4) and evaporated to dryness and the residue was recrystallized to give 900 mg (90%) of methyl 4-acetamido-4,6-dideoxy-2-*O*-methylsulfonyl-α-D-allopyranoside (**36**): mp 134°; ir 3500 (OH), 3425 (NH), 1675 (amide), 1155 cm^{-1} (OSO_2CH_3). As a satisfactory elementary analysis could not be obtained for **36**, a portion of it (80 mg) was acetylated with acetic anhydride in pyridine and the product was recrystallized from acetone to give 80 mg (87%) of **37**, mp 157–158°, $[\alpha]^{25}D$ +146° (*c* 0.59, $CHCl_3$).

Anal. Calcd for $C_{12}H_{21}NO_8S$: C, 42.48; H, 6.19; N, 4.13; S, 9.14. Found: C, 42.41; H, 6.27; N, 4.13; S, 9.14.

Methyl 4-Acetamido-4,6-dideoxy-α-D-allopyranoside (33). A. From Compound 30.—A solution of 450 mg (2.07 mmol) of **30** (free base) in 10 ml of pyridine was mixed with 0.5 ml of acetic anhydride at 0° and then stirred at room temperature for 2 hr. The solvents were removed *in vacuo* and the residue was dissolved in $CHCl_3$ and washed with water. The $CHCl_3$ solution was dried (Na_2SO_4) and evaporated to dryness to give a gum which was dissolved in CH_3OH and stirred with a small amount of Dowex-50 X2 (H^+). The resin was filtered off and the solvent was removed under reduced pressure to give 410 mg (90%) of **33** which was recrystallized from methanol–ether, mp 150–152°, $[\alpha]^{25}D$ +235° (*c* 0.75, CH_3OH).

Anal. Calcd for $C_9H_{17}NO_5$: C, 49.31; H, 7.76; N, 6.39. Found: C, 49.09; H, 7.88; N, 6.43.

B. From Compound 36.—A solution of sodium naphthalene reagent[25] was prepared by stirring a mixture of 512 mg (40 mmol) of naphthalene and 92 mg (40 mmol) of sodium in 13 ml of ethylene glycol dimethyl ether under a nitrogen atmosphere overnight. A slurry of 297 mg (1.0 mmol) of **36** in 5 ml of the same solvent was added to the sodium naphthalene reagent and the mixture was stirred for 20 min. Ten drops of water were added and the solvents were removed under vacuum. The yellow solid was extracted ten times with 10 ml of hot $CHCl_3$. After the $CHCl_3$ was evaporated, the residue was extracted with pentane to remove naphthalene. Recrystallization of the remaining solid from ethanol–ether gave 126 mg (57%) of **33**, mp 148–150°; a mixture melting point with a previously prepared sample was undepressed.

Hydrolysis of 100 mg (0.455 mmol) of **33** with 173 mg of $Ba(OH)_2$ in 3 ml of water followed by treatment of the product with *p*-toluenesulfonic acid gave 57 mg (36%) of methyl 4-amino-4,6-dideoxy-α-D-allopyranoside (**32**) hydrogen *p*-toluenesulfonate, mp 183–185°, identical with a sample described earlier. Also, 100 mg (0.455 mmol) of **33** was degraded to 29 mg (32.5%) of D-allothreoninol hydrogen oxalate, mp 174° dec; a mixture melting point with an authentic compound[1b,17] was unchanged and the two samples had superimposable ir spectra.

Structural Correlation of 8 and 33.—A solution of 10 mg of **8** in 1.5 ml of CH_3OH containing 1% HCl was heated under reflux for 2 hr under a nitrogen atmosphere. The solution was evaporated to dryness and repeatedly azeotroped with CH_3OH and benzene to remove the last traces of HCl. The residue was dissolved in pyridine (1.5 ml) and treated with hexamethyldisilazane (0.1 ml) and trimethylchlorosilane (0.05 ml). The product was analyzed by gc using a 6 ft × 0.125 in. 3% SE-52 on a dichlorodimethylsilane-treated, acid-wated Chromosorb W column at 160° to give two peaks which corresponded to the di-*O*-trimethylsilyl ethers of authentic **8** (major) and **33** (minor). Also compound **33** gave an identical gas chromatogram after the same series of reactions.

Acknowledgment.—Financial support from the National Institutes of Health, Grant No. GM 11520, is gratefully acknowledged.

Registry No.—**1**, 14133-63-2; **2**, 2592-53-2; **3**, 32848-86-5; **4**, 14685-82-6; **6** oxime A, 36031-47-7; **6** oxime B, 35954-82-6; **7**, 42213-89-8; **7** TsOH, 35941-98-1; **8**, 35941-99-2; **9**, 35942-00-8; **10**, 42213-93-4; **10** hydrochloride, 42213-94-5; **11**, 42213-95-6; **11** TsOH, 42213-96-7; **12** hydrochloride, 42213-97-8; **13**, 42213-98-9; **14** hydrochloride, 42213-99-0; **15**, 42214-00-6; **16**, 42214-01-7; **17**, 42214-02-8; **18**, 37063-23-3; **19**, 7045-38-7; **20**, 42214-06-2; **21**, 42214-04-0; **22**, 42214-07-3; **23**, 6893-94-3; **24**, 6893-96-5; **25**, 42214-10-8; **26**, 42214-11-9; **27**, 33947-13-6; **28**, 33947-10-3; **29** oxime A, 42214-14-2; **29** oxime B, 42214-15-3; **30**, 42214-16-4; **30** TsOH, 42214-17-5; **32** TsOH, 42214-18-6; **33**, 42214-19-7; **35**, 42214-20-0; **36**, 42214-21-1; **37**, 42214-22-2; methyl 4-acetamido-4,6-dideoxy-2,3-*O*-isopropylidene-β-D-allopyranoside, 42214-23-3.