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Syntheses of 4-O-α-D-Galactopyranosyl-D-glucopyranose and 4-O-(6-Deoxy-α-D-galactopyranosyl)-D-glucopyranose by Chemical Modifications of Maltose

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The title compounds were synthesized starting from 1,6-anhydro-β-maltose, *via* 1,6-anhydro-4′,6′-O-benzylidene-β-maltose with several steps.

Heating of 2,2′,3,3′-tetra-O-acetyl-1,6-anhydro-4′,6′-di-O-mesyl-β-maltose (**9**) with sodium benzoate in hexamethylphosphoric triamide afforded 2,3-di-O-acetyl-1,6-anhydro-4-O-(2,3-di-O-acetyl-4,6-di-O-benzoyl-α-D-galactopyranosyl)-β-D-glucopyranose (**15**) as an amorphous powder. Deacylation of **15** and sequential reacetylation gave crystalline hexaacetate (**16**). The former of the title compound (**19**), mp 227—229, $[\alpha]_D^{26}$ +159.6°, was obtained after acetolysis of **16** followed by deacetylation.

Treatment of **9** with NaI in acetonitrile effected substitution of the mesyloxy at $C_{6'}$ to give the corresponding 6′-deoxy-6′-iodo-4′-O-mesyl derivative (**11**), from which 6′-deoxy compound (**13**) was prepared by catalytic hydrogenation. Benzoyloxy substitution with inversion at $C_{4'}$-mesyloxy in **13** gave 2,3-di-O-acetyl-1,6-anhydro-4-O-(2,3-di-O-acetyl-4-O-benzoyl-6-deoxy-α-D-galactopyranosyl)-β-D-glucopyranose (**20**), from which the latter of the title compound (**24**), hygroscopic, amorphous powder, $[\alpha]_D^{27}$ +128.3°, was obtained *via* the same pathway as for **19** from **15**.

Synthesis and characterization of the key intermediate (**9**) were described in full detail.

In the preceding paper of the same authors, the syntheses of maltose derivatives having sulfur atom in the reducing part were reported.[2] As further extension of our studies objecting chemical modifications at the non-reducing part in maltose, we now report on syntheses of the title compounds starting from 1,6-anhydro-β-maltose (maltosan). The key step in this pathway is bimolecular nucleophilic substitution reaction in 2,2′,3,3′-tetra-O-acetyl-1,6-anhydro-4′,6′-di-O-methanesulfonyl-β-maltose (**9**). In addition, this paper further indicates the usefulness of 1,6-anhydro-β-disaccharides as starting materials for chemical modifications of 1,4-α- or β-linked reducing disaccharides as it has been pointed out in the recent publications from our laboratory.[3]

Benzylidenation of maltosan (**1**) with zinc chloride afforded monobenzylidene maltosan (**2**) in 63% yield. As compound **2** was soluble in water, separation of **2** from **1** in the reaction mixture was effected by repeated extraction with warm acetone. Compound **2** consumed two molar equivalents of sodium metaperiodate with no concomitant formation of formic acid. From this result and structural correlations with monobenzylidene derivatives of benzyl β-maltoside,[4] phenyl α-maltoside,[5] and sucrose,[6] or dibenzylidene α,α-trehalose,[7]

1) Location: *Tanabe-dori, Mizuho-ku, Nagoya.*
2) M. Mori, M. Haga, and S. Tejima, *Chem. Pharm. Bull.* (Tokyo), **22**, 1331 (1974).
3) *a*) S. Tejima, *Carbohyd. Res.*, **20**, 123 (1971); *b*) S. Tejima and Y. Okamori, *Chem. Pharm. Bull.* (Tokyo), **20**, 2036 (1972); *c*) S. Tejima and T. Chiba, *ibid.*, **21**, 546 (1973); *d*) Y. Okamori, M. Haga, and S. Tejima, *ibid.*, **21**, 2538 (1973); *e*) T. Chiba, M. Haga, and S. Tejima, *ibid.*, **22**, 398 (1974).
4) A. Klemer, *Chem. Ber.*, **92**, 218 (1959).
5) H. Arita and Y. Matsushima, *J. Biochem.* (Tokyo), **70**, 795 (1971).
6) R. Khan, *Carbohyd. Res.*, **32**, 375 (1974).
7) L. Hough, P.A. Munroe, and A.C. Richardson, *J. Chem. Soc.* (*C*), **1971**, 1091.

and diethylidene α,α-trehalose,[8] the structure of **2** was tentatively assigned to 1,6-anhydro-4′,6′-O-benzylidene-β-maltose. The exact structural assignment was determined from the structures of the final products which were synthesized from **2** *via* unequivocal synthetic routes.

Acylation of **2** in pyridine with acetic anhydride or benzoyl chloride afforded crystalline tetraacetate (**3**) or tetrabenzoate (**4**), respectively. Treatment of **3** with N-bromosuccinimide and barium carbonate in carbon tetrachloride and 1,2-dichloroethane effected cleavage of the benzylidene acetal and, after column chromatography on silica gel, gave monobromo-monodeoxy derivative (**5**) as an amorphous powder. The nuclear magnetic resonance (NMR) spectroscopy of **5** showed signals corresponding to one benzoyl and four acetyls. The ring-opening with N-bromosuccinimide was reported first by Hanessian[9] and the method has been widely used for introduction of bromine in monosaccharides,[10,11b] however, reported example is little in disaccharides.[11a]

Catalytic hydrogenation of **5** over Raney nickel catalyst at room temperature under atmospheric pressure gave monodeoxy derivative (**6**) in good yield. The NMR of **6** showed a three proton doublet corresponding to the methyl (τ 8.74, $J_{5',6'}$=6 Hz). Deacylation of **6** and sequential acetylation of the deacylated product yielded crystals (**7**), mp 142—143°, $[\alpha]_D^{25}$ +51.5°. Compound **7** had almost the same physical constants with those of 2,2′,3,3′,4′-penta-O-acetyl-1,6-anhydro-6′-deoxy-β-maltose, mp 141—142°, $[\alpha]_D$+44.5°, which was reported by Dutton and Slessor.[12] Further, from the NMR data, the elemental analyses, and an unequivocal synthetic route, the structure of **7** was assigned to 2,2′,3,3′,4′-penta-O-acetyl-1,6-anhydro-6′-deoxy-β-maltose.

Therefore, the benzylidene acetal in **2**, **3**, or **4**, and the bromine in **5** attach at $C_{6'}$ position in maltosan.

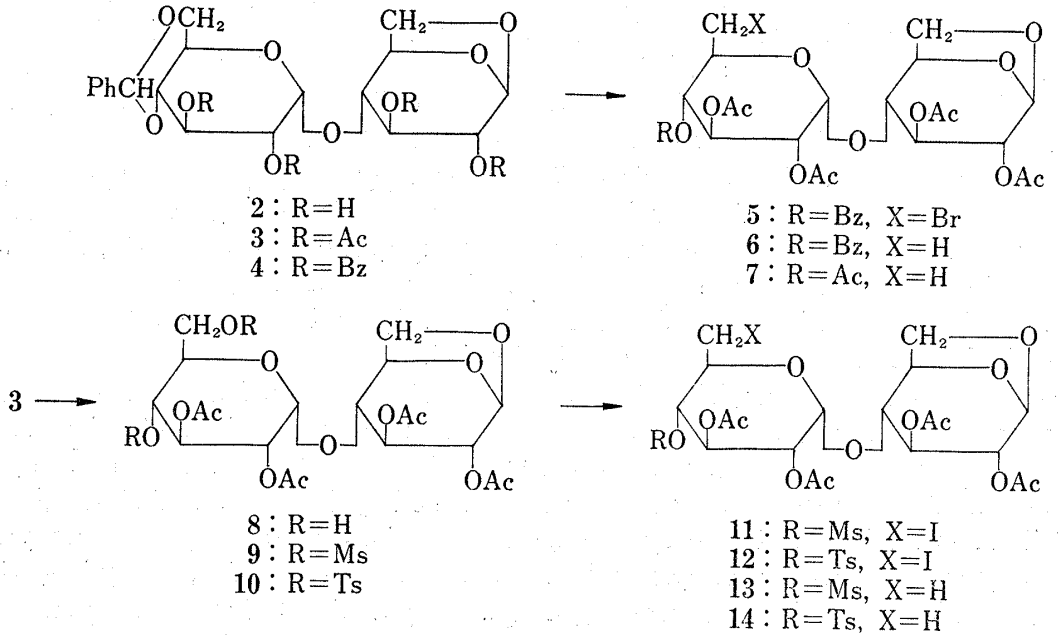

Chart 1. Ac=acetyl, Bz=benzoyl, Ms=mesyl, Ts=tosyl, Ph=phenyl

Debenzylidenation of **3** was effected by catalytic hydrogenation over palladium catalyst to afford crystalline tetraacetyl-1,6-anhydro-β-maltose (**8**). Compound **8** was also obtainable

8) G.G. Birch, *J. Chem. Soc.*, (*C*) **1966**, 1072.
9) S. Hanessian, *Carbohyd. Res.*, **2**, 86 (1966).
10) W.A. Szarek, "Advances in Carbohydrate Chemistry and Biochemistry," Vol. 28, Academic Press, New York and London, 1973, p. 225.
11) *a*) S. Hanessian and N.R. Plessas, *J. Org. Chem.*, **34**, 1035 (1969); *b*) *Idem, ibid.*, **34**, 1045 (1969).
12) G.G.S. Dutton and K.N. Slessor, *Can. J. Chem.*, **44**, 1069 (1966).

in good yield by mild acid hydrolysis of **3** with 80% acetic acid; no acetyl migration was observed under this condition. Sulfonylation of **8** with mesyl or tosyl chloride gave crystalline dimesylate (**9**) or ditosylate (**10**), respectively.

Treatment of **9** with sodium iodide in boiling acetonitrile caused replacement of one of the sulfonyloxy groups by iodine, and crystalline monoiodo-monodeoxy-monomesyl derivative (**11**) was obtained in 86% yield. Similarly, compound **10** gave the corresponding monodeoxy-monoiodo compound (**12**) in 73% yield as an amorphous powder. These results confirmed that one sulfonyl group in **9** or **10** was located on the primary alcohol group. Further proof of this structure was obtained by the following experiments. Catalytic hydrogenation of **11** over Raney nickel catalyst gave crystalline monodeoxy-monomesyl derivative (**13**) in good yield. The NMR spectrum of **13** showed a three proton doublet (τ 8.65, J=6 Hz) corresponding to the methyl at $C_{5'}$. Similarly, the corresponding monodeoxy compound (**14**) was obtained from **12** after purification by column chromatography, as an amorphous powder. The NMR spectrum of **14** also showed a three proton doublet (τ 8.73, $J_{5',6'}$=6 Hz).

The position of another sulfonyloxy group in **9** or **10** was determined by elucidation of the structure of a novel 1,6-anhydro-β-disaccharide (**17**) which was prepared from **9** as follows.

Heating of a mixture of **9** and sodium benzoate in hexamethylphosphoric triamide (HMPA) at 100—110° for 20 hr effected simultaneous substitutions at the two mesyloxy groups. After purification by column chromatography, a novel acylated 1,6-anhydro-β-disaccharide (**15**) was separated in 72% yield as an amorphous powder. The NMR spectrum of **15** showed signals corresponding to the two benzoyls and four acetyls. Deacylation of **15** and sequential acetylation of the deacylated product gave crystalline acetylated 1,6-anhydro-β-disaccharide (**16**). Deacetylation of **16** yielded crystalline 1,6-anhydro-β-disaccharide (**17**). Paper partition chromatography (PPC) of the acid hydrolyzate of **17** and gas chromatographic (GC) analysis of the trimethylsilylated acid hydrolyzate indicated that **17** was made up of glucose and galactose in the ratio of 1:1. Therefore, the structures of **15**, **16**, and **17** were assigned to 2,3-di-O-acetyl-1,6-anhydro-4-O-(2,3-di-O-acetyl-4,6-di-O-benzoyl-α-D-galactopyranosyl)-β-D-glucopyranose, 2,3-di-O-acetyl-1,6-anhydro-4-O-(2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl)-β-D-glucopyranose, and 1,6-anhydro-4-O-α-D-galactopyranosyl-β-D-glucopyranose, respectively. The formation of disaccharide derivatives containing D-galactopyranose form **9** suggested that the position of the secondary mesyloxy group in **9** was at $C_{4'}$, from which **15** was derived with inversion of the configuration. From this result, the position of the benzylidene acetal in **2** was undoubtedly decided as $C_{4'}$ and $C_{6'}$, and therefore, all structures of the compounds described before were completely decided.

According to the literature, S_N2 displacement reactions of 4-sulfonates of α-D-glucopyranosides in aprotic solvents, with such nucleophiles as benzoate, azide, and thiocyanate, give products with inversion of configuration at C_4.[13] In disaccharides containing D-glucopyranosyl linkage the analogous reactions have been accomplished by Kuzuhara and Emoto,[14] Khan,[15] and Tejima, *et al.*[3d] in order to synthesize disaccharides containing D-galactopyranose.

Acetolysis of **16** with acetolysis mixture effected cleavage of 1,6-anhydro-β-ring and, after purification by column chromatography, acetylated 4-O-(α-D-galactopyranosyl)-α-D-glucopyranose (**18**) was obtained as an amorphous powder. The NMR spectrum of **18** showed one proton doublet (τ 3.77, J=4 Hz) which could not be noticed in any 1,6-anhydro-β-maltose derivative mentioned before. We assigned it to the anomeric proton in the reducing part. According to the NMR data reported by Minnikin,[16] chemical shifts of anomeric proton in methyl α-glycosides of disaccharides appear in a region of τ 5.0—5.50 (J=3.5 Hz), while inter-

13) J. Hill, L. Hough, and A.C. Richardson, *Carbohyd. Res.*, **8**, 7, 19 (1968).
14) H. Kuzuhara and S. Emoto, *Agr. Biol. Chem.*, **30**, 122 (1966).
15) R. Khan, *Carbohyd. Res.*, **25**, 232 (1972).
16) D.E. Minnikin, *Carbohyd. Res.*, **23**, 139 (1972).

sugar α-linkage protons show a signal in a lower region, τ 4.3—5.00 (J=3.5 Hz). These data were not in accordance with our compound.

Deacetylation of **18** afforded 4-O-α-D-galactopyranosyl-D-glucopyranose (**19**). After recrystallization from methanol, **19** had mp 227—229° (decomp.) and $[\alpha]_D^{26}$ +159.6°. The specific rotation was far more dextrorotatory than that of lactose[17] and showed no mutarotation for 24 hr.

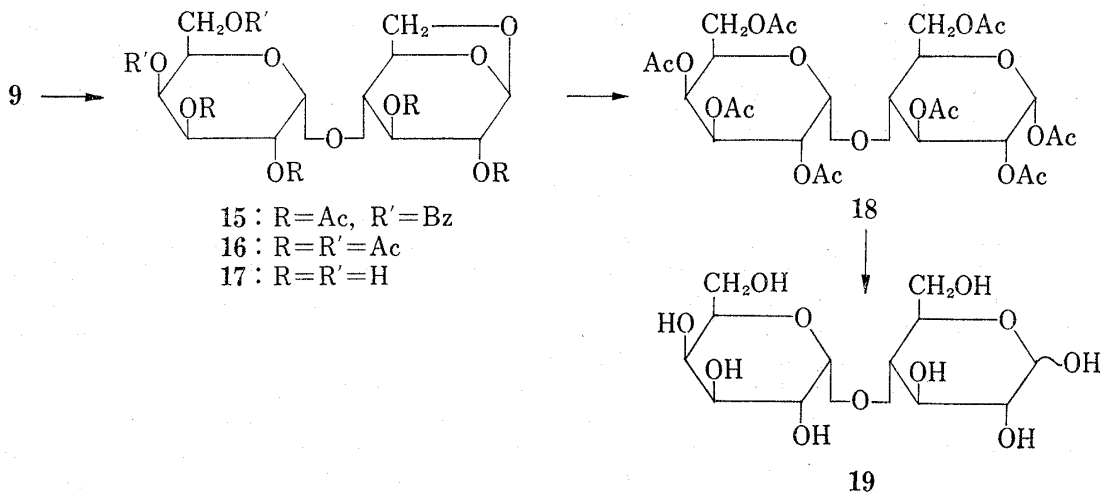

Chart 2. Ac=Acetyl, Bz=benzoyl

4-O-(6-Deoxy-α-D-galactopyranosyl)-D-glucopyranose was synthesized as follows. Nucleophilic substitution of the secondary mesyloxy in **13** with sodium benzoate in HMPA afforded the corresponding 4-O-benzoate (**20**) as an amorphous powder. Deacylation of **20** and sequential acetylation of the deacylated product yielded crystalline pentaacetate (**21**). Deacetylation of **21** afforded a novel 1,6-anhydro-6′-deoxy-β-disaccharide (**22**). After acid hydrolysis of **22** and treatment of the hydrolyzate with PPC, glucose and 6-deoxy-galactose were identified. Therefore, the structures of **20**, **21**, and **22** were assigned to 2,3-di-O-acetyl-1,6-anhydro-4-O-(2,3-di-O-acetyl-4-O-benzoyl-6-deoxy-α-D-galactopyranosyl)-β-D-glucopyranose, 2,3-di-O-acetyl-1,6-anhydro-4-O-(2,3,4-tri-O-acetyl-6-deoxy-α-D-galactopyranosyl)-β-D-glucopyranose, and 1,6-anhydro-4-O-(6-deoxy-α-D-galactopyranosyl)-β-D-glucopyranose, respectively.

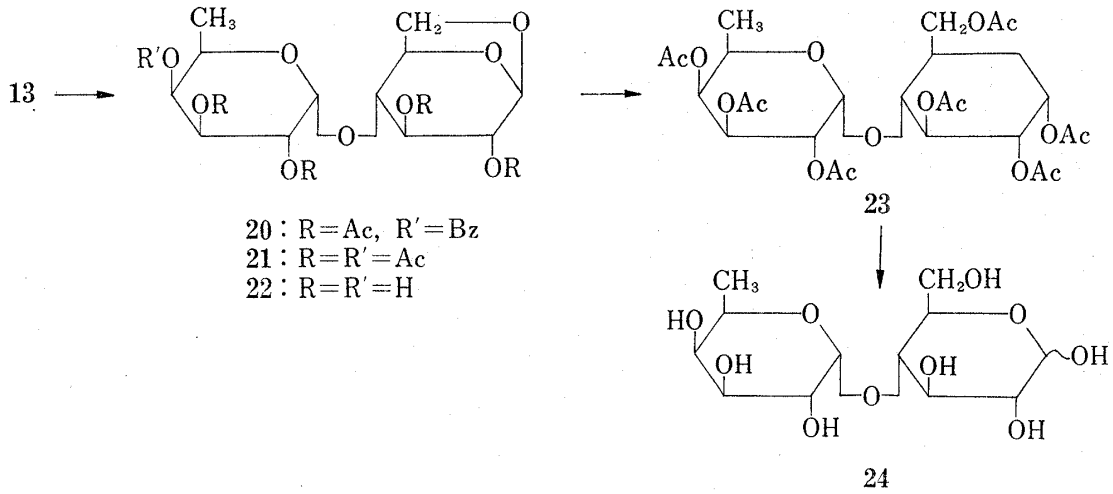

Chart 3. Ac=acetyl, Bz=benzoyl

17) J.R. Clamp, L. Hough, J.L. Hickson, and R.L. Whistler, "Advances in Carbohydrate Chemistry," Vol. 16, Academic Press, New York and London, 1961, p. 203.

Acetolysis of **21** afforded acetylated 4-O-(6-deoxy-α-D-galactopyranosyl)-α-D-glucopyranose (**23**). Similarly in **18**, in the NMR spectrum of **23**, the anomeric proton appeared as a one proton doublet (τ 3.74, J=3.5 Hz). Deacetylation of **23** yielded 4-O-(6-deoxy-α-D-galactopyranosyl)-D-glucopyranose (**24**) as an amorphous powder, $[\alpha]_D^{27}$ +128.3°.

One of the title compound (**19**) is a new reducing disaccharide having a binding structure of D-galactopyranose and D-glucopyranose with α-(1→4) glycosidic linkage; that is a structural isomer of lactose. The other is 4-O-(α-D-fucopyranosyl)-D-glucopyranose and also a new reducing disaccharide. Lactose and fucose are interesting sugars from biological view points and several attempts have been devoted to the syntheses of disaccharides containing L-fucopyranose.[18] In addition, chemical modifications of methyl β-maltoside have progressed recently by Hough, *et al.*[19] which are also interesting as compared with our results.

Experimental

Melting points were determined on a Yanagimoto micro melting point apparatus and uncorrected. Solutions were evaporated in a rotary evaporator below 40° under vacuum. Optical rotations were measured with a Yanagimoto Model OR-10 polarimeter in a 0.5 dm tube. Infrared (IR) spectra were recorded with a Jasco Model IRA-2 spectrometer. NMR spectra were recorded at 100 MHz with Jeol Model JNM-MH-100 spectrometer. Tetramethylsilane was used as the internal standard in $CDCl_3$. Chemical shifts are given on the τ scale. Thin-layer chromatography (TLC) on Silica gel GF_{254} (E. Merck, Darmstadt, Germany) activated at 110° was performed with solvent systems (A) 9: 1 (v/v) CH_2Cl_2–acetone, (B) 2: 1 ether–benzene, and (C) 2: 1 70% iso-PrOH–AcOEt. Detection was effected with H_2SO_4 and UV light (short wave length). PPC was performed on Toyo Filter Paper No. 50 by the ascending method[20] with solvent systems (D) 6: 4: 3 (v/v) *n*-BuOH–pyridine–H_2O, (E) 3: 3: 1 AcOEt–AcOH–H_2O, (F) 40: 11: 19 *n*-BuOH–EtOH–H_2O. Spots were detected by Tollens' reagent.[21] Column chromatography was effected on a column of Wako gel C-200 (Wako Pure Chemical Industries, Ltd., Osaka) as the adsorbent, with 1 g of the mixture to be separated per 20 g of adsorbent.

1,6-Anhydro-β-maltose (Maltosan) (1)——Compound **1** was prepared in 84% yield by deacetylation of maltosan hexaacetate[2] according to the method of Dutton and Slessor.[12] After recrystallization from MeOH–AcOEt, the product had mp 132—137°, $[\alpha]_D^{25}$ +76.6° (c=0.93, H_2O); TLC: *Rf* 0.40 (solvent C).

1,6-Anhydro-4′,6′-O-benzylidene-β-maltose (2)——A mixture of well dried and finely powdered **1** (15 g), freshly fused and powdered $ZnCl_2$ (15 g), and freshly distilled benzaldehyde (60 ml) was shaken for 20 hr at room temperature. The mixture was poured into ice-H_2O (100 ml) containing MeOH (10 ml). Excess benzaldehyde was removed by repeated extraction with petr. ether (bp 30—60°, 60 ml×5) and the organic layers were discarded. To the aqueous layer was added aq. Na_2CO_3 for neutralization, filtered, and the residue was washed with hot MeOH (40 ml×2). To combined filtrate and washings were evaporated to dryness and the residue was extracted with warm acetone (100 ml×10). Removal of acetone from the combined extracts gave an amorphous powder which crystallized from 85% EtOH (12 g, 63%). Recrystallization from 95% EtOH gave an analytically pure sample, mp 224—226°, $[\alpha]_D^{23}$ +56.4° (c=0.89, H_2O); TLC: *Rf* 0.72 (solvent C). *Anal.* Calcd. for $C_{19}H_{24}O_{10}$: C, 55.33; H, 5.87. Found: C, 55.28; H, 5.76. The $NaIO_4$-consumption (mole)[22] of **2** (100 mg) at room temperature was as follows: 0.68 (30 min), 0.81 (1 hr), 1.06 (2 hr), 1.82 (8 hr), and 2.12 (24 hr, constant).

2,2′,3,3′-Tetra-O-acetyl-1,6-anhydro-4′,6′-O-benzylidene-β-maltose (3)——To a solution of **2** (10.6 g) in dry pyridine (60 ml) was added Ac_2O (60 ml) at 0° under stirring, kept overnight at 5°, and then the mixture was poured into ice-H_2O (1.5 liter). The resulting precipitate was filtered, air-dried, and recrystallized twice from EtOH to give pure **3** (11.1 g, 72%), mp 215—216°, $[\alpha]_D^{24}$ +20° (c=1.01, $CHCl_3$); NMR ($CDCl_3$): 2.51—2.73 (5H, m, $C_6\underline{H}_5CH$), 4.51 (1H, s, $C_6H_5C\underline{H}$), 7.84, 7.93, 7.96 (12H, s, 4×OAc); TLC: *Rf* 0.54 (solvent A), 0.39 (B). *Anal.* Calcd. for $C_{27}H_{32}O_{14}$: C, 55.86; H, 5.56. Found: C, 55.89; H, 5.60.

1,6-Anhydro-2,2′,3,3′-tetra-O-benzoyl-4′,6′-O-benzylidene-β-maltose (4)——To an ice-cold solution of **2** (44 mg) in dry pyridine (2 ml) at 0° was added benzoyl chloride (0.1 ml) under stirring. After kept overnight at room temperature, the mixture was poured into ice-H_2O (20 ml) and extracted with CH_2Cl_2 (15 ml×3); the combined extracts were washed with cold dil. H_2SO_4, saturated $NaHCO_3$, and H_2O, dried ($CaCl_2$), and

18) H.M. Flowers, A. Levy, and N. Sharon, *Carbohyd. Res.*, **4**, 189 (1967); K.L. Matta, *ibid.*, **31**, 410 (1973); K.L. Matta, E.A.Z. Johnson, and J.J. Barlow, *ibid.*, **32**, 396, 418 (1974).
19) R.G. Edwards, L. Hough, A.C. Richardson, and E. Tarelli, *Carbohyd. Res.*, **35**, 111 (1974), and preceding parts of the series.
20) M. Ueda, *Yakugaku Zasshi*, **90**, 1332 (1970).
21) W.E. Travelyan, D.P. Procter, and J.S. Harrison, *Nature*, **166**, 444 (1950).
22) S. Okui, *Yakugaku Zasshi*, **75**, 1262 (1955).

evaporated to dryness which crystallized from EtOH–AcOEt (55 mg, 60%), mp 197—199°, $[\alpha]_D^{25}$ +75.3° (c=1.07, $CHCl_3$); TLC: *Rf* 0.74 (solvent A), 0.75 (B). *Anal.* Calcd. for $C_{47}H_{40}O_{14}$: C, 68.11; H, 4.86. Found: C, 68.18; H, 4.84.

2,2′,3,3′-Tetra-O-acetyl-1,6-anhydro-4′-O-benzoyl-6′-bromo-6′-deoxy-β-maltose (5)——A suspension of **3** (0.75 g), N-bromosuccinimide (0.27 g), and $BaCO_3$ (0.15 g) in CCl_4 (38 ml) and 1,2-dichloroethane (2 ml) was refluxed under stirring for 3 hr. The salts were removed by filtration and the filtrate was evaporated to dryness. To the residue was added ether (50 ml), filtered, and the filtrate was washed with H_2O (30 ml×3), dried (Na_2SO_4), and evaporated to dryness. The residue was purified by column chromatography on silica gel with benzene–ether (1: 2, v/v) as eluant. The combined fractions containing a single spot on TLC (solvent B) were evaporated to dryness to afford an amorphous powder (0.63 g, 76%), $[\alpha]_D^{25}$ −5° (c=1.21, $CHCl_3$); NMR ($CDCl_3$): 1.92—2.52 (5H, m, $C_6\underline{H}_5CO$), 7.77, 7.88, 7.90, 8.09 (12H, s, 4×OAc); TLC: *Rf* 0.62 (solvent A), 0.53 (B).

2,2′,3,3′-Tetra-O-acetyl-1,6-anhydro-4′-O-benzoyl-6′-deoxy-β-maltose (6)——Compound **5** (200 mg) was dissolved in EtOH (20 ml) containing triethylamine (10 drops), and hydrogenated over Raney Ni catalyst (freshly prepared from 2 g of alloy) at room temperature under atmospheric pressure; the theoretical amount of hydrogen was absorbed for 6 hr. After removal of the catalyst, the combined filtrate and washings were evaporated to dryness, and the residue was dissolved in CH_2Cl_2 (30 ml); the solution was washed with H_2O (20 ml×2), dried ($CaCl_2$), and evaporated to dryness, giving an amorphous powder which was purified by column chromatography on silica gel with CH_2Cl_2–acetone (20: 1, v/v) as eluant. Removal of solvent from the combined fractions containing a single spot on TLC (solvent A) gave an amorphous powder (190 mg, 83%); NMR ($CDCl_3$): 1.91—2.52 (5H, m, $C_6\underline{H}_5CO$), 7.76, 7.89, 7.91, 8.09 (12H, s, 4×OAc), 8.74 (3H, d, $J_{5',6'}$= 6 Hz, $C_{5'}$–$C\underline{H}_3$); TLC: *Rf* 0.55 (solvent A), 0.47 (B). $[\alpha]_D^{25}$ 0° (c=1.12, $CHCl_3$).

2,2′,3,3′,4′-Penta-O-acetyl-1,6-anhydro-6′-deoxy-β-maltose (7)——To a suspension of **6** (90 mg) in dry MeOH (2 ml) was added methanolic 0.1 N sodium methoxide (0.1 ml) at 0°. After stirring for few minutes to effect dissolution, the mixture was kept overnight in a refrigerator at 5°, made neutral with AcOH, and then evaporated to dryness. The residue was acetylated with Ac_2O (1 ml) and pyridine (1 ml) for 24 hr at room temperature. The mixture was evaporated by several co-distillations with toluene to afford a sirup which crystallized from EtOH. Recrystallization from iso-PrOH gave white crystals (50 mg, 62%), mp 142—143°, $[\alpha]_D^{25}$ +51.5° (c=0.93, $CHCl_3$) (lit.[12] mp 141—142°, $[\alpha]_D$ +44.5° (c=0.86, $CHCl_3$); NMR ($CDCl_3$): 7.80, 7.89, 7.93, 7.95, 7.99 (15H, s, 5×OAc), 8.81 (3H, d, $J_{5',6'}$=6 Hz, $C_{5'}$-$C\underline{H}_3$); TLC: *Rf* 0.51 (solvent A), 0.38 (B). *Anal.* Calcd. for $C_{22}H_{30}O_{14}$: C, 50.97; H, 5.83. Found: C, 51.04; H, 5.85.

2,2′,3,3′-Tetra-O-acetyl-1,6-anhydro-β-maltose (8)——1) Catalytic Hydrogenation of **3**: To a suspension of **3** (4.5 g) in MeOH (50 ml) was hydrogenated over Pd catalyst at room temperature under atmospheric pressure until absorption of hydrogen ceased. The Pd catalyst was freshly prepared from $PdCl_2$ (0.5 g) according to the method of Schmidt and Staad.[23] After removal of the catalyst, the filtrate was evaporated to dryness (3.7 g, 95%) which was used for further experiment. In order to obtain an analytical sample, a part of the residue was chromatographed on a column of silica gel with CH_2Cl_2–acetone (4: 1, v/v) as eluant. Removal of solvent from the combined fractions containing a single spot on TLC gave an amorphous powder which crystallized from AcOEt, mp 177—179°, $[\alpha]_D^{27}$ +39.1° (c=0.65, $CHCl_3$); TLC: *Rf* 0.61 (solvent 1: 1 v/v, CH_2Cl_2–acetone). *Anal.* Calcd. for $C_{20}H_{28}O_{14}$: C, 48.78; H, 5.73. Found: C, 48.83; H, 5.83.

2) Hydrolysis of **3** with 80% AcOH: A solution of **3** (2 g) in 80% AcOH (50 ml) was warmed at 45° for 7 hr, then evaporated to dryness by repeated co-distillation with EtOH, and the residue was triturated with ether–petr. ether to solidify. The solid (1.55 g, 91%) was collected by filtration and used for further experiment.

2,2′,3,3′-Tetra-O-acetyl-1,6-anhydro-4′,6′-di-O-methanesulfonyl-β-maltose (9)——To a cold solution of **8** (5 g) in dry pyridine (50 ml) was added mesyl chloride (3 ml) at −10° under stirring. After stirring for 30 min, the mixture was kept overnight at 5°, then poured into ice-H_2O (300 ml), and the resulting precipitate was filtered off. Recrystallization from EtOH gave white crystals (5.3 g, 81%), mp 199—200°, $[\alpha]_D^{24}$ +40.8° (c=1.46, $CHCl_3$); IR ν_{max}^{Nujol} cm^{-1}: 1180 (SO_2CH_3); NMR ($CDCl_3$): 6.92 (6H, s, 2×$SO_2C\underline{H}_3$), 7.82, 7.90, 7.91, 7.92 (12H, s, 4×OAc); TLC: *Rf* 0.31 (solvent A), 0.08 (B). *Anal.* Calcd. for $C_{22}H_{32}O_{18}S_2$: C, 40.74; H, 4.93. Found: C, 40.53; H, 5.12.

2,2′,3,3′-Tetra-O-acetyl-1,6-anhydro-4′,6′-di-O-*p*-toluenesulfonyl-β-maltose (10)——*p*-Toluenesulfonylation of **8** (1.5 g) in dry pyridine (15 ml) with tosyl chloride (2.1 g) afforded the tosylate. Recrystallization from EtOH gave pure **10** (2 g, 83%), mp 180—181°, $[\alpha]_D^{26}$ +36.2° (c=2.1, $CHCl_3$); NMR ($CDCl_3$): 2.17—2.70 (8H, m, 2×$SO_2C_6\underline{H}_4CH_3$), 7.56 (6H, s, 2×$SO_2C_6H_4C\underline{H}_3$), 7.91 7.95,, 8.08 (12H, s, 4×OAc); TLC: *Rf* 0.60 (solvent A), 0.35 (B). *Anal.* Calcd. for $C_{34}H_{40}O_{18}S_2$: C, 51.00; H, 5.04. Found: C, 50.70; H, 5.03.

2,2′,3,3′-Tetra-O-acetyl-1,6-anhydro-6′-deoxy-6′-iodo-4′-O-methanesulfonyl-β-maltose (11)——A mixture of **9** (4 g) and NaI (4 g) in acetonitrile (50 ml) was boiled for 8 hr under reflux, filtered, and the filtrate was evaporated to dryness. The residue was triturated with ice-H_2O to afford a solid, filtered, and the air-dried powder was recrystallized from EtOH to give pure **11** (3.6 g, 86%), mp 182—183°, $[\alpha]_D^{25}$ +36° (c=1.03,

23) O.Th. Schmidt and W. Staab, *Chem. Ber.*, **87**, 393 (1954).

$CHCl_3$); NMR ($CDCl_3$): 6.91 (3H, s, $SO_2C\underline{H}_3$), 7.83, 7.89, 7.91, 7.92 (12H, s, 4×OAc); TLC: *Rf* 0.53 (solvent A), 0.31 (B). *Anal.* Calcd. for $C_{21}H_{29}O_{15}IS$: C, 37.07; H, 4.30. Found: C, 37.36; H, 4.34.

2,2′,3,3′-Tetra-O-acetyl-1,6-anhydro-6′-deoxy-6′-iodo-4′-O-*p*-toluenesulfonyl-β-maltose (12)——A solution of **10** (0.4 g) and NaI (0.4 g) in acetonitrile (10 ml) was refluxed for 4 hr, filtered, and evaporated to dryness. The residue was dissolved in CH_2Cl_2–H_2O (30—20 ml). The organic layer was washed with 10% aq. $Na_2S_2O_3$ and H_2O, dried ($CaCl_2$), and evaporated to dryness to give an amorphous powder which was purified by column chromatography on silica gel with benzene–ether (2: 1, v/v) as eluant. Removal of solvent from the fractions containing a single spot on TLC gave an amorphous powder (275 mg, 73%), $[\alpha]_D^{27}$ +24.3° (*c*=1.40, $CHCl_3$); NMR ($CDCl_3$): 2.20—2.68 (4H, m, $SO_2C_6\underline{H}_4CH_3$), 7.55 (3H, s, $SO_2C_6H_4C\underline{H}_3$), 7.90, 7.93, 7.96, 8.10 (12H, s, 4×OAc); TLC: *Rf* 0.66 (solvent A), 0.46 (B). *Anal.* Calcd. for $C_{27}H_{33}O_{15}IS$: C, 42.87; H, 4.39. Found: C, 42.90; H, 4.04.

2,2′,3,3′-Tetra-O-acetyl-1,6-anhydro-6′-deoxy-4′-O-methanesulfonyl-β-maltose (13)——Compound **11** (2.7 g) was dissolved in AcOEt (270 ml) containing pyridine (1 ml) and hydrogenated over Raney Ni catalyst (freshly prepared from 27 g of alloy) at room temperature under atmospheric pressure; the theoretical amount of hydrogen was absorbed for 5 hr. After removal of the catalyst, the combined filtrate and washings were evaporated to dryness. The residue was dissolved in CH_2Cl_2 (100 ml), washed with 10% aq. $Na_2S_2O_3$ and H_2O, dried ($CaCl_2$), and evaporated to dryness, giving a sirup which crystallized from EtOH (2 g, 91%), mp 184—186°, $[\alpha]_D^{25}$ +34° (*c*=1, $CHCl_3$); NMR ($CDCl_3$): 6.96 (3H, s, $SO_2C\underline{H}_3$), 7.82, 7.91, 7.93, 7.94 (12H, s, 4×OAc), 8.65 (3H, d, $J_{5',6'}$=6 Hz, $C_{5'}$-$C\underline{H}_3$); TLC: *Rf* 0.48 (solvent A), 0.22 (B). *Anal.* Calcd. for $C_{21}H_{30}O_{15}S$: C, 45.49; H, 5.45. Found: C, 45.20; H, 5.50.

2,2′,3,3′-Tetra-O-acetyl-1,6-anhydro-6′-deoxy-4′-O-*p*-toluenesulfonyl-β-maltose (14)——Compound **12** (100 mg) was similarly hydrogenated as for **11** to afford the corresponding 6′-deoxy derivative. Purification by column chromatography with CH_2Cl_2–acetone (20: 1, v/v, 50 ml) as eluant gave **14** as an amorphous powder (60 mg, 72%), $[\alpha]_D^{24}$ +16.5° (*c*=1.07, $CHCl_3$); NMR ($CDCl_3$): 2.12—2.64 (4H, m, $SO_2C_6\underline{H}_4CH_3$), 7.52 (3H, s, $SO_2C_6H_4C\underline{H}_3$), 7.85, 7.89, 7.93, 8.10 (12H, s, 4×OAc), 8.73 (3H, d, $J_{5',6'}$=6 Hz, $C_{5'}$-$C\underline{H}_3$); TLC: *Rf* 0.59 (solvent A), 0.38 (B). *Anal.* Calcd. for $C_{27}H_{34}O_{15}S$: C, 51.42; H, 5.43. Found: C, 51.42; H, 5.44.

2,3-Di-O-acetyl-1,6-anhydro-4-O-(2,3-di-O-acetyl-4,6-di-O-benzoyl-α-D-galactopyranosyl)-β-D-glucopyranose (15)——A mixture of **9** (2.5 g) and sodium benzoate (2.5 g) in HMPA (50 ml) was heated at 100—110° for 20 hr, then poured into ice–H_2O (300 ml), and extracted with AcOEt (100 ml×3); the combined extracts were washed with H_2O (50 ml×3), dried ($MgSO_4$), and evaporated to dryness. The residue was purified by column chromatography on silica gel successively with CH_2Cl_2 (180 ml) and CH_2Cl_2–acetone (30: 1 and 20: 1, v/v, each 240 ml) as mobile phases. Removal of solvent from the combined fractions containing a single spot on TLC gave an amorphous powder (1.93 g, 72%), $[\alpha]_D^{26}$ +58.8° (*c*=0.71, $CHCl_3$); NMR ($CDCl_3$): 1.89—2.59 (10H, m, 2×$COC_6\underline{H}_5$), 7.81, 7.89, 7.93, 8.02 (12H, s, 4×OAc); TLC: *Rf* 0.64 (solvent A), 0.52 (B). *Anal.* Calcd. for $C_{34}H_{36}O_{16}$: C, 58.29; H, 5.18. Found: C, 58.31; H, 5.44.

2,3-Di-O-acetyl-1,6-anhydro-4-O-(2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl)-β-D-glucopyranose (16)—To a suspension of **15** (1.86 g) in dry MeOH (25 ml) was added methanolic 1 N sodium methoxide (1.2 ml). After stirring for 1 hr, the mixture was kept overnight at 5°, neutralized with AcOH, and evaporated to dryness. The residue was treated with Ac_2O (15 ml) and pyridine (15 ml), kept overnight at 5°, and then poured into ice-H_2O (160 ml). The mixture was extracted with CH_2Cl_2 (30 ml×3); the combined extracts were washed with cold dil. H_2SO_4, saturated $NaHCO_3$, and H_2O, dried ($CaCl_2$), and evaporated to dryness, giving a sirup which crystallized from EtOH (1.2 g, 77%), mp 132—133°, $[\alpha]_D^{23}$ +54.5° (*c*=1.1, $CHCl_3$); NMR ($CDCl_3$): 7.84, 7.86, 7.90, 7.97, 8.01 (18H, s, 6×OAc); TLC: *Rf* 0.44 (solvent A), 0.30 (B). *Anal.* Calcd. for $C_{24}H_{32}O_{16}$: C, 50.00; H, 5.60. Found: C, 49.90; H, 5.50.

1,6-Anhydro-4-O-α-D-galactopyranosyl-β-D-glucopyranose (17)——To a suspension of **16** (150 mg) in dry MeOH (15 ml) was added methanolic 0.3 N sodium methoxide (0.5 ml). The mixture was stirred for 1 hr at room temperature and kept overnight. After neutralization [Amberlite IR-120 (H^+)] and evaporation afforded a sirup which crystallized from MeOH–acetone (73 mg, 87%), mp 197—200°, $[\alpha]_D^{26}$ +104.7° (*c*=1.41, H_2O); TLC: *Rf* 0.45 (solvent C). *Anal.* Calcd. for $C_{12}H_{20}O_{10}$: C, 44.44; H, 6.22. Found: C, 44.33; H, 6.21.

PPC of Acid Hydrolyzate of 17——A mixture of **17** (10 mg) and 1 N H_2SO_4 (1 ml) was heated at 95° for 5 hr. After neutralization with $BaCO_3$, the salts were removed by filtration and washed with hot EtOH. The combined filtrate and washings were evaporated to dryness. A part of the residue was dissolved in H_2O, in which galactose (*Rf* 0.37) and glucose (0.40) were identified by PPC (solvent D).

Ratio of Galactose against Glucose in Acid Hydrolyzate of 17——The conditions of GC analysis were as follows.[24] A Shimadzu GC-4BPTF, equipped with a flame ionization detector and a stainless column (200×0.3 cm) packed with 0.5% OV-1 on Gas Chrom Q (100—200 mesh) were employed. Column oven temperature was programmed from 110 to 162° at 3°/min, N_2 gas flow rate was 20 ml/min, and flame ionization detector was carried out at 250°. Mannitol was used as the internal standard.

24) S. Arakawa, T. Chiba, and S. Tejima, *Seikagaku*, **46**, 795 (1974).

Completely dried hydrolyzate of **17**, which had been used in PPC, was trimethylsilylated,[25] injected, and operated under the conditions mentioned above. Galactose and glucose were identified in the ratio of 1: 1. Relative retention times: galactose (0.80, 0.84, 0.92), glucose (0.89, 1.10), mannitol (1.00).

1,2,3,6-Tetra-O-acetyl-4-O-(2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl)-α-D-glucopyranose (18)——Compound **16** (0.85 g) was dissolved in acetolysis mixture (40 ml, 1: 70: 30, v/v, H_2SO_4–Ac_2O–AcOH). After stirring for 2 hr at room temperature, the mixture was poured into ice-H_2O (400 ml), stirred for 2 hr, and extracted with CH_2Cl_2 (50 ml×2); the combined extracts were washed with saturated $NaHCO_3$ and H_2O, dried ($CaCl_2$), and evaporated to dryness, giving a sirup. It was dissolved in CH_2Cl_2 (1 ml) and column chromatographed on silica gel with ether as eluant. Removal of solvent from the fractions containing a single spot on TLC gave an amorphous powder (0.5 g, 50%), $[\alpha]_D^{27}$ +117° (c=1.14, $CHCl_3$); NMR ($CDCl_3$): 3.77 (1H, d, $J_{1,2}$=4 Hz, C_1-H), 7.78, 7.86, 7.89, 7.91, 8.01 (24H, s, 8×OAc); TLC: *Rf* 0.49 (solvent A), 0.37 (B). *Anal.* Calcd. for $C_{28}H_{38}O_{19}$: C, 49.56; H, 5.65. Found: C, 49.55; H, 5.36.

4-O-α-D-Galactopyranosyl-D-glucopyranose (19)——Deacetylation of **18** (0.49 g) was effected in the same way as for **16**. Recrystallization from MeOH gave pure **19** (0.18 g, 71%), mp 227—229° (decomp.), $[\alpha]_D^{26}$ +159.6° (c=1.02, H_2O), no mutarotation for 24 hr; TLC: *Rf* 0.39 (solvent C); PPC: *Rf* 0.27 (solvent D), 0.16 (E), 0.21 (F). *Anal.* Calcd. for $C_{12}H_{22}O_{11}$: C, 42.12; H, 6.48. Found: C, 42.33; H, 6.71.

2,3-Di-O-acetyl-1,6-anhydro-4-O-(2,3-di-O-acetyl-4-O-benzoyl-6-deoxy-α-D-galactopyranosyl)-β-D-glucopyranose (20)——A mixture of **13** (1.9 g) and dry sodium benzoate (1.9 g) in HMPA (40 ml) was heated at 110—115° for 24 hr. The mixture was treated in the same way as for **15** to give an amorphous powder (1.3 g, 67%), $[\alpha]_D^{26}$ +76.1° (c=1.36, $CHCl_3$); NMR ($CDCl_3$): 1.83—2.54 (5H, m, $C_6\underline{H}_5CO$), 7.81, 7.89, 8.04 (12H, s, 4×OAc), 8.77 (3H, d, $J_{5',6'}$=6 Hz, $C_{5'}$-$C\underline{H}_3$); TLC: *Rf* 0.54 (solvent A), 0.41 (B).

2,3-Di-O-acetyl-1,6-anhydro-4-O-(2,3,4-tri-O-acetyl-6-deoxy-α-D-galactopyranosyl)-β-D-glucopyranose (21)——Deacylation and sequential acetylation of **20** (1.25 g) were effected in the same way as for **15**. Recrystallization from EtOH gave pure **21** (0.75 g, 66%), mp 140—141°, $[\alpha]_D^{24}$ +52.2° (c=1.02, $CHCl_3$); NMR ($CDCl_3$): 7.83, 7.84, 7.90, 7.91, 8.01 (15H, s, 5×OAc), 8.84 (3H, d, $J_{5',6'}$=6 Hz, $C_{5'}$-$C\underline{H}_3$); TLC: *Rf* 0.48 (solvent A), 0.36 (B). *Anal.* Calcd. for $C_{22}H_{30}O_{14}$: C, 50.97; H, 5.83. Found: C, 51.02; H, 6.05.

1,6-Anhydro-4-O-(6-deoxy-α-D-galactopyranosyl)-β-D-glucopyranose (22)——Deacetylation of **21** (0.15 g) was effected in the same way as for **16**. Recrystallization from MeOH–acetone gave pure **22** (80 mg, 88%), mp 192—194°, $[\alpha]_D^{26}$ +101.3° (c=0.47, H_2O); TLC: *Rf* 0.52 (solvent C). *Anal.* Calcd. for $C_{12}H_{20}O_9 \cdot 1/2H_2O$: C, 45.42; H, 6.67. Found: C, 45.40; H, 6.63.

PPC of Acid Hydrolyzate of 22——Authentic 6-deoxy-D-galactose was prepared by acid hydrolysis of methyl 6-deoxy-α-D-galactopyranoside.[11a] Acid hydrolysis of **22** and the working of the hydrolyzate were effected in the same way as those of **17** in which glucose (*Rf* 0.40) and 6-deoxy-D-galactose (0.50) were identified by PPC (solvent D).

1,2,3,6-Tetra-O-acetyl-4-O-(2,3,4-tri-O-acetyl-6-deoxy-α-D-galactopyranosyl)-α-D-glucopyranose(23)——Compound **21** (0.55 g) was dissolved in acetolysis mixture (25 ml) as for **16**. After stirring for 2 hr at room temperature, the mixture was poured into ice-H_2O (300 ml), stirred for further 1.5 hr, and the resulting precipitate was collected by filtration. Further crops of crystals were obtained from the filtrate after evaporation of the CH_2Cl_2-extracts, followed by crystallization with EtOH. Recrystallization from EtOH gave pure **23** (0.35 g, 54%), mp 186—189°, $[\alpha]_D^{25}$ +137.5° (c=1.1, $CHCl_3$); NMR ($CDCl_3$): 3.74 (1H, d, $J_{1,2}$=3.5 Hz, C_1-H), 7.77, 7.82, 7.86, 7.91, 7.94, 8.00, 8.01 (21H, s, 7×OAc), 8.88 (3H, d, $J_{5',6'}$=6 Hz, $C_{5'}$-$C\underline{H}_3$); TLC: *Rf* 0.53 (solvent A), 0.42 (B). *Anal.* Calcd. for $C_{26}H_{36}O_{17}$: C, 50.32; H, 5.84. Found: C, 50.70; H, 5.59.

4-O-(6-Deoxy-α-D-galactopyranosyl)-D-glucopyranose (24)——Deacetylation of **23** (0.24 g) was effected in the same way as for **16** to afford a hygroscopic, amorphous powder (0.11 g, 87%), $[\alpha]_D^{27}$ +128.3° (c=0.72, H_2O), homogeneous by TLC and PPC. TLC: *Rf* 0.43 (solvent C), PPC: *Rf* 0.37 (solvent D), 0.24 (E), 0.30 (F).

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25) C.C. Sweely, R. Bently, M. Makita, and W.W. Wells, *J. Am. Chem. Soc.*, **85**, 2497 (1963).