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FACILE SYNTHESIS OF 1,2-*trans*-*O*-ACETYL GLYCOSYL CHLORIDE DERIVATIVES OF CELLOBIOSE, LACTOSE, AND D-GLUCOSE

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ABSTRACT

Solutions of *O*-acetyl-α-glycosyl bromide derivatives of D-glucose, cellobiose, and lactose in hexamethylphosphoramide were converted into corresponding β-chlorides at room temperature by the action of lithium chloride. At 3:1 mM ratios of chloride ion to glycose, 5–10% w/v solutions of glycosyl bromide formed α- and β-chlorides in ratios of (or greater than) 1:19 within 2–13 min and produced crystalline β-chlorides in 70–80% yields. Anomeric compositions were determined by n.m.r. spectroscopy in hexamethylphosphoramide. Older methods of preparing 1,2-*trans*-*O*-acetylglycosyl chlorides, with aluminum chloride or titanium tetrachloride, gave the α- and β-cellobiosyl and -lactosyl chlorides in ratios that varied from 2:3 to 1:4 and reached 85–95% levels of β-chloride only with β-D-glucose pentaacetate. When hydrolyzed under conditions that controlled solution acidity, the β-cellobiosyl and -lactosyl chlorides each gave 2-hydroxy derivatives in yields that could be varied from 16 to 60%. Hepta-*O*-acetyl-2-*O*-methyl-α-cellobiose was prepared to demonstrate how these hydrolysis mixtures can be used to synthesize a 2-*O*-substituted derivative.

INTRODUCTION

Various methods have been used to prepare 1,2-*trans*-*O*-acylglycosyl halides[1–5]; two of the more successful were based on action of either titanium tetrachloride or aluminum chloride on 1,2-*trans*-*O*-acetylglycoses under conditions of kinetic control. In the nineteen-seventies, Igarashi and coworkers[6,7] synthesized β-D-glucosyl and -galactosyl chlorides by the reaction of tetraethylammonium chloride with various 2-*O*-substituted-α-D-glycosyl perchlorates derived from the corresponding α-chlorides or -bromides. Their work, which expands greatly the variety of compounds capable of being converted into 1,2-*trans*-glycosyl chlorides, is built on an extensive series of investigations by other groups[5,8–12] into the ability of *O*-acylglycosyl halides to undergo nucleophilic displacement reactions in solutions containing ionic halides.

*Mention of firm names or trade products does not imply that they are endorsed or recommended by the U.S. Department of Agriculture over other firms or similar products not mentioned.

In an effort to prepare the hepta-*O*-acetyl-β-cellobiosyl and -lactosyl chlorides, previously unreported derivatives capable of selective conversion into compounds having a free hydroxyl group at C-2, we evaluated three potential methods of synthesis: action of (*a*) aluminum chloride or (*b*) titanium tetrachloride on octa-*O*-acetyl-β-cellobiose and -lactose, as well as action of (*c*) lithium chloride on solutions of the hepta-*O*-acetyl-α-cellobiosyl and -lactosyl bromides in hexamethylphosphoramide (HMPA).

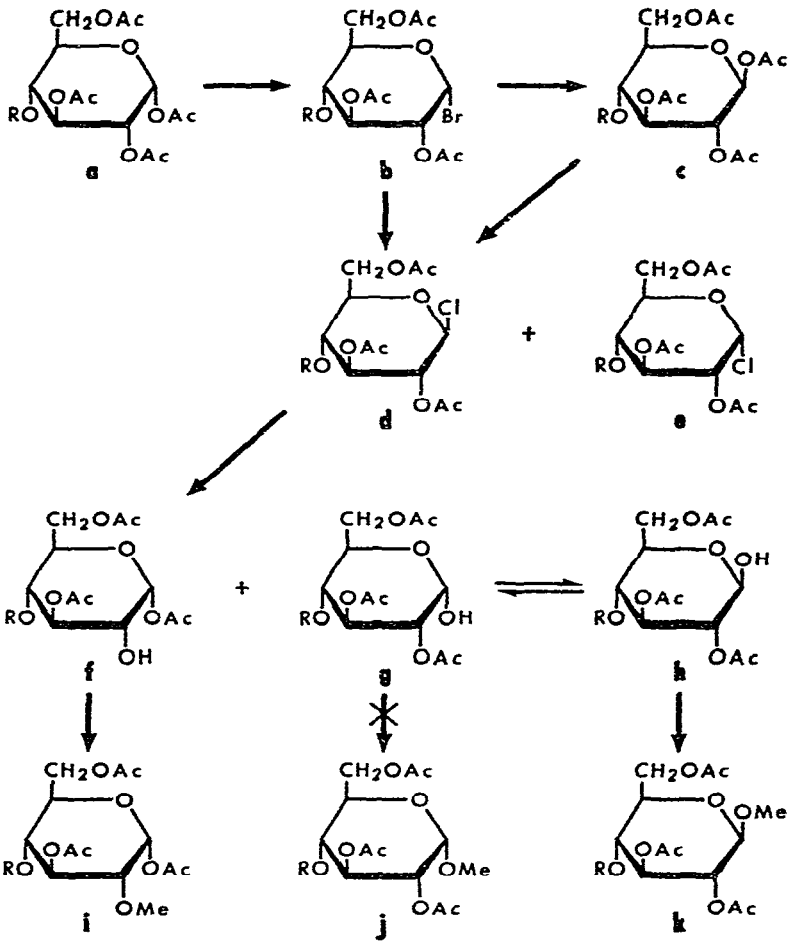
DISCUSSION

Even under mild reaction-conditions, either aluminum chloride or titanium tetrachloride acting on 1,2-*trans*-*O*-acetylglycoses produces mixtures of the 1,2-*cis*- and -*trans*-*O*-acetylglycosyl chlorides, the content of *cis* isomers varying from 5 to 40% of the total product-mixture for reactions derived from **1c** to **4c** (see Scheme). Although the levels of *cis*-glycosyl chlorides increase slightly when more metal chloride is added or the reaction is extended, conditions could not be found that convert **3c** or **4c** into **3d** or **4d** without isomerizing **d** products to **3e** or **4e**. Preparation of the pure D-gluco- or malto-analogs (**1d** and **2d**) depends on their separation from α-chloro forms by fractional crystallization, a technique unsuccessfully applied to **d, e** mixtures of **3** and **4**.

The anomeric configuration and approximate quantity of each component in the product-mixtures were determined in HMPA solutions by n.m.r. spectroscopy. HMPA is well suited for such analyses because it is free of solvent resonances within the range of τ 0 to 6.5, has two major resonances at τ 7.39 and 7.48, which can be used as internal-lock signals, and it separates H-1 resonances from one another and shifts them downfield from other methine resonances. Further, HMPA is purified easily, readily solubilizes glycosyl halides, and does not react appreciably during the analysis. By comparison, the perdeuterio derivatives of chloroform, benzene, acetone, and methyl sulfoxide used frequently with acetylated glycoses were unsatisfactory for various reasons: substrate insolubility (benzene), tendency for overlapping H-1 doublets of **1d–4d** with other methine resonances (chloroform and benzene), cost to purify by multiple distillations from phosphorus pentaoxide (acetone), or rapid reaction with glycosyl halides (methyl sulfoxide)[13]; in our experience the *cis* halide reacts far more slowly than the *trans*. For derivatives of **1–4**, the chemical shifts of H-1 resonances are listed in Table I.

Solutions of tetraethylammonium chloride in acetonitrile have been used to prepare **1d** by displacing either bromide or perchlorate ions from tetra-*O*-acetyl-α-D-glycosyl precursors[5,6]. Lemieux and Hayami[5] noted an 83% uptake of labelled chloride ion by **1b** after 90 min at 30°, but obtained **1d** in low yield. Igarashi and coworkers[6], however, isolated **1d** in 54% yield by substituting tetra-*O*-acetyl-α-D-glycopyranosyl perchlorate for **1b** and by decreasing the reaction time to 10 min at −20°.

Kinetic investigations into the action of dissolved ionic halides on selected



1, R = Ac
2, R = α-D-Glc $(OAc)_4$
3, R = β-D-Glc $(OAc)_4$
4, R = β-D-Gal $(OAc)_4$

TABLE I

H-1 CHEMICAL SHIFTS τ IN HEXAMETHYLPHOSPHORAMIDE[a]

Parent compound	*Derivative*[b]				
	b	**e**	**d**	**a**	**c**
1	3.13	3.48	3.88	3.84	3.94
2		3.51	3.80	3.90	3.94
3	3.19	3.57	3.92	3.91	4.15
4	3.24	3.58	3.94	3.91	4.14

[a]100 MHz; each as a doublet. [b]For α-, $J_{1,2} = 3.5$–4 Hz; for β-, $J_{1,2} = 8$–9 Hz.

1,2-*cis*- and -*trans*-*O*-acylglycosyl halides having O-2 equatorial established that the *cis* anomer (*a*, *e*) undergoes displacement with configurational inversion at C-1 far more rapidly than does the *trans* (*e*, *e*) form[5,10,11]. The rate at which *trans* forms are inverted to produce *cis* isomers is sufficiently rapid, however, to produce mixtures of **1d–4d** and -**e** products when **1b–4b** derivatives are treated with chloride salts unless: (*a*) conditions are adjusted to minimize the length of time newly formed **d** products are exposed to secondary, chloride-ion displacements or (*b*) the displacing agent is completely converted into a product, for example, a quaternary perchlorate salt[6], incapable of further interactions with **1d–4d** products.

Formation of hepta-*O*-acetyl-α-cellobiosyl and -lactosyl perchlorates with subsequent addition of equimolar amounts of a quaternary ammonium chloride salt was not attempted because the disaccharide bromides are insoluble and because the direct conversion of **3**- or **4b** into **3**- or **4d** uses less-expensive reagents and offers greater ease and speed.

Lithium chloride and hexadecyltrimethylammonium chloride were selected as displacing agents for preliminary experiments with **1b** in three solvents: acetonitrile, *N*,*N*-dimethylformamide (DMF), and HMPA. In solutions containing fixed amounts of **1b** and quantities of either displacing agent sufficient to provide a threefold molar excess, the reaction progress was monitored on a recording polarimeter. Neither ionic chloride could be evaluated in all three solvents; lithium chloride is relatively insoluble in acetonitrile, as is the quaternary salt in HMPA.

Data in the Experimental section demonstrate that hexadecyltrimethylammonium chloride is less efficient as a displacing agent than lithium chloride, the quaternary salt being least efficient in acetonitrile. As judged by the time each reaction required to reach a minimum specific rotation and by the magnitude of change in optical rotation at that point, lithium chloride in HMPA gave the best results. HMPA is known to form a complex with lithium chloride[14] and has been used for SN2 displacements with carbohydrate sulfonates[15,16].

When levels of **1b** were 5% (w/v), a 3:1 mM ratio of lithium chloride to **1b** offered nearly optimum conversion-rates for the formation of **1d**. The ratio of **1d** to **1e** exceeded 19:1, as judged by n.m.r. and by graphic estimates from minimum specific-rotation data.

The best way to prepare **3d** and **4d** was to increase the concentration of **3b** or **4b** to 10% while maintaining the 3:1 mM ratio of lithium chloride to either **b** derivative. N.m.r. spectroscopy showed that conversion of **3b** into **3d** was essentially complete at the point where the specific rotation reached a minimum value; the H-1 resonances for **3b** and **3e** could not be observed. Samples frozen and immediately processed at the point of minimum specific rotation had **d**:**e** ratios exceeding 19:1 after isolation, with average yields of 70–80%.

When hydrolyzed, the 1,2-*trans*-*O*-acetylglycosyl chlorides presumably pass through successive acetoxonium ion and orthoacid intermediates, with subsequent collapse to form 1-OH and 2-OH derivatives[17]. Additionally, the extent to which the 1-OH and 2-OH products are formed depends on the overall structure of the glycosyl

chloride, as well as the reaction conditions. The manner in which structural differences remote from the hydrolysis site may influence the ratio of hydrolysis products formed is not well understood. However, for a given glycosyl halide, more 2-OH product is formed in solutions that are highly acidic at the end of the reaction than in solutions (for example those containing pyridine or sodium acetate) capable of reacting with the hydrogen chloride generated by hydrolysis[18].

Hydrolyses of **3d** and **4d** were conducted in aqueous solutions of acetone, DMF, and pyridine. Progress of the hydrolyses was monitored by t.l.c., with the relative quantities of 1-OH and 2-OH derivatives being determined by g.l.c. of their mono-trimethylsilyl (Me_3Si) ethers. The results, and comparisons with data reported earlier[18] for **1d** and **2d**, are shown in Table II.

TABLE II

HYDROLYSES OF 1,2-*trans*-*O*-ACETYL-β-GLYCOPYRANOSYL CHLORIDES[a]

Aqueous solvent	*Compound*[b]							
	1d		**2d**		**3d**		**4d**	
	1-OH	*2-OH*	*1-OH*	*2-OH*	*1-OH*	*2-OH*	*1-OH*	*2-OH*
Acetone	31	69	60	40	40	60	50	50
N,*N*-Dimethylformamide	30	70	63	37	42	58	51	49
Pyridine	80	20	88	12	84	16	83	17

[a]Ratio of d–solvent–H_2O, 1:10:1 (w/v/v) at 25° for **1d** and **2d**, 23° for **3d** and **4d**. [b]Data for **1d** and **2d** from Ref. 18.

The ease with which **3d** and **4d** are converted into mixtures rich in 2-OH derivatives (**3f**, **4f**) allows the facile production of derivatives substituted selectively at O-2, provides compounds of potential interest as models for enzyme-substrate investigations, and either generates receptors for syntheses of oligosaccharides or supplies reaction-intermediates useful in chemical syntheses.

The chemical nature of **3f** is not well defined, as other workers[19,20] have failed to report concurring melting-point and specific-rotation data. Fortunately, a preliminary separation of **3f** from the 1-OH forms present in hydrolysis mixtures is not necessary for making 2-*O*-substituted derivatives. For example, a mixture of **3f**, **3g**, and **3h** was treated with diazomethane under conditions that selectively convert **3f** and **3h** to methoxyl derivatives. Because **3h** is present in small amounts, **3i** was readily separated from **3k** in a 40% yield by fractional crystallization. Deacetylation produced amorphous 2-*O*-methyl cellobiose, as Lindberg and coworkers[21] reported.

EXPERIMENTAL

General methods. — N.m.r. spectra were measured at 100 MHz on a Varian HA-100 spectrometer with tetramethylsilane ($\tau = 10.0$) as the internal standard.

Solute concentrations were approximately 20% (w/v) unless noted otherwise. Chemical shifts and coupling constants are first-order, measured directly from spectral spacings. A Hewlett–Packard research chromatograph, Model 5750 equipped with an electronic integrator, was used for g.l.c. The column was 1/8-in. o.d. × 2.5 ft stainless steel packed with 3% OV-17 on Gas Chrom Q (80–100 mesh). Column programming was isothermal, with helium as the carrier gas and flame ionization for detection.

Melting points were determined in capillary tubes. Optical rotations were measured at 546.1 nm in a 0.2-dm cell with a Bendix polarimeter, Model 1169. Multiplication by 0.85 allows comparison of 546.1 nm values with those measured at the D line of a sodium lamp. Solutions were evaporated under diminished pressure. Precoated plates of Silica Gel F-254 (0.25-mm layer thickness, E. Merck, Darmstadt, Germany) were used for t.l.c. For column chromatography, Baker analyzed silica gel No. 3405 (J. T. Baker Chemical Co.) was used without pretreatment. All chromatographic solvents were proportioned on a v/v basis. HMPA (Eastman Organic Chemicals) was dried over calcium hydride, filtered, distilled under diminished pressure and then stored in the dark over calcium hydride. Chloroform (ACS grade) was stored for 2–3 days in the dark over calcium hydride before use with titanium tetrachloride. Anhydrous lithium chloride was dissolved in HMPA by stirring overnight at 25° with subsequent dilution to 2% (w/v) solutions. Hexadecyltrimethylammonium chloride was recrystallized from acetone and dried at 60° in a vacuum oven.

Starting materials. — For **1–4**, derivatives **a–c** were prepared by methods described elsewhere[22–26].

Action of aluminum chloride. — Three samples of a derivative from the **1c–4c** series (**1c**, 1.2 g; **2c–4c**, 2 g) were weighed into 2-dram, stoppered bottles, dissolved in dichloromethane (**1c**, 5 ml; **2c–4c**, 3 ml), and then treated with anhydrous aluminum chloride (**1c**, 0.25 g; **2c–4c**, 0.5 g). Each bottle was shaken vigorously in a horizontal plane at 25° (**1c**, 45 min; **2c–4c**, 4 h), and then the mixtures were dissolved in chloroform (250 ml) and washed three times with 200-ml slurries of ice and water. The organic phase was stirred for 1 h with anhydrous calcium chloride, filtered, and evaporated; the residues were examined by n.m.r. spectroscopy in HMPA. Conversion of **1c–4c** into the corresponding **d**, **e** product mixtures was complete, with levels of **1d** reaching 90–95% and **2d–4d** averaging 60–80%, as judged by relative peak areas. For **3c**, two- and four-fold increases of aluminum chloride gave ratios of **3d**:**3e** similar to those found at the 0.5-g level of aluminum chloride. Attempts to separate **d**, **e** mixtures of **3** and **4** by fractional crystallization were unsuccessful, but **1d** and **2d** crystallized readily from ether[4].

Action of titranium tetrachloride. — Pacsu's synthesis[27] of **4e** was adapted for use with **1c–4c**. Duplicate 3-g samples of **1c–4c** were dissolved in solutions of titanium tetrachloride in chloroform (**1c**, 0.9 ml in 40 ml; **2c–4c**, 0.5 ml in 20 ml) and protected from moisture. One member of each series was kept at 25° for the reaction period (**1c**, 15 min; **2c–4c**, 1 h) and the other was refluxed on a steam bath (**1c**, 45 min; **2c–4c**, 2 h). Product mixtures were isolated as already described and examined by

n.m.r. spectroscopy in HMPA. Conversion into mixtures of **1d–4d**, and -**e** products was complete for each series. Levels of **1e–4e** averaged 10–15% in the reaction mixtures at 25° and reached the expected 95–100% levels in the refluxed solutions. Product mixtures weighed 2.4–2.8 g, yielding **1d**, **2d**, and mixtures of **3d**, **e** and **4d**, **e** when crystallized. Crude samples of **1e–4e** served as n.m.r. standards without further purification.

Displacements of bromide ion from **1–4b**. — *General procedure.* All preliminary reactions were performed in 10-ml volumetric flasks containing 0.1–1.0 g of **1b–4b** and sufficient displacing agent to provide millimolar ratios of agent to **b** that varied from 1:1 to 4:1. Samples of **1b–4b** were either dissolved directly in solvents containing the displacing agent or taken up in the solvent of choice and made to volume with a calculated amount of stock solution containing the agent being tested. All samples were shaken vigorously 15–60 sec and then were monitored for changes in optical rotation until a minimum value was reached, at which time the reaction was stopped.

When products were to be isolated, samples were diluted immediately with 2 vol. of ethyl acetate, chilled previously in a solid carbon dioxide–acetone bath, and then stored in the bath until processing. Water-soluble materials were removed by washing with mixtures of ice and water as already described.

Approximate compositions for solutions of lithium chloride in HMPA were determined with the aid of a graph plotting specific rotation as a function of **b**, **d** composition. The specific-rotation values of pure **b** and **d** samples of the mono- or disaccharide being investigated were connected by a straight line for this purpose, disregarding contributions made by the small differences in the specific rotations of chloro and bromo analogs. Values used for **d** samples were measured in the presence of lithium chloride (3:1 moles/mole) because the salt significantly depressed the specific rotation below that recorded for the same compound in pure HMPA. For mixtures rich in the **d** product, values from n.m.r. and graphic techniques were nearly equal (±2–5% for **d**). Whether or not the specific rotation of **b** samples is altered by lithium chloride is unknown, but extrapolations of logarithmic plots of rate data suggest that any shift in rotation caused by the salt is less than 5–10% of the value in pure HMPA.

A. Two of four 0.3-g samples of **1b** were dissolved and made up to volume with 7% solutions of hexadecyltrimethylammonium chloride in either acetonitrile (I) or DMF (II). The third and fourth samples were dissolved in solutions containing lithium chloride (93 mg) in either DMF (III) or HMPA (IV). Molar ratios of chloride to **1b** were approximately 3:1 for each solution. Estimated levels of **1d** at the points of minimum optical rotation were: I, +104° after 90 min, 55%; II, +48°, 50 min, 75%; III, +33°, 38 min, 80%; IV, −4°, 3.4 min, 95%. Two 0.6-g samples of **1b**, when dissolved in solutions of DMF or HMPA containing 186 mg of lithium chloride, reached minimum specific rotations of +25° and −5° within 24 min and 2.1 min, respectively.

B. Four 0.2-g samples of **1b** were dissolved and made up to volume in solutions of lithium chloride–HMPA in which the chloride:**1b** ratios were varied from 1:1 to

4:1 in one-unit steps. Elapsed times required to reach specific rotations of +48° and +19° (estimated to be the points at which levels of **1d** reached 75% and 87%), and the times at which minimum specific rotations were recorded are: 1:1, 188 sec, 839 sec, 1,575 sec (+1.3°, 90–93% **1d**); 2:1, 74 sec, 237 sec, 505 sec (−2.3°, 92–95%); 3:1, 59 sec, 144 sec, 275 sec (−3.6°, 93–96%); 4:1, 39 sec, 84 sec, 217 sec (−5.7°, 94–97%).

C. Four samples of **1b**, weighing 0.1, 0.3, 0.5, and 0.67 g, respectively, were dissolved and made up to volume in lithium chloride–HMPA at a 3:1 ratio. Estimated conversion of **1b** into **1d** was 95% or greater for each reaction, as judged from the minimum specific rotations: 0.1 g, −4.1° after 420 sec; 0.3 g, −3.9°, 205 sec; 0.5 g, −3.8°, 135 sec; 0.67 g, −5.2°, 120 sec.

D. Preliminary experiments established that **3b** and **4b** react more slowly with lithium chloride in HMPA than **1b** does, but that the degree of conversion into **3d** and **4d** also reaches or exceeds 95% when concentrations of carbohydrate are increased to 10% (w/v) and a 3:1 mM ratio of lithium chloride to **b** is maintained.

E. Solutions of lithium chloride in HMPA (2%, 150 ml) were added to stoppered, 500-ml flasks containing 10 g of **1b** or 15 g of **3b** or **4b** and shaken vigorously for 60–120 sec. At the point of minimum specific rotation, each mixture was diluted and stored as described. Minimum specific rotations were: **1**, −5° within 2 min; **3**, −28° within 13 min; and **4**, −8° within 7.5 min. The cold solutions were diluted to 1,000 ml with additional ethyl acetate and washed once with 800 ml of ice and water. The aqueous layer was extracted with 250 ml of fresh ethyl acetate, and the combined extracts were washed three times more before stirring for 1 h over anhydrous calcium chloride (200 g). Each solution was filtered through talc and evaporated under diminished pressure below 45°. Small amounts (1–2 ml) of HMPA were present in each residue.

1d. — The crude product contained 10% of **1e** and was free from **1b** (n.m.r.). One crystallization from ether gave 6.2 g (69% of pure **1d**; $[\alpha]_{546}^{24}$ −10.9° (*c* 4.6, HMPA). In the presence of lithium chloride (2%), the $[\alpha]_{546}^{24}$ was −15° (*c* 5.2, HMPA).

3d. — The crystalline isolate was stored under ether (100 ml) for 24 h at −5° and then filtered. The crude **3d** (11.2 g, 80%) was free of **3b** and **3e** (n.m.r.) and was satisfactory for most uses. Recrystallization from ethyl acetate–ether gave pure **3d**; m.p. 172–173°, $[\alpha]_{546}^{22}$ −14.3 (*c* 4.3, HMPA). In the presence of lithium chloride (2%), the $[\alpha]_{546}^{23}$ was −32.7° (*c* 10.1, HMPA).

Anal. Calc. for $C_{26}H_{35}ClO_{17}$: C, 47.68; H, 5.39; Cl, 5.41. Found: C, 47.71; H, 5.63; Cl, 5.47.

4d. — The crude syrupy residue was free of **4b** and **4e** (n.m.r.). The crystalline product from ethyl acetate–ether was essentially pure **4d** (10.7 g, 76%), but contained 3–5% of an impurity that co-crystallized with **4d** and could not be separated from the product by repeated recrystallizations. Identity of the impurity, detected by a singlet at τ 3.30 in HMPA, is unknown. Trace amounts were detected in **3d** also. Crystalline **4d** softened at 70°, melting to form a clear froth at 76–78°, $[\alpha]_{546}^{25}$ −1.7° (*c* 5.3 in HMPA). In 2% lithium chloride, the $[\alpha]_{546}^{24}$ was −7.2° (*c* 4.2, HMPA).

Hydrolyses of **3d** *and* **4d**. — *A*. Samples (0.5 g) of **3d** or **4d** were weighed into 4-dram screw-capped bottles, dissolved in 5-ml portions of acetone, DMF, or pyridine; and then treated with 0.5-ml portions of water. Each homogeneous solution was allowed to react for 4 h at 23° and was monitored periodically by t.l.c. (ether, 2 ascents). Samples (0.2 ml) were removed at 1-h intervals, quenched in a solution of pyridine (1 ml), hexamethyldisilazane (1 ml), and chlorotrimethylsilane (0.5 ml), and analyzed by g.l.c. at 250°. The ratio of products at the end of each reaction is expressed as 1-OH:2-OH (**g**+**h**:**f**) (Table II).

B. A 10-g sample of **3d** was hydrolyzed at 25° in aqueous acetone (110 ml, 1:10 vol.) with added DMF (5 ml). After 3 h, the solution was diluted to 1,500 ml with ethyl acetate and freed of water-soluble components. The syrupy product-mixture (9.2 g) had a 1-OH:2-OH ratio of 2:3 (g.l.c.) and was used without further examination.

Methylation of **3f**. — Treatment of the mixture of **3f**, **3g**, and **3h** from procedure *B* with diazomethane in the presence of boron trifluoride etherate was accomplished as reported previously for a similar mixture of maltose analogs[18]. Conversion of **3f** and **3h** into the *O*-methyl derivatives, **3i** and **3k**, was essentially complete (g.l.c., 250°). After separation from unreacted starting materials on a 60×750 mm column of silica gel, the mixture of methylated products weighed 6.1 g. The syrupy mixture, which hardened when stored overnight under ether (50 ml) at −5°, was crystallized twice from ethanol to yield pure **3i** (3.9 g); m.p. 187.5–188.5°, $[\alpha]_{546}^{28}$ +60.1° (*c* 2.3, chloroform).

Anal. Calc. for $C_{27}H_{38}O_{18}$: C, 49.85; H, 5.89. Found: C, 49.55; H, 5.86.

N.m.r. data (benzene-d_6): τ 3.52 (doublet, $J_{1,2}$ 3.8 Hz, H-1), 4.30 (triplet, $J_{2,3} = J_{3,4}$ 10 Hz, H-3), 6.29 (triplet, $J_{4,5}$ 9.5 Hz, H-4), 6.83 (doublet of doublets, H-2), 6.93 (singlet, OMe), 8.07, 8.18, 8.27, 8.30 (2), 8.32, 8.43 (acetyl C-Me).

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