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Further examples of orthoesterification under kinetically controlled conditions Application to the selective acylation of sucrose, maltose and α,α-trehalose

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Abstract

Orthoesterification of sucrose with 1,1-dimethoxyethene under kinetic control gave 4,6-*O*-methoxyethylidenesucrose in 77% crude yield. Similar orthoesterification of maltose led essentially after acetylation to 1,2,3,6,2′,3′-hexa-*O*-acetyl-4′-6′-*O*-methoxyethylidenemaltose. Analogous treatment of α,α-trehalose gave 2,3,2′,3′-tetra-*O*-acetyl-4,6:4′,6′-di-*O*-methoxyethylidene-α,α-trehalose in 47% yield. The acid-catalyzed opening of these orthoesters was studied, and these reactions were shown to give disaccharides selectively protected by acetyl groups. © 1998 Elsevier Science Ltd.

Keywords: Orthoester; Orthoesterification; Ketene acetal; Disaccharides; Sucrose; Maltose; α,α-Trehalose

1. Introduction

Cyclic orthoesters have been reported as important intermediates in carbohydrate chemistry, and the best known of these are bicyclic 1,2-glycopyranosyl derivatives which may be prepared from glycosyl halides and have been used as intermediates in oligosaccharide synthesis [1]. A few orthoesters involving other positions have been mentioned in our previous papers [2,3]. These were easily prepared by a kinetically controlled orthoesterification of monosaccharides with 1,1-dimethoxyethene in *N*,*N*-dimethylformamide. This method provided access to orthoester sugar derivatives protected at positions different from those obtained by conventional orthoesterification with trimethyl orthoacetate. Thus, the reaction favored an initial attack at a primary hydroxyl group with subsequent ring closure involving the less sterically hindered hydroxyl group. Mild hydrolysis of these unusual orthoesters gave selectively acetylated monosaccharides [2–4]. In this paper we report the extension of this kinetically controlled orthoesterification to three disaccharides with biological and industrial importance, namely, sucrose, maltose and α,α-trehalose.

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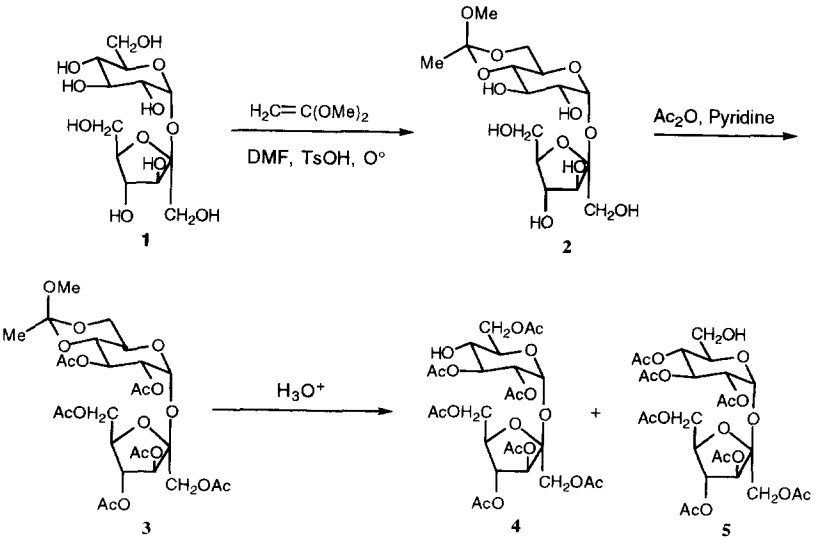
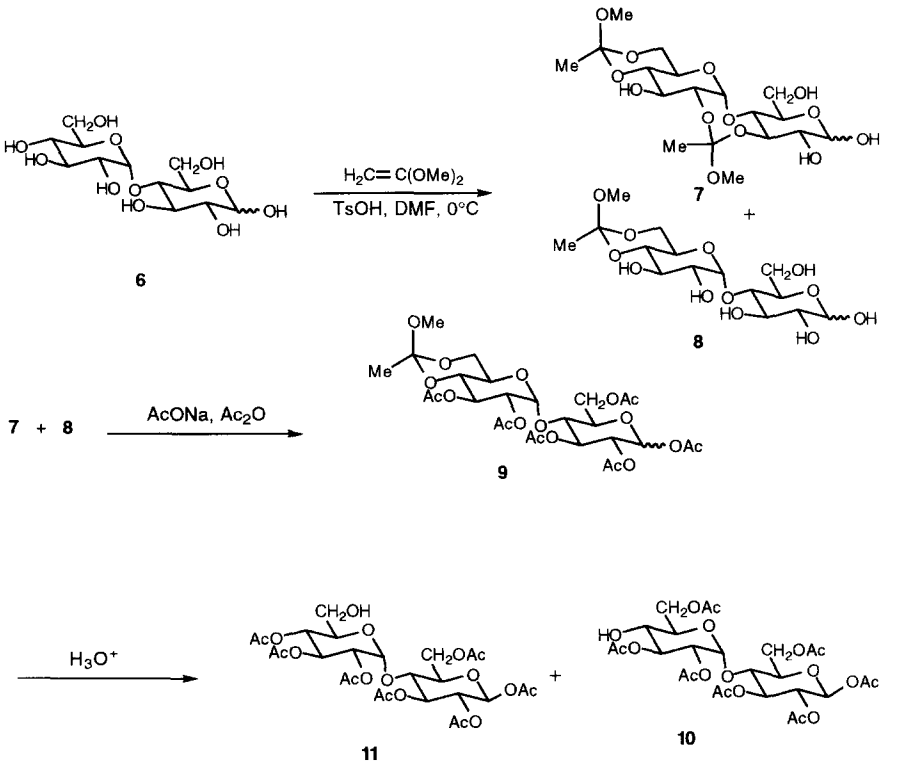
2. Results and discussion

Treatment of sucrose (**1**) (Scheme 1) with 1,1-dimethoxyethene in dry *N*,*N*-dimethylformamide at 0–5 °C in the presence of catalytic amount of *p*-toluenesulfonic acid afforded, after treatment, a clear colorless syrup. Purification of the crude product by column chromatography could not be performed without partial hydrolysis of the orthoester if the silica gel and the eluent were not carefully dried. Acetylation of the pure orthoester, followed by chromatographic purification, gave crystalline **3** for which the ^{1}H NMR data and physical constants were identical with those of the known [5] 2,3,1′,3′,4′,6′-hexa-*O*-acetyl-4,6-*O*-methoxyethylidenesucrose. In the ^{1}H NMR spectrum of **3** in deuteriobenzene, only resonances due to H-1, H-2, H-3, H-3′ and H-4′ were interpretable on a first-order basis. Partial hydrolysis of compound **3** was done with a 3:1 aqueous acetic acid solution and gave a mixture of two isomers. Their separation by column chromatography gave the pure 4-hydroxyl derivative **4** first in about 47% yield and then the 6-hydroxyl derivative **5** (yield 17%). Ballard et al. [6] reported that a mixture of hepta-*O*-acetylsucrose resulted from the deacetylation of a chloroform solution of octa-*O*-acetylsucrose on an aluminum oxide column. Amongst the products they identified 2,3,6,1′,3′,4′,6′-hepta-*O*-acetylsucrose (**4**) as a new component isolated with 2.7% yield. The synthesis of **4** was also reported from hepta-*O*-acetyl-6-*O*-tritylsucrose (**5**) by detritylation under conditions favorable for the migration of the 4-*O*-acetyl group to the 6-position [7,8]. Our method could be an excellent route to prepare compound **4** in good yield. The structures of **4** and **5** were confirmed by NMR spectroscopy and by their physical constants, which were similar to those of the literature [9]. In the spectra of **4** and **5**, the H-4 resonance appeared at relatively high field (3.52 and 5.06 ppm, respectively) in comparison with the H-4 signal for sucrose octaacetate, indicating that O-4 was not acetylated.

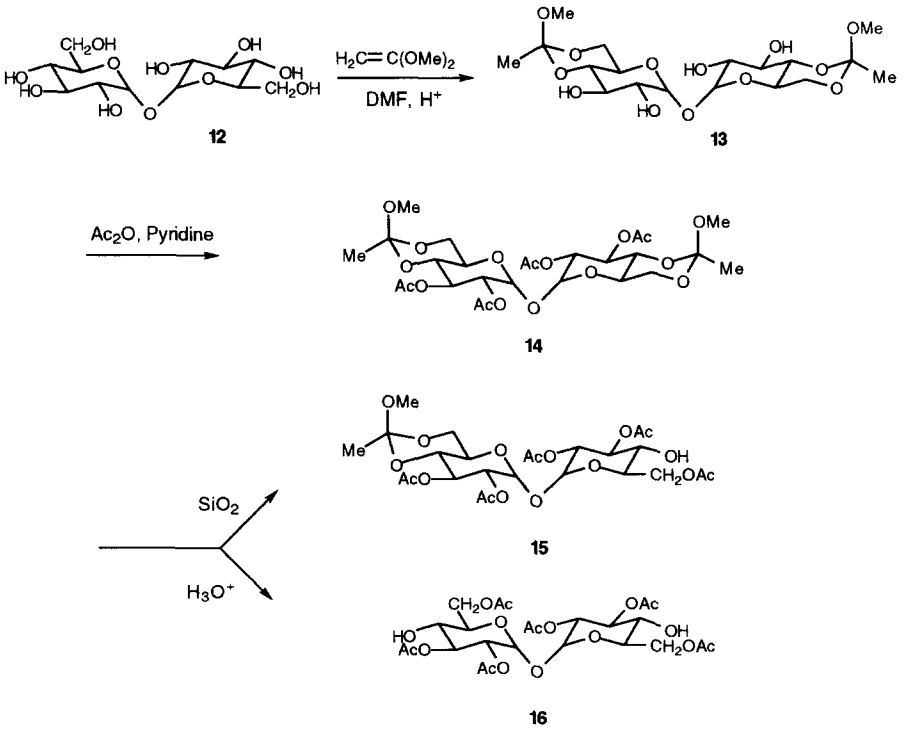
Orthoesterification of maltose **6** (Scheme 2) under the standard conditions with 2.5 molar equiv of 1,1-dimethoxyethene gave a mixture of two products. The ^{1}H NMR spectrum of the crude mixture revealed signals of orthoester groups. Intensities of these signals suggested that the mixture contained 4′,6′-*O*-methoxyethylidene-α,β-maltose (**8**) as the principal product that was accompanied by a very small amount of 3,2′:4′,6′-di-*O*-methoxyethylidene-α,β-maltose (**7**). As a direct separation of the two derivatives could not be accomplished, the crude mixture of **7** and **8** was acetylated with hot acetic anhydride–sodium acetate, and chromatography on silica gel allowed the isolation of a crystalline compound **9** (yield 49%) as the main product, which was identified by NMR spectroscopy. The spectrum of **9** in dry $CDCl_3$ showed at lower field a narrow doublet at δ 6.25 ($J_{1\alpha,2}$ = 3.7 Hz, H-1) and a wide doublet at δ 5.75 ($J_{1\beta,2}$ 8.2 Hz), corresponding to the α and β



Scheme 1.



Scheme 2.



Scheme 3.

anomers. Their relative intensity indicated an α,β anomeric ratio of 1:9. Partial hydrolysis of **9** was performed with aqueous acetic acid and gave a mixture of products. Only the two main components **10** and **11** could be isolated in reasonable yields by chromatography on silica gel, and these were identified by NMR spectroscopy as 1,2,3,6,2′,3′,6′-hepta-*O*-acetyl-β-maltose (**10**) and 1,2,3,6,2′,3′,4′-hepta-*O*-acetyl-β-maltose (**11**).

The disaccharide α,α-trehalose (**12**) (α-D-glucopyranosyl-α-D-glucopyranoside) is found in many fungi, in plants, and in the blood of most insects [10], where it probably plays an important part in carbohydrate metabolism [11]. Because of the symmetry of the molecule, the behavior of α,α-trehalose (**12**) compares with that of methyl α-D-glucopyranoside. Consequently, symmetrical 4,6:4′,6′-diorthoester **13** (Scheme 3) is normally produced in high crude yield (98%) when α,α-trehalose (**12**) (previously dried according to Birch [12]) is treated with 1,2-dimethoxyethene. Acetylation of **13** with acetic anhydride–pyridine gave a quantitative yield of the crystalline acetate **14**. The ^{1}H NMR spectrum of the acetate **14** showed H-1, H-2 and H-3 signals clearly observable at low field as a doublet, a quartet, and a triplet, respectively. When this acetate was purified on a column of silica gel, it was only partly isolated as a pure compound (yield 46%), and another more polar product was isolated (24%) and identified as the nonsymmetrical orthoester **15** with a free OH group at position 4. The selective introduction of a functional group on only one of the two glucosyl moieties to give a nonsymmetrical derivative of trehalose is determined to be quite difficult [13–15]. Therefore, this unexpected selective hydrolysis of **14** with SiO_2 is very interesting and opens the way for other transformations of trehalose. Hydrolysis of both orthoester groups of **14** was performed with equeous acetic acid and gave exclusively the symmetrical diol OH-4,4′ **16**. Analysis of the ^{1}H NMR spectrum of **16** in dimethyl sulfoxide showed in particular one doublet corresponding to the secondary OH group, which disappeared after addition of deuterium oxide. The simplicity of the sequence orthoesterification–hydrolysis confirms the interest of this method in the selective preparation of key synthetic intermediates in the chemical transformation of disaccharides.

3. Experimental

General methods.—Melting points were determined on a Büchi apparatus. Evaporations were performed under diminished pressure. Optical rotations were measured at room temperature on a Perkin–Elmer 141 polarimeter in 1 dm tubes (*c*, 1 at 20 °C). Column chromatography was performed with Silica Gel 60 (E. Merck 70–230 mesh) or 60A (E. Merck 35–70 mesh). TLC was carried out on precoated plates (E. Merck 5724), and compounds were visualized with a spray of 30% sulfuric acid in water, followed by heating. All organic solvents were dried and distilled. Pyridine was dried and distilled under reduced pressure. Me_2NCHO was stirred over CaH_2 and distilled under reduced pressure. Anhydrous Na_2SO_4 was used to dry organic extracts. ^{1}H NMR (300 or 400 MHz) and ^{13}C NMR (75 or 100 MHz) spectra were recorded on a Bruker MSL 300 or a AC 400 spectrometer. Chemical shift data are given in δ-units (ppm) measured downfield from internal Me_4Si, and spin–spin coupling values are in Hz (Tables 1–4). Microanalyses were performed by the Service Central d'Analyses du CNRS in Lyon, France.

Preparation of 4,6-O-methoxyethylidenesucrose (**2**).—To a suspension of sucrose (**1**) (5.0 g, 14.6 mmol), in dry Me_2NCHO (50 mL), containing 1 g of Sikkon (Fluka dehydrating agent) maintained at 0–5 °C (ice bath), were added 1,1-dimethoxyethene (2.5 g, 29.2 mmol) and *p*-toluenesulfonic acid (20 mg). The mixture was stirred magnetically at 0–5 °C until the monitoring by TLC (5:3:2 BuOH–EtOH–water) indicated that all starting material had disappeared (4 h), whereupon anhydrous sodium carbonate was added, and the cold mixture was stirred for one more hour. The mixture was filtered and concentrated to give a syrup. Fast purification of small portions of syrup on column chromatography (5:1 EtOAc–MeOH) gave pure **2** (4.45 g, 77%): $[\alpha]_D^{20}$ +41° (MeOH); ^{13}C NMR (Me_2SO-d_6): δ 111.93 (Me*C*OMe), 104.16 (C-2), 92.50 (C-1), 82.58 (C-5′), 76.73 (C-3′), 73.95 (C-4′), 73.00 (C-2), 72.37 (C-3), 69.28 (C-5), 62.21 (C-4), 62.02 (C-1′), 61.91 (C-6′), 61.23 (C-6), 50.12 (MeCO*Me*), 21.73 (*Me*COMe).

Preparation of 2,3,1′,3′,4′,6′-hexa-O-acetyl-4,6-methoxyethylidenesucrose (**3**).—Compound **2** (5 g, 12.5 mmol) was dissolved in dry pyridine (50 mL), and Ac_2O (15.3 g, 150.6 mmol) was added portionwise to the solution. The mixture was stirred at 0 °C and was then kept overnight at room temperature. The mixture was poured onto ice containing Na_2CO_3, and the product was extracted into CH_2Cl_2. The organic solution was washed with a saturated aqueous $NaHCO_3$ solution. After drying, the extracts were evaporated, and the residue was coevaporated with toluene to give **3** as an amorphous solid that was

Table 1
^{1}H NMR spectral data for sucrose derivatives **2** and **3**

Compound	Solvent	^{1}H NMR, δ														
		H-1	H-2	H-3	H-4	H-5	H-6a, H-6b	H-1′	H-3′	H-4′	H-5′	H-6′ a, H-6′b	OH	OMe	Me	OAc
2	Me_2SO-d_6	5.20 (d) ($J_{1,2}$ 3.9)	4.78 (dd) ($J_{2,3}$ 9.9)	5.15–5.00 (m)	5.15–5.00 (m)	← 3.90–3.35 (m) →			← 5.15–5.00 (m) →		← 3.90–3.35 (m) →		4.90 (m)	3.20 (s)	1.38 (s)	
3	$CDCl_3$	5.65 (d) ($J_{1,2}$ 3.9)	4.78 (dd) ($J_{2,3}$ 9.9)	5.36 (t) ($J_{3,4}$ 9.9)	3.90 (t) ($J_{4,5}$ 9.9)	← 4.35–3.76 (m) →			5.41 (d) ($J_{3',4'}$ 5.7)	5.34 (t) ($J_{4',5'}$ 5.7)	← 4.35–3.76 (m) →			3.28 (s)	1.43 (s)	2.08 (s) 2.03 (s) 2.00 (s) 2.10 (s) 2.15 (s) 2.00 (s)

Table 2
^{1}H NMR spectral data for sucrose derivatives **4** and **5**

Compound	Solvent	^{1}H NMR, δ												
		H-1	H-2	H-3	H-4	H-5	H-6a, H-6b	H-1′	H-3′	H-4′	H-5′	H-6′a H-6′b	OH	OAc
4	$CDCl_3$	5.61 (d) ($J_{1,2}$ 3.6)	4.78 (d) ($J_{2,3}$ 10.0)	5.38 (t) ($J_{3,4}$ 10.0)	3.52 (t) ($J_{4,5}$ 10.0)	4.47 (m)	4.11 (dd) ($J_{6a,6b}$ 10.0)	4.32 (d) ($J_{1'a,1'b}$ 14.0)	5.45 (d) ($J_{3',4'}$ 5.7)	5.34 (t) ($J_{4',5'}$ 5.7)	← 4.27–4.04 (m) →		3.24 (d) ($J_{OH,4}$ 5.8)	2.10 (4) (s), 2.12 (s), 2.13 (s), 2.14 (s)
5	$CDCl_3$	5.68 (d) ($J_{1,2}$ 3.7)	4.86 (dd) ($J_{2,3}$ 10.2)	5.43 (t) ($J_{3,4}$ 10.2)	5.06 (t) ($J_{4,5}$ 10.2)	4.40–4.10 (m)	3.52 (m)	4.40–4.10 (m)	5.45 (d) ($J_{3',4'}$ 5.5)	5.36 (t) ($J_{4',5'}$ 5.5)	4.40–4.10 (m)	3.52 (m)	2.70 (m)	2.02 (s), 2.05 (s), 2.08 (2) (s), 2.09 (2) (s), 2.13 (s)

Table 3
^{1}H NMR spectral data for maltose derivatives **8–11**

Compound	Solvent	^{1}H NMR, δ														
		H-1	H-2	H-3	H-4	H-5	H-6a, H-6b	H-1′	H-3′	H-4′	H-5′	H-6′a, H-6′b	OH	OMe	Me	OAc
8	$CDCl_3$	6.23 (d) ($J_{1\alpha,2}$ 3.7) 5.63 (d) ($J_{1\beta,2}$ 8.2)	4.83 (m)	5.23 (m)	4.03–4.23 (m)	← 3.96–3.56 (m) →		5.23 (m)	4.83 (m)	5.23 (m)	← 3.96–3.56 (m) →			3.30 (s)	1.23 (s)	
9	$CDCl_3$	6.25 (d) ($J_{1\alpha,s}$ 3.7) 5.75 (d) ($J_{1\beta,2}$ 8.2)	5.04 (t) ($J_{2,3}$ 9.2)	4.49 (dd) ($J_{3,4}$ 9.2)	4.43 (dd) ($J_{4,5}$ 9.2)	4.30–3.60 (m)	4.30–3.60 (m)	4.95 (dd) ($J_{1',2'}$ 4.0)	5.38 (dd) ($J_{2',3'}$ 10.5)		← 4.30–3.60 (m) →			3.30 (s)	1.40 (s)	2.0 (2) (s), 2.05 (2) (s), 2.10 (s), 2.15 (s)
10	$CDCl_3$	5.74 (d) ($J_{1,2}$ 8.2)	4.97 (dd) ($J_{2,3}$ 9.2)	5.29 (t) ($J_{3,4}$ 9.2)	4.01 (t) ($J_{4,5}$ 9.2)	3.86–3.70 (m)	4.48 (m)	5.35 (d) ($J_{1',2'}$ 4.0)	5.22 (t) ($J_{2',3'}$ 10.5)	3.71 (m)	3.86–3.70 (m)	4.20 (m)	3.20 (d) ($J_{OH,H-4'}$ 5.8)			1.95 (s), 2.00 (s), 2.01 (s), 2.02 (s), 2.02 (s), 2.03 (s), 2.09 (s), 2.12 (s)
11	$CDCl_3$	5.72 (d) ($J_{1,2}$ 8.2)	4.95 (dd) ($J_{2,3}$ 9.2)	5.28 (t) ($J_{3,4}$ 9.2)	4.00 (t) ($J_{4,5}$ 10.0)	3.85–3.75 (m)	4.20 (m)	5.34 (d) ($J_{1',2'}$ 4.0)	5.20 (t) ($J_{2',3'}$ 10)	4.46 (t) ($J_{4',5'}$ 10)	3.85–3.75 (m)	3.50–4.45 (m)	2.33 (m)			2.01 (2) (s), 2.10 (s), 2.12 (s), 2.15 (s), 2.18 (s), 2.20 (s)

Table 4
NMR spectral data for α,α-trehalose derivatives **12–15**

Compound	Solvent	^{1}H NMR															
		H-1	H-2	H-3	H-4	H-5	H-6a, H-6b	H-1′	H-2′	H-3′	H-4′	H-5′	H-6′a, H-6′b	OH	OMe	Me	OAc
12	Me_2CO-d_6	5.33 (d) ($J_{1,2}$ 4.0)	4.96 (dd) ($J_{2,3}$ 10.0)	5.50 (t) ($J_{1,2}$ 10.0)	← 4.10–3.63 (m) →			5.33 (d) ($J_{1',2'}$ 4.0)	4.96 (d) ($J_{2',3'}$ 10.0)	5.50 (t) ($J_{3',4'}$ 10.0)	← 4.10–3.63 (m) →		4.10–3.63 (m)	2.03 (s), 2.10 (s)	3.30(s)	1.40(s)	
13	C_6D_6	5.40 (d) ($J_{1,2}$ 4.0)	5.06 (dd) ($J_{2,3}$ 9.7)	5.87 (t) ($J_{3,4}$ 9.7)	3.88 (t) ($J_{4,5}$ 9.7)	3.64 (dd) ($J_{5,6}$ 4.3)	4.05 (m)	5.40 (d) ($J_{1',2'}$ 4.0)	5.06 (dd) ($J_{2',3'}$ 9.7)	5.87 (t) ($J_{3',4'}$ 9.7)	3.38 (t) ($J_{4',5'}$ 9.7)	3.64 (dd) ($J_{5',6'}$ 4.3)	4.05 (m)		3.01 (s)	1.39 (s)	1.70 (2) (s), 1.75 (2) (s)
14	Me_2SO-d_6	5.23 (d) ($J_{1,2}$ 4.0)	4.93 (dd) ($J_{2,3}$ 10.0)	5.30 (t) ($J_{3,4}$ 10.0)	4.20 (m)	← 4.06–3.60 (m) →		5.23 (d) ($J_{1',2'}$ 4.0)	4.93 (dd) ($J_{2',3'}$ 10.0)	5.30 (t) ($J_{3',4'}$ 10.0)	4.20 (m)		4.06–3.60 (m)	5.80 (d) ($J_{OH,4;4'}$ 6.4)	3.41 (s)	1.38 (s)	2.10 (3) (s), 2.13 (s)
15	Me_2SO-d_6	5.10 (d) ($J_{1,2}$ 4.0)	4.76 (dd) ($J_{2,3}$ 10.0)	5.33 (t) ($J_{3,4}$ 10.0)	4.20 (m)	← 4.0–3.36 (m) →		5.10 (d) ($J_{1',2'}$ 4.0)	4.76 (dd) ($J_{2',3'}$ 10.0)	5.33 (t) ($J_{3',4'}$ 10.0)	4.20 (m)		4.0–3.36 (m)	5.76 (d) ($J_{OH,4}$ 6.4)			2.00 (6) (s)

submitted to silica gel chromatography (2:1 EtOAc–hexane) to afford **3** (6.8 g, 84%): mp 78–80 °C, lit. [5] 79–81 °C; $[\alpha]_D^{20}$ +58.9° ($CHCl_3$), lit. [4] $[\alpha]_D^{20}$ +61° ($CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 170.68, 170.01, 169.93(2) (Me*C*O), 112.62 (Me*C*OMe), 104.10 (C-2′), 90.50 (C-1), 79.24 (C-5′), 75.82 (C-3′), 74.84 (C-2, C-4′), 71.21 (C-3), 70.55 (C-5), 68.63 (C-4), 63.35 (C-1′), 63.06 (C-6′), 61.18 (C-6), 50.71 (MeCO*Me*), 21.56 (*Me*COMe).

*Preparation of 2,3,6,1′,3′,4′,6′-hepta-*O*-acetylsucrose* (**4**) *and 2,3,4,1′,3′,4′,6′-hepta-*O*-acetylsucrose* (**5**).—A solution of **3** (3 g, 4.6 mmol) in 1:3 acetic acid–water was stirred for 30 min at room temperature. The reaction was monitored by TLC, and when it was complete the solution was freeze-dried to afford a solid residue. TLC, (1:1 EtOAc–hexane) indicated two components that were separated by column chromatography (1:1 EtOAc–hexane) to give **4** (1.5 g, 51%) and **5** (0.5 g, 17%). Compound **4**: $[\alpha]_D^{20}$ +46.5° (*c* 1.0 $CHCl_3$), lit. [9] +48.3° (*c* 1.0 $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 171.73, 171.20, 170.94, 170.42, 170.16, 170.07, 169.16 (Me*C*O), 104.19 (C-2′), 90.41 (C-1), 79.41 (C-5′), 75.61 (C-3′), 75.16 (C-4′), 71.95 (C-2), 71.03 (C-3), 70.41 (C-5), 69.06 (C-4), 64.04 (C-1′), 62.69 (C-6′), 62.16 (C-6), 20.94, 20.69, 20.79(2), 20.71(2), 20.60 (*Me*CO). Compound **5**: $[\alpha]_D^{20}$ +59.5° (*c* 1.0 $CHCl_3$), lit. [9] +61.3° (*c* 1.0 $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 170.18, 170.05, 169.84 (2) (Me*C*O), 103.82 (C-2′), 89.74 (C-1), 78.89 (C-5′), 75.64 (C-3′), 74.75 (C-4′), 71.12 (C-2), 70.41 (C-3), 69.35 (C-5), 63.02 (C-1′), 61.36 (C-6), 20.62(7) (*Me*CO).

*1.2.3.6.2′,3′-Hexa-*O*-acetyl-4′,6′-*O*-methoxyethylidenemaltose* (**9**).—A solution of maltose (6 g, 17.5 mmol) in anhydrous Me_2NCHO (60 mL) containing *p*-toluenesulfonic acid (25 mg) was maintained below 5 °C and 1,1-dimethoxyethene (3.52 g, 40 mmol) was added. The mixture was stirred until monitoring by TLC indicated that all of the starting material had disappeared (4 h), whereupon anhydrous Na_2CO_3 was added. The reaction mixture was filtered, and the filtrate was concentrated to give a syrupy mixture of **7** and **8** in 92% yield. Anhydrous sodium acetate (4.93 g) and Ac_2O (6.8 mL) were added to this mixture (6.4 g, 16 mmol) that was heated at 100 °C for 1 h with stirring until TLC indicated the disappearance of starting material. The mixture was cooled and poured onto ice and sodium carbonate, filtered and extracted with dichloromethane. The dried extracts were evaporated to give **9**, after purification by column chromatography (1:1 EtOAc–hexane), as an amorphous solid (5.6 g, 49%): mp 94–95 °C. $[\alpha]_D^{20}$ +69° (*c* 1.0 $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 170.53, 169.93 (2), 169.64, 169.48 and 168.83 (Me*C*O), 112.66 (Me*C*OMe), 96.65 (α) and 91.33 (β) (C-1), 72.38, 73.07, 75.28, 72.54, 62.58 (C-2,3,4,5,6), 95.79 (C-1′), 68.05, 71.01, 72.54, 70.48, 61.18 (C-2′,3′,4′,5′,6′), 50.71 (MeCO*Me*), 21.48, 20.83, 20.87 (*Me*COMe, *Me*CO). Anal. Calcd for $C_{27}H_{38}O_{18}$: C, 49.84; H, 5.84; O, 44.30. Found: C, 49.39; H, 5.85; O, 44.24.

*1,2,3,6,2′,3′,6′-Hepta-*O*-acetyl-β-maltose* (**10**) *and 1,2,3,6,2′,3′,4′-hepta-*O*-acetyl-β-maltose* (**11**).—A solution of **9** (4 g, 6.1 mmol) treated as described for the hydrolysis of **3** gave, after lyophilization, a residue that which was chromatographed (1:1 EtOAc–hexane) to afford **10** (1.37 g, 35%) and **11** (0.64 g, 16%). Compound **10**: mp 71–72 °C; $[\alpha]_D^{20}$ +35.6° (*c* 1.0 $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 171.58, 171.20, 170.82, 170.14, 169.70, and 168.90 (Me*C*O), 95.97 (C-1), 71.73, 73.21, 75.41, 62.69 (C-2,3,4,5,6), 91.32 (C-1′), 68.84, 70.40, 71.02, 71.32, 61.18 (C-2′,3′,4′,5′,6′), 20.69, 20.70 and 20.62 (*Me*CO). Compound **11**: mp 76–78 °C; $[\alpha]_D^{20}$ +50.4° (*c* 1.0 $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 171.49, 171.11, 170.79, 170.15, 169.68 and 168.89 (Me*C*O), 95.92 (C-1), 71.67, 73.16, 75.33, 72.37 and 62.66 (C-2,3,4,5,6), 91.30 (C-1′), 68.78, 71.23, 70.28, 69.76 and 62.53 (C-2′,3′,4′,5′,6′), 20.84, 20.66 and 20.57 (*Me*CO).

2, 3, 2′, 3′ - Tetra - O - acetyl - 4, 6:4′:6′ - di - O - methoxyethylidene-α,α-trehalose (**14**) *and 2,3,2′,3′,6′-penta - O - acetyl - 4, 6 - O - methoxyethylidene - α, α - trehalose* (**15**).—Treatment of α,α-trehalose (5.8 g, 16.9 mmol previously dried according to the method described by Birch [12]) with 1,1-dimethoxyethene by the foregoing general procedure gave a residue. TLC showed only one component **13** (5.78 g, 75%): $[\alpha]_D^{20}$ +125° ($CHCl_3$). Treatment of **13** (6.0 g, 13.2 mmol) with Ac_2O (7.9 g, 78 mmol) (see Section 3.6) led to a solid residue that was composed (TLC; 1:1 EtOAc–hexane) of two products that were separated by chromatography (1:2 EtOAc–hexane) to afford successively **14** (3.8 g, 46%) and **15** (1.97 g, 24%). Compound **14**: mp 75–76 °C; $[\alpha]_D^{20}$ +125.6° ($CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 169.25, 168.73 (Me*C*O), 111.62 (Me*C*OMe), 91.80, 92.16 (C-1, C-1′), 69.97, 69.71, 67.83, 61.79, 60.23 (C-2,3,4,5,6), 49.66 (MeCO*Me*), 20.46, 19.81, 19.49 (*Me*COMe and *Me*CO). Anal. Calcd for $C_{26}H_{38}O_{17}$: C, 50.16; H, 6.10; O, 43.72 Found: C, 50.40; H, 6.11; O, 43.79. Compound **15**: mp 161–162 °C; $[\alpha]_D^{20}$ +138.7° ($CHCl_3$). ^{13}C NMR ($CDCl_3$): δ 169.97, 169.64 (Me*C*O), 112.64 (Me*C*OMe), 93.17, 92.19 (C-1, C-1′), 73.25, 73.09, 70.43, 69.97, 69.58, 68.87, 62.96,

62.82, 61.27 (C-2,3,4,5,6 and C-2′,3′,4′,5′,6′), 50.16 (MeCO*Me*), 20.85, 20.59 (*Me*COMe and *Me*CO). Anal. Calcd for $C_{25}H_{36}O_{17}$: C, 49.34; H, 5.92; O, 44.73. Found: C, 49.59; H, 5.91; O, 44.52.

2,3,6,2′,3′,6′-Hexa-O-*acetyl-α,α-trehalose* (**16**).—A solution of **14** (4 g, 6.4 mmol), treated as described for the hydrolysis of **3**, gave after lyophilization and purification (1:1 EtOAc–hexane) **16** as a solid compound (1.2 g, 31%); mp 175–176 °C; $[\alpha]_D^{20}$ +146° ($CDCl_3$); ^{13}C NMR (Me_2SO-d_6): δ 170.45, 170.06, 169.55 (Me*C*O), 91.77 and 91.55 (C-1, C-1′), 71.82, 69.81, 68.19, 63.05, 59.67 (C-2,2′,3,3′,4,4′,5,5′,6,6′), 20.95, 20.56, 19.92 (*Me*CO). Anal. Calcd for $C_{24}H_{34}O_{17}$: C, 48.48; H, 5.72; O, 45.79. Found: C, 48.81; H, 5.90; O, 45.71.

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