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2,3,4-Tri-*O*-acetyl-1,6-anhydro-β-D-mannopyranose, an artifact produced during carbohydrate analysis. A total synthesis of 2,3,5-tri-*O*-acetyl-1,6-anhydro-β-D-mannofuranose

Sukumar Manna [a,*], Bill H. McAnalley [a] and Herman L. Ammon [b]

[a] *Synthetic Organic Division, Carrington Laboratories, Inc., P.O. Box 569500, Dallas, TX 75356-9500 (USA)*

[b] *Department of Chemistry and Biochemistry, University of Maryland, College Park, MD 20742 (USA)*

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ABSTRACT

This study confirms that 2,3,4-tri-*O*-acetyl-1,6-anhydro-β-D-mannopyranose is an artifact produced during carbohydrate analysis. A new synthesis of 2,3,5-tri-*O*-acetyl-1,6-anhydro-β-D-mannofuranose is also described, and a novel dimer, 1,6′:6,1′-dianhydro-2,3:2′,3′-di-*O*-isopropylidene-5,5′-di-*O*-(1-methoxyethyl)-di-α-D-mannofuranose, has been isolated. The structure of the dimer is confirmed by X-ray analysis of a derivative, 1,6′:6,1′-dianhydro-2,3:2′,3′-di-*O*-isopropylidene-di-α-D-mannofuranose.

INTRODUCTION

Polysaccharides are susceptible to degradation under harsh reaction conditions (for a review, see ref 1). For example, during routine analysis[2] of hydrolyzing polysaccharides with CF_3CO_2H to individual sugars, small amounts of degradation products[3,4] are always obtained. Even the simple sugar, D-mannose, upon treatment with CF_3CO_2H under conditions identical to that of polysaccharide analysis, produces an artifact. This paper deals with the identification of the artifact obtained from D-mannose and confirmation of its structure by comparison with an authentic, synthetic compound.

D-Mannose was converted to D-mannitol hexaacetate with and without prior treatment with CF_3CO_2H. The procedure involved: (*i*) treatment with 2 M CF_3CO_2H for 30 min at 110°C, (*ii*) reduction to D-mannitol with sodium borohy-

* Corresponding author (present address); Dr. Sukumar Manna, Claude Pepper Institute for Aging and Therapeutic Research, Florida Institute of Technology, 150 West University Boulevard, Melbourne, FL 32901-6988, USA.

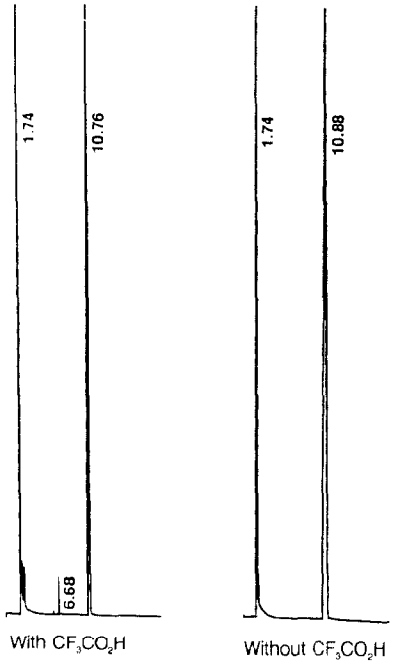
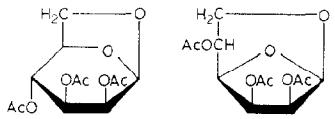


Fig. 1. Gas–liquid chromatogram of D-mannitol hexaacetate derived from D-mannose.

dride, and (iii) acetylation of the D-mannitol with acetic anhydride in pyridine to give D-mannitol hexaacetate. In the acid-treatment step there is always an artifact observed by GLC analysis (Fig. 1).

Gas chromatographic positive-ion chemical-ionization mass spectroscopic analysis of the artifact (peak at 6.68 min, Fig. 1) showed a single molecular ion at m/z 289 (M + 1) corresponding to the molecular weight m/z 288 and major fragmentation peaks at m/z 229, 169, and 109 due to the loss of three acetyl groups. This data suggests that the artifact is an anhydromannose, either 2,3,4-tri-*O*-acetyl-1,6-anhydro-β-D-mannopyranose (**1**) or 2,3,5-tri-*O*-acetyl-1,6-anhydro-β-D-mannofuranose (**2**).



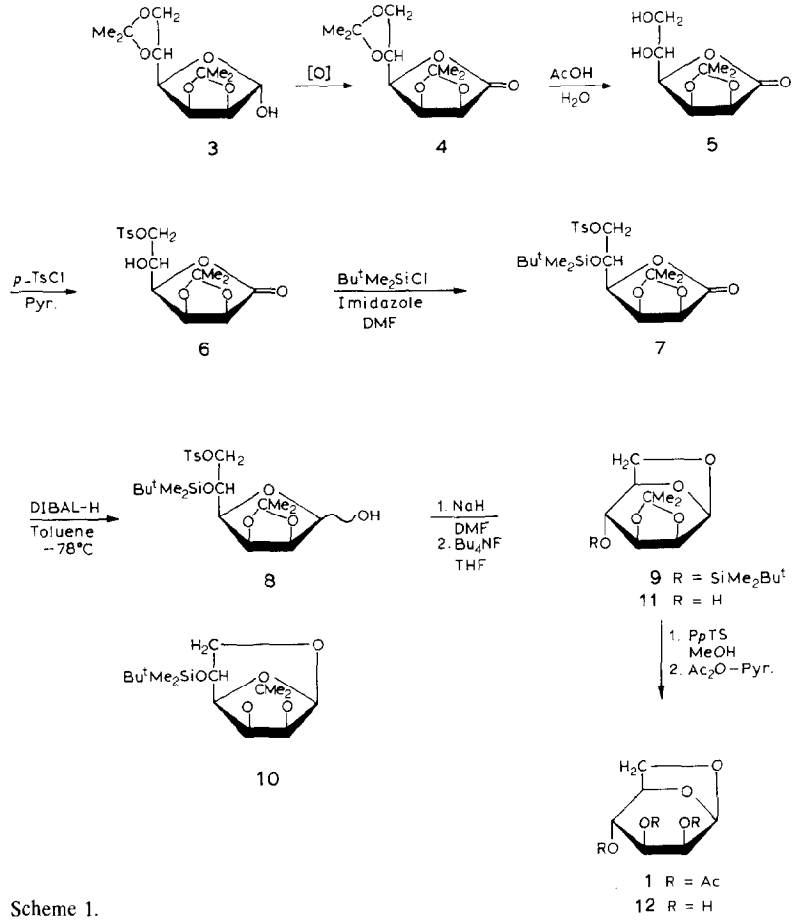
1 2

1,6-Anhydro-β-D-mannopyranose has been previously synthesized[5,6], and it is widely used in the synthesis of biologically active compounds[7]. Large quantities of anhydromannose can be obtained by a pyrolytic procedure[8] in low yield or via a high-yield synthesis[9] from D-mannose. In the present study, the need for an authentic sample of the compound and the lack of a reliable source of 1,6-

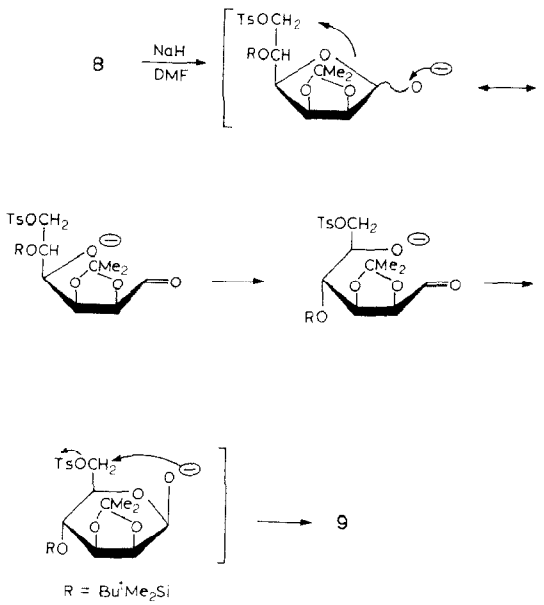
anhydro-β-D-mannofuranose[10,11] led us to investigate the total synthesis of this compound.

RESULTS AND DISCUSSIONS

2,3,4-Tri-*O*-acetyl-1,6-anhydro-β-D-mannopyranose (**1**) (ref 9) and 2,3,5-tri-*O*-acetyl-1,6-anhydro-β-D-mannofuranose (**2**) have been synthesized from D-mannose. 2,3:5,6-Di-*O*-isopropylidene-α-D-mannofuranose (**3**) was oxidized with Collins' reagent[12] or with Me_2SO–acetic anhydride[13] to the known[14] 2,3:5,6-di-*O*-isopropylidene-D-mannono-1,4-lactone (**4**) (Scheme 1). Selective hydrolysis of the 5,6-*O*-isopropylidene group with acetic acid in water at 60°C produced 2,3-*O*-isopropylidene-D-mannono-1,4-lactone (**5**). The primary hydroxyl group was tosylated to give

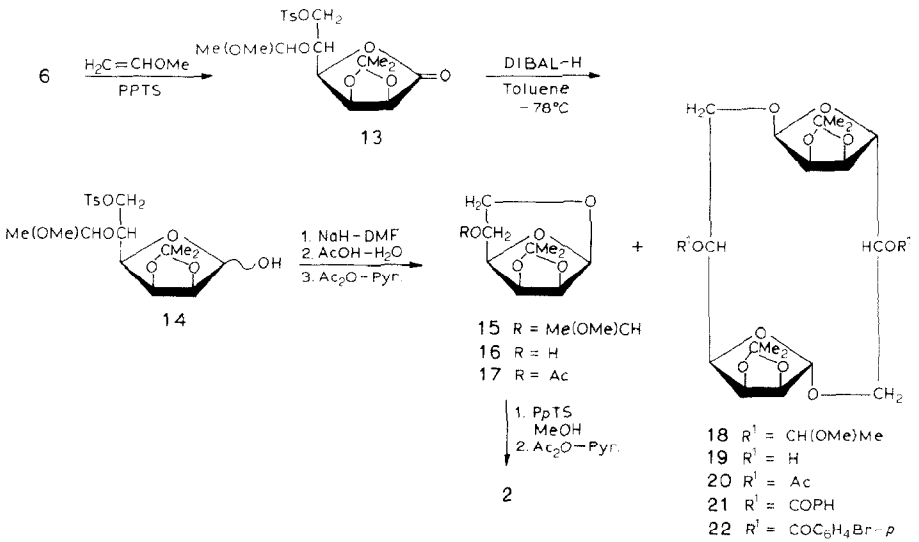


Scheme 1.



Scheme 2.

6 using a limited amount of *p*-toluenesulfonyl chloride in pyridine, and the C-5 hydroxyl group was subsequently protected as the *tert*-butyldimethylsilyl ether using *tert*-butylchlorodimethylsilane and imidazole in DMF[15] to obtain 2,3-*O*-isopropylidene-5-*O*-*tert*-butyldimethylsilyl-6-*O*-*p*-tolylsulfonyl-D-mannono-1,4-lactone (**7**). The 1,4-lactone was reduced to the lactol **8** using diisobutylaluminum hydride



Scheme 3.

(DIBAL-H)[16] in toluene at −78°C, and no overreduced product was obtained. It was expected that, by treatment with base, lactol **8** should undergo internal nucleophilic substitution to form 1,6-anhydro-D-mannofuranose (**10**). Contrary to this expectation, lactol **8**, upon treatment with a base such as sodium hydride in DMF, underwent smooth rearrangement, followed by internal nucleophilic substitution[17], to form 1,6-anhydro-2,3-*O*-isopropylidene-4-*O*-*tert*-butyldimethylsilyl-β-D-mannopyranose (**9**), along with some *O*-desilylated product (**11**) (Scheme 2). (Note that similar rearrangements have been previously observed. See ref 17.) The alcohol **9** was deprotected[15] with tetrabutylammonium fluoride to give the known compound[8,18], 2,3-*O*-isopropylidene-1,6-anhydro-β-D-mannopyranose (**11**). Treatment of **11** with pyridinium *p*-toluenesulfonate (P*p*TS)[19] in refluxing methanol afforded 1,6-anhydro-β-D-mannopyranose (**12**) which, upon acetylation, produced

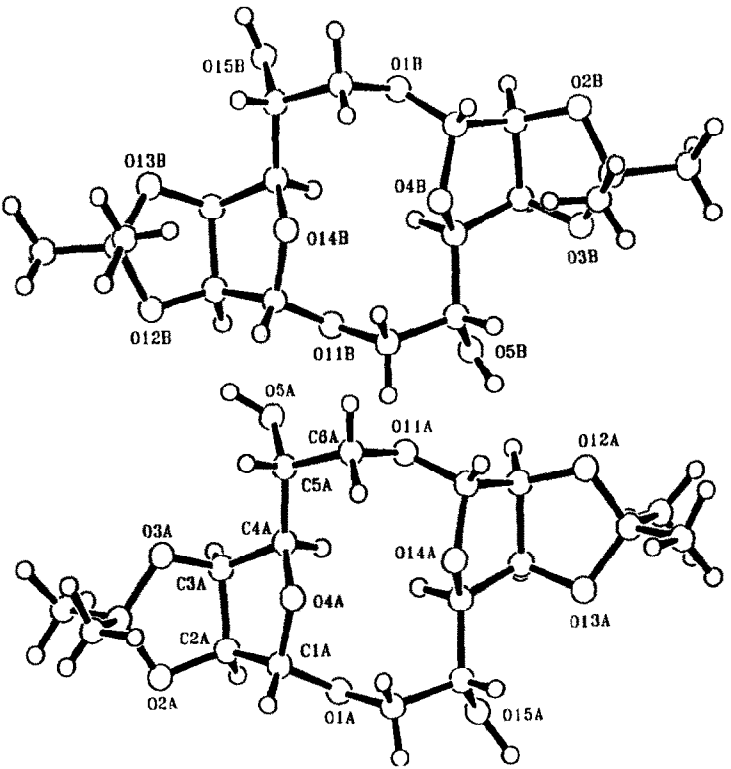


Fig. 2. Ball-and-stick representations of the two crystallographically independent molecules of dimer-diol **19**. The molecules have been drawn to illustrate the similar conformations of the central 12-membered rings. The oxygen atoms have been labeled. The oxygen atom labels show the pseudocentrosymmetric relationship between the two molecules: e.g., this relationship is present between (O1A, O1B), (O4A, O4B), etc.

2,3,4-tri-*O*-acetyl-1,6-anhydro-β-D-mannopyranose (**1**), identical in all respects to the compound previously generated.

In order to alleviate the problem of ring expansion, the C-5 HO-group in **6** was protected as its 1-methoxyethyl ether[20] using methyl vinyl ether in the presence of P*p*TS (Scheme 3, *p*-toluenesulfonic acid[20] has been replaced with P*p*TS to minimize polymerization of methyl vinyl ether). The resultant diasteriomeric mixture of 2,3-*O*-isopropylidene-5-*O*-(1-methoxyethyl)-6-*O*-(*p*-tolylsulfonyl-D-mannono-1,4-lactone (**13**) was reduced by diisobutylaluminum hydride (DIBAL-H)[16] to lactol **14**. Upon treatment with sodium hydride in DMF, lactol **14** produced two compounds which were separated by chromatography. The slower moving compound 1,6-anhydro-2,3-*O*-isopropylidene-5-*O*-(1-methoxyethyl)-β-D-mannofuranose (**15**), upon hydrolysis of the 1-methoxyethyl protecting group, produced the known[10] 1,6-anhydro-2,3-*O*-isopropylidene-β-D-mannofuranose (**16**) that was further characterized as its 5-acetate[10] **17**. Acetate **17**, upon hydrolysis of the acetonide protecting group with P*p*TS in refluxing methanol, followed by acetylation with acetic anhydride in pyridine, furnished 1,6-anhydro-2,3,5-tri-*O*-acetyl-β-D-mannofuranose (**2**).

The faster moving compound, a dimer, 1,6′:6,1′-dianhydro-2,3:2′,3′-di-*O*-isopropylidene-5,5′-di-*O*-(1-methoxyethyl)-di-α-D-mannofuranose (**18**), upon hydrolysis of the 1-methoxyethyl protecting group, gave a single compound, a dimer-diol, 1,6′:6,1′-dianhydro-2,3:2′,3′-di-*O*-isopropylidene-di-α-D-mannofuranose (**19**). Mass spectroscopic analyses of the dimer-diol (**19**) and its diacetate derivative (**20**) confirmed the dimeric structure. Detailed analyses of the ^{1}H and ^{13}C NMR spectra of the dimer-diol (**19**), dimer-diacetate (**20**), dimer-dibenzoate (**21**), and dimer-di-*p*-bromobenzoate (**22**) confirmed that they were symmetrical dimers and

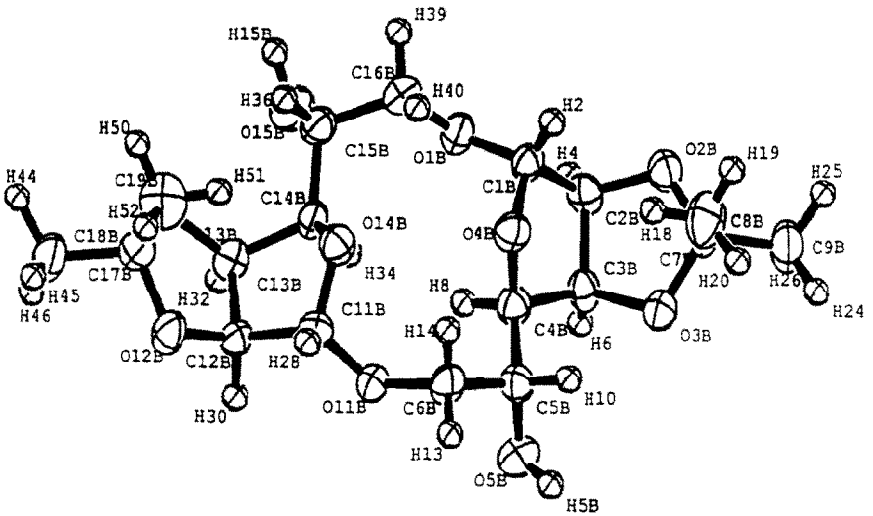


Fig. 3. ORTEP drawing of dimer-diol **19** with complete atom numbering.

TABLE I

Crystallographic data for dimer-diol **19**

Crystal dimensions	0.09 × 0.11 × 0.26 mm, rectangular shape
Empirical formula	$C_{18}H_{28}O_{10}$
Formula weight	404.4
Crystal system	triclinic
Lattice parameters:	$a = 9.930\ (2)$ Å,
	$b = 10.118\ (1)$ Å
	$c = 11.177\ (1)$ Å
	$\alpha = 87.58\ (1)^\circ$
	$\beta = 67.76\ (1)^\circ$
	$\gamma = 75.74\ (1)^\circ$
Unit cell volume	$V = 944.9\ (6)$ Å^3
Space group	$P1$ (#1)
Z value	2
Calcd crystal density	1.421 g cm^{-3}
$F(000)$	432 e
Diffractometer	Enraf–Nonius CAD-4
X-radiation	Cu $K\alpha$ ($\lambda = 1.54178$ Å, graphite monochromator)
μ (Cu $K\alpha$)	9.4 cm^{-1}
Temperature	23°C
2θ maximum for data collection	119.9°
Data summary:	
No. total data measured	3109
No. data without standards	3021
No. unique data with $I \geq 3\sigma(I)$	2607
Number of variables	713
Residuals: R; wtd R	0.039; 0.068
Goodness-of-fit indicator	2.21
Maximum shift/error in final l s	0.07
Min and max in final difference map	−0.25, 0.20 e Å

the anomeric configurations were α. Finally, a single-crystal X-ray crystallographic analysis of the dimer-diol **19** firmly established its structure.

The crystal structure of **19** contains two independent molecules in the acentric triclinic space group $P1$. The molecules are related by an approximate center of symmetry; a preliminary crystallographic model in the centric space group $P1$ with one molecule per asymmetric unit was refined to an R factor of 0.35. Ball-and-stick model drawings of the molecules are shown in Fig. 2, and an ORTEP drawing is shown in Fig. 3. The X-ray crystallographic data and the positional parameters of dimer-diol (**19**) are shown in Tables I and II, respectively. The structures and conformations of the central 12-membered rings of the two molecules are virtually identical. A rigid-body, least-squares fit of the 12-atom rings gave rms and maximum deviations in position of 0.093 and 0.158 Å, respectively. The major differences between the molecules are associated with the conformations of the acetone–ketal five-membered rings. A search of the Cambridge Structural

TABLE II

Atomic coordinates for dimer-diol **19**

Atom	x [a]	y [a]	z [a]	B_{eq} [a]
O-1A	0.7505	0.3368	0.2242	3.1 (3)
O-1B	0.2606 (6)	0.6719 (5)	0.7924 (6)	3.2 (3)
O-2A	0.5085 (8)	0.1548 (6)	0.1597 (7)	4.6 (4)
O-2B	0.5090 (7)	0.8547 (6)	0.8497 (6)	3.7 (3)
O-3A	0.2896 (7)	0.3360 (6)	0.2202 (6)	3.7 (3)
O-3B	0.7385 (7)	0.6894 (6)	0.7645 (6)	3.4 (3)
O-4A	0.4774 (7)	0.4119 (6)	0.3431 (6)	3.1 (3)
O-4B	0.4699 (7)	0.5469 (6)	0.8468 (6)	3.1 (3)
O-5A	0.2277 (7)	0.6743 (6)	0.2261 (6)	4.0 (3)
O-5B	0.8568 (7)	0.3893 (6)	0.6008 (6)	4.1 (3)
O-11A	0.4170 (7)	0.7656 (5)	0.3361 (6)	3.1 (3)
O-11B	0.6003 (6)	0.2490 (6)	0.6666 (6)	3.2 (3)
O-12A	0.6764 (7)	0.9493 (6)	0.3716 (6)	3.8 (3)
O-12B	0.3343 (7)	0.0568 (6)	0.6546 (6)	3.8 (3)
O-13A	0.8913 (7)	0.7699 (6)	0.3107 (6)	3.2 (3)
O-13B	0.1299 (7)	0.2400 (6)	0.6673 (6)	3.5 (3)
O-14A	0.6148 (7)	0.6528 (6)	0.4096 (6)	3.0 (3)
O-14B	0.3317 (7)	0.3214 (6)	0.7969 (6)	3.2 (3)
O-15A	1.0001 (7)	0.4727 (6)	0.1783 (6)	4.1 (3)
O-15B	0.0760 (7)	0.5723 (7)	0.6771 (6)	4.3 (4)
C-1A	0.6031 (9)	0.3014 (7)	0.2687 (8)	3.1 (4)
C-1B	0.3691 (9)	0.6788 (7)	0.8503 (8)	2.9 (4)
C-2A	0.565 (1)	0.2746 (8)	0.1524 (8)	3.4 (4)
C-2B	0.478 (1)	0.7667 (7)	0.7722 (8)	3.2 (4)
C-3A	0.4238 (9)	0.3929 (8)	0.1600 (8)	3.1 (4)
C-3B	0.6391 (9)	0.6665 (7)	0.7013 (8)	3.0 (4)
C-4A	0.4264 (8)	0.4958 (7)	0.2522 (7)	2.7 (4)
C-4B	0.5992 (8)	0.5296 (7)	0.7215 (7)	3.0 (4)
C-5A	0.2749 (9)	0.6021 (7)	0.3242 (8)	3.0 (4)
C-5B	0.730 (1)	0.4059 (7)	0.7246 (7)	3.1 (4)
C-6A	0.2997 (9)	0.6952 (8)	0.4124 (8)	3.3 (4)
C-6B	0.665 (1)	0.2798 (8)	0.7580 (8)	3.4 (5)
C-7A	0.3408 (9)	0.1908 (7)	0.1933 (7)	3.0 (4)
C-7B	0.6497 (9)	0.7906 (7)	0.8695 (7)	3.1 (4)
C-8A	0.302 (1)	0.152 (1)	0.0838 (9)	4.7 (6)
C-8B	0.617 (1)	0.721 (1)	0.995 (1)	5.1 (7)
C-9A	0.260 (1)	0.129 (1)	0.317 (1)	5.2 (7)
C-9B	0.744 (1)	0.896 (1)	0.859 (1)	4.7 (6)
C-11A	0.5215 (8)	0.7831 (7)	0.3946 (7)	2.8 (4)
C-11B	0.4574 (8)	0.2103 (7)	0.7256 (7)	3.1 (4)
C-12A	0.6401 (9)	0.8561 (7)	0.3025 (7)	3.0 (4)
C-12B	0.4059 (8)	0.1680 (7)	0.6202 (8)	3.0 (4)
C-13A	0.7974 (9)	0.7430 (7)	0.2438 (7)	2.8 (4)
C-13B	0.2725 (9)	0.2890 (7)	0.6178 (7)	2.9 (4)
C-14A	0.7431 (8)	0.6141 (7)	0.2869 (7)	2.8 (4)
C-14B	0.2757 (8)	0.3982 (7)	0.7050 (7)	2.7 (4)
C-15A	0.8685 (9)	0.4895 (7)	0.2976 (7)	3.0 (4)
C-15B	0.1222 (9)	0.5033 (7)	0.7760 (7)	3.1 (4)
C-16A	0.800 (1)	0.3651 (7)	0.3265 (8)	3.2 (5)
C-16B	0.143 (1)	0.6001 (8)	0.8643 (8)	3.5 (5)

TABLE II (continued)

Atom	x [a]	y [a]	z [a]	B_{eq} [a]
C-17A	0.844 (1)	0.9156 (8)	0.3383 (9)	3.9 (5)
C-17B	0.167 (1)	0.1021 (7)	0.7085 (8)	3.2 (4)
C-18A	0.927 (1)	0.985 (1)	0.217 (1)	5.2 (7)
C-18B	0.101 (1)	0.014 (1)	0.648 (1)	4.2 (6)
C-19A	0.876 (1)	0.947 (1)	0.454 (1)	5.4 (7)
C-19B	0.101 (1)	0.105 (1)	0.854 (1)	5.4 (7)
H-1	0.626 (7)	0.222 (7)	0.313 (6)	3 (1)
H-2	0.320 (7)	0.710 (6)	0.937 (6)	2 (1)
H-3	0.656 (8)	0.256 (6)	0.078 (6)	2 (1)
H-4	0.437 (8)	0.822 (7)	0.712 (6)	3 (1)
H-5	0.43 (1)	0.419 (9)	0.08 (1)	6 (2)
H-6	0.696 (8)	0.679 (7)	0.611 (7)	3 (1)
H-7	0.511 (9)	0.536 (7)	0.206 (6)	3 (1)
H-8	0.55 (1)	0.512 (7)	0.658 (7)	4 (2)
H-9	0.187 (8)	0.557 (7)	0.381 (6)	3 (1)
H-10	0.765 (7)	0.427 (6)	0.796 (5)	2 (1)
H-11	0.203 (9)	0.764 (7)	0.451 (7)	3 (1)
H-12	0.34 (1)	0.63 (1)	0.476 (9)	6 (2)
H-13	0.747 (8)	0.199 (7)	0.764 (6)	3 (1)
H-14	0.569 (8)	0.300 (7)	0.846 (7)	3 (1)
H-15	0.17 (1)	0.16 (1)	0.121 (9)	7 (2)
H-16	0.35 (1)	0.05 (1)	0.06 (1)	8 (3)
H-17	0.36 (1)	0.201 (8)	0.004 (8)	5 (2)
H-18	0.55 (1)	0.660 (9)	0.995 (8)	5 (2)
H-19	0.56 (1)	0.784 (8)	1.064 (8)	4 (2)
H-20	0.715 (9)	0.691 (7)	1.006 (7)	4 (1)
H-21	0.14 (2)	0.17 (1)	0.36 (1)	10 (3)
H-22	0.30 (2)	0.16 (1)	0.39 (1)	12 (4)
H-23	0.28 (1)	0.04 (1)	0.311 (7)	4 (2)
H-24	0.84 (1)	0.85 (1)	0.875 (8)	6 (2)
H-25	0.69 (1)	0.98 (1)	0.93 (1)	7 (2)
H-26	0.76 (1)	0.94 (1)	0.77 (1)	8 (3)
H-27	0.467 (6)	0.822 (5)	0.482 (5)	1 (1)
H-28	0.467 (8)	0.135 (7)	0.780 (6)	3 (1)
H-29	0.609 (6)	0.909 (5)	0.241 (5)	1 (1)
H-30	0.507 (8)	0.137 (6)	0.536 (6)	3 (1)
H-31	0.859 (7)	0.739 (6)	0.145 (6)	2 (1)
H-32	0.299 (7)	0.305 (6)	0.535 (7)	2 (1)
H-33	0.701 (6)	0.590 (5)	0.223 (5)	0.8 (9)
H-34	0.36 (1)	0.43 (1)	0.656 (9)	6 (2)
H-35	0.894 (7)	0.508 (7)	0.371 (6)	3 (1)
H-36	0.044 (7)	0.456 (6)	0.831 (6)	2 (1)
H-37	0.889 (6)	0.291 (5)	0.332 (5)	1 (1)
H-38	0.706 (9)	0.383 (7)	0.408 (7)	3 (1)
H-39	0.035 (9)	0.670 (8)	0.898 (7)	4 (2)
H-40	0.17 (1)	0.553 (9)	0.925 (9)	6 (2)
H-41	0.93 (1)	0.948 (9)	0.138 (8)	5 (2)
H-42	1.05 (1)	0.958 (7)	0.198 (7)	4 (2)
H-43	0.90 (1)	1.09 (1)	0.239 (9)	6 (2)
H-44	−0.03 (1)	0.04 (1)	0.680 (9)	7 (2)

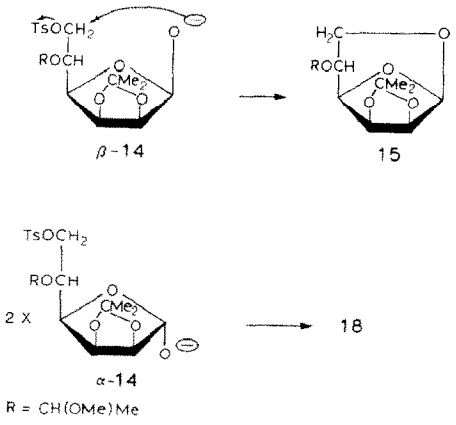
TABLE II (continued)

Atom	x [a]	y [a]	z [a]	B_{eq} [a]
H-45	0.12 (1)	−0.06 (1)	0.68 (1)	6 (2)
H-46	0.146 (8)	0.013 (6)	0.547 (7)	3 (1)
H-47	1.00 (1)	0.93 (1)	0.42 (1)	6 (2)
H-48	0.81 (1)	0.89 (1)	0.53 (1)	9 (3)
H-49	0.82 (1)	1.04 (1)	0.492 (9)	6 (2)
H-50	−0.02 (1)	0.133 (8)	0.888 (8)	5 (2)
H-51	0.13 (1)	0.17 (1)	0.89 (1)	9 (3)
H-52	0.13 (1)	0.01 (1)	0.89 (1)	8 (3)
H-15B	−0.0321	0.6063	0.7167	4 (2)
H-15A	1.1158	0.4401	0.1820	12 (3)
H-5A	0.1253	0.6641	0.2319	10 (3)
H-5B	0.9307	0.3621	0.6308	11 (4)

[a] Esd's appear in parentheses and refer to the last significant digit.

Database current to July, 1992 revealed no other compounds with this 12-membered ring.

The formation of products **15** and **18** can be rationalized mechanistically. Lactol **14** (β-form), upon treatment with strong base, can undergo internal nucleophilic substitution to give 1,6-anhydro-β-D-mannofuranose (**15**), or the α-form can displace the tosyl group in a bimolecular reaction to give the dimeric structure **18** (Scheme 4). Selective hydrolysis of the acetonide protecting group of the dimeric diol **19** was unsuccessful. During treatment of **19** with P*p*TS in refluxing methanol, the labile 1,6-anhydro linkage underwent hydrolytic cleavage, along with the acetonide group, producing methyl D-mannopyranoside. GLC and GLC–MS anal-



Scheme 4.

yses showed that the artifact was identical with the synthetic 2,3,4-tri-*O*-acetyl-1,6-anhydro-β-D-mannopyranose (**1**) and different from 2,3,5-tri-*O*-acetyl-1,6-anhydro-β-D-mannofuranose (**2**).

EXPERIMENTAL

Melting points were determined on an Electrothermal melting-point apparatus and are uncorrected. The ^1H and ^{13}C NMR spectra were recorded on an IBM WP 270 SY at 270 MHz and 69.75 MHz, respectively, in $CDCl_3$ (Me_4Si as internal standard) unless otherwise stated. IR spectra were recorded on an IBM IR/32 (FTIR) spectrophotometer. GLCS were recorded on a Varian 6000 gas chromatograph (oven temperature 235°C, detector and ionization temperature 250°C, fid, column SP 2330, 30 m). Electron-ionization mass spectra (EIMS) were recorded on a Hewlett–Packard 5890 MSDS. Low-ionization mass spectra were obtained by chemical ionization with methane as reagent gas on a Finnigan 4021 spectrometer, and high-resolution MS (HRMS) was determined on a Kratos MS-50. Optical rotations were recorded on a Perkin–Elmer 241 MC polarimeter. Column chromatography was performed on Silica Gel-60 (70–230 mesh, E. Merck), and thin-layer chromatography (TLC) was carried out on silica gel G plates (0.25 mm thickness, E Merck).

*Preparation of 2,3,4-tri-*O*-acetyl-1,6-anhydro-β-D-mannopyranose* (**1**).—*Method A.* A solution of D-mannose (0.5 g, 2.77 mmol) in pyridine (10 mL) and *p*-toluenesulfonyl chloride (0.7 g, 3.67 mmol) was stirred for 12 h at room temperature. The pyridine was evaporated, and the final traces were removed by azeotropic distillation with toluene. The crude product (6-*O*-*p*-tolylsulfonyl-D-mannose) was dissolved in anhyd DMF (10 mL), and hexane-washed NaH (0.4 g) was added. After stirring for 15 h at room temperature the reaction mixture was cooled to 0°C, and excess NaH was quenched with glacial acetic acid. Excess acetic acid was removed by azeotropic distillation with toluene, and the crude product, 1,6-anhydro-β-D-mannopyranose, was acetylated with Ac_2O (20 mL) in pyridine (20 mL). The mixture was poured onto ice and extracted with CH_2Cl_2. The organic extract was washed with water, then with brine, and dried (Na_2SO_4). After evaporation of solvent, pyridine residues were removed by azeotropic distillation with toluene. Product **1** was purified by column chromatography over silica gel using 1 : 1 EtOAc hexane as eluent: yield, 0.47 g (59%). The product was identical with the product from method *B* below.

Method B. A solution of D-mannose (0.5 g, 2.77 mmol) in pyridine (10 mL) and *p*-toluenesulfonyl chloride (0.7 g, 3.67 mmol) was stirred for 12 h at room temperature. The pyridine was evaporated, and trace amounts of solvent-base were removed by azeotropic distillation with toluene. The resulting crude 6-*O*-*p*-tolylsulfonyl-D-mannose was refluxed in MeOH (8 ML) with NaOMe (1 mL, 25 wt% in MeOH) for 20 h. The reaction mixture was cooled to 0°C, acetic acid (2 mL) was added, and the solvent was removed by distillation under aspirator

vacuum. The crude product, 1,6-anhydro-β-D-mannopyranose, was acetylated with Ac_2O (20 mL) in pyridine (20 mL). After workup and purification as described earlier, 2,3,4-tri-*O*-acetyl-1,6-anhydro-β-D-mannopyranose was obtained in 58% yield; mp 83°C [lit.[8] 90–91°C]; $[\alpha]_D^{25}$ −124.76° (*c* 1, $CHCl_3$), [lit.[8] −123.6°]; ^1H NMR: δ 5.44 (s, 3 H), 5.28 (dd, 1 H, *J* 5.5, 1.6 Hz), 5.02 (dd, 1 H, *J* 5.5, 1.6 Hz), 4.82 (s, 1 H), 4.63 (d, 1 H, *J* 5.8 Hz), 4.25 (dd, 1 H, *J* 7.8, 0.8 Hz), 3.87 (dd, 1 H, *J* 7.8, 5.8 Hz), 2.17 (s, 3 H), 2.15 (s, 3 H), and 2.07 (s, 3 H); ^{13}C NMR: δ 169.75, 169.69, 169.50, 99.44, 73.75, 71.83, 67.63, 66.87, 65.27, 20.91, 20.80, and 20.61; HRMS Calcd for $C_{12}H_{17}O_8$ $(M + H)^+$ *m/z* 289.0924; found *m/z* 289.0924.

*Preparation of 2,3:5,6-di-*O*-isopropylidene-*D*-mannono-1,4-lactone* (**4**).—*Method A.* A solution of 2,3:5,6-di-*O*-isopropylidine-α-D-mannofuranose (3; 1.0 g, 3.84 mmol) in CH_2Cl_2 (5 mL) was added to a stirred solution of Collins' reagent[12] (6.0 g, 23.3 mmol) in CH_2Cl_2 (120 mL), and the reaction mixture was stirred for 30 min at room temperature. The organic solution was then decanted and washed with water, brine, and dried (Na_2SO_4). Product **4** was purified by column chromatography over silica gel using 1:1 EtOAc–hexane: yield, 0.8 g (80%); mp 125°C [lit.[14] 126°C]; IR (KBr) 1784 cm^{-1}; ^1H NMR: δ 4.65–4.91 (m, 2 H), 4.38–4.47 (m, 2 H,), 4.04–4.18 (m, 2 H), 1.48 (s, 3 H), 1.47 (s, 3 H), 1.45 (s, 3 H), 1.43 (s, 3 H).

Method B. A solution of compound **3** (1.4 g, 5.38 mmol) in Me_2SO (19 mL) was treated[13] with Ac_2O (12.7 mL, 134 mmol), and the mixture was stirred for 2 h at room temperature. The mixture was poured over ice, and the product was extracted with ether. The ether extract was washed with water, brine, and dried (Na_2SO_4). Product **4** was purified by crystallization from ether–hexane; yield, 79%. The product was identical with the product from method *A* above.

*Preparation of 2,3-O-isopropylidene-4-*O*-tert-butyldimethylsilyl-1,6-anhydro-β-D-mannopyranose* (**9**).–A solution of **4** (0.8 g, 3.1 mmol) in glacial acetic acid (6 mL) and water (1 mL) was stirred for 4 h at 60°C. The solvent was removed by azeotropic distillation with toluene under reduced pressure to obtain the 2,3-*O*-isopropylidene-D-mannono-1,4-lactone (**5**). The crude product was used for the next step without further purification: IR (KBr) 3450 and 1786 cm^{-1}.

A solution of **5** (0.8 g, 3.63 mmol) in pyridine (6 mL) and *p*-toluenesulfonyl chloride (0.9 g, 4.72 mmol) was stirred for 10 h at room temperature. The mixture was poured into ice and extracted with CH_2Cl_2. The organic extract was washed successively with water, cold N HCl, water, aq $NaHCO_3$, water, and brine, and then it was dried (Na_2SO_4). After evaporation of the solvent the product, 2,3-*O*-isopropylidene-6-*O*-*p*-tolylsulfonyl-D-mannono-1,4-lactone (**6**), was purified by column chromatography over silica gel using 1:1 EtOAc–hexane as eluent: yield, 0.7 g (61%); IR (KBr) 3500, 1796 cm^{-1}; ^1H NMR: δ 7.81 (d, 2 H, *J* 7.0 Hz), 7.37 (d, 2 H, *J* 7.0 Hz), 4.83–4.94 (m, 2 H), 4.16–4.50 (m, 4 H), 2.46 (s, 3 H), 1.45 (s, 3 H), and 1.41 (s, 3 H).

A mixture of **6** (0.3 g, 0.8 mmol), imidazole (143 mg, 2.10 mmol) and *tert*-butylchlorodimethylsilane (158 mg, 1.05 mmol) in anhyd DMF (3 mL) was stirred for 10 h at room temperature. The mixture was diluted with CH_2Cl_2 and water,

and the organic extract was washed with water, aq $NaHCO_3$, water, and brine, and then it was dried (Na_2SO_4). After evaporation of the solvent under reduced pressure, the crude product, 2,3-*O*-isopropylidene-5-*O*-*tert*-butyldimethylsilyl-6-*O*-*p*-tolylsulfonyl-D-mannono-1,4-lactone (**7**), was dried under vacuum and used for the next step; yield, 98%; IR (KBr) 1797 cm^{-1}.

Diisobutylaluminum hydride (1.5 mL, M in hexane) was added dropwise by syringe under a positive flow of N_2 to a cold, stirred solution (−78°C) of γ-lactone **7** (0.4 g, 0.82 mmol) in anhyd toluene (5 mL). The stirring was continued for 4 h at −78°C. It was quenched with acetic acid (0.2 mL) and diluted with EtOAc and water. The organic extract was washed with dil NaOH, water, and brine, and dried (Na_2SO_4). The solvent was evaporated under reduced pressure, and the crude product, 2,3-*O*-isopropylidene-5-*O*-*tert*-buyldimethylsilyl-6-*O*-*p*-tolylsulfonyl-D-mannofuranose (**8**), was used for the next step: yield, 90%; ^1H NMR: δ 7.77 (d, 2 H, *J* 8.2 Hz), 7.32 (d, 2 H, *J* 8.2 Hz), 5.24 (s, 1 H), 4.0–4.71 (m, 6 H), 2.41 (s, 3 H), 1.35 (s, 3 H), 1.25 (s, 3 H), 0.75 (s. 9 H), 0.03 (s, 3 H), and 0.02 (s, 3 H).

A solution of **8** (350 mg, 0.71 mmol) in anhyd DMF (5 mL) was stirred with NaH (30 mg, prewashed with hexane, 1.25 mmol) for 90 min at ambient temperature. After cooling to 0°C, the mixture was quenched with acetic acid (0.2 mL) and diluted with water and EtOAc. The organic extract was washed with water, then with brine, and dried (Na_2SO_4). After evaporation of the solvent, the products were purified by column chromatography over silica gel using 1:1 EtOAc–hexane as eluent. Compound **9** was obtained in 35% yield: mp 105–106°C; ^1H NMR: 5.36 (s, 1 H), 4.41 (d, 1 H, *J* 7.0 Hz), 4.10 (m, 2 H), 3.96 (d, 2 H, *J* 7.0 Hz), 3.74 (t, 1 H, *J* 7.0 Hz), 1.60 (s, 3 H), 1.40 (s, 3 H), 0.95 (s, 9 H), 0.16 (s, 6 H); HRMS: Calcd for $C_{15}H_{28}O_5SiH$, m/z $(M+1)^+$ 317.1784; found 317.1790. Some *O*-desilylated product, 2,3-*O*-isopropylidene-1,6-anhydro-β-D-mannopyranose (**11**) was also obtained: yield, 12%; mp 155–156°C [lit.[18] 161–162°C, lit.[8] 157–160°C).

Preparation of 2,3-O-isopropylidene-1,6-anhydro-β-D-mannopyranose (**11**).—A solution of **9** (34 mg, 0.11 mmol) and tetrabutylammonium fluoride (35 mg, 0.11 mmol) in dry tetrahydrofuran (2 mL) was stirred for 10 min. The mixture was diluted with EtOAc and water, and the organic extract was washed with water, then with brine, and dried (Na_2SO_4). Product **11** was purified by column chromatography over silica gel using 1:1 EtOAc–hexane as eluent: yield, 70%; mp 154–155°C [lit.[18] 161–162°C, lit.[8] 157–160°C]; ^1H NMR: δ 5.36 (d, 1 H, *J* 2.8 Hz), 4.53 (dd, 1 H, *J* 6.0, 1.2 Hz), 4.23 (d, 1 H, *J* 6.0 Hz), 3.98–4.10 (m, 3 H), 3.78 (t, 1 H, *J* 7.0 Hz), 1.54 (s, 3 H), and 1.33 (s, 3 H).

Preparation of 2,3,4-tri-O-acetyl-1,6-anhydro-β-D-mannopyranose (**1**) *from 2,3-O-isopropylidene-1,6-anhydro-β-D-mannopyranose* (**11**).—A solution of **11** (20 mg, 0.1 mmol) and *p*TS (20 mg, 0.08 mmol) in dry MeOH (5 mL) was refluxed under N_2 for 30 h. The solution was evaporated to dryness, and the crude 1,6-anhydro-β-D-mannopyranose (**12**) was acetylated with Ac_2O (1 mL) in pyridine (1 mL). After usual workup and purification, 2,3,4-tri-*O*-acetyl-1,6-anhydro-β-D-mannopyranose

(**1**) was obtained in 90% yield; mp 83°C. This compound is identical in all respects with the compound synthesized above.

2,3-O-Isopropylidene-5-O-(1-methoxyethyl)-1,6-anhydro-β-D-mannofuranose (**15**) *and 1,6′:6,1′-dianhydro-2,3:2′,3′di-O-isopropylidene-5,5′-di-O-(1-methoxyethyl)-di-α-D-mannofuranose* (**18**).—Methyl vinyl ether (4 mL) was condensed with the aid of a cold finger in a flask containing γ-lactone **6** (1.4 g, 3.76 mmol) and P*p*TS (200 mg, 0.8 mmol) in dry $CHCl_3$ (10 mL) under N_2. The mixture was stirred at ambient temperature for 48 h. Excess methyl vinyl ether was removed by bubbling N_2 through the mixture. The mixture was diluted with CH_2Cl_2 and water. The organic extract was washed with water, then with brine, and dried (Na_2SO_4). The crude product, 2,3-*O*-isopropylidene-5-*O*-(1-methoxyethyl)-6-*O*-*p*-tolylsulfonyl-D-mannono-1,4-lactone (**13**) (1.5 g) was used as such for the next step: IR (KBr) 1790 cm^{-1}; ^1H NMR: δ 7.80 (d, 2 H, *J* 8.0 Hz), 7.35 (d, 2 H, *J* 8.0 Hz), 4.0–4.9 (m, 5 H), 3.60–3.73 (m, 2 H), 3.23–3.30 (m, 3 H), 2.45 (s, 3 H), 1.42 (s, 3 H), 1.38 (s, 3 H), and 1.22–1.31 (m, 3 H).

Diisobutylaluminum hydride (5 mL, M solution in hexane) was added dropwise to a cold (−78°C) solution of γ-lactone **13** (0.7 g, 1.6 mmol) in dry toluene (10 mL) under N_2. The mixture was stirred for 7 h at −78°C. After quenching with acetic acid (1 mL), the mixture was diluted with dil NaOH (1%, 100 mL). The product was extracted with EtOAc. The organic extract was washed with water, then with brine, and dried (Na_2SO_4). The crude product, 2,3-*O*-isopropylidene-5-*O*-(1-methoxyethyl)-6-*O*-*p*-tolylsulfonyl-D-mannofuranose (**14**) was used for the next step without further purification: yield, 0.6 g; ^1H NMR: δ 7.81 (d, 2 H, *J* 8.0 Hz), 7.34 (d, 2 H, *J* 8.0 Hz), 5.26 and 5.30 (s each, 1 H,), 4.02–4.85 (m, 7 H,), 3.18 and 3.29 (s each, 3 H,), 2.43 (s, 3 H), and 1.23–1.46 (m, 9 H).

A mixture of lactol **14** (0.6 g, 1.38 mmol) and NaH (0.1 g, prewashed with hexane, 4.16 mmol) in anhyd DMF (10 mL) was stirred at ambient temperature for 15 h. After quenching with acetic acid at 0°C, the mixture was diluted with EtOAc and water. The organic extract was washed with water, then with brine, and dried (Na_2SO_4). The products were purified by column chromatography over silica gel using 1:1 EtOAc–hexane as eluent. The faster moving compound, dimer (**18**), was isolated in 20–25% yield; ^1H NMR: δ 4.93 (s, 2 H), 4.68–4.88 (m, 6 H), 3.80–4.20 (m, 8 H), 3.33 and 3.38 (s each, 6 H), 1.42 (s, 6 H), 1.31–1.39 (m, 6 H), 1.30 (s, 6 H). The slower moving compound, the desired **15**, was obtained in 25–30% yield: ^1H NMR: δ 5.25 (d, 1 H, *J* 4.18 Hz), 4.37–4.99 (m, 5 H), 3.79–3.86 (m, 2 H), 3.33 and 3.31 (s each, 3 H), 1.64 (s, 3 H), 1.44 (s, 3 H), 1.36–1.40 (m, 3 H); HRMS: Calcd for $C_{12}H_{20}O_6$ NH_4 $(M + NH_4)^+$ *m/z* 278.1603; found *m/z* 278.1600.

Preparation of 2,3-O-isopropylidene-1,6-anhydro-β-D-mannofuranose (**16**).—A solution of **15** (40 mg, 0.15 mmol)) in acetic acid (2 mL) and water (0.2 mL) was stirred at ambient temperature for 2 h. After workup, the product **16** was purified by chromatography: yield, 95%; mp 95–96°C [lit.[10] 93–94°C]; ^1H NMR: δ 5.21 (d, 1 H, J 4.3 Hz), 4.99 (dd, 1 H, *J* 8.8, *J* 6.5 Hz), 4.70–4.78 (m, 2 H), 4.34 (d, 1 H, *J* 6.4 Hz), 3.77 (d, 1 H, *J* 12.4 Hz), 3.70 (br s, 1 H), 3.15 (br s, 1 H), 1.65 (s, 3 H), 1.45 (s,

3 H); HRMS: Calcd for $C_8H_{11}O_5$ $(M - CH_3)^+$ m/z 187.0606; found m/g 187.0605.

Preparation of 2,3-O-isopropylidene-5-O-acetyl-1,6-anhydro-β-D-mannofuranose (**17**).—Compound **16** (30 mg, 0.148 mmol) was acetylated with Ac_2O (1 mL) in pyridine (2 mL) at 0°C. After workup the acetate (**17**) was obtained in 95% yield; mp 100–101°C, [lit.[10] 102–103°C]; ^1H NMR: δ 5.27 (d, 1 H, J 4.13 Hz), 4.99 (dd, 1 H, J 8.53, 6.60 Hz), 4.88 (s, 1 H), 4.72–4.79 (m, 2 H), 4.43 (d, 1 H, J 6.34 Hz), 3.82 (d, 1 H, J 13.25 Hz), 2.17 (s, 3 H), 1.66 (s, 3 H), and 1.45 (s, 3 H).

Preparation of 2,3,5-tri-O-acetyl-1,6-anhydro-β-D-mannofuranose (**2**).—A solution of **17** (30 mg, 0.123 mmol) and PpTS (25 mg, 0.1 mmol) in dry MeOH was refluxed under N_2 for 4–5 h. After evaporation of solvent, the crude product was acetylated with Ac_2O (1 mL) in pyridine (2 mL) at 0°C. Usual workup and column chromatography over silica gel using 1:1 EtOAc–hexane furnished **2** as an oil: yield, 85%; $[\alpha]_D^{25}$ − 86.8° (c 0.1, $CHCl_3$) [lit.[10] − 86.8°]; IR (neat) 1751 cm^{-1}; ^1H NMR: δ 5.46 (d, 1 H, J 4.5 Hz), 5.41 (dd, 1 H, J 9.6, 7.0 Hz), 5.16 (dd, 1 H, J 9.6, 4.5 Hz), 4.78 (br s, 1 H), 4.55 (d, 1 H, J 7.0 Hz), 4.40 (dd, 1 H, J 13.5, 3.0 Hz), 3.86 (dd, 1 H, J 13.5, 1.5 Hz), 2.20 (s, 3 H), 2.17 (s, 3 H), and 2.12 (s, 3 H); ^{13}C NMR: δ 170.69, 169.33, 169.20, 95.79, 74.96, 68.20, 66.41, 66.31, 63.67, 21.12 and 20.36 (2 C); CIMS (CH_4): m/z (*rel* intensity) 289 (M + 1, 100), 317 (M + 29, 5), 329 (M + 41, 4), 229 (10), 127 (15), and 109 (10); HRMS (EI): Calcd for $C_{10}H_{13}O_7$ (M − $COCH_3$), m/z 245.0661; found m/z 245.0664.

1,6′ : 6,1′-Dianhydro-2,3 : 2′3′-di-O-isopropylidene-di-α-D-mannofuranose (**19**, dimer-diol).—A solution of the dimer **18** (40 mg) in acetic acid (2 mL) and water (0.2 mL) was stirred at ambient temperature for 2 h. After aqueous workup, the dimer-diol **19** was obtained: yield, 95%; mp 248–250°C; ^1H NMR (250 MHz): δ 4.98 (s, 2 H), 4.80 (dd, 2 H, J 10.0, 2.5 Hz), 4.66 (d, 2 H, J 10.0 Hz), 4.09 (dd, 2 H, J 12.0, 2.5 Hz), 3.88–4.02 (m, 6 H), 2.30 (br s, 2 H), 1.40 (s, 6 H), and 1.30 (s, 6 H); ^{13}C NMR (62.89 MHz): δ 113.29, 107.09, 85.23, 79.62, 77.81, 68.97, 68.70, 26.42, and 25.37; HRMS (EI): Calcd for $C_{18}H_{24}O_8$ (M − 2 × H_2O), m/z 368.3442; found m/z 368.3445.

Single-crystal X-ray crystallographic analysis of dimer-diol **19**.—A rectangular-shaped crystal was used for X-ray measurements on an Enraf–Nonius CAD-4 diffractometer equipped with a Cu X-ray source and incident beam graphite monochromator, $\lambda(CuK\alpha) = 1.5418$ Å. Cell parameters from 25 reflections measured in the range of $10.0 \leqslant \theta \leqslant 38.1°$. Data were collected with the $2\theta/\theta$ scan method at a constant speed of 5.49° min^{-1}, $\theta_{range} = 1.5$ $(0.46 + 0.14 \tan \theta)$, maximum $\theta = 59.9°$. Each scan recorded as 96 steps with the upper and lower 16 steps used for background correction. Eight standard intensities, recorded at intervals of 1 h of X-ray exposure, showed an average change of −2.3% and were used to apply a decay correction. A ψ-scan absorption correction was applied; the correction factors ranged from 0.86–1.0. A total of 3109 data were measured; 2812 unique data; 2607 data with $I \geqslant 3\sigma$ (I). All calculations were performed with the TEXSAN system (TEXSAN, Single Crystal Structure Analysis Software, 1989, v.

5.0, Molecular Structure Corporation., 3200 A Research Forest Drive, The Woodlands, Texas 77381) running on either a DEC VaxStation II or a Dec 3100. Initial attempts to solve the structure with direct methods in $P1$ were unsuccessful. The intensity statistics were appropriate for $P\bar{1}$, and a preliminary solution was obtained with the SIR direct methods link[21] in this space group. The model, which showed substantial "disorder", was refined to an R-value of 0.35. With the $P\bar{1}$ model as a partial structure, a subsequent SIR calculation in $P1$ revealed the two crystallographically independent molecules. Preliminary positions for the methyl and hydroxyl hydrogen atoms were obtained from a difference map; positions for the other hydrogens were calculated from the C and O framework. The structure refinement used anisotropic temperature factors for C and O and isotropic terms for H and included a correction for secondary extinction. The quantity minimized was $\Sigma w(F_o\text{-}F_c)^2$, $w = 1/\sigma^2\ (F_o)$. The final R, weighted R, and goodness-of-fit values are 0.039, 0.068, and 2.21, respectively; 0.07 maximum shift/error; minimum and maximum values in the $\Delta\rho$ map of -0.25 and 0.20 e Å^3. For crystallographic data, see Table I; for atomic coordinates, see Table II.

*1,6′ : 6,1′-Dianhydro-2,3 : 2′,3′-di-*O*-isopropylidene-5,5′-di-*O*-acetyl-di-α-*D*-mannofuranose* (**20**).—The dimer-diol **19** (20 mg, 0.05 mmol) was acetylated with Ac_2O (1 mL) in pyridine (2 mL) at 0°C (12 h). After usual workup, the diacetate was obtained in 95% yield; mp 233–235°C; $[\alpha]_D^{25} - 22.8°$ (*c* 0.1, $CHCl_3$); IR (KBr) 1745 cm^{-1}; ^{1}H NMR: δ 5.07 (d, 2 H, *J* 10 Hz), 4.95 (s, 2 H), 4.64–4.70 (m, 4 H), 4.28 (dd, 2 H, *J* 10.2, 2.4 Hz), 4.13 (d, 2 H, *J* 11.61 Hz), 3.85 (d, 2 H, *J* 11.3 Hz), 2.12 (s, 6 H), 1.40 (s, 6 H), and 1.29 (s, 6 H); ^{13}C NMR: δ169.66, 113.16, 107.21, 84.93, 79.22, 75.39, 70.79, 66.63, 26.21, 25.34, and 21.15; HRMS: Calcd for $C_{21}H_{29}O_{12}$ ($M^+ - CH_3$), *m/z* 473.1659; found *m/z* 473.1656; CIMS (CH_4): *m/z* (*rel* intensity) 489 (M + 1, 100), 517 (M + 29, 8), 529 (M + 41, 5), 473 (10), 429 (8), and 245 (24).

*Preparation of 1,6′ : 6,1′-dianhydro-2,3 : 2′,3′-di-*O*-isopropylidene-5,5′-di-*O*-benzoyl-di-α-*D*-mannofuranose* (**21**).—A solution of the dimer-diol **19** (20 mg, 0.05 mmol) in pyridine (3 mL) was treated with benzoyl chloride (0.5 mL) at 0°C for 2 h. After usual workup, the dibenzoate **21** was purified by column chromatography over silica gel using 4 : 25 EtOAc–hexane: yield, 95%; mp 270°C; ^{1}H NMR: δ 7.81 (d, 4 H, *J* 7.0 Hz), 7.31 (m, 2 H), 7.19 (d, 4 H, *J* 7.0 Hz), 5.05 (d, 2 H, *J* 10.12 Hz), 4.73 (s, 2 H), 4.51 (dd, 2 H, *J* 5.6, 2.8 Hz), 4.37 (d, 2 H, *J* 5.6 Hz), 4.25 (dd, 2 H, *J* 10.2, 2.8 Hz), 4.03 (dd, 2 H, *J* 11.9, 1.5 Hz), 3.71 (dd, 2 H, *J* 11.9, 1.5 Hz), 1.13 (s, 6 H), and 0.95 (s, 6 H); ^{13}C NMR: δ 165.28, 133.09, 130.21, 129.83, 128.36, 113.24, 107.33, 85.06, 79.32, 75.60, 71.47, 66.71, 26.27, and 25.34.

*Preparation of 1,6′ : 6,1′-dianhydro-2,3 : 2′,3′-di-*O*-isopropylidene-5,5′-di-*O*-p-bromobenzoyl-di-α-*D*-mannofuranose* (**22**).—A solution of the dimer-diol **19** (30 mg, 0.074 mmol) in pyridine (3 mL) and *p*-bromobenzoyl chloride (0.15 mL) was stirred for 90 min at 0°C. After usual workup, the product **22** was purified by column chromatography over silica gel using 1 : 9 EtOAc–hexane as eluent: yield, 95%; mp 270°C; IR (KBr) 1734 cm^{-1}; ^{1}H NMR: δ 7.94 (d, 4 H, *J* 8.0 Hz), 7.61 (d, 4 H, *J* 8.0

Hz), 5.32 (d, 2 H, *J* 9.2 Hz), 5.01 (s, 2 H), 4.77 (dd, 2 H, *J* 5.6, 2.8 Hz), 4.65 (d, 2 H, *J* 5.6 Hz), 4.51 (dd, 2 H, *J* 10.0, 2.8 Hz), 4.29 (dd, 2 H, *J* 12.0, 1.4 Hz), 3.98 (dd, 2 H, *J* 12.0, 1.4 Hz), 1.41 (s, 6 H), 1.23 (s, 6 H); ^{13}C NMR: δ 164.52, 131.68, 131.32, 129.01, 128.24, 113.29, 107.29, 85.00, 79.24, 75.50, 71.72, 66.60, 26.22, and 25.29.

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