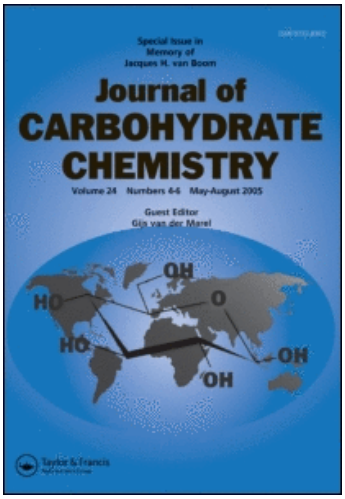

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DEHYDRATION OF SOME HEXITOLS

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ABSTRACT

Heating galactitol, D-glucitol, D-mannitol and L-iditol in a 5% aqueous sulfuric acid solution at 200 °C for 30 min afforded 1,4-, 3,6-, 1,5-, 2,6- and 1,6-monoanhydrohexitols with retained configuration as well as 2,5-monoanhydrohexitols with inverted configuration at C-2 or C-5. 1,4;3,6-, 1,5;2,6- and 1,4;2,6- ≡ 1,5;3,6-Dianhydrohexitols were also identified. Cyclization of the hexitols *via* their *O*-tosyl derivatives in pyridine gave products completely free of 2,5-anhydrohexitols but with increased amounts of dianhydrohexitols. All mixtures were separated by capillary GC (CGC) and their components identified by CGC-MS and by co-injection with standards.

INTRODUCTION

The dehydration of alditols[1-3] in aqueous hydrochloric or sulfuric acid has been known to afford a variety of cyclic products depending on the conditions of reaction and structure of reactants. Thus, tetritols in a 50% sulfuric acid solution gave 1,4-anhydrotetritols[4] and 2,5-di-(1,2-dihydroxyethyl)-1,4-dioxans[5] as a result of intra- and intermolecular elimination of water, respectively.

Inspection of the cyclization products of pentitols in 2M HCl or in 1% and 5% H_2SO_4 revealed five-membered anhydropentitols with either retained[6-8] or inverted[9] configuration at C-2 or C-4.[9] The presence of diastereomeric cyclic products can be explained in terms of isomerization taking place during cyclization. Reactions of pentitols with concentrated hydrochloric acid in a sealed ampoule[10] afforded cyclic products with retained or inverted configuration at C-2 or C-4 and also chlorodeoxy, and dichlorodideoxy derivatives of pentitols and anhydropentitols.

Cyclization of *O*-tosyl derivatives of pentitols gave monoanhydropentitols, their chlorodeoxy and dichlorodideoxy derivatives and also dianhydropentitols.[11]

Heating of hexitols in concentrated sulfuric acid[12,13] gave 1,4(3,6)-mono- and 1,4;3,6-dianhydrohexitols. Refluxing of D-mannitol in 3M sulfuric acid[14] or hydrochloric acid[15] afforded a mixture of 1,4- and 1,5-monoanhydrohexitols with retained configuration of the reactant and 2,5-anhydrohexitol with inverted configuration at C-2 or C-5.

Analogous reactions of D-mannitol in a sealed ampoule afforded the aforementioned mono- and dianhydrohexitols and also their monochloro derivatives.[16]

RESULTS AND DISCUSSION

Heating a 5% aqueous sulfuric acid solution of galactitol, D-glucitol, D-mannitol and L-iditol for 30 min at 200 °C gave a variety of mono- and dianhydrohexitols. The products, as their peracetates, and product yields are listed in the Table. CGC's of the dehydrations are presented in FIGs. 1-4.

Mixtures of the dehydration (cyclization) products were separated by Capillary Gas Chromatography as their peracetates (CGC, FIGs. 1-4) and particular components were identified by CGC-MS and by co-injection with standards. Comparison of the recorded mass spectra with those taken from

Table 1

Relative percentages of particular components of the mixture of monoanhydrohexitols[a] resulting from dehydration of hexitols in 5% sulfuric acid at 200 °C for 30 min.

Reactant	Acetylated monoanhydrohexitol	Peak no in GC	Rel. percentage
Galactitol	1,5-anhydro-D-galactitol ≈ 2,6-anhydro-L-galactitol	2[b]	traces
FIG. 1a	2,6-anhydro-D-galactitol ≈ 1,5-anhydro-L-galactitol		
	1,4-anhydro-D-galactitol ≈ 3,6-anhydro-L-galactitol	3[b] 26	99.5
	3,6-anhydro-D-galactitol ≈ 1,4-anhydro-L-galactitol		
	1,6-anhydrogalactitol	4	0.5
D-Glucitol	1,4-anhydro-D-glucitol = 3,6-anhydro-L-gulitol	3[c]	68.
FIG. 2a	3,6-anhydro-D-glucitol = 1,4-anhydro-L-gulitol		
	1,5-anhydro-D-glucitol = 2,6-anhydro-L-gulitol	4[c]	2.
	2,6-anhydro-D-glucitol = 1,5-anhydro-L-gulitol		
	2,5-anhydro-D-mannitol	5	3.
	2,5-anhydro-L-iditol	6	27.
	1,6-anhydro-D-glucitol	7	traces
D-Mannitol	1,4-anhydro-D-mannitol = 3,6-anhydro-D-mannitol	4	37.
FIG. 3a	1,5-anhydro-D-mannitol = 2,6-anhydro-D-mannitol	5	2.
	2,5-anhydro-D-glucitol	6	61.
L-Iditol	1,4-anhydro-L-iditol = 3,6-anhydro-L-iditol	2	96.
FIG. 4a	1,5-anhydro-L-iditol = 2,6-anhydro-L-iditol	3	4.

a. Calculated from GC peak areas assuming the sum of peaks of monoanhydrohexitols in the particular mixture equal to 100%;
b. Racemic mixture; c. Compounds not separated chromatographically.

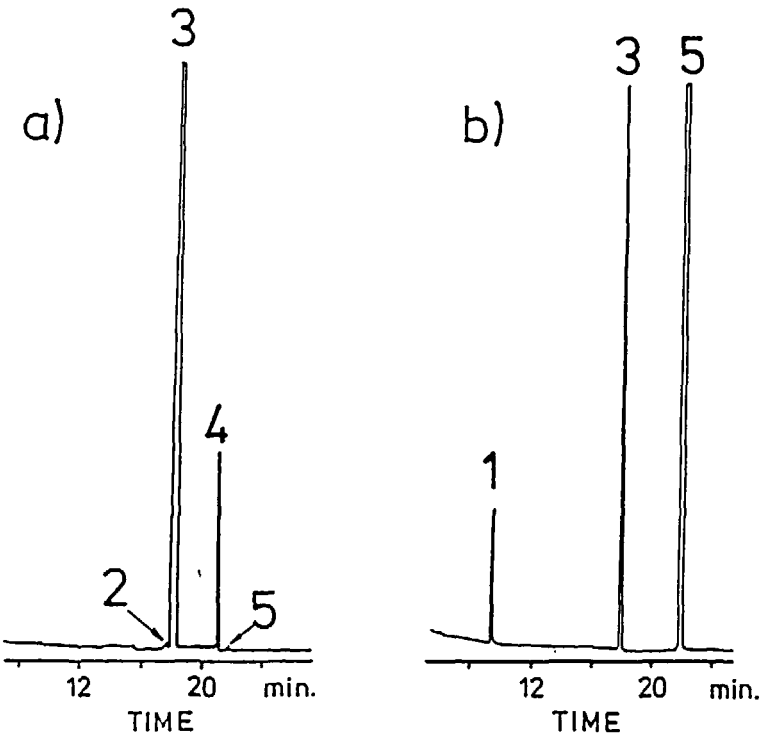


FIG. 1. CGC of per-O-acetylated dehydration (cyclization) products of galactitol: a) in 5% H_2SO_4, 200 °C, 30 min; b) via its O-tosyl derivatives in basic medium (pyridine, sodium methoxide).

Peak: 1 = 1,4:2,6-dianhydrogalactitol; 2 = 1,5-anhydrogalactitol; 3 = 1,4-anhydrogalactitol; 4 = 1,6-anhydrogalactitol; 5 = galactitol

the literature allowed only the size of the heterocyclic ring to be established. A suggested cyclization (dehydration) pathway of the hexitols is shown in Scheme 1 using D-glucitol as an example.

The results presented in the Table show that monoanhydrohexitols with tetrahydrofuran rings, i.e. 1,4-anhydro-D,L- galactitol (99% yield), 1,4-anhydro-D-glucitol and -L-gulitol (together, 68%), 2,5-anhydro-L-iditol (27%), 1,4-anhydro-D-mannitol (37%), 2,5-anhydro-D-glucitol (61%)

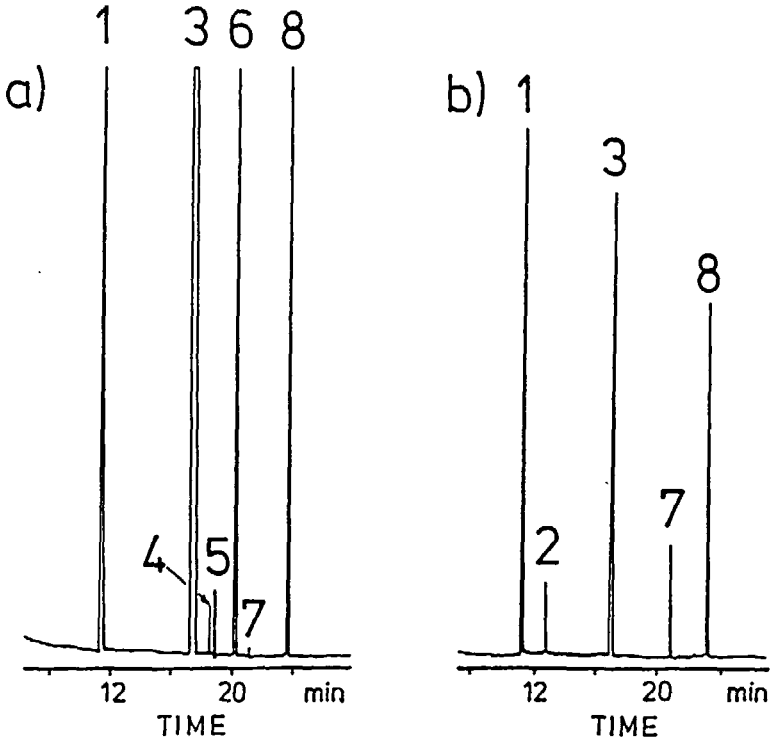


FIG. 2. CGC of per-O-acetylated dehydration (cyclization) products of D-glucitol: a) in 5% H_2SO_4; 200 °C, 30 min; b) via its O-tosyl derivatives in basic medium (pyridine, sodium methoxide).

Peak: 1 = 1,4:3,6-dianhydroglucitol; 2 = 1,5:3,6-dianhydroglucitol; 3 = 1,4-anhydroglucitol and 3,6-anhydroglucitol; 4 = 1,5-anhydroglucitol and 2,6-anhydroglucitol; 5 = 2,5-anhydromannitol; 6 = 2,5-anhydroiditol; 7 = 1,6-anhydroglucitol; 8 = glucitol

and 1,4-anhydro-L-iditol (96%) are formed in the highest amounts irrespective of the acidic reaction conditions. This outcome is in keeping with the spatial requirements of the molecules being formed. For instance, the favorable arrangement of bulky substituents (devoid of 1,2-*cis* groupings) favors formation of 1,4-anhydro-D-galactitol (99%) on the one hand whereas unfavorable interactions (two *cis*-1,2 groupings) result in formation of much less 1,4-anhydro-*D*-mannitol (37%).

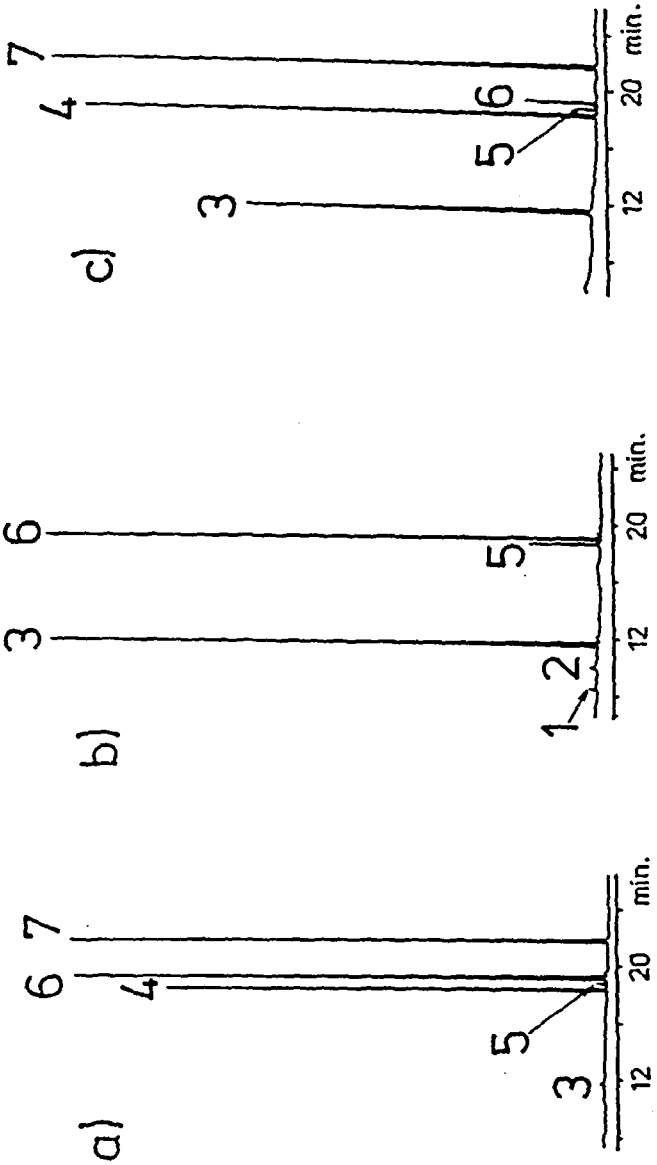


FIG. 3. GGC of per-O-acetylated dehydration (cyclization) products of D-mannitol: a) in 5% H_2SO_4; 200 °C, 30 min; b) in 5% H_2SO_4; 200 °C, 40 h; c) via its O-tosyl derivatives in basic medium (pyridine, sodium methoxide). Peak: 1 = 1,5:2,6-dianhydromannitol; 2 = 1,4:2,6-dianhydromannitol; 3 = 1,4:3,6-dianhydromannitol; 4 = 1,4(3,6)-anhydromannitol; 5 = 1,5(2,6)-anhydromannitol; 6 = 2,5-anhydroglucitol; 7 = mannitol.

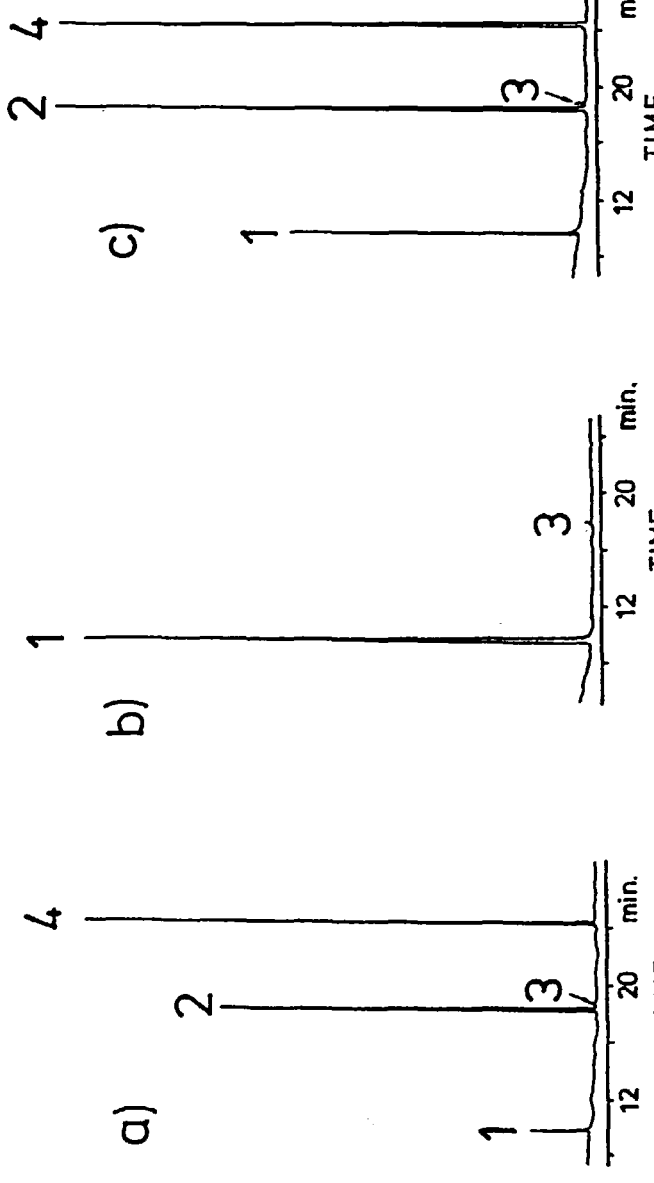
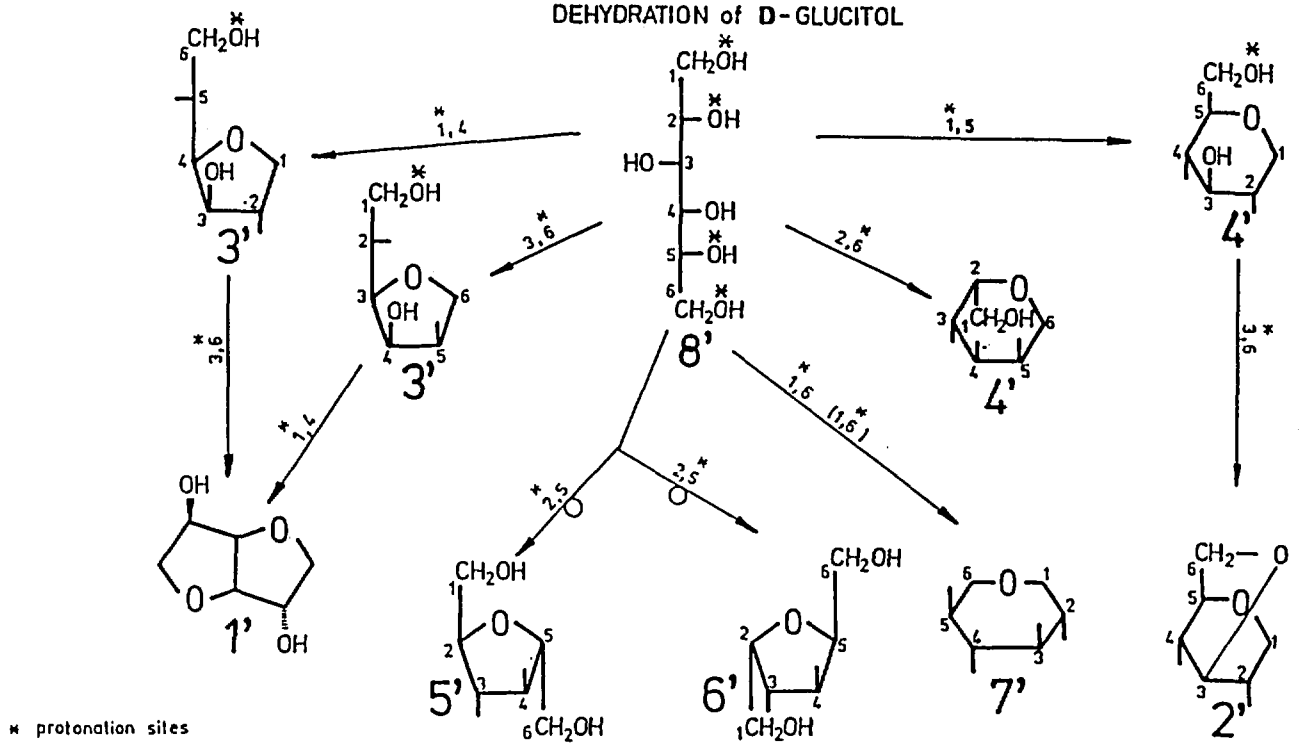


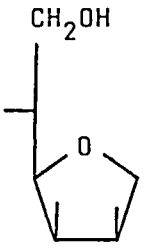
FIG. 4. CGC of per-O-acetylated dehydration (cyclization) products of L-iditol: a) in 5% H_2SO_4; 200 °C, 30 min; b) in 5% H_2SO_4; 200 °C, 90 min; c) via its O-tosyl derivatives in basic medium (pyridine, sodium methoxide). Peak : 1 = 1,4:3,6-dianhydroiditol; 2 = 1,4(3,6)-anhydroiditol; 3 = 1,5(2,6)-anhydroiditol; 4 = iditol.



'Numbering of the structures is based on peak numbers in FIG. 2 corresponding to per-O-acetylated derivatives of these compounds.

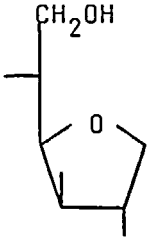
Scheme 1

1,4-anhydro-D-galactitol

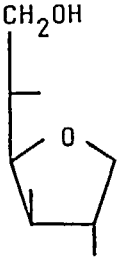


1,4-anhydro-D-mannitol

In the two remaining cases, 1,4-anhydro-D-glucitol (68%)[17] and -L-iditol (96%), respectively the stability of those molecules is each influenced by a single *cis* 1,2-grouping.



1,4-anhydro-D-glucitol



1,4-anhydro-L-iditol

The six-membered 1,5- and 2,6-monoanhydrohexitols are formed in low yields, this resembling the dehydration experiments with pentitols.[9] However, unlike pentitols, isomers with inverted configuration at C-4 and C-3 were missing in the 1,4(3,6) dehydration products of hexitols, possibly due to the shielding effect of the -CH_2OH group (at C-5 or C-2) during attack of the oxygen atom bonded with C-1 or C-6 on positively charged C-4 or C-3.

Cyclization of D-glucitol gave 2,5-anhydrohexitols with inversion of configuration at C-2 or C-5, in overall yield of 30%. The 2,5 dehydration of D-glucitol (Table) results in varying yields ranging from 3% for 2,5-anhydro-D-mannitol (inversion of C-2; FIG. 2a, peak 5) to 27% for 2,5-anhydro-L-iditol (inversion of C-5; FIG. 2a, peak 6). Under the acidic

conditons employed in the cyclization of hexitols, dianhydrohexitols are also formed. Again formation of a 5-membered ring is preferred (FIG. 2a, peak 1; FIG. 3b, peak 3; FIG. 4b, peak 1) rather than a 6-membered one.

The dehydration of hexitols *via* corresponding *O*-tosyl products in pyridine in the cold, followed by heating the mixture with sodium methoxide proceeds readily. First, *O*-tosyl derivatives of only primary alcoholic groups are formed which undergo rapid cyclization (mostly 1,4 or 3,6) to form 5-membered rings (FIG. 1b, peak 3, FIG. 2b, peak 3, FIG. 3c peak 4 and FIG. 4c, peak 2). The formed monoanhydrohexitols undergo secondary cyclization (mostly 3,6 or 1,4) to form primarily 5-membered rings (FIG. 2b, peak 1, FIG. 3c, peak 3, FIG. 4c, peak 1).

EXPERIMENTAL

Reaction 1. Dehydration of hexitols in 5% aqueous sulfuric acid.

a. Sealed ampoules each containing 20 mg (0.11 mmol) of an alditol (galactitol, D-glucitol, D-mannitol or L-iditol) and 0.2 mL of 5% H_2SO_4 were heated at 200 °C for 30 min. The reaction mixtures were allowed to cool to room temperature, neutralized with $BaCO_3$, filtered and the filtrates concentrated to dryness under a nitrogen stream. The residues were acetylated with 0.6 mL of acetic anhydride in the presence of catalytic amounts of sodium acetate during 1h at 100 °C.

The procedure was repeated but with extended heating at 200 °C for D-mannitol (40 h) and L-iditol (1.5 h).

Reaction 2. Cyclization of hexitols *via* *O*-tosylation.

a. D-Glucitol or D-mannitol (5.5 mg; 0.03 mmol each) were placed in two screw capped glass vials to which 14.3 mg (0.075 mmol) of p-toluenesulfonyl chloride (TsCl) and 0.3 mL of freshly distilled pyridine were added. The tightly closed vials were left for 5 days at ambient temperature. The solvent was then expelled under nitrogen and 0.1 mL of abs

methanol together with 0.3 mL of 0.31 M methanolic solution of sodium methoxide were added to each vial. The mixtures were heated for 2 h at 70 °C, cooled, neutralized with N H_2SO_4 and concentrated to dryness under a nitrogen stream. The residue was acetylated with 0.3 mL of acetic anhydride as in 1a.

b. Galactitol and L-iditol (5.5 mg; 0.03 mmol each) were placed in separate screw capped vials to which 11.5 mg (0.06 mmol) of TsCl and 0.3 mL of freshly distilled pyridine were added. The tightly closed vials were heated at 60 °C for 4 h. After cooling, the solvent was removed under a nitrogen stream and the residue was cyclized in the methanolic sodium methoxide solution as described for 2a.

Reaction products 1 and 2 were analyzed by CGC.

Isolation of 3,6-anhydro-D-glucitol.

The mother liquors left after isolation of 1,4-anhydro-D-glucitol, obtained by dehydration of D-glucitol,[12] were dissolved in boiling ethyl acetate and treated with ethanol. The resulting precipitate was dissolved in boiling ethyl acetate and reprecipitated with ethanol. The procedure was repeated four times to give a homogeneous, crystalline substance with the mp and optical rotation identical with those of 3,6-anhydro-D-glucitol (1,4-anhydro-L-gulitol).[18]

The following standards have been synthesized by the cited methods: 1,4-anhydro-D-galactitol,[19] 1,4-anhydro-D-glucitol,[12] 3,6-anhydro-D-glucitol,[18] 1,4-anhydro-D-mannitol,[20] 1,5-anhydro-D-galactitol,[21] 1,5-anhydro-D-glucitol,[21] 2,6-anhydro-D-glucitol,[22] 1,5-anhydro-D-mannitol,[21] 2,5-anhydro-D-glucitol,[23] 2,5-anhydro-D-mannitol,[24] 1,4;3,6-dianhydro-D-glucitol,[25] 1,4;3,6-dianhydro-D-mannitol,[26] 1,4;3,6-dianhydro-L-iditol,[27] 1,4;2,6-dianhydro-D-galactitol,[28] 1,5;3,6-dianhydro-D-glucitol,[29] 1,5;3,6-dianhydro-D-mannitol,[29] 1,5;2,6-dianhydro-D-mannitol.[26]

Capillary Gas Chromatography (CGC)

The instrument used was a CHROM-5 (Laboratorni Pristroje, Prague) gas chromatograph equipped with a flame ionization detector (FID) and a capillary column (50m x 0.3mm) coated

with an SP-2340 stationary phase (film thickness 0.15μm on $BaCO_3$).[29] Hydrogen was used as a carrier gas. The temperature of both the detector and injection port was held at 240 °C. The oven temperature was programmed as follows: 140 °C, 4 °C/min.

Capillary Gas Chromatography - Mass Spectrometry (CGC-MS)

Mass spectra were recorded on a Hewlett-Packard CG-MS System Model 5992B instrument equipped with a capillary column (Carbowax 20M; 20m x 0.2mm). The injection port temperature was 240 °C. The mass spectrometer was equipped with a jet separator. Samples were ionized with a 70-eV beam of electrons.

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REFERENCES AND FOOTNOTES

1. L. F. Wiggins, *Adv. Carbohydr. Chem.*, 5, 191 (1950).

2. L. Hough, A. C. Richardson, in Rodd·s Chemistry of Carbon Compounds, Vol. I, Part F, S. Coffey, Ed., 2nd edn, Elsevier, Amsterdam, 1 (1967).

3. S. Soltzberg, *Adv. Carbohydr. Chem. Biochem.*, 25, 229 (1970).

4. H. Klosterman, F. Smith, *J. Am. Chem. Soc.*, 74, 5336 (1952).

5. A. H. Haines, A. G. Wells, *Carbohydr. Res.*, 27, 261 (1973).

6. J. F. Carson, W. D. Maclay, *J. Am. Chem. Soc.*, 67, 1808 (1945).

7. J. Baddiley, J. G. Buchanan, B. Carss, A. P. Mathias, *J. Chem. Soc.*, 1956, 4583.

8. D. L. MacDonald, J. D. Crum, R. Barker, *J. Am. Chem. Soc.*, 67, 3379 (1958).

9. A. Wisniewski, J. Szafranek, J. Sokolowski, *Carbohydr. Res.*, 97, 229 (1981).

10. A. Wisniewski, J. Sokolowski, J. Szafranek, *J. Carbohydr. Chem.*, 2, 293 (1983).

11. A. Wisniewski, E. Skorupowa, J. Sokolowski, D. Glod, G. Descotes, *J. Carbohydr. Chem.*, 8, 59 (1989).

12. S. Soltzberg, R. M. Goepp, *Jr.*, W. Freudenberg, *J. Am. Chem. Soc.*, 68, 919 (1946).

13. R. C. Hockett, H. G. Fletcher, *Jr.*, E. L. Sheffield, R. M. Goepp, *Jr.*, *J. Am. Chem. Soc.*, 68, 927 (1946).

14. K. Bock, Ch. Pedersen, H. Thogersen, *Acta Chim. Scand.*, B(35), 441 (1981).

15. T. A. W. Koerner, *Jr.*, R. J. Voll, E. S. Younathan, *Carbohydr. Res.*, 59, 403 (1977).

16. J. Szafranek, A. Wisniewski, *J. Chromatogr.*, 161, 213 (1978).

17. The lower yields of 1,4-anhydro-D-glucitol and -L-gulitol is due to the fact that under the conditions used (200 °C; 30 min) the product of successive dehydration, 1,4;3,6-dianhydro-D-glucitol, arises at their expense. The yield obtained after shorter heating (10 min) when successive cyclization failed to occur was 94%.

18. E. Fischer, K. Zach, *Ber.*, 45, 2068 (1912).

19. R. K. Ness, H. G. Fletcher, *Jr.*, C. S. Hudson, *J. Am. Chem. Soc.*, 73, 3742 (1951).

20. H. G. Fletcher, *Jr.*, H. W. Diehl, *J. Am. Chem. Soc.*, 74, 3175 (1952).

21. R. K. Ness, H. G. Fletcher, *Jr.*, C. S. Hudson, *J. Am. Chem. Soc.*, 72, 4547 (1950).

22. R. K. Ness, H. G. Fletcher, *Jr.*, *J. Am. Chem. Soc.*, 75, 2619 (1953).

23. T. A. W. Koerner, *Jr.*, R. J. Voll, E. S. Younathan, *Carbohydr. Res.*, 59, 403 (1977).

24. D. Horton, K. D. Philips, *Carbohydr. Res.*, 30, 367 (1973).

25. R. Montgomery, L. F. Wiggins, *J. Chem. Soc.*, 390, (1946).

26. R. Jeanloz, H. G. Fletcher, *Jr.*, C. S. Hudson, *J. Am. Chem. Soc.*, 70, 4052 (1948).

27. H. G. Fletcher, *Jr.*, R. M. Goepp, *Jr.*, *J. Am. Chem. Soc.*, 68, 939 (1946).

28. A. Wisniewski, E. Skorupowa, J. Sokolowski, L. Rozanski, D. Glod, G. Descotes, *J. Carbohydr. Chem.*, 8, 73 (1989).

29. K. Grob. G. Grob, *J. Chromatogr.*, 125, 471 (1976).