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Note

Efficient synthesis of α,ω-dibromodideoxyalditols as precursors for α,ω-dithioalkylalditols

Caroline Crombez-Robert, Mohammed Benazza, Catherine Fréchou, Gilles Demailly *

Laboratoire de Chimie Organique, Université de Picardie Jules Verne, 33 rue Saint-Leu, F-80039 Amiens, France

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Abstract

The regioselective bromination of unprotected alditols (D-arabinitol, xylitol, ribitol, D-glucitol, and D-mannitol) was achieved with acetyl bromide as the brominating reagent. The α,ω-dibromodideoxyalditols were isolated after acetylation in good overall yields (51–80%). 1,5-Dithioalkylpentitols, 1,6-dithioalkyl-D-mannitol, and D-glucitol were obtained from the dibromo derivatives and sodium alkanethiolates (with R = *n*-butyl, *n*-octyl, *n*-dodecyl, and *n*-hexadecyl). © 1997 Published by Elsevier Science Ltd.

Keywords: Alditols; α,ω-Dibromoalditols; α,ω-Dithioalkylalditols; Thioetherification; Regioselective bromination; Acetoxonium ion

Bromodeoxyalditols are used as alkylating agents in chemotherapy [1], and as intermediates leading to potential glycosidase inhibitors and anti-HIV iminocyclitols [2].

In our investigation on the functionalisation of unprotected carbohydrates, regioselective bromination at the primary carbon atoms of alditols leading to the α,ω-dibromo derivatives dominated. In previous work, we reported some chlorination [3,4] and bromination [$Me_2(OAc)COBr$, Scheme 1] [5] reactions in which heterocyclisation was avoided by using neutral conditions and cyclic intermediates [6,7]. This was attributed to the fact that hydroxyl groups involved in the cyclodehydration reaction were simultaneously protected in the bromination process.

Under neutral conditions, cyclic iminium salts [8] and acetoxonium ions [5] are intermediates. When the acetoxonium ion was used, the nature of the by-products was found to depend greatly upon the alditol structure and the halogenating reagent (1-bromocarbonyl-1-methylethyl acetate or hydrogen bromide/acetic acid). It is important to emphasise that, with hydrogen bromide–acetic acid as brominating reagent, the resulting α,ω-dibromodideoxyhexitol derivatives were obtained in modest yields with large amounts of anhydro derivatives as by-products [5]. This is probably due to competitive hydroxyl protonation inducing cyclodehydration with loss of one molecule of water [9].

Acetyl bromide, commonly used as an acylating reagent, can also be used as a brominating reagent

* Corresponding author. E-mail: Demailly.gilles@sc.u-picardie.fr

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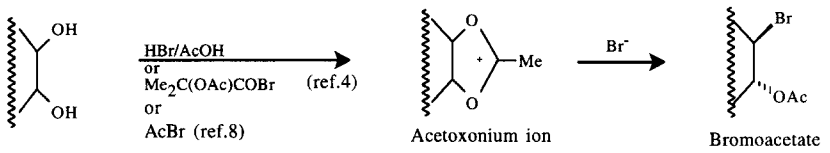


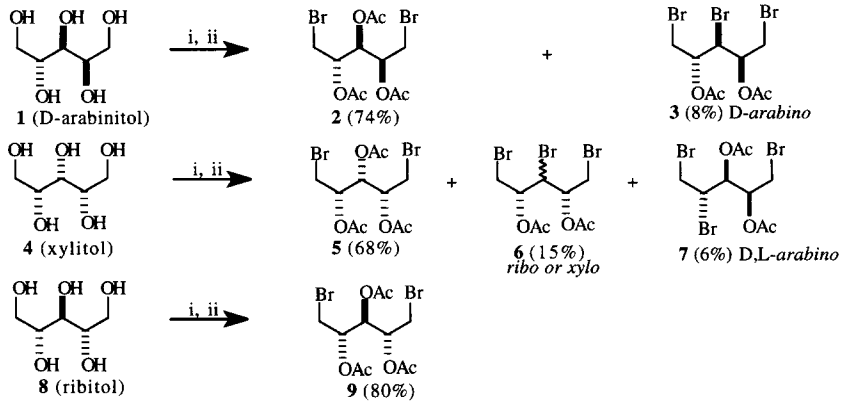
Scheme 1.

when two *cis* vicinal hydroxyl groups are present (Scheme 1) [10]. For instance, in the carbohydrate field, bromination occurred on vicinal *cis* secondary hydroxyl groups by 1,2-acetoxonium ring opening (five-membered ring) leading to bromoacetoxy derivatives [11] with configurational inversion.

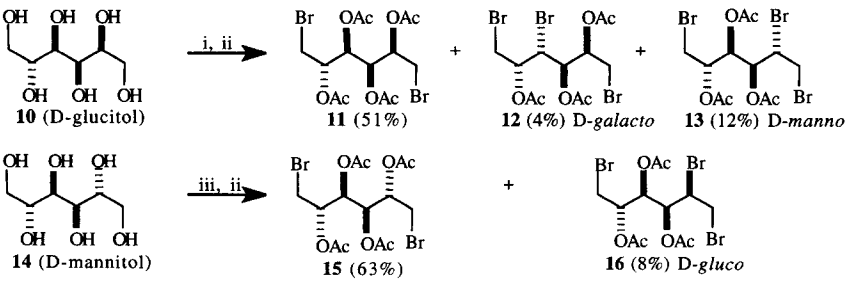
In the present work, we report the direct synthesis of α,ω-dibromodideoxyalditol derivatives which subsequently gives α,ω-dithioalkylalditol derivatives in good yields.

Bromination of alditols was performed in 1,4-dioxane as a non-polar solvent. D-Arabinitol (**1**), xylitol (**4**), and ribitol (**8**) were treated with acetyl bromide (3 equiv) at room temperature for 16 h. After acetylation of the crude product, 2,3,5-tri-*O*-acetyl-1,5-dibromo-1,5-dideoxy-D-arabinitol (**2**), xylitol (**5**), and ribitol (**9**) were isolated by chromatography in 74, 68, and 80% yields, respectively (Scheme 2). From **1** and **4**, only linear tribromotrideoxyalditol derivatives **3** (*arabino*), **6** (*xylo* or *ribo*), and **7** (*arabino*) were obtained in lower yields.

With hexitols, 2.4 equiv of acetyl bromide were required. With D-mannitol, prolonged reaction time (72 h) was necessary. Thus, D-glucitol (**10**) and D-mannitol (**14**) gave, after acetylation, 2,3,4,5-tetra-*O*-acetyl-1,6-dibromo-1,6-dideoxy-D-glucitol (**11**) and -D-mannitol (**15**) in 51 and 63% yields, respectively (Scheme 3). The linear tribromo derivatives **12**, **13**, and **16** with D-*galacto*, D-*manno*, and D-*gluco* configurations, respectively, were obtained in small amounts. With both pentitols and hexitols, anhydro derivatives were not detected. Furthermore, bromination at C-2 of **10** and **14** (see compounds **13** and **16**) imply that the initial bromination at the primary carbon atoms takes place via a 1,3-acetoxonium ion ring opening (six-membered ring) [4].



Scheme 2. (i) 0.5 g, 3 equiv of AcBr, RT, 16 h, 1,4-dioxane; (ii) Ac_2O, pyridine.

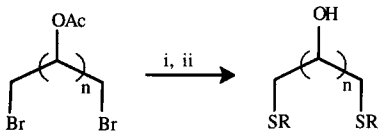


Scheme 3. (i) 0.5 g, 2.4 equiv of AcBr, RT, 16 h, 1,4-dioxane; (ii) Ac_2O, pyridine; (iii) 0.5 g, 2.4 equiv of AcBr, RT, 72 h, 1,4-dioxane.

Table 1
^{1}H Chemical shifts (δ, ppm) and coupling constants (J, Hz) for peracetylated dibromoalditol derivatives (in $CDCl_3$) and for unprotected dithioalkylalditol derivatives (in C_5D_5N)

Compd	Chemical shifts									Coupling constants										
	H-1	H-1′	H-2	H-3	H-4	H-5	H-5′	H-6	H-6′	$J_{1,1'}$	$J_{1,2}$	$J_{1',2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{4,5'}$	$J_{5,5'}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$
2	3.27(dd)	3.33(dd)	5.30(m)	5.41(dd)	5.08(m)	3.37(dd)	3.51(dd)			10.8	7.2	5.5	2.2	8.5	5.5	3.3	11.6			
3	3.42(dd)	3.47(dd)	5.21(m)	4.57(dd)	5.09(m)	3.73(dd)	3.84(dd)			10.18	8.3	6.3	1.76	10.1	2.85	3.7	11.8			
5	3.39(dd)	3.43(dd)	5.31(dd)	5.52(t)	5.31(dd)	3.39(dd)	3.43(dd)			11.2	5.9	4.8	5.1	5.1	5.9	4.8	11.2			
6	3.62(dd)	3.62(dd)	5.21(dd)	4.41(t)	5.21(dd)	3.62(dd)	3.62(dd)			–	5.0	5.0	6.2	6.2	5.0	5.0	11.2			
7	3.32(dd)	3.39(dd)	5.54(m)	5.49(dd)	4.24(dd)	3.66(dd)	3.70(dd)			10.6	6.8	6.2	2.5	8.18	5.9	5.7	11.5			
9	3.32(dd)	3.51(dd)	5.14(dd)	5.19(t)	5.14(dd)	3.32(dd)	3.51(dd)			11.2	7.4	3.1	4.9	4.9	7.4	3.1	11.2			
11	3.49(dd)	3.51(dd)	5.06(m)	5.47(dd)	5.31(dd)	5.02(m)		3.38(dd)	3.52(dd)	11.3	4.5	3.7	7.1	3.3	7.3			5.7	5.8	11.6
12	3.27(dd)	3.34(dd)	5.61(m)	5.44(dd)	4.42(dd)	5.01(m)		3.42(dd)	3.46(dd)	10.6	6.9	6.4	1.7	10.3	1.7			8.2	6	10.4
13	3.62(dd)	3.71(dd)	4.16(m)	5.38(dd)	5.62(dd)	5.09(m)		3.33(dd)	3.49(dd)	11.3	6.3	6.3	8.1	1.9	8.4			6.2	3.6	11.6
15	3.30(dd)	3.48(dd)	5.04(m)	5.35(d)	5.35(d)	5.04(m)		3.30(dd)	3.48(dd)	11.6	6	3.8	8.1	–	8.1			6	3.8	11.6
16	3.60(dd)	3.76(dd)	4.23(m)	5.55(dd)	4.39(dd)	5.06(m)		3.38(dd)	3.45(dd)	11.1	7.9	4.7	4.2	3.7	7.4			5.6	3.5	11.6
17	3.18(dd)	3.18(dd)	4.74(t)	4.23(t)	4.55(ddd)	3.12(dd)	3.48(dd)			13.4	7	7	1,5	8.3	8	3	13.4			
18	3.15(dd)	3.15(dd)	4.72(t)	4.24(d)	4.54(ddd)	3.11(dd)	3.46(dd)			13.6	6.8	6.8	–	8.3	8	2.6	13.4			
19	3.25(dd)	3.25(dd)	4.85(t)	4.32(d)	4.63(t)	3.21(dd)	3.59(dd)			13.2	6.8	6.8	–	8.0	7.5	3	13.4			
20	3.21(dd)	3.21(dd)	4.79(t)	4.26(d)	4.58(t)	3.16(dd)	3.53(dd)			13.0	6.9	6.9	–	8.1	7.9	2.4	13.4			
21	3.15(dd)	3.30(dd)	4.48(m)	4.37(t)	4.48(m)	3.15(dd)	3.30(dd)			13.2	7	5.8	3.4	3.4	7	5.8	13.2			
22	3.16(dd)	3.28(dd)	4.46(m)	4.35(t)	4.46(m)	3.16(dd)	3.28(dd)			13.2	7	5.9	3.5	3.5	7	5.9	13.2			
23	3.26(dd)	3.38(dd)	4.46(m)	4.57(d)	4.46(m)	3.26(dd)	3.38(dd)			13.2	6.9	5.8	3.2	3.2	6.9	5.8	13.2			
24	3.18(dd)	3.30(dd)	4.51(m)	4.38(s)	4.51(m)	3.18(dd)	3.30(dd)			13.2	7.1	5.9	–	–	7.1	5.9	13.2			
25	3.10(dd)	3.35(dd)	4.46(m)	4.25(t)	4.46(m)	3.10(dd)	3.35(dd)			13.5	8.5	2.8	6.4	6.4	8.5	2.8	13.5			
26	3.19(dd)	3.45(dd)	4.54(m)	4.30(t)	4.54(m)	3.19(dd)	3.45(dd)			13.4	8.7	2.8	6	6	8.7	2.8	13.4			
27	3.19(dd)	3.45(dd)	4.55(m)	4.33(t)	4.55(m)	3.19(dd)	3.45(dd)			13.5	8.6	2.7	6.4	6.4	8.6	2.7	13.5			
28	3.25(dd)	3.51(dd)	4.60(m)	4.36(t)	4.60(m)	3.25(dd)	3.51(dd)			13.3	8.4	2.2	6.4	6.4	8.4	2.2	13.3			
29	3.17(dd)	3.50(dd)	4.60(m)	4.35(dd)	4.76(dd)	4.51(m)		3.13(dd)	3.27(dd)	13.4	7.3	2.8	7.8	1.9	3.43			6.3	5.6	13.3
30	3.18(dd)	3.53(dd)	4.59(m)	4.36(dd)	4.73(d)	4.50(m)		3.14(dd)	3.27(dd)	13.5	7.3	2.6	7.6	1.8	–			6.9	5.7	13.3
31	3.20(dd)	3.52(dd)	4.61(m)	4.35(d)	4.76(s)	4.52(m)		3.15(dd)	3.30(dd)	13.4	7.3	2	8	–	–			6.1	5.6	13.3
32 [a]	2.53(dd)	2.62(dd)	5.08(m)	5.47(t)	5.38(t)	5.00(m)			2.72(dd)	15.3	7	5.5	5.2	5.2	5.2			6.9	4.8	14.4
33	3.15(dd)	3.54(dd)	4.61(m)	4.65(d)	4.65(d)	4.61(m)		3.15(dd)	3.54(dd)	13.4	8.2	2.7	8	–	8			8.2	2.7	13.4
34	3.14(dd)	3.53(dd)	4.58(ddd)	4.66(d)	4.66(d)	4.58(ddd)		3.14(dd)	3.53(dd)	13.6	8.2	2.6	8.2	–	8.2			8.2	2.6	13.6
35	3.16(dd)	3.55(dd)	4.63(m)	4.72(d)	4.72(d)	4.63(m)		3.16(dd)	3.55(dd)	13.4	8.2	2.7	8.1	–	8.1			8.2	2.7	13.4
36 [a]	2.51(dd)	2.68(dd)	5.01(m)	5.33(d)	5.33(d)	5.01(m)		2.51(dd)	2.68(dd)	14.2	8	4.3	7.1	–	7.1			8	4.3	14.2

[a] ^{1}H NMR data for peracetylated derivatives in $CDCl_3$.



Scheme 4. $n = 3$ (pentitols), 4 (hexitols); RSH/NaH, THF–Me_2SO; (ii) MeONa, MeOH.

The structures of the tribromotrideoxyalditols were determined by ^1H NMR spectroscopy (Table 1). The *syn–anti* methine coupling constants ($J_{2,3}$ and $J_{3,4}$), for compounds **3** and **7** indicate that both derivatives adopt a planar zig-zag conformation and the D-*arabino* configuration [7]. Similarly, with hexitol derivatives, the arrangement *syn–anti–syn* in **12**, *anti–syn–anti* in **13**, and *syn–syn–anti* methine as deduced from the coupling constants ($J_{2,3}$, $J_{3,4}$, and $J_{4,5}$) in **16** are consistent with the D-*galacto*, D-*manno*, and D-*gluco* configuration, respectively. On the other hand, in **6**, both *xylo* and *ribo* configurations could be considered since $J_{2,3}$ and $J_{3,4}$ have the same values. Therefore, in all cases the bromination of secondary alcools occurred with inversion of configuration.

The introduction of alkylthio groups in the α,ω-dibromodideoxyalditol derivatives could be performed by using available alkylthiolate ion (e.g. sodium alkylthiolate) or alkylthiol/base for preparation *in situ* of the alkylthiolate ion [12]. The latter was preferred in order to avoid oxidation of the thiol to bis(dialkyl disulfide) [13]. However, with peracetylated α,ω-dibromodideoxyalditols, the use of base such as sodium methoxide or sodium hydroxide was excluded due to deacetylation and subsequent heterocyclisation of the free dibromo derivatives. With sodium hydride, the acetyl groups were preserved and thioetherification could be performed (Scheme 4).

In the present work, the thioalkylation was performed with alkylthiol/sodium hydride as thioalkylating reagent. Hence, the 1,5-dibromodideoxypentitol derivatives (**2**, **5**, and **9**) and 1,6-dibromodideoxyhexitol derivatives (**11** and **15**) were treated with alkanethiol (2.4 equiv of RSH, R = C_4H_9, C_8H_{17}, $C_{12}H_{25}$, and $C_{16}H_{33}$) and sodium

Table 2
Yields and physical data of 1,5-dideoxy-1,5-dithioalkylpentitols and 1,6-dideoxy-1,6-dithioalkylhexitols

Substrats	Isolated yields (%) [a]	mp (°C) [b]	$[\alpha]_D$ [c]	R_f [e]
2	**17** (90) (C-4) [d]	78–79 (from hexane)	+50.6 (*c* 1.04, $HCCl_3$)	0.51
	18 (92) (C-8) [d]	86–87 (from hexane)	−61.6 (*c* 1.06, $HCCl_3$)	0.62
	19 (93) (C-12)	90.5–91.5 (from CH_2Cl_2)	+30.5 (*c* 1.04, $HCCl_3$)	0.70
	20 (92) (C-16)	98.5–99.5 (from CH_2Cl_2)	−94.8 (*c* 1, C_5H_5N)	0.81
5	**21** (94) (C-4) [d]	42–43 (from hexane)		0.32
	22 (92) (C-8) [d]	56–57 (from hexane)		0.44
	23 (93) (C-12)	75–76 (from CH_2Cl_2)		0.52
	24 (93) (C-16)	88–89 (from CH_2Cl_2)		0.69
9	**25** (90) (C-4) [d]	38–39 (from hexane)		0.53
	26 (89) (C-8) [d]	54–55 (from hexane)		0.68
	27 (92) (C-12)	74–75 (from CH_2Cl_2)		0.74
	28 (95) (C-16)	83–84 (from CH_2Cl_2)		0.85
11	**29** (92) (C-4) [d]	51–52 (from hexane)	−59 (*c* 1.07, $HCCl_3$)	0.62
	30 (93) (C-8)	65–66 (from CH_2Cl_2)	+39.6 (*c* 1.10, $HCCl_3$)	0.76
	31 (89) (C-12)	70–81 (from CH_2Cl_2)	+12.3 (*c* 1.01, C_5H_5N)	0.87
	32 (91) (C-16)	87–88 (from CH_2Cl_2)	+21 (*c* 0.99, $HCCl_3$) [f]	0.93
15	**33** (91) (C-4) [d]	123–124 (from hexane)	−44.5 (*c* 0.63, $HCCl_3$)	0.36
	34 (93) (C-8)	130–131 (from CH_2Cl_2)	+51.3 (*c* 1, $HCCl_3$)	0.45
	35 (90) (C-12)	133.5–134.5 (from CH_2Cl_2)	+28.5 (*c* 1, C_5H_5N)	0.60
	36 (95) (C-16)	138–139 (from CH_2Cl_2)	+50.4 (*c* 1.3, $HCCl_3$) [f]	0.75

[a] Thioetherification occurred with RSH (2.4 equiv) (R = C-4, C-8, C-12, or C-16 = alkyl chain size), NaH (2.2 equiv), RT, 1:1 THF–Me_2SO (40 mL), 15 min, 1 g of peracetylated dibromodideoxyalditol derivatives.
[b] Mp are uncorrected.
[c] Optical rotations were obtained at 24 °C.
[d] Soluble in MeOH.
[e] With 3:4 AcOEt–hexane for pentitol derivatives and 1:1 AcOEt–hexane for hexitol derivatives.
[f] Optical rotation for peracetylated derivatives.

hydride (2.2 equiv) at room temperature in 1:1 tetrahydrofurane–dimethyl sulfoxide as solvent. In all cases, the thioetherification occurred in less than 15 min. The peracetylated dithioether derivatives were extracted with ether. Deacetylation with sodium methoxide in methanol, led to pure α,ω-dithioalkylalditol derivatives without further purification. Following this procedure, four thioaliphatic chains were introduced in good overall yields (see Table 2).

The structure elucidation of the unprotected dithioalkylalditol derivatives was done by NMR spectroscopy (Tables 1 and 3) and confirmed by elemental analysis.

In conclusion, an easy and inexpensive direct access to 1,5- and 1,6-dibromodideoxyalditol derivatives from unprotected alditols is now available. Although the hydroxyl groups carried a basic sensitive protecting group (acetyl group), no side-reactions (acetyl cleavage or heterocyclisation reactions) were observed during thioetherification. Twenty dithioetherified alditol derivatives were obtained in good overall yields.

1. Experimental

General methods.—Melting points were determined with a Büchi 535 digital melting point apparatus and are uncorrected. Optical rotations were measured with a DIP-370 digital polarimeter. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 300 WB spectrometer; chemical shifts are reported in δ (ppm)

Table 3
^{13}C Chemical shifts (δ, ppm) for peracetylated dibromoalditol derivatives (in $CDCl_3$) and for unprotected dithioalkylalditol derivatives (in C_5D_5N)

Compd	C-1	C-2	C-3	C-4	C-5	C-6	CO(Ac)	Me(Ac)
2	29.08	69.83	70.71	68.96	30.97		169.53; 169.66; 169.80	
3	29.49	67.99	50.92	69.09	32.85		169.47; 168.55; 168.64	
5	29.64	70.28	71.15	70.28	29.64		169.55; 169.91	20.50; 20.72
6	30.69	70.89	51.13	70.89	30.69		168.46	19.69
7	27.97	70.08	71.62	47.48	32.18		168.46; 168.61	19.63; 19.75
9	29.90	70.79	71.47	70.79	29.90		169.13; 169.67	
11	29.75	70.17	69.36	69.73	69.36	30.01	169.49; 169.71	20.46; 20.67
12	27.74	70.35	69.61	48.53	67.99	29.08	168.50; 168.98	
13	31.64	47.29	69.77	69.17	68.43	29.51	168.64	19.69
15	29.69	68.17	67.97	67.97	68.17	29.69	168.64; 168.74	
16	32.25	49.16	67.75	70.47	68.57	29.14	168.64	19.46; 19.70; 19.79
17	35.74	69.38	73.73	71.23	37.30			
18	37.33	70.90	75.24	72.76	38.83			
19	37.39	71.00	75.28	72.86	38.85			
20	37.28	70.83	75.21	72.71	38.79			
21	37.22	73.75	73.94	73.75	37.22			
22	37.21	73.76	73.93	73.76	37.21			
23	37.26	73.79	74.03	73.79	37.26			
24	37.16	73.76	73.76	73.76	37.16			
25	37.25	73.69	76.56	73.69	37.25			
26	37.10	73.52	76.33	73.52	37.10			
27	37.71	74.18	77.05	74.18	37.71			
28	36.16	72.63	75.54	72.63	36.16			
29	38.30	72.67	76.48	71.98	74.71	38.76		
30	38.10	72.66	76.47	71.92	74.71	38.43		
31	37.10	72.60	76.54	71.98	74.70	38.25		
32 [a]	32.23	70.31	71.17	69.81	69.81	31.84	169.81	20.72
33	38.76	72.97	73.64	73.64	72.97	38.76		
34	38.47	73.02	73.62	73.62	73.02	38.74		
35	38.75	72.99	73.61	73.61	72.99	38.75		
36 [a]	31.91	68.08	69.06	69.06	68.08	31.91	168.83	19.77

[a] ^{13}C NMR data for peracetylated derivatives in $CDCl_3$.

relative to Me_4Si. All ^{13}C NMR signals were assigned through C–H correlated spectra. TLC was performed on Silica Gel 60 F_{254} (230 mesh, E. Merck) with hexane–EtOAc as eluent, and zones were detected by the vanillin–H_2SO_4 reagent. The silica gel used in column chromatography was 35–70 μ (Amicon).

General alditol (pentitols, D-*glucitol, and* D-*mannitol) bromination procedure with AcBr.*—To a suspension of 0.5 g of the alditol [D-arabinitol (**1**), xylitol (**4**), ribitol (**8**), D-glucitol (**10**), and D-mannitol (**14**)] in dry 1,4-dioxane (8 mL) was added AcBr under the conditions reported in Schemes 2 and 3 (for pentitols and hexitols, respectively). Removal of the solvent gave a syrup which was treated overnight with an excess of Ac_2O in anhyd pyridine. Concentration resulted in a residue which was passed through a column of silica gel (150 g) with 6:1 hexane–EtOAc as eluent.

The following pentitol and hexitol derivatives were prepared according to this general procedure.

*2,3,4-Tri-O-acetyl-1,5-dibromo-1,5-dideoxy-*D-*arabinitol* (**2**).—0.98 g (74%); mp 76–78 °C (from EtOH); $[\alpha]_D^{23}$ +28.9° (*c* 1.42, CH_2Cl_2); R_f 0.61 in 5:2 hexane–EtOAc. Anal. Calcd for $C_{11}H_{16}Br_2O_6$: C, 32.69; H, 3.99; Br, 39.55. Found: C, 32.95; H, 3.95; Br, 39.53.

*2,4-Di-O-acetyl-1,3,5-tribromo-1,3,5-trideoxy-*D-*arabinitol* (**3**).—0.119 (8%); mp 34–35 °C (from EtOH); $[\alpha]_D^{23}$ +2.4° (*c* 1.69, CH_2Cl_2).

2,3,4-Tri-O-acetyl-1,5-dibromo-1,5-dideoxy-xylitol (**5**).—0.90 g (68%); mp 63–65 °C (from EtOH); R_f 0.47 in 5:2 hexane–EtOAc. Anal. Calcd for $C_{11}H_{16}Br_2O_6$: C, 32.69; H, 3.99; Br, 39.55. Found: C, 32.97; H, 4.02; Br, 39.15.

2,4-Di-O-acetyl-1,3,5-tribromo-1,3,5-trideoxy-ribitol or -xylitol (**6**).—Syrup, 0.21 g (15%); R_f 0.73 in 5:2 hexane–EtOAc.

*2,3-Di-O-acetyl-1,4,5-tribromo-1,4,5-trideoxy-*D,L-*arabinitol* (**7**).—0.08 g (6%); mp 64–66 °C; R_f 0.57 in 5:2 hexane–EtOAc.

2,3,4-Tri-O-acetyl-1,5-dibromo-1,5-dideoxy-ribitol (**9**).—Syrup, 1.11 g (80%); R_f 0.65 in 6:2 hexane–EtOAc. Anal. Calcd for $C_{11}H_{16}Br_2O_6$: C, 32.69; H, 3.99; Br, 39.55. Found: C, 32.91; H, 4.08; Br, 39.12.

*2,3,4,5-Tetra-O-acetyl-1,6-dibromo-1,6-dideoxy-*D-*glucitol* (**11**).—Syrup, 0.67 g (51%); R_f 0.48 in 5:2 hexane–EtOAc. Anal. Calcd for $C_{14}H_{20}Br_2O_8$: C, 35.32; H, 4.23; Br, 33.56. Found: C, 35.52; H, 4.53; Br, 33.45.

*2,3,5-Tri-O-acetyl-1,4,6-tribromo-1,4,6-trideoxy-*D-*galactitol* (**12**).—0.05 g (4%); mp 93–95 °C (from EtOH); $[\alpha]_D^{23}$ −3.2° (*c* 1.32, CH_2Cl_2); R_f 0.62 in 5:2 hexane–EtOAc.

*3,4,5-Tri-O-acetyl-1,2,6-tribromo-1,2,6-trideoxy-*D-*mannitol* (**13**).—0.16 g (12%); mp 101–102 °C (from EtOH); $[\alpha]_D^{23}$ +39.1° (*c* 1, CH_2Cl_2); R_f 0.68 in 5:2 hexane–EtOAc.

*2,3,4,5-Tetra-O-acetyl-1,6-dibromo-1,6-dideoxy-*D-*mannitol* (**15**).—0.83 g (63%); mp 121–123 °C (from EtOH); $[\alpha]_D^{23}$ +29.6° (*c* 1.2, CH_2Cl_2); R_f 0.52 in 5:2 hexane–EtOAc. Anal. Calcd for $C_{14}H_{20}Br_2O_8$: C, 35.32; H, 4.23; Br, 33.56. Found: C, 35.59; H, 4.34; Br, 33.58.

*3,4,5-Tri-O-acetyl-1,2,6-tribromo-1,2,6-trideoxy-*D-*glucitol* (**16**).—Syrup, 0.11 g (8%); $[\alpha]_D^{23}$ +28.5° (*c* 1.24, CH_2Cl_2); R_f 0.61 in 5:2 hexane–EtOAc.

General thioetherification procedure of 1,5-dibromo-1,5-dideoxypentitol derivatives (**2**, **5** *and* **9**) *and 1,6-dibromo-1,6-dideoxyhexitol derivatives* (**11** *and* **15**).—To the α,ω-dibromoalditol derivative (1 g) in 1:1 THF–Me_2SO (20 mL), was added 2.4 equiv of RSH (R = *n*-butyl, *n*-octyl, *n*-decyl, or *n*-hexadecyl) and 2.2 equiv of NaH at room temperature. The mixture was stirred for 15 min. The soln was concd under reduced pressure and extracted with Et_2O–H_2O. The organic phase was concd and the crude product was deacetylated with MeONa in MeOH. When the free dithioetherified derivatives were not soluble in MeOH (see Table 2), they were collected by filtration and washed with MeOH and hexane. When, after deacetylation, the soln remained homogeneous, neutralisation with Amberlist-15, filtration, and concn gave dithio derivatives as syrups which crystallised by addition of hexane. Yields and physical data are summarised in Table 2.

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