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Note

Regioselective chlorination study of unprotected pentitols: syntheses of some 1,5-dichloro-1,5-dideoxypentitol derivatives

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Besides their use as starting materials for carbohydrate-based organic synthesis [1], chlorodeoxy sugars are sweetening [2], anticariogenic [3] and potential male contraceptive agents [4]. The latter effect led us to initiate a program focused on chlorosugar syntheses and more especially 1,5-dichloro-1,5-dideoxypentitol derivatives.

Methods commonly used to prepare chlorinated sugars are based on the following sequences: (i) hydroxyl-group activation and (ii) subsequent chlorination in acidic [5] or basic [6] medium. However, in both cases, the direct regioselective chlorination of unprotected alditols at primary carbon atoms competes with intramolecular cyclodehydration [5,6].

More recently, we achieved the direct synthesis of some 1,5-dichloro-1,5-dideoxypentitol derivatives starting from unprotected pentitols under nearly neutral conditions using iminium salts **1** [7], **2** [8], and **3** [9], and an acid chloride, **4** [10] as chlorinating reagents. Herein, a compilation of experimental results and NMR data is summarized.

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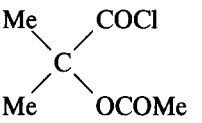
$Me_2\overset{+}{N}=CXY, Cl^-$

1 X = H, Y = OMs
2 X = H, Y = Cl
3 X = Y = Cl



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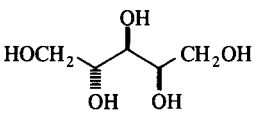
Our first attempt to chlorinate unprotected D-arabinitol (**5**), xylitol (**6**), and ribitol (**7**) (Scheme 1), was carried out with mesyloxymethylene-*N*,*N*-dimethyliminium chloride (**1**) in *N*,*N*-dimethylformamide (MsCl in DMF) [7]. While **5** gave mainly the



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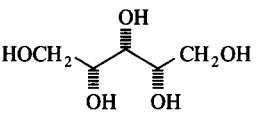

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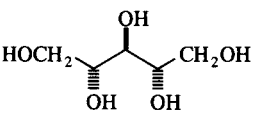

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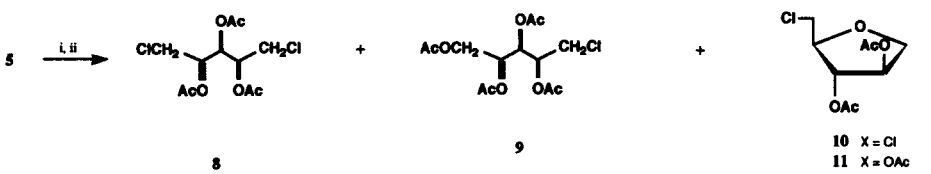
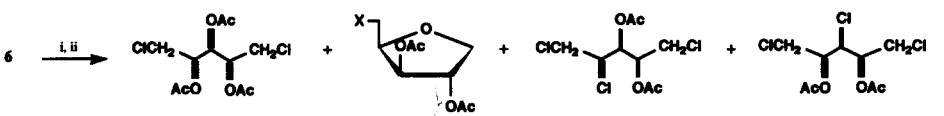
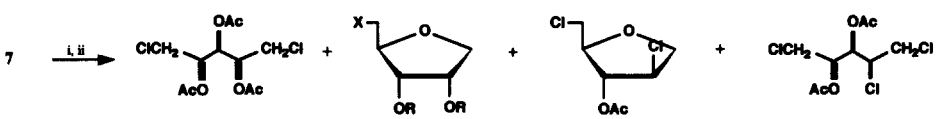


8 **9** **10** X = Cl **11** X = OAc



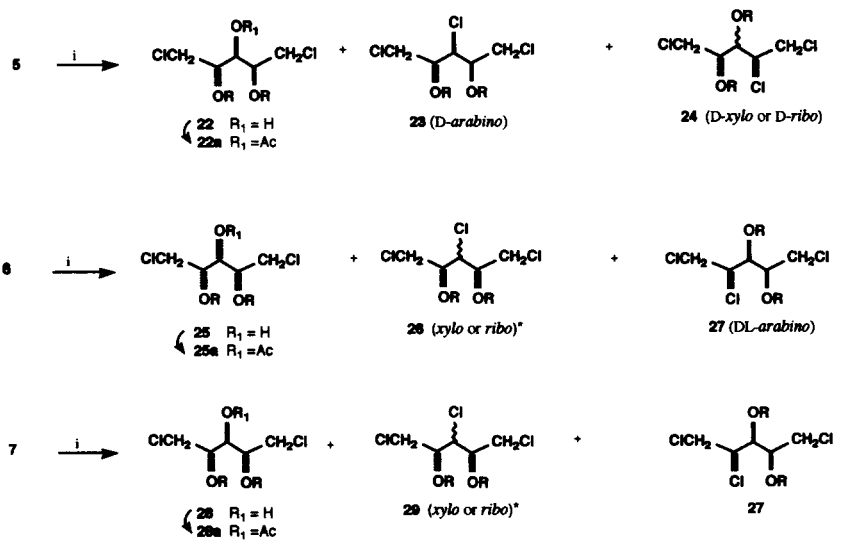
12 **13** X = OAc **14** X = Cl **15** (DL-*arabino*) **16** (*ribo*)



17 **18** X = R = Ac **19** X = Cl, R = Ac **19a** X = Cl, R = H **19b** X = Cl, R = $Me_2C<$ **20** (DL-*arabino*) **21** (DL-*arabino*)

i- 6 equiv MsCl in DMF (iminium salt **1**), 65 °C, 16 h; ii- Ac_2O, pyridine, 0 °C, 16 h.

Scheme 1.



i- Iminium salt **3** in 1,4-dioxane; * NMR data of compounds **26** and **29** are different; R = -$CONMe_2$

Scheme 2.

1,5-dichloro-1,5-dideoxy-D-arabinitol derivative **8** (50% yield after acetylation) (Scheme 1), **6** and **7** produced the anhydro derivatives **13, 14** and **18, 19, 20**, respectively, in good overall yields. The 1,5-dichloro-1,5-dideoxy derivatives **12** and **17** were obtained in small amounts (5 and 11% yields, respectively).

Although chlorination reactions with the iminium salts **1** and **2** (Vilsmeier–Haack salt) involve the same alkoxymethyleneiminium salt intermediate ($[ROCH{=}NMe_2]^+Cl^-$) [7,8], with reagent **2**, compounds **8, 12** and **17** were obtained with 77, 50 and 53% yields, respectively. This unexpected result seems to be dependent on the inorganic acid formed during the chlorination reaction (CH_3SO_3H with **1** and HCl with **2**) [8].

The subsequent use of phosgene iminium salt **3** (Viehe–Janouseck salt) as chlorinating reagent in 1,4-dioxane, under mild conditions (1 h 15–2 h 30 min, 20–40°C instead of 12 h, 55–60°C), with **2** allowed significant increase in the yields of 1,5-dichloro-1,5-dideoxy derivatives [9]. Thereby, compounds **22, 25**, and **28** were obtained in 73, 70, and 79% yields, respectively (Scheme 2). It is of interest that an excess of reagent, higher temperature or reaction time, favored to a great extent the formation of linear trichloropentitol derivatives (**23, 24, 26, 27**, and **29**).

Similar results were obtained with the 1-chlorocarbonyl-1-methylethyl acetate **4** as chlorinating reagent. Thus, D-arabinitol (**5**) gave mainly 2,4-di-*O*-acetyl-1,5-dichloro-1,5-dideoxy-D-arabinitol (**30**) (58%) in which OH-3 remains free. Chlorination of **5** followed by acetylation led to 1,5-dichloro-1,5-dideoxy derivative **8** in higher yield (80%). With xylitol (**6**) and ribitol (**7**), only peracetylated 1,5-dichloro-1,5-dideoxy derivatives **12** and **17** could be isolated after acetylation (70 and 72%, respectively).

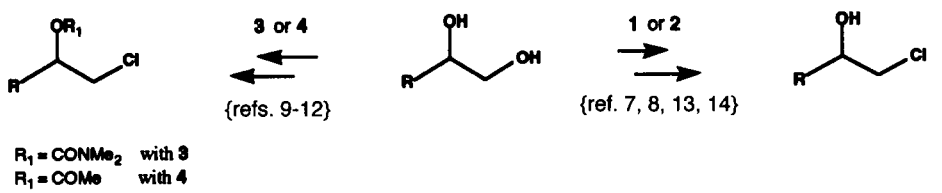
Table 1
Isolated yields of 1,5-dichloro-1,5-dideoxy derivatives of D-arabinitol (**5**), xylitol (**6**), and ribitol (**7**) obtained by direct chlorination using chlorinating reagents **1**, **2**, **3**, and **4**

Chlorinating reagents	1,5-dichloropentitol derivatives			
	5	**6**	**7**	ref.
(1) Me_2N^+ =CHOMs, Cl^- [a,b]	50% (**8**)	5% (**12**)	11% (**17**)	7
(2) Me_2N^+ =CHCl, Cl^- [a,b]	77% (**8**)	50% (**12**)	53% (**17**)	8
(3) Me_2N^+ =CCl_2, Cl^- [d]	73% (**22**)	70% (**25**)	79% (**28**)	9
(4) Me_2C(OAc)COCl [e,f]	80% (**8**)	70% (**12**)	72% (**17**)	10

[a] Chlorination was followed by acetylation with Ac_2O in pyridine; [b] 6 Equiv of **1**, 65°C, 16 h; [c] 4 Equiv of commercial iminium salt **2** or **4** equiv of $SOCl_2$ in DMF; [d] See Experimental section for conditions; [e] For experimental procedure see ref. [10]; [f] Chlorinated products are isolated after acetylation

This result shows that the one-pot chlorination and acetylation does not necessarily occur on vicinal hydroxyl groups, as with chlorination and carbamoylation with the iminium salt **3**.

The resistance of pentitols towards ring closure, as observed with both chlorinating reagents **3** and **4**, may be ascribed in large part to simultaneous protection of secondary hydroxyl groups (Scheme 3) [11].



Scheme 3.

Table 1 summarizes the yields of 1,5-dichloro-1,5-dideoxypentitol derivatives prepared by the chlorinating reagents **1–4**. The iminium salt **2**, the phosgene iminium derivative **3**, and the acid chloride **4** gave the higher yields of 1,5-dichloro-1,5-dideoxy derivatives.

Structural determination was based on the NMR data reported in Tables 2–4. With dichlorodideoxy and trichlorotrideoxy derivatives **8, 9, 15**, and **21** (Scheme 1), **22, 23**, and **27** (Scheme 2), an anti-methine coupling constant $J_{3,4} > 8$ Hz and *gauche* coupling constant $J_{2,3} < 2.5$ Hz (Table 2), indicate the *arabino* configuration. For compounds **26** and **29** (Scheme 2), $J_{2,3} = J_{3,4}$ could indicate either the *ribo* or *xylo* configuration, since C-3 chlorination could occur with inversion or retention of configuration.

In conclusion, this work shows that iminium salts and α-acetoxy acid chloride are the most efficient reagents for the regioselective chlorination of unprotected pentitols, leading to 1,5-dichloro-1,5-dideoxypentitols in high yields.

Table 2
^{1}H NMR [a] data for chlorodeoxypentitol derivatives

Compound	Chemical shifts (δ)								
	H-1a	H-1b	H-2	H-3	H-4	H-5a	H-5b	CH_3(Ac)	$(CH_3)_2N$
8	3.41(dd)	3.49(dd)	5.28(m)	5.41(dd)	5.12(m)	3.53(dd)	3.64(dd)	2.03 (6H); 2.08 (3H)	
9	3.41(dd)	3.47(dd)	5.27(m)	5.38(dd)	5.05(m)	4.04(dd)	4.16(dd)	1.98 (3H); 2 (3H); 2.03 (3H); 2.06 (3H)	
10	3.94(m)	3.99(dd)	5.08(ddd)	5.02(dd)	3.96(m)	3.61(dd)	3.67(dd)	1.95 (3H); 1.98 (3H)	
11	3.74(dd)	3.82(dd)	4.93(ddd)	4.81(m)	3.78(m)	3.96(dd)	4.08(dd)	1.86 (6H); 1.85 (3H)	
12	3.45(dd)	3.51(dd)	5.06(dd)	5.39(t)	5.06(dd)	3.45(dd)	3.51(dd)	2.08 (3H); 2.07 (6H)	
13	3.45(dd)	3.97(m)	4.83(m)	5.04(dd)	4.00(dd)	3.84(dd)	3.93(m)	1.80 (3H); 1.79 (3H); 1.77 (3H)	
14	3.50(dd)	3.98(dd)	4.85(m)	5.07(d)	4.03(dd)	3.35(d)	3.35(dd)	1.85 (3H); 1.82 (3H)	
15	3.64(dd)	3.72(dd)	5.41(m)	5.33(dd)	4.12(m)	3.43(dd)	3.49(dd)	2.28 (3H); 2.07 (3H)	
16	3.70(t)	3.70(t)	5.02(dd)	4.34(t)	5.02(dd)	3.70(t)	3.70(t)	2.04 (6H)	
17	3.45(dd)	3.62(dd)	5.10(m)	5.18(t)	5.10(m)	3.45(dd)	3.62(dd)	2.06 (6H); 2.02 (3H)	
18	3.79(dd)	4.09(dd)	5.39(dd)	5.23(t)	4.16(m)	4.16(m)	4.30(dd)	1.89 (6H); 1.88 (3H)	
19	3.59(dd)	3.95(dd)	5.09(m)	4.92(d)	3.92(dd)	3.40(d)	3.49(dd)	1.81 (3H); 1.79 (3H)	
19a [b]	3.83(dd)	4.10(dd)	4.30(m)	4.18(dd)	4.04(m)	3.72(dd)	3.87(dd)		
19b	3.89(m)	3.89(m)	4.73(m)	4.61(dd)	4.14(m)	3.39(dd)	3.45(dd)	(1.40 (3H); 1.23 (3H)) [c]	
20	3.78(dd)	3.88(dd)	4.07(m)	4.83(m)	3.74(m)	3.46(dd)	3.52(dd)	1.79 (3H)	
21	3.62(dd)	3.66(dd)	4.23(dd)	4.62(dd)	5.26(m)	3.56(dd)	4.82(dd)	2.12 (3H); 2.10 (3H)	
22	3.70(d)	3.70(d)	4.91(dd)	4.22(d)	4.86(m)	3.83(dd)	3.89(dd)		2.85 (12H)
22a	3.47(d)	3.47(d)	5.06(ddd)	5.42(dd)	4.99(m)	3.49(dd)	3.66(dd)	2.01 (3H)	2.79 (12H)
23	3.61(dd)	3.67(dd)	5.19(m)	4.61(dd)	5.05(m)	3.85(dd)	3.97(dd)		2.88 (3H); 2.82 (3H); 2.84 (3H); 2.85 (3H)
24	3.67(dd)	3.89(dd)	4.32(m)	5.39(dd)	5.31(m)	3.66(dd)	3.81(dd)		2.92 (12H)
25	3.60(dd)	3.65(dd)	4.83(dd)	4.05(t)	4.83(dd)	3.60(dd)	3.65(dd)		2.81 (6H); 2.79 (6H)
25a	3.61(dd)	3.67(dd)	5.10(m)	5.63(t)	5.10(m)	3.61(dd)	3.67(dd)	2.03 (3H)	2.86 (12H)
26	3.76(dd)	3.80(dd)	5.16(m)	4.50(t)	5.16(m)	3.76(dd)	3.80(dd)		2.92 (6H); 2.88 (6H)
27	3.52(dd)	3.61(dd)	5.35(ddd)	5.27(dd)	4.20(m)	3.68(dd)	3.82(dd)		2.88 (9H); 2.90 (3H)
28	3.78(dd)	3.85(dd)	4.99(m)	4.17(t)	4.99(m)	3.78(dd)	3.85(dd)		2.96 (6H); 2.95 (6H)
28a	3.49(dd)	3.63(dd)	5.07(m)	5.29(t)	5.07(m)	3.49(dd)	3.63(dd)	1.96 (3H); 2.79 (12H)	
29	3.76(t)	3.76(t)	5.14(dd)	4.49(t)	5.14(dd)	3.76(t)	3.76(t)		2.90 (6H); 2.87 (6H)
30	3.59(dd)	3.67(dd)	5.10(m)	4.18(dd)	4.93(m)	3.80(dd)	3.86(dd)	2.04 (3H); 2.03 (3H)	

[a] Recorded at 300 MHz for solutions in $CDCl_3$–Me_4Si; [b] For solutions in D_2O–DSS; [c] $(CH_3)_2C<$.

Table 3
^{1}H NMR [a] coupling constants (Hz) for chlorodeoxypentitol derivatives

Compound	$J_{1a,1b}$	$J_{1a,2}$	$J_{1b,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5a}$	$J_{4,5b}$	$J_{5a,5b}$
8	11.5	7.3	6.0	2.2	8.7	5.2	3.3	12.4
9	11.5	7.2	6.1	2.3	8.8	4.8	2.5	12.5
10	10.9	—	4.1	—	—	6.3	5.3	11.5
11	10.8	1.6	4.3	2.3	3.4	6.5	4.7	12.1
12	12.2	5.6	4.9	5.0	5.0	5.6	4.9	12.2
13	10.6	2.3	4.6	1.1	3.6	6.8	—	11.2
14	10.6	1.8	4.6	0	4.0	6.8	6.8	12.2
15	11.4	6.7	6.4	2.4	8.8	5.8	4.2	11.6
16	—	4.9	4.9	6.1	6.1	4.9	4.9	—
17	12.1	6.9	3.0	5.2	5.2	6.9	3.0	12.1
18	10.1	3.8	5.1	5.4	5.4	—	5.5	13.6
19	10.3	3.6	4.9	5.4	6.4	4.5	3.8	11.4
19a [b]	10.1	2.4	4.1	4.7	7.4	5.5	3.2	12.2
19b	—	—	—	6.2	1.7	6.6	5.2	11.5
20	10.7	2.0	4.1	2.0	3.1	6.7	5.4	12.4
21	11.7	7.0	7.4	2.0	8.4	4.3	3.3	12.2
22	—	7.0	7.0	2.3	8.5	3.1	3.6	12.1
22a	10.5	6.2	6.2	3.2	8.0	4.8	3.5	12.2
23	10.6	8.2	5.7	1.8	9.8	2.7	3.0	12.4
24	11.9	7.7	5.6	3.8	6.9	5.0	3.4	12.2
25	11.6	5.6	5.3	4.8	4.8	5.6	5.3	11.6
25a	12.0	4.6	5.1	5.4	5.4	4.6	5.1	12.1
26	12.1	4.3	5.4	6.2	6.2	4.3	5.4	12.1
27	10.6	6.7	6.2	2.4	8.1	6.8	4.7	12.1
28	12.0	3.8	5.3	5.4	5.4	3.8	5.3	12.0
28a	12.0	6.5	3.7	5.5	5.5	6.5	3.7	12.0
29	—	4.4	4.4	6.3	6.3	4.4	4.4	—
30	11.0	6.7	7.4	1.7	9.3	3.6	3.6	16.3

[a] Recorded at 300 MHz for solutions in $CDCl_3$–Me_4Si; [b] For solutions in D_2O–DSS.

Table 4
^{13}C NMR [a] data for chlorodeoxypentitol derivatives

Compound	Chemical shifts (δ)								
	C-1	C-2	C-3	C-4	C-5	CH_3(Ac)	CO(Ac)	$(CH_3)_2N$	$CO(NMe_2)$
8	41.79	69.86	69.32	69.06	42.96	20.49; 20.60	169.41; 169.42; 169.77		
9	41.67	69.83	68.37	68.01	61.60	20.69; 20.49	168.88; 169.70; 169.51		
10	72.08	77.07	78.73	83.58	43.64	20.64; 20.73	169.75; 169.92		
11	71.63	77.22	78.03	81.43	63.11	20.32; 20.39	169.55; 169.39		
12	42.15	70.44	69.56	70.44	42.15	20.56; 20.36	169.44; 169.81		
13	71.49	77.05	75.68	77.05	61.54	20.00; 20.44	168.88; 169.17; 170.20		
14	71.58	76.79	75.17	79.31	40.19	20.00; 20.17	168.88; 169.17		
15	41.46	70.53	71.15	57.52	45.63	20.44; 20.34	169.41; 169.25		
16	42.68	72.01	53.20	72.01	42.68	20.47	169.52		
17	42.25	70.90	70.11	70.90	42.25	20.51; 20.41	168.97; 169.52		
18	70.73	71.81	72.26	78.63	63.90	20.23; 20.32	170.40; 169.88; 169.80		
19	70.53	71.15	72.34	79.24	44.29	20.09; 20.19	169.52; 169.53		
19a [b]	75.56	73.85	75.69	83.19	47.79				
19b	73.53	81.00	83.01	84.02	43.59	(26.54; 24.91) [c]	112.95 [c]		
20	74.11	59.56	81.30	83.75	44.18	20.33	169.39		
21	44.41	59.42	68.92	70.72	42.60	20.48; 20.72	169.33		
22	41.48	73.41	68.13	72.53	44.46			36.54; 35.96	155.25; 155.08
22a	42.07	71.28	69.89	70.71	43.33	20.47	169.36	33.48; 35.74	154.80
23	41.50	71.57	57.51	70.72	44.83			35.85; 36.58	155.45; 154.26
24	45.08	60.96	73.08	72.07	43.51			35.37; 36.73	154.53
25	42.61	73.89	69.35	73.89	42.61			36.46; 35.81	155.65
25a	42.83	71.41	70.17	71.41	42.83	20.43	169.50	36.45; 35.72	154.94
26	42.36	71.98	58.00	71.98	42.36			35.66; 34.96	153.66
27	41.41	71.02	71.98	57.82	44.81			34.90; 35.72; 35.89	153.80; 154.03
28	43.53	74.66	69.56	74.66	43.53			36.46; 35.84	155.45
28a	42.79	71.81	70.52	71.81	42.79	20.51	168.92	35.74; 36.40	154.66
29	43.27	72.93	58.94	72.93	43.27			36.55; 35.86	154.58
30	41.01	71.04	67.83	70.39	44.03	20.67; 20.55	169.96; 170.12		

[a] Recorded at 300 MHz for solutions in $CDCl_3$–Me_4Si; [b] For solutions in D_2O–DSS; [c] $(CH_3)_2C <$.

1. Experimental

General methods.—Melting points were determined with an Electrothermal 1A 9200 digital melting-point apparatus and are uncorrected. Optical rotations were measured with a DIP-370 digital polarimeter. ^{1}H and ^{13}C NMR spectra (Tables 2–4) were recorded on a Bruker 300 WB spectrometer Aspect 3000 and chemical shifts are reported in δ units (ppm) relative to Me_4Si or $Me_3Si(CH_2)_3SO_3Na$. All ^{13}C spectra are assigned through 2D-XH-correlated spectra using the XHCORRD. AUR program. TLC was performed on Silica Gel 60F-254 (E. Merck, 230 mesh) with hexane–EtOAc as eluent, and zones were detected by vanillin–H_2SO_4). The silica gel used in column chromatography was 35–70 μm (Amicon).

For pentitol chlorination using MsCl in DMF (iminium salt **1**), see ref. [7]. D-Arabinitol (**5**), xylitol (**6**), and ribitol (**7**) (0.2 g) were chlorinated by chloromethylene-*N,N*-dimethyliminium chloride **2** (4 equiv, 55–60°C, 12 h) (Aldrich), or formed in situ by reaction of $SOCl_2$ with DMF. The general procedure is the same as that described in [7] (see also [8]). The following compounds were isolated after acetylation of the crude product (Ac_2O in pyridine).

2,3,4-Tri-O-*acetyl-1,5-dichloro-1,5-dideoxy*-D-*arabinitol* (**8**).—From **5** (0.2 g), 320 mg, (77%); R_f 0.46 in 4:1 hexane–EtOAc; mp 76–77°C (EtOH) (Lit. [7] 75–76°C); $[\alpha]_D^{22}$ +41.5 (*c* 1.34, $CHCl_3$) (Lit. [7] +42°). Anal. Calcd for $C_{11}H_{16}Cl_2O_6$: C, 41.90; H, 5.08; Cl, 22.54. Found: C, 41.98; H, 5.20; Cl, 22.33.

2,3,4-Tri-O-*acetyl-1,5-dichloro-1,5-dideoxyxylitol* (**12**).—From **6** (0.2 g), 200 mg, (49%); R_f 0.28; mp 64–66°C (EtOH) (Lit. [7] 65–66°C). Anal. Calcd for $C_{11}H_{16}Cl_2O_6$: C, 41.90; H, 5.08; Cl, 22.54. Found: C, 41.87; H, 5.15; Cl, 22.39.

2,3-Di-O-*acetyl-1,4-anhydro-5-chloro-5-deoxy*-DL-*xylitol* (**14**).—From **6** (0.2 g), 30 mg, (10%); R_f 0.37; syrup. Anal. Calcd for $C_9H_{13}ClO_5$: C, 45.66; H, 5.50; Cl, 15.01. Found: C, 45.37; H, 5.75; Cl, 14.41.

2,3-Di-O-*acetyl-1,4,5-trichloro-1,4,5-trideoxy*-DL-*arabinitol* (**15**).—From **6** (0.2 g), 30 mg (8%); R_f 0.51; mp 75°C (EtOH) (Lit. [7] 74–75°C). Anal. Calcd for $C_9H_{13}Cl_3O_4$: C, 37.05; H, 4.46; Cl, 36.54. Found: C, 37.59; H, 4.59; Cl, 36.41.

2,3-Di-O-*acetyl-1,4,5-trichloro-1,4,5-trideoxy*-DL-*arabinitol* (**17**).—From **7** (0.2 g), 220 mg, (53%); R_f 0.35; syrup. Anal. Calcd for $C_{11}H_{16}Cl_2O_6$: C, 41.90; H, 5.08; Cl, 22.54. Found: C, 42.01; H, 5.17; Cl, 22.37.

2,3-Di-O-*acetyl-1,4-anhydro-5-chloro-5-deoxy*-DL-*ribitol* (**19**).—From **7** (0.2 g), (20 mg, (6%); R_f 0.29; syrup. Anal. Calcd for $C_9H_{13}ClO_5$: C, 45.66; H, 5.50; Cl, 15.01. Found: C, 45.38; H, 5.51; Cl, 15.21.

3,4-Di-O-*acetyl-1,2,5-trichloro-1,2,5-trideoxy*-DL-*arabinitol* (**21**).—From **7** (0.2 g), 20 mg, (6%); R_f 0.52; mp 126–127°C (Lit. [7] 125–127°C). Anal. Calcd for $C_9H_{13}Cl_3O_4$: C, 37.05; H, 4.46; Cl, 36.54. Found: C, 37.51; H, 4.50; Cl, 36.60.

1,4-Anhydro-5-chloro-5-deoxy-DL-*ribitol* (**19a**).—Obtained by de-*O*-acetylation (4.23 10^{-3} mol) (NaOMe–MeOH at 0°C) of **19** (1 g), 530 mg, (82%); R_f 0.64 in 4:1 EtOAc–hexane. Anal. Calcd for $C_5H_9ClO_3$: C, 39.34; H, 5.90; Cl, 23.28. Found: C, 39.13; H, 5.94; Cl, 23.45.

1,4-Anhydro-5-chloro-5-deoxy-2,3-O-*isopropylidene*-DL-*ribitol* (**19b**).—Obtained by acetonation (H_2SO_4–acetone) of **19a** (126 mg), 100 mg, (79%); R_f 0.49 in 8:1 hexane–EtOAc.

*General pentitol chlorination procedure by dichloromethylene-*N,N*-dimethyliminium chloride* (**3**).—A mixture of pentitol and iminium salt **3** in 1,4-dioxane was stirred at the desired temperature and reaction time. The solution was stirred with MeOH (8 mL) for 30 min and solvents were evaporated under reduced pressure. The resulting syrup was purified by flash chromatography on silica gel (100 g) with a suitable hexane–EtOAc mixture.

D-Arabinitol (**5**) (0.2 g), 3 equiv of **3**, 20°C, 1 h 30, gave the following products after flash chromatography with 2:1 hexane–EtOAc as eluent.

*1,5-Dichloro-1,5-dideoxy-2,4-di-*O*-[*N,N*-dimethylcarbamoyl]-*D*-arabinitol* (**22**).—Yield 320 mg, (73%); R_f 0.52 in 3:2 hexane–EtOAc; mp 101–104°C (hexane–EtOAc); $[\alpha]_D^{22}$ +22,3° (*c* 1.52, CH_2Cl_2). Anal. Calcd for $C_{11}H_{20}Cl_2N_2O_5$: C, 39.88; H, 6.04; Cl, 21.45; N, 8.46. Found: C, 39.64; H, 6.19; Cl, 21.21; N, 8.24.

At 20°C during 48 h, **5** gave **22** in only 51% yield plus the following by-products. The flash chromatography was performed with 2:1 followed by 3:2 hexane–EtOAc as eluents.

*1,3,5-Trichloro-1,3,5-trideoxy-2,4-di-*O*-[dimethylcarbamoyl]-*D*-arabinitol* (**23**).—Yield 130 mg, (28%); R_f 0.66 in 3:2 hexane–EtOAc; mp 92–94°C. Anal. Calcd for $C_{11}H_{19}Cl_3N_2O_4$: C, 37.77; H, 5.44; Cl, 30.47; N, 8.01. Found: C, 37.18; H, 5.88; Cl, 29.59; N, 7.57.

*1,2,5-Trichloro-1,2,5-trideoxy-2,4-di-*O*-[*N,N*-dimethylcarbamoyl]-*D*-xylitol or* -D-*ribitol* (**24**).—Yield 20 mg, (4%), R_f 0.74 in 3:2 hexane–EtOAc. Anal. Calcd for $C_{11}H_{19}Cl_3N_2O_4$: C, 37.77; H, 6.44; Cl, 30.47; N, 8.01. Found: C, 37.61; H, 6.53; Cl, 30.05; N, 7.75.

*3-*O*-Acetyl-1,5-dichloro-1,5-dideoxy-2,4-di-*O*-[*N,N*-dimethylcarbamoyl]-*D*-arabinitol* (**22a**).—Obtained by acetylation of **22** (Ac_2O–pyridine). R_f 0.42 in 1:1 hexane–EtOAc. Anal. Calcd for $C_{13}H_{22}Cl_2N_2O_6$: C, 41.82; H, 5.9; Cl, 19.03; N, 7.51. Found: C, 42.64; H, 6.24; Cl, 19.64; N, 7.03.

Chlorination of xylitol (**6**) (0.2 g) by iminium salt **3** (2.2 equiv, 40°C, 1 h 15 min) gave after chromatography with 5:2 hexane–EtOAc as an eluent, *1,5-dichloro-1,5-dideoxy-2,4-di-*O*-[*N,N*-dimethylcarbamoyl]xylitol* (**25**) 305 mg, (70%); R_f 0.32 in 1:1 hexane–EtOAc; mp 81–83°C (hexane–EtOAc). Anal. Calcd for $C_{11}H_{20}Cl_2N_2O_5$: C, 39.88; H, 6.04; Cl, 21.45; N, 8.46. Found: C, 39.72; H, 5.95; Cl, 21.52; N, 8.56.

From **6** (0.2 g), using 3 equiv of **3**, **25** was obtained in 59% yield plus the following trichloro derivatives (chromatography with 5:2 followed by 2:3 hexane–EtOAc as eluents).

*1,3,5-Trichloro-1,3,5-trideoxy-2,4-di-*O*-[*N,N*-dimethylcarbamoyl]-ribitol or* -*xylitol* (**26**).—Yield 97 mg, (21%); R_f 0.78. Anal. Calcd for $C_{11}H_{19}Cl_3N_2O_4$: C, 37.77; H, 5.44; Cl, 30.47; N, 8.01. Found: C, 37.62; H, 5.72; Cl, 30.32; N, 8.46.

*1,4,5-Trichloro-1,4,5-trideoxy-2,3-di-*O*-[*N,N*-dimethylcarbamoyl]-*DL*-arabinitol* (**27**).—Yield 46 mg, (10%); R_f 0.68. Anal. Calcd for $C_{11}H_{19}Cl_3N_2O_4$: C, 37.77; H, 5.44; Cl, 30.47; N, 8.01. Found: C, 38.05; H, 5.53; Cl, 31.15; N, 8.73.

*3-*O*-Acetyl-1,5-dichloro-1,5-dideoxy-2,4-di-*O*-[*N,N*-dimethylcarbamoyl]-*D*-xylitol* (**25a**).—Obtained after acetylation of **25**; R_f 0.17 in 2:1 hexane–EtOAc; mp 118–120°C. Anal. Calcd for $C_{13}H_{22}Cl_2N_2O_6$: C, 41.82; H, 5.90; Cl, 19.03; N, 7.51. Found: C, 41.75; H, 6.05; Cl, 19.73; N, 7.35.

Chlorination of ribitol (**7**) (0.2 g) (3 equiv of **3**, 25°C, 2 h 30 min) gave, after chromatography with 2:1 hexane–EtOAc as eluent, *1,5-dichloro-1,5-dideoxy-2,4-di*-O-*[*N,N-*dimethylcarbamoyl]ribitol* (**28**) 344 mg, (79%); mp 63–65°C (hexane–EtOAc); R_f 0.44 in 1:1 hexane–EtOAc. Anal. Calcd for $C_{11}H_{20}Cl_2N_2O_5$: C, 39.88; H, 6.04; Cl, 21.45; N, 8.46. Found: C, 39.62; H, 6.32; Cl, 21.65; N, 8.42.

Increasing the reaction time (26 h) gave **28** in only 47% yield and the following by-products isolated with 2:1 followed by 1:1 hexane–EtOAc as eluents.

1,3,5-Trichloro-1,3,5-trideoxy-2,4-di-O-*[*N,N-*dimethylcarbamoyl]-ribitol or -xylitol* (**29**).—Yield 97 mg, (21%), R_f 0.77. Anal. Calcd for $C_{11}H_{19}Cl_3N_2O_4$: C, 37.77; H, 5.44; Cl, 30.47; N, 8.01. Found: C, 37.75; H, 5.92; Cl, 30.01; N, 8.52.

1,4,5-Trichloro-1,4,5-trideoxy-2,3-di-O-*[*N,N-*dimethylcarbamoyl]*-DL-*arabinitol* (**27**).—Yield 92 mg, (20%).

3-O-*Acetyl-1,5-dichloro-1,5-dideoxy-2,4-di*-O-*[*N,N-*dimethylcarbamoyl]-ribitol* (**28a**).—Obtained by acetylation of **28**. R_f 0.31 in 2:1 hexane–EtOAc. Anal. Calcd for $C_{13}H_{22}Cl_2N_2O_6$: C, 41.82; H, 5.90; Cl, 19.03; N, 7.51. Found: C, 41.62; H, 6.32; Cl, 20.79; N, 7.45.

For direct chlorination of unprotected pentitols by acid chloride **4** see ref. [10].

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