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Note

Regioselective synthesis of alditol vicinal bis-cyclic thionocarbonates via alditol stannylene acetal complexes as a short and efficient route to α,ω-diiodoalditol derivatives

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Abstract

The bis-cyclic thionocarbonates of alditols (pentitols and hexitols) were quickly and easily obtained from alditol stannylene complexes and phenyl chlorothionoformate (PhOC(S)Cl) in good yields. Acetylation of isolated free alditol bis-thionocarbonates and subsequent iodination using methyl iodide under pressure led to α,ω-diiodo derivatives of alditols in good to excellent isolated yields (67–93%).

Keywords: Alditols; Bis-thionocarbonates; α,ω-Diiodoalditols; Pentitols, hexitols, iodination

1. Introduction

The halogenoalditol derivatives are of interest as synthesis intermediates,[1,2] and as enzyme inhibitors,[3] alkylating agents used in chemotherapy,[4] or as sweeteners [5].

In a previous work we reported that regioselective halogenation on free primary alditol sites via bis-electrophilic intermediates such as bis-iminium or bis-phosphonium (respectively obtained using a mesyloxyiminium chloride [$(Me_2N{=}CHOMs)^+$, Cl^-][6] or CX_4–PPh_3–pyridine complex (with X = Cl, Br or I)[7] as halogenating reagents) led mainly to O-heterocyclisation reactions. We showed that the basic medium was a favourable parameter for the heterocyclisation reaction. Furthermore, we showed that the combination of neutral conditions with electrophilic cyclic intermediates such as acetoxonium or iminium ions enables the synthesis of α,ω-dihalogenated derivatives of alditols in good yields. Thus, the use of the bis-cyclic acetoxonium ion or the bis-cyclic iminium alditol salt (using $Me_2C(OAc)COCl$[8] or [$(Me_2N{=}CCl_2)^+$, Cl^-][9] as chlorinating reagents, respectively) allowed the synthesis of the 1,5-dichlorinated derivatives of pentitols and the 1,6-dichlorinated derivatives of some hexitols in good yields. α,ω-Dibrominated derivatives were also synthesised via the acetoxonium intermediate using $Me_2C(OAc)COBr$[10] or AcBr[2b] as brominating agents. With most of the alditols studied, heterocyclisation was avoided through the simultaneous protection by acetates or carbamates of the OH groups usually involved in the cyclodehydration (Scheme 1, Paths a and b). For regioselective iodination of primary alditol sites, no general effective method has been described up to now.

The development of the chemistry of cyclic alditol intermediates in our laboratory has led us to investigate other intermediates such as cyclic sulfites and sulfates. Certain substitution reactions (azidation)[11] and heterocyclisation reactions (thia and aza-heterocyclisation)[12] have been respectively achieved. To conclude our work on the α,ω-regioselective halogenation of alditols, we chose another cyclic intermediate, the thionocarbonate group; by analogy with the chlorination and bromination via the unstable cyclic iminium or acetoxonium

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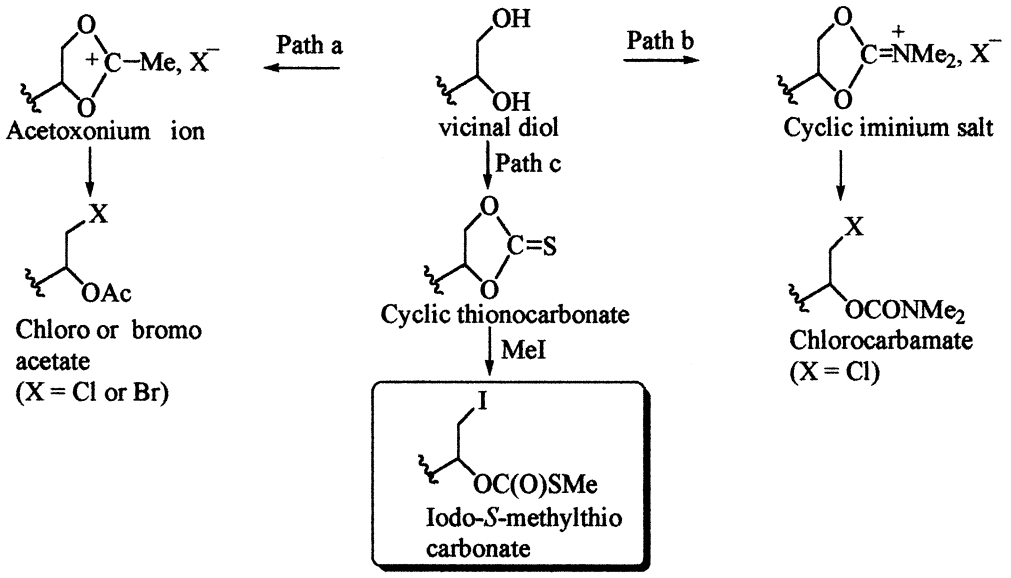
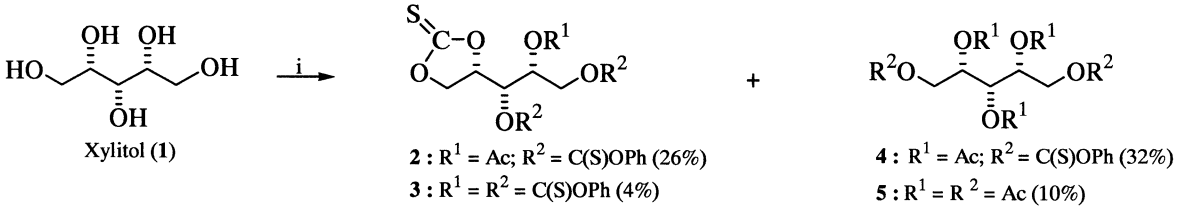


Scheme 1. Regioselective halogenation of alditols via a cyclic intermediate.



Scheme 2. Reagents and conditions: (i) (a) PhOC(S)Cl (2.2 equiv), pyridine (2.2 equiv) $HCCl_3$, 72 h, rt; (b) Ac_2O, pyridine.

ions,[8,9] this stable intermediate undergoes a one pot iodination of the primary site and simultaneous protection of the vicinal OH in the form of *S*-methylthiocarbonate by reaction with methyl iodide (Path c).[13] The use of this iodination reaction was limited until now to erythritol and partially protected D-mannitol.[13d]

2. Results and discussion

In the present work, we first describe an easy synthesis of bis-thionocarbonates of complex polyols: the alditols [including pentitols (xylitol **1**, ribitol **10** and D-arabinitol **14**) and hexitols (D-mannitol **18** and galactitol **24**)]. We then describe the subsequent synthesis of the corresponding α,ω-dideoxy-α,ω-diiodooalditol derivatives.

Among the main reagents used in the synthesis of cyclic thionocarbonates of vicinal diols are phenoxythiocarbonyl chloride (PhOC(S)Cl),[14] diimidazol-1-yl thioketone[13] and chlorothiophosgene.[15] The vicinal diol is often activated by a base such as pyridine or triethylamine.

Our first alditols thionocarbonatation attempt was carried out on xylitol **1** using PhOC(S)Cl with pyridine as base (reaction time of 72 h to complete disappearance of the substrate). After acetylation of the crude product, we obtained a mixture consisting mainly of four products namely: 2-*O*-acetyl-1,3-di-*O*-phenoxythiocarbonyl-D,L-xylitol-4,5-thionocarbonate (**2**), 1,2,3-tri-*O*-phenoxythiocarbonyl-D,L-xylitol-4,5-thionocarbonate (**3**), 2,3,4-tri-*O*-acetyl-1,5-di-*O*-phenoxythiocarbonylxylitol (**4**) and peracetylated xylitol (**5**) in yields of 26, 4, 32 and 10%, respectively (Scheme 2). The cyclisation of phenoxythiocarbonyl groups in cyclic thionocarbonate with free vicinal OH groups seems to be difficult under these conditions.

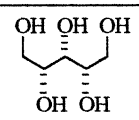
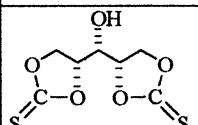
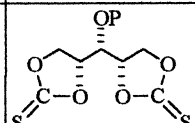
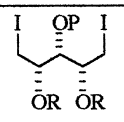
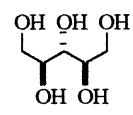
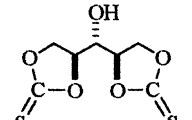
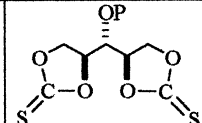
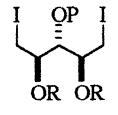
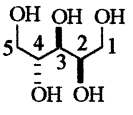
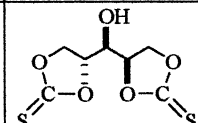
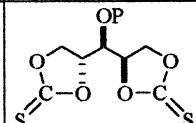
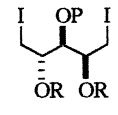
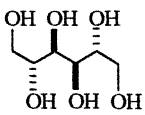
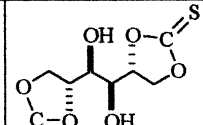
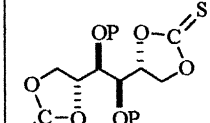
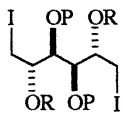
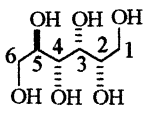
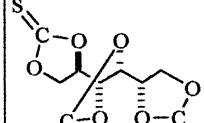
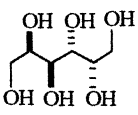
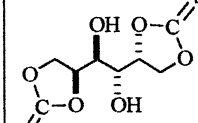
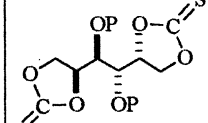
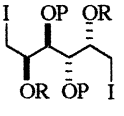
Following our work on the acylation of xylitol via its stannylene acetal complex (using *n*-Bu_2SnO as organotin activating reagent),[16] we tried the bis-thionocarbonatation on the same organotin complex (with 2.2 equiv of PhOC(S)Cl at rt, 4 h, in $CHCl_3$ as solvent). Surprisingly, the target xylitol-1,2:4,5-bis-thionocarbonate (**8**) was obtained as the main product in excellent yield (87%) (Table 1, entry 1). The same conditions, applied to the stannylene acetal complexes of ribitol **10**, D-arabinitol **14**, and D-mannitol **18**, led, respectively, to the corresponding bis-thionocarbonates in 63, 55 and 69% yields (entries 2, 3 and 4). In the case of D-glucitol **22** (entry 5), thionocarbonation involved all the OH-

vicinal groups. Only the tris-thionocarbonate assumed to be **23** was formed in good yield (75%) (with *n*-Bu_2SnO 3 equiv and PhOC(S)Cl 3 equiv). The latter was characterised in ^{13}C NMR by three signals at 190.0, 191.6 and 191.7 ppm corresponding to the thiocarbonyl groups. With galactitol **24** (entry 6), the reaction in $CHCl_3$ was very slow since even under drastic conditions—refluxed $CHCl_3$ and a large excess of reagent (4 equiv)—the starting material was isolated in non-negligible amount. On the other hand, in 1,4-dioxane as a solvent, the corresponding bis-thionocarbonate derivative **25** was obtained in excellent yield (90%). The coordinating character of 1,4-dioxane could explain this result. Unfortunately, using this solvent instead of chloroform with the previously investigated alditols did not change the result.

Apart from compound **25**, which was isolated by filtration, in all the other cases of alditols investigated, the corresponding cyclic thionocarbonate derivatives were obtained by flash chromatography on silica gel with mixtures of CH_2Cl_2–AcOEt or CH_2Cl_2–acetone as eluents.

To obtain the iodinated derivatives via the cyclic thionocarbonates of vicinal diols, two routes may be considered. The first involves displacement of the thionocarbonyl group by an iodide ion. This route can be ruled out as it would lead to a transformation of the thionocarbonate into thiolcarbonate.[17] The second

Table 1
Isolated yields of α,ω-diiodoalditol derivatives obtained via the reaction of corresponding acetylated vicinal alditol bis-thionocarbonates with methyl iodide under pressure

Entry	Substrate*	Bis-thionocarbonate**	Yield (%)	Acetylated Bis-thionocarbonate P = Ac (%)	α,ω-diiodoalditol P = Ac R = CO(SMe)	Yield (%)
1	 Xylitol (**1**)	 **8**	87	 **6** (95)	 **9**	93
2	 Ribitol (**10**)	 **11**	63	 **12** (90)	 **13**	88
3	 D-arabinitol (**14**)	 **15**	55	 **16** (95)	 **17**	91
4	 D-mannitol (**18**)	 **19**	69	 **20** (92)	 **21**	67
5	 D-glucitol (**22**)	 **23**	75[a]	**23**	Complex mixture	-
6	 Galactitol (**24**)	 **25**	90[b]	 **26** (90)	 **27**	89

*Used as their stannylene complexes; **Easily obtained from alditol stannylene complexes and phenoxythiocarbonyl chloride in $HCCl_3$ as solvent; [a]Performed with 3 equiv of Bu_2SnO/PhOC(S)Cl system; [b]Reaction occurred in 1,4-dioxane as solvent.

route involves treatment of the thionocarbonate, at ordinary pressure or under pressure by methyl iodide.[13] Regioselective iodination of the primary sites of the alditols should occur with simultaneous protection of the secondary hydroxyl-group involved in the thionocarbonate ring. With this second route, treatment of the bis-thionocarbonates **8**, **11**, **15**, **19** and **25**, and the tris-thionocarbonate **23** by MeI in a closed reactor led systematically to complex mixtures. Surprisingly, the same reaction carried out on the acetylated bis-thionocarbonates derivatives **6**, **12**, **16**, **20** and **26** led to the corresponding α,ω-diiodoalditol derivatives **9** (xylo), **13** (ribo), **17** (D-arabino), **21** (D-manno) and **27** (galacto) in very good yields (67–93%, see Table 1). The thionocarbonate ring is thus systematically opened through regioselective attack by an iodide ion on the primary site according to the mechanism previously reported in the literature.[13a]

3. Conclusions

In conclusion, alditol bis-cyclic thionocarbonates have proved to be an excellent alternative to other methodologies[†] in the synthesis of α,ω-diiodoalditol derivatives. By analogy with the acetoxonium ion[2b,8,10] or the cyclic iminium salt,[9] the cyclic thionocarbonate group once more confirms the effectiveness of cyclic intermediates in avoiding the formation of anhydride byproducts usually observed with alditols.

4. Experimental

General methods.—Melting points were determined with a Büchi 535 apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 300 WB spectrometer; chemical shifts are reported in δ (ppm) 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 or CH_2Cl_2–acetone as eluent, and detection by the vanillin–H_2SO_4 reagent. The silica gel used in column chromatography was 35–70 μ Amicon. Mass spectroscopy analyses were performed by the 'Service d'Analyse de la Faculté de Pharmacie, Laboratoire de Chimie Thérapeutique U.R.A. au CNRS, (Université de Reims Champagne Ardenne)'. Elemental analyses were performed by the 'Service de Microanalyse du CNRS' (Laboratoire de Chimie Bioorganique, Université de Reims Champagne Ardenne'.

Reaction of phenoxythiocarbonyl chloride with xylitol.—To xylitol (400 mg, 2.6 mmol) in pyridine (0.47 mL, 5.78 mmol), phenoxythiocarbonyl chloride (0.8 mL, 5.78 mmol) in anhyd $CHCl_3$ (5 mL) was added. The mixture was stirred for 3 days until homogenisation of the solution. The reaction mixture was dried and acetylated with an excess of Ac_2O in pyridine at rt. The resulting product was chromatographed on silica gel with 9:1 hexane–EtOAc yielding **2**, **3** and **4** (for yields, see Scheme 2).

*2-*O*-Acetyl-1,3-di-*O*-phenoxythiocarbonyl-*D,L*-xylitol-4,5-thionocarbonate* (**2**). Syrup, R_f 0.76 in 5:4 hexane–EtOAc; ^{13}C NMR ($CDCl_3$): δ 194.5 (C(S)OPh × 2), 190.1 (CS, thionocarbonate), 170.4 (CO, Ac), 153.7 (C-ipso), 122.1, 127.4, 130.1 (Ph), 80.9 (C-3), 79.9 (C-4), 71.0 (C-5), 69.9 (C-1), 68.9 (C-2), 21.1 (CH_3); ^{1}H NMR: δ 7.3 (m, 10 H, Ph), 5.58 (ddd, 1 H, $J_{2,3}$ 2.6, $J_{2,1a}$ 5.8, $J_{2,1b}$ 6.0 Hz, H-2), 5.19 (dd, 1 H, $J_{3,4}$ 5.6 Hz, H-3), 5.10 (m, 1 H, H-4), 4.89 (dd, 1 H, $J_{5a,5b}$ 12.6, $J_{5b,4}$ 3.0 Hz, H-5b), 4.77 (m, 3 H, H-1a,1b,5a), 2.22 (s, 3 H, CH_3).

*1,2,3-Tri-*O*-phenoxythiocarbonyl-*D,L*-xylitol-4,5-thionocarbonate* (**3**). Syrup, R_f 0.83 in 5:4 hexane–EtOAc; ^{13}C NMR ($CDCl_3$): δ 194.5, 194.8 (C(S)OPh), 189.5 (C=S), 153.1 (C-ipso), 121.9, 122.0, 122.1, 127.4, 127.6, 130.4 (Ph), 79.5, 80.3 (C-2,3), 77.5 (C-4), 70.6 (C-1), 69.3 (C-5); ^{1}H: δ 7.3 (m, 15 H, Ph), 5.29 (m, 2 H, $J_{3,4}$ 2.8 Hz, H-2,3), 5.19 (ddd, 1 H, H-4), 5.08 (dd, 1 H, $J_{5b,4}$ 5.3 Hz, H-5b), 5.00 (dd, 1 H, $J_{5a,5b}$ 11.9, $J_{5a,4}$ 5.3 Hz, H-5a), 4.93 (dd, 1 H, $J_{1b,2}$ 3.4 Hz, H-1b), 4.79 (dd, 1 H, $J_{1a,1b}$ 12.7, $J_{1a,2}$ 3.6 Hz, H-1a).

*2,3,4-Tri-*O*-acetyl-1,5-di-*O*-phenoxythiocarbonylxylitol* (**4**). Syrup, R_f 0.70 in 5:4 hexane–EtOAc; ^{13}C NMR ($CDCl_3$): δ 195.0 (C(S)OPh), 170.2 (C=O, Ac), 153.8 (C-ipso), 122.2, 127.2, 130.0 (Ph), 71.3 (C-1,5), 71.3 (C-3), 68.9 (C-2,4), 21.0, 21.3 (CH_3, Ac).

General procedure for the preparation of bis-cyclic thionocarbonate derivatives of alditols.—A mixture of alditol (400 mg) and dibutyltin oxide (2.1 equiv) was refluxed in toluene for a few hours. The solvent was removed by evaporation, and the residue was dissolved in $CHCl_3$. Phenoxythiocarbonyl chloride (2.2 equiv) was added dropwise and the mixture was stirred vigorously during 4 h at rt. The mixture obtained after evaporation was extracted by flash chromatography (EtOAc or CH_2Cl_2–acetone). The resulting alditol bis-cyclic thionocarbonate was subsequently acetylated with an excess of Ac_2O in pyridine at rt (for yields, see Table 1).

Xylitol-1,2:4,5-bis-thionocarbonate (**8**). Mp 168–169 °C; R_f 0.61 in EtOAc; ^{13}C NMR ($(CD_3)_2SO$): δ 192.8 (C=S), 82.8 (C-2,4), 71.9 (C-1,5), 69.7 (C-3); ^{1}H: δ 6.42 (d, 1 H, $J_{OH,3}$ 6.4 Hz, OH), 5.34 (m, 2 H, $J_{2,3}$ 4.0 Hz, H-2,4), 4.88 (t, 2 H, $J_{1b,2}$ 8.7 Hz, H-1b,5b), 4.55 (dd, 2 H, $J_{1a,1b}$ 8.7, $J_{1a,2}$ 6.9 Hz, H-1a,5a), 4.48 (dd, 1 H, $J_{3,4}$ 4.0 Hz, H-3). Anal. Calcd for $C_7H_8O_5S_2$: C, 35.58; H, 3.41; O, 33.86; S, 27.14. Found: C, 35.14; H, 3.37.

[†] Following the halogenation procedure previously described by Whistler et al.,[7b] using CX_4–PPh_3–pyridine complex as halogenating reagent (X = Cl, Br, I), both free pentitols and hexitols studied gave mainly 1,4-*O*-heterocyclisation.

3-O-*Acetylxylitol-1,2:4,5-bis-thionocarbonate* (**6**). Mp 181–183 °C; R_f 0.41 in 4:5 hexane–EtOAc; ^{13}C NMR ($(CD_3)_2SO$): δ 192.2 (C=S), 170.5 (carbonyl), 80.3 (C-2,4), 71.9 (C-1,5), 70.9 (C-3), 21.2 (CH_3); ^{1}H: δ 5.48 (t, 1 H, $J_{3,4}$ 4.5 Hz, H-3), 5.34 (m, 2 H, $J_{2,3}$ 4.5 Hz, H-2,4), 4.88 (t, 2 H, $J_{1b,2}$ 9.0 Hz, H-1b,5b), 4.55 (dd, 2 H, $J_{1a,1b}$ 9.0, $J_{1a,2}$ 6.2 Hz, H-1a,5a), 2.09 (s, 3 H, CH_3). Anal. Calcd for $C_9H_{10}O_6S_2$: C, 38.84; H, 3.62; O, 34.49; S, 23.04. Found: C, 38.24; H, 3.45.

Ribitol-1,2:4,5-bis-thionocarbonate (**11**). Mp 139–141 °C; R_f 0.60 in EtOAc; ^{13}C NMR ($(CD_3)_2SO$): δ 192.4 (C=S), 81.9 (C-2,4), 71.1 (C-1,5), 69.0 (C-3); ^{1}H: δ 6.57 (d, 1 H, $J_{OH,3}$ 6.1 Hz, OH), 5.12 (m, 2 H, $J_{2,3}$ 4.1 Hz, H-2,4), 4.78 (t, 2 H, $J_{1b,2}$ 7.9 Hz, H-1b,5b), 4.62 (t, 2 H, $J_{1a,1b}$ 7.9, $J_{1a,2}$ 7.9 Hz, H-1a,5a), 4.22 (dd, 1 H, $J_{3,4}$ 4.1 Hz, H-3). Anal. Calcd for $C_7H_8O_5S_2$: C, 35.58; H, 3.41; O, 33.86; S, 27.14. Found: C, 35.27; H, 3.45.

3-O-*Acetylribitol-1,2:4,5-bis-thionocarbonate* (**12**). Syrup; R_f 0.49 in 1:1 hexane–EtOAc; ^{13}C NMR ($(CD_3)_2SO$): δ 192.4 (C=S), 170.1 (C=O), 79.3 (C-2,4), 71.1 (C-1,5), 70.9 (C-3), 21.1 (CH_3); ^{1}H: δ 5.46 (t, 1 H, $J_{3,4}$ 3.8 Hz, H-3), 5.19 (m, 2 H, $J_{2,3}$ 3.8 Hz, H-2,4), 4.88 (t, 2 H, $J_{1b,2}$ 9.5 Hz, H-1b,5b), 4.68 (dd, 2 H, $J_{1a,1b}$ 9.5, $J_{1a,2}$ 6.9 Hz, H-1a,5a), 2.11 (s, 3 H, CH_3). Anal. Calcd for $C_9H_{10}O_6S_2$: C, 38.84; H, 3.62; O, 34.49; S, 23.04. Found: C, 38.33; H, 3.55.

D-*Arabinitol-1,2:4,5-bis-thionocarbonate* (**15**). Mp 139–141 °C; R_f 0.51 in 2:5 hexane–EtOAc; ^{13}C NMR ($(CD_3)_2SO$): δ 192.3, 192.6 (C=S), 82.5, 82.6 (C-2,4), 71.2, 72.1 (C-1,5), 68.9 (C-3); ^{1}H: δ 6.52 (d, 1 H, $J_{OH,3}$ 6.2 Hz, OH), 5.21 (m, 2 H, H-2,4), 4.82 (dd, 2 H, $J_{1b,2}$ 8.3 Hz, H-1b,5b), 4.58 (m, 2 H, $J_{1a,1b}$ 16.1 Hz, H-1a,5a), 4.08 (m, 1 H, H-3). Anal. Calcd for $C_7H_8O_5S_2$: C, 35.58; H, 3.41; O, 33.86; S, 27.14. Found: C, 35.33; H, 3.47.

3-O-*Acetyl*-D-*arabinitol-1,2:4,5-dithionocarbonate* (**16**). Mp 134–136 °C; R_f 0.38 in 4:5 hexane–EtOAc; ^{13}C NMR ($(CD_3)_2SO$): δ 192.3, 192.6 (C=S), 170.4 (C=O), 79.5, 79.46 (C-2,4), 71.1, 70.8, (C-1,5), 70.2 (C-3), 20.9 (CH_3); ^{1}H: δ 5.52 (dd, 1 H, $J_{2,3}$ 1.5, $J_{3,4}$ 4.9 Hz, H-3), 5.30 (m, 2 H, H-2,4), 4.82 (m, 3 H, H-1b,5b,5a), 4.45 (dd, 1 H, $J_{1a,1b}$ 16.1, $J_{1a,2}$ 8.0 Hz, H-1a), 2.21 (s, 3 H, CH_3). Anal. Calcd for $C_9H_{10}O_6S_2$: C, 38.84; H, 3.62; O, 34.49; S, 23.04. Found: C, 38.73; H, 3.60.

D-*Mannitol-1,2:5,6-bis-thionocarbonate* (**19**). Mp 141–142 °C; R_f 0.42 in 3:5 hexane–EtOAc; ^{13}C NMR ($(CD_3)_2SO$): δ 192.5 (C=S), 84.1 (C-2,5), 71.1 (C-1,6), 69.6 (C-3,4); ^{1}H: δ 5.92 (d, 1 H, OH), 5.15 (t, 2 H, H-2,5), 4.71 (d, 4 H, H-1a,1b,6a,6b), 4.04 (s, 2 H, H-3,4). Anal. Calcd for $C_8H_{10}O_6S_2$: C, 36.08; H, 3.79; O, 36.05; S, 24.08. Found: C, 35.93; H, 3.65.

3,4-Di-O-*acetyl*-D-*mannitol-1,2:5,6-bis-thionocarbonate* (**20**). Mp 154–156 °C; R_f 0.35 in 1:1 hexane–EtOAc; ^{13}C NMR ($(CD_3)_2SO$): δ 191.8 (C=S), 170.1 (C=O), 81.3 (C-2,5), 71.0 (C-3,4), 69.5 (C-1,6), 21.3 (CH_3); ^{1}H: δ 5.48 (s, 2 H, H-3,4), 5.32 (t, 2 H, H-2,5), 4.82 (t, 2 H, $J_{1b,2}$ 8.3 Hz, H-1b,6b), 4.67 (t, 2 H, $J_{1a,1b}$ 8.3, $J_{1a,2}$ 8.3 Hz, H-1a,6a), 2.09 (s, 6 H, CH_3). Anal. Calcd for $C_{12}H_{14}O_8S_2$: C, 41.14; H, 4.03; O, 36.53; S, 18.30. Found: C, 40.97; H, 3.97.

D-*Glucitol-1,2:3,4:5,6-tris*-thionocarbonate (**23**). Mp 93–95 °C; R_f 0.59 in EtOAc; ^{13}C NMR ($(CD_3)_2SO$): δ 190.0, 191.6, 191.7 (C=S), 81.6, 81.2, 80.8 ($\times 2$) (C-2,3,4,5), 70.7, 71.9 (C-1,6). Anal. Calcd for $C_9H_8O_6S_3$: C, 35.06; H, 2.62; O, 31.13; S, 31.20. Found: C, 35.12; H, 2.69.

Galactitol-1,2:5,6-bis-thionocarbonate (**25**). Mp 196–198 °C; R_f 0.45 in 3:5 hexane–EtOAc; ^{13}C NMR ($(CD_3)_2SO$): δ 193.1 (C=S), 82.9 (C-2,5), 72.0 (C-1,6), 69.6 (C-3,4); ^{1}H: δ 6.08 (s, 1 H, OH), 5.34 (m, 2 H, H-2,5), 4.78 (t, 2 H, $J_{1b,2}$ 8.7 Hz, H-1b,6b), 4.56 (dd, 2 H, $J_{1a,1b}$ 8.7, $J_{1a,2}$ 6.2 Hz, H-1a,6a), 3.63 (m, 2 H, H-3,4). Anal. Calcd for $C_8H_{10}O_6S_2$: C, 36.08; H, 3.79; O, 36.05; S, 24.08. Found: C, 36.15; H, 3.81.

3,4-Di-O-*acetylgalactitol-1,2:5,6-bis-thionocarbonate* (**26**). Mp 203–205 °C; R_f 0.62 in 4:5 hexane–EtOAc; ^{13}C NMR ($(CD_3)_2SO$): δ 192.6 (C=S), 170.3 (C=O), 80.6 (C-2,5), 72.2 (C-1,6), 70.0 (C-3,4), 21.3 (CH_3); ^{1}H: δ 5.35 (m, 4 H, H-2,3,4,5), 4.77 (t, 2 H, $J_{1b,2}$ 9.0 Hz, H-1b,6b), 4.39 (dd, 2 H, $J_{1a,1b}$ 9.0, $J_{1a,2}$ 5.4 Hz, H-1a,6a), 2.11 (s, 6 H, CH_3). Anal. Calcd for $C_{12}H_{14}O_8S_2$: C, 41.14; H, 4.03; O, 36.53; S, 18.30. Found: C, 40.91; H, 3.96.

General procedure for iodination.—A mixture of acetylated alditol bis-cyclic thionocarbonate derivative and methyl iodide (1.25 μL/mg) was heated at 80 °C with stirring for 1 day in a closed reactor. The solvent was evaporated to dryness under diminished pressure and the residue was dissolved in CH_2Cl_2. The organic layer was washed with a satd $Na_2S_2O_3$ solution and evaporated to dryness. The crude product was purified by flash chromatography (4:1, hexane–EtOAc) to give the corresponding α,ω-diiodoalditols derivatives (for yields, see Table 1).

3-O-*Acetyl-2,4-di*-O-*(methylthio)carbonyl-1,5-dideoxy-1,5-diiodoxylitol* (**9**). Syrup; R_f 0.65 in 7:3 hexane–EtOAc; ^{13}C NMR ($CDCl_3$): δ 170.0 (C=O), 171.8 (*C*O(SMe)), 73.8 (C-2,4), 73.1 (C-3), 20.9 (CH_3, Ac.), 14.1 (SCH_3), 1.3 (C-1,5); ^{1}H: δ 5.57 (dd, 2 H, $J_{2,3}$ 5.0 Hz, H-2,4), 5.46 (t, 1 H, $J_{3,4}$ 5.0 Hz, H-3), 3.33 (dd, 2 H, $J_{1b,2}$ 5.3 Hz, H-1b,5b), 3.28 (dd, 2 H, $J_{1a,1b}$ 11.2, $J_{1a,2}$ 6.1 Hz, H-1a,5a), 2.40 (s, 6 H, SCH_3), 2.15 (s, 3 H, CH_3, Ac.). Anal. Calcd for $C_{11}H_{16}I_2O_6S_2$: C, 23.50; H, 2.87; I, 45.15; O, 17.08; S, 11.41. Found: C, 23.62; H, 3.00.

3-O-*Acetyl-2,4-di*-O-*(methylthio)carbonyl-1,5-dideoxy-1,5-diiodoribitol* (**13**). Syrup; R_f 0.78 in 5:3 hexane–EtOAc; ^{13}C NMR ($CDCl_3$): δ 171.5 (*C*O(SMe)), 169.7 (C=O), 74.3 (C-2,4), 73.3 (C-3), 21.1 (CH_3, Ac.), 14.1 (SCH_3), 2.0 (C-1,5); ^{1}H: δ 5.22 (t, 1 H, $J_{3,4}$ 4.8 Hz, H-3), 5.19 (m, 2 H, $J_{2,3}$ 4.8 Hz, H-2,4), 3.44 (dd, 2

H, $J_{1b,2}$ 3.7 Hz, H-1b,5b), 3.25 (dd, 2 H, $J_{1a,1b}$ 11.3, $J_{1a,2}$ 7.6 Hz, H-1a,5a), 2.40 (s, 6 H, SCH_3), 2.08 (s, 3 H, CH_3, Ac.). Anal. Calcd for $C_{11}H_{16}I_2O_6S_2$: C, 23.50; H, 2.87; I, 45.15; O, 17.08; S, 11.41. Found: C, 23.58; H, 2.93.

*3-*O*-Acetyl-2,4-di-*O*-(methylthio)carbonyl-1,5-dideoxy-1,5-diiodo-*D*-arabinitol* (**17**). Syrup; R_f 0.75 in 5:3 hexane–EtOAc; ^{13}C NMR ($CDCl_3$): δ 171.2, 171.4 (*C*O(SMe)), 169.8 (C=O), 73.7 (C-2), 73.3 (C-4), 72.4 (C-3), 21.2 (CH_3, Ac.), 14.2 (SCH_3), 2.8 (C-1), 1.0 (C-5); ^1H: δ 5.38 (dd, 1 H, $J_{3,4}$ 5.3 Hz, H-3), 5.28 (m, 1 H, H-4), 4.97 (m, 1 H, $J_{2,3}$ 2.4 Hz, H-2), 3.39 (dd, 1 H, $J_{1a,1b}$ 11.4, $J_{1b,2}$ 3.9 Hz, H-1b), 3.19 (m, 3 H, H-1a,5a,5b), 2.32 (2s, 2×3 H, SCH_3), 2.11 (s, 3 H, CH_3, Ac.). Anal. Calcd for $C_{11}H_{16}I_2O_6S_2$: C, 23.50; H, 2.87; I, 45.15, O, 17.08; S, 11.41. Found: C, 23.43; H, 2.83.

*3,4-Di-*O*-acetyl-2,5-di-*O*-(methylthio)carbonyl-1,6-dideoxy-1,6-diiodo-*D*-mannitol* (**21**). Mp 117–119 °C; R_f 0.78 in 5:4 hexane–EtOAc; ^{13}C NMR ($CDCl_3$): δ 171.5 (*C*O(SMe)), 170.0 (C=O), 73.3 (C-2,5), 69.9 (C-3,4), 21.3 (CH_3, Ac.), 14.0 (SCH_3), 1.7 (C-1,6); ^1H NMR: δ 5.33 (d, 2 H, $J_{4,5}$ 6.3 Hz, H-3,4), 5.18 (m, 2 H, $J_{2,3}$ 6.3 Hz, H-2,5), 3.39 (dd, 2 H, $J_{1b,2}$ 4.3 Hz, H-1b,6b), 3.23 (dd, 2 H, $J_{1a,1b}$ 11.2, $J_{1a,2}$ 7.3 Hz, H-1a,6a), 2.37 (s, 6 H, SCH_3), 2.13 (s, 6 H, CH_3, Ac.),. Anal. Calcd for $C_{14}H_{20}I_2O_8S_2$: C, 26.51; H, 3.18; I, 40.02; O, 20.18; S, 10.11. Found: C, 26.63; H, 3.22.

*3,4-Di-*O*-acetyl-2,5-di-*O*-(methylthio)carbonyl-1,6-dideoxy-1,6-diiodogalactitol* (**27**). Mp 171–173 °C; R_f 0.55 in 3:1 hexane–EtOAc; ^{13}C NMR ($CDCl_3$): δ 171.9 (*C*O(SMe)), 170.2 (C=O), 73.8 (C-2,5), 69.8 (C-3,4), 21.1 (CH_3, Ac.), 14.1 (SCH_3), 1.0 (C-1,6); ^1H: δ 5.32 (m, 4 H, $J_{2,3}$ 6.3 Hz, H-2,3,4,5), 3.23 (dd, 2 H, $J_{1b,2}$ 5.6 Hz, H-1b,6b), 3.13 (dd, 2 H, $J_{1a,1b}$ 10.9, $J_{1a,2}$ 8.2 Hz, H-1a,6a), 2.38 (s, 6 H, SCH_3), 2.18 (s, 6 H, CH_3, Ac.). Anal. Calcd for $C_{14}H_{20}I_2O_8S_2$: C, 26.51; H, 3.18; I, 40.02; O, 20.18; S, 10.11. Found: C, 26.65; H, 3.24.

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