Carbohydrate Research, 171 (1987) 13–24
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

DICHLOROMETHYLENATION OF 1,4-LACTONES. A NEW ACCESS TO 1-DEOXY-1-*C*-METHYL-*C*-GLYCOSYL COMPOUNDS*

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(Received December 23rd, 1985; accepted for publication, February 5th, 1986)

ABSTRACT

Sugar 1,4-lactones reacted with hexamethylphosphorous triamide–tetrachloromethane to give dichloroolefins in one step. These compounds are versatile intermediates. Treatment of these 1,1-dichloro-1,1-dideoxy-3,4,-*O*-isopropylidene derivatives with lithium diisopropylamide gave the corresponding 4-deoxy-3-ulo derivatives. Reduction of the dichloromethylene group gave a methyl group with high stereospecifity. This opens the way to a set of 2,5-anhydro-1-deoxyalditols.

INTRODUCTION

The discovery of *C*-nucleosides and their biological properties[1] prompted the search for the synthesis of *C*-glycosyl compounds. Some methods have been proposed which allowed the introduction of a highly functionalized chain at the anomeric center. The functionality permitted the construction of various nitrogen-containing heterocycles. These syntheses have been the topic of a review[2]. Nevertheless, the formation of a carbon–carbon bond at the anomeric center with a high degree of stereoselectivity remained a problem which has been partially solved in the past few years with the synthesis of recently discovered, highly-complex structures[3] of some natural products. Oxolane and oxane rings present in these structures have been synthetized, as well as model compounds. Several methods have been published, for example the reaction of allylsilanes[4] and enol ethers[5], Claisen[6] and Ferrier[7] rearrangements, the Wittig reaction[8], and the generation of carbanions[9] at C-1 or radical chemistry[10].

Only a few reports of the use of lactones as starting materials for *C*-glycosyl compounds synthesis have been published[11,12]. Sugar lactones are often commercially available or readily obtained from the corresponding alcohol. Nucleophilic additions on the carbonyl group, followed by subsequent dehydration led to the

*Part of this work was presented at the IIIrd European Symposium on Carbohydrates, Grenoble, September 1985.
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0008-6215/87/$03.50

TABLE I

DICHLOROMETHYLENATION OF 1,4-LACTONES

Starting compound	*Product*	*Reaction conditions*		*Yield*
		Temp. (°)	*Time (h)*	*(%)*
1	2	−30	1	79
4	5	−30	1	92
8	9	0	3	52
12	13	0	4	75
16	17	−30	1	67
19	20	−30	3	90

formation of a carbon–carbon double bond. If the reagent is able to perform both reactions, the oxygen atom of the lactone may be replaced by a substituted carbon atom.

N, N, N', N', N'', N'' - Hexamethylphosphorous triamide – tetrachloromethane ($(Me_2N)_3P$–CCl_4), a reagent known for the activation of sugar hydroxyl groups[13], has been also used for the transformation of a carbonyl into a dihalogenomethylene group. This reaction was applied to some aldehydes and ketones[14]*, including keto sugars[16]. 1,4-Lactones derived from sugars react with $(Me_2N)_3P$–CCl_4 to form dichloroolefins in good yields[17], and we report now some applications of this reaction to the field of deoxy-*C*-glycosyl compounds.

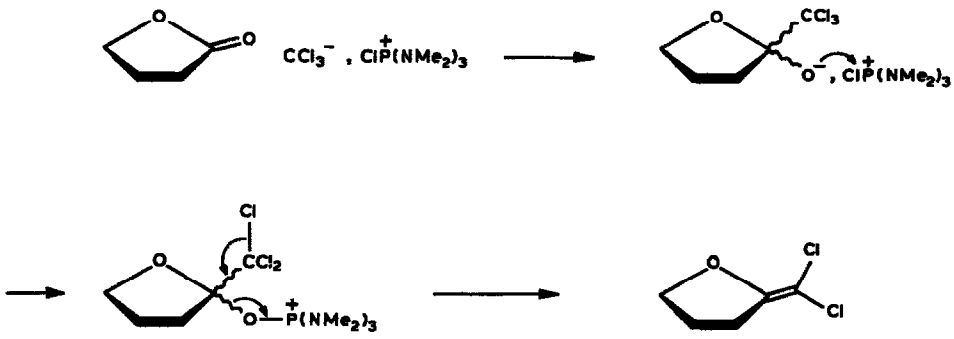
RESULTS AND DISCUSSION

Treatment of some 1,4-lactones with the reagent in dry oxolane at low temperature gave the corresponding dichloroolefins in good yields. The reaction can be performed by slow addition of the phosphine to a solution of carbon tetrachloride at −30°, followed by addition of the lactone, or by adding the phosphine to the mixture of carbon tetrachloride and lactone in dry oxolane with a motor-driven syringe, thus allowing a very slow addition.

The use of carbon tetrabromide instead of carbon tetrachloride gave complex mixtures which darkened rapidly at −30°. The triphenylphosphine–carbon tetrachloride system, which is known to react well with ketones and aldehydes to give dichloroolefins, gave no reaction with 1,4-lactones. This observation supports an ionic mechanism rather than a phosphorane-type mechanism as triphenylphosphine could give phosphorane whereas $(Me_2N)_3P$ could not [18].

The reaction is believed to proceed *via* trichloromethylide formation, followed by condensation of this unstable compound with the carbonyl group of the lactone. Oxytris(dimethylamino)phosphonium salt formation arose from the reaction of the tertiary alcoholate with the chlorophosphonium salt. Subsequent positive halogen

*For a silicon based reagent, see ref. 15.



Scheme 1.

abstraction by the phosphine or the complex phosphine–carbon tetrachloride afforded the dichloromethylene group and hexamethylphosphoric triamide (see Scheme 1). Thus, with sterically hindered lactone as in the D-*ribo* series, condensation of the trichloromethylide anion became sluggish. There is a delicate balance between the nucleophilic attack of the anion and its decomposition, which could explain the excess of phosphine needed and the observed yield. Replacement of the bulky (1,1-dimethylethyl)dimethylsilyl group by acetate led to a better yield of dichloroolefins 13, this observation supporting our hypothesis. On the other hand, these results demonstrated the excellent chemoselectivity of the reagent, which distinguished between ester and lactone. The mildness of the reaction conditions allowed the use of the acetate, mesylate, or silyl group to protect alcohol groups.

For further transformation of the sugar in the presence of a dichloromethylene group, which may act as a carbonyl protecting group, the stability of this group was examined. Thus, acid hydrolysis of 5 in aqueous acetic acid led to 6 in nearly quantitative yield, and deacetylation of 13 with sodium methoxide gave 15 in the same yield.

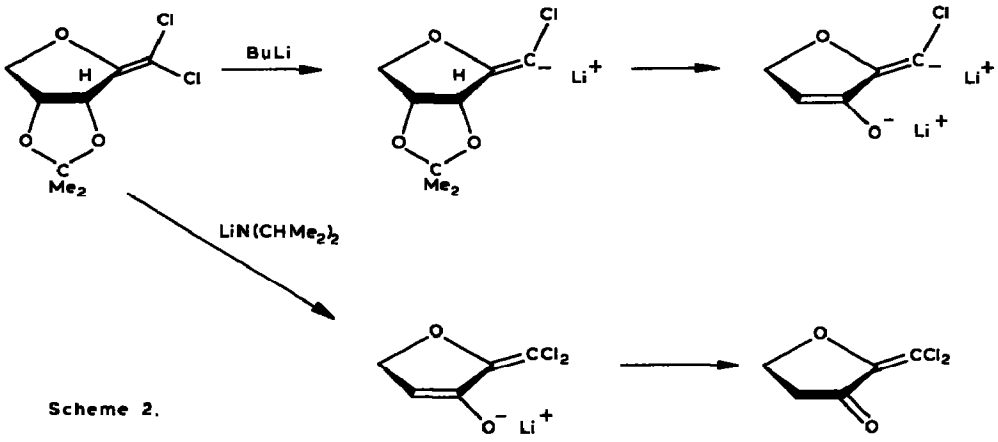
The reduction of the dichloromethylene to a methyl group giving a *cis* arrangement of the methyl and 3,4,-*O*-isopropylidene groups was efficiently achieved

TABLE II

RANEY NICKEL REDUCTION OF DICHLOROMETHYLENE COMPOUNDS

Starting compound	*Product*	*Reaction time (h)*	*Yield (%)*
2	3	3	71
5	7	2	90
9	10 + 11[a]	5	82
13	14	5	83
17	18	5	72
20	21	3	65

[a] 9.1 Ratio by ^{1}H-n.m.r. estimation.



Scheme 2.

by the use of freshly prepared Raney nickel in ethyl acetate. The reaction was completely stereospecific, except in the case of the D-*ribo* derivative **9**. It was possible to detect the *trans* isomer **11** by ^{1}H-n.m.r. spectroscopy although we were unable to isolate **11** in the pure form without contamination of the *cis* isomer **10**. Table II summarizes these results.

Action of strong bases on dichloro compounds was then examined. This investigation began with **5** which, upon treatment with butyllithium, gave a new product. Careful spectral analysis revealed that a mixture of ketones had been obtained (Scheme 2). In fact, two concurrent reactions occured, a metal-to-halogen exchange of one chlorine atom and an H-3* abstraction by butyllithium, thus giving rise to the formation of deoxyketones[19]. The reaction was very difficult to monitor and needed a large excess of alkyllithium and so we eventually turned to other strong bases. Lithium diisopropylamide [$LiN(CHMe_2)_2$] was found to be very efficient, the metal-to-halogen exchange being suppressed. Dichloroolefins were treated with an excess of amide in dry oxolane to give the expected ketones in good yield. Upon treatment of **20** with an excess of amide, both the 3,4-*O*-isopropylidene and 6-*O*-

TABLE III

TREATMENT OF DICHLOROOLEFINS WITH LITHIUM DIISOPROPYLAMIDE

Starting compound	*Product*	*Reaction conditions*		*Yield*
		Temp. (°)	*Time (h)*	*(%)*
2	**22**	−30	2	69
5	**23**	−30	2	90
9	**24**	−30	3	57

*Refers to heptose numbering.

TABLE IV

RANEY NICKEL REDUCTION OF KETONES

Starting compound	Product	Reaction time (h)	Yield (%)
22	25 + 26 (9:1)	1	70[a]
23	27 + 28	2	10 85
24	29 + 30	3	65 10

[a] Pure isolated 26

acetyl groups were removed, thus giving a complex mixture of different ketones.

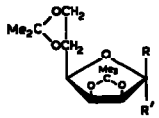
Attempts to protect the starting lactone with the base-stable (1,1-dimethylethyl)dimethylsilyl group were unsuccessful. This transformation opens the way to branched-chain carbohydrate, owing to the possible alkylation of intermediate ketone enolates according to our recent method[20]. The results obtained with lithium diisopropylamide are summarized in Table III.

Finally, we attemped the reduction of the dichloroketones obtained. Raney nickel was found to be very efficient to reduce both double bonds and carbon–chlorine bonds, thus a new route to dideoxy-*C*-glycosyl compounds was opened. Our results are summarized in Table IV.

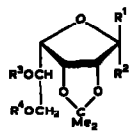
In conclusion, the convenient dichloromethylenation of sugar 1,4-lactones gives a new access to deoxy-*C*-glycosyl- or dideoxy-*C*-glycosyl compounds after Raney nickel reduction. Indeed, the introduced methyl group may be regarded as the C-5′ of a *C*-glycosyl compounds bearing a chiral functionalized appendage of one to three carbon atoms. This may be of interest for N the synthesis of natural products, such as muscarin and furanomycin *i.a.* Compounds such as **2** and **22** are potentially useful in the synthesis of more complex molecules.

EXPERIMENTAL

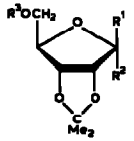
General methods. — Optical rotations were measured with a Perkin–Elmer



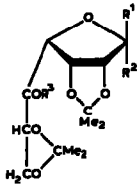
1 R, R′ = O
2 R, R′ = CCl_2
3 R = Me, R′ = H



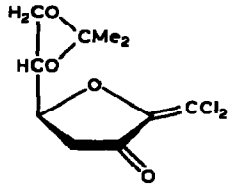
4 R^1, R^2 = O; $R^3 = R^4 = CMe_2$
5 $R^1, R^2 = CCl_2$; $R^3, R^4 = CMe_2$
6 $R^1, R^2 = CCl_2$; $R^3 = R^4$ = H
7 R^1 = H; R^2 = Me



8 R^1, R^2 = O; $R^3 = Bu^tMe_2Si$
9 $R^1, R^2 = CCl_2$; $R^3 = Bu^tMe_2Si$
10 R^1 = H; R^2 = Me; $R^3 = Bu^tMe_2Si$
11 R^1 = Me; R^2 = H; $R^3 = Bu^tMe_2Si$
12 R^1, R^2 = O; R^3 = Ac
13 $R^1, R^2 = CCl_2$; R^3 = Ac
14 R^1 = H; R^2 = Me; R^3 = Ac
15 $R^1, R^2 = CCl_2$; R^3 = H



16 R^1, R^2 = O; R^3 = Ms
17 $R^1, R^2 = CCl_2$; R^3 = Ms
18 R^1 = H; R^2 = Me; R^3 = Ms
19 R^1, R^2 = O; R^3 = Ac
20 $R^1, R^2 = CCl_2$; R^3 = Ac
21 R^1 = H; R^2 = Me; R^3 = Ac



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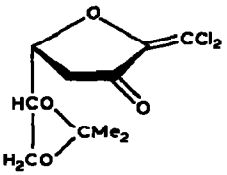

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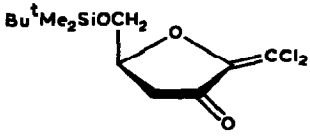

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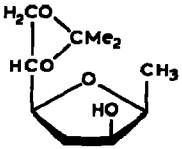

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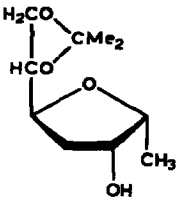

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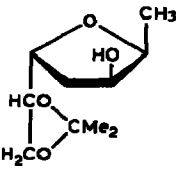

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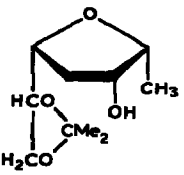

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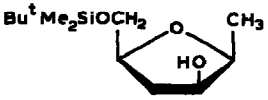

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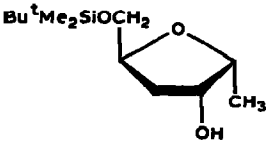

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141 polarimeter. I.r. spectra were recorded for thin films with a Perkin–Elmer 580 B spectrometer, and ^{1}H-n.m.r. spectra for solutions in (^{2}H)chloroform with tetramethylsilane as the internal standard with a Bruker Aspect 3000 (400 MHz) instrument. T.l.c. was performed on Merck precoated plates of Silica gel 60 and detection was effected by spraying the plates with H_2SO_4 in methanol and heating under an i.r. lamp. Oxolane was distilled immediately prior to use from sodium–benzophenone. N,N,N′,N′,N″,N″-Hexamethylphosphorous triamide was purchased from Aldrich and distilled before use. Raney nickel was prepared according to Burgstahler and Abdel-Rahman[21]. Starting lactones **1**, **4**, **8**, **12**, **16**, and **19** were prepared according to references cited by standard procedures (respectively refs. 22, 23, 11, 24, 25 and 25). Microanalyses were performed by the Service Central de Microanalyses du C.N.R.S. (Vernaison, France): amorphous compounds **2**, **5**, **9**, **13**, **15**, **17**, **24**, **29**, and **30** were unstable and gave unsatisfactory results.

Procedures for dichloromethylenation of lactones. — Method A. To a solution of carbon tetrachloride (1.2 g, 8 mmol) in anhydrous oxolane (30 mL)

under Ar was added dropwise a solution of $(Me_2N)_3P$ (980 mg, 6 mmol) in anhydrous oxolane (10 mL) at −30°. A white precipitate was formed. A solution of the lactone (1 or 4: 516 mg, 2 mmol) in oxolane (20 mL) was subsequently added. Stirring was continued for 1 h at −30°. T.l.c. indicated complete transformation of the starting compound. The mixture was then poured into water and the product extracted with diethyl ether (3 × 100 mL). After rapid washing with dilute HCl (10 mL) and water (50 mL), the organic layer was dried ($MgSO_4$) and evaporated. Column chromatography of the residue afforded pure dichloroolefins.

Method B. To a solution of lactone (2 mmol) and carbon tetrachloride (1.2 g, 8 mmol) in anhydrous oxolane (30 mL) under Ar was added over 2 h with a motor-driven syringe (or very slowly) a solution of $(Me_2N)_3P$ (980 mg, 6 mmol) in anhydrous oxolane (10 mL) at the temperature indicated in Table I. The reaction was monitored by t.l.c. If some starting material remained, the treatment was repeated by adding further amount of carbon tetrachloride and phosphine until complete disappearance of starting material. The products were recovered by Method A.

*2,5-Anhydro-1,1-dichloro-1-deoxy-3,4:6,7-di-*O*-isopropylidene-*D*-manno-hept-1-enitol* (2). — Yield 512 mg (79%), $[\alpha]_D^{20}$ +172° (*c* 0.5, chloroform), R_F 0.7 (2:1 hexane–ethylacetate); ν_{max} 1665 cm^{-1}; ^{1}H-n.m.r. (250 MHz): δ 1.38 (s, 3 H), 1.42 (s, 3 H), 1.45 (s, 3 H), 1.48 (s, 3 H, CMe_2); 4.12 (m, 3 H, H-7, 7′, 5), 4.5 (m, 1 H, H-6), 4.87 (m, 1 H, H-4), and 5.3 (d, 1 H, H-3).

*3,6-Anhydro-7,7-dichloro-7-deoxy-1,2:4,5-di-*O*-isopropylidene-*L*-gluco-hept-6-enitol* (5). — Yield 598 mg (92%), $[\alpha]_D^{20}$ −175° (*c* 0.5, chloroform), R_F 0.57 (1:1 hexane–ethylacetate); ν_{max} 1660 cm^{-1}, ^{1}H-n.m.r. (250 MHz): δ 1.37 (s, 3 H), 1.4 (s, 3 H), 1.46 (s, 6 H, CMe_2), 3.75 (dd, 1 H, $J_{1,2}$ 7 $J_{1,1'}$ 8.5 Hz, H-1), 4.19 (dd, 1 H, $J_{3,4}$ 4, $J_{3,2}$ 8.5 Hz, H-3), 4.23 (dd, 1 H, $J_{1',2}$ 7 Hz, H-1′), 4.45 (dd, 1 H, H-2), 4.75 (dd, 1 H, $J_{3,4}$ 4 Hz, H-4), and 5.31 (d, 1 H, $J_{4,5}$ 6 Hz, H-5).

*2,5-Anhydro-1,1-dichloro-1-deoxy-3,4-*O*-isopropylidene-6-*O*-[(1,1-dimethylethyl)dimethylsilyl]-*D*-ribo-hex-1-enitol* (9). — Yield 377 mg (51%), $[\alpha]_D^{22}$ −145° (*c* 0.5, chloroform), R_F 0.5 (9:1 hexane–ethyl acetate); ν_{max} 1660 cm^{-1}, ^{1}H-n.m.r.: δ 0.06 (s, 6 H, CH_3Si), 0.88 (s, 9 H, Bu^tSi), 1.4 (s, 3 H), 1.47 (s, 3 H), 3.76 (dd, 1 H, $J_{5,6}$ 1.5, $J_{6,6'}$ 11 Hz, H-6), 3.84 (dd, 1 H, $J_{5,6'}$ 2.5 Hz, H-6′), 4.6 (t, 1 H, H-5), 4.81 (d, 1 H, $J_{3,4}$ 6 Hz, H-4), and 5.23 (d, 1 H, H-3).

*6-*O*-Acetyl-2,5-anhydro-1,1-dichloro-1-deoxy-3,4-*O*-isopropylidene-*D*-ribo-hex-1-enitol* (13). — Yield 445 mg (75%), $[\alpha]_D^{22}$ −154° (*c* 0.5, chloroform), R_F 0.56 (2:1 hexane–ethyl acetate); ν_{max} 1750, 1665 cm^{-1}; ^{1}H-n.m.r.: δ 1.4 (s, 3 H), 1.5 (s, 3 H, CMe_2), 2.1 (s, 3 H, $COCH_3$), 4.1 (dd, 1 H, $J_{6,5}$ 3.5, $J_{6,6'}$ 12 , H-6), 4.35 (dd, 1 H, $J_{5,6'}$ 3.5 Hz, H-6), 4.75 (m, 2 H, H-4,5), and 5.3 (d, 1 H, $J_{3,4}$ 6 Hz, H-3).

*2,5-Anhydro-1,1-dichloro-1-deoxy-3,4:7,8-di-*O*-isopropylidene-6-*O*-methanesulfonyl-*D*-glycero-*D*-gluco-oct-1-enitol* (17). — Yield 290 mg (67%), $[\alpha]_D^{22}$ −112° (*c* 0.5, chloroform), R_F 0.45 (3:2 hexane–ethyl acetate); ν_{max} 1660 cm^{-1}, ^{1}H-n.m.r.: δ 1.38 (s, 3 H), 1.4 (s, 3 H), 1.42 (s, 3 H), 1.45 (s, 3 H, CMe_2), 3.15 (s, 3 H, SO_2CH_3), 4.0–4.2 (m, 4 H, H-5, 7,8,8′), 4.8 (dd, 1 H, $J_{4,5}$ 4, $J_{3,4}$ 6 Hz, H-4), 5.08

(dd, 1 H, $J_{6,7}$ 4, $J_{5,6}$ 9 Hz, H-6), and 5.33 (d, 1 H, H-3).

*6-O-Acetyl-2,5-anhydro-1,1-dichloro-1-deoxy-3,4:7,8-di-O-isopropylidene-*D-glycero-D-gluco-*oct-1-enitol* (**20**). — Yield 715 mg (90%), m.p. 77° (hexane), $[\alpha]_D^{22}$ −85° (*c* 0.5, chloroform), R_F 0.55 (2:1 hexane–ethyl acetate); ν_{max} 1745, 1665 cm^{-1}, ^{1}H-n.m.r.: δ 1.3 (s, 3 H), 1.39 (s, 3 H), 1.42 (s, 3 H), 1.48 (s, 3 H, CMe_2), 2.1 (s, 3 H, $COCH_3$), 3.97 (dd, 1 H, $J_{7,8}$ 6, $J_{8,8'}$ 9 Hz, H-8), 4.05 (dd, 1 H, $J_{7,8'}$ 6.5 Hz, H-8'), 4.2 (dd, 1 H, $J_{4,5}$ 3.5, $J_{5,6}$ 7 Hz, H-5), 4.3 (dd, 1 H, $J_{6,7}$ 5.5 Hz, H-7), 4.8 (dd, 1 H, $J_{3,4}$ 5.5, $J_{4,5}$ 3.5 Hz, H-4), 5.3 (d, 1 H, H-3), and 5.55 (dd, 1 H, H-6).

Anal. Calc. for $C_{16}H_{22}Cl_2O_7$: C, 48.38; H, 5.58; Cl, 17.85. Found: C, 48.21; H, 5.65; Cl, 18.28.

*3,6-Anhydro-7,7-dichloro-7-deoxy-4,5-*O*-isopropylidene-*L-gluco-*hept-6-enitol* (**6**). — Compound **5** (230 mg, 0.7 mmol) was dissolved in aqueous acetic acid (40 mL, 7:3, v:v). The mixture was heated at 50°. T.l.c. monitoring showed complete disappearance of starting material after 1 h. The solvent was evaporated and, after three codistillations with toluene, the residue was directly chromatographed on silica gel; yield 190 mg (95%); m.p. 118°, $[\alpha]_D^{20}$ −200° (*c* 0.5, chloroform), R_F 0.33 (2:3 hexane–ethyl acetate); ν_{max} 3600 cm, 1660 cm^{-1}, ^{1}H-n.m.r.: δ 1.4 (s, 3 H), 1.48 (s, 3 H, CMe_2), 2.5 (b.m., 1 H, CH_2OH), 3.15 (m, 1 H, CHOH), 3.8 (dd, 1 H, $J_{7,7'}$ 11.5, $J_{6,7}$ 4.5 Hz, H-7), 3.9 (dd, 1 H, $J_{6,7'}$ 3.5, H-7'), 4.15 (q, 1 H, $J_{5,6}$ 7 Hz, H-6), 4.28 (dd, 1 H, $J_{4,5}$ 3.5 Hz, H-5), 4.88 (dd, 1 H, $J_{3,4}$ 6 Hz, H-4), and 5.35 (d, 1 H, H-3).

Anal. Calc. for $C_{10}H_{14}Cl_2O_5$: C, 42.13; H, 4.95; Cl, 24.87. Found: C, 41.77; H, 4.98; Cl, 23.98.

*2,5-Anhydro-1,1-dichloro-1-deoxy-3,4-*O*-isopropylidene-*D-ribo-*hex-1-enitol* (**15**). — Compound **13** (450 mg, 1.5 mmol) was dissolved in dry methanol (40 mL). A catalytic amount of Na (3 mg) was then added. After 3 h of stirring at room temperature, the mixture was made neutral with Dowex 50W (H^+). Filtration and evaporation gave pure **15** (380 mg, 95%), $[\alpha]_D^{20}$ −128° (*c* 0.5, chloroform), R_F 0.4 (2:1 hexane–ethyl acetate); ν_{max} 3600, 1665 cm^{-1}, ^{1}H-n.m.r.: δ 1.2 (s, 3 H), 1.3 (s, 3 H, CMe_2), 3.05 (m, 1 H, OH), 3.7 (dd, 1 h, $J_{6,6'}$ 7 $J_{5,6}$ 3 Hz, H-6), 3.85 (dd, 1 H, $J_{5,6'}$ 2.5 Hz, H-6'), 4.6 (s, 1 H, H-5), 4.8 (d, 1 H, $J_{3,4}$ 6 Hz, H-4), and 5.3 (d, 1 H, H-3).

Procedure for Raney nickel reduction. — The dichloromethylene derivative (1 mmol) was dissolved in dry ethyl acetate. About 200 mg of freshly prepared Raney nickel, previously washed with ethyl acetate, were added and the mixture vigourously stirred until complete transformation of the starting material (t.l.c. monitoring). The mixture was filtered through a pad of Celite and the filtrate evaporated. Column chromatography afforded pure products.

*2,5-Anhydro-1-deoxy-3,4:6,7-di-*O*-isopropylidene-*D-glycero-D-manno-*hept-itol* (**3**). — Yield 183 mg (71%), $[\alpha]_D^{20}$ −20.8° (*c* 0.5, chloroform), R_F 0.47 (3:2 hexane–ethyl acetate); ^{1}H-n.m.r.: δ 1.3 (d, 3 H, *J* 6 Hz, Me), 1.33 (s, 3 H), 1.36 (s, 3 H), 1.43 (s, 3 H), 1.47 (s, 3 H, CMe_2), 3.47 (dd, 1 H, $J_{4,5}$ 3.5 $J_{5,6}$ 7.5 Hz, H-5), 3.64 (m, 1 H, H-1), 4.05 (m, 2 H, H-7,7'), 4.38 (m, 1 H, H-5), 4.55 (dd, 1 H, $J_{3,4}$ 6, $J_{3,2}$ 3.5 Hz, H-3), and 4.73 (dd, 1 H, H-4).

Anal. Calc. for $C_{13}H_{22}O_5$: C, 60.45; H, 8.59. Found: C, 60.10; H, 8.50.

3,6-Anhydro-7-deoxy-1,2:4,5-di-O-*isopropylidene*-D-glycero-L-gluco-*heptitol* (7). — Yield 232 mg (90%), $[\alpha]_D^{20}$ +21° (*c* 0.5, chloroform), R_F 0.53 (3:2 hexane–ethyl acetate); ^{1}H-n.m.r.: δ 1.3 (s, 3 H, CMe_2), 1.38 (d, 3 H, *J* 6 Hz, H-7), 1.59 (s, 3 H, CMe_2), 1.63 (s, 6 H, CMe_2), 3.53 (dd, 1 H, $J_{3,4}$ 4, $J_{2,3}$ 8 Hz, H-3), 3.56 (m, 2 H, H-6,1), 4.23 (dd, 1 H, $J_{1,2}$ 7, $J_{1,1'}$ 8.5 Hz, H-1'), 4.41 (q, 1 H, H-2), 4.78 (dd, 1 H, $J_{5,6}$ 4, $J_{4,5}$ 6.5 Hz, H-2), and 4.83 (dd, 1 H, H-5).

Anal. Calc. for $C_{13}H_{22}O_5$: C, 60.45; H, 8.59. Found: C, 60.19; H, 8.53.

2,5-Anhydro-1-deoxy-3,4-O-*isopropylidene-6*-O-*[(1,1-dimethylethyl)dimethylsilyl]*-D-*altritol* (10). — Yield 247 mg (82%), $[\alpha]_D^{22}$ −4.4° (*c* 0.5, chloroform), R_F 0.35 (9:1 ether–hexane); ^{1}H-n.m.r.: δ 0.06 (s, 6 H, Me_2Si), 0.9 (s, 9 H, Bu^tSi), 1.27 (d, 3 H, *J* 6 Hz, H-1), 1.36 (s, 3 H, CMe_2), 1.51 (s, 3 H, CMe_2), 3.3 (m, 2 H, H-6,6'), 4.05 (t, 1 H, $J_{5,6}$ 4 Hz, H-5), 4.2 (dq, 1 H, $J_{2,3}$ 4 Hz, H-2), 4.59 (dd, 1 H, $J_{3,4}$ 6.5 Hz, H-3), and 4.81 (d, 1 H, H-4).

6-O-*Acetyl-2,5-anhydro-1-deoxy-3,4*-O-*isopropylidene*-D-*altritol* (14). — Yield 191 mg (83%), $[\alpha]_D^{22}$ +9.7° (*c* 0.5, chloroform), R_F 0.45 (2:1 hexane–ethyl acetate); ν_{max} 1740 cm^{-1}; ^{1}H-n.m.r.: δ 1.3 (d, 3 H, J 6.5 Hz, H-1), 1.35 (s, 3 H), 1.55 (s, 3 H, CMe_2), 2.1 (s, 3 H, CH_3CO), 4.0 (dd, 1 H, $J_{6,6'}$ 11.5, $J_{5,6}$ 5 Hz, H-6), 4.1 (dd, 1 H, $J_{2,3}$ 3.5 Hz, H-2), 4.15 (dd, 1 H, $J_{5,6'}$ 6.5 Hz, H-6'), 4.25 (t, 1 H, H-5), and 4.6 (m, 2 H, H-3,4).

Anal. Calc. for $C_{11}H_{18}O_5$: C, 57.39; H, 7.82. Found: C, 56.96; H, 7.92.

2,5-Anhydro-1-deoxy-3,4:7,8-di-O-*isopropylidene-6*-O-*methylsulfonyl*-D-erythro-L-galacto-*octitol* (18). — Yield 263 mg (72%), $[\alpha]_D^{22}$ +2.2° (*c* 0.5, chloroform), R_F 0.30 (3:2 hexane–ethyl acetate); ^{1}H-n.m.r.: δ 1.29 (d, 3 H, J 6 Hz, H-1), 1.31 (s, 3 H), 1.37 (s, 3 H), 1.48 (s, 3 H, CMe_2), 3.1 (s, 3 H, SO_3CH_3), 3.5 (dd, 1 H, $J_{4,5}$ 3.5 $J_{5,6}$ 9 Hz, H-4), 3.63 (dq, 1 H, $J_{2,3}$ 3.5, *J* 6 Hz, H-2), 4.06 (m, 2 H, H-8,8'), 4.37 (dt, 1 H, $J_{7,8}$ 6.5, $J_{7,8'}$ 6.5 Hz, H-7), 4.6 (dd, 1 H, $J_{3,4}$ 6 Hz, H-3), 4.68 (dd, 1 H, H-3), and 5.08 (dd, 1 H, $J_{6,7}$ 4 Hz, H-6).

Anal. Calc. for $C_{15}H_{26}O_8S$: C, 49.17; H, 7.15; S, 8.75. Found: C, 48.92; H, 7.09; S, 8.50.

6-O-*Acetyl-2,5-anhydro-1-deoxy-3,4:7,8-di*-O-*isopropylidene*-D-erythro-L-galacto-*octitol* (21). — Yield 214 mg (65%), $[\alpha]_D^{20}$ +6.9° (*c* 0.5, chloroform), R_F 0.47 (1:1 hexane–ethyl acetate); ν_{max} 1740 cm^{-1}; ^{1}H-n.m.r.: δ 1.29 (s, 3 H, H-1), 1.30 (s, 3 H), 1.35 (s, 3 H), 1.42 (s, 3 H), 1.49 (s, 3 H, CMe_2), 2.15 (s, 3 H, CH_3CO), 3.48 (dd, 1 H, $J_{4,5}$ 3.5, $J_{5,6}$ 7 Hz, H-5), 3.6 (m, 1 H, *J* 6, $J_{2,3}$ 3.5 Hz, H-2), 4.0 (m, 2 H, $J_{7,8}$ 8, $J_{7,8'}$ 7, $J_{8,8}$ 9 Hz, H-8,8'), 4.35 (m, 1 H, $J_{6,7}$ 4.5 Hz, H-7), 4.6 (dd, 1 H, $J_{3,4}$ 6 Hz, H-3), 4.67 (dd, 1 H, H-4), and 5.53 (dd, 1 H, H-6).

Anal. Calc. for $C_{16}H_{26}O_7$: C, 58.17; H, 7.87. Found: C, 58.80; H, 8.07.

General procedure for ketone formation with lithium diisopropylamide. — Dichloroolefin (1 mmol) was dissolved in dry oxolane (20 mL) under Ar at −30°. Lithium diisopropylamide (2.2 mmol) solution [prepared at 0° from diisopropylamine (220 mg, 2.2 mmol) and butyllithium (2.5M solution, 0.9 mL) in dry oxolane (20 mL) at 0°] was added dropwise over 10 min. After complete disappearence of starting compound (t.l.c. monitoring), the mixture was hydrolyzed with a saturated

ammonium chloride solution (50 mL). Extraction with ether (3 × 100 mL), washing with water, drying (Na_2SO_4), and evaporation afforded a crude product which was chromatographed on a silica gel column.

*2,5-Anhydro-1,1-dichloro-1,4-dideoxy-6,7-*O*-isopropylidene-*D*-erythro-hex-1-enitol-3-ulose* (**22**). — Yield 184 mg (69%), m.p. 83–85° (hexane), $[\alpha]_D^{20}$ −27° (*c* 0.5, chloroform), R_F 0.48 (2:1 hexane–ethyl acetate); υ_{max} 1740, 1600 cm^{-1} ^{1}H-n.m.r. δ 1.35 (s, 3 H), 1.45 (s, 3 H) CMe_2, 2.85 (t, 2 H, $J_{4,5}$ 7.5, $J_{4',5}$ 5.5 Hz, H-4,4'), 3.85 (dd, 1 H, $J_{7,7'}$ 9, $J_{6,7}$ 5 Hz, H-7), 4.2 (dd, 1 H, $J_{6,7'}$ 6.5 Hz, H-7'), 4.35 (m, 1 H, $J_{5,6}$ 5 Hz, H-6), and 4.6 (m, 1 H, H-5).

Anal. Calc. for $C_{10}H_{12}Cl_2O_4$: C, 44.97; H, 4.53; Cl, 26.55. Found: C, 44.87; H, 4.44; Cl, 25.71.

*2,5-Anhydro-1,1-dichloro-1,4-dideoxy-6,7-*O*-isopropylidene-*D*-threo-hex-1-enitol-3-ulose* (**23**). — Yield 240 mg (90%), m.p. 89° (hexane), $[\alpha]_D^{22}$ +26.6° (*c* 0.5, chloroform), R_F 0.44 (2:1 hexane–ethyl acetate); υ_{max} 1740, 1600 cm^{-1}; ^{1}H-n.m.r.: δ 1.3 (s, 6 H, CMe_2), 2.75 (dd, 1 H, $J_{4,5}$ 4.5, $J_{4,4'}$ 18 Hz, H-4), 2.97 (dd, 1 H, $J_{4',5}$ 8.5 Hz, H-4'), 4.1 (dd, 2 H, $J_{6,7}$ 7, $J_{6,7'}$ 2.5 Hz, H-7,7'), 4.25 (m, 1 H, $J_{5,6}$ 2.5 Hz, H-6), and 4.75 (m, 1 H, H-5).

Anal. Calc. for $C_{10}H_{12}Cl_2O_4$: C, 44.97; H, 4.53; Cl, 26.55. Found: C, 44.81; H, 4.56; Cl, 25.96.

*2,5-Anhydro-1,1-dichloro-1,4-dideoxy-6-*O*-[(1,1-dimethylethyl)dimethylsilyl]-*D*-glycero-hex-1-enitol-3-ulose* (**24**). — Yield 160 mg (57%), $[\alpha]_D^{20}$ −24.8° (*c* 0.5, chloroform), R_F 0.48 (4:1 hexane–ethyl acetate); υ_{max} 1740, 1600 cm^{-1}; ^{1}H-n.m.r.: δ 0.1 (s, 6 H, Me_2Si), 0.8 (s, 9 H, Bu^t), 2.80 (dd, 1 H, $J_{4,4'}$ 13, $J_{4,5}$ 8 Hz, H-4), 2.86 (dd, 1 H, $J_{4',5}$ 5 Hz, H-4'), 3.70 (dd, 1 H, $J_{6,6'}$, 11.5, $J_{5,6}$ 2 Hz, H-6), 4.05 (dd, 1 H, $J_{5,6'}$ 2.5 Hz, H-6'), and 4.75 (m, 1 H, H-5).

The above ketones (1 mmol) were hydrogenated over Raney nickel as already described and isolated in the same way.

*2,5-Anhydro-1,4-dideoxy-6,7-*O*-isopropylidene-*D*-gluco-hepitol* (**25**). — Yield 141 mg (70%), $[\alpha]_D^{22}$ +16.7° (*c* 0.5, chloroform), R_F 0.42 (1:1 hexane–ethyl acetate); υ_{max} 3600 cm^{-1}; ^{1}H-n.m.r.: δ 1.3 (d, 3 H, *J* 6.5 Hz, H-1), 1.4 (s, 3 H), 1.5 (s, 3 H, CMe_2), 1.95 (dd, 1 H, $J_{4,4'}$ 14, $J_{4,5}$ 3 Hz, H-4), 2.3 (m, 1 H, $J_{4',5}$ 10, $J_{3,4'}$ 5 Hz, H-4'), 3.3 (m, 1 H, OH), 3.58 (q, 1 H, $J_{7,7'}$ 8, $J_{6,7}$ 6.5 Hz, H-7), 3.8 (dq, 1 H, $J_{2,3}$ 2.5 Hz, H-2), 3.95 (d, 1 H, $J_{3,4}$ 5 Hz, H-3), 4.1 (m, 2 H, $J_{6,7'}$ 2.5, $J_{5,6}$ 6 Hz, H-5,7'), and 4.4 (m, 1 H, H-6).

Anal. Calc. for $C_{10}H_{18}O_4$: C, 59.40; H, 8.91. Found: C, 59.22; H, 8.65.

*2,5-Anhydro-1,4-dideoxy-6,7-*O*-isopropylidene-*D*-altro-heptitol* (**26**). — Pure **27** was not obtained without contamination of **26**. The proportion was determined by integration of ^{1}H-n.m.r. signals of the crude mixture of **25** and **26**.

*2,5-Anhydro-1,4-dideoxy-6,7-*O*-isopropylidene-*D*-galacto-heptitol* (**27**). - Yield 19 mg (10%), $[\alpha]_D^{20}$ +10.5° (*c* 0.5, chloroform), R_F 0.24 (1:1 hexane–ethyl acetate); υ_{max} 3600 cm^{-1}; ^{1}H-n.m.r.: δ 1.25 (d, 3 H, *J* 7 Hz, H-1), 1.37 (s, 3 H), 1.44 (s, 3 H, CMe_2), 1.82 (ddd, 1 H, $J_{4,4'}$ 13, $J_{3,4}$ 2.5, $J_{4,5}$ 6 Hz, H-4), 1.9 (ddd, 1 H, $J_{3,4'}$ 6.5, $J_{4',5}$ 9 Hz, H-4'), 2.0 (m, 1 H, OH), 3.7 (dd, 1 H, $J_{7,7'}$ 8, $J_{6,7}$ 7 Hz, H-7), 3.9 (m,

1 H, $J_{2,3}$ 3.5 Hz, H-2), and 4–4.2 (m, 4 H, H-3,5,6,7').

Anal. Calc. for $C_{10}H_{18}O_4$: C, 59.40; H, 8.91. Found: C, 59.18; H, 8.75.

*2,5-Anhydro-1,4-dideoxy-6,7-O-isopropylidene-*D*-ido-heptitol* (**28**). — Yield 171 mg (85%), $[\alpha]_D^{20}$ −28.6° (*c* 0.5, chloroform), R_F 0.34 (1:1 hexane–ethyl acetate); υ_{max} 3600 cm^{-1}; ^{1}H-n.m.r.: δ 1.27 (d, 3 H, *J* 6 Hz, H-1), 1.4 (s, 3 H), 1.47 (s, 3 H, CMe_2), 1.95 (dd, 1 H, $J_{4,4'}$ 14, $J_{3,4}$ 2.5 Hz, H-4), 2.4 (dd, 1 H, $J_{4',5}$ 4, $J_{3,4'}$ 9 Hz, H-4'), 3.63 (m, 1 H, OH), 3.85 (m, 1 H, $J_{2,3}$ 2.5 Hz, H-2), 3.94 (m, 1 H, H-3), and 3.95–4.1 (m, 4 H, H-5,6,7,7').

Anal. Calc. for $C_{10}H_{18}O_4$: C, 59.40; H, 8.91. Found: C, 59.27; H, 8.70.

*2,5-Anhydro-1,4-dideoxy-6-O-[(1,1-dimethylethyl)dimethylsilyl]-*D*-xylo-hexitol* (**29**). — Yield 160 mg (65%), $[\alpha]_D^{20}$ +37° (*c* 0.5, chloroform), R_F 0.51 (2:1 hexane–ethyl acetate); υ_{max} 3600 cm^{-1}; ^{1}H-n.m.r.: δ 0.13 (2 s, 6 H, Me_2Si), 0.92 (s, 9 H, Bu^t), 1.26 (d, 3 H, *J* 6.5 Hz, H-1), 1.94 (dd, 1 H, $J_{4,5}$ 2.5 Hz, H-4), 2.35 (ddd, 1 H, $J_{4',3}$ 5, $J_{4',5}$ 10, $J_{4,4'}$ 14 Hz, H-4'), 3.5 (dd, 1 H, $J_{5,6}$ 1.5, $J_{5,6'}$ 11 Hz, H-5), 3.82 (m, 3 H, H-2,3,5), 3.9 (m, 1 H, OH), and 4.18 (ddd, 1 H, H-5).

*2,5-Anhydro-1,4-dideoxy-6-O-[(1,1-dimethylethyl)dimethylsilyl]-*D*-arabino-hexitol* (**30**). — Yield 24 mg (10%), $[\alpha]_D^{20}$ −9.8° (*c* 0.5, chloroform), R_F 0.30 (2:1 hexane–ethyl acetate); υ_{max} 3600 cm^{-1}; ^{1}H-n.m.r.: δ 0.06 (s, 6 H, $SiCH_3$), 0.85 (s, 9 H, Bu^t), 1.15 (d, 3 H, *J* 6 Hz, H-1), 1.6 (m, 1 H, OH), 1.79 (ddd, 1 H, $J_{4,4'}$ 13, $J_{3,4}$ 3, $J_{4,5}$ 6.5 Hz, H-4), 2.0 (ddd, 1 H, $J_{3,4'}$, 6.5 $J_{4',5}$ 8 Hz, H-4'), 3.6 (d, 2 H, $J_{5,6} = J_{5,6'}$ = 4.5 Hz, H-6,6'), 3.82 (dq, 1 H, $J_{2,3}$ 3.5 Hz, H-2), 3.92 (m, 1 H, H-3), and 4.15 (m, 1 H, H-5).

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