

A CASE OF OLIGOMERIZATION ON ATTEMPTED CHLORINATION OF AN  $\alpha$ -HYDROXY  
 ACETAL WITH THE TRIPHENYLPHOSPHINE TETRACHLOROMETHANE REAGENT

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Summary :

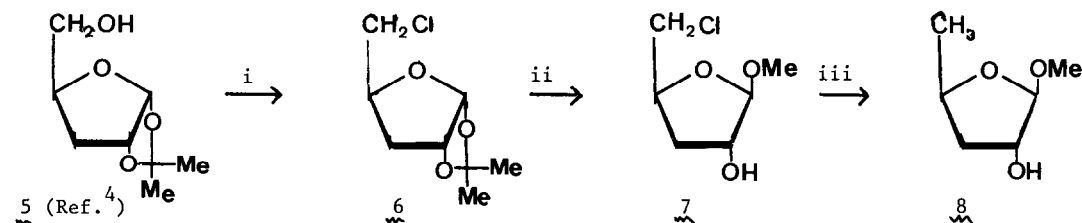
Treatment of methyl 3,5-dideoxy- $\beta$ -D-erythro-pentofuranoside **1** with the  $\text{Ph}_3\text{P-CCl}_4$  reagent gave none of the expected 2-chloro derivative but a mixture of 1 $\rightarrow$ 2 linked oligosaccharides, **9**, **10** with some higher homologues, terminated by a 2-chloro-2,3,5-trideoxy- $\alpha$ -D-threo-pentofuranosyl unit at the non reducing end.

Treatment of the furanosides **1** (Ref.<sup>1</sup>) or **2** (Ref.<sup>2</sup>) by a  $\text{Ph}_3\text{P-CCl}_4$  mixture gave, as expected,<sup>3</sup> chlorides with inverted configurations **3** and **4**. However there is at the same time



inversion of the configuration of the seemingly not involved, adjacent, anomeric carbon, so that this apparent conformity to the rule conceals a more complicated mechanism. To assess the extent of the participation of the acyloxy groups in **1** and **2** to this reaction, we have prepared the reduced furanoside **8** (Scheme and Table II) and examined its behaviour with the same reagent.

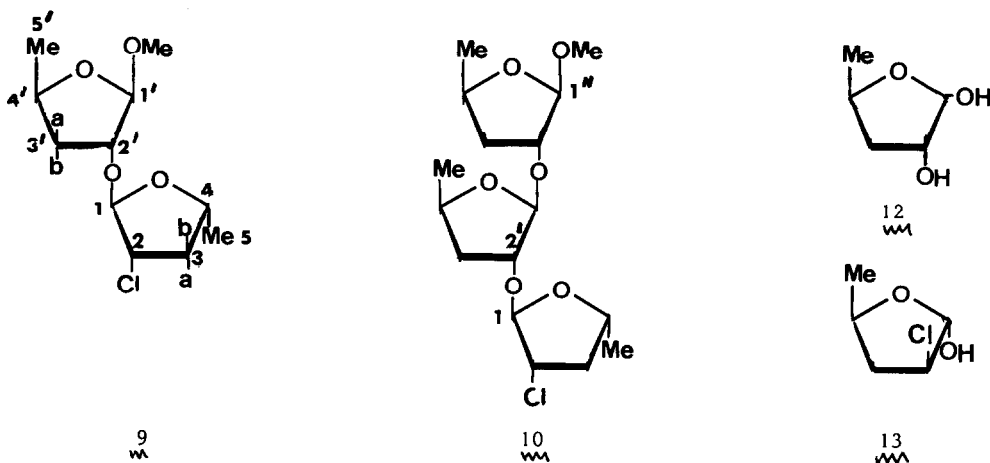
Scheme.



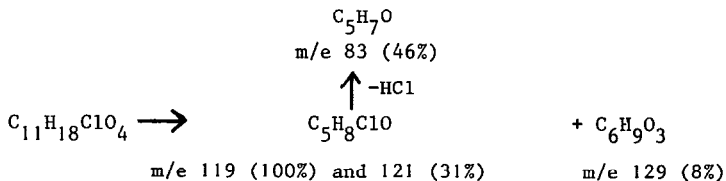
Reagents : i,  $\text{Ph}_3\text{P-CCl}_4$  (89%); ii, Dowex-50 ( $\text{H}^+$ ) in dry MeOH (96%); iii,  $\text{Bu}_3\text{SnH}$  (74%).

The effect of the  $\text{Ph}_3\text{P-CCl}_4$  reagent on the  $\alpha$ -hydroxy acetal **8** was most unexpected. After a 3 h period of refluxing a solution of **8** (7 mmoles) in  $\text{CCl}_4$  (50 ml) in the presence of  $\text{Ph}_3\text{P}$  (1.5 equivalent), there was no more starting material, but no product with the

expected volatility for a methyl 2-chloro-2,3,5-trideoxy-pentofuranoside was found on V.P.C. examination of the  $\text{CCl}_4$  solution. After the removal of the solvent and  $\text{Ph}_3\text{PO}$ , silica gel column chromatography (ether-light petroleum, 1:3, v/v) gave in succession disaccharide **9** (0.64 mmole), trisaccharide **10** (0.28 mmole), and a mixture of higher oligosaccharides, **11** (Table II).

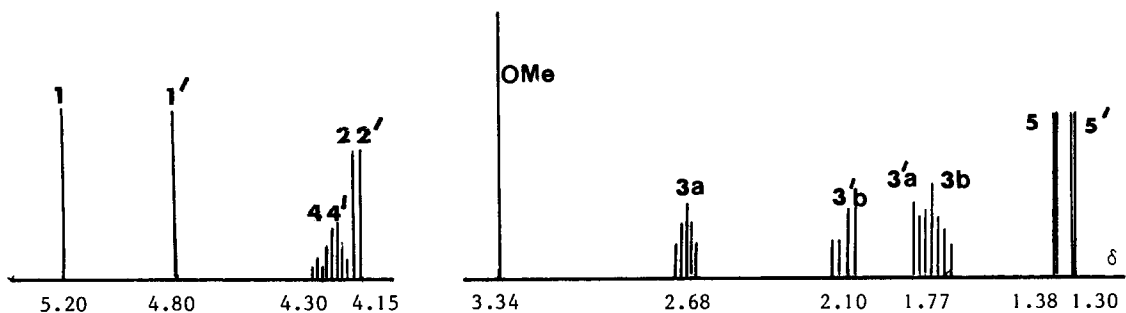


Structure **9** rests on the following evidence : one major m.s. fragmentation can be interpreted as the severance of the C(1)-O(2') bond :



$^1\text{H}$  n.m.r. signals could be allotted by double irradiation experiments at frequencies corresponding to  $\delta$  1.30, 2.10 and 2.68, with the assumption that protons cis to chlorine are more deshielded than protons cis to oxygen.<sup>5</sup> (Figure and Table I). The spectrum of **9** is the superposition of three, completely first-order, practically independent spectra, A for the chlorinated unit, B for the reducing unit minus  $\text{OCH}_3$ , C for  $\text{OCH}_3$ . Because of the flexibility of the furanose ring, configuration inferences from n.m.r. spectra are not always perfectly safe. While the configuration of the reducing unit (spectrum B) seems out of question, J values (Table I) indicate a different one for the chlorinated unit (spectrum A) and fit best (although not perfectly) formula **9**.

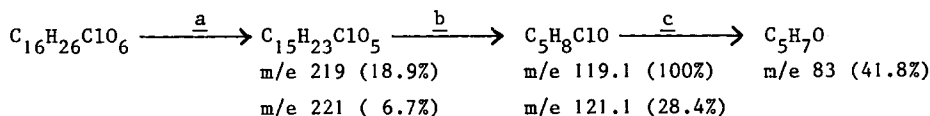
Finally, acidic hydrolysis of disaccharide **9** (dioxane-2M aqueous HCl, 1:1, v/v; 10 min at  $100^\circ\text{C}$ ) gave its component units, **12** and **13** which could be separated by silica gel column chromatography (ether-light petroleum, 1:1, v/v). Furanose **13** (b.p.  $85^\circ$  at 12 mm) showed a n.m.r. spectrum which, but for the shifting of the signal of 1-H to 5.52 p.p.m., was almost identical with spectrum A ( $J_{1,2}$  0,  $J_{2,3a}$  7,  $J_{2,3b}$  3.5,  $J_{3a,b}$  14,  $J_{3a,4}$  7,  $J_{3b,4}$  6 Hz). The other unit **12** was obtained as an anomeric mixture (Table II).

Figure.  $^1\text{H}$  n.m.r. spectrum of disaccharide 9 (250 MHz,  $\text{CDCl}_3$ ,  $\text{Me}_4\text{Si}$ ).Table I.  $J_{x,y}$  values and dihedral angles<sup>a</sup> in disaccharide 9.

Protons x, y	$J_{x,y}$ (Hz)	$(\text{H}_x-\text{C}-\text{C}-\text{H}_y)^\circ$	Protons x, y	$J_{x,y}$ (Hz)	$(\text{H}_x-\text{C}-\text{C}-\text{H}_y)^\circ$
1,2	0	100	1',2'	0	100
2,3a	7	150	2',3'a	4.5	40
2,3b	3.5	50	2',3'b	0	80
3a,3b	14		3'a,3'b	13.5	
3a,4	7	150	3'a,4'	8.5	170
3b,4	7	20	3'b,4'	6	30

<sup>a</sup>No correction for electronegativity.

We now come to trisaccharide 9. The following m.s. fragmentation was observed :

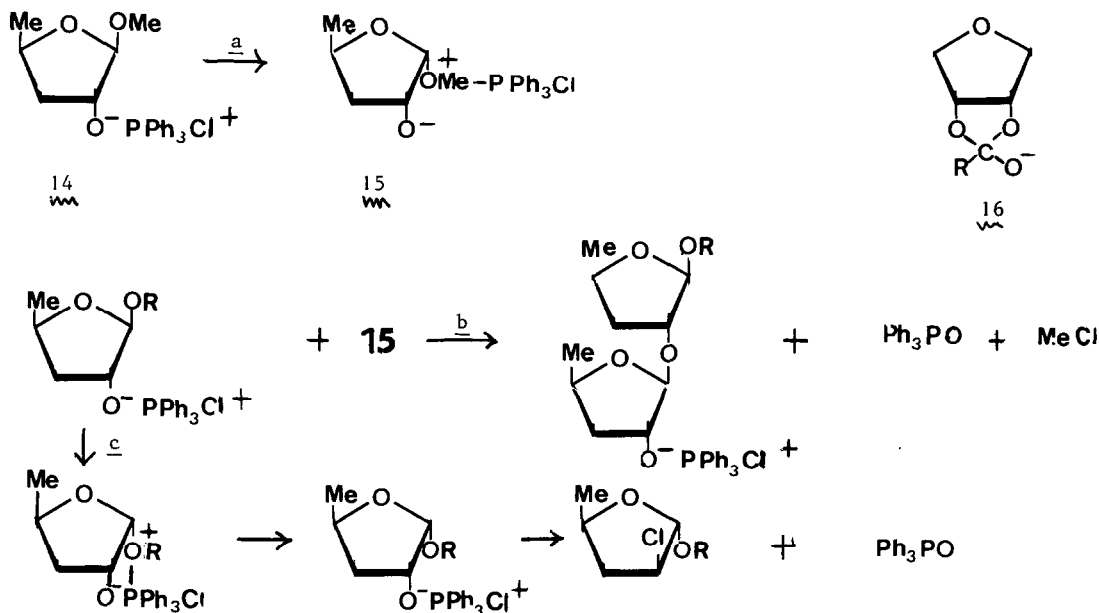


Fragmentation a corresponds to the loss of  $\text{CH}_3\text{O}$  and b to the severance of bond  $\text{C}(1)-\text{O}(2')$  as above. The n.m.r. spectrum, this time, is the superposition of one spectrum A, one signal for  $\text{OCH}_3$ , and two spectra B, with only a slight shifting of the signals of 1'-H and 1''-H ( $\delta$  4.98 and 4.94).

The  $^1\text{H}$  n.m.r. spectrum of fraction 11 may again be described in the same way : one spectrum A, one signal for  $\text{OCH}_3$  and three spectra B.

On the next page, tentative common intermediates are suggested for the chlorination-anomerization and oligomerization reactions, starting from the usual ion-pair 14. For some reasons, 14 does not give a chloride, and slowly isomerizes to 15 (a). Lewis acids are known to be anomerization catalysts and the  $\text{Ph}_3\text{PCl}^+$  cation acts in this way. The concentration of 15 is always small, as it reacts quickly in the chain propagation reaction b. Reaction c, as slow as a, terminates the oligomerization, and becomes the only possible one when there is no more 15.

Now, the reactions of 1 and 2 gave an appreciable yield of monomeric chlorides. Oligomerization may have been a relatively slow process, because of the greater bulk, or steric hindrance to approach, of these bigger molecules. Structures such as 16 (known intermediates in base-catalyzed acyl migration) may also be involved, but their meaning is difficult to assess

Table II. Characterization of new compounds.<sup>a</sup>

Compound	b.p.	$ \alpha _D^{20}$ (c ca 1 in $\text{CH}_2\text{Cl}_2$ )
<u>6</u>	65°C/0.02 mm Hg	-17°
<u>7</u>	85°C/0.02 mm Hg	-82°
<u>8</u>	94°C/12 mm Hg	-134°
<u>9</u>	145-150°C/12 mm Hg	+37°
<u>10</u>	180°C/12 mm Hg	-16°
<u>12</u>	90°C/0.05 mm Hg	-12° <sup>b</sup>

<sup>a</sup> Satisfactory analyses for C, H, Cl, O and compatible  $^1\text{H}$  n.m.r. spectra were found for all these compounds. <sup>b</sup> Anomeric mixture.

#### References.

- <sup>1</sup> S. David and G. de Sennyey, *Carbohydr.Res.*, 1979, 77, 79.
- <sup>2</sup> G. Ritzmann, R.S. Klein, D.H. Hollenberg, and J.J. Fox, *Carbohydr.Res.*, 1975, 39, 227.
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- <sup>4</sup> M. Macheboeuf and J. Delsal, *Bull.Soc.Chim.Biol.*, 1943, 25, 116.
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